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Office of Chemical Safety and
Pollution Prevention

Data Quality Evaluation Information for Human Health Hazard Epidemiology for Asbestos Part 2 – Supplemental Evaluation Including Legacy Uses and Associated Disposals of Asbestos

Systematic Review Support Document for the Risk Evaluation

CASRN: 1332-21-4

November 2024

This supplemental file contains the data quality evaluation results for data sources that met the screening criteria for the *Risk Evaluation for Asbestos Part 2: Supplemental Evaluation Including Legacy Uses and Associated Disposals of Asbestos*. Details regarding the data quality evaluation process implemented are described in the *Risk Evaluation for Asbestos Part 2: Supplemental Evaluation Including Legacy Uses and Associated Disposals of Asbestos – Systematic Review Protocol* as well as the *White Paper: Quantitative Human Health Approach to be Applied in the Risk Evaluation for Asbestos Part 2 – Supplemental Evaluation including Legacy Uses and Associated Disposals of Asbestos*.

As described in Section 4.6.2 of the *Risk Evaluation for Asbestos Part 2: Supplemental Evaluation Including Legacy Uses and Associated Disposals of Asbestos – Systematic Review Protocol* and Appendix B.2 of the *White Paper: Quantitative Human Health Approach to be Applied in the Risk Evaluation for Asbestos Part 2 – Supplemental Evaluation including Legacy Uses and Associated Disposals of Asbestos*, additional screening was conducted based on whether the data source used standardized mortality ratios (SMR) or regression and whether the data source contained dose-response data. Specifically, following full-text PECO-based screening, for those references that met PECO screening criteria and used SMR or regression, data quality evaluation was conducted for data sources that received Medium or High metric ratings for Metrics 4 and 5. Data sources that received either Low or Critically Deficient metric ratings for Metric 4 or Metric 5 did not proceed to data quality evaluation; the metric ratings and comments for Metrics 4 and 5 are included in this supplemental file.

References that assessed the same cohort were linked and evaluated as a group of references or as multiple subgroups of references from the same cohort. However, each health outcome assessed in a paper or cohort group of papers was evaluated independently such that each reference or cohort group of references may have different overall quality determinations (OQD) for different health outcomes. Additional comments providing a brief summary including strengths and weaknesses of the study are presented adjacent to the OQD. If a reference also was evaluated for an evidence stream other than epidemiology, those evaluations will be presented in a separate supplemental file with the Risk Evaluation. U.S. EPA conducted data quality evaluation based on author-reported descriptions and results (including associated methods papers).

As described in Section 5.5.2 of the *Risk Evaluation for Asbestos Part 2: Supplemental Evaluation Including Legacy Uses and Associated Disposals of Asbestos – Systematic Review Protocol* and Appendix B.2 of the *White Paper: Quantitative Human Health Approach to be Applied in the Risk Evaluation for Asbestos Part 2 – Supplemental Evaluation including Legacy Uses and Associated Disposals of Asbestos* , data quality evaluation forms from Asbestos Part 1 were modified to reflect the change in scope for Asbestos Part 2. For mesothelioma, the mesothelioma data quality evaluation form used in Asbestos Part 1 was used for Asbestos Part 2, with some modifications based on calibration. For other outcomes, the lung cancer data quality evaluation form from Asbestos Part 1 was used with additional modifications to evaluate other outcomes that were not considered in Asbestos Part 1. The Table of Contents lists data sources based on whether the endpoints were either mesothelioma or other health outcome categories. In some circumstances, although a study assessed both mesothelioma and other health outcomes, the mesothelioma data were not sufficient to undergo data quality evaluation (*e.g.*, the reference might not have met PECO screening criteria for mesothelioma), and the rationale for not evaluating mesothelioma is documented in the 'Additional Comments' field. Modifications to the forms are further described under Section 5.5.2 of the *Risk Evaluation for Asbestos Part 2: Supplemental Evaluation Including Legacy Uses and Associated Disposals of Asbestos – Systematic Review Protocol* that accompanies the *Risk Evaluation for Asbestos Part 2: Supplemental Evaluation Including Legacy Uses and Associated Disposals of Asbestos*.

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Study Citation:	Amandus, H. (1986). The morbidity and mortality of vermiculite miners and millers exposed to tremolite-actinolite. NIOSH(59):19861986.
Health Outcome:	Mesothelioma
Target Organ(s):	Lung/Respiratory: mesothelioma; Cancer/Carcinogenesis: mesothelioma
Asbestos Fiber Type(s):	Asbestos- Libby amphibole: 1318-09-8; Asbestos - Tremolite: 14567-73-8; Asbestos - Actinolite: 12172-67-7
Linked HERO ID(s):	3100838, 29839, 759132, 783513
HERO ID:	3100838

Domain	Metric	Rating	Comments
Additional Comments:			None of the studies included in this cohort evaluated mesothelioma in a way that is appropriate for full evaluation (no SMRs or regression analyses) (Amandus, 1986, 3100838; Amandus & Wheeler, 1987, 29839; Amandus et al., 1988, 783513). For Amandus & Wheeler, the authors describe that there were two cases of mesothelioma observed, and they provided information on tenure, general exposure levels, and proportional mortality rate (1987, 29839).For Amandus et al., the authors only note the number of mesothelioma diagnoses indicated on death certificates, with no mortality rates or SMRs/regressions (1988, 783513).For the Amandus study, the author provides some details about tenure, latency, and the number of cases of mesothelioma detected. Proportional mortality rates are also reported (1986, 3100838).

* No biomarkers were identified for this evaluation.

Study Citation:	Armstrong, B. K., de Klerk, N. H., Musk, A. W., Hobbs, M. S. (1988). Mortality in miners and millers of crocidolite in Western Australia. British Journal of Industrial Medicine 45(1):13-May.
Health Outcome:	Mesothelioma
Target Organ(s):	Cancer/Carcinogenesis: Mesothelioma mortality; Lung/Respiratory: Mesothelioma mortality; Mortality: Mesothelioma mortality
Asbestos Fiber Type(s):	Asbestos - Crocidolite (riebeckite): 12001-28-4
Linked HERO ID(s):	3083076, 6874474
HERO ID:	3083076

Domain	Metric		Rating	Comments
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Low	Dust concentration measurements were taken periodically at the mine and mill. A koniometer, which is a device used to estimate the amount of dust in the air, was utilized between 1948 and 1958. This only measured total dust per cubic centimeter (ppcc), and it had an upper limit of 1,000 ppcc. This limit was often exceeded. A survey was undertaken to determine the concentration of airborne crocidolite fibers greater than 5 microns in length in 1966. A Casella long running thermal precipitator was used to generate the data. A Casella gravimetric dust sampler and a Hexhelt were also used to estimate dust mass. No impingers or PCM/TEM were utilized in this study.This metric is rated low because the studies or any cited methods source does not explicitly mention the use of PCM or TEM (Armstrong et al., 1988, 3083076; Reid et al., 2018, 6874474).
	Metric 5:	Exposure Levels	Medium	The figure included in the Armstrong et al., 1988, (HERO ID: 3083076) paper displays mesothelioma mortality amongst the miners and millers at various exposure levels. They are split into groups as follows: <10 f/cc y, 10-100 f/cc y, and >100 f/cc y. They also include all exposures combined, which includes unknown exposures.The levels of exposure in the Reid et al. 2018 (HERO ID: 6874474) paper included <10 f/mL years, 10-50 f/mL years, and >50. These values allow for the development of an exposure-response estimate.

Additional Comments:	NOTE: This cohort was rated "Low" for Metric 4, and thus does not meet the criteria for usefulness for dose-response. Only outcome inventory, fiber types, and Metrics 4 and 5 received a full QC.There are some concerns about the methods used to analyze mesothelioma outcomes. 32 mesothelioma deaths were reported in this study, but there was no SMRs or associated confidence intervals reported. They did mention that there was a statistically significant excess of mesothelioma deaths, but there is no information from the analysis to further support this.

* No biomarkers were identified for this evaluation.

** As described in Appendix B.2 of the *White Paper: Quantitative Approach to the Human Health Assessment for the Risk Evaluation for Asbestos Part 2: Supplemental Evaluation Including Legacy Uses and Associated Disposals of Asbestos*, to be considered as being informative for dose-response analysis, metrics 4 and 5 would need metric ratings of Medium or High. This reference did not satisfy this requirement; therefore data quality evaluation is presented for only for metrics 4 and 5.

Study Citation:	Berry, G., Pooley, F., Gibbs, A., Harris, J., Mcdonald, J. (2009). Lung fiber burden in the Nottingham gas mask cohort. Inhalation Toxicology 21(2):168-172.
Health Outcome:	Mesothelioma
Target Organ(s):	Cancer/Carcinogenesis: Mesothelioma-pleural, Mesothelioma-peritoneal; Mortality: Mesothelioma-pleural, Mesothelioma-peritoneal; Lung/Respiratory: Mesothelioma-pleural
Asbestos Fiber Type(s):	Asbestos - Crocidolite (riebeckite): 12001-28-4
Linked HERO ID(s):	No linked references.
HERO ID:	709467

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Medium	Key elements of study design were reported in this retrospective case study of a subset of the original Nottingham Gas Mask Cohort of n=1,154 mostly female employees who assembled military gas masks, 1940-1945, using filter pads containing 20% crocidolite asbestos. Within this cohort, a subset was selected of those with tissue samples. Lung tissue samples were obtained from 50 (77%) of the n=65 cases of mesothelioma, (and n=20 deaths from other causes). Duration of employment was recorded in only 51 of the 70 deaths.
	Metric 2:	Attrition	Medium	Exclusions of subjects from the original cohort or analyses were adequately described for the cases (n=70) with lung tissue samples selected out of the original cohort (n=1,154) and those with employment duration data (n=-51 of n=70).
	Metric 3:	Comparison Group	N/A	This study focused upon mesothelioma outcomes.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Medium	Crocidolite asbestos fiber levels per microgram of dried lung were analyzed by transmission electron microscopy.
	Metric 5:	Exposure Levels	Medium	The range and distribution of lung crocidolite fiber concentrations presented in Tables 1 and 2 by decade of death and categories (4 categories) of length (months) of exposure are sufficient to develop an exposure response relationship.
	Metric 6:	Temporality	High	The study establishes appropriate temporality and the interval between exposure and outcome is long enough for consideration of latency of the outcome. The period of possible exposure to crocidolite was noted to be September 1940 to March 1945 with follow-up for deaths through 1994.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	High	ICD codes were not detailed within the main text, however data regarding deaths was described in the referenced original Nottingham cohort study by McDonald et al., 2006 (HERO ID 709504) and indicate use of ICD-9 as well as employment and pathological records for traced former workers with all deaths due to mesothelioma described as confirmed by pathology.

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Study Citation: Berry, G., Pooley, F., Gibbs, A., Harris, J., Mcdonald, J. (2009). Lung fiber burden in the Nottingham gas mask cohort. Inhalation Toxicology 21(2):168-172.
Health Outcome: Mesothelioma
Target Organ(s): Cancer/Carcinogenesis: Mesothelioma-pleural, Mesothelioma-peritoneal; Mortality: Mesothelioma-pleural, Mesothelioma-peritoneal; Lung/Respiratory: Mesothelioma-pleural
Asbestos Fiber Type(s): Asbestos - Crocidolite (riebeckite): 12001-28-4
Linked HERO ID(s): No linked references.
HERO ID: 709467

Domain	Metric		Rating	Comments
	Metric 8:	Reporting Bias	High	There were no concerns for selective reporting as all outcomes which were outlined within methods were also reported within the results. Results for fiber concentrations within lungs were reported across year of death and cause of death categories within Table 1, and the regression equation was detailed in the text for the % fibers by year of death in Figure 2.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Low	Other than stratification of fiber concentration results across year and cause of death categories, no adjustments for gender, age or race appear to have been made and the distribution of primary covariates and potential confounders was not reported.
	Metric 10:	Covariate Characterization	N/A	Potential confounders were not detailed as considered.
	Metric 11:	Co-exposure Counfounding	Medium	The members of the cohort were workers at the Nottingham military gas mask factory 1940 through 1945. Although co-exposures were not addressed, there was no evidence that there was an unbalanced provision of co-exposures among exposure groups. Considerations for workers who might have initially left and worked elsewhere with additional exposures but eventually returned to the gas mask factory for study were not detailed. Authors noted that masks consisted of 20% crocidolite, but details regarding the remaining composition of masks were not provided.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	Medium	The study design was appropriate to address the main objective of analyzing lung fiber burdens over time. The percentage of fibers longer than 6μm was analyzed by logistic regression with respect to year of death. Median geometric mean crocidolite fibers in lung tissue were presented in Table 1 for year of death categories and cause of death.
	Metric 13:	Statistical Power	Medium	The number of participants (n=70 total with n=51 with duration of employment data) was minimal for regression analyses, although additional covariates did not appear to have been considered within modeling.
	Metric 14:	Reproducibility of Analyses	Medium	The description of analysis is sufficient to understand how to generally reproduce the analyses. Transformation of exposure variables was described in detail. Imputation of exposures with zero values as one-half of the limit of detection was also detailed.
	Metric 15:	Statistical Analysis	Low	Model building was not described in terms of the reasoning for lack of considerations for potential confounders.
Domain 6: Other (if applicable) Considerations for Biomarker Selection and Measurement (Lakind et al. 2014)				
	Metric 16:	Use of Biomarker of Exposure	Low	Evidence exists for a relationship between lung fiber concentrations and external exposure, internal dose or target dose, but there has been no assessment of accuracy and precision or none was reported.

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Study Citation:	Berry, G., Pooley, F., Gibbs, A., Harris, J., Mcdonald, J. (2009). Lung fiber burden in the Nottingham gas mask cohort. Inhalation Toxicology 21(2):168-172.
Health Outcome:	Mesothelioma
Target Organ(s):	Cancer/Carcinogenesis: Mesothelioma-pleural, Mesothelioma-peritoneal; Mortality: Mesothelioma-pleural, Mesothelioma-peritoneal; Lung/Respiratory: Mesothelioma-pleural
Asbestos Fiber Type(s):	Asbestos - Crocidolite (riebeckite): 12001-28-4
Linked HERO ID(s):	No linked references.
HERO ID:	709467

Domain	Metric		Rating	Comments
	Metric 17:	Effect Biomarker	N/A	No biomarkers of effect were used.
	Metric 18:	Method Sensitivity	Medium	Authors noted, "For three zero values, half of the detection limit (0.005, 0.005, 0.05 fibers/μg) was substituted". Analytical method utilized transmission electron microscopy.
	Metric 19:	Biomarker Stability	Low	Lung fiber sample storage history and stability not detailed.
	Metric 20:	Sample Contamination	Medium	There is no information included regarding contamination.
	Metric 21:	Method Requirements	High	Transmission electron microscopy utilized to provide identification and quantitation of lung fibers.
	Metric 22:	Matrix Adjustment	N/A	A biomarker of exposure was utilized.

Additional Comments: This study focused upon post-mortem crocidolite lung fiber concentrations in a subset (n=70: n=50 mesothelioma and n=20 deaths from other causes) of the Nottingham Gas Mask cohort of n=1,154 employees with lung tissue samples who had worked 1940-1945 on the manufacture of military gas masks with filter pads containing 20% crocidolite and who were followed through 2003. Crocidolite asbestos fiber levels per microgram of dried lung were presented by decade of death and cause of death (Table 1), duration of exposure (Table 2), and the percentage of fibers longer than 6μm was analyzed with year of death by logistic regression (Figure 2). The crocidolite counts ranged from 0 to 1,949 (mean 234, median 47) fibers/μg.

Overall Quality Determination — Medium

Study Citation:	Brims, F. J. H., Kong, K., Harris, E. J. A., Sodhi-Berry, N., Reid, A., Murray, C. P., Franklin, P. J., Musk, A. B., e Klerk, N. H. (2020). Pleural plaques and the risk of lung cancer in asbestos-exposed subjects. American Journal of Respiratory and Critical Care Medicine 201(1):57-62.
Health Outcome:	Mesothelioma
Target Organ(s):	Lung/Respiratory: Malignant mesothelioma
Asbestos Fiber Type(s):	Asbestos - Crocidolite (riebeckite): 12001-28-4
Linked HERO ID(s):	733541, 709469, 3079298, 3520653, 3531364, 6868332
HERO ID:	6868332

Domain	Metric		Rating	Comments
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Low	This metric is rated Low because the study or any cited methods source does not explicitly mention the use of PCM or TEM. Dust concentrations were measured using koniometer between 1948 and 1958. In 1966, fiber counting was done using a Casella long running thermal precipitator. Personal and fixed monitors were utilized in 1973. Additional measurements were taken in 1977, 1978, 1980, 1984, 1986, and 1992, using interpolation to estimate concentrations for years that surveys were not conducted. According to Hansen et al., 1997 2219991, all samples examined were analyzed using the standard membrane filter method. Some exceptions were surveys in 1984 and 1986 which used SEM, and in 1992 which used TEM. Although later surveys utilized TEM, the current study does not describe estimates in a way to know outcomes based on exposures measured from 1992 and after.
	Metric 5:	Exposure Levels	Medium	The distribution of exposure appears to be sufficient to develop an exposure-response estimate. Cumulative exposure was utiliized in statistical models.

Additional Comments: None

** As described in Appendix B.2 of the *White Paper: Quantitative Approach to the Human Health Assessment for the Risk Evaluation for Asbestos Part 2: Supplemental Evaluation Including Legacy Uses and Associated Disposals of Asbestos*, to be considered as being informative for dose-response analysis, metrics 4 and 5 would need metric ratings of Medium or High. This reference did not satisfy this requirement; therefore data quality evaluation is presented for only for metrics 4 and 5.

Study Citation:	Churg, A., Vedal, S. (1994). Fiber burden and patterns of asbestos-related disease in workers with heavy mixed amosite and chrysotile exposure. American Journal of Respiratory and Critical Care Medicine 150(3):663-669.		
Health Outcome:	Mesothelioma		
Target Organ(s):	Lung/Respiratory: Mesothelioma		
Asbestos Fiber Type(s):	Asbestos - Amosite (grunerite): 12172-73-5; Asbestos - Tremolite: 14567-73-8; Asbestos - Chrysotile (serpentine): 12001-29-5		
Linked HERO ID(s):	No linked references.		
HERO ID:	758904		

Domain	Metric	Rating	Comments
Domain 2: Exposure Characterization			
	Metric 4: Measurement of Exposure	Low	Methods for fiber count included fiber morphology and fiber chemistry determined through energy-dispersive x-ray spectroscopy, followed by calculating fiber concentration using an algorithm that accounted for weight of lung tissue used in the study and number of grid squares. However, authors did not utilize PCM or TEM, thus warranting a low rating per the guidance.
	Metric 5: Exposure Levels	Low	Actual measured exposure data were not available for the cases and are estimations based on historic data and calculations. Authors stated that exposure was not included in their models as they felt combining years of exposure with fiber burden did not make sense analytically nor is there a correlation between the two.

Additional Comments: Authors stated crocidolite fibers were detected in a small number of cases but were excluded from analyses. Examining the association between chrysotile or tremolite with disease was not conducted due to low concentrations, but concentrations are reported.

* No biomarkers were identified for this evaluation.

** As described in Appendix B.2 of the *White Paper: Quantitative Approach to the Human Health Assessment for the Risk Evaluation for Asbestos Part 2: Supplemental Evaluation Including Legacy Uses and Associated Disposals of Asbestos*, to be considered as being informative for dose-response analysis, metrics 4 and 5 would need metric ratings of Medium or High. This reference did not satisfy this requirement; therefore data quality evaluation is presented for only for metrics 4 and 5.

Study Citation:	Churg, A., Wright, J. L., Vedal, S. (1993). Fiber burden and patterns of asbestos-related disease in chrysotile miners and millers. American Review of Respiratory Disease 148(1):25-31.
Health Outcome:	Mesothelioma
Target Organ(s):	Cancer/Carcinogenesis: Mesothelioma, lung cancer; Lung/Respiratory: Asbestosis, airway fibrosis, pleural plaques, lung cancer, mesothelioma
Asbestos Fiber Type(s):	Asbestos - Chrysotile (serpentine): 12001-29-5; Asbestos - Tremolite: 14567-73-8
Linked HERO ID(s):	No linked references.
HERO ID:	1481523

Domain		Metric	Rating	Comments
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Medium	Fiber concentrations were measured using analytic electron microscopy. Summary statistics of exposure year and latency were reported. The nature of the study design determined exposure measured at only one time period.
	Metric 5:	Exposure Levels	Low	Very limited description of exposure range. The geometric means of asbestos concentration reported in cases (by disease type) and subjects without asbestos-related disease.

Additional Comments:	The mesothelioma measurement is uninformative because no death certificate or ICD codes used. The participation selection lack of description of key elements and attrition rate is high. Covariates were not sufficiently considered and comparison group is not ideal.

* No biomarkers were identified for this evaluation.

** As described in Appendix B.2 of the *White Paper: Quantitative Approach to the Human Health Assessment for the Risk Evaluation for Asbestos Part 2: Supplemental Evaluation Including Legacy Uses and Associated Disposals of Asbestos*, to be considered as being informative for dose-response analysis, metrics 4 and 5 would need metric ratings of Medium or High. This reference did not satisfy this requirement; therefore data quality evaluation is presented for only for metrics 4 and 5.

Study Citation:	Consonni, D., Calvi, C., De Matteis, S., Mirabelli, D., Landi, M. T., Caporaso, N. E., Peters, S., Vermeulen, R., Kromhout, H., Dallari, B., Pesatori, A. C., Riboldi, L., Mensi, C. (2019). Peritoneal mesothelioma and asbestos exposure: A population-based case-control study in Lombardy, Italy. Occupational and Environmental Medicine 76(8):545-553.
Health Outcome:	Mesothelioma
Target Organ(s):	Lung/Respiratory: Peritoneal mesothelioma
Asbestos Fiber Type(s):	Asbestos - Not specified: 1332-21-4
Linked HERO ID(s):	No linked references.
HERO ID:	6868714

Domain	Metric		Rating	Comments
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Low	Neither PCM nor TEM were used for measuring exposure. The study measures asbestos exposure in both a qualitative and quantitative approach. Quantitative measures came from linking ISCO-68 codes to SYN-JEM which provided yearly exposure intensity values for each job. From this, authors calculated individual lifetime cumulative exposures to asbestos (ff/mL-years). The qualitative measure came from expert evaluations of the ReNaM questionnaire (a standardized questionnaire that focuses on life-time job-history) where asbestos exposure categories (never-exposed, extra-occupational, occupational probable/possible, and definite occupational exposure) were created. Recall and interviewer bias is of concern since completing the questionnaire was done via an interview by trained personnel (as opposed to occupational records) and assessment of cases were non-blinded.
	Metric 5:	Exposure Levels	Medium	Four levels of exposure are defined for cumulative asbestos exposure (ff/mL-years): never exposed, <0.888, <3.158, 3.158 and over. Continuous cumulative and log-transformed cumulative exposure are also calculated.

Additional Comments: While asbestos fiber type is not assessed in this study, authors state that chrysotile and amphiboles were often used in Italy.

* No biomarkers were identified for this evaluation.

** As described in Appendix B.2 of the *White Paper: Quantitative Approach to the Human Health Assessment for the Risk Evaluation for Asbestos Part 2: Supplemental Evaluation Including Legacy Uses and Associated Disposals of Asbestos*, to be considered as being informative for dose-response analysis, metrics 4 and 5 would need metric ratings of Medium or High. This reference did not satisfy this requirement; therefore data quality evaluation is presented for only for metrics 4 and 5.

Study Citation:	Cookson, W. O., Musk, A. W., Glancy, J. J., de Klerk, N. H., Yin, R., Mele, R., Carr, N. G., Armstrong, B. K., Hobbs, M. S. (1985). Compensation, radiographic changes, and survival in applicants for asbestosis compensation. British Journal of Industrial Medicine 42(7):461-468.
Health Outcome:	Mesothelioma
Target Organ(s):	Mortality: Respiratory neoplasms mortality; Lung/Respiratory: Respiratory neoplasms mortality; Cancer/Carcinogenesis: Respiratory neoplasms mortality
Asbestos Fiber Type(s):	Asbestos - Crocidolite (riebeckite): 12001-28-4
Linked HERO ID(s):	No linked references.
HERO ID:	3083452

Domain	Metric		Rating	Comments
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Low	This metric is rated low because neither the study nor any cited methods sources explicitly mention the use of PCM or TEM to quantify asbestos fibers.
	Metric 5:	Exposure Levels	Medium	Respiratory neoplasms, which included mesothelioma, were only assessed as ”exposed” vs. ”unexposed” and thus have a limited range of exposure.

Additional Comments:	This study was not fully evaluated because metric 4 was rated as low, due to no explicit mention in the study or cited sources about the use of PCM or TEM.

** As described in Appendix B.2 of the *White Paper: Quantitative Approach to the Human Health Assessment for the Risk Evaluation for Asbestos Part 2: Supplemental Evaluation Including Legacy Uses and Associated Disposals of Asbestos*, to be considered as being informative for dose-response analysis, metrics 4 and 5 would need metric ratings of Medium or High. This reference did not satisfy this requirement; therefore data quality evaluation is presented for only for metrics 4 and 5.

Study Citation:	Cuccaro, F., Nannavecchia, A. M., Silvestri, S., Angelini, A., Coviello, V., Bisceglia, L., Magnani, C. (2019). Mortality for mesothelioma and lung cancer in a cohort of asbestos cement workers in BARI (Italy): Time related aspects of exposure. Journal of Occupational and Environmental Medicine 61(5):410-416.			
Health Outcome:	Mesothelioma			
Target Organ(s):	Peritoneal mesothelioma: Peritoneal mesothelioma mortality; Lung/Respiratory: Pleural mesothelioma mortality; Cancer/Carcinogenesis: Pleural mesothelioma mortality, Peritoneal mesothelioma mortality; Mortality: Peritoneal mesothelioma, Pleural mesothelioma			
Asbestos Fiber Type(s):	Asbestos - Chrysotile (serpentine): 12001-29-5; Asbestos - Crocidolite (riebeckite): 12001-28-4; Asbestos - Amosite (grunerite): 12172-73-5			
Linked HERO ID(s):	No linked references.			
HERO ID:	6867273			

Domain		Metric	Rating	Comments
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Low	Between 1970 and 1974 several industrial hygiene investigations were carried out with measurement of the concentration of the airborne fibers (Coviello, et al., 2002, HERO ID 3080488). This metric is rated Low because authors in this paper do not explicitly cite use of PCM or TEM, and the cited methods paper (Coviello et al. 2002, 3080488) is not freely available or through HERO. PubMed also indicated that the article is in Italian.
	Metric 5:	Exposure Levels	Medium	The authors of this cohort study used an exposure index to evaluate individual cumulative exposure as proxy of asbestos dose and reported 3 or more levels of exposure (3 tertiles).

Additional Comments: QC was not completed for metrics other than Metrics 4 and 5 because the study does not have sufficient exposure information to be useful for dose-response analysis.Metric 4 is rated Low because authors in this paper do not explicitly cite use of PCM or TEM, and the cited methods paper (Coviello et al. 2002, 3080488) is not freely available. For Metric 5, this cohort study used an exposure index to evaluate individual cumulative exposure as proxy of asbestos dose, and reported 3 or more levels of exposure (3 tertiles). Mesothelioma and other outcomes forms filled for Metrics 4 and 5 and evaluation stopped.

** As described in Appendix B.2 of the *White Paper: Quantitative Approach to the Human Health Assessment for the Risk Evaluation for Asbestos Part 2: Supplemental Evaluation Including Legacy Uses and Associated Disposals of Asbestos*, to be considered as being informative for dose-response analysis, metrics 4 and 5 would need metric ratings of Medium or High. This reference did not satisfy this requirement; therefore data quality evaluation is presented for only for metrics 4 and 5.

Study Citation:	Dawson, A., Gibbs, A. R., Pooley, F. D., Griffiths, D. M., Hoy, J. (1993). Malignant mesothelioma in women. Thorax 48(3):269-274.
Health Outcome:	Mesothelioma
Target Organ(s):	Lung/Respiratory: Malignant mesothelioma
Asbestos Fiber Type(s):	Asbestos - Chrysotile (serpentine): 12001-29-5; Asbestos - Crocidolite (riebeckite): 12001-28-4; Asbestos - Tremolite: 14567-73-8; Asbestos - Amosite (grunerite): 12172-73-5
Linked HERO ID(s):	No linked references.
HERO ID:	718578

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Medium	Key elements of study design were reported. Participation is not likely biased and exposure-outcome distribution of participants is likely representative of those eligible for inclusion,. However, total number of patients, from which cases with post-mortem evaluations were chosen, with malignant mesothelioma but with no postmortem analyses records was not provided. Authors did acknowledged the potential non-representativeness of this population due to the patient-referred nature of cases which included wartime dockyard and gas mask workers known to have suffered from heavy asbestos exposure. All available pathological, occupational and lung fiber mineralogical data on n=177 female malignant mesothelioma cases from unspecified file records and unspecified geographic residential origin 1963-1990 were reviewed and compared with n=31 female controls from Exeter, Liverpool, Befast, Dublin, and Cardiff with post-mortem examinations and no known history of exposure to dusts and no mesothelioma or lung cancer. Source of data for controls not detailed but assumed to have been from the same files as cases.
	Metric 2:	Attrition	Medium	Missing information was noted for several subsets of outcome and exposure, and authors acknowledged the lack of completeness of exposure data, however it was unclear if this was related to exposure and/or outcome. The total number of participants with tumor tissue slides available (n=151) was a subset of the total number of mesothelioma cases (n=177). Tumor tissue slides were available for n=151 of a total of n=177 cases. Two cases of the total cases tested (n=103 of the n=151 with histologic slides available) were positive for carcinoembryonic antigen and were excluded from further analyses. Lung tissue fiber burden was examined by transmission electron microscopy for n=105 tumors of known sites (Table 2). Exposure classification according to Zielhuis et al., 1978 (HERO ID 6910362) data was available for n= 93 cases.

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Study Citation:	Dawson, A., Gibbs, A. R., Pooley, F. D., Griffiths, D. M., Hoy, J. (1993). Malignant mesothelioma in women. Thorax 48(3):269-274.
Health Outcome:	Mesothelioma
Target Organ(s):	Lung/Respiratory: Malignant mesothelioma
Asbestos Fiber Type(s):	Asbestos - Chrysotile (serpentine): 12001-29-5; Asbestos - Crocidolite (riebeckite): 12001-28-4; Asbestos - Tremolite: 14567-73-8; Asbestos - Amosite (grunerite): 12172-73-5
Linked HERO ID(s):	No linked references.
HERO ID:	718578

Domain	Metric		Rating	Comments
	Metric 3:	Comparison Group	Medium	Inclusion criteria and methods of participant selection for cases and controls was reported. Geographic residential origin of controls, but not cases (other than one case from Antolia) was reported. Other than restriction of cases and controls to women and reporting the mean (range) age of n=102 malignant mesothelioma cases (60.5 years (18-89)) and n=31 controls (68.0 years (30-93)) for which age data was available, details regarding other potentially relevant demographic and occupational covariate differences between cases and controls were not considered. Statistical analyses of potential demographic or other relevant covariate differences between cases and controls was lacking, and multivariate statistical control for differences, particularly age, between groups was not detailed. It is unclear to what extent, if any, the healthy worker effect was involved within results including those cases classified within Table 4 as having direct occupational exposure in comparison with the population controls.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Medium	Methods used to quantify exposure were well defined, with sources of methods reported. Lung tissue fiber (106 fibers/g), fiber length and diameter analyses were assessed by Transmission Electron Microscopy (TEM) with energy dispersive x ray analysis using an "EDAX" machine according to the methods within Pooley et al., 1979 (HERO ID: 3084350). Asbestos exposure classification methods for cases only were conducted as in Zielhuis et al., HERO ID 6910362. Exposure to asbestos was classified for n=93 (of total n=177 cases) malignant mesothelioma cases according to Zielhuis18 into categories of (la) direct occupational exposure; (lb) indirect occupational exposure-for example, workers in the vicinity of asbestos contaminated work situations; (2) paraoccupational exposure-for example, the wives of men working with asbestos; (3) neighborhood exposure-for example, people living in the vicinity of asbestos mines or processing factories; (4) exposure in ambient air; and (5) no known exposure. Only n=74 (80% of the total n=93 cases with Zielhuis classified exposure history data of the total n=177 malignant mesothelioma cases) cases had a history of known exposure to asbestos. Zielhuis classification of potential historical exposure for controls was not detailed.
	Metric 5:	Exposure Levels	Medium	The range and distribution of exposure is sufficient to develop and exposure-response estimate. Table 4 presents fiber burden (x 10^6 fibers/g lung) geometric mean (range) results for n=93 mesothelioma cases across five Zielhuis et al., 1978 (HERO ID 6910362) exposure categories of direct occupational, indirect occupational, domestic, neighborhood, ambient air and no known exposure categories. Table 3 reports lung fiber burden (x 10^6 fibers/g lung) across five fibrosis grade categories for n=116 cases.
	Metric 6:	Temporality	Low	This study reported cross-sectional results of fiber burdens in mesothelioma cases as well as cross-sectional analyses of the relationship between postmortem fibrosis and lung fiber burdens in mesothelioma cases and controls for which temporality cannot be established.

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Study Citation:	Dawson, A., Gibbs, A. R., Pooley, F. D., Griffiths, D. M., Hoy, J. (1993). Malignant mesothelioma in women. Thorax 48(3):269-274.
Health Outcome:	Mesothelioma
Target Organ(s):	Lung/Respiratory: Malignant mesothelioma
Asbestos Fiber Type(s):	Asbestos - Chrysotile (serpentine): 12001-29-5; Asbestos - Crocidolite (riebeckite): 12001-28-4; Asbestos - Tremolite: 14567-73-8; Asbestos - Amosite (grunerite): 12172-73-5
Linked HERO ID(s):	No linked references.
HERO ID:	718578

Domain	Metric		Rating	Comments
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Medium	Outcome of mesothelioma was assessed. Mesothelioma case histological subtypes were confirmed by immunohistochemistry, although classification of n=26 cases for which no tumor or tissue slides were available were described as classified as with previous records from Dr JC Wagner.
	Metric 8:	Reporting Bias	Medium	There were no concerns for selective reporting as all outcomes which were outlined within methods were also reported within the results. Additional n=1,184 male cases of mesothelioma were reported, but analyses of males was not a subset of reported objectives and comparisons were only made within text with results from previous studies of males. No formal statistical analyses between cases and controls was conducted, and no effect estimates were reported,
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Low	Analyses were restricted to female cases and controls. Additional statistical control for potentially relevant demographic or other variables was not conducted.
	Metric 10:	Covariate Characterization	Low	Source of covariate data (age only) was not directly stated, nor validated, but assumed to have been obtained from the files from which patient data were obtained.
	Metric 11:	Co-exposure Counfounding	Low	The patient population under study included mesothelioma case workers in Table 4 to have had direct and indirect occupational exposure, however potential confounding due to co-exposures was not reported as considered.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	Medium	The study method chosen was appropriate for the cross-sectional data available.
	Metric 13:	Statistical Power	Medium	The number of cases and controls are generally adequate to detect an effect in the overall population. Authors acknowledged the inadequacy of the sample size for analyses of fiber types on outcomes of interest.
	Metric 14:	Reproducibility of Analyses	Medium	The description of analysis is sufficient to understand how to conceptually reproduce the data within the presented tables, although raw data was not reported.
	Metric 15:	Statistical Analysis	N/A	This study did not utilize multivariate statistical modeling methods.
Domain 6: Other (if applicable) Considerations for Biomarker Selection and Measurement (Lakind et al. 2014)				
	Metric 16:	Use of Biomarker of Exposure	Low	Asbestos bodies were assessed by light microscopy in the background lung of n=133 cases, with results indicating presence of asbestos bodies in n=70 (53%) cases. Total amphibole counts analyzed by transmission electron microscopy (TEM) of n=49 of the n=70 specimens positive for asbestos bodies were less than the n=50 specimens analyzed with no asbestos bodies.

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Study Citation:	Dawson, A., Gibbs, A. R., Pooley, F. D., Griffiths, D. M., Hoy, J. (1993). Malignant mesothelioma in women. Thorax 48(3):269-274.
Health Outcome:	Mesothelioma
Target Organ(s):	Lung/Respiratory: Malignant mesothelioma
Asbestos Fiber Type(s):	Asbestos - Chrysotile (serpentine): 12001-29-5; Asbestos - Crocidolite (riebeckite): 12001-28-4; Asbestos - Tremolite: 14567-73-8; Asbestos - Amosite (grunerite): 12172-73-5
Linked HERO ID(s):	No linked references.
HERO ID:	718578

Domain	Metric		Rating	Comments
	Metric 17:	Effect Biomarker	N/A	Asbestos bodies were assessed in background lung as markers of exposure.
	Metric 18:	Method Sensitivity	Low	LOD/LOQ was not detailed.
	Metric 19:	Biomarker Stability	Low	Sample storage history and stability data were not detailed.
	Metric 20:	Sample Contamination	Medium	No information was provided regarding sample contamination.
	Metric 21:	Method Requirements	Medium	Asbestos bodies in background lung samples were assessed by light microscopy.
	Metric 22:	Matrix Adjustment	N/A	Matrix adjustment is not required for assessment of biomarker.

Additional Comments: This study reported cross-sectional results of postmortem fibrosis and lung fiber burdens from an initial total population of n=177 female malignant mesothelioma cases 1963-1990 (geographic origin not detailed) and n=31 female controls from Exeter, Liverpool, Belfast, Dublin, and Cardiff with no initially known exposure history to dusts and no mesothelioma or lung cancer. Cases (n=102 of total n=177) with age data were described as being of mean (range) age 60.5 years (18-89 years) with n=31 controls aged 68 years (30-93 years). Mesothelioma cases had notably higher total amphibole counts than controls. Fibrosis was noted within some controls.

Overall Quality Determination Low

Study Citation:	de Klerk, N. H., Armstrong, B. K., Musk, A. W., Hobbs, M. S. T. (1989). Cancer mortality in relation to measures of occupational exposure to crocidolite at Wittenoom Gorge in Western Australia. British Journal of Industrial Medicine 46(8):529-536.		
Health Outcome:	Mesothelioma		
Target Organ(s):	Lung/Respiratory: Mortality from malignant mesothelioma of the pleura; Mortality: Mortality from malignant mesothelioma of the pleura; Cancer/Carcinogenesis: Mortality from malignant mesothelioma of the pleura		
Asbestos Fiber Type(s):	Asbestos - Crocidolite (riebeckite): 12001-28-4		
Linked HERO ID(s):	783917, 3079799, 3080174		
HERO ID:	783917		

Domain	Metric	Rating	Comments
Domain 2: Exposure Characterization			
	Metric 4: Measurement of Exposure	Low	This metric is rated low because Klerk et al. 1989 783917, Reid et al. 2006 3079799, and Reid et al. 2004 3080174 relied on historic dust measures (konimeters, thermal precipitators) without documenting the use of appropriate conversions. These papers cited the single time point membrane filter PCM fiber concentration measures that were taken in 1966, shortly before the facility closed (publication not available in HERO or other online sources, Major 1968 entitled the First Australian Pneumoconiosis Conference). However, they did not mention or cite a dust-to-fiber conversion factor, and no such factors were identified in the literature. Concerns regarding the validity and utility of occupational exposure measures used in Wittenoom studies have been expressed by the industrial hygienist responsible for the membrane filter measures (e.g., Rogers and Major 2002 HEROID 3080506).
	Metric 5: Exposure Levels	Low	The distribution of exposure provided in de Klerk et al 783917 appears to be sufficient to develop an exposure-response estimate. Cumulative exposure was used in analyses either as a continuous variable or in 4 categories. As noted above, however, there are important concerns remain regarding the validity of exposure estimates.

Additional Comments: Klerk et al. 1989 783917 was/were not evaluated for any metrics except Metric 4 and 5 and had no data extracted because it/they did not have sufficient exposure information to be useful for dose-response analysis.

** As described in Appendix B.2 of the *White Paper: Quantitative Approach to the Human Health Assessment for the Risk Evaluation for Asbestos Part 2: Supplemental Evaluation Including Legacy Uses and Associated Disposals of Asbestos*, to be considered as being informative for dose-response analysis, metrics 4 and 5 would need metric ratings of Medium or High. This reference did not satisfy this requirement; therefore data quality evaluation is presented for only for metrics 4 and 5.

Study Citation:	de Klerk, N. H., Musk, A. W., Cookson, W. O., Glancy, J. J., Hobbs, M. S. (1993). Radiographic abnormalities and mortality in subjects with exposure to crocidolite. British Journal of Industrial Medicine 50(10):902-906.
Health Outcome:	Mesothelioma
Target Organ(s):	Lung/Respiratory: Lung cancer mortality, mesothelioma mortality, pneumoconiosis mortality; Cancer/Carcinogenesis: Mesothelioma mortality
Asbestos Fiber Type(s):	Asbestos - Crocidolite (riebeckite): 12001-28-4
Linked HERO ID(s):	No linked references.
HERO ID:	3081932

Domain		Metric	Rating	Comments
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Low	Study reports that estimates of crocidolite from Wittenoom Gorge were collected from existing industry records of fibre. The exact tool utilized to measure the asbestos is not mentioned, but methods state that fibers in the air >5mu in length from 1966 were used to create cumulative exposure measures.
	Metric 5:	Exposure Levels	Low	The exposure ranges are appropriate to the study using intensity (f/mL), days of exposure (average), and cumulative exposure (f/mL-years).

Additional Comments: For the year of the study and the 5 different case-control analyses conducted, I agree with the rating. There are some discrepancies, such as how the asbestos was measured and exposures to various forms of asbestos which were not regarded.

* No biomarkers were identified for this evaluation.

** As described in Appendix B.2 of the *White Paper: Quantitative Approach to the Human Health Assessment for the Risk Evaluation for Asbestos Part 2: Supplemental Evaluation Including Legacy Uses and Associated Disposals of Asbestos*, to be considered as being informative for dose-response analysis, metrics 4 and 5 would need metric ratings of Medium or High. This reference did not satisfy this requirement; therefore data quality evaluation is presented for only for metrics 4 and 5.

Study Citation:	Dunning, K. K., Adjei, S., Levin, L., Rohs, A. M., Hilbert, T., Borton, E., Kapil, V., Rice, C., Lemasters, G. K., Lockey, J. E. (2012). Mesothelioma associated with commercial use of vermiculite containing Libby amphibole. Journal of Occupational and Environmental Medicine 54(11):1359-1363.
Health Outcome:	Mesothelioma
Target Organ(s):	Mortality: Mesothelioma mortality; Cancer/Carcinogenesis: Mesothelioma mortality; Lung/Respiratory: Mesothelioma mortality
Asbestos Fiber Type(s):	Asbestos- Libby amphibole: 1318-09-8; Asbestos - Not specified: 1332-21-4; Asbestos - Winchite: 12425-92-2; Asbestos- Richterite: 17068-76-7; Asbestos - Tremolite: 14567-73-8
Linked HERO ID(s):	No linked references.
HERO ID:	1066036

Domain	Metric		Rating	Comments
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Low	Analyses use cumulative fiber exposure. Additional details about exposure measurement are reported in Lockey et al., 1984, HEROID 29685. Samples were collected via membrane filters either by following an employee with a sampler (from 1972-1976) or by breathing zone sampling (after 1976). Authors note that exposure of fiber was defined as ”particles with a length greater than 5 um, a diameter less than 3 um, and an aspect ratio of 3:1 or greater”. Thus, fiber type was unknown, and samples likely included fibers other than asbestos. Samples were reviewed through polarized light microscopy, scanning electron microscopy, and TEM. Indexes were created for each department within the facility. Study authors used work histories reported by workers in 1980 to calculate the cumulative fiber exposure level for each employee. Previous estimates were revised to include additional data related to exposure collected in 2010, such as adjustments for vermiculite source and changes in duration of work by season (Borton et al., 2012, HEROID 1066035). Borton et al. also estimated exposures from 1957-1971 using estimates from 1972 with adjustments for dustier historical conditions. This study also reported comparisons between personal and area samples and found approximately equal means and ranges.
	Metric 5:	Exposure Levels	Low	For SMR analyses of mesothelioma, exposure is presented in two groups (exposed workers and unexposed workers). Authors note the possibility that associations were not observed due to the low exposure levels among the study population, which introduces concern about the influence of the exposure distribution on the ability to detect an effect.

Additional Comments:	QC was not completed for metrics other than Metrics 4 and 5 because the study does not have sufficient exposure information to be useful for dose-response analysis.This retrospective occupational cohort study examined the association between asbestos exposure and mesothelioma mortality among workers mining and milling contaminated vermiculite. There were no major concerns with the study, aside from limited exposure distributions among the study population and concerns about the number of mesothelioma cases in the cohort. The approach for exposure measurement and statistical analysis was strong, and there were no concerns about selection bias resulting from population recruitment approaches.

* No biomarkers were identified for this evaluation.

** As described in Appendix B.2 of the *White Paper: Quantitative Approach to the Human Health Assessment for the Risk Evaluation for Asbestos Part 2: Supplemental Evaluation Including Legacy Uses and Associated Disposals of Asbestos*, to be considered as being informative for dose-response analysis, metrics 4 and 5 would need metric ratings of Medium or High. This reference did not satisfy this requirement; therefore data quality evaluation is presented for only for metrics 4 and 5.

Study Citation:	e La Provôté, S., Desoubeaux, N., Paris, C., Letourneux, M., Raffaelli, C., Galateau-Salle, F., Gignoux, M., Launoy, G. (2002). Incidence of digestive cancers and occupational exposure to asbestos. European Journal of Cancer Prevention 11(6):523-528.
Health Outcome:	Mesothelioma
Target Organ(s):	Lung/Respiratory: Pleural and peritoneal mesothelioma; Gastrointestinal: Pleural and peritoneal mesothelioma; Cancer/Carcinogenesis: Pleural and peritoneal mesothelioma
Asbestos Fiber Type(s):	Asbestos - Chrysotile (serpentine): 12001-29-5; Asbestos - Crocidolite (riebeckite): 12001-28-4
Linked HERO ID(s):	3520580, 3077730, 3078903, 3520549
HERO ID:	3520580

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Medium	Clin et al. 2011, HERO ID: 3078903 analyzed the risk of mesotheliomas among salaried and retired workers (men and women) from an asbestos reprocessing plant (textiles and friction materials) in the Calvados department in Normandy, France. Eligibility was based on: (i) working at the plant for at least 1 year; (ii) being alive in 1978 when the regional cancer registry was established; (iii) having resided in Calvados during at least part of the 1978 to 1995 initial follow-up period, with known vital status (de la Provote et al al. 2002, HERO ID: 3520580). As noted by Clin et al. 2011, HERO ID: 3078903, "... since one of our inclusion criteria was that subjects had to be alive in 1978, there may be a selection bias related to the 'healthy worker effect'." Including retired workers, however, would have helped to reduce this bias. The number of workers who did not meet eligibility criteria was not provided; it is unknown whether a large number of workers of similar age and employment duration as those in the cohort had cancer diagnoses prior to 1978, which could bias results. The factories had operated using asbestos in various capacities since 1928. All cancer cases from 1978 to 2004 were included, resulting in 2024 subjects (1604 men).
	Metric 2:	Attrition	High	Clin et al. 2011, HERO ID: 3078903 reported that 107 subjects (5.3%) had missing vital status at the end of 2004 and were excluded from analysis. It is unclear why vital status was missing, but given the relatively small share of subjects and that it would not be expected to be related exposure and outcome make this a limited concern for bias.
	Metric 3:	Comparison Group	Medium	In calculating relative risk for mesothelioma, workers with varying concentrations of exposures were compared amongst each other. There is no indication that groups were similar but there is no indication of healthy worker effect.
Domain 2: Exposure Characterization				

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Study Citation:	e La Provôté, S., Desoubeaux, N., Paris, C., Letourneux, M., Raffaelli, C., Galateau-Salle, F., Gignoux, M., Launoy, G. (2002). Incidence of digestive cancers and occupational exposure to asbestos. European Journal of Cancer Prevention 11(6):523-528.
Health Outcome:	Mesothelioma
Target Organ(s):	Lung/Respiratory: Pleural and peritoneal mesothelioma; Gastrointestinal: Pleural and peritoneal mesothelioma; Cancer/Carcinogenesis: Pleural and peritoneal mesothelioma
Asbestos Fiber Type(s):	Asbestos - Chrysotile (serpentine): 12001-29-5; Asbestos - Crocidolite (riebeckite): 12001-28-4
Linked HERO ID(s):	3520580, 3077730, 3078903, 3520549
HERO ID:	3520580

Domain	Metric		Rating	Comments
	Metric 4:	Measurement of Exposure	Medium	Exposure estimates were assigned to individuals based on job functions and timing/duration of employment and fiber count measures. As described by de la Provote et al. 2002, HERO ID: 3520580, fiber counts were measured at different locations in the plant as follows: (i) 1973 -1995 data were collected by Casella pumps on a membrane filter, with PCM (phase-contrast light microscopy) counts of fibers longer than 5μ m, less than 3μ m in diameter, with a length/diameter ratio greater than 3; (ii) 1960-1974 data were collected on soluble filters by an ARM (Avy–Raillere–Martin) apparatus, with light microscopy fiber counts as particles per liter of air; and (iii) estimates prior to 1959/1960 were based on production reports for 1939-1945 [50% of 1960 levels], linearly extrapolated to 1960. Date cutoffs differed slightly across manuscripts [e.g. ARM started in 1959 vs 1960 according to Clin et al. 2011, HERO ID: 3078903]. Side-by-side Casella vs. ARM method measures in 1974 were used to develop a conversion factor for the different methods. A cumulative exposure index (CEI) for the entire career (fibers/mL * year) was calculated as the sum of exposure * duration for each job position. A mean exposure concentration (MEC), also referred to as averaged exposure (AEL) was also calculated and expressed in fibers/mL). Clin et al. 2009, HERO ID: 3520549 and Boulanger et al. 2017, HERO ID: 3077730 explain these same methods but in lesser detail. Clin et al. 2011, HERO ID: 3078903 uses CEI and AEL exposure categories with a 10-year lag to account for latency.
	Metric 5:	Exposure Levels	Medium	To estimate mesothelioma risk, only Clin et al. 2011, HERO ID: 3078903 categorized asbestos exposure variables using 3 ordinal levels.In de la Provote et al. 2002, HERO ID: 3520580, Clin et al. 2009, HERO ID: 3520549 and Boulanger et al. 2015, HERO ID: 307773, SIRs are only calculated using 2 exposure categories of cumulative exposure, such as exposed/unexposed or <= vs > 80 fibers/mL-year, all of which merit a Low rating for this metric. Because of this, de la Provote et al. 2002, HERO ID: 3520580, Clin et al. 2009, HERO ID: 3520549, and Boulanger et al. 2015, HERO ID: 307773, are only evaluated for metrics 4 and 5.
	Metric 6:	Temporality	High	While Clin et al. 2011, HERO ID: 3078903 gives limited detail on temporality, de la Provote et al. 2002, HERO ID: 3520580 shows that 69% of workers had at least 10 years at work, and 50% had >= 20 years.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	High	Clin et al. 2011, HERO ID: 3078903 reported using ICD-O 3 codes to identify mesothelioma cases, further stating that mesothelioma cases were assessed and validated by an expert pathologist from the French mesothelioma panel. ICD-O 3 codes are not given.

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Study Citation:	e La Provôté, S., Desoubeaux, N., Paris, C., Letourneux, M., Raffaelli, C., Galateau-Salle, F., Gignoux, M., Launoy, G. (2002). Incidence of digestive cancers and occupational exposure to asbestos. European Journal of Cancer Prevention 11(6):523-528.		
Health Outcome:	Mesothelioma		
Target Organ(s):	Lung/Respiratory: Pleural and peritoneal mesothelioma; Gastrointestinal: Pleural and peritoneal mesothelioma; Cancer/Carcinogenesis: Pleural and peritoneal mesothelioma		
Asbestos Fiber Type(s):	Asbestos - Chrysotile (serpentine): 12001-29-5; Asbestos - Crocidolite (riebeckite): 12001-28-4		
Linked HERO ID(s):	3520580, 3077730, 3078903, 3520549		
HERO ID:	3520580		

Domain	Metric		Rating	Comments
	Metric 8:	Reporting Bias	High	Clin et al. 2011, HERO ID: 3078903 reported findings in the abstract, results, and discussion sections adequately, where confidence intervals are provided for relative risk estimates. P-values and numbers of cases were also presented in detail.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	High	Clin et al. 2011, HERO ID: 3078903 adjusted models by sex and age (time dependent). Data on smoking were not available. Race was not discussed, although it is likely that the population was largely white.
	Metric 10:	Covariate Characterization	Medium	Information on covariates was obtained from the company's occupational health department records.
	Metric 11:	Co-exposure Counfounding	N/A	For mesothelioma, there is not likely to be any co-exposures for these subjects or in their settings, resulting in an "N/A" (not applicable) rating.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	Medium	Clin et al. 2011, HERO ID: 3078903 used a Cox hazard model to analyze the dose-response relationship of occupational asbestos exposure and risk of mesothelioma.
	Metric 13:	Statistical Power	Medium	Clin et al. 2011, HERO ID: 3078903 likely has adequate power to detect an association (n cases=24, total n=2024).
	Metric 14:	Reproducibility of Analyses	Medium	The descriptions of analyses are clear and sufficiently well-written to conceptually reproduce analyses.
	Metric 15:	Statistical Analysis	Medium	The authors describe appropriate methods, including using exposure lags, categorizing exposure to avoid assumptions of linearity, and examining alternative time scales in Cox models.

Additional Comments: Note that for de la Provote et al. 2002, HERO ID: 3520580, Clin et al. 2009, HERO ID: 3520549 and Boulanger et al. 2015, HERO ID: 307773, SIRs are only calculated using 2 exposure categories of cumulative exposure, such as exposed/unexposed or <= vs > 80 fibers/mL-year, all of which merit a Low rating for this metric. Because of this, de la Provote et al. 2002, HERO ID: 3520580, Clin et al. 2009, HERO ID: 3520549, and Boulanger et al. 2015, HERO ID: 307773 are only evaluated for metrics 4 and 5, and QC was not performed for any other metrics. Only Clin et al. 2011, HERO ID: 3078903 was evaluated for all metrics. The only outcome evaluated here is pleural and peritoneal mesothelioma.

Overall Quality Determination High

* No biomarkers were identified for this evaluation.

Study Citation:	Farioli, A., Straif, K., Brandi, G., Curti, S., Kjaerheim, K., Martinsen, J. I., Sparen, P., Tryggvadottir, L., Weiderpass, E., Biasco, G. (2018). Occupational exposure to asbestos and risk of cholangiocarcinoma: a population-based case-control study in four Nordic countries. Occupational and Environmental Medicine 75(3):191-198.
Health Outcome:	Mesothelioma
Target Organ(s):	Cancer/Carcinogenesis: Mesothelioma; Lung/Respiratory: Mesothelioma
Asbestos Fiber Type(s):	Asbestos - Not specified: 1332-21-4
Linked HERO ID(s):	5029590, 6875563
HERO ID:	5029590

Domain	Metric		Rating	Comments
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Low	This metric is rated low because the study or any cited methods sources do not explicitly mention the use of PCM or TEM (Plato et al., 2018, 6875563). Exposure in this study was estimated using a generic job-exposure matrix that was specifically developed for this cohort, but did not include personal measurements based on PCM or TEM (Kauppinen et al., 2009, 699236).
	Metric 5:	Exposure Levels	Medium	A range of exposure levels is reported within the study. For Plato et al. (2018, 6875563) these groupings include 0 fibers/ml, >0-0.2 fibers/ml, >0.2-1.25 fibers/ml, and >1.25-2.0 fibers/ml.

Additional Comments: This evaluation was not completed because metric 4 was rated as low. This is due to no explicit mention of the use of PCM or TEM for exposure measurements.

** As described in Appendix B.2 of the *White Paper: Quantitative Approach to the Human Health Assessment for the Risk Evaluation for Asbestos Part 2: Supplemental Evaluation Including Legacy Uses and Associated Disposals of Asbestos*, to be considered as being informative for dose-response analysis, metrics 4 and 5 would need metric ratings of Medium or High. This reference did not satisfy this requirement; therefore data quality evaluation is presented for only for metrics 4 and 5.

Study Citation:	Ferrante, D., Mirabelli, D., Tunesi, S., Terracini, B., Magnani, C. (2015). Pleural mesothelioma and occupational and non-occupational asbestos exposure: a case-control study with quantitative risk assessment. Occupational and Environmental Medicine 73(3):147-153.
Health Outcome:	Mesothelioma
Target Organ(s):	Lung/Respiratory: Pleural malignant mesothelioma (PMM); Cancer/Carcinogenesis: Pleural malignant mesothelioma (PMM)
Asbestos Fiber Type(s):	Asbestos - Crocidolite (riebeckite): 12001-28-4; Asbestos - Chrysotile (serpentine): 12001-29-5
Linked HERO ID(s):	No linked references.
HERO ID:	3008803

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	High	This population-based case-control study included the incident cases of pleural malignant mesothelioma (PMM) diagnosed between 1 January 2001 and 30 June 2006 among residents of the Casale Monferrato Local Health Authority (LHA) in Italy. Cases were also recruited from a random sample of the corresponding general population. The LHA included the town of Casale Monferrato, where an asbestos plan was operational for 80 years, and the surrounding area of approximately 60 towns and villages. Cases were identified via units of pathology, pneumology, oncology, internal medicine, oncology, internal medicine, thoracic surgery and radiotherapy of hospitals in the study area. The authors report that 200 out of 223 eligible cases agreed to join the study and that the ascertained cases represented 96% of all cases of PMM in the area. No inclusion or exclusion criteria appear to be used. Participants were invited by their attending clinician.
	Metric 2:	Attrition	High	The authors do not report any subject withdrawal or attrition from the analysis sample after formal recruitment. Outcome and exposure data appear to be complete.
	Metric 3:	Comparison Group	High	Controls were selected randomly from the population rosters of the Casale Monferatto LHA. Cases and controls were matched by date of birth (±18 months) and gender. To increase power in the younger age classes, the case control ratio was 1:2 for cases 60 years and older, and 1:4 for younger cases. Controls were invited by letter after their general practitioners were informed. The authors report that 348 out of 552 controls agreed to participate in the study. The distribution of cases and controls was similar by sex, and cases were older than controls due to over-sampling of controls matched to cases under 60 and "the different age distribution of non-participating controls." Information on exposure and covariates was gathered directly via interviews from controls, while 46% of interviews with cases were conducted with a close relative due to the case being dead or being in poor health condition. All of these differences (gender, age, and type of interview) were controlled for in statistical analysis. The potential for the healthy worker effect is not discussed, but is unlikely to produce significant bias since both controls and cases had occupational experience and exposure.
Domain 2: Exposure Characterization				

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Study Citation:	Ferrante, D., Mirabelli, D., Tunesi, S., Terracini, B., Magnani, C. (2015). Pleural mesothelioma and occupational and non-occupational asbestos exposure: a case-control study with quantitative risk assessment. Occupational and Environmental Medicine 73(3):147-153.
Health Outcome:	Mesothelioma
Target Organ(s):	Lung/Respiratory: Pleural malignant mesothelioma (PMM); Cancer/Carcinogenesis: Pleural malignant mesothelioma (PMM)
Asbestos Fiber Type(s):	Asbestos - Crocidolite (riebeckite): 12001-28-4; Asbestos - Chrysotile (serpentine): 12001-29-5
Linked HERO ID(s):	No linked references.
HERO ID:	3008803

Domain	Metric		Rating	Comments
	Metric 4:	Measurement of Exposure	Medium	The authors do not directly reference PCM or TEM quantitative measures of exposure in the methods. In the methods they cite various sources for where reference values for fiber concentrations came from, but these references are in Italian and thus could not be assessed for their usage of PCM or TEM by the QC team. However, in the discussion section the authors state that the ”information on airbone asbestos fiber concentration in Casale Monferrato were presented by Maule et al and are only sumarised here.” The cited reference specifies that ”fibers were counted on transmission electron microscope (TEM, detection limit not provided) and were identified by EDXA” (Maule et al., 2007, HERO ID: 3089896). However, other analyses from the Maule paper indicate that SEM was used for some years and TEM in other years - it is not entirely clear which measurements were used in the present analysis, although it may be reasonably assumed that both were used for their respective years. The other sources of data, that were unable to be retrieved in English, appear to be fiber measurements from the Balangero asbestos mine, asbestos cement production, asbestos-textile works, and production of brake and clutch linings.To assign exposure to individuals, asbestos exposure was assessed without knowledge of case/control status. The assessment took into account the whole exposure experience of each individual, including occupational and non-occupational sources (environmental, familial, domestic). Individuals with multiple potential sources of occupational exposure were looked at separately. Study raters assessed the probability, frequency, intensity, and duration of exposure for each potential source for each individual based on existing literature and the subject's interview results in order to assign an index value in fiber-ml years. There is some potential recall bias due to information coming from personal interviews rather than company records. This is a larger concern for the 46% of cases for whom interviews were conducted with close relatives rather than the actual subject who may not know the exact tasks subjects performed on the job. However, among participants who were directly interviewed recall bias is unlikely to be significantly differential by outcome status. To account for the potential recall bias among ”proxy” interviewees, whether or not interviews were conducted with the actual subject was an adjustment factor in statistical analysis.
	Metric 5:	Exposure Levels	Medium	The range and distribution of exposure is sufficient or adequate to develop an exposure-response estimate. Exposure was occupational or non-occupational and determined in fibers/mL-years. Groups were <0.1, ≥ 0.1–<1, ≥ 1–<10, or ≥ 10. Mean and range of fibre/mL-years are reported in Table 2.

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Study Citation: Ferrante, D., Mirabelli, D., Tunesi, S., Terracini, B., Magnani, C. (2015). Pleural mesothelioma and occupational and non-occupational asbestos exposure: a case-control study with quantitative risk assessment. Occupational and Environmental Medicine 73(3):147-153.
Health Outcome: Mesothelioma
Target Organ(s): Lung/Respiratory: Pleural malignant mesothelioma (PMM); Cancer/Carcinogenesis: Pleural malignant mesothelioma (PMM)
Asbestos Fiber Type(s): Asbestos - Crocidolite (riebeckite): 12001-28-4; Asbestos - Chrysotile (serpentine): 12001-29-5
Linked HERO ID(s): No linked references.
HERO ID: 3008803

Domain	Metric		Rating	Comments
	Metric 6:	Temporality	High	There is an appropriate consideration of latency in this case-control study, as this study was designed to assess outcomes 20 years after cessation of the industrial activity that was responsible for asbestos exposure. Duration of exposure ranges are not provided for the total population, but subjects with <1 f/mL year exposure had a mean of 28 years of exposure (SD 17) and subjects with >=10 f/mL year exposure had a mean of 53 years (SD 17) of exposure.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	High	The study only included cases of pleural malignant mesothelioma with diagnosis confirmed after examination of histological and/or cytological samples, identified through active search in the area referral hospitals.
	Metric 8:	Reporting Bias	Medium	All of the study's findings that are discussed in the methods are clearly presented in the results. However, p-values are not presented in the paper but are mentioned in the abstract.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Medium	Analyses were conducted using unconditional logistic regression models adjusting for gender, age at diagnosis and type of interview (direct or proxy respondents). There is no discussion of why those specific variables were chosen and not others.
	Metric 10:	Covariate Characterization	High	Potential confounders were assessed using standardized questionnaires that were completed in interviews by trained professionals (residence at interview, no mention of other confounders).
	Metric 11:	Co-exposure Counfounding	Low	Potential co-exposures in occupational settings are otherwise not discussed.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	Medium	The study used unconditional logistic regression modeling to assess differences in PMM diagnosis between cases and controls, which is an appropriate design.
	Metric 13:	Statistical Power	Medium	The final sample consisted of 548 individuals (200 cases and 348 controls), which is sufficiently large to detect an effect. The authors do not calculate overall statistical power, but mention using a 1:4 case:control ratio in younger cases to increase power.
	Metric 14:	Reproducibility of Analyses	Low	Exposure estimation processes are not clearly defined, and would be difficult to reproduce given access to the analytic data. Other aspects of the study are well-described.
	Metric 15:	Statistical Analysis	Medium	Unconditional logistic regression modeling was used to calculate odds ratios and rationale around variables that were included were transparent.

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Study Citation:	Ferrante, D., Mirabelli, D., Tunesi, S., Terracini, B., Magnani, C. (2015). Pleural mesothelioma and occupational and non-occupational asbestos exposure: a case-control study with quantitative risk assessment. Occupational and Environmental Medicine 73(3):147-153.
Health Outcome:	Mesothelioma
Target Organ(s):	Lung/Respiratory: Pleural malignant mesothelioma (PMM); Cancer/Carcinogenesis: Pleural malignant mesothelioma (PMM)
Asbestos Fiber Type(s):	Asbestos - Crocidolite (riebeckite): 12001-28-4; Asbestos - Chrysotile (serpentine): 12001-29-5
Linked HERO ID(s):	No linked references.
HERO ID:	3008803

Domain	Metric	Rating	Comments
Additional Comments:	Case-control study with 300 pleural malignant mesothelioma (PMM) cases and 348 controls. Asbestos type in this study is specific to 'amphibole' but another methods paper that was referenced in methods ((Maule et al., 2007, 3089896) discusses chrysotile and crocidolite, so those were included. Exposure was for occupational and non-occupational populations. Methods around the measurement of exposure and duration of exposure are unclear, although another study was referenced in the methodology for measuring fibers which cited TEM, however since non-occupational exposed cases exposure was not measured with TEM, Metric 4 was rated as Medium despite the large amount of uncertainty. The authors observed significant associations between asbestos exposure and odds of PMM.		

Overall Quality Determination — Medium

⋆ No biomarkers were identified for this evaluation.

Study Citation:	Finkelstein, M. M. (1984). Mortality among employees of an Ontario asbestos-cement factory. American Review of Respiratory Disease 129(5):754-761.
Health Outcome:	Mesothelioma
Target Organ(s):	Lung/Respiratory: Mesothelioma mortality; Cancer/Carcinogenesis: Mesothelioma mortality; Mortality: Mesothelioma mortality
Asbestos Fiber Type(s):	Asbestos - Chrysotile (serpentine): 12001-29-5; Asbestos - Crocidolite (riebeckite): 12001-28-4
Linked HERO ID(s):	No linked references.
HERO ID:	3083612

Domain	Metric		Rating	Comments
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Low	This metric is rated Low because the study or any cited methods source does not explicitly mention the use of PCM or TEM.The estimated average cumulative exposure of the production workers was about 60 fiber-years/mL (chrysotile and crocidolite). The estimated mean cumulative exposure within the board shop, in which chrysotile was the sole asbestos type utilized, was 39 f-y/mL. Air sampling data from government, insurance and company hygienists initiated in late 1969 were utilized along with company employment records to classify each production worker (n=186) according to estimated annual cumulative asbestos exposure as described within Finkelstein et al., 1983 (HERO ID 3100548), which also referenced Finkelstein, 1982 (HERO ID 76). Microscopic method of fiber analysis (PCM or TEM) was not detailed in main or referenced text. Air sampling data was obtained from only later factory years (late 1969 onward) and was not representative of earlier years, although assumptions for exposure levels for those earlier years were supported by impinger area sampling data. Air sampling data from government, insurance and company hygienists initiated in late 1969 were utilized along with company employment records to classify each production worker (n=186) according to estimated annual cumulative asbestos exposure as described within Finkelstein et al., 1983 (HERO ID 3100548) and Finkelstein, 1982 (HERO ID 76). Eighteen-year cumulative exposures were calculated for the production workers (Table 7) by combining work histories and exposure estimates, with job-related exposures multiplied by the time spent at each job and summed over the 18 years from first exposure. Workers were assigned to an exposure category according to their 18-year exposure totals. Exposures were assumed to have been unchanged from 1962 to 1970, to have been 30% higher from 1955 to 1961, and to have been twice as high from 1948 to 1954, with assumptions supported by impinger area sampling performed 1949 through the 1960's. Raw materials in the production worker pipe manufacturing process included cement, silica and both chrysotile and crocidolite asbestos, while the asbestos cement board production utilized chrysotile asbestos only. Comparison control workers were primarily within the rock wool/fiberglass insulation production area, although authors noted it was possible for employees to be assigned to the pipe shop for brief clean-up duties, or re-assigned from non-asbestos to asbestos work areas, such that some control workers were exposed as well. Exposures for maintenance workers were not calculated due to inadequate data.
	Metric 5:	Exposure Levels	Medium	The range and distribution of asbestos exposure in Table 7 presented across five exposure categories ranging from <=30 fiber-years/mL through >150 fiber-years/mL for production workers is sufficient to develop an exposure-response estimate.

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Study Citation:	Finkelstein, M. M. (1984). Mortality among employees of an Ontario asbestos-cement factory. American Review of Respiratory Disease 129(5):754-761.
Health Outcome:	Mesothelioma
Target Organ(s):	Lung/Respiratory: Mesothelioma mortality; Cancer/Carcinogenesis: Mesothelioma mortality; Mortality: Mesothelioma mortality
Asbestos Fiber Type(s):	Asbestos - Chrysotile (serpentine): 12001-29-5; Asbestos - Crocidolite (riebeckite): 12001-28-4
Linked HERO ID(s):	No linked references.
HERO ID:	3083612

Domain	Metric	Rating	Comments
Additional Comments:	QC was not completed for metrics other than Metrics 4 and 5 because the study does not have sufficient exposure information to be useful for dose-response analysisNOTE: this study was not evaluated for any metrics except Metric 4 and 5 and had no data extracted because it did not have sufficient exposure information to be useful for dose-response analysis. Within this retrospective cohort study, mortality among asbestos exposed (n=535, production and maintenance workers) and control (n=205) male employees (total n=740) of an asbestos cement pipe manufacturing factory with a minimum of one year employment who had been hired prior to 1960 was compared with mortality of the Ontario, Canada male general population over a period of 10 to 34 years of follow-up. Workers were divided into three groups for study: production workers involved in asbestos cement pipe manufacture, maintenance workers, and those involved in rock wool and fiberglass insulation or other minimal exposure areas who were classified as non-exposed controls. Factory production of asbestos cement pipe in one shed and rock wool (later fiberglass) insulation in another shed began in 1948, and asbestos cement board was produced in a separate building from 1955 to 1970. Air sampling data from government, insurance and company hygienists initiated in late 1969 were utilized along with company employment records to classify each production worker (n=186) according to estimated annual cumulative asbestos exposure. Air sampling data was obtained from only later factory years (late 1969 onward) and was not representative of earlier years, although assumptions for exposure levels for those earlier years were supported by impinger area sampling data. In the period 20 years from first exposure, the production workers had a standardized mortality ratio of 181 for all causes of death, 320 for non-malignant respiratory disease, and 58 for ischemic heart disease.		

* No biomarkers were identified for this evaluation.

** As described in Appendix B.2 of the *White Paper: Quantitative Approach to the Human Health Assessment for the Risk Evaluation for Asbestos Part 2: Supplemental Evaluation Including Legacy Uses and Associated Disposals of Asbestos*, to be considered as being informative for dose-response analysis, metrics 4 and 5 would need metric ratings of Medium or High. This reference did not satisfy this requirement; therefore data quality evaluation is presented for only for metrics 4 and 5.

Study Citation:	Finkelstein, M. M. (1983). Mortality among long-term employees of an Ontario (Canada) asbestos-cement factory. British Journal of Industrial Medicine 40(2):138-144.
Health Outcome:	Mesothelioma
Target Organ(s):	Mortality: Mesothelioma mortality; Cancer/Carcinogenesis: Mesothelioma mortality; Lung/Respiratory: Mesothelioma mortality
Asbestos Fiber Type(s):	Asbestos - Chrysotile (serpentine): 12001-29-5; Asbestos - Crocidolite (riebeckite): 12001-28-4
Linked HERO ID(s):	No linked references.
HERO ID:	3100548

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Medium	Key elements of the study design were reported within this retrospective cohort study of long-term male workers in which n=339 male asbestos workers hired prior to 1960 and employed by the same company in Ontario, Canada for at least nine years were followed until 31 October 1980 for mortality outcomes of interest. An additional n=11 men (3.2% of the total) could not be properly classified from their work histories as production, maintenance or rock wool/fiberglass workers and were excluded from the current analysis. Participants were identified from company records of all hourly and salaried employees who had worked at the plant of interest. Employees were excluded if they did not work for at least nine years to account for the long latency of asbestos-related diseases and difficulties of tracing short-term employees. There is no evidence to suggest inclusion or exclusion from the sample differed significantly by outcome or exposure status.
	Metric 2:	Attrition	Low	Official death certificates were obtained for all men who had died. However, a total of five (2.7%) of the n=186 production workers, three (5.5%) of the n=55 maintenance workers and five (5.7%) of the n=87 unexposed or minimally exposed workers were unable to be traced for mortality outcomes and were assumed still alive for analysis. A group of 55 maintenance workers were originally included, but later excluded as the study reported that it ”was not thought possible to estimate exposures for the maintenance men.”

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Study Citation:	Finkelstein, M. M. (1983). Mortality among long-term employees of an Ontario (Canada) asbestos-cement factory. British Journal of Industrial Medicine 40(2):138-144.
Health Outcome:	Mesothelioma
Target Organ(s):	Mortality: Mesothelioma mortality; Cancer/Carcinogenesis: Mesothelioma mortality; Lung/Respiratory: Mesothelioma mortality
Asbestos Fiber Type(s):	Asbestos - Chrysotile (serpentine): 12001-29-5; Asbestos - Crocidolite (riebeckite): 12001-28-4
Linked HERO ID(s):	No linked references.
HERO ID:	3100548

Domain	Metric		Rating	Comments
	Metric 3:	Comparison Group	Medium	Inclusion criteria and methods of participant selection were reported. Workers within the rock wool/fiber glass operations (n=87) were classified as minimally exposed, had mortality described as similar to the general male Ontario population and were utilized as the comparison control workers. SMR analyses results utilized the age and calendar specific mortality experience of the male Ontario general population as a comparison group for expected mortality rates. The mean age at the start of exposure or employment was described as similar between the exposed and general populations. Comparison control workers were primarily within the rock wool/fiberglass insulation production area, although the author of the current study noted in another publication (Finkelstein et al., 1983, HERO ID 3083612) of workers in the same factory that it was possible for employees to be assigned to the pipe shop for brief clean-up duties, or re-assigned from non-asbestos to asbestos work areas, such that some control workers may have been exposed as well. There is potential for healthy worker effect in terms of left truncation bias, as the cohort for the current study was restricted to workers with at least nine years of employment, such that all workers had to survive for at least nine years to be included. However, Table 2 SMR results for non-malignant respiratory disease indicate no evidence of healthy worker effect in terms of the healthy hire or healthy worker survivor effect.

Domain 2: Exposure Characterization

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Study Citation:	Finkelstein, M. M. (1983). Mortality among long-term employees of an Ontario (Canada) asbestos-cement factory. British Journal of Industrial Medicine 40(2):138-144.
Health Outcome:	Mesothelioma
Target Organ(s):	Mortality: Mesothelioma mortality; Cancer/Carcinogenesis: Mesothelioma mortality; Lung/Respiratory: Mesothelioma mortality
Asbestos Fiber Type(s):	Asbestos - Chrysotile (serpentine): 12001-29-5; Asbestos - Crocidolite (riebeckite): 12001-28-4
Linked HERO ID(s):	No linked references.
HERO ID:	3100548

Domain	Metric		Rating	Comments
	Metric 4:	Measurement of Exposure	Medium	The microscopic method (PCM or TEM) of analysis of air sampling data reported in Table 1 with outcome mortality rates was not detailed. The average estimated cumulative exposure among production workers was reported for three groups of production workers of 62 men each as 44 f-y/ml, 92 f-y/ml, and 180 f-y/mL (chrysotile and crocidolite). Groups were created on the basis of ranking 18-year cumulative exposures. Air sampling data from government, insurance and company hygienists initiated in late 1969 was utilized along with company employment records to classify each production worker's exposure, however production within the plant began in 1948 and measured exposures for periods 1948-1970 were lacking and assumed as related to the quantitative measurements made beginning in 1969. Exposures for maintenance workers was described as not calculated due to inadequate data. Estimated cumulative exposure for only the first 18 years of employment was utilized such that for men employed less than 18 years this parameter was used and for men employed more than 18 years, the potential exposures after 18 years were excluded. Exposures were assumed to have been unchanged from 1962 to 1970, to have been 30% higher from 1955 to 1961, and to have been twice as high from 1948 to 1954, with assumptions supported by impinger area sampling performed 1949 through the 1960's. Based on subsequent discussion and review of additional information, the rating was adjusted based on impinger data was collected and personal membrane sampling was conducted beginning in late 1969 and detailed employment records were used to construct exposure histories.
	Metric 5:	Exposure Levels	Medium	The range and distribution of estimated exposures is reported within Table 1 for production workers as 8 to 420 fiber-years/mL. Table 1 provides the mortality rates for production workers across three groups of exposure categories.
	Metric 6:	Temporality	High	The study presents an appropriate temporality and the interval between exposure and outcome is appropriate considering the latency of disease. Workers were required to have been hired before 1960 and were followed up until 1980, ensuring at least 20 years of follow-up for the cohort.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Medium	Workers were followed up until 31 October 1980, and as such only pre-ICD 10 coding was utilized as indicated for ICD codes reported in official death certificate data obtained for all deaths in Table 2. Additional clinical, pathological and necropsy reports were available for n=44 of the n=58 deaths among production workers.
	Metric 8:	Reporting Bias	Medium	There were no concerns for selective reporting. SMR's in Table 2 and mortality rates across age and time since first exposure groups per man years in production workers in Table 3 were reported as single values, with no measures of variation or confidence intervals. Confidence intervals for specific outcomes were reported within the text.

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Study Citation:	Finkelstein, M. M. (1983). Mortality among long-term employees of an Ontario (Canada) asbestos-cement factory. British Journal of Industrial Medicine 40(2):138-144.
Health Outcome:	Mesothelioma
Target Organ(s):	Mortality: Mesothelioma mortality; Cancer/Carcinogenesis: Mesothelioma mortality; Lung/Respiratory: Mesothelioma mortality
Asbestos Fiber Type(s):	Asbestos - Chrysotile (serpentine): 12001-29-5; Asbestos - Crocidolite (riebeckite): 12001-28-4
Linked HERO ID(s):	No linked references.
HERO ID:	3100548

Domain	Metric		Rating	Comments
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Medium	Other than stratification for years since first exposure and age, no additional adjustments or consideration for differences between exposed and non-exposed groups regarding distributions of relevant covariates were detailed. The cohort for study was restricted to males. The authors mention that information for smoking was available for 70% of the cohort, but this information is not used in statistical analyses. The authors state that data was available for 9 of 11 men who had died of mesothelioma: 2 never smoked, 2 had quit for 10 or more years, and 5 were smokers. Based on subsequent discussion and review of additional information, the rating was adjusted based on stratification by age and only males being included in the study.
	Metric 10:	Covariate Characterization	Medium	Finkelstein, 1982 provides evidence of detailed personnel files use for TSFE, age, job history, etc.
	Metric 11:	Co-exposure Counfounding	N/A	This metric is not applicable for mesothelioma.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	Medium	The study design was appropriate as an early study to address the research aims. Two types of comparisons were performed, internal and external. Table 2 SMR results were obtained through external comparisons by applying the Ontario general population mortality rates as reference and presented for production, maintenance and control workers. Table 3 mortality rate results were presented for production workers stratified across age and years since first exposure groups. Tests for trend were not reported.
	Metric 13:	Statistical Power	Medium	The number of participants was adequate, however formal statistical comparisons between exposed and non-exposed workers, or across time since first exposure groups, were not presented. SMR results in Table 2 were reported for the n=328 workers, while results in Table 3 were reported only for the n=186 production workers.
	Metric 14:	Reproducibility of Analyses	Medium	The data are presented in Table 1 that were used used in the 1986 analysis. Reporting errors are present in Table 2, but these data are not used in the 1986 analysis.
	Metric 15:	Statistical Analysis	Medium	Model building was not conducted. The construction of SMRs appears appropriate.

Additional Comments: This was an occupational retrospective cohort study reporting SMRs of long-term male workers in which n=339 male asbestos workers hired prior to 1960 and employed by the same company in Ontario, Canada for at least nine years were followed until 31 October 1980 for mortality outcomes of interest. Concerns included the assumption that workers unable to be traced for mortality outcomes were still alive at the end of follow-up, with no sensitivity analyses conducted to examine results with and without these workers. Mesothelioma mortality was obtained utilizing pre-ICD 10 coding. Exposure concentrations are provided for three groups of exposure in relation to a reference population of Ontario men by outcome - however, no statistical analysis is done to compare mortality using exposure concentration data, limiting the study's usefulness for dose-response analysis.

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Study Citation:	Finkelstein, M. M. (1983). Mortality among long-term employees of an Ontario (Canada) asbestos-cement factory. British Journal of Industrial Medicine 40(2):138-144.
Health Outcome:	Mesothelioma
Target Organ(s):	Mortality: Mesothelioma mortality; Cancer/Carcinogenesis: Mesothelioma mortality; Lung/Respiratory: Mesothelioma mortality
Asbestos Fiber Type(s):	Asbestos - Chrysotile (serpentine): 12001-29-5; Asbestos - Crocidolite (riebeckite): 12001-28-4
Linked HERO ID(s):	No linked references.
HERO ID:	3100548

Domain	Metric	Rating	Comments
Overall Quality Determination		**Medium**	

* No biomarkers were identified for this evaluation.

Study Citation: Finkelstein, M. M. (1985). A study of dose-response relationships for asbestos associated disease. British Journal of Industrial Medicine 42(5):319-325.
Health Outcome: Mesothelioma
Target Organ(s): Lung/Respiratory: Mesothelioma mortality; Mortality: Mesothelioma mortality; Cancer/Carcinogenesis: Mesothelioma mortality
Asbestos Fiber Type(s): Asbestos - Crocidolite (riebeckite): 12001-28-4; Asbestos - Chrysotile (serpentine): 12001-29-5
Linked HERO ID(s): No linked references.
HERO ID: 709685

Domain	Metric		Rating	Comments
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Low	This metric is rated Low because the study or any cited methods source does not explicitly mention the use of PCM or TEM.Air sampling was conducted by different entities including the government, the asbestos cement company, and insurance hygienists (Finkelstein, 1982, HEROID: 76). Measurements were primarily made through impinger area sampling (Finkelstein, 1982, HEROID: 76). In 1969, personal membrane filters were used (Finkelstein, 1982, HEROID: 76). Because of the infrequent consistency of reporting exposure, extrapolations were needed for missing time frames (Finkelstein, 1982, HEROID: 76).Authors described the following for calculation expose and dose estimation: "Cumulative exposures were calculated for each man by summing annual exposures accumulated during the first 18 years from the start of exposure. Asbestos dosages were calculated by assuming that a fixed proportion of the workplace air concentrations were deposited in the lungs, and each year's accumulation was weighted by the residence time in lung tissue (the formulas used are given in the appendix). Cumulative exposures had been estimated to be accurate to within a factor of 3 to 5."
	Metric 5:	Exposure Levels	Medium	The distribution of exposure appears to be sufficient to develop an exposure-response estimate. Cumulative exposure (f-y/ml) and dose (f/ml*yr-squared) for calculating cumulative risk were utilized in statistical models. Range or other measure distribution is not present in this paper, however Figure 3 shows values ranging from 0-6,500 fibers/mL x year^2.

Additional Comments: Finklestein et al, 1985 709685 was not evaluated for any metrics except Metric 4 and 5 and had no data extracted because it did not have sufficient exposure information to be useful for dose-response analysis. QC was not completed for metrics other than Metrics 4 and 5 because the study does not have sufficient exposure information to be useful for dose-response analysis.

* No biomarkers were identified for this evaluation.

** As described in Appendix B.2 of the *White Paper: Quantitative Approach to the Human Health Assessment for the Risk Evaluation for Asbestos Part 2: Supplemental Evaluation Including Legacy Uses and Associated Disposals of Asbestos*, to be considered as being informative for dose-response analysis, metrics 4 and 5 would need metric ratings of Medium or High. This reference did not satisfy this requirement; therefore data quality evaluation is presented for only for metrics 4 and 5.

Study Citation:	Franklin, P., Alfonso, H., Reid, A., Olsen, N., Shilkin, K. B., Brims, F., de Klerk, N., Musk, A. W. (2016). Asbestos exposure and histological subtype of malignant mesothelioma. Occupational and Environmental Medicine 73(11):749-752.
Health Outcome:	Mesothelioma
Target Organ(s):	Cancer/Carcinogenesis: malignant mesothelioma (cytology only), malignant mesothelioma (sarcomatoid), malignant mesothelioma (biphasic), malignant mesothelioma (epithelioid); Lung/Respiratory: malignant mesothelioma (biphasic), malignant mesothelioma (epithelioid), malignant mesothelioma (cytology only), malignant mesothelioma (sarcomatoid)
Asbestos Fiber Type(s):	Asbestos - Crocidolite (riebeckite): 12001-28-4; Asbestos - Amosite (grunerite): 12172-73-5; Asbestos - Chrysotile (serpentine): 12001-29-5; Asbestos - Not specified: 1332-21-4
Linked HERO ID(s):	733541, 709469, 3079298, 3520653, 3531364, 6868332
HERO ID:	3520653

Domain	Metric		Rating	Comments
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Low	This metric is rated Low. The exposures used to calculate the effect estimates reported in Table 2 stemmed from data that came from historical records like questionnaires and clinical documents. Questions about asbestos exposure covered various characteristics including ”duration of exposure (for occupational cases only), time since first exposure, source of asbestos exposure (occupational or non-occupational), form of asbestos handled (raw, processed or unclear), type of asbestos (crocidolite only or mixed fibres) and cumulative exposure (for crocidolite only).” Measurements of these characteristics did not suggest the use of PCM or TEM. Additionally, cited methods for exposure measurement based on historical records reported the following: Armstrong et al., 1986 3083076 did not use either PCM or TEM. Counting method was with a Casella long running thermal precipitator. Hansen et al., 1997 2219991 described that the first survey to count fiber was in 1966, which was done by an industrial hygienist using a Casella long running thermal precipitator. All samples examined in this particular study were analyzed using the standard membrane filter method. Some exceptions were surveys in 1984 and 1986 which used SEM, and in 1992 which used TEM. So, their latest samples were analyzed using TEM. However, the study being evaluated does not describe estimates in a way to know outcomes based on exposures measured from 1992 and after. Based on Table 1, time since first exposure was over 40 years for this sample of mesothelioma cases so I presume peak exposure for them was way before 1992. Lastly, these papers described methods for those tied to Wittenoom so it’s still not clear how exposure measurements were conducted for those who reported exposure unrelated to Wittenoom. Analysis of lung specimens from select cases (n=122) did measure asbestos fibers via TEM, and estimates are reported in Table 4. However, they were non-regression and non-SMR.
	Metric 5:	Exposure Levels	Low	Regression analyses only present exposure in terms of ”exposed vs. unexposed” and thus have a limited range of exposure.

Additional Comments: Due to ”Low” ratings for both Metric 4 and Metric 5, this study was determined not to be useful for dose-response analysis and thus did not receive a full evaluation.

** As described in Appendix B.2 of the *White Paper: Quantitative Approach to the Human Health Assessment for the Risk Evaluation for Asbestos Part 2: Supplemental Evaluation Including Legacy Uses and Associated Disposals of Asbestos*, to be considered as being informative for dose-response analysis, metrics 4 and 5 would need metric ratings of Medium or High. This reference did not satisfy this requirement; therefore data quality evaluation is presented for only for metrics 4 and 5.

Study Citation:	Gardner, M. J., Winter, P. D., Pannett, B., Powell, C. A. (1986). Follow up study of workers manufacturing chrysotile asbestos cement products. British Journal of Industrial Medicine 43(11):726-732.		
Health Outcome:	Mesothelioma		
Target Organ(s):	Cancer/Carcinogenesis: Mesothelioma; Lung/Respiratory: Mesothelioma		
Asbestos Fiber Type(s):	Asbestos - Chrysotile (serpentine): 12001-29-5		
Linked HERO ID(s):	No linked references.		
HERO ID:	3083223		

Domain	Metric	Rating	Comments
Domain 2: Exposure Characterization			
	Metric 4: Measurement of Exposure	Low	Atmospheric fibre concentrations were made during period 1968-82 by company and were assigned codes to job ittles to reflect levels of probable exposure (table 2). Over 70% of readings are based on use of personal samplers. "For the period before 1968 it would be reasonable to assume that levels were higher because of less extensive exhaust ventilation and more direct handling of raw asbestos".
	Metric 5: Exposure Levels	Low	"Since 10=970 fibre levels have generally bene low with mean levels under 1 f/ml throughout factory. Only a few exposures over 2f/ml have been recorded and most measured concentrations have been under 0.5f/ml."

Additional Comments: Overall, information on the measurement of exposure metric (M4) to assess exposure was limited. Additionally, the exposure levels metric (M5) information reported was limited to determine exposure-response relationships.

** As described in Appendix B.2 of the *White Paper: Quantitative Approach to the Human Health Assessment for the Risk Evaluation for Asbestos Part 2: Supplemental Evaluation Including Legacy Uses and Associated Disposals of Asbestos*, to be considered as being informative for dose-response analysis, metrics 4 and 5 would need metric ratings of Medium or High. This reference did not satisfy this requirement; therefore data quality evaluation is presented for only for metrics 4 and 5.

Study Citation: Gilham, C., Rake, C., Burdett, G., Nicholson, A. G., Davison, L., Franchini, A., Carpenter, J., Hodgson, J., Darnton, A., Peto, J. (2015). Pleural mesothelioma and lung cancer risks in relation to occupational history and asbestos lung burden. Occupational and Environmental Medicine 73(5):290-299.

Health Outcome: Mesothelioma

Target Organ(s): Cancer/Carcinogenesis: Mesothelioma cases and mesothelioma mortality; Lung/Respiratory: Mesothelioma cases and mesothelioma mortality; Mortality: Mesothelioma cases and mesothelioma mortality

Asbestos Fiber Type(s): Asbestos - Amosite (grunerite): 12172-73-5; Asbestos - Crocidolite (riebeckite): 12001-28-4; Asbestos - Chrysotile (serpentine): 12001-29-5; Asbestos - Not specified: 1332-21-4; Asbestos - Tremolite: 14567-73-8; Asbestos - Anthophyllite: 17068-78-9

Linked HERO ID(s): No linked references.

HERO ID: 3077660

Domain	Metric	Rating	Comments
Domain 1: Study Participation			
	Metric 1: Participant Selection	Medium	This study built on a case-control study referred to as the MALCS study (Rake et al., 2009, HERO ID 733522). Telephone interviews of 622 mesothelioma patients and 1420 population controls in England, Wales, and Scotland were conducted between 2001 and 2006 as part of the MALCS study. Additionally, 420 patients with resected lung cancer born since 1940 were interviewed as controls for the mesothelioma patients as part of the present study (Gilham et al., 2015, HERO ID 3077660), though the dates of these interviews were not specified.Patients with lung cancer and mesothelioma were identified through physicians, nurses, and Hospital Episode Statistics (HES) notifications from 170 hospitals throughout Britain. Detailed selection methods are provided in the MALCS paper (Rake et al., 2009, HERO ID 733522). In the cited MALCS case-control study paper, it was reported that the exclusion criteria for both mesothelioma cases and population controls were: being "physically or mentally unfit for interview", not having access to a telephone, or not speaking English (Rake et al., 2009, HERO ID 733522).The MALCS paper reported "Overall 39% of 1396 notified mesothelioma patients (423 too ill or dead, 87 no GP or consultant permission and 31 ineligible or not traced) and 18% of 2897 controls (169 too ill or dead, 169 no permission, 191 ineligible or untraced) were not invited for interview. The proportion of those invited who were interviewed, sometimes after several reminders, consisted of 73% (624 out of 857) of mesothelioma cases and 60% (1420 out of 2368) of controls. As expected, response rates in controls were higher in more affluent areas (69% in the top two quintiles of socioeconomic status and 46% in the lowest)." The analysis of lung samples in the present paper was conducted on mesothelioma patients and lung cancer patients, but not the population controls from the MALCS study. The present paper (Gilham et al., 2015, HERO ID 3077660) reported that written informed consent was obtained from 346 (77%) patients with mesothelioma and their next of kin for postmortem samples to be analyzed and from 406 (96%) patients with lung cancer for analysis of resected tissue." Thus, although some elements were not present, the available information does not indicate substantial risk of selection bias.

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Study Citation:	Gilham, C., Rake, C., Burdett, G., Nicholson, A. G., Davison, L., Franchini, A., Carpenter, J., Hodgson, J., Darnton, A., Peto, J. (2015). Pleural mesothelioma and lung cancer risks in relation to occupational history and asbestos lung burden. Occupational and Environmental Medicine 73(5):290-299.
Health Outcome:	Mesothelioma
Target Organ(s):	Cancer/Carcinogenesis: Mesothelioma cases and mesothelioma mortality; Lung/Respiratory: Mesothelioma cases and mesothelioma mortality; Mortality: Mesothelioma cases and mesothelioma mortality
Asbestos Fiber Type(s):	Asbestos - Amosite (grunerite): 12172-73-5; Asbestos - Crocidolite (riebeckite): 12001-28-4; Asbestos - Chrysotile (serpentine): 12001-29-5; Asbestos - Not specified: 1332-21-4; Asbestos - Tremolite: 14567-73-8; Asbestos - Anthophyllite: 17068-78-9
Linked HERO ID(s):	No linked references.
HERO ID:	3077660

Domain	Metric		Rating	Comments
	Metric 2:	Attrition	Medium	The authors reported that ”written informed consent was obtained from 346 (77%) patients with mesothelioma and their next of kin for postmortem samples to be analyzed and from 406 (96%) patients with lung cancer for analysis of resected tissue.” The use of postmortem samples for mesothelioma patients indicates that the analyses could not include samples from mesothelioma patients who were still alive. The use of resected tissue for lung cancer patients implies that the lung cancer patients may have been alive at the time of sample collection. The authors reported that samples were analyzed as they became available, such that transmission electron microscopy (TEM) was performed on 133 mesothelioma samples and 262 lung cancer samples. All of the analyzed samples were from patients born since 1940, with the exception of 11 female mesothelioma patients born between 1925-1939, who were excluded from most of the analyses. Thus, lung samples were analyzed for 133/346 (38%) of the mesothelioma patients and 262/406 (65%) of the lung cancer patients for whom consent was obtained. Thus, there was at least moderate exclusion from the analysis sample.
	Metric 3:	Comparison Group	Medium	The authors selected lung cancer patients as the control group for mesothelioma patients because ”resected lung cancers provide the only adequate national source of lung samples in people who can be identified systematically, are available for interview and have an age distribution similar to mesothelioma. Only a small proportion of all lung cancers are caused by asbestos, so the asbestos lung burdens of this national sample are reasonably representative of the general population except for a few per cent with very high burdens.”The cited MALCS study indicated that information obtained via interview included smoking histories and potential environmental exposures (Rake et al., 2009, HERO ID 733522), but it is unclear whether the mesothelioma patients and the lung cancer patients differed on these variables. The statistical analyses adjusted for period of birth and sex, although neither was statistically significant. Several analyses were restricted to only males due to the small number of females.In addition to comparison of mesothelioma cases to lung cancer cases, ”the lifetime risk (probability of dying by age 90) was calculated actuarially in each lung burden category assuming current (2013) UK rates for all other causes of death. These lifetime risks were standardized to the projected probabilities of dying by age 90 for mesothelioma (0.86%) and lung cancer (4.67%) of all British men born in 1945.” SMRs in each lung burden category were determined ”for the cohort of British men whose central date of birth is the beginning of 1945, (The median date of birth of our mesothelioma cases was September 1944.)”Thus, information about some demographic and exposure variables was not available to compare between groups. For example, race was not mentioned. However, age and sex were addressed in the analyses.

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Study Citation:	Gilham, C., Rake, C., Burdett, G., Nicholson, A. G., Davison, L., Franchini, A., Carpenter, J., Hodgson, J., Darnton, A., Peto, J. (2015). Pleural mesothelioma and lung cancer risks in relation to occupational history and asbestos lung burden. Occupational and Environmental Medicine 73(5):290-299.
Health Outcome:	Mesothelioma
Target Organ(s):	Cancer/Carcinogenesis: Mesothelioma cases and mesothelioma mortality; Lung/Respiratory: Mesothelioma cases and mesothelioma mortality; Mortality: Mesothelioma cases and mesothelioma mortality
Asbestos Fiber Type(s):	Asbestos - Amosite (grunerite): 12172-73-5; Asbestos - Crocidolite (riebeckite): 12001-28-4; Asbestos - Chrysotile (serpentine): 12001-29-5; Asbestos - Not specified: 1332-21-4; Asbestos - Tremolite: 14567-73-8; Asbestos - Anthophyllite: 17068-78-9
Linked HERO ID(s):	No linked references.
HERO ID:	3077660

Domain	Metric		Rating	Comments
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Medium	Lifetime occupational history was obtained from telephone interviews of 622 mesothelioma patients, 1420 population controls, and 420 patients with resected lung cancer. Then “job titles were assigned to Standard Occupational Classification 1990 (SOC 90) and Standard Industrial Classification 1992 (SIC 92) codes and grouped into main job categories” (Gilham et al., 2015, 733522). The authors reported that ”subjects were assigned to the highest-ranking occupation they had worked in irrespective of duration”. Thus, although lifetime work history was obtained, the assignment of occupation was based on only a portion of this history.Transmission electron microscopy (TEM) was used to analyze 133 post-mortem lung tissue samples from a subset of the mesothelioma patients and 262 resected lung tissue samples from a subset of the lung cancer patients. The authors reported that ”lung samples were anonymized and sent to the Health and Safety Laboratory (HSL) for TEM counting of asbestos fibers longer than 5 um.”Lung tissue samples were analyzed as they became available. Because tissue samples, but not environmental samples, were analyzed, the samples were only analyzed at one time point for each individual, but this time point is representative of cumulative asbestos lung fiber burden.
	Metric 5:	Exposure Levels	Medium	The range and distribution of exposure, expressed as million fibers longer than 5 um per dry gram (mf/g) asbestos lung burden and displayed in Table 1, was sufficient to develop an exposure-response relationship, as shown in Figure 2.
	Metric 6:	Temporality	Low	The exposure measurement of asbestos burden in lung tissue occurred post-mortem for mesothelioma patients. Since the diagnosis of these patients was determined while they were alive, the exposure measurement was obtained after the outcome measurement. However, the study also included occupational history data, which indicates occupational exposures that occurred before death from mesothelioma. Some possibility remains that some of the fiber accumulation that was assessed after death could have occurred after disease development. Therefore, the temporality of exposure and outcome is uncertain.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	High	The authors state that lung cancer and mesothelioma patients were “identified through chest physicians, lung cancer nurse specialists and Hospital Episode Statistics (HES)” from 170 hospitals throughout Britain (Gilham et al., 2015, HERO ID 733522). The MALCS study methods paper says that ”histological confirmation was obtained for 92% of interviewedmesothelioma cases” (Rake et al., 2009, HERO ID 733522).

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Study Citation:	Gilham, C., Rake, C., Burdett, G., Nicholson, A. G., Davison, L., Franchini, A., Carpenter, J., Hodgson, J., Darnton, A., Peto, J. (2015). Pleural mesothelioma and lung cancer risks in relation to occupational history and asbestos lung burden. Occupational and Environmental Medicine 73(5):290-299.
Health Outcome:	Mesothelioma
Target Organ(s):	Cancer/Carcinogenesis: Mesothelioma cases and mesothelioma mortality; Lung/Respiratory: Mesothelioma cases and mesothelioma mortality; Mortality: Mesothelioma cases and mesothelioma mortality
Asbestos Fiber Type(s):	Asbestos - Amosite (grunerite): 12172-73-5; Asbestos - Crocidolite (riebeckite): 12001-28-4; Asbestos - Chrysotile (serpentine): 12001-29-5; Asbestos - Not specified: 1332-21-4; Asbestos - Tremolite: 14567-73-8; Asbestos - Anthophyllite: 17068-78-9
Linked HERO ID(s):	No linked references.
HERO ID:	3077660

Domain	Metric		Rating	Comments
	Metric 8:	Reporting Bias	Medium	Mesothelioma findings are reported throughout the paper. Some of the estimates are reported with confidence intervals, such as in Table 1, while others are not, such as in Table 3 (Gilham et al., 2015, HERO ID 3077660).
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Medium	The analyses adjusted for sex and age but did not adjust for race. In Table 1, the odds ratios are adjusted for sex and period of birth (1940-1944, 1945-1949, 1950-1954, and 1955+), although neither was statistically significant.
	Metric 10:	Covariate Characterization	Medium	Although the authors did not discuss whether the questionnaires used to interview participants were validated, there is no evidence to suggest any concerns about the validity of the method. It is unlikely that the participants would have incorrectly reported sex or age.
	Metric 11:	Co-exposure Counfounding	N/A	The assessment of potential co-exposures was not necessary for mesothelioma because there are few other causes of mesothelioma.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	Medium	The study design used appropriate statistical methods including odds ratios and logistic regression for case-control analyses, and SMR for comparison to the British population.
	Metric 13:	Statistical Power	Medium	Although the authors did not provide an explicit discussion of power, there was an adequate number of participants such that an association was observed between asbestos lung burden and mesothelioma.
	Metric 14:	Reproducibility of Analyses	Medium	The analyses were described in sufficient detail in the paper and in ”Appendix 1: Statistical Methods” (Gilham et al., 2015, 3077660).
	Metric 15:	Statistical Analysis	Medium	Although some details could have been explained better, the methods for calculating the risk estimates were sufficiently transparent.
Domain 6: Other (if applicable) Considerations for Biomarker Selection and Measurement (Lakind et al. 2014)				
	Metric 16:	Use of Biomarker of Exposure	High	This study asbestos used fiber concentrations in lung tissue samples as a biomarker of asbestos exposure, which has a clear relationship with target dose. Transmission electron microscopy (TEM) was used to measure this biomarker. In the lung cancer and mesothelioma lung tissue samples assessed in this study, 75% of the counted fibers were amosite, 18% were crocidolite, 1.9% were chrysotile, 1 % were tremolite, 2 % were anthophyllite, 0.6% were actinolite, and 1.7% were uncharacterized amphiboles. Thus, several different fiber types were identified in this study because TEM can distinguish between fiber types, thus determining specific biomarkers of exposure (fiber concentrations in lung tissue) for each specific fiber type.

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Study Citation:	Gilham, C., Rake, C., Burdett, G., Nicholson, A. G., Davison, L., Franchini, A., Carpenter, J., Hodgson, J., Darnton, A., Peto, J. (2015). Pleural mesothelioma and lung cancer risks in relation to occupational history and asbestos lung burden. Occupational and Environmental Medicine 73(5):290-299.
Health Outcome:	Mesothelioma
Target Organ(s):	Cancer/Carcinogenesis: Mesothelioma cases and mesothelioma mortality; Lung/Respiratory: Mesothelioma cases and mesothelioma mortality; Mortality: Mesothelioma cases and mesothelioma mortality
Asbestos Fiber Type(s):	Asbestos - Amosite (grunerite): 12172-73-5; Asbestos - Crocidolite (riebeckite): 12001-28-4; Asbestos - Chrysotile (serpentine): 12001-29-5; Asbestos - Not specified: 1332-21-4; Asbestos - Tremolite: 14567-73-8; Asbestos - Anthophyllite: 17068-78-9
Linked HERO ID(s):	No linked references.
HERO ID:	3077660

Domain	Metric		Rating	Comments
	Metric 17:	Effect Biomarker	N/A	The only biomarkers assessed were biomarkers of exposure. Biomarkers of effect were not assessed.
	Metric 18:	Method Sensitivity	Medium	As described in Appendix 2, the analytical sensitivity for fiber counts was 0.01 million fibers per dry gram. Only 2.8% of all samples, and 2/133 mesothelioma samples, did not achieve this sensitivity due to low fiber concentrations and high amounts of other particles. The sensitivity was later increased to 0.003 mf/g by using newer equipment for a selected subgroup of samples.
	Metric 19:	Biomarker Stability	Low	All lung tissue samples were sent to a pathology laboratory in Leeds for an initial assessment and preparation and then were sent to the Health and Safety Laboratory (HSL) for TEM analysis. Specific preparation for storage and transport was not detailed, though it was mentioned that blocks were waxed and de-waxed. The authors did not specifically discuss the stability of the biomarker.
	Metric 20:	Sample Contamination	High	The authors detail that "new disposable containers and filtration equipment were used for each sample to avoid cross-contamination and a process blank was run with each batch of analyses" (Gilham et al., 2015, 3077660)
	Metric 21:	Method Requirements	High	The use of transmission electron microscopy enabled appropriate identification and quantification of asbestos fibers in the samples.
	Metric 22:	Matrix Adjustment	N/A	Matrix adjustment is not required for assessment of this biomarker.

Additional Comments: This study built on the MALCS case-control study by comparing asbestos lung burden in a subset of the mesothelioma patients from the MALCS study to that of a sample of patients with lung cancer. The study also assessed SMR in comparison to the British male population born in 1945. The strengths of the study include the use of transmission electron microscopy for the quantification of asbestos fibers in lung tissue samples, and description of details pertaining to method sensitivity and statistical methods. There were some limitations due to the comparison groups used (lung cancer cases and the British male general population born in 1945). Some methodological details were unclear or were not described in sufficient detail. For example, the authors stated that consent was obtained for postmortem samples from mesothelioma patients and resected tissue from lung cancer patients. It is unclear what proportion of the lung cancer patients were alive at the time of sampling, or why the number of samples analyzed was substantially lower than the number of consent forms received.

Overall Quality Determination **Medium**

Study Citation:	Gilham, C., Rake, C., Hodgson, J., Darnton, A., Burdett, G., Peto Wild, J., Newton, M., Nicholson, A. G., Davidson, L., Shires, M. (2018). Past and current asbestos exposure and future mesothelioma risks in Britain: The Inhaled Particles Study (TIPS). International Journal of Epidemiology 47(6):1745-1756.
Health Outcome:	Mesothelioma
Target Organ(s):	Mortality: mesothelioma mortality; Cancer/Carcinogenesis: mesothelioma mortality; Lung/Respiratory: mesothelioma mortality
Asbestos Fiber Type(s):	Asbestos - Tremolite: 14567-73-8; Asbestos - Not specified: 1332-21-4; Asbestos - Actinolite: 12172-67-7; Asbestos - Anthophyllite: 17068-78-9; Asbestos - Crocidolite (riebeckite): 12001-28-4; Asbestos - Amosite (grunerite): 12172-73-5
Linked HERO ID(s):	No linked references.
HERO ID:	6869402

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Medium	This study estimated the average asbestos lung burden among all individuals in the United Kingdom (UK) born in each of 5 time periods: 1940-44, 1945-49, 1950-54, 1955-59, and 1960-64. The study then estimates the association between the average lung burden estimated among individuals in each time period (referred to as ”birth cohorts”) and the corresponding national cumulative mesothelioma mortality rate by age 50. The unit of analyses is the birth cohort rather than the individual. Lung cancer and mesothelioma patients in the Inhaled Particle Study (TIPS) were from a hospital-based case-control study. Since each cohort includes all individuals born in the UK between 1940-1964 and this is a national study, bias due to selection criteria may not be a concern.
	Metric 2:	Attrition	Medium	The study interviewed and measured asbestos levels in lung samples from 257 patients treated for pneumothorax and 262 with resected lung cancer. This resected lung cancer and mesothelioma patients are from a national case-control study and they are born in the United Kingdom during 1940-1964, with the analytic dataset constructed from administrative data (e.g., birth records, death records). All eligible pneumothorax patients recruited from 13 hospital centers in England and Wales Overall 42% of them them replied agreeing to be interviewed, of whom 91% gave consent for their lung material to be analyzed. The exclusion of subjects from analyses was adequately addressed, and reasons were documented.
	Metric 3:	Comparison Group	Medium	This aim of the Inhaled Particle Study (TIPS) were to determine whether the linear relationship between mesothelioma risk and asbestos lung burden in individuals is also seen in national mesothelioma death rates and population average burdens, and to predict future occupational and environmental mesothelioma rates from the lung burdens of exposed workers and of the general population born since 1965. Analyses are stratified by sex and year of birth, and groups are comparable with respect to age by definition (i.e., the mortality rate by age 50 is computed for each group defined by birth year). The authors do not discuss other potential factors that could be different between birth cohorts and could be related to mesothelioma mortality. Given that this study involves comparisons made over time, it is possible that improvements in treatment (such that individuals born in later cohorts who develop mesothelioma are more likely to live past the age of 50 than individuals born in earlier cohorts) could affect the results observed in this study. However, there is no evidence to support or refute this possibility in the study.
Domain 2: Exposure Characterization				

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Study Citation:	Gilham, C., Rake, C., Hodgson, J., Darnton, A., Burdett, G., Peto Wild, J., Newton, M., Nicholson, A. G., Davidson, L., Shires, M. (2018). Past and current asbestos exposure and future mesothelioma risks in Britain: The Inhaled Particles Study (TIPS). International Journal of Epidemiology 47(6):1745-1756.
Health Outcome:	Mesothelioma
Target Organ(s):	Mortality: mesothelioma mortality; Cancer/Carcinogenesis: mesothelioma mortality; Lung/Respiratory: mesothelioma mortality
Asbestos Fiber Type(s):	Asbestos - Tremolite: 14567-73-8; Asbestos - Not specified: 1332-21-4; Asbestos - Actinolite: 12172-67-7; Asbestos - Anthophyllite: 17068-78-9; Asbestos - Crocidolite (riebeckite): 12001-28-4; Asbestos - Amosite (grunerite): 12172-73-5
Linked HERO ID(s):	No linked references.
HERO ID:	6869402

Domain	Metric		Rating	Comments
	Metric 4:	Measurement of Exposure	Medium	This study estimated the association between average asbestos lung burdens among all individuals born in the UK in 5-year increments between 1940-1964 and national rates of mesothelioma mortality by age 50. Average asbestos lung burdens for the entire UK population in each cohort was estimated via a job-exposure matrix developed from TEM asbestos fiber counts in lung tissue in a sample of 262 lung cancer patients (resected 1999-2010), 133 pleural mesothelioma patients (resected postmortem), and 271 pneumothorax patients (surgically treated 2002-2010). The justification for the "medium" rating is due to the development of a JEM for the entire UK population based on fiber counts in a small number of patients.
	Metric 5:	Exposure Levels	Medium	Table 2 showed the male amphibole lung burden from occupational exposure at three exposure levels (high risk, medium risk and any occupational exposure) in the year of birth 1940-54.
	Metric 6:	Temporality	Medium	The outcome measure in this study is the rate of mesothelioma mortality by age 50. For individuals who are primarily exposed in the environment, particularly if exposure occurs early in life or in young adulthood, this may reflect adequate follow-up time (e.g., > 20 years). For individuals who are primarily exposed in the workplace, the restriction of the outcome measure to mortality by age 50 may not ensure adequate follow-up in some cases, particularly if exposure occurred in mid-life.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	High	The paper states that national mesothelioma death rates by age 50 were obtained from the Health and Safety Executive (HSE) (Health and Safety Executive, 2017, no HERO ID). Tables available from HSE indicate that mesothelioma cases were identified by searching death records for mention of mesothelioma. The available information does not state whether or not all death record fields were searched.
	Metric 8:	Reporting Bias	High	All findings described in the methods section and statistical appendix are reported on in the results section and/or in the figures and tables. Effect estimates from regression models include 95% confidence intervals.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Low	While analyses are stratified by sex and age is accounted for by design, the study does not describe whether other factors that differ between groups could be related to the outcome, and no additional adjustment is made in regression models (i.e., there is indirect evidence that considerations were not made for confounder adjustment).
	Metric 10:	Covariate Characterization	High	The methods for assessing the covariates considered in this analysis (age, sex) were not explicitly described, but can be reasonably assumed to have been assessed using either birth or death records.

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Study Citation: Gilham, C., Rake, C., Hodgson, J., Darnton, A., Burdett, G., Peto Wild, J., Newton, M., Nicholson, A. G., Davidson, L., Shires, M. (2018). Past and current asbestos exposure and future mesothelioma risks in Britain: The Inhaled Particles Study (TIPS). International Journal of Epidemiology 47(6):1745-1756.
Health Outcome: Mesothelioma
Target Organ(s): Mortality: mesothelioma mortality; Cancer/Carcinogenesis: mesothelioma mortality; Lung/Respiratory: mesothelioma mortality
Asbestos Fiber Type(s): Asbestos - Tremolite: 14567-73-8; Asbestos - Not specified: 1332-21-4; Asbestos - Actinolite: 12172-67-7; Asbestos - Anthophyllite: 17068-78-9; Asbestos - Crocidolite (riebeckite): 12001-28-4; Asbestos - Amosite (grunerite): 12172-73-5
Linked HERO ID(s): No linked references.
HERO ID: 6869402

Domain	Metric		Rating	Comments
	Metric 11:	Co-exposure Counfounding	N/A	Co-exposures are not discussed in this paper.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	Medium	The method used to analyze data in this study was a linear regression of average asbestos lung burdens and cumulative mesothelioma mortality rates by age 50, where the unit of analysis was the birth cohort rather than the individual. Lifetime occupational histories were obtained from resected lung cancer and mesothelioma patients in a national case-conrol study. These methods are appropriate to the research question described in the paper.
	Metric 13:	Statistical Power	Uninformative	The unit of analysis in the regression model constructed in this paper was the birth cohort rather than the individual. More specifically, for each of 5 birth cohorts consisting of all individuals born in the UK within a 5-year period, the exposure entered into the model was the average asbestos lung burden for the entire cohort, and the outcome entered in the model was the cohort's cumulative mesothelioma mortality rate by age 50. While each cohort consists of a large number of individuals, the total number of data points in the regression model is n=5 due to aggregation to the cohort level. As such, the statistical power of the regression model is likely limited.
	Metric 14:	Reproducibility of Analyses	Medium	The description of the analysis is detailed enough to conceptually reproduce the analysis.
	Metric 15:	Statistical Analysis	Medium	Detailed information regarding the form and variables of the linear regression model are provided in the statistical appendix of this paper. The distribution of lung burden ins approximately lognormal (Figure 1).

Additional Comments: This paper uses linear regression to assess the relationship between average asbestos lung burden estimated across all individuals born in the United Kingdom within each of 5 time windows (1940-44, 1945-49, 1950-54, 1955-59, and 1960-64) and each group's corresponding cumulative mesothelioma mortality rate by age 50. In addition to this analysis of observed data, the paper develops predictions of future mesothelioma rates to age 90 in these groups, as well as predictions of future mesothelioma rates among individuals born more recently. Chrysotile fibers were also analyzed in the lung tissue samples used to develop exposure estimates but were excluded from regression analyses.

Overall Quality Determination — Uninformative

* No biomarkers were identified for this evaluation.

Study Citation:	Hagmar, L., Akesson, B., Nielsen, J., Andersson, C., Linden, K., Attewell, R., Moller, T. (1990). Mortality and cancer morbidity in workers exposed to low levels of vinyl chloride monomer at a polyvinyl chloride processing plant. American Journal of Industrial Medicine 17(5):553-565.		
Health Outcome:	Mesothelioma		
Target Organ(s):	Cancer/Carcinogenesis: mesothelioma mortality; Mortality: mesothelioma mortality		
Asbestos Fiber Type(s):	Asbestos - Chrysotile (serpentine): 12001-29-5		
Linked HERO ID(s):	No linked references.		
HERO ID:	675185		

Domain	Metric	Rating	Comments
Domain 2: Exposure Characterization			
	Metric 4: Measurement of Exposure	Low	Estimates of asbestos exposure were obtained from breathing zone samples conducted in 1971 and 1975. Details on the sampling method were minimal. Other time periods were not sampled, but industrial hygienists estimated job- and department-specific . Time-weighted averages were assumed to be 40% lower after 1969 compared to prior years. Cumulative exposure was determined by adding years of exposure.
	Metric 5: Exposure Levels	Low	For cancer mortality, SMRs were calculated without stratification, indicating two levels of exposure (exposed and unexposed).

Additional Comments: This study utilized an occupational cohort to examine the relative mortality rates for mesothelioma compared to the general population. SMRs calculated for mesothelioma were not specific to mesothelioma, including other lung cancer mortality. As a result, the results are difficult to interpret for mesothelioma alone.

* No biomarkers were identified for this evaluation.

** As described in Appendix B.2 of the *White Paper: Quantitative Approach to the Human Health Assessment for the Risk Evaluation for Asbestos Part 2: Supplemental Evaluation Including Legacy Uses and Associated Disposals of Asbestos*, to be considered as being informative for dose-response analysis, metrics 4 and 5 would need metric ratings of Medium or High. This reference did not satisfy this requirement; therefore data quality evaluation is presented for only for metrics 4 and 5.

Study Citation: Hansen, J., de Klerk, N. H., Musk, A. W., Hobbs, M. S. T. (1998). Environmental exposure to crocidolite and mesothelioma: Exposure-response relationships. American Journal of Respiratory and Critical Care Medicine 157(1):69-75.
Health Outcome: Mesothelioma
Target Organ(s): Lung/Respiratory: Lung cancer mortalityLung cancer incidenceRespiratory system mortalityMesothelioma incidenceMesothelioma mortality; Cancer/Carcinogenesis: Mesothelioma incidenceMesothelioma mortalityLung cancer incidenceLung cancer mortalityCancer incidence, all and specific types (SIRs for exposed/gen pop, no dose-reponse)Cancer mortality, all and specific types (SMRs for exposed/gen pop, no dose-response); Mortality: Mesothelioma mortalityLung cancer mortalityAll-cause mortality (SMR for exposed/gen pop, no dose-response)Respiratory system mortality (SMR for exposed/gen pop, no dose-response)Digestive system mortality (SMR for exposed/gen pop, no dose-response)Signs/symptoms ill-defined (SMR for exposed/gen pop, no dose-response)Nervous system mortality (SMR, no dose-response)
Asbestos Fiber Type(s): Asbestos - Crocidolite (riebeckite): 12001-28-4
Linked HERO ID(s): 709618, 709466, 709501, 2088306, 6869529
HERO ID: 709618

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Medium	As detailed in Hansen et al. 1998, 709618, the Wittenoom residents' cohort recruited all individuals who: (i) lived in Wittenoom for ≥1 month between 1943 and 1993 and (ii) had not been employed in the asbestos industry. Cohort size varied slightly with updates over time, including 4,768 participants (2608 women, 2160 men) at the end of 2000 (Reid 2008 709466; Reid 2006 709501). Members were identified using multiple sources to identification of former residents (e.g., doctors/hospitals, schools, vitamin A trial participants, former asbestos workers), but inclusion rates cannot be determined. The authors reduced the likelihood of "healthy resident" bias by including persons with only 1 month of residence over a wide span of time. However, by 1993 when 27 cases had been identified in residents, 17 additional mesotheliomas were identified among individuals who resided in Wittenoom for less than one month. Although suggests that exposure durations of less than one month are relevant, according to the authors, all of these cases had reportedly worked with asbestos and likely had more intense exposure (Hansen et al 1998 709618). The authors did not discuss the number of non-workers identified who resided at Wittenoom for less than one month.
	Metric 2:	Attrition	Medium	In Hansen et al 1998 (709618), about 29% of the cohort could not be traced. The remaining studies, published after 2000, reported ~20% loss to follow-up (e.g., Reid 2018 6869529). The extent to which this attrition may be selective is not known, since characteristics of untraced subjects (e.g., age, sex) were not described. However, the authors partially addressed attrition bias at the analysis stage in several papers (Reid et al. 2012, 2088306; Reid et al. 2018, 6869529) by comparing the impact of different censoring assumptions for subjects lost to follow-up. Alternative analyses assumed these persons: (i) were all still alive until censored at age 85y; vs. (ii) were eligible to contribute person-years until the last date their status or age 85y. The first method likely overestimates and the second underestimates person-years at risk.

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Study Citation:	Hansen, J., de Klerk, N. H., Musk, A. W., Hobbs, M. S. T. (1998). Environmental exposure to crocidolite and mesothelioma: Exposure-response relationships. American Journal of Respiratory and Critical Care Medicine 157(1):69-75.
Health Outcome:	Mesothelioma
Target Organ(s):	Lung/Respiratory: Lung cancer mortalityLung cancer incidenceRespiratory system mortalityMesothelioma incidenceMesothelioma mortality; Cancer/Carcinogenesis: Mesothelioma incidenceMesothelioma mortalityLung cancer incidenceLung cancer mortalityCancer incidence, all and specific types (SIRs for exposed/gen pop, no dose-reponse)Cancer mortality, all and specific types (SMRs for exposed/gen pop, no dose-response); Mortality: Mesothelioma mortalityLung cancer mortalityAll-cause mortality (SMR for exposed/gen pop, no dose-response)Respiratory system mortality (SMR for exposed/gen pop, no dose-response)Digestive system mortality (SMR for exposed/gen pop, no dose-response)Signs/symptoms ill-defined (SMR for exposed/gen pop, no dose-response)Nervous system mortality (SMR, no dose-response)
Asbestos Fiber Type(s):	Asbestos - Crocidolite (riebeckite): 12001-28-4
Linked HERO ID(s):	709618, 709466, 709501, 2088306, 6869529
HERO ID:	709618

Domain	Metric		Rating	Comments
	Metric 3:	Comparison Group	Medium	Within-cohort analyses were used to estimate associations between mesothelioma and exposure. Analysis samples included all identified eligible residents, avoiding bias due to questionnaire non-response (47% non-response reported in Hansen et al. 1998, 709618). Because a high proportion (41%) of the cohort identified from doctors, hospitals, and schools or a vitamin A trial (14%) there may have been some bias in favor of including less healthy short-term residents (Reid et al., 2008 709466; Hansen et al. 1998, 709618). Western Australia data was used as a referent for SMRs; the authors described ascertainment as almost complete (Reid et al., 2007, 2088306). Expected mortality for 1950-1969 was extrapolated from 1970-74 as period specific rates were not available.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Medium	Residential exposure estimates were based on a series of fiber measures initiated in 1966 (Hansen et al. 1997, 2219991). A 1966 value of 0.5 f/mL was based on measures taken prior to the mill/mine closure in 1966 (0.5 f/mL), and subsequent values were interpolated through 1992 using measures from personal and/or fixed monitors: 1973 (median 0.22 f/mL), 1977, and 1978 using PCM counts; 1984 and 1986 using scanning electron microscopy (SEM); and 1992 using TEM. The 1966 outdoor fiber samples were recounted in 1986 using PCM and updated guidelines according to Rogers and Major 2002 (3080506). Since 1948-1966 measures (1948-1966) were of dust by konimeter, intensity prior to the 1958 new mill was extrapolated as 1.0 f/mL based on estimates that the exposure was halved (Hansen 2219991). Concerns include the limited number, location, and quality of samples, as well as less precise SEM. Cumulative exposure was calculated based on duration of residence, assuming 24 h a day, 7 d a week exposure. Duration estimates used: (i) detailed mesothelioma registry data; (ii) questionnaire responses, worker employment dates for relatives, or family member questionnaires if available; (iii) records at hospitals, schools, etc; and (iv) a value of 6 months if still unknown. Proportions estimated using each method were not shown. An important concern is potential for differential measurement error by mesothelioma case status. Another source of error includes the lack of information on specific locations and activities that would affect individual exposure (only lived with, likely washed clothes of an asbestos worker were estimated). The most recent study indicated that exposure was missing for about 5% of the sample (Reid et al. 2018, 6869529).

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Study Citation: Hansen, J., de Klerk, N. H., Musk, A. W., Hobbs, M. S. T. (1998). Environmental exposure to crocidolite and mesothelioma: Exposure-response relationships. American Journal of Respiratory and Critical Care Medicine 157(1):69-75.

Health Outcome: Mesothelioma

Target Organ(s): Lung/Respiratory: Lung cancer mortalityLung cancer incidenceRespiratory system mortalityMesothelioma incidenceMesothelioma mortality; Cancer/Carcinogenesis: Mesothelioma incidenceMesothelioma mortalityLung cancer incidenceLung cancer mortalityCancer incidence, all and specific types (SIRs for exposed/gen pop, no dose-reponse)Cancer mortality, all and specific types (SMRs for exposed/gen pop, no dose-response); Mortality: Mesothelioma mortalityLung cancer mortalityAll-cause mortality (SMR for exposed/gen pop, no dose-response)Respiratory system mortality (SMR for exposed/gen pop, no dose-response)Digestive system mortality (SMR for exposed/gen pop, no dose-response)Signs/symptoms ill-defined (SMR for exposed/gen pop, no dose-response)Nervous system mortality (SMR, no dose-response)

Asbestos Fiber Type(s): Asbestos - Crocidolite (riebeckite): 12001-28-4

Linked HERO ID(s): 709618, 709466, 709501, 2088306, 6869529

HERO ID: 709618

Domain	Metric		Rating	Comments
	Metric 5:	Exposure Levels	Medium	Cumulative exposure (f/mL-years) was analyzed with respect to mesothelioma as a continuous variable in all 4 papers, and in some studies using 3 or more categories. The estimated mean (SD) was on the order of 5.5 (8.0) f/mL year (Reid et al. 2007, 709501). Variability was adequate overall and in sub-group analyses (e.g., in individuals exposed as children median [IQR] = 3.3 [1.4-7.5], range 0.1 to 64.4; Reid et al., 2012 2088306).
	Metric 6:	Temporality	High	All analyses had appropriate sequencing and lengthy follow-up. In the earliest analysis with follow-up through 1993 (Hansen et al. 1998, 709618), only 12.5% of the cohort had a lag of less than 20 years since first residence at Wittenoom. Subsequent analyses had follow-up through 2002 or later (Reid et al. 2007, 709501). In the most recent analysis (of mortality through 2014), the mean time since first exposure was 51 years in children and 42 years in adults (Reid et al. 2018, 6869529).
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Medium	Record linkage to official sources was used was used to identify mesotheliomas; linkage methods were not described. Mesotheliomas were identified by the Western Australia Mesothelioma Registry (part of the regional cancer registry) and the Australian Mesothelioma Surveillance Programme. ICD codes for mesothelioma were not provided, but a 2005 Western Australia Cancer Registry report ("Cancer in Western Australia: Incidence and mortality 2003 and Mesothelioma 1960-2003") provided tables indicating that over 95% of mesotheliomas were microscopically confirmed since 1960.
	Metric 8:	Reporting Bias	High	Results for mesothelioma analyses were presented adequately and appropriately in all papers.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	High	Associations between mesothelioma and cumulative asbestos exposure were adjusted for age and sex; Hansen et al 1998 709618 also adjusted simultaneously for different dimensions of exposure. Analyses also included appropriate interaction terms to test the significance of hypothesized differences in gender and age at exposure (e.g., gender x exposure in Reid et al. 2007, 709501).
	Metric 10:	Covariate Characterization	High	Age and sex data was based on records and questionnaires.
	Metric 11:	Co-exposure Counfounding	N/A	Per mesothelioma-specific guidance, concern about co-exposures is limited for mesothelioma, meriting a "not applicable" rating.

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Study Citation:	Hansen, J., de Klerk, N. H., Musk, A. W., Hobbs, M. S. T. (1998). Environmental exposure to crocidolite and mesothelioma: Exposure-response relationships. American Journal of Respiratory and Critical Care Medicine 157(1):69-75.
Health Outcome:	Mesothelioma
Target Organ(s):	Lung/Respiratory: Lung cancer mortalityLung cancer incidenceRespiratory system mortalityMesothelioma incidenceMesothelioma mortality; Cancer/Carcinogenesis: Mesothelioma incidenceMesothelioma mortalityLung cancer incidenceLung cancer mortalityCancer incidence, all and specific types (SIRs for exposed/gen pop, no dose-reponse)Cancer mortality, all and specific types (SMRs for exposed/gen pop, no dose-response); Mortality: Mesothelioma mortalityLung cancer mortalityAll-cause mortality (SMR for exposed/gen pop, no dose-response)Respiratory system mortality (SMR for exposed/gen pop, no dose-response)Digestive system mortality (SMR for exposed/gen pop, no dose-response)Signs/symptoms ill-defined (SMR for exposed/gen pop, no dose-response)Nervous system mortality (SMR, no dose-response)
Asbestos Fiber Type(s):	Asbestos - Crocidolite (riebeckite): 12001-28-4
Linked HERO ID(s):	709618, 709466, 709501, 2088306, 6869529
HERO ID:	709618

Domain	Metric		Rating	Comments
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	Medium	Analytic methods were appropriate. Hazard ratios or relative risks used Cox regression models (Reid 2018 6869529, Hansen 1998 709618, Reid 2007 709501), and odds ratios in an age-matched nested case-control analysis used conditional logistic regression (Reid et al. 2008, 709466). SMRs/SIRs for mesothelioma were calculated using Western Australia as an appropriate referent population (Reid et al. 2012, 2088306). To examine the potential influence of loss to follow-up on results, some analyses studies compared alternative censoring methods as described earlier (see Attrition comments).
	Metric 13:	Statistical Power	Medium	With nearly 5,000 subjects, sample size was adequate overall as well as in analyses of women (Reid et al. 2008, 709466) and individuals exposed as children (Reid et al. 2018, 6869529). There were a large number of mesothelioma cases (n=27 in the first analysis by Hansen et al. 1998, 709618, n=119 in Reid et al. 2018, 6869529).
	Metric 14:	Reproducibility of Analyses	Medium	Descriptions of all analyses were clear and sufficient for reproduction.
	Metric 15:	Statistical Analysis	Medium	The models and methods used were adequately described for both SMRs/SIRs and regression models.

Additional Comments: These studies analyzed >5,000 individuals who had lived in Wittenoom, Australia for ≥1 month from 1943-1993 to evaluate associations between residential asbestos exposure and mesothelioma (all 4 studies). The cohort excluded asbestos workers. In the most recent study geometric mean (IQR) cumulative exposure was 3.02 (1.4-7.70) f/mL-years in children and 2.05 (0.90-5.75) f/mL-years in adults, with 119 mesotheliomas identified by 2014. Increasing exposure was consistently associated with risk of mesothelioma incidence and/or mortality. Though differences narrowed with longer follow-up, individuals first exposed as adults had a higher risk vs. those exposed as children (Reid et al. 2007, 709501 vs. Reid et al. 2018, 6869529). Initial gender differences were not significant after longer follow-up. SMRs for residents exposed as children were significantly higher for mesothelioma. Key concerns include exposure measurement error, particularly prior to 1966 when mining ceased: a single value was extrapolated to the entire period as no fiber measures were taken. Differential measurement error with respect to mesothelioma is a concern, since detailed residential and work histories were available for those cases, while duration of residence was estimated from limited public records for half of the remaining cohort. There was also a 20% loss to follow-up, addressed in some studies by comparing different assumptions on the status of these subjects. Associations with mesothelioma remained robust with differing assumptions.

Overall Quality Determination — Medium

* No biomarkers were identified for this evaluation.

Study Citation:	Howel, D., Gibbs, A., Arblaster, L., Swinburne, L., Schweiger, M., Renvoize, E., Hatton, P., Pooley, F. (1999). Mineral fibre analysis and routes of exposure to asbestos in the development of mesothelioma in an English region. Occupational and Environmental Medicine 56(1):51-58.
Health Outcome:	Mesothelioma
Target Organ(s):	Cancer/Carcinogenesis: malignant mesothelioma; Lung/Respiratory: malignant mesothelioma
Asbestos Fiber Type(s):	Asbestos - Amosite (grunerite): 12172-73-5; Asbestos - Crocidolite (riebeckite): 12001-28-4; Asbestos - Chrysotile (serpentine): 12001-29-5
Linked HERO ID(s):	No linked references.
HERO ID:	3081021

Domain	Metric		Rating	Comments
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	High	Quantitative estimates of exposure were consistently assessed (i.e., using the same method and sampling timeframe) during multiple time periods and using TEM. Samples were obtained postmortem and prepared to be measured by TEM. All fibers >0.5um were counted.
	Metric 5:	Exposure Levels	Low	The range and distribution of exposure is limited. There are only 2 exposure groups, high ("defined as being in the top third of values foundin all subjects for that fibre type") and low, being reviewed for the odds ratios analyses.

Additional Comments: QC was not completed for metrics other than Metrics 4 and 5 because the study does not have sufficient exposure information to be useful for dose-response analysis.

* No biomarkers were identified for this evaluation.

** As described in Appendix B.2 of the *White Paper: Quantitative Approach to the Human Health Assessment for the Risk Evaluation for Asbestos Part 2: Supplemental Evaluation Including Legacy Uses and Associated Disposals of Asbestos*, to be considered as being informative for dose-response analysis, metrics 4 and 5 would need metric ratings of Medium or High. This reference did not satisfy this requirement; therefore data quality evaluation is presented for only for metrics 4 and 5.

Study Citation:	Hughes, J. M., Weill, H. (1991). Asbestosis as a precursor of asbestos related lung cancer: Results of a prospective mortality study. British Journal of Industrial Medicine 48(4):229-233.
Health Outcome:	Mesothelioma
Target Organ(s):	Lung/Respiratory: Mesothelioma mortality; Cancer/Carcinogenesis: Mesothelioma mortality; Mortality: Mesothelioma mortality
Asbestos Fiber Type(s):	Asbestos - Chrysotile (serpentine): 12001-29-5; Asbestos - Crocidolite (riebeckite): 12001-28-4
Linked HERO ID(s):	No linked references.
HERO ID:	2223821

Domain	Metric		Rating	Comments
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Low	”This outcome is rated Low due to the lack of PCM or TEM being used in the study.Authors refer to a different study for all information regarding to exposure to asbestos (Hughes et al. 1987, 3583332) That paper notes that air sampling data was collected by a mix of the government, industry, and insurance companies with a midget impinger (recorded in millions of particles per cubic foot(mppcf)). This was done from the 1950s-1960s. Membrane filter sampling (measured in fibers per milliliter) was also noted to have been carried out starting in 1969. Authors note that because of the employment population occurring from 1940-1950, all exposure estimates were converted into mppcf. These air sampling data in combination with job history data were used to estimate cumulative exposure.”
	Metric 5:	Exposure Levels	Low	SMRs for mesothelioma do not provide results by levels of exposure. Authors only provide categorical cumulative exposure levels for small opacities (<25, 25-99, 100-149, and >=150 mppcf-y) and for lung cancer (<51, 51-85, 86-121, 122-169, and >=170 mppcf-y).

Additional Comments: Overall, this study is well-designed and references most methods to a previous paper (Hughes et al. 1987, 3583332).Note that the cancerous health outcomes were not evaluated for any metrics except Metric 4 and 5 and had no data extracted because they did not have sufficient exposure information to be useful for dose-response analysis.

** As described in Appendix B.2 of the *White Paper: Quantitative Approach to the Human Health Assessment for the Risk Evaluation for Asbestos Part 2: Supplemental Evaluation Including Legacy Uses and Associated Disposals of Asbestos*, to be considered as being informative for dose-response analysis, metrics 4 and 5 would need metric ratings of Medium or High. This reference did not satisfy this requirement; therefore data quality evaluation is presented for only for metrics 4 and 5.

Study Citation:	Hughes, J. M., Weill, H., Hammad, Y. Y. (1987). Mortality of workers employed in two asbestos cement manufacturing plants. Occupational and Environmental Medicine 44(3):161-174.
Health Outcome:	Mesothelioma
Target Organ(s):	Lung/Respiratory: Mesothelioma mortality; Cancer/Carcinogenesis: Mesothelioma mortality; Mortality: Mesothelioma mortality
Asbestos Fiber Type(s):	Asbestos - Chrysotile (serpentine): 12001-29-5; Asbestos - Amosite (grunerite): 12172-73-5; Asbestos - Crocidolite (riebeckite): 12001-28-4
Linked HERO ID(s):	No linked references.
HERO ID:	281

Domain	Metric	Rating	Comments
Additional Comments:	Mesothelioma was not analyzed in an SMR/Regression analysis.		

Study Citation:	Hughes, J. M., Weill, H., Hammad, Y. Y. (1987). MORTALITY OF WORKERS EMPLOYED IN 2 ASBESTOS CEMENT MANUFACTURING PLANTS. British Journal of Industrial Medicine 44(3):161-174.		
Health Outcome:	Mesothelioma		
Target Organ(s):	Cancer/Carcinogenesis: Mesothelioma		
Asbestos Fiber Type(s):	Asbestos - Chrysotile (serpentine): 12001-29-5; Asbestos - Crocidolite (riebeckite): 12001-28-4		
Linked HERO ID(s):	No linked references.		
HERO ID:	3583332		

Domain	Metric	Rating	Comments
Domain 2: Exposure Characterization			
	Metric 4: Measurement of Exposure	Low	This metric is rated as low because the study or any cited methods source does not explicitly mention the use of PCM or TEM.
	Metric 5: Exposure Levels	Medium	SMRs were calculated using 5 categories of employment duration that ranged from a few months to >15 years (different values for each plant), and using 5 categories of cumulative exposure (<c to >= 100 mppcf).

Additional Comments: NOTE: This study was not fully evaluated because the rating for metric 4 was low, due to no explicit mention of PCM or TEM. Analyses of the 10 mesotheliomas identified were not evaluated.

** As described in Appendix B.2 of the *White Paper: Quantitative Approach to the Human Health Assessment for the Risk Evaluation for Asbestos Part 2: Supplemental Evaluation Including Legacy Uses and Associated Disposals of Asbestos*, to be considered as being informative for dose-response analysis, metrics 4 and 5 would need metric ratings of Medium or High. This reference did not satisfy this requirement; therefore data quality evaluation is presented for only for metrics 4 and 5.

Study Citation:	Iwatsubo, Y., Pairon, J. C., Boutin, C., Ménard, O., Massin, N., Caillaud, D., Orlowski, E., Galateau-Salle, F., Bignon, J., Brochard, P. (1998). Pleural mesothelioma: dose-response relation at low levels of asbestos exposure in a French population-based case-control study. American Journal of Epidemiology 148(2):133-142.
Health Outcome:	Mesothelioma
Target Organ(s):	Lung/Respiratory: Pleural mesothelioma; Cancer/Carcinogenesis: Pleural mesothelioma
Asbestos Fiber Type(s):	Asbestos - Not specified: 1332-21-4
Linked HERO ID(s):	3081164, 2569475, 3077945, 3078290, 3863052
HERO ID:	3081164

Domain		Metric	Rating	Comments
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Low	These studies utilized a job exposure matrix to develop a semi-quantitative measurement of exposure. Industrial hygienists evaluated the occupational exposure to asbestos, and allowed for each job period of the subjects to be classified based on the probability, frequency, and intensity of asbestos exposure (Iwatsubo et al., 1998, 3081164; Lacourt et al., 2012, 2569475; Lacourt et al., 2013, 3078290; Lacourt et al., 2014, 3077945; Lacourt et al., 2017, 3863052). This metric was rated as low because the study or any cited methods source does not explicitly mention the use of PCM or TEM (Iwatsubo et al., 1998, 3081164; Lacourt et al., 2012, 2569475; Lacourt et al., 2013, 3078290; Lacourt et al., 2014, 3077945; Lacourt et al., 2017, 3863052).
	Metric 5:	Exposure Levels	Medium	Each of the studies included in this cohort included a range of exposures based on the JEMs, and three or more levels were reported in each study (Iwatsubo et al., 1998, 3081164; Lacourt et al., 2012, 2569475; Lacourt et al., 2013, 3078290; Lacourt et al., 2014, 3077945; Lacourt et al., 2017, 3863052).

Additional Comments:	A complete evaluation of this cohort was not completed because they only utilized a job exposure matrix to semquantitatively determine asbestos exposure levels. As this was based on professional judgment and did not include TEM or PCM, the metric pertaining to measurement of exposures was rated as low (Iwatsubo et al., 1998, 3081164; Lacourt et al., 2012, 2569475; Lacourt et al., 2013, 3078290; Lacourt et al., 2014, 3077945; Lacourt et al., 2017, 3863052). Metric five was rated as high because there were several levels of exposure created in the JEM, representing a range of exposures.

* No biomarkers were identified for this evaluation.

** As described in Appendix B.2 of the *White Paper: Quantitative Approach to the Human Health Assessment for the Risk Evaluation for Asbestos Part 2: Supplemental Evaluation Including Legacy Uses and Associated Disposals of Asbestos*, to be considered as being informative for dose-response analysis, metrics 4 and 5 would need metric ratings of Medium or High. This reference did not satisfy this requirement; therefore data quality evaluation is presented for only for metrics 4 and 5.

Study Citation:	Jiang, Z., Xia, H., Wu, W., Chen, R., Morinaga, K., Lou, J., Zhang, X., Chen, T., Chen, J., Ying, S. (2018). Hand-spinning chrysotile exposure and risk of malignant mesothelioma: A case-control study in Southeastern China. International Journal of Cancer 142(3):514-523.
Health Outcome:	Mesothelioma
Target Organ(s):	Lung/Respiratory: Cases of malignant mesothelioma; Cancer/Carcinogenesis: Cases of malignant mesothelioma
Asbestos Fiber Type(s):	Asbestos - Chrysotile (serpentine): 12001-29-5
Linked HERO ID(s):	No linked references.
HERO ID:	6860340

Domain	Metric		Rating	Comments
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Low	Individual exposure was not directly measured, but was determined based on a cumulative exposure index (CEI), which was based on job classification.It is unclear whether PCM or TEM or another method was used.Raw materials from 18 asbestos textile plants were randomly sampled from the 1980s-2010s using X-Ray diffraction, which determined that the raw materials were chrysotile mixed with other chemical impurities.Airborne asbestos samples from 1987-2011 from 49 hand-spinning asbestos plants and 12 hand-spinning from home workplaces were analyzed using a weighting method. Measurements were taken at a flow rate of 2 L/min for a duration of 15-20 minutes. Mass concentrations were transformed into fiber number concentrations in fibers/ml using a formula described in a paper that was not found in HERO (Huang J. 1994). The estimated median concentration of asbestos was 8.0 fibers per milliliter (f/mL) for hand-spinning at plants and 0.6 f/mL for hand-spinning at home.The study authors cited several papers in their methods description, some of which were reviewed and were not found to mention use of PCM or TEM, but at least one methods paper (Huang J. 1994) wasn't readily accessible and the method for quantifying fiber counts is not fully known based on the available information.To assess individual exposure levels, participants were interviewed following a structured questionnaire, which included occupational history. The occupations and industrial activities of all participants was classified using the International Standard Classification of Occupation (ISCO) codes and the International Standard Industrial Classification (ISIC) codes, respectively. Two experts independently assessed exposure probability based on fiber concentration measurements (unclear whether PCM, TEM, or other) and expert judgement. The cumulative exposure index (CEI) of asbestos was expressed as fibers per milliliter years (f/mL-years) and was calculated based on the sum of the products of probability, frequency, intensity, and duration of each job exposure.
	Metric 5:	Exposure Levels	Medium	The range and distribution of exposure is sufficient to develop an exposure-response estimate. Table 4 presents odds ratios for malignant mesothelioma stratified by asbestos exposure levels. Asbestos exposure categories were defined in several different ways, including categorization by cumulative exposure index (CEI). There were three categories of CEI: >0–0.5, >0.5–29, and >29 fibers per milliliter years (f/mL-years).

Additional Comments:	None

** As described in Appendix B.2 of the *White Paper: Quantitative Approach to the Human Health Assessment for the Risk Evaluation for Asbestos Part 2: Supplemental Evaluation Including Legacy Uses and Associated Disposals of Asbestos*, to be considered as being informative for dose-response analysis, metrics 4 and 5 would need metric ratings of Medium or High. This reference did not satisfy this requirement; therefore data quality evaluation is presented for only for metrics 4 and 5.

Study Citation:	Konen, T., Johnson, J. E., Lindgren, P., Williams, A. (2019). Cancer incidence and mortality associated with non-occupational and low dose exposure to Libby vermiculite in Minnesota. Environmental Research 175(Elsevier):449-456.		
Health Outcome:	Mesothelioma		
Target Organ(s):	Lung/Respiratory: Mesothelioma mortality; Cancer/Carcinogenesis: Mesothelioma mortality; Mortality: Mesothelioma mortality		
Asbestos Fiber Type(s):	Asbestos- Libby amphibole: 1318-09-8		
Linked HERO ID(s):	No linked references.		
HERO ID:	6866465		

Domain	Metric		Rating	Comments
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Low	Asbestos exposure was estimated, and no quantitative measurements were taken. The authors reported that the exposure estimates were calculated ”based on total months of residency (duration) and addresses in the study area and using results of modeled ambient asbestos concentration levels during three different time periods during plant operations (1938-1989).”
	Metric 5:	Exposure Levels	Medium	The range of exposure was adequate to create an exposure-response estimate. The study’s analyses included 3 exposed groups (<50th percentile, 50th - 75th percentile, and >75th percentile).

Additional Comments: METRIC 4 WAS RATED AS LOW - STOPPED EVALUATING BASED ON NEW GUIDANCE ON 1.27.23Information on the measurement of exposure metric (M4) to assess exposure is limited (low rating) as no quantitative measurements were taken. However, the exposure levels metric (M5) information reported is sufficient to determine exposure-response relationships.

** As described in Appendix B.2 of the *White Paper: Quantitative Approach to the Human Health Assessment for the Risk Evaluation for Asbestos Part 2: Supplemental Evaluation Including Legacy Uses and Associated Disposals of Asbestos*, to be considered as being informative for dose-response analysis, metrics 4 and 5 would need metric ratings of Medium or High. This reference did not satisfy this requirement; therefore data quality evaluation is presented for only for metrics 4 and 5.

Study Citation:	Kurumatani, N., Kumagai, S. (2008). Mapping the risk of mesothelioma due to neighborhood asbestos exposure. American Journal of Respiratory and Critical Care Medicine 178(6):624-629.			
Health Outcome:	Mesothelioma			
Target Organ(s):	Mortality: Mesothelioma mortality; Lung/Respiratory: Mesothelioma mortality			
Asbestos Fiber Type(s):	Asbestos - Crocidolite (riebeckite): 12001-28-4; Asbestos - Chrysotile (serpentine): 12001-29-5			
Linked HERO ID(s):	No linked references.			
HERO ID:	2601091			
Domain	Metric		Rating	Comments
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Low	Exposure was estimated utilizing professional judgement of plant concentration with meteorological data to estimate “relative asbestos concentrations” for the population of interest and no use of quantitative exposure measures. Authors noted in Supplemental material that the “relative asbestos concentrations” for the population of interest surrounding the plant were estimated using an assumed fiber concentration (professional judgement) emitted from the plant because actual concentrations and emission rates of airborne asbestos fibers during the period of interest were unknown. No quantitative asbestos sampling was reported or utilized within calculations. Authors assumed the emission point of asbestos was the center of the plant, and airborne asbestos emitted from the plant was the sole industrial source of exposure.
	Metric 5:	Exposure Levels	Medium	Dose-response relations between mesothelioma SMR’s and relative asbestos concentration levels divided into five exposure groups were presented within Figure 3.
Additional Comments:	HERO ID 2601091 Kurumatani (2008) was not evaluated for any metrics except Metrics 4 and 5 and had no data extracted because it did not have sufficient exposure information to be useful for dose-response analysis.			

** As described in Appendix B.2 of the *White Paper: Quantitative Approach to the Human Health Assessment for the Risk Evaluation for Asbestos Part 2: Supplemental Evaluation Including Legacy Uses and Associated Disposals of Asbestos*, to be considered as being informative for dose-response analysis, metrics 4 and 5 would need metric ratings of Medium or High. This reference did not satisfy this requirement; therefore data quality evaluation is presented for only for metrics 4 and 5.

Study Citation:	Lacourt, A., Gramond, C., Rolland, P., Ducamp, S., Audignon, S., Astoul, P., Chamming's, S., Gilg Soit Ilg, A., Rinaldo, M., Raherison, C., Galateau-Salle, F., Imbernon, E., Pairon, J. C., Goldberg, M., Brochard, P. (2014). Occupational and non-occupational attributable risk of asbestos exposure for malignant pleural mesothelioma. Thorax 69(6):532-539.			
Health Outcome:	Mesothelioma			
Target Organ(s):	Lung/Respiratory: Pleural mesothelioma; Cancer/Carcinogenesis: Pleural mesothelioma			
Asbestos Fiber Type(s):	Asbestos - Not specified: 1332-21-4			
Linked HERO ID(s):	No linked references.			
HERO ID:	3078046			

Domain	Metric		Rating	Comments
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Low	The assessment of asbestos exposure was done by two experts who examined the questionnaires of participants. Occupational exposure was broken down into four parameters, including probability of exposure, frequency of exposure, intensity of exposure, and route of exposure (Lacourt et al., 2014, 3078046). There was no indication of actual tools or instruments used, and only professional judgment was used to estimate exposure. This metric is rated low because the study or any cited methods source does not explicitly mention the use of PCM or TEM (Lacourt et al., 2014, 3078046).
	Metric 5:	Exposure Levels	Medium	The authors reported a range of exposure that is sufficient to develop an exposure-response estimate. Table 1 presents the groupings for intensity of exposure, which is reported in f/mL (Lacourt et al., 2014, 3078046).

Additional Comments: Due to the rating for measurement of exposure, this study was not evaluated fully. Utilization of professional judgment and a job exposure matrix, without actual quantitative measurement of asbestos fibers, lead to a low rating. However, they did provide several levels of intensity of exposure which was determined semiquantitatively (Lacourt et al., 2014, 3078046).

** As described in Appendix B.2 of the *White Paper: Quantitative Approach to the Human Health Assessment for the Risk Evaluation for Asbestos Part 2: Supplemental Evaluation Including Legacy Uses and Associated Disposals of Asbestos*, to be considered as being informative for dose-response analysis, metrics 4 and 5 would need metric ratings of Medium or High. This reference did not satisfy this requirement; therefore data quality evaluation is presented for only for metrics 4 and 5.

Study Citation:	Larson, T. C., Antao, V. C., Bove, F. J. (2010). Vermiculite worker mortality: Estimated effects of occupational exposure to Libby amphibole. Journal of Occupational and Environmental Medicine 52(5):555-560.
Health Outcome:	Mesothelioma
Target Organ(s):	Lung/Respiratory: Mesothelioma; Mortality: Mesothelioma
Asbestos Fiber Type(s):	Asbestos- Libby amphibole: 1318-09-8
Linked HERO ID(s):	709497, 709457, 711560, 2238712
HERO ID:	711560

Domain	Metric		Rating	Comments
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Low	This metric is rated Low because the study or any cited methods source does not explicitly mention the use of PCM or TEM to develop quantitative estimates of exposure.
	Metric 5:	Exposure Levels	Medium	The distribution of exposure appears to be sufficient to develop an exposure-response estimate. Cumulative exposure was utilized in dose-response calculations and were represented in four levels: <1.4 f/cc-y, 1.4 to <8.6 f/cc-y, 8.6 to <44.0 f/cc-y, and >=44.0 f/cc-y.

Additional Comments: QC was not completed for metrics other than Metrics 4 and 5 because the study does not have sufficient exposure information to be useful for dose-response analysis. Metric 4 had a low level of confidence because the authors do not mention using PCM or TEM to develop quantitative estimates of exposure.

** As described in Appendix B.2 of the *White Paper: Quantitative Approach to the Human Health Assessment for the Risk Evaluation for Asbestos Part 2: Supplemental Evaluation Including Legacy Uses and Associated Disposals of Asbestos*, to be considered as being informative for dose-response analysis, metrics 4 and 5 would need metric ratings of Medium or High. This reference did not satisfy this requirement; therefore data quality evaluation is presented for only for metrics 4 and 5.

Study Citation:	Madkour, M. T., El Bokhary, M. S., Awad Allah, H. I., Awad, A. A., Mahmoud, H. F. (2009). Environmental exposure to asbestos and the exposure-response relationship with mesothelioma. Eastern Mediterranean Health Journal 15(1):25-38.
Health Outcome:	Mesothelioma
Target Organ(s):	Cancer/Carcinogenesis: Malignant Pleural Mesothelioma; Lung/Respiratory: Malignant Pleural Mesothelioma
Asbestos Fiber Type(s):	Asbestos - Chrysotile (serpentine): 12001-29-5
Linked HERO ID(s):	No linked references.
HERO ID:	2593920

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Medium	This study, conducted in 2003 and 2004 in Egypt, included two groups exposed to asbestos: (i) 2913 environmentally exposed individuals residing in 6 neighborhoods ranging from 100 meters to 2.5 km from the Sigwart chrysotile asbestos manufacturing plant in greater Cairo; and (ii) 487 workers currently employed at the asbestos plant (all departments). The plant operated from 1948 to 2004. Participants were adults aged >20y. An unexposed comparison group was also included. High confidence for environmentally exposed: The environmentally exposed group is likely representative of environmental exposure and health outcomes; individuals with “any history suggestive of any occupational exposure to asbestos” were excluded. Health center workers recruited these individuals, selecting from a target population identified using cluster sampling (not specified if drawn from population or clinic registries). No other selection criteria were mentioned (e.g. based on health status, employment status, duration of residence) that could have biased the exposure-outcome distribution. Medium confidence for occupationally exposed: The occupationally exposed group was limited to currently active workers, which induced risk of a healthy worker bias (potential selection of less healthy people out of the workforce). This is of concern as the study began after a 2002 report of asbestos-related pleuropulmonary disorders at the plant.
	Metric 2:	Attrition	High	Participation rates were high in all three groups. Environmental: the authors report a response rate of 95% (2913 of the 3059 invited). Occupational: 89% if the 543 current employees participated (35 refused, 21 were lost to follow-up). Comparison group: 979 of 1041 invited (94%) participated.
	Metric 3:	Comparison Group	Low	The comparison group comprised residents in an agricultural area (Banha city) 40 km from the plant. None of the individuals had a history of occupational or environmental exposure. No other selection criteria were mentioned. The appropriateness of comparisons with the two exposed groups is very uncertain as the authors do not provide any information on the distribution of age, sex, socioeconomic indicators, employment status, or health status in this group.
Domain 2: Exposure Characterization				

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Study Citation:	Madkour, M. T., El Bokhary, M. S., Awad Allah, H. I., Awad, A. A., Mahmoud, H. F. (2009). Environmental exposure to asbestos and the exposure-response relationship with mesothelioma. Eastern Mediterranean Health Journal 15(1):25-38.
Health Outcome:	Mesothelioma
Target Organ(s):	Cancer/Carcinogenesis: Malignant Pleural Mesothelioma; Lung/Respiratory: Malignant Pleural Mesothelioma
Asbestos Fiber Type(s):	Asbestos - Chrysotile (serpentine): 12001-29-5
Linked HERO ID(s):	No linked references.
HERO ID:	2593920

Domain	Metric		Rating	Comments
	Metric 4:	Measurement of Exposure	Medium	Exposure was quantified based on: air sample concentrations; duration (of residence or employment); and cumulative fiber-years (concentration x duration). 10-year categories of exposure duration ranged from 0-10 to >40 years. Concentrations (fibers/cc) were quantified based on PCM counts of fibers > 5 μm using samples collected on membrane filters using a known air flow rate (type of pump or impinger not specified), prepared using OSHA methods. Exposure was estimated in each group, but there were differences in the measures and methodologic information provided across groups, complicating comparisons and making validity uncertain. Historic exposure measures were not included. –Occupational exposure: Medium confidence. 45 air samples were taken at breathing height (1.5 meters) from 8 areas including manufacturing, milling, and offices, over 8h from 9:00-17:00h. Mean fiber concentration, but not mean fiber concentrations-year or mean duration of employment, were shown for each of these 8 areas (Table 8; overall mean 0.59 f/mL-years). Potential source of error: Measures were taken inside the plant from January 2003 to March 2004 when it was fully functioning and after it closed in November 2004. The paper does not specify when measures were taken in each area, or whether measures after plant closure were included in the estimates. –Environmental exposure: Medium confidence. Fiber counts were estimated using 5 air samples collected in each of the 6 residential areas, which were characterized based on mean distance from the plant. Mean concentrations were reported for each area (Table 9; overall mean 0.38 f/mL), but not cumulative fiber-years or mean duration of residence. Uncertainties: The authors did not specify sample collection height, flow rates, hours of the day, or dates. –Control area exposure: Medium confidence. Air sample collection was reported. The mean fiber concentration was reported as 0.0021 fibers/mL (Tables 8 and 9); mean duration of residence was not shown so mean fiber-years were uncertain. Uncertainties: There was no description of the methods used to collect samples, including: the number of samples; height, flow rate, hours of the day, dates of collection.
	Metric 5:	Exposure Levels	Medium	In addition to any vs no known exposure, exposure levels associated with prevalent mesothelioma were shown using: 5 categories of exposure duration; by area of residence/distance from the plant (n=6); location of work (n=8) with differing exposure concentrations. For the study population as a whole (Table 10), the authors used two categories of exposure concentration and three categories of cumulative exposure; it is uncertain how cutoffs were selected as numbers were imbalanced.
	Metric 6:	Temporality	Medium	Temporality is established. Although outcomes and exposure were measured contemporaneously, exposure duration was estimated retrospectively using categories that included >40 years of known exposure, an adequate timeframe for development of mesothelioma.
Domain 3: Outcome Assessment				

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Study Citation: Madkour, M. T., El Bokhary, M. S., Awad Allah, H. I., Awad, A. A., Mahmoud, H. F. (2009). Environmental exposure to asbestos and the exposure-response relationship with mesothelioma. Eastern Mediterranean Health Journal 15(1):25-38.
Health Outcome: Mesothelioma
Target Organ(s): Cancer/Carcinogenesis: Malignant Pleural Mesothelioma; Lung/Respiratory: Malignant Pleural Mesothelioma
Asbestos Fiber Type(s): Asbestos - Chrysotile (serpentine): 12001-29-5
Linked HERO ID(s): No linked references.
HERO ID: 2593920

Domain	Metric		Rating	Comments
	Metric 7:	Outcome Measurement or Characterization	Medium	Malignant pleural mesothelioma (MPM) was identified using a four-step process: (1) screening of all participants using mass miniature radiography (MMR, by qualified and experienced readers for parenchymarous and pleural diseases); (2) standard chest radiographs for cases with MMR abnrormalities; (3) high resolution computerized scans of individuals with abnormal radiographs to localize lesions; (4) admission to chest hospital for pleural biopsy using methods that included CT-guided biopsy. ICD codes were not provided, but procedures involved specialists and included biopsies. Screening of all participants reduced the likelihood of differential misclassification related to detection bias. The screening identified other pleuropulmonary disorders including pleural plaques and diffuse pleural thickening. Potential source of bias: prevalence-incidence bias may be present, since the most severe cases may not have been available for screening (e.g. death, hospitalized, moved).
	Metric 8:	Reporting Bias	Medium	The study presented findings in accordance with its aims: to evaluate the prevalence of malignant pleural mesothelioma (MPM) among individuals with environmental and occupational exposure; to examine the exposure response-curve for environmental exposure. The statistical methods described in the methods section were used (t-tests or chi-square tests for various descriptive tables; relative risk for any vs no exposure). However, the paper did not include multivariable-adjusted estimates to account for confounding, relative risks for increasing exposure, or effect estimates with confidence intervals or standard errors. In addition, the manuscript failed to present characteristics of the comparison group.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Low	Analyses did not adjust for any confounders, despite the differences shown in the age and gender distribution among individuals with vs without malignant pleural mesothelioma. Information on smoking habits and on SES was not discussed or shown.
	Metric 10:	Covariate Characterization	Low	The authors describe taking a “full history” of relevant background; however, assessment of potential confounders such as age and SES was not discussed.
	Metric 11:	Co-exposure Counfounding	N/A	For mesothelioma, there are no established risk factors other than exposure to asbestos. Therefore, no known co-exposures are of concern.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	Medium	The authors present appropriate descriptive and statistical tests. However, there was no consideration of confounding, and the relative risk shown did not examine dose-response
	Metric 13:	Statistical Power	Medium	The sample size and the number of cases were both large.

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Study Citation:	Madkour, M. T., El Bokhary, M. S., Awad Allah, H. I., Awad, A. A., Mahmoud, H. F. (2009). Environmental exposure to asbestos and the exposure-response relationship with mesothelioma. Eastern Mediterranean Health Journal 15(1):25-38.
Health Outcome:	Mesothelioma
Target Organ(s):	Cancer/Carcinogenesis: Malignant Pleural Mesothelioma; Lung/Respiratory: Malignant Pleural Mesothelioma
Asbestos Fiber Type(s):	Asbestos - Chrysotile (serpentine): 12001-29-5
Linked HERO ID(s):	No linked references.
HERO ID:	2593920

Domain	Metric		Rating	Comments
	Metric 14:	Reproducibility of Analyses	Medium	Reproducing the analyses linking the prevalence of mesothelioma to exposure would be straightforward.
	Metric 15:	Statistical Analysis	Low	The statistical analyses are not fully appropriate as they do not take into account potential confounding or evaluate dose-response.

Additional Comments: This study conducted in Egypt in 2003-04 screened three population groups to identify prevalent malignant pleural mesothelioma (MPM): residents living at varying distanced from an urban chrysotile asbestos plant; active workers at the plant; and residents in a rural community with minimal/no exposure. A total of 88 cases were identified, 83 in the environmentally exposed group. The study provides important insights on MPM risk in individuals with high levels of environmental exposure. However, HWE bias is an important concern in analyses of occupational exposure based on current workers in a facility where health risks had already been reported, that closed while the study was conducted. Other issues include the lack of accounting for confounding, the lack of information on the comparison group, and some uncertainties in exposure assessment methods. Nonetheless, the study is well-powered to contribute information on the dose-response relationship of high concentrations of environmental asbestos exposure and risk of MPM.

Overall Quality Determination — Medium

* No biomarkers were identified for this evaluation.

Study Citation:	Mcdonald, J. C., Armstrong, B. G., Edwards, C. W., Gibbs, A. R., Lloyd, H. M., Pooley, F. D., Ross, D. J., Rudd, R. M. (2001). Case-referent survey of young adults with mesothelioma: I. Lung fibre analyses. Annals of Occupational Hygiene 45(7):513-518.
Health Outcome:	Mesothelioma
Target Organ(s):	Lung/Respiratory: Mesothelioma diagnosis
Asbestos Fiber Type(s):	Asbestos - Crocidolite (riebeckite): 12001-28-4; Asbestos - Amosite (grunerite): 12172-73-5; Asbestos - Tremolite: 14567-73-8; Asbestos - Not specified: 1332-21-4; Asbestos - Chrysotile (serpentine): 12001-29-5
Linked HERO ID(s):	No linked references.
HERO ID:	758954

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Medium	The current study noted that details regarding case selection were reported within Mcdonald et al., 2001 (HERO ID 709579). Starting in 1989, approximately 85% of all respiratory and occupational medicine consultants in the UK voluntarily reported new cases of occupational respiratory disease to the national Surveillance of Work-related and Occupational Respiratory Disease (SWORD) study. Eligibility was described as all cases of malignant mesothelioma reported by physicians to SWORD between 1990 and 1996, born from 1943 onwards; these were selected for study and followed until the end of 1997. Of the n=180 eligible cases, exclusions were made for n=18 reported twice, n=14 described as too old, n=5 described as overseas, and n=3 for which diagnosis had been changed to benign pleural disease, inflammatory disease or adenocarcinoma, leaving n=140 men and women suitable for study. Of these, n=11 males and n=1 female was excluded due to lack of work history, leaving n=115 males and n=13 females for study. Of these, those without autopsies and lung burden analysis were excluded, leaving n=69 males and n=4 females for study. Final analyses for the current study excluded the females and was restricted to n=69 male mesothelioma cases. Eligibility for n=57 potential controls was described as those with autopsies from accidental or sudden cardiac deaths conducted by the same pathologists as cases, matched to cases by age and geographic region. Distributions of relevant exposure, outcome, demographic and other variables between those included and excluded were not detailed.
	Metric 2:	Attrition	Medium	Exposure and outcome data were complete for selected cases, although n=5 eligible cases were originally noted as lost to follow-up (“overseas”).
	Metric 3:	Comparison Group	Medium	Key elements of study design were reported (inclusion criteria and methods of participant selection) and indicate subjects were recruited during the same time period from the same eligible population. Differences in all potential confounding variables between groups were not detailed, although cases and controls were compared across matching variable categories of age and geographic region in Table 1.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	High	Autopsied lung fiber burden within mesothelioma cases and controls was measured utilizing Transmission Electron Microscopy (TEM).
	Metric 5:	Exposure Levels	Medium	Exposure distribution is adequate for exposure-response analyses. Final regression models incorporated odds ratios across quartiles of fiber concentration per microgram (f/ug) tissue within autopsied tissue samples including 0.0 f/ug, 0.1-0.9 f/ug, 1.0-9.9 f/ug, >=10.0 f/ug, as well as linear models utilizing a continuous measure of exposure.

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Study Citation:	Mcdonald, J. C., Armstrong, B. G., Edwards, C. W., Gibbs, A. R., Lloyd, H. M., Pooley, F. D., Ross, D. J., Rudd, R. M. (2001). Case-referent survey of young adults with mesothelioma: I. Lung fibre analyses. Annals of Occupational Hygiene 45(7):513-518.
Health Outcome:	Mesothelioma
Target Organ(s):	Lung/Respiratory: Mesothelioma diagnosis
Asbestos Fiber Type(s):	Asbestos - Crocidolite (riebeckite): 12001-28-4; Asbestos - Amosite (grunerite): 12172-73-5; Asbestos - Tremolite: 14567-73-8; Asbestos - Not specified: 1332-21-4; Asbestos - Chrysotile (serpentine): 12001-29-5
Linked HERO ID(s):	No linked references.
HERO ID:	758954

Domain	Metric		Rating	Comments
	Metric 6:	Temporality	Low	Temporality of exposure with outcome is uncertain within this cross-sectional study where physician diagnosis of mesothelioma within original database was confirmed at autopsy along with lung fiber analysis for the current study.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	High	Initial diagnoses were made by respiratory and occupational medicine consultants referring mesothelioma cases to the original SWORD study. Mcdonald et al., 2001 (ID 709259) indicates that research assistant confirmation of data was obtained from medical records, occupational histories, coroners and subject general practitioners. Formal validation of diagnoses was made through histological examination of lung tissue and tumor samples for cases and controls described as conducted independently by two pathologists considerably experienced in mesothelioma diagnosis.
	Metric 8:	Reporting Bias	High	There were no concerns for selective reporting as all outcomes which were outlined within methods were also reported within the results. Effect estimates within Tables 2 and 4 are reported as unadjusted and adjusted Odds Ratios (OR's) and 95% confidence intervals. The number of cases and controls within regression results was clearly detailed.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Medium	Controls were matched to cases on age and geographic region. Analysis was restricted to males. Consideration for race was not detailed.
	Metric 10:	Covariate Characterization	High	Covariates were assessed using reliable methodologies, cases and controls were matched on age and geographic region, but not race not discussed. Mcdonald et al., 2001 (ID 709259) indicates that research assistant confirmation of occupational data was obtained from medical records, occupational histories, coroners and subject general practitioners.
	Metric 11:	Co-exposure Counfounding	N/A	Per mesothelioma-specific guidance, concern about co-exposures is limited for mesothelioma, meriting a "not applicable" rating.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	Medium	This cross-sectional design was appropriate for an initial investigation of exposure and outcome. Conditional logistic regression was utilized for matched case control analyses.
	Metric 13:	Statistical Power	Medium	Analyses of n=69 mesothelioma cases with n=57 controls was minimal for this matched case control analyses. Analyses within some higher exposure quartiles across asbestos types was sometimes not possible due to the lack of cases and/or controls (Tables 2 and 4).
	Metric 14:	Reproducibility of Analyses	Medium	Statistical tests and matching variables were described and general methods were described in a way that would facilitate reproducibility with access to the analytic data.

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Study Citation: Mcdonald, J. C., Armstrong, B. G., Edwards, C. W., Gibbs, A. R., Lloyd, H. M., Pooley, F. D., Ross, D. J., Rudd, R. M. (2001). Case-referent survey of young adults with mesothelioma: I. Lung fibre analyses. Annals of Occupational Hygiene 45(7):513-518.
Health Outcome: Mesothelioma
Target Organ(s): Lung/Respiratory: Mesothelioma diagnosis
Asbestos Fiber Type(s): Asbestos - Crocidolite (riebeckite): 12001-28-4; Asbestos - Amosite (grunerite): 12172-73-5; Asbestos - Tremolite: 14567-73-8; Asbestos - Not specified: 1332-21-4; Asbestos - Chrysotile (serpentine): 12001-29-5
Linked HERO ID(s): No linked references.
HERO ID: 758954

Domain	Metric		Rating	Comments
	Metric 15:	Statistical Analysis	Medium	Conditional logistic regression models were adequately described and there were no indications of a lack of adherence to model assumptions.
Domain 6: Other (if applicable) Considerations for Biomarker Selection and Measurement (Lakind et al. 2014)				
	Metric 16:	Use of Biomarker of Exposure	High	Lung tissue fiber analyses was conducted by TEM and were presented for each fiber type assessed (Table 2).
	Metric 17:	Effect Biomarker	N/A	A biomarker of exposure was assessed in the current study.
	Metric 18:	Method Sensitivity	Low	LOD/LOQ values were not stated.
	Metric 19:	Biomarker Stability	Low	Storage history of samples was not detailed.
	Metric 20:	Sample Contamination	Medium	Contamination information was not detailed.
	Metric 21:	Method Requirements	Medium	Transmission electron microscopy provides a measure of degree of confidence for the lung tissue samples selected from what was described as different parts of each lung.
	Metric 22:	Matrix Adjustment	N/A	Matrix adjustment is not required.

Additional Comments: This cross-sectional study of a limited number (n=69 male mesothelioma cases and n=57 controls) with lung fiber analyses by transmission electron microscopy (TEM)) indicated lung amosite and crocidolite fibers could account for about 80% of cases of mesothelioma, and tremolite for some 7%. A steep linear trend in mesothelioma odds ratios (ORs) were noted for all amphiboles combined with an indication for additive effects.

Overall Quality Determination **Medium**

Study Citation:	Mcdonald, J. C., Armstrong, B., Case, B., Doell, D., Mccaughey, W. T., Mcdonald, A. D., Sébastien, P. (1989). Mesothelioma and asbestos fiber type. Evidence from lung tissue analyses. Cancer 63(8):1544-1547.
Health Outcome:	Mesothelioma
Target Organ(s):	Lung/Respiratory: mesothelioma; Mortality: mesothelioma
Asbestos Fiber Type(s):	Asbestos - Amosite (grunerite): 12172-73-5; Asbestos - Crocidolite (riebeckite): 12001-28-4; Asbestos - Tremolite: 14567-73-8; Asbestos - Anthophyllite: 17068-78-9; Asbestos - Chrysotile (serpentine): 12001-29-5
Linked HERO ID(s):	No linked references.
HERO ID:	3082766

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	High	This was a cross-sectional study design of asbestos fiber levels and the risk of mesothelioma mortality. Lung samples from n=78 mesothelioma cases autopsied from 1982-1983 were collected from registries from nine Canadian provinces. Cases were included in the study if the pathologist deemed the diagnosis ”more likely than not”. Lung samples for deaths not caused by malignant or respiratory disease were collected from the following years: 1979, 1980, 1981, and half of 1984. These controls (n=78) were selected from the same autopsy register that cases were selected from. Controls were matched by sex, date of death (within one year), type of tissue, and date of birth. Authors note that British Columbia was excluded from the sample due to an existing study occurring in the region.
	Metric 2:	Attrition	High	Authors report a total of 167 diagnosed mesothelioma cases in the study area during the sampling period, with only a portion being fatal (n=83) and only 78 samples available. There is no evidence of further restricting the sample for analyses. As the study was conducted among subjects whose diseases were fatal, attrition and loss to follow up are not of concern.
	Metric 3:	Comparison Group	Medium	Authors selected referent population from the same autopsy registry but during slightly different years (1982 and 1983 for cases; 1979, 1980, 1981, and the first half of 1984 for controls). Controls were matched for sex, date of death, type of tissue, and date of birth. A full comparison of demographic characteristics of cases and controls is not provided, thus other demographic differences cannot be completely ruled out.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Medium	Fiber levels in lung samples were assessed using analytic TEM to identify short (<8 um fiber length) and long (>=8 um fiber length) fibers. As samples were collected after subject death, levels only represent one time period, which is anticipated to reasonably represent the period of interest prior to subject death.
	Metric 5:	Exposure Levels	Medium	Fiber concentrations ranged from <0.1 to 100 per ug dry weight of lung sample, which represents a sufficient range to examine the exposure-outcome relationship.
	Metric 6:	Temporality	Medium	This study represents a cross-sectional analysis of a disease with a long latency period. Fiber levels were measured after mesothelioma death, thus it can be assumed that the latency period was accounted for in the study.
Domain 3: Outcome Assessment				

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Study Citation:	Mcdonald, J. C., Armstrong, B., Case, B., Doell, D., Mccaughey, W. T., Mcdonald, A. D., Sébastien, P. (1989). Mesothelioma and asbestos fiber type. Evidence from lung tissue analyses. Cancer 63(8):1544-1547.
Health Outcome:	Mesothelioma
Target Organ(s):	Lung/Respiratory: mesothelioma; Mortality: mesothelioma
Asbestos Fiber Type(s):	Asbestos - Amosite (grunerite): 12172-73-5; Asbestos - Crocidolite (riebeckite): 12001-28-4; Asbestos - Tremolite: 14567-73-8; Asbestos - Anthophyllite: 17068-78-9; Asbestos - Chrysotile (serpentine): 12001-29-5
Linked HERO ID(s):	No linked references.
HERO ID:	3082766

Domain	Metric		Rating	Comments
	Metric 7:	Outcome Measurement or Characterization	High	Deaths from mesothelioma were assessed by examining information from the autopsy registries in Canadian provinces. Fatal mesothelioma case samples were examined and confirmed histologically (by biopsy or at autopsy).
	Metric 8:	Reporting Bias	Medium	While anticipated results of analyses are reported, the results do not always include all information needed for dose-response analyses. Odds ratios are reported by fiber concentration in Table 1 along with case and referent numbers, but no measure of variance accompanies the effect estimate. Additionally, the risk increment and 95% CI, along with the attributable risk, are reported, but case and referent numbers are not reported.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Medium	Sex, year of death, type of tissue, and age were appropriately adjusted for using matching of cases and referents. While age and sex are two important confounders, information on other potential confounders is not provided, thus limiting the ability to assess is adjustment was complete.
	Metric 10:	Covariate Characterization	Low	While it could be reasonably assumed that information on confounders was collected from registries, the source of confounder information is not explicitly stated in the study.
	Metric 11:	Co-exposure Counfounding	N/A	Per mesothelioma-specific guidance, concern about co-exposures is limited for mesothelioma, meriting a "not applicable" rating.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	Medium	This cross-sectional assessment of the case and referent populations was appropriate, as was the use of multivariate logistic regression to assess the relationship between the exposure and outcome.
	Metric 13:	Statistical Power	Medium	The number of cases (n=78) and matched referents (n=78) is adequate to detect an effect in the population.
	Metric 14:	Reproducibility of Analyses	Medium	The information provided about the analysis is sufficient to conceptually reproduce the approach.
	Metric 15:	Statistical Analysis	Medium	Authors explicitly provide information about the construction of statistical models and why certain covariates were included.
Domain 6: Other (if applicable) Considerations for Biomarker Selection and Measurement (Lakind et al. 2014)				
	Metric 16:	Use of Biomarker of Exposure	High	Lung samples were analyzed to assess the number of asbestos fibers (by type) present per ug dry weight tissue. Lung tissues are an appropriate matrix to accurately assess asbestos fiber levels.
	Metric 17:	Effect Biomarker	High	Lung tissue samples were histologically examined to assess mesothelioma. Lung is an appropriate matrix to accurately assess this health outcome.

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Study Citation:	Mcdonald, J. C., Armstrong, B., Case, B., Doell, D., Mccaughey, W. T., Mcdonald, A. D., Sébastien, P. (1989). Mesothelioma and asbestos fiber type. Evidence from lung tissue analyses. Cancer 63(8):1544-1547.
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Linked HERO ID(s):	No linked references.
HERO ID:	3082766

Domain	Metric		Rating	Comments
	Metric 18:	Method Sensitivity	Medium	LOD <0.01 for fibers appears low enough to capture a wide range of exposure levels to address the research hypothesis.
	Metric 19:	Biomarker Stability	High	Stability and storage losses are not of concern for the lung samples collected in this study.
	Metric 20:	Sample Contamination	Medium	There is no information related to sample contamination, but there are no major concerns about contamination of lung tissue samples with asbestos fibers.
	Metric 21:	Method Requirements	Medium	Methods with high degrees of confidence are used to assess biomarkers of effect and of exposure.
	Metric 22:	Matrix Adjustment	N/A	Matrix adjustment was not required for any of the biomarkers assessed in this study.

Additional Comments: This cross-sectional study examines autopsy tissue from deceased mesothelioma patients to assess fiber levels and compare those levels to lung tissue from a deceased referent population. While some information about consideration of confounders and details of results from statistical analyses are limited, the study reasonably assesses the exposure-outcome relationship through appropriate participant selection, exposure analysis, statistical analysis, and outcome ascertainment.

Overall Quality Determination — Medium

Study Citation:	Mcdonald, J. C., Mcdonald, A. D. (1997). Chrysotile, tremolite and carcinogenicity. Annals of Occupational Hygiene 41(6):699-705.
Health Outcome:	Mesothelioma
Target Organ(s):	Cancer/Carcinogenesis: Mesothelioma mortality; Lung/Respiratory: Mesothelioma mortality; Mortality: Mesothelioma mortality
Asbestos Fiber Type(s):	Asbestos - Chrysotile (serpentine): 12001-29-5; Asbestos - Tremolite: 14567-73-8
Linked HERO ID(s):	No linked references.
HERO ID:	7836

Domain	Metric		Rating	Comments
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Uninformative	Details on exposure measurement methods were not reported in the present reference or cited references (HERO ID 3081408 and 3651098). Men were compared by years of employment.
	Metric 5:	Exposure Levels	Medium	Participants were compared using logistic regression, suggesting a continuous measure of exposure (years of employment).

Additional Comments: None

* No biomarkers were identified for this evaluation.

** As described in Appendix B.2 of the *White Paper: Quantitative Approach to the Human Health Assessment for the Risk Evaluation for Asbestos Part 2: Supplemental Evaluation Including Legacy Uses and Associated Disposals of Asbestos*, to be considered as being informative for dose-response analysis, metrics 4 and 5 would need metric ratings of Medium or High. This reference did not satisfy this requirement; therefore data quality evaluation is presented for only for metrics 4 and 5.

Study Citation:	Mcdonald, J. C., Mcdonald, A. D., Armstrong, B., Sebastien, P. (1986). Cohort study of mortality of vermiculite miners exposed to tremolite. Occupational and Environmental Medicine 43(7):436-444.
Health Outcome:	Mesothelioma
Target Organ(s):	Cancer/Carcinogenesis: mesothelioma mortality; Lung/Respiratory: mesothelioma mortality; Mortality: mesothelioma mortality
Asbestos Fiber Type(s):	Asbestos- Libby amphibole: 1318-09-8
Linked HERO ID(s):	29964, 709547, 709695
HERO ID:	29964

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Medium	Description of study setting was provided, and other elements including inclusion criteria and case ascertainment, primarily from McDonald et al. 1986, HERO ID: 29964, with McDonald and Armstrong 2003, HERO ID: 709547 giving a briefer version of the info. The study population includes male workers from a Libby mining company who have been hired before 1963. In total, 406 males worked at the site for at least one net year were included, 12 of which were employed before 1940. No other description of additional inclusion or exclusion criteria. There is limited information on subjects not included or participation rate, which introduces potential for selection bias.
	Metric 2:	Attrition	High	In McDonald et al. 1986, HERO ID: 29964, at the end of the follow-up period (July 1st, 1983), 226 were alive and 165 were dead. 14 men were found alive on 1981 but subsequent status was not available. In total, vital status of 405 out of 406 men included in this study were traced. Death certificates were obtained for 163 of the 165 deceased. In McDonald and Armstrong 2003, HERO ID: 709547, at the end of the follow-up period (July 1st, 1983), the remaining 241 (vs 240 in McDonald et al. 1986, HERO ID: 29964) known to be alive at the end of the 1983 follow up period were traced via the National Death Index to 1998, where another 120 were confirmed dead.There is little loss to follow up.
	Metric 3:	Comparison Group	Medium	In McDonald et al. 1986, HERO ID: 29964 mesothelioma case-referent analyses, "controls for each case were chosen as men surviving beyond the age of death of the case, who had been born and had started work at Libby mine within three years of the case."In McDonald and Armstrong 2003, HERO ID: 709547, comparison was made among other workers. Age and sex were considered in the analyses.Thus, there is only indirect evidence that groups are not similar to each other.
Domain 2: Exposure Characterization				

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Study Citation:	Mcdonald, J. C., Mcdonald, A. D., Armstrong, B., Sebastien, P. (1986). Cohort study of mortality of vermiculite miners exposed to tremolite. Occupational and Environmental Medicine 43(7):436-444.
Health Outcome:	Mesothelioma
Target Organ(s):	Cancer/Carcinogenesis: mesothelioma mortality; Lung/Respiratory: mesothelioma mortality; Mortality: mesothelioma mortality
Asbestos Fiber Type(s):	Asbestos- Libby amphibole: 1318-09-8
Linked HERO ID(s):	29964, 709547, 709695
HERO ID:	29964

Domain	Metric		Rating	Comments
	Metric 4:	Measurement of Exposure	Medium	Details on exposure assessment are primarily from McDonald et al. 1986, HERO ID: 29964, with McDonald and Armstrong 2003, HERO ID: 709547 citing this paper. The measurement of exposure (a mix of personal and area) changed during the study period but was ultimately based employment records and quantitative estimates of exposure using a combination of midget impingers and PCM (cited as optical microscopy while referencing Walton 1982, HERO ID: 29649, which clarifies it as phase contrast optical microscopy) for a portion of participant's work history of exposure, requiring extrapolation for earlier years. Air samples were collected using midget impinger before 1970 and using membrane filters after 1970. Samples before 1970 only measured dust concentrations without conversion factors. Limited amount of samples were collected before 1965, and the measurements were much higher after 1975 when the company introduced a systematic air sampling program. Authors assumed that fiber exposure measures made before 1965 (engineering controls installed at this point to reduce dust/fiber levels), were a fraction of those measured afterwards. Authors further note: "For the other operation locations fiber measurements were available only for the recent periods. When the data were considered inadequate to describe past conditions, because of changes in process or control practice, arbitrary correction factors were applied. This was done after discussion with the company's representatives and especially with a previous manager who had spent almost all his career with Libby and who had extensive knowledge of the operations." Samples were taken until 1982. Cumulative exposure levels were calculated based on job histories, operation locations, and estimated average fiber concentrations.In McDonald and Armstrong 2003, HERO ID: 709547, they used three different indices for exposure: "...(A) average intensity over first five years of employment (f/ml); (B) cumulative exposure (f/ml.y); and (C) residence weighted cumulative exposure, for which each year's exposure is weighted according to the number of years since it was experienced (f/ml.y)."
	Metric 5:	Exposure Levels	Medium	In McDonald et al. 1986, HERO ID: 29964, cumulative continuous exposure levels were used for case-referent analysis of mesothelioma. In McDonald and Armstrong 2003, HERO ID: 709547, both continuous and categorical exposure levels were used in Poisson regression analyses for mesothelioma.
	Metric 6:	Temporality	High	The follow-up period is greater than 20 years in this cohort for >2/3 of deaths (as shown in McDonald et al. 1986, HERO ID: 29964), suggesting there is sufficient consideration of latency of mesothelioma. The temporality is established and exposure occurred before outcome.
Domain 3: Outcome Assessment				

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Study Citation:	Mcdonald, J. C., Mcdonald, A. D., Armstrong, B., Sebastien, P. (1986). Cohort study of mortality of vermiculite miners exposed to tremolite. Occupational and Environmental Medicine 43(7):436-444.		
Health Outcome:	Mesothelioma		
Target Organ(s):	Cancer/Carcinogenesis: mesothelioma mortality; Lung/Respiratory: mesothelioma mortality; Mortality: mesothelioma mortality		
Asbestos Fiber Type(s):	Asbestos- Libby amphibole: 1318-09-8		
Linked HERO ID(s):	29964, 709547, 709695		
HERO ID:	29964		
Domain	Metric	Rating	Comments
	Metric 7: Outcome Measurement or Characterization	High	In McDonald et al. 1986, HERO ID: 29964, the cases were ascertained from death certificates and underlying cause of death was coded by a single qualified nosologist according to ICD-8 codes (163, 199, and 515). In McDonald and Armstrong 2003, HERO ID: 709547, the additional deaths were coded by State nosologists in ICD-9 (codes not specified).
	Metric 8: Reporting Bias	High	Findings of the study were reported in abstract and results. Analyses show relative risk with 95% CI (McDonald et al. 1986, HERO ID: 29964, McDonald and Armstrong 2003, HERO ID: 709547). McDonald and Armstrong 2003, HERO ID: 709547 also reports a p-trend. Reporting bias is not likely to be introduced.
Domain 4: Potential Confounding / Variability Control			
	Metric 9: Covariate Adjustment	Medium	For case-referent analysis, age, sex, and date of hire were matched (McDonald et al. 1986, HERO ID: 29964), while in McDonald and Armstrong 2003, HERO ID: 709547, there is no covariate adjustment, except for sex and race.
	Metric 10: Covariate Characterization	Medium	The source of covariates were not described but likely collected from employment records.
	Metric 11: Co-exposure Counfounding	N/A	Co-exposure is not applicable for mesothelioma because there are no established risk factors other than exposure to asbestos.
Domain 5: Analysis			
	Metric 12: Study Design and Methods	Medium	The case-referent and Poisson analyses were appropriate method to evaluate the exposure-outcome associations.
	Metric 13: Statistical Power	N/A	This metric is rated as not applicable according to EPA guidance for mesothelioma (i.e., mark not applicable when no analyses are performed for mesothelioma).
	Metric 14: Reproducibility of Analyses	Medium	The descriptions of the methods and analyses are sufficient and conceptually reproducible.
	Metric 15: Statistical Analysis	Medium	Descriptions of case-referent and Poisson models are clear.
Additional Comments:	This is a cohort of 2 studies (McDonald et al. 1986, HERO ID: 29964, McDonald and Armstrong 2003, HERO ID: 709547), with latter being a follow-up on the same cohort of workers in a Libby asbestos mine, with more deaths added for analyses. Metrics 11 and 13 are marked as NA as per instructions specific for mesothelioma.		
Overall Quality Determination		**Medium**	

* No biomarkers were identified for this evaluation.

Study Citation:	Menegozzo, S., Comba, P., Ferrante, D., De Santis, M., Gorini, G., Izzo, F., Magnani, C., Pirastu, R., Simonetti, A., Tùnesi, S., Menegozzo, M. (2011). Mortality study in an asbestos cement factory in Naples, Italy. Annali dell'Istituto superiore di sanità 47(3):296-304.
Health Outcome:	Mesothelioma
Target Organ(s):	Lung/Respiratory: malignant neoplasms respiratory tract (160-165) mortality, malignant neoplasms pleura (163) mortality, malignant neoplasms peritoneum (158) mortality; Mortality: malignant neoplasms respiratory tract (160-165) mortality, malignant neoplasms pleura (163) mortality, malignant neoplasms peritoneum (158) mortality; Cancer/Carcinogenesis: malignant neoplasms respiratory tract (160-165) mortality, malignant neoplasms pleura (163) mortality, malignant neoplasms peritoneum (158) mortality
Asbestos Fiber Type(s):	Asbestos - Amosite (grunerite): 12172-73-5; Asbestos - Crocidolite (riebeckite): 12001-28-4; Asbestos - Chrysotile (serpentine): 12001-29-5
Linked HERO ID(s):	No linked references.
HERO ID:	3078781

Domain	Metric		Rating	Comments
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Low	This metric is rated Low because the study or any cited methods source does not explicitly mention the use of PCM or TEM.Authors provided a detailed history of asbestos work in the plant, but methodology of exposure measurement is limited. Generic dust measures were available from the 1960s and in 1979, 64 airborne asbestos fiber samplings were available (crocidolite specific). No information is provided regarding how measures were taken.
	Metric 5:	Exposure Levels	Medium	The study cohort includes workers hired from 1950-1986, and follow-up is from 1965-2005. Even though the environmental airborne generic asbestos fiber and crocidolite sampling in different areas in 1979, this study only presented "duration of exposure" that can be used as a surrogate of exposure assessment for several diseases and to determine exposure-response relationships.

Additional Comments:	NOTE: This study would not be fully evaluated under the current guidelines. This is due to the low rating for metric 4, as no PCM or TEM was mentioned in the study or a cited source.This study provides a comprehensive analysis of SMRs from workers in the Bagnoli factory cohort. Overall, the study describes metrics well, but lacks proper covariables and excluded smoking in their analyses. There is very little information regarding the measurements of asbestos dusts within the factory, with no mention of what tools were used or measures for non-crocidolite asbestos exposures.

* No biomarkers were identified for this evaluation.

** As described in Appendix B.2 of the *White Paper: Quantitative Approach to the Human Health Assessment for the Risk Evaluation for Asbestos Part 2: Supplemental Evaluation Including Legacy Uses and Associated Disposals of Asbestos*, to be considered as being informative for dose-response analysis, metrics 4 and 5 would need metric ratings of Medium or High. This reference did not satisfy this requirement; therefore data quality evaluation is presented for only for metrics 4 and 5.

Study Citation:	Metintas, S., Metintas, M., Ak, G., Kalyoncu, C. (2012). Environmental asbestos exposure in rural Turkey and risk of lung cancer. International Journal of Environmental Health Research 22(5):468-479.
Health Outcome:	Mesothelioma
Target Organ(s):	Lung/Respiratory: Malignant mesothelioma; Cancer/Carcinogenesis: Malignant mesothelioma
Asbestos Fiber Type(s):	Asbestos - Tremolite: 14567-73-8
Linked HERO ID(s):	No linked references.
HERO ID:	2325159

Domain		Metric	Rating	Comments
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Medium	White soil exposure was assessed both indoors and outdoors (two samples for each environment) in each village. Inclusion for indoor measurements included white-washed walls with white soil. Outdoor samples were taken from the center of the village on the main road. Samples were sent to specialists in the National Institute of Workers Health and Security (ISGUM), Ankara. A PCM was used to count fibres longer than 5 um. This has been marked medium as the authors don't clarify if multiple time periods were used for measures.
	Metric 5:	Exposure Levels	Low	Levels of exposure are by exposed and unexposed villages and by men and women. As there are only two levels of exposure, the metric is rated Low.

Additional Comments:	HEROID 235159 was not evaluated for any metrics except Metric 4 and 5 and had no data extracted because it did not have sufficient exposure information to be useful for dose-response analysis. Metric 5 only provided 2 exposure levels, thus receiving a Low rating. Comments can still be found for all metric, but they are not rated.

** As described in Appendix B.2 of the *White Paper: Quantitative Approach to the Human Health Assessment for the Risk Evaluation for Asbestos Part 2: Supplemental Evaluation Including Legacy Uses and Associated Disposals of Asbestos*, to be considered as being informative for dose-response analysis, metrics 4 and 5 would need metric ratings of Medium or High. This reference did not satisfy this requirement; therefore data quality evaluation is presented for only for metrics 4 and 5.

Study Citation:	Moshammer, H., Neuberger, M. (2009). Lung function predicts survival in a cohort of asbestos cement workers. International Archives of Occupational and Environmental Health 82(2):199-207.		
Health Outcome:	Mesothelioma		
Target Organ(s):	Mortality: Mesothelioma mortality; Cancer/Carcinogenesis: Mesothelioma mortality		
Asbestos Fiber Type(s):	Asbestos - Chrysotile (serpentine): 12001-29-5; Asbestos - Crocidolite (riebeckite): 12001-28-4		
Linked HERO ID(s):	No linked references.		
HERO ID:	2079066		

Domain	Metric	Rating	Comments
Domain 2: Exposure Characterization			
	Metric 4: Measurement of Exposure	Low	Estimated cumulative exposure was described as based upon historical spot measurements analyzed by light microscopy and exposure classifications assigned to each work area. Workplace asbestos exposure spot measurement records were available from 1950 until 1981. Each worker was assigned a specific category of exposure for every year that worker worked at the asbestos cement factory. Details regarding consideration for changes in job area or task during that year were not provided. Authors did not discuss the potential for exposure misclassification within these methods, but the misclassification was likely non-differential. Mean (IQR) estimated cumulative exposure was reported in Table 2 as 72.62 fiber years (fibers x years/cm^3) (70.81).
	Metric 5: Exposure Levels	Low	The range and distribution of estimated exposure across five workplace areas in Table 1 is sufficient to develop exposure-response estimates. Separate mesothelioma mortality analyses results within Table 4 utilized only binary (yes/no) amphibole exposure as an exposure predictor variable.

Additional Comments: Metric 4 rating changed to low due to no mention of PCM/TEM in exposure assessmentMa

* No biomarkers were identified for this evaluation.

** As described in Appendix B.2 of the *White Paper: Quantitative Approach to the Human Health Assessment for the Risk Evaluation for Asbestos Part 2: Supplemental Evaluation Including Legacy Uses and Associated Disposals of Asbestos*, to be considered as being informative for dose-response analysis, metrics 4 and 5 would need metric ratings of Medium or High. This reference did not satisfy this requirement; therefore data quality evaluation is presented for only for metrics 4 and 5.

Study Citation: Neuberger, M., Kundi, M. (1990). Individual asbestos exposure: Smoking and mortality—a cohort study in the asbestos cement industry. British Journal of Industrial Medicine 47(9):615-620.
Health Outcome: Mesothelioma
Target Organ(s): Cancer/Carcinogenesis: Mesothelioma; Lung/Respiratory: Mesothelioma
Asbestos Fiber Type(s): Asbestos - Crocidolite (riebeckite): 12001-28-4
Linked HERO ID(s): No linked references.
HERO ID: 3082545

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Medium	Eligibility criteria not described in detail (e.g., of the 2816 persons eligible for the study), but other key details of participants described. A brief description of the study setting and asbestos use was provided.
	Metric 2:	Attrition	Medium	A total of 121 persons lost to follow up. Authors note this was mostly due to emigration.
	Metric 3:	Comparison Group	High	A nested case-control analysis was completed for mesothelioma. Controls were matched by year of first employment, duration of employment, and year of birth.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Medium	”Individual exposures were estimated (from 1973) from personal records onduration of exposure at different workplaces, estimations of dust concentration until 1965, dust measurements mainly by a conimeter method until 1975, and by personal air samplers and membrane filter methods (Asbestos International Association, HERO 3648707) subsequently. ” The referenced study (HERO 3648707) cites the use of PCM methodology to count fibres. Details on implementation for this study were limited, but it appears they followed a standard protocol.
	Metric 5:	Exposure Levels	Medium	Reports 4 exposure groups (high, high/medium, medium, and neglible).
	Metric 6:	Temporality	Medium	Study authors note that all persons who had not been observed for more than 15 years from start of exposure were excluded.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Medium	Follow up on vital status for participants was undertaken using government registration offices, death registries, physicians, and pathologists. Mesothelioma was identified using ICD-9 163.
	Metric 8:	Reporting Bias	High	Table 3 indicates crocidolite exposure of four cases of mesothelioma verified by necropsy and controls matched for sex, age, time of first employment, and duration of employment. Chi-square results are provided in the discussion.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	High	Cases and controls were matched on several factors: year of first employment, duration of employment, and year of birth.
	Metric 10:	Covariate Characterization	Medium	Authors note they used a ”standardised questionnaire on occupational exposures and smoking.” Age was presumably determined from personnel records.

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Study Citation:	Neuberger, M., Kundi, M. (1990). Individual asbestos exposure: Smoking and mortality—a cohort study in the asbestos cement industry. British Journal of Industrial Medicine 47(9):615-620.
Health Outcome:	Mesothelioma
Target Organ(s):	Cancer/Carcinogenesis: Mesothelioma; Lung/Respiratory: Mesothelioma
Asbestos Fiber Type(s):	Asbestos - Crocidolite (riebeckite): 12001-28-4
Linked HERO ID(s):	No linked references.
HERO ID:	3082545

Domain	Metric		Rating	Comments
	Metric 11:	Co-exposure Counfounding	Low	In an occupational setting, potential co-exposures are not discussed.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	Medium	A chi-square test was used to compare exposure among the cases and controls.
	Metric 13:	Statistical Power	Medium	Only four confirmed mesothelioma cases were observed, and study authors made comparisons with a nested group of 16 controls.
	Metric 14:	Reproducibility of Analyses	Medium	Simple comparisons were made between groups. No concerns for reproducibility.
	Metric 15:	Statistical Analysis	Medium	No concerns regarding use of chi-square to determine differences between groups.

Additional Comments: Historical prospective cohort study analyzing 49 lung cancer and 4 mesothelioma cases from asbestos-exposed cement factory workers. Methods were generally standard, but some details were not present regarding selection and exposure measurement, however, this is not likely to appreciably impact the results. Mesothelioma was analyzed in a nested case-control design with a small set of controls (n=16).

Overall Quality Determination — Medium

* No biomarkers were identified for this evaluation.

Study Citation:	Nicholson, W. J., Selikoff, I. J., Seidman, H., Lilis, R., Formby, P. (1979). Long-term mortality experience of chrysotile miners and millers in Thetford Mines, Quebec. Annals of the New York Academy of Sciences, Vol. 330 330:21-Nov.
Health Outcome:	Mesothelioma
Target Organ(s):	Cancer/Carcinogenesis: Mesothelioma; Lung/Respiratory: Mesothelioma; Mortality: Mesothelioma
Asbestos Fiber Type(s):	Asbestos - Chrysotile (serpentine): 12001-29-5
Linked HERO ID(s):	No linked references.
HERO ID:	158

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Medium	This study revolved around a cohort of men employed for at least 20 years in one of four companies that mine and mill chrysotile, exclusively. This represented 544 individuals from four separate operations. These operations were examined in Thetford Mines, Quebec, Canada. The participants included represented a variety of potential job classifications. However, not many details beyond this were included pertaining to inclusion criteria, such as the total number of individuals that could have potentially been included.
	Metric 2:	Attrition	Medium	There was moderate exclusion of participants from analyses. The aim of this study was to determine mortality outcomes for participants enrolled from the asbestos mines. The authors were able to obtain 172 of 178 certificates of death, and there were an additional 130 cases for which the authors obtained clinical, surgical, and pathological data to supplement death certificate information.
	Metric 3:	Comparison Group	Medium	The expected number of deaths/illnesses included in this study were derived from the age-specific death rate data for white Canadian males. It is important to note that they did not use data specific to Quebec, but it is noted that ”national rates are not importantly different from those of Quebec province but are likely to be significantly higher than those of the rural mining counties in which these workers lived” (Nicholson et al., 1979). The authors also explicitly discuss the potential for healthy worker effect, but they mention that ”the effects of asbestos exposure appear to overcome the beneficial health status usually associated with employability” (Nicholson et al., 1979). As mentioned, the participants were compared to white Canadian males, but there was no discussion of the racial makeup of employees.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	High	The authors report that 97 air samples were collected from various work locations within five operating asbestos mines/mills. These samples were collected between 1973 and 1975, and a majority of them were personal samples. The concentrations varied greatly, but it is reported that ”in virtually all work categories average dust concentrations exceeded the asbestos standard then current in the United States of 5 fibers longer than 5 micrometers/milliliter (5 f/ml)” (Nicholson et al., 1979). The authors detail that they followed the methods outlined by the National Institute of Occupational Safety and Health to determine asbestos concentrations, which utilizes a microscope with phase contrast optics (1972, 145).

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Study Citation:	Nicholson, W. J., Selikoff, I. J., Seidman, H., Lilis, R., Formby, P. (1979). Long-term mortality experience of chrysotile miners and millers in Thetford Mines, Quebec. Annals of the New York Academy of Sciences, Vol. 330 330:21-Nov.
Health Outcome:	Mesothelioma
Target Organ(s):	Cancer/Carcinogenesis: Mesothelioma; Lung/Respiratory: Mesothelioma; Mortality: Mesothelioma
Asbestos Fiber Type(s):	Asbestos - Chrysotile (serpentine): 12001-29-5
Linked HERO ID(s):	No linked references.
HERO ID:	158

Domain	Metric		Rating	Comments
	Metric 5:	Exposure Levels	Medium	Multiple levels of asbestos exposure were presented in the study. Table 3 includes a range, mean, and number of samples of asbestos in each of the mine/mill locations. It is also further divided into various work areas/activities, including general mill air, bagging asbestos, quality control laboratory, crusher, dryer, shops, and nonwork areas. This table highlights that a majority of the cohort was employed in facility two, and concentrations are reported in fibers longer than 5 micrometers/ml of air.
	Metric 6:	Temporality	High	One of the requirements to be included in this study was that the workers must have been employed for at least 20 years. This means that there is an appropriate temporality between exposure and outcome such that exposure occurred prior to the outcome.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	High	Death certificates were examined to determine the causes of death of participants. There was no mention of ICD coding schemes present in this study.
	Metric 8:	Reporting Bias	Medium	The findings are reported at various points throughout the study. Expected and observed deaths are reported, along with the O/E calculations. However, information such as confidence intervals are not reported, contributing to the medium rating.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Low	No description is provided in this study that discusses considerations for potential confounders or their adjustment.
	Metric 10:	Covariate Characterization	N/A	Covariates were not assessed in this study.
	Metric 11:	Co-exposure Counfounding	N/A	Because mesothelioma has few other causes than asbestos exposure, this metric was not rated.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	Medium	The study design and methods are appropriate for the research question being examined.
	Metric 13:	Statistical Power	Medium	Even though an explicit discussion of power was not included, the number of participants is adequate to detect an effect.
	Metric 14:	Reproducibility of Analyses	Low	There is a very limited discussion of the analysis presented in this study.
	Metric 15:	Statistical Analysis	Medium	SMRs were utilized, and it is clear why this analysis method was used.

Additional Comments: This study had some strengths and limitations. One benefit was the temporality component, since one of the inclusion criteria was that employees must have worked there for at least 20 years, providing a sufficient time from exposure to outcome. There was also an adequate number of participants included in the study to determine an effect. However, these results could be limited. It would have also been beneficial for the authors to provide more information about the causes of deaths, such as a discussion about diagnoses or specific indications, such as through cytological or histological means, for mesothelioma.

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Study Citation:	Nicholson, W. J., Selikoff, I. J., Seidman, H., Lilis, R., Formby, P. (1979). Long-term mortality experience of chrysotile miners and millers in Thetford Mines, Quebec. Annals of the New York Academy of Sciences, Vol. 330 330:21-Nov.
Health Outcome:	Mesothelioma
Target Organ(s):	Cancer/Carcinogenesis: Mesothelioma; Lung/Respiratory: Mesothelioma; Mortality: Mesothelioma
Asbestos Fiber Type(s):	Asbestos - Chrysotile (serpentine): 12001-29-5
Linked HERO ID(s):	No linked references.
HERO ID:	158

Domain	Metric	Rating	Comments
Overall Quality Determination		**Medium**	

* No biomarkers were identified for this evaluation.

Study Citation:	Nokso-Koivisto, P., Pukkala, E. (1994). Past exposure to asbestos and combustion products and incidence of cancer among Finnish locomotive drivers. Occupational and Environmental Medicine 51(5):330-334.
Health Outcome:	Mesothelioma
Target Organ(s):	Gastrointestinal: Stomach cancer, Rectal cancer, Colon cancer, Oral cavity and pharynx cancer; Lung/Respiratory: Lung and trachea cancer, Mesothelioma; Renal/Kidney: Kidney cancer, Bladder, ureter, urethra cancer; Skin/Connective Tissue: Skin (non-melanoma) cancer, Skin melanoma; Immune/Hematological: Leukemia, Hodgkin's disease, Non-Hodgkin's lymphoma; Reproductive/Developmental: Prostate cancer; Cancer/Carcinogenesis: All site cancer, Oral cavity and pharynx cancer, Stomach cancer, Colon cancer, Rectal cancer, Lung and trachea cancer, Mesothelioma, Prostate cancer, Kidney cancer, Bladder, ureter, urethra cancer, Skin melanoma, Skin (non-melanoma), Non-Hodgkin's lymphoma, Hodgkin's disease, Leukemia
Asbestos Fiber Type(s):	Asbestos - Anthophyllite: 17068-78-9; Asbestos - Chrysotile (serpentine): 12001-29-5
Linked HERO ID(s):	No linked references.
HERO ID:	3081842

Domain	Metric		Rating	Comments
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Low	To estimate pre-1970s steam engine maintenance exposures in Finland, working conditions were reconstructed in two workshops with the assistance of workers who had been exposed. During reconstructed dismantling of the outer covers of the boilers of two engines, eight personal air samples were collected. The authors state that "asbestos exposure was measured with standardized techniques," but they don't specify what these techniques were. Therefore, it is unclear whether PCM, TEM, or another method was used. The authors also reported that asbestos concentrations in cabins of diesel locomotives with asbestos pipe insulation was measured.
	Metric 5:	Exposure Levels	Low	The range and distribution of exposure was limited. The authors reported that "the average number of fibres > 5 um was 5.0 (range 2.5-7.5)/cm^3, indicating medium exposure" (Nokso-Koivisto & Pukkala, 1994) for the reconstructed steam engine dismantling. The number of fibers was undetectable for diesel locomotive cabins. Furthermore, although different time periods were assessed, the study only assessed two exposure levels – standardized incidence ratios were used to compare locomotive drivers (exposed) to the Finnish population (presumed unexposed or lower exposed). Therefore, this study does not include sufficient information for dose-response assessment.

Additional Comments: None

** As described in Appendix B.2 of the *White Paper: Quantitative Approach to the Human Health Assessment for the Risk Evaluation for Asbestos Part 2: Supplemental Evaluation Including Legacy Uses and Associated Disposals of Asbestos*, to be considered as being informative for dose-response analysis, metrics 4 and 5 would need metric ratings of Medium or High. This reference did not satisfy this requirement; therefore data quality evaluation is presented for only for metrics 4 and 5.

Study Citation:	Nuyts, V., Vanhooren, H., Begyn, S., Nackaerts, K., Nemery, B. (2017). Asbestos bodies in bronchoalveolar lavage in the 21st century: a time-trend analysis in a clinical population. Occupational and Environmental Medicine 74(1):59-65.
Health Outcome:	Mesothelioma
Target Organ(s):	Lung/Respiratory: mesothelioma; Cancer/Carcinogenesis: mesothelioma
Asbestos Fiber Type(s):	Asbestos - Not specified: 1332-21-4
Linked HERO ID(s):	No linked references.
HERO ID:	3531256

Domain	Metric		Rating	Comments
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Low	Asbestos bodies were quantified in BAL samples using light microscopy.
	Metric 5:	Exposure Levels	Medium	The range and distribution of exposure is sufficient to develop an exposure-response estimate, and an exposure-response model using a continuous measure of exposure was used for the analysis. Exposures ranged from 0 to 164.5 asbestos bodies (AB)/mL, with a median of 0.5 AB/mL and an arithmetic mean of 5 AB/mL.

Additional Comments: None

** As described in Appendix B.2 of the *White Paper: Quantitative Approach to the Human Health Assessment for the Risk Evaluation for Asbestos Part 2: Supplemental Evaluation Including Legacy Uses and Associated Disposals of Asbestos*, to be considered as being informative for dose-response analysis, metrics 4 and 5 would need metric ratings of Medium or High. This reference did not satisfy this requirement; therefore data quality evaluation is presented for only for metrics 4 and 5.

Study Citation:	Offermans, N. S., Vermeulen, R., Burdorf, A., Goldbohm, R. A., Kauppinen, T., Kromhout, H., van den Brandt, P. A. (2014). Occupational asbestos exposure and risk of pleural mesothelioma, lung cancer, and laryngeal cancer in the prospective Netherlands cohort study. Journal of Occupational and Environmental Medicine 56(1):19-Jun.
Health Outcome:	Mesothelioma
Target Organ(s):	Cancer/Carcinogenesis: pleural mesothelioma, lung cancer, laryngeal cancer (glottis and supraglottis cancers); Lung/Respiratory: pleural mesothelioma, lung cancer, laryngeal cancer (glottis and supraglottis cancers)
Asbestos Fiber Type(s):	Asbestos - Not specified: 1332-21-4
Linked HERO ID(s):	No linked references.
HERO ID:	3078062

Domain	Metric		Rating	Comments
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Low	The study employed two job exposure matrices - the DOMJEM (the Netherlands) and the FINJEM (Finland) - however, only one matrix appears to leverage quantitative measures of exposure to asbestos, but it is unclear if TEM or PCM were used. It appears that the DOMJEM uses expert judgment only to assign semiquantitative exposure values with corresponding weighting. The FINJEM uses expert judgment and exposure measurement, though there is no discussion of the methodology used to make those measurements.
	Metric 5:	Exposure Levels	Medium	This study examines exposure by tertile of cumulative exposure, tertile of duration of exposure, and, among the exposed only, tertile of duration of high exposure. Many of the analyses use those who were not exposed to asbestos as the referent group. There is an appropriate range of exposure among the study population to assess the exposure-response relationship.

Additional Comments:	This case-cohort study leverages the NLCS cohort to assess the association between occupational asbestos exposure and pleural mesothelioma cases. The study design and methodological approaches are robust, and the study employed the ICD-O-3 to identify mesothelioma cases. There are no major concerns about residual bias in the observed results.

* No biomarkers were identified for this evaluation.

** As described in Appendix B.2 of the *White Paper: Quantitative Approach to the Human Health Assessment for the Risk Evaluation for Asbestos Part 2: Supplemental Evaluation Including Legacy Uses and Associated Disposals of Asbestos*, to be considered as being informative for dose-response analysis, metrics 4 and 5 would need metric ratings of Medium or High. This reference did not satisfy this requirement; therefore data quality evaluation is presented for only for metrics 4 and 5.

Study Citation:	Peto, J. (1980). Lung cancer mortality in relation to measured dust levels in an asbestos textile factory. IARC Scientific Publications (30):829-836.
Health Outcome:	Mesothelioma
Target Organ(s):	Cancer/Carcinogenesis: pleural mesothelioma mortality; Mortality: pleural mesothelioma mortality; Lung/Respiratory: pleural mesothelioma mortality
Asbestos Fiber Type(s):	Asbestos - Chrysotile (serpentine): 12001-29-5; Asbestos - Crocidolite (riebeckite): 12001-28-4
Linked HERO ID(s):	No linked references.
HERO ID:	163

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Medium	This study is an extended follow up of the same North England asbestos textile factory worker cohort recruited from the work areas with highest expected asbestos exposure: fiberizing, carding, spinning, weaving, and plaiting. (Knox et al. 1968, HEROID: 115; Peto et al. 1977, HEROID: 3084525). Here, 679 men who had begun work after 1933 and who had accrued >10 total years of service by 1972 were included in the study. There is limited detail on recruitment or other inclusion criteria. There may be some selection bias, as only healthier workers would be able to complete >10 years of work in select high-exposure areas.
	Metric 2:	Attrition	High	Follow up for mortality continued through 1978 by the National Health Central Register and the factory personnel department. 41 of 679 (6%) men were unable to be traced. In this analysis, they were assumed to have been alive at the previous follow up date (12/31/1974), but their subsequent man-years were not included here. Deaths of workers over 85 are ignored. There is no other mention of drop-out or loss that was not included in follow-up.
	Metric 3:	Comparison Group	Low	The study only mentions ”unaffected controls” in the section on lung cancer mortality and dust levels. Another study using the same cohort (Knox et al. 1968, HEROID: 115) notes comparisons to ”national rates,” however it’s not clear if this is the same comparison group for this study. The study does compare in text results workers first exposed before 1951 and those in 1951 and later (i.e., cohort 1 and 2).
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Low	Asbestos fiber exposure concentrations were reportedly measured using a thermal precipitator in years between 1951-1961. Additional support for understanding past area dust measures in particles/mL were taken in conversations with hygiene officers from the factory. Static membrane filters in years after 1961. Authors state that for each area of the factory, representative combinations of measures were used and averaged to be converted to modern counting methods. ”The revised estimates are based on preliminary data abstracted from a detailed analysis that is currently being conducted by T.B.A. Industrial Products Ltd and must be regarded as provisional. However, they indicate that average dust levels were in the region of 30 fibre/ml in 1951 and remained high until about 10 years ago.”
	Metric 5:	Exposure Levels	Low	Asbestos exposure appears to be continuous, however SMR analyses are stratified by years since first exposure and year of first exposure, not by a quantitative measure of asbestos exposure. This suggests the exposure for SMR analyses is dichotomous.

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Study Citation: Peto, J. (1980). Lung cancer mortality in relation to measured dust levels in an asbestos textile factory. IARC Scientific Publications (30):829-836.
Health Outcome: Mesothelioma
Target Organ(s): Cancer/Carcinogenesis: pleural mesothelioma mortality; Mortality: pleural mesothelioma mortality; Lung/Respiratory: pleural mesothelioma mortality
Asbestos Fiber Type(s): Asbestos - Chrysotile (serpentine): 12001-29-5; Asbestos - Crocidolite (riebeckite): 12001-28-4
Linked HERO ID(s): No linked references.
HERO ID: 163

Domain	Metric		Rating	Comments
	Metric 6:	Temporality	Medium	There is appropriate temporality reported (>10 years) to follow-up to establish exposure-outcome, however it is not clear what share of workers has longer follow up time, as only man-years are reported, not total workers by years of service. In the paper on the same cohort published prior to this one, which had more subjects (Peto et al. 1977, HEROID: 3084525), 406/1085 (37%) of workers had >20 years of service. It seems reasonable to assume a similar proportion in the current study.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Medium	No ICD codes were used to establish mortality, except for gastrointestinal cancer, however no version is explicitly listed. Authors report that follow-up was itself completed by National Health Central Register (NHCR) and by the factory personnel department.
	Metric 8:	Reporting Bias	High	Mesothelioma is reported in all parts of study. Rate of pleural mesothelioma mortality is reported without effect estimates (in tables). Some data is available in text with confidence limits.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Low	Sex is adjusted for based on inclusion of only men. There is brief mention of adjustment for man-years in the analysis, but no other variables are discussed.
	Metric 10:	Covariate Characterization	Low	Covariate is assumed to have been collected from factory personnel records. No explicit detail is provided.
	Metric 11:	Co-exposure Counfounding	N/A	There are no applicable co-exposures for mesothelioma.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	Medium	The study design is appropriate for measuring relative risk and mortality rates of workers from the textile factory.
	Metric 13:	Statistical Power	Medium	The number of subjects (n=679) should be sufficient to find any true relationships between exposure and outcome.
	Metric 14:	Reproducibility of Analyses	Medium	The methods described in the paper are clear enough to be conceptually replicated.
	Metric 15:	Statistical Analysis	Medium	SMR analyses were appropriate, with no explicit assumptions to be met.

Additional Comments: Asbestos fiber types are detailed in an earlier iteration of the current study (Knox et al., 1968, HEROID: 115). There is limited detail on recruitment and participation methods and rates, as well as how outcomes were ascertained by the National Health Central Register and factory personnel departments.

Overall Quality Determination — Medium

* No biomarkers were identified for this evaluation.

Study Citation: Peto, J., Seidman, H., Selikoff, I. J. (1982). Mesothelioma mortality in asbestos workers: implications for models of carcinogenesis and risk assessment. British Journal of Cancer 45(1):124-135.
Health Outcome: Mesothelioma
Target Organ(s): Mortality: Mesothelioma; Cancer/Carcinogenesis: Mesothelioma; Lung/Respiratory: Mesothelioma
Asbestos Fiber Type(s): Asbestos - Not specified: 1332-21-4; Asbestos - Amosite (grunerite): 12172-73-5; Asbestos - Chrysotile (serpentine): 12001-29-5; Asbestos - Crocidolite (riebeckite): 12001-28-4
Linked HERO ID(s): No linked references.
HERO ID: 165

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Low	This study examined mesothelioma death rates among current and former 17,800 insulation workers in North America, however this is not entirely certain given how the study was written. Authors cite a previous work for details (Selikoff et al. 1979), but this was not available at the time of evaluation. There is no information given on the study population or its recruitment.
	Metric 2:	Attrition	Low	The number of participants were not reported at the different stages of the studies discussed in the manuscript.
	Metric 3:	Comparison Group	Low	The comparison groups belong to different studies (i.e., settings), exposed to different asbestos fiber types in different locations (as suggested by the limited descriptions provided on Table III). It is uncertain if they belonged to the same eligible population.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Medium	Based on additional review of related publications and the 1986 assessment, asbestos measurements were conducted using stand membrane filter technique of the US Public Health Service, presented in Nicholson 1976. Membrane filters were counted using PCM.
	Metric 5:	Exposure Levels	Medium	Based on information presented in the 1986 assessment and Nicholson 1976, cumulative exposures for workers were determined based on length of work history and asbestos fiber counts presented in Nichols 1976.
	Metric 6:	Temporality	High	Selikoff, 1979 presents complete data on years from exposure onset including 35+ years of follow-up. This study is part of the foundation establishing the latency of effect.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Medium	The authors did not provide details about how the outcome was diagnosed in the reviewed studies. Medium is the most appropriate rating but still does not adequately match with the study.
	Metric 8:	Reporting Bias	High	The authors reported results for the outcomes mentioned in the abstract, allowing a detailed extraction.
Domain 4: Potential Confounding / Variability Control				

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Study Citation: Peto, J., Seidman, H., Selikoff, I. J. (1982). Mesothelioma mortality in asbestos workers: implications for models of carcinogenesis and risk assessment. British Journal of Cancer 45(1):124-135.
Health Outcome: Mesothelioma
Target Organ(s): Mortality: Mesothelioma; Cancer/Carcinogenesis: Mesothelioma; Lung/Respiratory: Mesothelioma
Asbestos Fiber Type(s): Asbestos - Not specified: 1332-21-4; Asbestos - Amosite (grunerite): 12172-73-5; Asbestos - Chrysotile (serpentine): 12001-29-5; Asbestos - Crocidolite (riebeckite): 12001-28-4
Linked HERO ID(s): No linked references.
HERO ID: 165

Domain	Metric		Rating	Comments
	Metric 9:	Covariate Adjustment	Medium	Some adjustments were made (age, sex, years of exposure) but not described in detail. There is indirect evidence that appropriate adjustments were also made, e.g., the footnote on p. 130 indicates that the authors made assumptions of white male rates for all causes of death to adjust the authors ”lifelong risk” estimates.
	Metric 10:	Covariate Characterization	Medium	The methods used for confounder assessment are of unknown validity as details were not provided. They are likely provided from company or employment records.
	Metric 11:	Co-exposure Counfounding	N/A	Not applicable (mesothelioma outcome).
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	Medium	The authors used appropriate statistical methods (SMRs, survival relative risk) to report the distribution of mesothelioma mortality cases by age and years since first exposure.
	Metric 13:	Statistical Power	Medium	The number of subjects analyzed (n=17,800 for North American insulation workers, not including other cohorts in thi) is sufficiently large to detect the effect in the exposed population (reporting 236 cases of mesothelioma deaths).
	Metric 14:	Reproducibility of Analyses	Medium	Reviewing the relevant information across publications and the 1986 assessment provides sufficient detail to conceptually understand the analysis.
	Metric 15:	Statistical Analysis	Medium	Methods for calculating mortality risks are transparent.

Additional Comments: This article is a review. While it may reanalyze or represent analyses of Selikoff et al. 1979, it does not appear to be original data in any way. The measurement of exposure was uninformative as PCM or TEM were not mentioned, and details about exposure measurements were not provided. Fiber types are those reported by any study in the review.

Overall Quality Determination — Medium

* No biomarkers were identified for this evaluation.

Study Citation:	Rogers, A. J., Leigh, J., Berry, G., Ferguson, D. A., Mulder, H. B., Ackad, M. (1991). Relationship between lung asbestos fiber type and concentration and relative risk of mesothelioma. A case-control study. Cancer 67(7):1912-1920.
Health Outcome:	Mesothelioma
Target Organ(s):	Cancer/Carcinogenesis: Mesothelioma
Asbestos Fiber Type(s):	Asbestos - Crocidolite (riebeckite): 12001-28-4; Asbestos - Amosite (grunerite): 12172-73-5; Asbestos - Chrysotile (serpentine): 12001-29-5; Asbestos - Not specified: 1332-21-4
Linked HERO ID(s):	No linked references.
HERO ID:	3082405

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	High	This study employed a case-control study design. Cases were obtained from the Australian Mesothelioma Surveillance Program, which was in place from January 1, 1980 to December 31, 1985. Notifications to this program helped the authors obtain participants, and "voluntary notifications were sought from clinicians and pathologists throughout Australia" (Rogers et al., 1991). Cancer registries in each Australian state were examined for cross-checking purposes. The only individuals allowed into the study were those with a definite or probably mesothelioma diagnosis as determined by five experienced pathologists appointed by the Royal College of Pathologists of Australasia. There were 697 total cases with these diagnoses, but only 221 had lung tissue materials available. This included 209 individuals with a definite designation, and 12 with a probable designation.
	Metric 2:	Attrition	High	While there were 697 potential participants identified as having definite or probable mesothelioma diagnoses, only 221 cases were included in the analyses because of the availability of lung tissue samples. The authors mention that "postmortem material from five possible cases was also available but was excluded from the current study" (Rogers et al., 1991). No information was provided as to why these samples were excluded; however, this represented a minimal level of attrition.
	Metric 3:	Comparison Group	Low	This study utilized an unmatched method for obtaining controls. Formalin-preserved lung tissue was obtained for another study from consecutive autopsies at the Royal Prince Alfred Hospital in Sydney, Australia. These necropsies took place during the same time period as the cases. Exclusion criteria for these controls included pneumoconiosis, emphysema, pneumonia, or gastrointestinal cancer. 359 control samples were included in this study. They did mention that there was "reasonable frequency matching for age and sex" (Rogers et al., 1991).
Domain 2: Exposure Characterization				

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Study Citation:	Rogers, A. J., Leigh, J., Berry, G., Ferguson, D. A., Mulder, H. B., Ackad, M. (1991). Relationship between lung asbestos fiber type and concentration and relative risk of mesothelioma. A case-control study. Cancer 67(7):1912-1920.
Health Outcome:	Mesothelioma
Target Organ(s):	Cancer/Carcinogenesis: Mesothelioma
Asbestos Fiber Type(s):	Asbestos - Crocidolite (riebeckite): 12001-28-4; Asbestos - Amosite (grunerite): 12172-73-5; Asbestos - Chrysotile (serpentine): 12001-29-5; Asbestos - Not specified: 1332-21-4
Linked HERO ID(s):	No linked references.
HERO ID:	3082405

Domain	Metric		Rating	Comments
	Metric 4:	Measurement of Exposure	Medium	Overall, 0.5 gram tissue samples were prepared and used for the examination of fiber concentrations. Samples were filtered onto Millipore 0.8 um filters, which were then examined using light microscopy. Nuclepore 0.4 um filters were used for the examination with transmission electron microscopy. The authors only counted fibers that were > 2um (as determined by TEM), or > 5um (as determined by light microscopy). The sensitivity was 15,000 fibers/g for light microscopy, and 200,000 fibers/g for TEM. It is important to note that light microscopy fiber counts ”were made on all 221 cases and 359 controls. Electron microscopic fiber counts, EDAX, and fiber length measurements were made on all 221 cases and 103 male controls, drawn randomly from the total group of 276” (Rogers et al., 1991). Because these samples were examined in necropsied lung tissues, fiber concentrations were only determined at one point in time.
	Metric 5:	Exposure Levels	Medium	The range of exposures is sufficient to develop an exposure-response estimate.
	Metric 6:	Temporality	Low	The temporality of exposure and outcome is uncertain. However, because asbestos concentrations were estimated from lung tissue samples, it can reasonably be assumed that exposure preceded the outcome of mesothelioma.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	High	Mesothelioma diagnosis was determined by a panel of five experienced pathologists, who were all appointed by the Royal College of Pathologists of Australasia. Potential classifications included definite, probably, possible, and not mesothelioma based on histologic classification. The scores for determining these classifications were 1, 0.75, 0.50, and 0, respectively. Only definite and probably classifications were included in the study, and ”the definite diagnosis was regarded as the category with score nearest to the mean score” (Rogers et al., 1991).
	Metric 8:	Reporting Bias	High	Mesothelioma findings are reported throughout the study, and odds ratios are provided with their associated 95% confidence intervals.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	High	The authors described in their discussion section that they included age as a confounding variable, as it was a way to frequency match cases and controls.
	Metric 10:	Covariate Characterization	Low	The authors did not provide a description of the methods used for covariate characterization.
	Metric 11:	Co-exposure Counfounding	N/A	As this was a mesothelioma study, there was no need to evaluate potential co-exposures, as there are few other causes than asbestos exposure, meriting a ”not applicable” rating.
Domain 5: Analysis				

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Study Citation:	Rogers, A. J., Leigh, J., Berry, G., Ferguson, D. A., Mulder, H. B., Ackad, M. (1991). Relationship between lung asbestos fiber type and concentration and relative risk of mesothelioma. A case-control study. Cancer 67(7):1912-1920.
Health Outcome:	Mesothelioma
Target Organ(s):	Cancer/Carcinogenesis: Mesothelioma
Asbestos Fiber Type(s):	Asbestos - Crocidolite (riebeckite): 12001-28-4; Asbestos - Amosite (grunerite): 12172-73-5; Asbestos - Chrysotile (serpentine): 12001-29-5; Asbestos - Not specified: 1332-21-4
Linked HERO ID(s):	No linked references.
HERO ID:	3082405

Domain	Metric		Rating	Comments
	Metric 12:	Study Design and Methods	Medium	The study design implemented is appropriate for the research question being examined.
	Metric 13:	Statistical Power	Medium	The authors did not provide an explicit discussion of the power for this study, but there was an adequate number of participants to detect an effect in the exposed population.
	Metric 14:	Reproducibility of Analyses	Medium	Given the amount of detail provided by the authors, this study is reproducible. Overall, the authors calculated the relative risk, estimated by odds ratios. Fiber content levels were used to group participants, and each level was compared with the zero-exposure group, which was defined as <15,000 fibers by might microscopy, or <200,000 fibers by TEM. The significance of linear trends was determined with the Mantel-Haenszel chi-squared test. Multiple logistic regression models were also estimated.
	Metric 15:	Statistical Analysis	Medium	The model used for calculating the risk estimates is transparent. The logistics regression model operates under the assumption that the distribution of the outcome is binomial.
Domain 6: Other (if applicable) Considerations for Biomarker Selection and Measurement (Lakind et al. 2014)				
	Metric 16:	Use of Biomarker of Exposure	High	The examination of fiber concentrations in lung tissue allow for a quantitative relationship with external exposure. Even though there was the potential for multiple fiber types to be present in the study, the authors were able to identify the specific fiber types by "comparing the energy dispersive x-ray analysis (EDAX) spectrum of the fiber with those of the International Union Against Cancer (UICC) asbestos specimens prepared in the same manner" (Rogers et al., 1991).
	Metric 17:	Effect Biomarker	N/A	The only biomarkers assessed in this study were biomarkers of exposure, as the authors were examining fiber counts in lung tissue.
	Metric 18:	Method Sensitivity	Medium	The authors detailed the analytical sensitivity for both light microscopy and TEM. The sensitivity for light microscopy was 15,000 fibers per gram, and the limit was 200,000 fibers per gram for TEM.
	Metric 19:	Biomarker Stability	Low	The authors detail that the lung tissue was preserved in formalin, and they were generally comprised of a "5x5x5 cm blocks from the lower lobe of the uninvolved lung" (Rogers et al., 1991). They did not describe the storage history further or information pertaining to stability.
	Metric 20:	Sample Contamination	Medium	There is no information provided about the potential contamination of the samples.
	Metric 21:	Method Requirements	Medium	The authors utilized light microscopy and transmission electron microscopy to determine fiber concentrations.
	Metric 22:	Matrix Adjustment	Low	There was no description of matrix adjustments performed in this study.

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Study Citation:	Rogers, A. J., Leigh, J., Berry, G., Ferguson, D. A., Mulder, H. B., Ackad, M. (1991). Relationship between lung asbestos fiber type and concentration and relative risk of mesothelioma. A case-control study. Cancer 67(7):1912-1920.
Health Outcome:	Mesothelioma
Target Organ(s):	Cancer/Carcinogenesis: Mesothelioma
Asbestos Fiber Type(s):	Asbestos - Crocidolite (riebeckite): 12001-28-4; Asbestos - Amosite (grunerite): 12172-73-5; Asbestos - Chrysotile (serpentine): 12001-29-5; Asbestos - Not specified: 1332-21-4
Linked HERO ID(s):	No linked references.
HERO ID:	3082405

Domain	Metric	Rating	Comments
Additional Comments:	This study sought to examine the relationship between mesothelioma and asbestos fiber type and concentration found in postmortem lung tissue samples. One of the strengths of this study was that the authors utilized a panel of pathologists to identify, on a scale, a histologic classification of mesothelioma. Another strength was their use of TEM for the quantification of asbestos fibers. Some limitations included a lack of information surrounding storage and contamination for the lung tissue samples, as well as the temporality. However, because this study examined postmortem samples, it can still be assumed that exposure preceded the outcome.		

Overall Quality Determination Medium

Study Citation:	Roggli, V. L., Pratt, P. C., Brody, A. R. (1986). Asbestos content of lung tissue in asbestos associated diseases: a study of 110 cases. British Journal of Industrial Medicine 43(1):18-28.		
Health Outcome:	Mesothelioma		
Target Organ(s):	Lung/Respiratory: mesothelioma; Cancer/Carcinogenesis: mesothelioma		
Asbestos Fiber Type(s):	Asbestos - Amosite (grunerite): 12172-73-5; Asbestos - Crocidolite (riebeckite): 12001-28-4; Asbestos - Anthophyllite: 17068-78-9; Asbestos - Tremolite: 14567-73-8; Asbestos - Actinolite: 12172-67-7; Asbestos - Chrysotile (serpentine): 12001-29-5		
Linked HERO ID(s):	No linked references.		
HERO ID:	3083350		

Domain	Metric	Rating	Comments
Domain 2: Exposure Characterization			
	Metric 4: Measurement of Exposure	Low	Asbestos bodies in lung tissue samples were quantified by LM and SEM, post-mortem.
	Metric 5: Exposure Levels	Medium	The range and distribution of exposure is sufficient to develop an exposure-response estimate, which was done using a continuous measure of exposure.Median and range asbestos bodies (AB) exposures measured via LM were as follows:. Asbestosis: 106,000 (range: 2,400 – 684,000) AB/g. Mesothelioma: 550 (range: 0.2 – 13,3000) AB/g. Lung cancer: 102 (0.8 – 46,000) AB/g. Idiopathic pulmonary fibrosis: 9 (0.8 – 148) AB/g. Normal lungs: 3 (0.2 – 22) AB/g.

Additional Comments: Overall, information on the measurement of exposure metric (M4) to assess exposure was limited or rated low (authors used Asbestos bodies in lung tissue samples were quantified by LM and SEM, post-mortem). The exposure levels metric (M5) information reported was adequate to determine exposure-response relationships.

** As described in Appendix B.2 of the *White Paper: Quantitative Approach to the Human Health Assessment for the Risk Evaluation for Asbestos Part 2: Supplemental Evaluation Including Legacy Uses and Associated Disposals of Asbestos*, to be considered as being informative for dose-response analysis, metrics 4 and 5 would need metric ratings of Medium or High. This reference did not satisfy this requirement; therefore data quality evaluation is presented for only for metrics 4 and 5.

Study Citation:	Roggli, V. L., Vollmer, R. T., Butnor, K. J., Sporn, T. A. (2002). Tremolite and mesothelioma. Annals of Occupational Hygiene 46(5):447-453.
Health Outcome:	Mesothelioma
Target Organ(s):	Cancer/Carcinogenesis: mesothelioma
Asbestos Fiber Type(s):	Asbestos - Tremolite: 14567-73-8; Asbestos - Chrysotile (serpentine): 12001-29-5; Asbestos - Actinolite: 12172-67-7; Asbestos - Anthophyllite: 17068-78-9
Linked HERO ID(s):	No linked references.
HERO ID:	758980

Domain		Metric	Rating	Comments
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Medium	The authors indicated the use of scanning electron microscopy to analyze fiber presence on lung tissue samples, estimating the quantity of fibers present per gram of wet lung tissue.
	Metric 5:	Exposure Levels	Low	The authors only reported the median and range of fiber concentrations in lung samples as they related to the presence of mesothelioma (Table 1). Multivariate analyses were conducted using continuous measures of talc and chrysotile, but only as they related to the presence of tremolite and the presence of all three of tremolite, actinolite, and anthophyllite in lung tissue, rather than the presence of mesothelioma (Table 4).

Additional Comments: None

** As described in Appendix B.2 of the *White Paper: Quantitative Approach to the Human Health Assessment for the Risk Evaluation for Asbestos Part 2: Supplemental Evaluation Including Legacy Uses and Associated Disposals of Asbestos*, to be considered as being informative for dose-response analysis, metrics 4 and 5 would need metric ratings of Medium or High. This reference did not satisfy this requirement; therefore data quality evaluation is presented for only for metrics 4 and 5.

Study Citation:	Rubino, G. F., Piolatto, G., Newhouse, M. L., Scansetti, G., Aresini, G. A., Murray, R. (1979). Mortality of chrysotile asbestos workers at the Balangero Mine, northern Italy. Occupational and Environmental Medicine 36(3):187-194.
Health Outcome:	Mesothelioma
Target Organ(s):	Cancer/Carcinogenesis: Mesothelial malignancy occurrence; Lung/Respiratory: Mesothelial malignancy occurrence
Asbestos Fiber Type(s):	Asbestos - Chrysotile (serpentine): 12001-29-5
Linked HERO ID(s):	178, 6861719
HERO ID:	178

Domain		Metric	Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	High	The rating is based on asbestos part 1 evaluation description: ”Subjects included men from the Balangero mine worker cohort that were employed in an Italian asbestos mine. The initial cohort ((Rubino et al., 1979, HEROID: 178), pg 188) consisted of 952 men employed between 1/1/1930 and 12/31/1965, with at least 30 calendar days’ employment during that period.” and the description in the paper of interest (Ferrante et al., 2020, HEROID: 6861719: ”The cohort included 974 male workers employed for at least 6 months and active at the Balangero mine on 1st January 1946 or hired subsequently until the cessation of activity.” While these accounts differ, it is likely meant to suggest that only subjects with mortality, which began 1/1/46, are included in Ferrante et al., which extended mortality follow up to 5/31/2013.
	Metric 2:	Attrition	High	In Ferrante et al., 2020, HEROID: 6861719, only 21/974 (2%) workers were lost by follow up in 2013.
	Metric 3:	Comparison Group	Medium	As per asbestos part 1, this is rated high, however the paper in question Ferrante et al., 2020, HEROID 6861719 does not explicitly address this metric. As per asbestos part 1: ”The most complete data on comparison groups is available from the most recent follow-up (Pira et al., 2017). General population mortality rates using the whole country from 1955 until 1980 and specifically the Piedmont Region (where the mine is located) from 1981 onwards (no regional rates available prior to 1981). The 1955-1959 rates were applied to 1946-1954 period (no available data); this may have led to an underestimate of expected deaths which may have showed and increased rate during this period. Expected numbers of deaths (overall and selected cancers) were computed using age-specific and calendar-year-specific (5-year categories) male death rates (Pira et al., 2017) pg 559.”
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Medium	From asbestos part 1: ”Most complete report of exposure assessment is in initial cohort study ((Rubino et al., 1979) pg 189). Chrysotile fiber counts were first measured in 1969 using membrane filter collection and phase contrast microscopy (frequency not reported). To estimate exposure from 1946-1969, factory records on daily production, equipment used, characteristics of the job and number of hours/day were used (this method has considerable limitations due to basis on mean values for large job categories and no allowance for changes in weather). Simulated and measured data were made comparable by using weighting factors (e.g., more dusty operation for 1-2 hr/d compared with longer working hours in the past).”

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Study Citation:	Rubino, G. F., Piolatto, G., Newhouse, M. L., Scansetti, G., Aresini, G. A., Murray, R. (1979). Mortality of chrysotile asbestos workers at the Balangero Mine, northern Italy. Occupational and Environmental Medicine 36(3):187-194.
Health Outcome:	Mesothelioma
Target Organ(s):	Cancer/Carcinogenesis: Mesothelial malignancy occurrence; Lung/Respiratory: Mesothelial malignancy occurrence
Asbestos Fiber Type(s):	Asbestos - Chrysotile (serpentine): 12001-29-5
Linked HERO ID(s):	178, 6861719
HERO ID:	178

Domain	Metric		Rating	Comments
	Metric 5:	Exposure Levels	Medium	The range and distribution of the cumulative exposure is sufficient to develop exposure-response relations and the study reports 3 levels of exposure for analyses completed in Ferrante et al., 2020, HEROID: 6861719, table 3.
	Metric 6:	Temporality	High	Ferrante et al., 2020, HEROID: 6861719 presents appropriate temporality between the exposure to asbestos and the outcome of mesothelioma incidence, with follow up spanning into 2013.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	High	Ferrante et al., 2020, HEROID: 6861719 notes that mesothelioma cases were extracted form a regional registry.
	Metric 8:	Reporting Bias	High	Ferrante et al., 2020, HEROID: 6861719 reports Poisson regression outcomes with relative risks and 95% CIs.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Medium	Ferrante et al., 2020, HEROID: 6861719 adjusted for age explicitly and sex and race discretely based on the initial recruitment makeup of subjects, however there was no adjustment for smoking.
	Metric 10:	Covariate Characterization	High	Ferrante et al., 2020, HEROID: 6861719 used occupational data from employers: ”The list of cohort members and their working periods and job assignments were extracted from the factory rosters, stored after the mine bankruptcy in the Turin section of the Italian State Archives, where we had access to them.”
	Metric 11:	Co-exposure Counfounding	Low	Ferrante et al., 2020, HEROID: 6861719 did not adjust for coexposures.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	Medium	The study design (cohort with follow up and analyses of mesothelioma incidence counts by Poisson regression) was appropriate (Ferrante et al., 2020, HEROID: 6861719). However it is unclear why authors did not complete a Cox survival model.
	Metric 13:	Statistical Power	Medium	The number of participants (n=953) are adequate to detect an effect in the exposed population (Ferrante et al., 2020, HEROID: 6861719).
	Metric 14:	Reproducibility of Analyses	Medium	The description of the analysis is sufficient to understand how to conceptually reproduce the analysis with access to the analytic data (Ferrante et al., 2020, HEROID: 6861719).
	Metric 15:	Statistical Analysis	Low	Relative risks were calculated for mesothelioma incidence using Poisson regression, however model assumptions were not explicitly addressed (i.e., does outcome data fit the Poisson distribution?). Authors state only: ”95% CI were estimated assuming the Poisson distribution of observed cases.” However, it is unclear if they mean all outcomes or a specific one (potentially only mesothelioma).

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Study Citation:	Rubino, G. F., Piolatto, G., Newhouse, M. L., Scansetti, G., Aresini, G. A., Murray, R. (1979). Mortality of chrysotile asbestos workers at the Balangero Mine, northern Italy. Occupational and Environmental Medicine 36(3):187-194.
Health Outcome:	Mesothelioma
Target Organ(s):	Cancer/Carcinogenesis: Mesothelial malignancy occurrence; Lung/Respiratory: Mesothelial malignancy occurrence
Asbestos Fiber Type(s):	Asbestos - Chrysotile (serpentine): 12001-29-5
Linked HERO ID(s):	178, 6861719
HERO ID:	178

Domain	Metric	Rating	Comments
Additional Comments:	Evaluations were only completed for Ferrante et al., 2020, HEROID: 6861719 for mesothelioma analyses with results shown in table 3.		
Overall Quality Determination		**Medium**	

* No biomarkers were identified for this evaluation.

Study Citation:	Rödelsperger, K., Woitowitz, H. J., Brückel, B., Arhelger, R., Pohlabeln, H., Jöckel, K. H. (1999). Dose-response relationship between amphibole fiber lung burden and mesothelioma. Cancer Detection and Prevention 23(3):183-193.
Health Outcome:	Mesothelioma
Target Organ(s):	Cancer/Carcinogenesis: Mesothelioma; Lung/Respiratory: Mesothelioma
Asbestos Fiber Type(s):	Asbestos - Chrysotile (serpentine): 12001-29-5; Asbestos - Not specified: 1332-21-4; Asbestos - Amosite (grunerite): 12172-73-5; Asbestos - Crocidolite (riebeckite): 12001-28-4; Asbestos - Tremolite: 14567-73-8; Asbestos - Actinolite: 12172-67-7; Asbestos - Anthophyllite: 17068-78-9
Linked HERO ID(s):	3081025, 3080703
HERO ID:	3081025

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Medium	66 cases and 66 controls from five towns across seven clinical centers in West Germany between January 1, 1988 and December 31, 1991. Cases had definite diagnosis of diffuse malignant mesothelioma confirmed by a panel of pathologists. Inclusion criteria for cases included the presence of a lung tissue sample, for which only 66 of the 324 confirmed mesothelioma cases. The 66 controls were selected from a combined pool of 315 hospital patients treated by surgical lung resection for something other than mesothelioma and 182 population controls. Controls were matched to cases using age, sex, and region of residence. Both cases and controls needed to be of German nationality. It is unclear how many controls were sourced from the hospital patients and how many were sourced from the population.
	Metric 2:	Attrition	High	There was no reported subject withdrawal from the study of the matched 66 cases with lung tissue samples and controls and the outcome and exposure data were both largely complete.
	Metric 3:	Comparison Group	Medium	Cases and controls had to be of German nationality, had to be willing and able to give an interview, and had to provide written informed consent. Control group mostly had lung cancer, and for some of these controls lung cancer might be caused by an asbestos exposure, introducing possible bias. Controls were matched to cases according to age (±5 years), sex, and region of residence. It is unclear how many controls were sourced from hospital patients and how many were sourced from the population. Also, occupation was not used in matching criteria.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Medium	Lung tissue fiber analysis by TEM - single time point of measurement.
	Metric 5:	Exposure Levels	Medium	Unconditional logistic regression analysis of concentration of fibers longer than 5 µm from lung tissue on mesothelioma split the analysis sample into five categories of exposure: <0.05, 0.05-<0.1, 0.1-<0.2, 0.2-<0.5, and >=0.5 f/µg, and odds ratios compare odds of mesothelioma in each of the four upper exposure categories to the to the lowest exposure category.
	Metric 6:	Temporality	Low	The temporality of exposure and outcome is uncertain. Sources of data and details of methods of assessment were not sufficiently reported for duration of follow-up and periods of exposure.
Domain 3: Outcome Assessment				

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Study Citation:	Rödelsperger, K., Woitowitz, H. J., Brückel, B., Arhelger, R., Pohlabeln, H., Jöckel, K. H. (1999). Dose-response relationship between amphibole fiber lung burden and mesothelioma. Cancer Detection and Prevention 23(3):183-193.
Health Outcome:	Mesothelioma
Target Organ(s):	Cancer/Carcinogenesis: Mesothelioma; Lung/Respiratory: Mesothelioma
Asbestos Fiber Type(s):	Asbestos - Chrysotile (serpentine): 12001-29-5; Asbestos - Not specified: 1332-21-4; Asbestos - Amosite (grunerite): 12172-73-5; Asbestos - Crocidolite (riebeckite): 12001-28-4; Asbestos - Tremolite: 14567-73-8; Asbestos - Actinolite: 12172-67-7; Asbestos - Anthophyllite: 17068-78-9
Linked HERO ID(s):	3081025, 3080703
HERO ID:	3081025

Domain	Metric		Rating	Comments
	Metric 7:	Outcome Measurement or Characterization	High	Out of 450 incident patients with a suspicious diagnosis of diffuse malignant mesothelioma (DMM), 324 had a definite diagnosis confirmed by a panel of pathologists (66 of which were cases in this study).
	Metric 8:	Reporting Bias	High	Mesothelioma findings are reported in the abstract, results, and discussion sections. Odds ratios are reported with 95% confidence intervals, and the number of cases/controls that fall into each exposure category are reported as well.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Medium	Confounding was addressed by controlling for a continuous variable for age and binary variables for the clinical center (Hamburg/others) and sex. Race was not adjusted for in the models, and it is unclear if the study participants were of multiple races as this was not reported. Also, study authors had information on smoking habits but did not control for this information in models.
	Metric 10:	Covariate Characterization	Medium	It is assumed that confounder information was assessed from the standardized questionnaire to collect detailed occupational history that is mentioned in the methods section, though it is not clear from the study details exactly where confounder information was sourced.
	Metric 11:	Co-exposure Counfounding	N/A	Odds ratios related to Chrysotile and all ”other mineral fibers” were adjusted for the concentration of amphibole fibers longer than 5 μm.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	Medium	Case-control design was appropriate, and appropriate statistical methods (logistic regression) were used.
	Metric 13:	Statistical Power	Medium	With only 66 cases and 66 controls split into five exposure groups, the sample size is relatively small, but there is sufficient sample size to detect an effect. However, confidence intervals are very wide, suggesting imprecise estimates of effect due to the small number of cases/controls in each cell.
	Metric 14:	Reproducibility of Analyses	Medium	The description of the analysis is generally sufficient to understand how to conceptually reproduce the analysis with access to the analytic data, however the authors note that they perform a logarithmic transformation to asbestos and amphibole fiber concentrations, but they did not specify the base that was used.

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Study Citation:	Rödelsperger, K., Woitowitz, H. J., Brückel, B., Arhelger, R., Pohlabeln, H., Jöckel, K. H. (1999). Dose-response relationship between amphibole fiber lung burden and mesothelioma. Cancer Detection and Prevention 23(3):183-193.
Health Outcome:	Mesothelioma
Target Organ(s):	Cancer/Carcinogenesis: Mesothelioma; Lung/Respiratory: Mesothelioma
Asbestos Fiber Type(s):	Asbestos - Chrysotile (serpentine): 12001-29-5; Asbestos - Not specified: 1332-21-4; Asbestos - Amosite (grunerite): 12172-73-5; Asbestos - Crocidolite (riebeckite): 12001-28-4; Asbestos - Tremolite: 14567-73-8; Asbestos - Actinolite: 12172-67-7; Asbestos - Anthophyllite: 17068-78-9
Linked HERO ID(s):	3081025, 3080703
HERO ID:	3081025

Domain	Metric		Rating	Comments
	Metric 15:	Statistical Analysis	Medium	The method for calculating risk estimates is transparent. Study authors estimated odds ratios relating fiber concentrations in the lung to mesothelioma diagnoses. The authors explained that they log transformed the fiber concentrations because they were inherently right skewed distributions, and added 0.1 f/μg to each concentrations to avoid taking the logarithm of zero. Authors adjusted the odds ratios by age, sex, and region as these variables were used to match cases to controls.
Domain 6: Other (if applicable) Considerations for Biomarker Selection and Measurement (Lakind et al. 2014)				
	Metric 16:	Use of Biomarker of Exposure	High	Fibers present in the lung tissue samples were able to be classified into asbestos-specific categories of chrysotile and amphibole (with subcategories of amosite/crocidolite, actinolite/tremolite, and anthophyllite), and also measured for length. Lung fibers themselves are derived from multiple parent chemicals, but the lung fibers were able to be classified into asbestos-specific categories when appropriate.
	Metric 17:	Effect Biomarker	N/A	Health outcome was measured by diagnosis from a panel of pathologists, rather than a specific biomarker of effect.
	Metric 18:	Method Sensitivity	Low	Median detection limits were reported as 0.16 fibers/μg of dried lung tissue for fibers of all lengths and 0.029 fibers/μg dry weight for fibers longer than 5 μm. However, median concentrations of 0.02 fibers/μg dry weight are reported in Table III, calling into question the actual limit of detection.
	Metric 19:	Biomarker Stability	High	Detailed methodology for lung tissue fiber analysis by STEM were described in detail including low temperature ashing. No known losses during storage were reported.
	Metric 20:	Sample Contamination	Medium	There is no information included in the study about contamination.
	Metric 21:	Method Requirements	High	Scanning transmission electron microscope (TEM) was performed to examine asbestos fiber species together with other mineral fibers in human lung tissue. TEM is considered the best method for counting asbestos fibers.
	Metric 22:	Matrix Adjustment	N/A	Matrix adjustment is not required for assessment of lung fiber concentrations.

Additional Comments: Study could have been improved with higher sample size, as well as additional details about logarithmic adjustment, but the study contains data that could be potentially useful for dose-response in measuring the relationship between asbestos lung fiber concentrations and mesothelioma.

Overall Quality Determination — Medium

Study Citation:	Seidman, H. (1984). Short-term asbestos work exposure and long-term observation.
Health Outcome:	Mesothelioma
Target Organ(s):	Mortality: Pleural mesothelioma mortality, Peritoneal mesothelioma mortality, Mesothelioma (non-pleural and non-peritoneal) mortality; Lung/Respiratory: Pleural mesothelioma mortality, Peritoneal mesothelioma mortality, Mesothelioma (non-pleural and non-peritoneal) mortality; Cancer/Carcinogenesis: Pleural mesothelioma mortality, Peritoneal mesothelioma mortality, Mesothelioma (non-pleural and non-peritoneal) mortality
Asbestos Fiber Type(s):	Asbestos - Amosite (grunerite): 12172-73-5
Linked HERO ID(s):	No linked references.
HERO ID:	257

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	High	In this retrospective cohort study, Seidel et al 1984 (HEROID 257) examined cause-specific mortality in a cohort of male workers at an amosite asbestos factory in Paterson, NJ that operated from June 1941 to November 1954. The cohort was described as almost entirely white (mentioned in Seidman et al., 1979 HEROID 94625). This study excluded deaths in the first five years, analyzing mortality occurring 5-40 years after employment. Of all 933 men recruited to work from June 1941 to December 1945, this study excluded 113: 35 who worked with asbestos elsewhere (21 before starting and 14 afterwards); 40 who died within 5 years; and 38 lost to follow-up shortly after leaving the plant. The remaining 820 participants had worked at the facility for as little as one month up to several years. The mean age at employment was 41.9 years (50.8% aged >40 years). Three aspects of participant selection helped to limit bias. First, the study avoided healthy worker selection bias because all workers were eligible for inclusion regardless of date of initial employment, and regardless of duration of employment. In addition, the study used an exposure lag to reduce potential bias by taking disease latency into account: asbestos exposure at this plant may not have been causally related to disease outcomes with latency periods of ≥5 years. Finally, participants exposed to asbestos in other work settings were excluded.
	Metric 2:	Attrition	High	Only a few eligible workers (n=38) had been lost to follow-up at the start of this study. There was little additional attrition of the 820 participants in this follow-up through 1982, which included: 4 additional men lost to follow-up, and 5 who contributed person-time until starting asbestos work elsewhere (i.e., became ineligible; see p. 3). Of the 811 remaining men, 593 had died and 218 were still alive, accounting for the complete cohort. A later publication (Seidman et al., 1986, HEROID 290) reported similar numbers (5 lost to follow-up, 6 who began asbestos work elsewhere, 216 alive). Table 1 shows, for each 5-year period of follow-up, the number of workers at risk, the mean age of those workers, and the number of deaths that occurred, along with the small number lost to follow-up.
	Metric 3:	Comparison Group	High	Standardized mortality ratios were calculated comparing all eligible workers in the cohort to white male residents of New Jersey in the same 5-year age groups during the same calendar periods. The authors reported elsewhere (Seidman et al., 1979 HEROID 94625) that death rates from cancer in New Jersey were "among the highest in the United States". The choice of the state referent helped to account for the regional background rates of cancer mortality.

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Study Citation:	Seidman, H. (1984). Short-term asbestos work exposure and long-term observation.
Health Outcome:	Mesothelioma
Target Organ(s):	Mortality: Pleural mesothelioma mortality, Peritoneal mesothelioma mortality, Mesothelioma (non-pleural and non-peritoneal) mortality; Lung/Respiratory: Pleural mesothelioma mortality, Peritoneal mesothelioma mortality, Mesothelioma (non-pleural and non-peritoneal) mortality; Cancer/Carcinogenesis: Pleural mesothelioma mortality, Peritoneal mesothelioma mortality, Mesothelioma (non-pleural and non-peritoneal) mortality
Asbestos Fiber Type(s):	Asbestos - Amosite (grunerite): 12172-73-5
Linked HERO ID(s):	No linked references.
HERO ID:	257

Domain	Metric		Rating	Comments
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Low	No fiber or dust count measures were available for this facility. Estimates were based on measures taken in 1967, 1970 and 1971 at two other plants run by the same company (in Tyler, TX; Port Allegany, PA) making the same products with the same machinery. Details on sampling equipment and procedures, or references to obtain that information, were not provided. Dr. William Nicholson helped to "assign plausible estimates" to "particular jobs" (i.e., estimates were extrapolated from later measures at other facilities using professional judgment). There were no details on how data were used, no discussion of comparable ventilation/dust extraction, and no references cited. It is not possible to ascertain the likely validity of fiber count estimates. Fiber-years/cc for each worker were calculated by multiplying estimated fiber counts for each job duty by the duration of work in that post. The median count of fibers > 5µ per cc across jobs was 50; counts for a list of job titles were shown in Table 5 (e.g., 5 for office workers, 15 for inspectors and foremen, 50 for production supervisors, 100 for pulverizers). Potential sources of error noted by the authors included: (i) the tendency for industrial hygienists to over-sample dustier areas (counts too high, underestimate dose-response); (ii) the possibility that short-term workers "may have experienced an apprenticeship period in which they did some of the dirtier work in their department" (counts too low, over-estimate effect of short-term exposure); and (iii) lack of information on use of respirators (measurement error, uncertain if a source of bias). The study reports that there was a "concerted effort to have the Paterson plant workers use respirator protectors" although no details on compliance are provided.
	Metric 5:	Exposure Levels	Medium	Exposure was analyzed using categories of fiber-years/cc and work duration. Data were presented using 8 categories of fiber-years/cc (<6, 6-11.9, 12-24.9, 25-49.9, 50-99.9, 100-149.9, 150-249.9, 250+ fiber-years/cc), as well as dichotomized (<25 vs 25+ fiber-years/cc). Exposure duration was classified in 7 categories (<1 month, 1 month, 2 months, 3-5 months, 6-11 months, 1 year, 2+ years); boundaries for these periods were not provided. In addition, some analyses calculated SMRs classified by department of work (e.g., Table 11 in HEROID 257; see also Table XIII in Seidman et al, 1986 HEROID 290). Only incidence is provided for mesothelioma outcomes, with no statistical analysis.
	Metric 6:	Temporality	High	Temporality and duration of follow-up was appropriate for the outcomes evaluated (multiple cancers, mesothelioma, and asbestosis). Follow-up ranged from a minimum of 5 to a maximum of 40 years.
Domain 3: Outcome Assessment				

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Study Citation: Seidman, H. (1984). Short-term asbestos work exposure and long-term observation.
Health Outcome: Mesothelioma
Target Organ(s): Mortality: Pleural mesothelioma mortality, Peritoneal mesothelioma mortality, Mesothelioma (non-pleural and non-peritoneal) mortality; Lung/Respiratory: Pleural mesothelioma mortality, Peritoneal mesothelioma mortality, Mesothelioma (non-pleural and non-peritoneal) mortality; Cancer/Carcinogenesis: Pleural mesothelioma mortality, Peritoneal mesothelioma mortality, Mesothelioma (non-pleural and non-peritoneal) mortality
Asbestos Fiber Type(s): Asbestos - Amosite (grunerite): 12172-73-5
Linked HERO ID(s): No linked references.
HERO ID: 257

Domain	Metric		Rating	Comments
	Metric 7:	Outcome Measurement or Characterization	Medium	ICD codes for mesotheliomas were not provided or discussed. The authors reported the “best evidence (BE)” available to classify cause of death, in addition to death certificate (DC) information. Tables comparing BE and DE indicated that additional information increased the number of mesotheliomas identified, as well as knowledge of the site of mesotheliomas. Best evidence included additional information from autopsy, surgical specimens, x-ray films and clinical findings (Seidman et al., 1979 HEROID 94625). Details on BE sources used to characterize mesotheliomas were not discussed, but insights can be inferred from acknowledgements (e.g., see Seidman et al, 1986 HEROID 290), which mention receiving generous help from medical facilities including hospitals, pathologists, and state health departments, with several facilities and clinicians listed by name.
	Metric 8:	Reporting Bias	High	Information is presented for all outcomes described. The authors present details on the observed and expected numbers of deaths stratified by categories of exposure or time period, along with the resulting SMRs; statistical significance is indicated. There is no evidence of selective reporting.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Medium	Because of small numbers and limited data, analyses of mortality from mesothelioma were based on death rates per million-man years overall, stratified by follow-up time, and by indicators of exposure. Counts of mesotheliomas were also shown overall as well as stratified by exposure and duration of follow-up.
	Metric 10:	Covariate Characterization	Medium	Analyses specific to mesothelioma did not include covariates; no confounding bias was expected.
	Metric 11:	Co-exposure Counfounding	Low	In this occupational setting, potential co-exposures are not discussed. There is no information to suggest the presence of other important co-exposures in this setting. The factory supplied the US. Navy with asbestos insulation for the pipes, boilers, and turbines of its ships. The manufacturing procedures carried out in the factory were described on p. 5 of the manuscript (HEROID 257).
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	Medium	The retrospective cohort design was appropriate and mortality rates were calculated appropriately.
	Metric 13:	Statistical Power	Medium	Based on best evidence, there were 17 mesotheliomas identified during the 5-to-40-year follow-up (9 peritoneal, 8 pleural).
	Metric 14:	Reproducibility of Analyses	Medium	The descriptions of analyses are brief but adequate. Tables included detailed counts of deaths, including mesotheliomas.

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Study Citation:	Seidman, H. (1984). Short-term asbestos work exposure and long-term observation.
Health Outcome:	Mesothelioma
Target Organ(s):	Mortality: Pleural mesothelioma mortality, Peritoneal mesothelioma mortality, Mesothelioma (non-pleural and non-peritoneal) mortality; Lung/Respiratory: Pleural mesothelioma mortality, Peritoneal mesothelioma mortality, Mesothelioma (non-pleural and non-peritoneal) mortality; Cancer/Carcinogenesis: Pleural mesothelioma mortality, Peritoneal mesothelioma mortality, Mesothelioma (non-pleural and non-peritoneal) mortality
Asbestos Fiber Type(s):	Asbestos - Amosite (grunerite): 12172-73-5
Linked HERO ID(s):	No linked references.
HERO ID:	257

Domain	Metric	Rating	Comments
	Metric 15: Statistical Analysis	Medium	Death rates per million person-years were calculated for mesothelioma. As the authors note, person-years were limited due to the high mortality in the cohort.

Additional Comments: This retrospective cohort study evaluated mortality in 820 workers at an amosite factory in New Jersey that operated between 1941 and 1954. Workers were almost exclusively white males. The authors reduced the likelihood of healthy worker selection bias by including all workers who were not exposed to asbestos elsewhere regardless of date of initial employment, and regardless of duration of employment. The authors were able to access medical records that appear to have improved the characterization of outcomes such as mesotheliomas (e.g., see Selikoff et al., 1992 HEROID 709720). With a high mean age at initial employment (>40 years) mortality was high even after relatively short follow-up. Employment patterns facilitated the analysis of mortality in workers with as little as one month of work. The study estimated death rates per million man-years for mesotheliomas overall and for two sites (pleural, peritoneal) stratified by exposure in fiber-years/cc (observed as low as 6-11.9 fiber-years/cc) and by duration of time worked (observed as low as 2 months). The major weakness of the study is that fiber count data were not available for this facility. Estimates were extrapolated based on measures taken at later dates at other locations operated by the same company, based on professional judgment. Validity of these estimates cannot be ascertained.

Overall Quality Determination — Medium

* No biomarkers were identified for this evaluation.

Study Citation:	Seidman, H., Selikoff, I. J., Gelb, S. K. (1986). Mortality experience of amosite asbestos factory workers: Dose-response relationships 5 to 40 years after onset of short-term work exposure. American Journal of Industrial Medicine 10(5-6):479-514.
Health Outcome:	Mesothelioma
Target Organ(s):	Cancer/Carcinogenesis: All cancer, lung cancer, pleural mesothelioma, peritoneal mesothelioma, mesothelioma non-specified, larynx buccal and pharynx cancer, esophagus cancer, stomach cancer, colon-rectum cancer, kidney cancer, bladder cancer, pancreas cancer, other and unspecified cancer mortality, Pleural mesothelioma mortality, Mesothelioma (not specified) mortality; Mortality: Pleural mesothelioma mortality, Peritoneal mesothelioma mortality, Mesothelioma (not specified) mortality; Lung/Respiratory: Peritoneal mesothelioma mortality, Mesothelioma (not specified) mortality
Asbestos Fiber Type(s):	Asbestos - Amosite (grunerite): 12172-73-5
Linked HERO ID(s):	No linked references.
HERO ID:	290

Domain	Metric		Rating	Comments
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Low	This metric is rated Low because the study or any cited methods source does not explicitly mention the use of PCM or TEM.Authors state that there was ”no direct observations of fiber counts in this factory”. Instead, fiber counts from other Paterson factories were used in this study. There is more information of the earlier version of this study, which reports that that Paterson factory used the same fibers and followed the same production process. Samples were made in October 1971 and followed ”5u + fibers averaged as high as 23 fibers/ml (Seidman et al., 1979). There is no defining of what tools were used to measure fibers in either study.
	Metric 5:	Exposure Levels	Medium	Range of exposure is appropriate, as it ranges in elapsed number of years since onset of work as 5-9 years, 5-14 years, 5-19 years, 5-24 years, 5-29 years, 5-34 years, and 5-39 years. However, the exposure dose is not based on fiber concentration but on exposure time.

Additional Comments: Please note that this study would not be fully evaluated under the current guidelines. This is due to the low rating for metric 4, as no PCM or TEM was mentioned in the study or a cited source.This study is a follow-up to RefID 94625 by the same authors. Comments referencing this study will be cited as (Seidman et al., 1979).Overall, this study provides an analysis of workers from the Paterson factory to that of the general New Jersey population. There is some discrepancy when it comes to the race of the cohort and the comparison groups, and age is not provided in the study. Confidence intervals are also not provided in the study results of SMRs and SIRs, but significant is noted when appropriate.

* No biomarkers were identified for this evaluation.

** As described in Appendix B.2 of the *White Paper: Quantitative Approach to the Human Health Assessment for the Risk Evaluation for Asbestos Part 2: Supplemental Evaluation Including Legacy Uses and Associated Disposals of Asbestos*, to be considered as being informative for dose-response analysis, metrics 4 and 5 would need metric ratings of Medium or High. This reference did not satisfy this requirement; therefore data quality evaluation is presented for only for metrics 4 and 5.

Study Citation:	Smailyte, G., Kurtinaitis, J., Andersen, A. (2004). Cancer mortality and morbidity among Lithuanian asbestos-cement producing workers. Scandinavian Journal of Work, Environment and Health 30(1):64-70.
Health Outcome:	Mesothelioma
Target Organ(s):	Cancer/Carcinogenesis: Pleura cancer (mesothelioma); Lung/Respiratory: Pleura cancer (mesothelioma)
Asbestos Fiber Type(s):	Asbestos - Chrysotile (serpentine): 12001-29-5
Linked HERO ID(s):	No linked references.
HERO ID:	3080235

Domain	Metric		Rating	Comments
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Low	No measurements were taken at factory A, so no data is available. Factory B had annual dust mass measurements from 1975-1993, and fibers per milliliter were available for 1996-1998. There was no discussion of the tools used to ascertain these measurements.This metric is rated low because the study or any cited methods source does not explicitly mention the use of PCM or TEM.
	Metric 5:	Exposure Levels	Low	The authors report the concentrations of asbestos in factory B varied from 1.9-4.0 mg/m^3 for 1975-89, and was 1.2-2.2 mg/m^3 from 1990-1993. In 1996-1998, fiber measurement shows the concentration 0.5-1.0 f/ml. These values are only available for factory B as no measurements were taken at facility A.

Additional Comments:	With regards to mesothelioma outcomes, there is not a lot of information provided. Only one female participant had a case of mesothelioma, and the authors included expected numbers of mesothelioma cases in men. The lack of data on asbestos concentrations in one of the factories examined may also limit the results discussed in the paper.NOTE: Metric 4 was rated as low because there was no mention of PCM or TEM in the study or any cited source. Under current guidelines, this would have resulted in the evaluation not being completed.

* No biomarkers were identified for this evaluation.

** As described in Appendix B.2 of the *White Paper: Quantitative Approach to the Human Health Assessment for the Risk Evaluation for Asbestos Part 2: Supplemental Evaluation Including Legacy Uses and Associated Disposals of Asbestos*, to be considered as being informative for dose-response analysis, metrics 4 and 5 would need metric ratings of Medium or High. This reference did not satisfy this requirement; therefore data quality evaluation is presented for only for metrics 4 and 5.

Study Citation:	Sullivan, P. A. (2007). Vermiculite, respiratory disease, and asbestos exposure in Libby, Montana: update of a cohort mortality study. Environmental Health Perspectives 115(4):579-585.
Health Outcome:	Mesothelioma
Target Organ(s):	Mortality: Mesothelioma mortality; Lung/Respiratory: Mesothelioma mortality; Cancer/Carcinogenesis: Mesothelioma mortality
Asbestos Fiber Type(s):	Asbestos- Libby amphibole: 1318-09-8; Asbestos- Richterite: 17068-76-7; Asbestos - Winchite: 12425-92-2; Asbestos - Tremolite: 14567-73-8
Linked HERO ID(s):	709497, 709457, 711560, 2238712
HERO ID:	709497

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Medium	Subjects were vermiculite miners, millers, and processors from a mine operating in Libby, Montana. The authors specify that some subjects may have been "assigned jobs in the screening plant, railroad loading dock, expansion plants, or an office located in the town of Libby (several miles from the mine)." The cohort was designed to include all white males hired at Libby from September 1935 to December 1981, and the total cohort was identified in May 1982 and subjects were followed through December 2001. It is not clear exactly how subjects were recruited or identified, though it is likely that the authors used data from an existing NIOSH database. Demographic data was collected from a NIOSH database and then validated against microfilm company records. One person originally identified (presumably from the NIOSH database) was removed due to company records stating that the employee never actually worked. After excluding 9 participants for missing demographic data, there were 1,871 study subjects. However, after additional exclusions based on missing outcome data and to limit the analysis sample to only white men, the final analytic sample consisted of 1,672 workers (Sullivan et al. 2007 HERO ID: 709497).Moolgavkar et al. 2010 (HERO ID: 709457) used the same cohort as Sullivan et al. 2007 (HERO ID: 709497) but they also excluded 10 individuals were missing vital status and thus resulted in a final analytic sample of 1,662.
	Metric 2:	Attrition	High	In Sullivan et al. 2007 (HERO ID: 709497), after 1,871 subjects were identified for inclusion, 104 were excluded due to not being white males, and 95 were exclude due to dying or being lost to follow-up before 1960. Prior to 1960 comparison rates for asbestosis in NIOSH Life Table Analysis system were not available, requiring exclusion from the analysis sample. In Moolgavkar et al. 2010 (HERO ID: 709457) an additional 10 participants were excluded due to missing vital status, although it is not clear how these cases were handled in the original study. There is overall a low rate of attrition and it is unlikely to be influenced by both exposure and outcome.
	Metric 3:	Comparison Group	Medium	In Sullivan et al. 2007 (HERO ID: 709497) and SMRs were calculated as the primary statistical analysis. Reference mortality rates were pulled from the NIOSH Life Table Analysis system. It is not specified whether this reference population was the general US population or an occupational-only population. Since the analysis samples only contained white males, there was no need to adjust by race or sex. However, SMRs were adjusted for age at risk and calendar-year of follow-up in Sullivan et al. 2007 (HERO ID: 709497). Moolgavkar et al. 2010 (HERO ID: 709457) also performed a regression analysis for mesothelioma that did not report any adjustments.

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Study Citation:	Sullivan, P. A. (2007). Vermiculite, respiratory disease, and asbestos exposure in Libby, Montana: update of a cohort mortality study. Environmental Health Perspectives 115(4):579-585.
Health Outcome:	Mesothelioma
Target Organ(s):	Mortality: Mesothelioma mortality; Lung/Respiratory: Mesothelioma mortality; Cancer/Carcinogenesis: Mesothelioma mortality
Asbestos Fiber Type(s):	Asbestos- Libby amphibole: 1318-09-8; Asbestos- Richterite: 17068-76-7; Asbestos - Winchite: 12425-92-2; Asbestos - Tremolite: 14567-73-8
Linked HERO ID(s):	709497, 709457, 711560, 2238712
HERO ID:	709497

Domain	Metric		Rating	Comments
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Medium	In this cohort, all studies used the exact same method of assessing exposure through quantification using PCM and assignment to participants via a job-exposure matrix, based on one used in an earlier NIOSH study (Amandus and Wheeler, 1987 HERO ID: 29839). In Sullivan et al. 2007 (HERO ID: 709497) and Moolgavkar et al. 2010 (HERO ID: 709457) adjustments to the JEM were made, most notably to assign workers with the "common laborer" job assignments or unknown job assignments the average estimated exposure intensity for all unskilled jobs, as opposed to using the relatively low exposure estimate for the mill yard in Libby. Thus, estimates of cumulative exposure were higher in this cohort study than other studies using the same JEM. Additionally, obtaining work histories for these studies resulted in additional jobs that were not detailed in the original NIOSH JEM. Exposure estimates for these jobs and corresponding calendar periods were extrapolated based on review of exposure records from other studies of Libby workers and professional judgment. Work history to assign exposure was gathered from a NIOSH database created in the 1980's and was validated against microfilm company records. The authors do not specify how many samples were analyzed for use in the JEM. In statistical analysis results were presented in terms of cumulative exposure (fiber/cc-years).
	Metric 5:	Exposure Levels	Medium	All studies in the cohort have an adequate distribution of exposure to detect an effect. All studies report at least three levels of exposure or use a continuous model of exposure in their SMR analyses.
	Metric 6:	Temporality	High	In all studies there was a minimum of 20 years of follow-up since a participant's first exposure, and the workers hired earliest had >65 years of prior exposure data since the study was designed to capture those employed between 1935 and 1981.
Domain 3: Outcome Assessment				

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Study Citation: Sullivan, P. A. (2007). Vermiculite, respiratory disease, and asbestos exposure in Libby, Montana: update of a cohort mortality study. Environmental Health Perspectives 115(4):579-585.
Health Outcome: Mesothelioma
Target Organ(s): Mortality: Mesothelioma mortality; Lung/Respiratory: Mesothelioma mortality; Cancer/Carcinogenesis: Mesothelioma mortality
Asbestos Fiber Type(s): Asbestos- Libby amphibole: 1318-09-8; Asbestos- Richterite: 17068-76-7; Asbestos - Winchite: 12425-92-2; Asbestos - Tremolite: 14567-73-8
Linked HERO ID(s): 709497, 709457, 711560, 2238712
HERO ID: 709497

Domain	Metric		Rating	Comments
	Metric 7:	Outcome Measurement or Characterization	Medium	Vital status was determined through 2001 by the National Death Index resources, the Social Security Administration resources, the internet (Ancestry.com; RootsWeb.com, and electronic links to state death records). And a tracking service. Workers found to be alive on or after 1/1/1979, when the National Death Index tracking began, but not found in the Index, were assumed to be alive as of 12/31/2001. Vital status follow-up was successful for 97.8% of the cohort. While some of the resources have a high degree of certainty, others such as the internet-based resources are of questionable quality. There is no explanation of what percentage each resource was used to ascertain vital status, but the more reliable method such as National Death Index are likely to be more informative and thus used more often. Thus, while there is some uncertainty that the vital status ascertainment was fully accurate, it is unlikely that a significant number of participants would have their vital status changed or that this would be related to their exposure status. .For 97% of the participants known to be deceased, exact cause of death was pulled from death certificates and coded using the ICD codes relevant at the time of death, ranging from ICD-8 to ICD-10. Deaths prior to 1979 were coded by a single National Center for Health Statistics-trained nosologist; after 1979 ICD codes were obtained from the National Death Index. Final results present ICD-9 codes, so it can be assumed that all codes were converted to that system, although their methodology is not explained.The ICD-10 code presented for mesothelioma was reported as C45.
	Metric 8:	Reporting Bias	High	All stated outcomes are reported in the results.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Medium	In Sullivan et al. 2007 (HERO ID: 709497) SMRs were calculated and the sample only included white males, so there was no need to adjust for race and gender. Sullivan et al. 2007 (HERO ID: 709497) state that they also adjusted for age at risk and calendar year of follow-up. Moolgavkar et al. 2010 (HERO ID: 709457) also performed a Cox proportional hazards model analysis in which they adjusted for year of birth. They state that they used year of birth as a “rough surrogate” for smoking habits as well, which is not a sufficient consideration for smoking.
	Metric 10:	Covariate Characterization	Medium	All covariate information was obtained from the NIOSH database and cross-checked against microfilmed company records.
	Metric 11:	Co-exposure Counfounding	Low	In this occupational setting, no co-exposures are adjusted for. Sullivan et al. 2007 (HERO ID: 709497) notes that there was insufficient data to estimate exposure to other contaminants such as diesel particulate generated by mine machinery, or exposure to silica.
Domain 5: Analysis				

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Study Citation:	Sullivan, P. A. (2007). Vermiculite, respiratory disease, and asbestos exposure in Libby, Montana: update of a cohort mortality study. Environmental Health Perspectives 115(4):579-585.
Health Outcome:	Mesothelioma
Target Organ(s):	Mortality: Mesothelioma mortality; Lung/Respiratory: Mesothelioma mortality; Cancer/Carcinogenesis: Mesothelioma mortality
Asbestos Fiber Type(s):	Asbestos- Libby amphibole: 1318-09-8; Asbestos- Richterite: 17068-76-7; Asbestos - Winchite: 12425-92-2; Asbestos - Tremolite: 14567-73-8
Linked HERO ID(s):	709497, 709457, 711560, 2238712
HERO ID:	709497

Domain	Metric		Rating	Comments
	Metric 12:	Study Design and Methods	Medium	The use of SMRs and regression analyses to understand the long-term impact of asbestos exposure on mortality is appropriate. The use of a cohort design is also appropriate to assess outcomes with a long latency such as lung cancer.
	Metric 13:	Statistical Power	Medium	The number of participants used in the analysis sample varies by study but is always sufficiently large to detect an effect. Sullivan et al. 2007 (HERO ID: 709497) had a final analysis sample of 1,672; Moolgavkar et al. 2010 (HERO ID: 709457) had a final analysis sample of 1,662. There is not a significant discussion of power, but Sullivan et al. 2007 (HERO ID: 709497) states that the study has low power for lung cancer outcomes at lower exposure levels. There are some potential concerns for low power since the overall incidence of mesothelioma was low (n=2).
	Metric 14:	Reproducibility of Analyses	Medium	While several details are not explained in detail, such as how the ICD-8 through ICD-10 codes were converted to ICD-9 codes, overall the descriptions of methods across the cohort are detailed enough that it would be possible to reproduce the results given access to the analytic data.
	Metric 15:	Statistical Analysis	Medium	While there is no formal discussion of assumptions in statistical models in both Sullivan et al. 2007 (HERO ID: 709497) and Bateson et al. 2014 (HERO ID: 2238712, there are no assumptions in SMR or Cox proportional hazards model that would reasonably expect to be unmet. Moolgavkar et al. 2010 (HERO ID: 709457) contains those same analyses without a formal discussion of assumptions, but also analyses mesothelioma using a maximum likelihood equation in which they assume a Poisson distribution.

Additional Comments: In these cohort studies of Libby, Montana employees exposure was measured via PCM and assigned using a JEM. Participants were followed up for a minimum of 20 years from first exposure, and mortality outcomes were examined in relation to asbestos exposure through SMR and regression analysis. While there is some potential for outcome and exposure misclassification, the impact of potential misclassification is unlikely to significantly bias the results of the cohort. Significant effects were found mesothelioma mortality across the cohort.The measurement exposure (M4) and/or exposure levels (M5) metrics are rated as medium upon review by both set of reviewers. Also, the overall quality determination (OQD) is rated medium. Extraction has been completed and quality control reviewed.

Overall Quality Determination **Medium**

* No biomarkers were identified for this evaluation.

Study Citation:	Szeszenia-Dąbrowska, N., Wilczyńska, U., Szymczak, W., Strzelecka, A. (2002). Mortality study of workers compensated for asbestosis in Poland, 1970-1997. International Journal of Occupational Medicine and Environmental Health 15(3):267-278.
Health Outcome:	Mesothelioma
Target Organ(s):	Lung/Respiratory: Pleural mesothelioma; Mortality: Pleural mesothelioma
Asbestos Fiber Type(s):	Asbestos - Not specified: 1332-21-4
Linked HERO ID(s):	No linked references.
HERO ID:	3080436

Domain	Metric		Rating	Comments
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Low	Study authors mentioned that weighted asbestos concentrations were typically used until 1981 for assessing exposure. They did not provide any information about measurement tools such as midget impingers, TEM, or PCM.
	Metric 5:	Exposure Levels	Medium	Table 4 displays the distribution of the cohort by cumulative dose of asbestos fibers for most of the cohort. This distribution and range of exposure was sufficient to assess exposure-outcome relationships.

Additional Comments: This study assessed the risk of asbestos-related malignancies (including mesothelioma) among persons with diagnosed asbestosis. In terms of exposure, the authors used weighted asbestos concentrations to assessing exposures. They did not provide any information about measurement tools such as midget impingers, TEM, or PCM. On the other hand, they used ICD-9 codes to ascertain health and mortality outcomes.While information on the measurement of exposure metric (M4) to assess exposure was limited or rated low. The exposure levels metric (M5) information reported was adequate or rated medium to determine exposure-response relationships. The overall rating for this outcome/study is medium.

* No biomarkers were identified for this evaluation.

** As described in Appendix B.2 of the *White Paper: Quantitative Approach to the Human Health Assessment for the Risk Evaluation for Asbestos Part 2: Supplemental Evaluation Including Legacy Uses and Associated Disposals of Asbestos*, to be considered as being informative for dose-response analysis, metrics 4 and 5 would need metric ratings of Medium or High. This reference did not satisfy this requirement; therefore data quality evaluation is presented for only for metrics 4 and 5.

Study Citation:	Tuomi, T., Huuskonen, M. S., Virtamo, M., Tossavainen, A., Tammilehto, L., Mattson, K., Lahdensuo, A., Mattila, J., Karhunen, P., Liippo, K. (1991). Relative risk of mesothelioma associated with different levels of exposure to asbestos. Scandinavian Journal of Work, Environment and Health 17(6):404-408.
Health Outcome:	Mesothelioma
Target Organ(s):	Lung/Respiratory: Mesothelioma; Cancer/Carcinogenesis: Mesothelioma
Asbestos Fiber Type(s):	Asbestos - Not specified: 1332-21-4
Linked HERO ID(s):	No linked references.
HERO ID:	3082320

Domain	Metric		Rating	Comments
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Low	Exposure was assessed during one time period during diagnostic thoracotomy or autopsy. Though the authors stated that asbestos fibers in lung tissues were counted both by TEM and SEM in the method section, the result section reported exposure data measured by SEM only.
	Metric 5:	Exposure Levels	Medium	The study provided a range of exposure groups (overall 2 exposure groups: < 1 x 10^6 and >= 1 x 10^6 fibers/g dry tissue. For the ones >= 1 x 10^6, 3 groups were further reported: > 10 x 10^6, 100 x 10^6, and 1000 x 10^6 fibers/g dry tissue).

Additional Comments: QC was not completed for metrics other than Metrics 4 and 5 because the study does not have sufficient exposure information to be useful for dose-response analysis. The authors mentioned using TEM to develop quantitative estimates of exposure but only reported SEM results, resulting in a low confidence level for metric 4,

** As described in Appendix B.2 of the *White Paper: Quantitative Approach to the Human Health Assessment for the Risk Evaluation for Asbestos Part 2: Supplemental Evaluation Including Legacy Uses and Associated Disposals of Asbestos*, to be considered as being informative for dose-response analysis, metrics 4 and 5 would need metric ratings of Medium or High. This reference did not satisfy this requirement; therefore data quality evaluation is presented for only for metrics 4 and 5.

Study Citation:	Visona, S. D., Capella, S., Bodini, S., Borrelli, P., Villani, S., Crespi, E., Frontini, A., Colosio, C., Belluso, E. (2021). Inorganic Fiber Lung Burden in Subjects with Occupational and/or Anthropogenic Environmental Asbestos Exposure in Broni (Pavia, Northern Italy): An SEM-EDS Study on Autoptic Samples. International Journal of Environmental Research and Public Health 18(4):2053-2053.
Health Outcome:	Mesothelioma
Target Organ(s):	Lung/Respiratory: Mesothelioma; Mortality: Mesothelioma
Asbestos Fiber Type(s):	Asbestos - Chrysotile (serpentine): 12001-29-5; Asbestos - Crocidolite (riebeckite): 12001-28-4; Asbestos - Amosite (grunerite): 12172-73-5; Asbestos - Tremolite: 14567-73-8; Asbestos - Actinolite: 12172-67-7; Asbestos - Anthophyllite: 17068-78-9
Linked HERO ID(s):	No linked references.
HERO ID:	7460031

Domain	Metric		Rating	Comments
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Low	Asbestos fiber concentration in lung tissue samples collected at forensic autopsy was measured via Scanning Electron Microscope (SEM) and type of fiber was examined via energy dispersive spectroscopy (EDS). Both fiber level and asbestos body (AB) load was measured on a 2mm^2 filter area at 2000M. In analyses, the following groupings were made to assess type of fiber: chrysotile/asbestiform antigorite, tremolite/actinolite asbestos. Exposure was measured in autopsied lungs, thus the measurements represent a single time period but likely qualify cumulative asbestos exposures.Unfortunately, the exposure was assessed using a quantitative method other than PCM or TEM and conversion factors were not determined.
	Metric 5:	Exposure Levels	Low	The range and distribution of exposure are not adequate to develop an exposure-response estimate.

Additional Comments:	This case-control study had largely adequate approaches to assessing the relationship between asbestos exposure and mesothelioma. A primary weakness of the study is the approach to statistical analyses, as the Mann-Whitney test fails to allow for the inclusion of covariates. The methods for measuring exposure and identifying mesothelioma mortality were appropriate.

** As described in Appendix B.2 of the *White Paper: Quantitative Approach to the Human Health Assessment for the Risk Evaluation for Asbestos Part 2: Supplemental Evaluation Including Legacy Uses and Associated Disposals of Asbestos*, to be considered as being informative for dose-response analysis, metrics 4 and 5 would need metric ratings of Medium or High. This reference did not satisfy this requirement; therefore data quality evaluation is presented for only for metrics 4 and 5.

Study Citation:	Wang, X. R., Yu, I. T. S., Qiu, H., Wang, M. Z., Lan, Y. J., Tse, L. Y., Yano, E., Christiani, D. C. (2012). Cancer mortality among Chinese chrysotile asbestos textile workers. Lung Cancer 75(2):151-155.
Health Outcome:	Mesothelioma
Target Organ(s):	Lung/Respiratory: lung cancer mortality, nonmalignant respiratory disease mortality, asbestosis mortality, mesothelioma mortality
Asbestos Fiber Type(s):	Asbestos - Chrysotile (serpentine): 12001-29-5
Linked HERO ID(s):	No linked references.
HERO ID:	2638749

Domain		Metric	Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Medium	This prospective occupational study examined the health effects of asbestos exposure among a group of workers from an asbestos textile factory in China. Male workers were included in the study if they were registered workers in the factory on January 1972 and did not have signs of malignant tumors. Follow up continued through 2008. 586 workers were recruited for the original cohort, and 577 workers remained through the follow up period (98.5% participation rate at final follow up). While the study boasts a high participation rate, it is unclear what percentage of the total eligible workers were initially recruited in 1972, preventing a high rating in this domain.
	Metric 2:	Attrition	High	This study had a participation rate of 98.5% at the final follow up, a high rate that minimizes concerns about bias introduced via subject attrition. Analyses were limited to the 577 subjects that had complete follow up information. Outcome and exposure data are complete for study subjects.
	Metric 3:	Comparison Group	High	Authors provide a description of comparisons between the three exposure groups and noted differences in age, exposure duration, and smoking in the three groups. These variables were included as cofounders in Cox proportional hazard models, thus effectively controlling for the differences between the groups.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Medium	Asbestos levels in the factory were quantitatively measured via TEM in 1982 and 2006, with an assertion that levels remained over 2 mg/m^3 during the study period. Personal sampling was conducted to assess the levels in different areas of the factory, which was ultimately used to construct three exposure groups (high, medium, low). Authors note that 70% of the workers had stable positions in the factory for the duration of the study. These positions were used to place workers into exposure categories. While these exposure estimates were based on quantitative measures and the role in the factory, there is still potential for nondifferential misclassification of exposure due to the limited quantitative measuring and the lack of specificity about those who did have varying roles during their employment.
	Metric 5:	Exposure Levels	Medium	Exposure categories were high, medium, and low, based on the job description of workers and sampling results from the factory.
	Metric 6:	Temporality	High	This study has over 30 years of follow-up, and subjects did not have signs of malignancies during recruitment. This is an appropriate timeframe to assess mesothelioma with a latency period of 20 years.

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Study Citation:	Wang, X. R., Yu, I. T. S., Qiu, H., Wang, M. Z., Lan, Y. J., Tse, L. Y., Yano, E., Christiani, D. C. (2012). Cancer mortality among Chinese chrysotile asbestos textile workers. Lung Cancer 75(2):151-155.
Health Outcome:	Mesothelioma
Target Organ(s):	Lung/Respiratory: lung cancer mortality, nonmalignant respiratory disease mortality, asbestosis mortality, mesothelioma mortality
Asbestos Fiber Type(s):	Asbestos - Chrysotile (serpentine): 12001-29-5
Linked HERO ID(s):	No linked references.
HERO ID:	2638749

Domain	Metric		Rating	Comments
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Uninformative	Authors note that two deaths from mesothelioma were identified among the study cohort. One case was pleural and one peritoneal. Deaths were identified through employment records and through municipal registries. There is no indication that ICD codes were used to identify the cases, nor that death records captured non-site specific cases of mesothelioma.
	Metric 8:	Reporting Bias	Medium	Authors report two mesothelioma cases in the results and discussion, but do not report quantitative results (effect estimates with confidence intervals, etc.) that would be useful for extraction).
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	High	The authors appropriately adjust for variables that vary among the three exposure groups. Age, duration of exposure, and smoking were included as covariates in Cox proportional hazard models.
	Metric 10:	Covariate Characterization	Medium	Data on covariates was collected from factory records. Additionally, smoking information was collected from individuals via interview or from family members via interview. There was no indication of validation of factory records, though the records can be assumed to be fairly accurate, thus meriting a medium rating.
	Metric 11:	Co-exposure Counfounding	N/A	Per mesothelioma-specific guidance, concern about co-exposures is limited or likely not relevant for mesothelioma, meriting a ”not applicable” rating.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	Medium	This study used a prospective cohort design to assess mesothelioma, which has a long latency period. This is an appropriate design for this health outcome. Additionally a Cox proportional hazard model was used to compare the medium and high exposure groups to the low exposure group (referent).
	Metric 13:	Statistical Power	N/A	Per instructions, this metric was not rated for mesothelioma.
	Metric 14:	Reproducibility of Analyses	N/A	Per instructions, this metric was not rated for mesothelioma. Additionally, an analysis was not conducted for mesothelioma cases.
	Metric 15:	Statistical Analysis	N/A	Per instructions, this metric was not rated for mesothelioma. Additionally, a statistical model was not built for mesothelioma cases.

Additional Comments: This study is uninformative for mesothelioma outcomes, as the authors did not conduct statistical analyses for the two mesothelioma cases. Additionally, the mesothelioma outcome was not assessed using ICD codes. The examination of mesothelioma through employee records seems to only assess pleural and peritoneal cases, meriting and uninformative rating.

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Study Citation:	Wang, X. R., Yu, I. T. S., Qiu, H., Wang, M. Z., Lan, Y. J., Tse, L. Y., Yano, E., Christiani, D. C. (2012). Cancer mortality among Chinese chrysotile asbestos textile workers. Lung Cancer 75(2):151-155.
Health Outcome:	Mesothelioma
Target Organ(s):	Lung/Respiratory: lung cancer mortality, nonmalignant respiratory disease mortality, asbestosis mortality, mesothelioma mortality
Asbestos Fiber Type(s):	Asbestos - Chrysotile (serpentine): 12001-29-5
Linked HERO ID(s):	No linked references.
HERO ID:	2638749

Domain	Metric	Rating	Comments
Overall Quality Determination		**Uninformative**	

* No biomarkers were identified for this evaluation.

Study Citation:	Abramson, M. J., Murambadoro, T., Alif, S. M., Benke, G. P., Dharmage, S. C., Glaspole, I., Hopkins, P., Hoy, R. F., Klebe, S., Moodley, Y., Rawson, S., Reynolds, P. N., Wolfe, R., Corte, T. J., Walters, E. H. (2020). Occupational and environmental risk factors for idiopathic pulmonary fibrosis in Australia: Case-control study. Thorax 75(10):864-869.
Health Outcome:	Idiopathic pulmonary fibrosis
Target Organ(s):	Lung/Respiratory: Idiopathic pulmonary fibrosis
Asbestos Fiber Type(s):	Asbestos - Not specified: 1332-21-4
Linked HERO ID(s):	No linked references.
HERO ID:	6869440

Domain		Metric	Rating	Comments
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Low	It is unclear how the authors measured asbestos concentrations or how these data were collected for their use in the manuscript.
	Metric 5:	Exposure Levels	Medium	The authors provided a wide range of fiber-years included in the analysis of 4 exposure levels (Table 3).

Additional Comments: None

* No biomarkers were identified for this evaluation.

** As described in Appendix B.2 of the *White Paper: Quantitative Approach to the Human Health Assessment for the Risk Evaluation for Asbestos Part 2: Supplemental Evaluation Including Legacy Uses and Associated Disposals of Asbestos*, to be considered as being informative for dose-response analysis, metrics 4 and 5 would need metric ratings of Medium or High. This reference did not satisfy this requirement; therefore data quality evaluation is presented for only for metrics 4 and 5.

Study Citation:	Akkurt, I., Onal, B., Demir, A. U., Tüzün, D., Sabir, H., Ulusoy, L., Karadağ, K. O., Ersoy, N., Cöplü, L. (2006). Respiratory health in Turkish asbestos cement workers: the role of environmental exposure. American Journal of Industrial Medicine 49(8):609-616.
Health Outcome:	Pulmonary Function/Spirometry Results; Small irregular parenchymal opacities
Target Organ(s):	Lung/Respiratory: Forced vital capacity (FVC), Forced expiratory volume in 1 second (FEV1), Small irregular parenchymal opacities (>=1/0), Small irregular parenchymal opacities (>=1/1), Forced expiratory volume in 1 second/Forced vital capacity (FEV1/FVC) %, Restrictive lung function (FVC <80% of the predicted values based on age, sex and height), Obstructive lung function (FEV1/FVC<70% of predicted values based on age, sex and height)
Asbestos Fiber Type(s):	Asbestos - Chrysotile (serpentine): 12001-29-5
Linked HERO ID(s):	No linked references.
HERO ID:	2078953

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Low	Among 474 active workers currently employed in any 6 cement factories spread throughout Turkey, the study enrolled 424 (89%). ”The number of workers were 36, 42, 44, 62, 81 and 159, respectively” per asbestos factory. Authors do not describe recruitment methods, the share of workers per factory recruited, or any additional inclusion criteria. There is no discussion on whether exposure-outcome distribution may have varied by those included vs. those excluded.
	Metric 2:	Attrition	Low	Of the initial 424 workers enrolled, authors reported that 406 responded to survey questions on birthplace, and among those, 334 (82.3%) had chest x-rays of acceptable quality. Authors note that workers who had unusable chest x-rays were older and had longer duration of work, resulting in bias of the sample, with younger subjects with lower durations of exposure and presumably better respiratory health. There is no discussion of this potential bias beyond stating the reason why subjects did not have usable x-rays. In addition, only 260 workers have both workplace asbestos exposure and lung function test results, allowing them to be included in models.
	Metric 3:	Comparison Group	Medium	Authors describe comparison groups as workers ”who were titled with the jobs not related to asbestos dust”. Age, duration of work, and radiological findings were used for each outcome. Authors illustrate few differences (only in opacities and lung function outcomes) among groups. There is limited detail on the comparison group with jobs not related to asbestos exposure.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Medium	Authors report following the methods of the Asbestos International Association guidance of 1982. Samples were ”collected on 25 mm diameter cellulose ester membrane filters with 1.2 mm pores in open face cowled casettes made of conductive plastic. Filters were mounted on glass slides and cleared with acetone vapor. One hundred fields of a Walton Beckett granule were counted at 400 times magnification with phase contrast microscope.” It is unclear how often these samples were taken (one time measure or multiple times), when, or what duration. Asbestos fibers were reported in fibre/mL.
	Metric 5:	Exposure Levels	Medium	Asbestos exposures are presented dichotomously (No/Possible), as well as continuously (natural log transformed). The median and range of concentrations is 0.22 fiber/mL and 0.02-0.76 fiber/mL. This distribution is likely sufficient to develop a dose-response estimate.

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Study Citation: Akkurt, I., Onal, B., Demir, A. U., Tüzün, D., Sabir, H., Ulusoy, L., Karadağ, K. O., Ersoy, N., Cöplü, L. (2006). Respiratory health in Turkish asbestos cement workers: the role of environmental exposure. American Journal of Industrial Medicine 49(8):609-616.
Health Outcome: Pulmonary Function/Spirometry Results; Small irregular parenchymal opacities
Target Organ(s): Lung/Respiratory: Forced vital capacity (FVC), Forced expiratory volume in 1 second (FEV1), Small irregular parenchymal opacities (>=1/0), Small irregular parenchymal opacities (>=1/1), Forced expiratory volume in 1 second/Forced vital capacity (FEV1/FVC) %, Restrictive lung function (FVC <80% of the predicted values based on age, sex and height), Obstructive lung function (FEV1/FVC<70% of predicted values based on age, sex and height)
Asbestos Fiber Type(s): Asbestos - Chrysotile (serpentine): 12001-29-5
Linked HERO ID(s): No linked references.
HERO ID: 2078953

Domain		Metric	Rating	Comments
	Metric 6:	Temporality	Low	Authors note that 44.1% of subjects worked >10 years, making established temporality between exposure and outcomes less certain.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	High	Pulmonary Function/Spirometry Results: Spirometry was performed following the American Thoracic Society, 1987 guidelines: "Each subject was seated while wearing a nose clip. A portable spirometer (Gold Pulmonary Analysis Computer, and Pulmograph, Holland) was used to measure the forced vital capacity (FVC) and forced expiratory volume in 1 s (FEV1). At least three forced expiratory maneuvers were completed with the highest two FEV1 and FVC values within 5% of each other. The highest value of three maneuvers was recorded and used in the analysis." Authors report using the spirometry results for "Predicted values of FEV1 and FVC based on gender, height, and age, as adopted by Knudson et al. [1983], were used to calculate the predicted FEV1 and FVC."; Other Non-Cancer Outcomes: Authors report obtaining standard posteroanterior chest x-rays which were evaluated by two chest physicians individually. The physicians were blinded and followed revised version of 1980 International Labour Organization (ILO) Classifications. A third physician was brought in the case of inconsistency between two initial readers.
	Metric 8:	Reporting Bias	High	The methods and results are reported throughout the paper, where regression coefficients and standard errors or odds ratios and related confidence intervals and p-values are provided for analyses. The number of workers used in each analysis are reported in the footnotes of tables.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	High	Lung function linear regression analyses were adjusted for age, sex, height, smoking pack-years, and duration of work. Parenchymal opacities logistic regression analyses were adjusted for age, ever smoking, finishing secondary school, and duration of work.
	Metric 10:	Covariate Characterization	Medium	The questionnaire used for this study was conducted by an interviewer who collected informed consent from all workers. "The questionnaire included information on demographics, occupational history, respiratory symptoms, and smoking habits." There was no validation of smoking answers.
	Metric 11:	Co-exposure Counfounding	Low	Authors do not discuss occupational co-exposures and if they may vary by factory. They do discuss environmental or community exposures to naturally occuring asbestos in soil (erionite) as based on birthplace. The questionnaire included a question about this exposure, and only one worker noted that they were born in an area with high erionite exposure. Authors note that this did not impact their findings.

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Study Citation: Akkurt, I., Onal, B., Demir, A. U., Tüzün, D., Sabir, H., Ulusoy, L., Karadağ, K. O., Ersoy, N., Cöplü, L. (2006). Respiratory health in Turkish asbestos cement workers: the role of environmental exposure. American Journal of Industrial Medicine 49(8):609-616.

Health Outcome: Pulmonary Function/Spirometry Results; Small irregular parenchymal opacities

Target Organ(s): Lung/Respiratory: Forced vital capacity (FVC), Forced expiratory volume in 1 second (FEV1), Small irregular parenchymal opacities (>=1/0), Small irregular parenchymal opacities (>=1/1), Forced expiratory volume in 1 second/Forced vital capacity (FEV1/FVC) %, Restrictive lung function (FVC <80% of the predicted values based on age, sex and height), Obstructive lung function (FEV1/FVC<70% of predicted values based on age, sex and height)

Asbestos Fiber Type(s): Asbestos - Chrysotile (serpentine): 12001-29-5

Linked HERO ID(s): No linked references.

HERO ID: 2078953

Domain	Metric		Rating	Comments
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	Medium	Study design and methods are appropriate. The association of lung function and ranges of exposure to asbestos were ”adjusted for potential confounders by stepwise multiple linear regression analysis with inclusion and exclusion criteria of 0.10 and 0.15, respectively.” Multiple logistic regression was used to adjust with radiological findings of asbestosis. Analyses report p-value cutoffs of <0.05, 0.01, and 0.0001.
	Metric 13:	Statistical Power	Medium	Population size is adequate to analyze the outcomes for respiratory function and parenchymal opacities (n=406 for full sample and n=260 for subsample analysis among workers with workplace asbestos exposure during survey and lung function test).
	Metric 14:	Reproducibility of Analyses	Medium	The methods and analysis sections are clear enough to understand and conceptually reproduce the analyses.
	Metric 15:	Statistical Analysis	Low	The models for lung function and small irregular parenchymal opacities in asbestos workers are transparent. No assumptions are explicitly discussed, however authors do note they log-transformed asbestos exposure concentration to obtain a normal distribution.

Additional Comments: Overall, this study is well designed to analyze respiratory function in occupational workers. PCM was used to count asbestos fibres, thus rating Metric 4 as a medium. Major concerns for bias lie in lack of details on recruitment and higher attrition among older, likely higher-exposed workers. There is no detail about sampling duration, timing, or frequency.

Overall Quality Determination **Medium**

* No biomarkers were identified for this evaluation.

Study Citation:	Albin, M., Johansson, L., Pooley, F. D., Jakobsson, K., Attewell, R., Welinder, H. (1988). Mineral fibres, fibrosis, and asbestos bodies in lung tissue from deceased asbestos-cement workers. Arhiv za Higijenu Rada i Toksikologiju 39(4):447-453.
Health Outcome:	fibrosis, mortality
Target Organ(s):	Lung/Respiratory: fibrosis
Asbestos Fiber Type(s):	Asbestos - Chrysotile (serpentine): 12001-29-5; Asbestos - Crocidolite (riebeckite): 12001-28-4; Asbestos - Tremolite: 14567-73-8; Asbestos - Anthophyllite: 17068-78-9; Asbestos - Amosite (grunerite): 12172-73-5
Linked HERO ID(s):	3082921, 3082513
HERO ID:	3082921

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Medium	Some key elements of the study design were not present but available information indicates a low risk of selection bias. Cases (n=89) were deceased individuals who worked for more than three months between 1907 and 1977 (employed before the beginning of 1976) at an asbestos cement plant located in a small community in the south of Sweden (Johansson et al., 1987 HeroID:3083094). The cohort that the cases came from appeared to include both males and females (Johansson et al., 1987 HeroID:3083094) but the distribution for this demographic characteristic is not provided in the study. Among these, 69 has lung tissue that were further analyzed. Characteristics such as mean age, year of first employment, employment duration, and time between end of exposure and death are provided in Table 1. Exclusion criteria are not specified. Authors mentioned non-random sampling of the tissue specimens is possible as asbestotic lesions tend to be in a specific area of the lungs and have higher counts of fibres than other parts of the lungs. Tissues from these parts of the lungs may have been observed in some of the exposed workers, which could explain difference between the exposed workers and their controls, although they say this is “highly unlikely.”
	Metric 2:	Attrition	High	This study reports retrospective data of deceased individuals, thus subject withdrawal from the study is not of concern. None of the cases were excluded for analyses. Outcome and exposure data appear to be complete.
	Metric 3:	Comparison Group	Medium	There is indirect evidence that cases and controls are similar. Cases were matched with controls by sex, age, and year and place of death. Necropsy files came from the University Hospital of Lund, which is one of the three departments where necropsy files for the cases came from (Johansson et al., 1987 HeroID:3083094). The main occupation is not known or “was specified as labourer” for 46 controls (Johansson et al., 1987 HeroID:3083094), so healthy worker effect may not be of substantial concern if these 46 controls were in fact employed.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Medium	Lung tissues were analyzed by TEM. Energy dispersive x ray spectrometry was used to determine the type of asbestos fiber. These appear to be assessed during one time period but meant to be reasonably representative of the entire study period.

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Study Citation:	Albin, M., Johansson, L., Pooley, F. D., Jakobsson, K., Attewell, R., Welinder, H. (1988). Mineral fibres, fibrosis, and asbestos bodies in lung tissue from deceased asbestos-cement workers. Arhiv za Higijenu Rada i Toksikologiju 39(4):447-453.
Health Outcome:	fibrosis, mortality
Target Organ(s):	Lung/Respiratory: fibrosis
Asbestos Fiber Type(s):	Asbestos - Chrysotile (serpentine): 12001-29-5; Asbestos - Crocidolite (riebeckite): 12001-28-4; Asbestos - Tremolite: 14567-73-8; Asbestos - Anthophyllite: 17068-78-9; Asbestos - Amosite (grunerite): 12172-73-5
Linked HERO ID(s):	3082921, 3082513
HERO ID:	3082921

Domain	Metric		Rating	Comments
	Metric 5:	Exposure Levels	Medium	Until 1952, the highest reported concentration was 10 fibres/ml. "During the 1970s the highest exposure concentration was 4 f/ml." Average concentrations above 2 f/ml applied to millers, mixers, and workers engaged in polishing and sawing operations. Mean cumulative exposure is provided with a range of 0-230 f-y/ml and "the logarithm of the fibre concentrations was used as the dependent variable in the multiple linear regression." Additionally, Figure 3 illustrates the cumulative distribution of amphibole content among workers without mesothelioma, while Figure 4 illustrates cumulative distribution of chrysotile and tremolite content among workers and controls.
	Metric 6:	Temporality	Medium	Based on the case data, a >15-year latency appears to be established if we can assume that this study was conducted after 1984, which is 15 years after 1969 (the latest year reported for year of first employment; see Table 1). However, it is unclear if fibrosis preceded exposure which the authors admit to by saying "it cannot be judged whether the fibres accumulated first, causing fibrosis, or if the fibrosis occurred first, causing a deterioration of the alveolar clearance of fibre particles."
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Medium	Other Non-Cancer Outcomes: Authors examined lung tissue specimens and stated that interstitial fibrosis was scored 0-4 according to the classification proposed by Hinson et al." (Hinson et al., 1974 HeroID:3099579). Some analyses dichotomized the presence of fibrosis.
	Metric 8:	Reporting Bias	Medium	Most results seem to be reported in all aspects of the report, including p-values and sample sizes. There is one instance where exact fiber concentrations are discussed in the abstract text but not in the study. Some results are provided in text but not presented in tables or figures.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Medium	Final regression analyses adjusted for age and smoking. Although males and females were included in the cohort, there is no discussion of adjusting for sex.
	Metric 10:	Covariate Characterization	Medium	As an occupational study, it can be assumed that covariate data were collected from personnel records. Information such as mean age, year of first employment, employment duration, and time between end of exposure and death are provided in Table 1.
	Metric 11:	Co-exposure Counfounding	Low	Co-exposures were not appropriated adjusted for in analyses. Authors stated that exposed workers higher levels of the following non-asbestos fibres than controls: mullite, iron, rutile, muscovite, aluminum, and silicon.
Domain 5: Analysis				

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Study Citation:	Albin, M., Johansson, L., Pooley, F. D., Jakobsson, K., Attewell, R., Welinder, H. (1988). Mineral fibres, fibrosis, and asbestos bodies in lung tissue from deceased asbestos-cement workers. Arhiv za Higijenu Rada i Toksikologiju 39(4):447-453.
Health Outcome:	fibrosis, mortality
Target Organ(s):	Lung/Respiratory: fibrosis
Asbestos Fiber Type(s):	Asbestos - Chrysotile (serpentine): 12001-29-5; Asbestos - Crocidolite (riebeckite): 12001-28-4; Asbestos - Tremolite: 14567-73-8; Asbestos - Anthophyllite: 17068-78-9; Asbestos - Amosite (grunerite): 12172-73-5
Linked HERO ID(s):	3082921, 3082513
HERO ID:	3082921

Domain	Metric		Rating	Comments
	Metric 12:	Study Design and Methods	Medium	The study design was appropriate to address the research question. "The Mann-Whitney U test was used to compare concentrations of fibre or mass estimates between the groups and Kendall's test was used to evaluate rank correlates between fibre concentration or mass estimate and several variables (employment time, fibrosis grade, amount of smoking, and counts of asbestos bodies)." As a case-control study, logistic regression and multiple linear regression analyses were conducted.
	Metric 13:	Statistical Power	Medium	The case-control study had small sample sizes (cases = 76; controls = 96); however, authors were able to still detect effects. Despite lower measurements of exposure, effect estimates among controls were more pronounced than cases, to the authors' surprise.
	Metric 14:	Reproducibility of Analyses	Medium	The description of the analyses is sufficient to understand how to conceptually reproduce the analysis with access to the analytic data.
	Metric 15:	Statistical Analysis	Low	Description of assumptions made in the models are not provided.
Domain 6: Other (if applicable) Considerations for Biomarker Selection and Measurement (Lakind et al. 2014)				
	Metric 16:	Use of Biomarker of Exposure	High	To confirm asbestos exposure, authors assessed lung tissue specimens for presence of asbestos fibers.
	Metric 17:	Effect Biomarker	N/A	Biomarkers of effect are not relevant to this study.
	Metric 18:	Method Sensitivity	Medium	Fiber measurement was conducted through TEM. LOD/LOQ are not relevant for this study's analyses.
	Metric 19:	Biomarker Stability	Medium	Storage of lung specimens is not discussed. Stability of lung specimens are not a concern for this study.
	Metric 20:	Sample Contamination	Medium	Contamination of samples are not discussed nor is of concern.
	Metric 21:	Method Requirements	High	TEM was conducted to measure asbestos fibers.
	Metric 22:	Matrix Adjustment	N/A	Matrix adjustment is not applicable for this biomarker.

Additional Comments: Biomarker evaluation was completed with assistance from project lead. Fiber counts among workers with mesothelioma; however, but no with SMR or regression were used in analysis for mesothelioma. HeroID:3082921 and HeroID:3082513 are duplicates of the same study. Evaluation should be considered applicable to both HERO IDs.

Overall Quality Determination — Medium

Study Citation:	Alexander, B. H., Raleigh, K. K., Johnson, J., Mandel, J. H., Adgate, J. L., Ramachandran, G., Messing, R. B., Eshenaur, T., Williams, A. (2012). Radiographic evidence of nonoccupational asbestos exposure from processing Libby vermiculite in Minneapolis, Minnesota. Environmental Health Perspectives 120(1):44-49.
Health Outcome:	Pleural abnormalities (pleural thickening or pleural plaques)
Target Organ(s):	Lung/Respiratory: Pleural abnormalities (pleural thickening or pleural plaques)
Asbestos Fiber Type(s):	Asbestos- Libby amphibole: 1318-09-8
Linked HERO ID(s):	No linked references.
HERO ID:	1005285

Domain	Metric		Rating	Comments
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Low	The exposure source was vermiculite ore originally from a mine near Libby, Montana known to be contaminated with amphibole asbestos and sent for processing to plants across the U.S., including the WM/WRG facility in Minneapolis, Minnesota. Potential community member airborne asbestos fiber exposure was estimated through a combination of Minnesota Pollution Control Agency dispersion modeling estimates of air concentrations in the community resulting from plant operations and questionnaire-derived activity-based modeling to establish exposure profiles for the enumerated cohort. Exposures were estimated for the period of plant operations 1938-1989. To obtain a sample representative of the range of community exposures, the popula¬tion was stratified into groups to represent three exposure scenarios: a) intense intermit¬tent exposure, b) long-term high ambient background exposure, and c) low ambient background exposure. We classified people with a childhood history of playing in the piles of waste rock outside the plant as the group with intense intermittent exposures to potentially high concentrations of asbes¬tos fibers. The long-term high and low back¬ground exposure groups were selected based on residential history and frequency matched to the age distribution of the intense intermit¬tent exposure category Details of exposure assessments were described as reported in full within Adgate et al., 2011 (HERO ID 105280). Adgate et al., 2011 noted that potential activity-based exposure pathways were ascertained based on previous Libby asbestos studies and questionnaire responses from the MDH/ATSDR cohort members with direct contact with waste rock, waste piles or vermiculite insulation. Background exposure for those with no reported activity-based exposure was determined by length of residence in the affected community and estimates of airborne fiber concentration. Adgate et al., 2011 noted that asbestos concentration data was reported within previous publications, including Kelly et al., 2006 (HERO ID 709511). Kelly et al., 2006 noted that exposure to Libby asbestos at the WRG plant was obtained from 1970's industrial hygiene data in air samples analyzed by phase-contrast light microscopy. Regression models within the current study utilized categories of activity exposure (f/cc x months), pile-playing exposure (f/cc x months), background exposure (f/cc x months) and total exposure (f/cc x months). Authors noted that activity-based exposure was derived from self-reported activities as assessed in 2001 when the cohort was enumerated, with assumptions of activity duration likely introducing some exposure misclassification. Furthermore, air dispersion models assumed an equivalent exposure opportunity for all people, regardless of where they spent their day.

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Study Citation:	Alexander, B. H., Raleigh, K. K., Johnson, J., Mandel, J. H., Adgate, J. L., Ramachandran, G., Messing, R. B., Eshenaur, T., Williams, A. (2012). Radiographic evidence of nonoccupational asbestos exposure from processing Libby vermiculite in Minneapolis, Minnesota. Environmental Health Perspectives 120(1):44-49.
Health Outcome:	Pleural abnormalities (pleural thickening or pleural plaques)
Target Organ(s):	Lung/Respiratory: Pleural abnormalities (pleural thickening or pleural plaques)
Asbestos Fiber Type(s):	Asbestos- Libby amphibole: 1318-09-8
Linked HERO ID(s):	No linked references.
HERO ID:	1005285

Domain	Metric		Rating	Comments
	Metric 5:	Exposure Levels	Medium	The range and distribution of estimated exposure is sufficient to develop exposure-response estimates. Regression model results within the current study were reported across three exposure f/cc x month categories based upon cut points at the 50th and 75th percentile of the exposure distribution for each exposure category. Estimated exposure levels in f/cc x months for regression categories of background exposure (<0.034, 0.034 to <0.077, and >=0.077 f/cc x months), exposure from pile playing (<0.158, 0.158 to <0.549, and >=0.549 f/cc x months), total exposure (<0.0523, 0.0523 to 0.245, and >= 0.245 f/cc x months), and total activity exposure (<0.082, 0.082 to <0.422, and >=0.422 f/cc x months) were detailed.

Additional Comments: This study investigated the association between radiographic pleural abnormalities, parenchymal opacities and other evidence of asbestosis in 461 individuals with radiographic assessments and a history before 1980 of nonoccupational direct contact with, or ever playing with, Libby vermiculite ore processing waste at the Western Minerals/W.R. Grace (WM/WRG) facility in Minneapolis, Minnesota who had never worked at the processing plant or never lived with a plant worker. Residents were described as often hauling the freely offered rock from the waste piles and using it for gardening and as fill material for driveways and yards. Neighborhood children also played on the piles of vermiculite processing waste, as access to the site was not restricted. As part of the Northeast Minneapolis Community Vermiculite Investigation (NMCVI), the Michigan Department of Health (MDH) and ATSDR surveyed over 1,600 properties and worked with the EPA to document contamination on more than 260 properties subsequently cleaned by EPA under the federal Superfund program as part of an initial community exposure characterization. A history of direct contact with the waste and ever playing in the waste piles was associated with pleural abnormalities, with a reported odds ratio of [OR] 2.78 [95% confidence inter¬val (CI): 1.26, 6.10] and 2.17 (95% CI: 0.99, 4.78), respectively, when adjusted for background exposure.NOTE: QC was not completed for metrics other than Metrics 4 and 5 because the study does not have sufficient exposure information to be useful for dose-response analysis

* No biomarkers were identified for this evaluation.

** As described in Appendix B.2 of the *White Paper: Quantitative Approach to the Human Health Assessment for the Risk Evaluation for Asbestos Part 2: Supplemental Evaluation Including Legacy Uses and Associated Disposals of Asbestos*, to be considered as being informative for dose-response analysis, metrics 4 and 5 would need metric ratings of Medium or High. This reference did not satisfy this requirement; therefore data quality evaluation is presented for only for metrics 4 and 5.

Study Citation:	Alfonso, H. S., Fritschi, L., de Klerk, N. H., Olsen, N., Sleith, J., Musk, A. W. (2004). Effects of asbestos and smoking on the levels and rates of change of lung function in a crocidolite exposed cohort in Western Australia. Thorax 59(12):1052-1056.
Health Outcome:	Asbestosis; Pulmonary Function/Spirometry Results; Pleural Plaques; locus of control
Target Organ(s):	Lung/Respiratory: Asbestosis, Pleural plaques and diffuse pleural thickening, carbon monoxide diffusing capacity, FEV1, FVC, FEV1/FVC; Neurological/Behavioral: locus of control (LOC)
Asbestos Fiber Type(s):	Asbestos - Crocidolite (riebeckite): 12001-28-4
Linked HERO ID(s):	733567, 2079051, 3077939, 3079889
HERO ID:	733567

Domain	Metric		Rating	Comments
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Low	Neither PCM nor TEM were used for measuring exposure. Exposure data were estimated from the 1966 survey of crocidolite fibers conducted by the Mines Department of Western Australia. Measurements for former residents were based on periodic surveys of fiber counts conducted by the Health Department of Western Australia made in Wittenoom as well as personal monitors (Alfonso et al., 2004 733567). There is concern that these measurements were not as precise as those done for former workers (Alfonso et al., 2005 2079051).
	Metric 5:	Exposure Levels	Medium	The distribution of exposure appears to be sufficient to develop an exposure-response estimate. Cumulative exposure was utilized in statistical models (f/ml-y) (Alfonso et al., 2004 733567, Alfonso et al., 2005 2079051, Franklin & Robinson 2015 3077939).

Additional Comments: Authors admitted that the selected participants for final analyses may not be representative of the whole cohort. This might warrant further review by QC to determine whether this is grounds for rating Metric 1 as uninformative. As QC reviewer, I agree with this concern from the initial reviewer that there is potentially some issues with participants selection bias in this study, but overall, I think it has multiple strengths that adds to the body of literature.The measurement exposure (M4) and/or is rated low upon review by both set of reviewers. However, exposure levels (M5) metrics is rated as medium. Also, the overall quality determination (OQD) is rated medium.

* No biomarkers were identified for this evaluation.

** As described in Appendix B.2 of the *White Paper: Quantitative Approach to the Human Health Assessment for the Risk Evaluation for Asbestos Part 2: Supplemental Evaluation Including Legacy Uses and Associated Disposals of Asbestos*, to be considered as being informative for dose-response analysis, metrics 4 and 5 would need metric ratings of Medium or High. This reference did not satisfy this requirement; therefore data quality evaluation is presented for only for metrics 4 and 5.

Study Citation:	Amandus, H. (1986). The morbidity and mortality of vermiculite miners and millers exposed to tremolite-actinolite. NIOSH(59):19861986.
Health Outcome:	Lung Cancer; Stomach, digestive; Pleural Plaques; NMRD, pleural changes, all cause mortality, ischemic heart disease, diseases of the circulatory system
Target Organ(s):	Lung/Respiratory: Small opacities with profusion greater >/= ILO category 1/0, Unilateral or bilateral pleural change, Unilater or bilateral pleural calcification on the wall, diaphragm, or other site, Unilateral or bilateral pleural plaque or diffuse pleural thickening on the lung wall, Non-malignant respiratory disease (NMRD) mortality, Pneumonia, Emphysema, Tuberculosis; Cardiovascular: All diseases of the circulatory system, Ischemic heart disease; Mortality: All diseases of the circulatory system, Ischemic heart disease, Non-malignant respiratory disease (NMRD) mortality, Pneumonia mortality, Emphysema mortality, Tuberculosis mortality, All cause mortality
Asbestos Fiber Type(s):	Asbestos- Libby amphibole: 1318-09-8; Asbestos - Tremolite: 14567-73-8; Asbestos - Actinolite: 12172-67-7
Linked HERO ID(s):	3100838, 29839, 759132, 783513
HERO ID:	3100838

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Low	This study incorporated various sections, including both a morbidity and a mortality study. For the morbidity study, the sample incorporated 191 men employed between 1975 and 1982 and had worked there for at least five years. This group was incorporated because over 50% of workers did not have radiographs available, due to either working less than five years or being terminated before 1975. The number of study participants for the mortality analysis was larger, being comprised of 589 white male and female employees. All of these individuals were hired before 1970 and had been employed for at least one year. December 31, 1981 was the end of the follow-up period when vital status was determined. 581 of these workers had their vital status determined, and 417 were alive. This means that there were 164 deceased workers, and death certificates were obtained for 162 of them. The Social Security Administration records were used to determine date of death for the two workers without death certificates available. More details about the total number of potential employees within the vermiculite mine/mill, participation rates, and specific inclusion/exclusion criteria would be beneficial for this study.
	Metric 2:	Attrition	High	The attrition level in the mortality study was low, with many of the death certificates available for 98.8% of the decedents. The attrition level was somewhat higher in the morbidity study, with only 184 and 121 of the 191 men having radiographs and questionnaire results available, respectively. This rating would be medium for this portion of the overall paper.
	Metric 3:	Comparison Group	Medium	To calculate the SMR, expected deaths were determined from the U.S. white male death rates. For the morbidity study, the author utilized an external control group for smoking, which was comprised of three groups without asbestos exposure. These groups included blue-collar workers without pneumoconiosis, non-asbestos cement plant workers, and coal miners with less than five years of employment. Control group members were excluded for various reasons, including if they had worked in a dusty trade, had a radiograph with rounded opacities greater than 0/1, or never smoked regularly. There author did not provide much of a discussion pertaining to similarities between the exposed and control groups in this study, which would have been beneficial to ensure that analyses were conducted appropriately.
Domain 2: Exposure Characterization				

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Study Citation: Amandus, H. (1986). The morbidity and mortality of vermiculite miners and millers exposed to tremolite-actinolite. NIOSH(59):19861986.
Health Outcome: Lung Cancer; Stomach, digestive; Pleural Plaques; NMRD, pleural changes, all cause mortality, ischemic heart disease, diseases of the circulatory system
Target Organ(s): Lung/Respiratory: Small opacities with profusion greater >/= ILO category 1/0, Unilateral or bilateral pleural change, Unilater or bilateral pleural calcification on the wall, diaphragm, or other site, Unilateral or bilateral pleural plaque or diffuse pleural thickening on the lung wall, Non-malignant respiratory disease (NMRD) mortality, Pneumonia, Emphysema, Tuberculosis; Cardiovascular: All diseases of the circulatory system, Ischemic heart disease; Mortality: All diseases of the circulatory system, Ischemic heart disease, Non-malignant respiratory disease (NMRD) mortality, Pneumonia mortality, Emphysema mortality, Tuberculosis mortality, All cause mortality
Asbestos Fiber Type(s): Asbestos- Libby amphibole: 1318-09-8; Asbestos - Tremolite: 14567-73-8; Asbestos - Actinolite: 12172-67-7
Linked HERO ID(s): 3100838, 29839, 759132, 783513
HERO ID: 3100838

Domain	Metric		Rating	Comments
	Metric 4:	Measurement of Exposure	High	For the morbidity study, the date of the most recent radiograph examination was used to calculate the cumulative exposure levels. As detailed in the section for the mortality study, air dust samples were collected at various timepoints in different areas of the mill/mine. Midget impingers were used to sample the dust in years prior to 1969, and these values were reported as million particles per cubic foot of air (mppcf). After 1967, membrane filter samples were collected, and values were instead reported as fibers per cubic centimeter of air (f/cc). This information was used to generate a fiber-year estimate for the individuals enrolled in the study. It is important to note that only samples taken between 1965 and 1971 were used for these calculations. Several steps were undertaken to determine job exposure estimates for the fiber-years accumulated for the participants. These steps included coding the workers' jobs and abstracting fiber concentrations, dividing the facility into various location-operations, determining the arithmetic mean to compute average f/cc concentrations, converting impingers measurements into appropriate units, estimating the exposure level at the various location-operations, utilizing a plant manager to estimate the hours worked at these locations, determining work histories, and computing the individual participant's cumulative exposure index. The authors also detail that some of the area samples of airborne dust were analyzed with phase contrast microscopy (Amandus, 1986, 3100838).
	Metric 5:	Exposure Levels	Medium	The authors reported a wide range of exposure levels in both the morbidity and the mortality studies. Examples of this include the results of man-year analyses in the mortality study were broken down into exposure groupings of <50, 50-99, 100-399, and >399 f-y, and the radiographic findings by fiber-years in the morbidity study, where results were reported in 0-15, 16-30, 31-85, and >86 fiber-year groupings.
	Metric 6:	Temporality	Medium	There was a range of latency groups included in the morbidity and mortality studies. While temporality is established for the participants, it is unclear if there was an adequate level of follow-up for the consideration of latency. For the mortality study, the average tenure was 8.3 years, while the average tenure for the morbidity study was 14 years. Because the inclusion criteria required workers to have been employed for at least one year, there is a wide range of potential latencies included in this study.
Domain 3: Outcome Assessment				

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Study Citation:	Amandus, H. (1986). The morbidity and mortality of vermiculite miners and millers exposed to tremolite-actinolite. NIOSH(59):19861986.
Health Outcome:	Lung Cancer; Stomach, digestive; Pleural Plaques; NMRD, pleural changes, all cause mortality, ischemic heart disease, diseases of the circulatory system
Target Organ(s):	Lung/Respiratory: Small opacities with profusion greater >/= ILO category 1/0, Unilateral or bilateral pleural change, Unilater or bilateral pleural calcification on the wall, diaphragm, or other site, Unilateral or bilateral pleural plaque or diffuse pleural thickening on the lung wall, Non-malignant respiratory disease (NMRD) mortality, Pneumonia, Emphysema, Tuberculosis; Cardiovascular: All diseases of the circulatory system, Ischemic heart disease; Mortality: All diseases of the circulatory system, Ischemic heart disease, Non-malignant respiratory disease (NMRD) mortality, Pneumonia mortality, Emphysema mortality, Tuberculosis mortality, All cause mortality
Asbestos Fiber Type(s):	Asbestos- Libby amphibole: 1318-09-8; Asbestos - Tremolite: 14567-73-8; Asbestos - Actinolite: 12172-67-7
Linked HERO ID(s):	3100838, 29839, 759132, 783513
HERO ID:	3100838

Domain	Metric		Rating	Comments
	Metric 7:	Outcome Measurement or Characterization	High	Lung Cancer: It is reported in the mortality study section that ”death certificates were obtained from the company and state vital statistics agencies” (Amandus, 1986, 3100838). Each of the underlying causes of death were recoded based on the International Classification of Diseases, Eighth Revision. Proper ICD codes were reported for the lung cancer causes of death, and are mentioned in Table 3.1.; Other Cancer(s): The underlying causes of death were reclassified and coded according to the International Classification of Diseases, Eighth Revision. ICD codes respective to the various outcomes are reported in Table 3.1. Death certificates were available for 98.8% of those who were deceased.; Pleural Plaques: As noted in the morbidity study section, the available radiographs for 184 of the 191 men were examined by three ”B” readers using the ILO classification of 1980. The films were ”taken in 1981-1982 for 134 workers, in 1976-1980 for 49 workers, and prior to 1975 for only 1 worker” (Amandus, 1986, 3100838). The readers evaluated a number of outcomes, which are detailed on page 56. It is important to note that the ”profusion of small opacities was derived from a median of the 3 readers, and for each pleural finding from a consensus of the readers” (Amandus, 1986, 3100838).; Other Non-Cancer Outcomes: Information on causes of mortality in the mortality study were determined from death certificates and vital statistic agencies. The causes of death were coded ”for statistical analysis according to the Eighth Revision of the International Classification of Diseases, adapted” (Amandus, 1986, 3100838). NMRD included such things as pneumonia, emphysema, and tuberculosis. These outcomes were reported with ICDA codes in Table 3.1.
	Metric 8:	Reporting Bias	Medium	There are a number of findings reported at various points throughout this study. Confidence intervals are reported in some tables for the mortality study, but not for all of them. This is similar to results presented in the morbidity study, as some tables, such as 4.11, provide regression coefficients and their associated standard errors.
Domain 4: Potential Confounding / Variability Control				

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Study Citation:	Amandus, H. (1986). The morbidity and mortality of vermiculite miners and millers exposed to tremolite-actinolite. NIOSH(59):19861986.
Health Outcome:	Lung Cancer; Stomach, digestive; Pleural Plaques; NMRD, pleural changes, all cause mortality, ischemic heart disease, diseases of the circulatory system
Target Organ(s):	Lung/Respiratory: Small opacities with profusion greater >/= ILO category 1/0, Unilateral or bilateral pleural change, Unilater or bilateral pleural calcification on the wall, diaphragm, or other site, Unilateral or bilateral pleural plaque or diffuse pleural thickening on the lung wall, Non-malignant respiratory disease (NMRD) mortality, Pneumonia, Emphysema, Tuberculosis; Cardiovascular: All diseases of the circulatory system, Ischemic heart disease; Mortality: All diseases of the circulatory system, Ischemic heart disease, Non-malignant respiratory disease (NMRD) mortality, Pneumonia mortality, Emphysema mortality, Tuberculosis mortality, All cause mortality
Asbestos Fiber Type(s):	Asbestos- Libby amphibole: 1318-09-8; Asbestos - Tremolite: 14567-73-8; Asbestos - Actinolite: 12172-67-7
Linked HERO ID(s):	3100838, 29839, 759132, 783513
HERO ID:	3100838

Domain	Metric		Rating	Comments
	Metric 9:	Covariate Adjustment	Low	While there was some discussion about the potential for confounding effects in the mortality study, such as with smoking, adjustments were not always made appropriately. There was an attempt to control for smoking in examinations of lung cancer, but there was no mention of this adjustment for endpoints such as NMRD. It is important to note that a small portion of the participants in the mortality study were female. Some results were indicated for the total group, while some were for the male participants only. In the morbidity study, radiographic findings and their relationship with f-y were controlled for both smoking and age. However, it was noted by the author that the association was hard to measure "because of the small number of cases among non-smokers and the tendency for most cases to be older, to have smoked, and to have a high f-y" (Amandus, 1986, 3100838). In the remainder of analyses, only age was controlled for.
	Metric 10:	Covariate Characterization	Medium	There was no information presented pertaining to the methods for validating the assessment of potential confounders. However, there was no indication that the method had poor validity.
	Metric 11:	Co-exposure Counfounding	Low	Both studies conducted are examining asbestos exposure and health outcomes amongst vermiculite workers. However, it does not appear that the author is controlling for vermiculite exposure itself. While they mention that "vermiculite has not been associated with significant health effects" there is still a potential for some impact of vermiculite dust on the workers (Amandus, 1986, 3100838), and it may have been beneficial to control for.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	Medium	The study design implemented is appropriate for the research question being examined. The use of SMRs was appropriate to examine the association between asbestos exposure and the various mortality outcomes in the mortality study.
	Metric 13:	Statistical Power	Medium	The number of participants in both the morbidity and mortality studies was sufficient to detect an effect in the exposed population. It is important to note that in the morbidity study, when looking at respiratory symptoms, "the number of cases were small and statistical power was low" (Amandus, 1986, 3100838).
	Metric 14:	Reproducibility of Analyses	Medium	The description of the analysis is sufficient to understand how to conceptually reproduce the analysis with access to the analytical data.
	Metric 15:	Statistical Analysis	Low	While some statistical models were used, there was no description of the model assumptions present within this study. Assumptions for the regressions performed in the morbidity study were not reported. However, the method for calculating SMRs in the mortality analysis were described.

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Study Citation:	Amandus, H. (1986). The morbidity and mortality of vermiculite miners and millers exposed to tremolite-actinolite. NIOSH(59):19861986.
Health Outcome:	Lung Cancer; Stomach, digestive; Pleural Plaques; NMRD, pleural changes, all cause mortality, ischemic heart disease, diseases of the circulatory system
Target Organ(s):	Lung/Respiratory: Small opacities with profusion greater >/= ILO category 1/0, Unilateral or bilateral pleural change, Unilater or bilateral pleural calcification on the wall, diaphragm, or other site, Unilateral or bilateral pleural plaque or diffuse pleural thickening on the lung wall, Non-malignant respiratory disease (NMRD) mortality, Pneumonia, Emphysema, Tuberculosis; Cardiovascular: All diseases of the circulatory system, Ischemic heart disease; Mortality: All diseases of the circulatory system, Ischemic heart disease, Non-malignant respiratory disease (NMRD) mortality, Pneumonia mortality, Emphysema mortality, Tuberculosis mortality, All cause mortality
Asbestos Fiber Type(s):	Asbestos- Libby amphibole: 1318-09-8; Asbestos - Tremolite: 14567-73-8; Asbestos - Actinolite: 12172-67-7
Linked HERO ID(s):	3100838, 29839, 759132, 783513
HERO ID:	3100838

Domain	Metric	Rating	Comments
Additional Comments:	It is important to note that this study was a dissertation. While the author examined both morbidity and mortality, some metrics were rated differently due to differences in outcome ascertainment, analysis etc. Another potential concern pertains to comparison groups, as they differed depending on the outcome being examined. It is important to note that for the mortality study, there were some female participants included. Some results were reported for the included cohort as a whole, while others were reported specifically for male participants. While this study was given a medium rating based on the calculated scores, there is potential for that to be downgraded to a low.The measurement exposure (M4) and/or exposure levels (M5) metrics are rated as medium upon review by both set of reviewers. Also, the overall quality determination (OQD) is rated medium. Extraction has been completed and quality control reviewed.		

Overall Quality Determination — Medium

* No biomarkers were identified for this evaluation.

Study Citation:	Amandus, H. (1986). The morbidity and mortality of vermiculite miners and millers exposed to tremolite-actinolite. NIOSH(59):19861986.
Health Outcome:	Respiratory symptoms including cough, phlegm, dyspnea, and wheezing
Target Organ(s):	Lung/Respiratory: Respiratory symptom: Cough, Respiratory symptom: Phlegm, Respiratory symptom: Dyspnea, Respiratory symptom: Wheezing
Asbestos Fiber Type(s):	Asbestos- Libby amphibole: 1318-09-8; Asbestos - Tremolite: 14567-73-8; Asbestos - Actinolite: 12172-67-7
Linked HERO ID(s):	3100838, 29839, 759132, 783513
HERO ID:	3100838

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Low	This study incorporated various sections, including both a morbidity and a mortality study. For the morbidity study, the sample incorporated 191 men employed between 1975 and 1982 and had worked there for at least ten years. This group was incorporated because over 50% of workers did not have radiographs available, due to either working less than five years or being terminated before 1975. More details about the total number of potential employees within the vermiculite mine/mill, participation rates, and specific inclusion/exclusion criteria would be beneficial for this study.
	Metric 2:	Attrition	Medium	The attrition level was somewhat higher in the morbidity study than in the mortality study, with only 184 and 121 of the 191 men having radiographs and questionnaire results available, respectively.
	Metric 3:	Comparison Group	Low	For the morbidity study, the author utilized an external control group for smoking, which was comprised of three groups without asbestos exposure. These groups included blue-collar workers without pneumoconiosis, non-asbestos cement plant workers, and coal miners with less than five years of employment. Control group members were excluded for various reasons, including if they had worked in a dusty trade, had a radiograph with rounded opacities greater than 0/1, or never smoked regularly. It is important to note that the coal miners were also excluded for the analysis examining a relationship between dyspnea and asbestos exposure. The author did not provide much of a discussion pertaining to similarities between the exposed and control groups in this study, which would have been beneficial to ensure that analyses were conducted appropriately.
Domain 2: Exposure Characterization				

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Study Citation: Amandus, H. (1986). The morbidity and mortality of vermiculite miners and millers exposed to tremolite-actinolite. NIOSH(59):19861986.
Health Outcome: Respiratory symptoms including cough, phlegm, dyspnea, and wheezing
Target Organ(s): Lung/Respiratory: Respiratory symptom: Cough, Respiratory symptom: Phlegm, Respiratory symptom: Dyspnea, Respiratory symptom: Wheezing
Asbestos Fiber Type(s): Asbestos- Libby amphibole: 1318-09-8; Asbestos - Tremolite: 14567-73-8; Asbestos - Actinolite: 12172-67-7
Linked HERO ID(s): 3100838, 29839, 759132, 783513
HERO ID: 3100838

Domain	Metric		Rating	Comments
	Metric 4:	Measurement of Exposure	High	For the morbidity study, the date of the most recent radiograph examination was used to calculate the cumulative exposure levels. As detailed in the section for the mortality study, air dust samples were collected at various timepoints in different areas of the mill/mine. Midget impingers were used to sample the dust in years prior to 1969, and these values were reported as million particles per cubic foot of air (mppcf). After 1967, membrane filter samples were collected, and values were instead reported as fibers per cubic centimeter of air (f/cc). This information was used to generate a fiber-year estimate for the individuals enrolled in the study. It is important to note that only samples taken between 1965 and 1971 were used for these calculations. Several steps were undertaken to determine job exposure estimates for the fiber-years accumulated for the participants. These steps included coding the workers' jobs and abstracting fiber concentrations, dividing the facility into various location-operations, determining the arithmetic mean to compute average f/cc concentrations, converting impingers measurements into appropriate units, estimating the exposure level at the various location-operations, utilizing a plant manager to estimate the hours worked at these locations, determining work histories, and computing the individual participant's cumulative exposure index. The authors also detail that some of the area samples of airborne dust were analyzed with phase contrast microscopy (Pearce, 1998, 3100838).
	Metric 5:	Exposure Levels	Medium	The authors reported a wide range of exposure levels in both the morbidity and the mortality studies. For example, Table 4.5 details radiographic findings by fiber-years, with groupings of 0-15, 16-30, 31-85, and >86 f-y.
	Metric 6:	Temporality	Medium	There was a range of latency groups included in the morbidity and mortality studies. While temporality is established for the participants, it is unclear if there was an adequate level of follow-up for the consideration of latency. The average tenure for the morbidity study was 14 years. Because the inclusion criteria required workers to have been employed for at least one year, there is a wide range of potential latencies included in this study.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Uninformative	Other Non-Cancer Outcomes: For respiratory symptoms in the morbidity study, symptoms were considered present if the participant gave an affirmative answer to their questions pertaining to cough, phlegm, dyspnea, and wheezing. Because these were self-reported, and there was no discussion of validation, the rating for this portion of the morbidity study is uninformative.

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Study Citation:	Amandus, H. (1986). The morbidity and mortality of vermiculite miners and millers exposed to tremolite-actinolite. NIOSH(59):19861986.
Health Outcome:	Respiratory symptoms including cough, phlegm, dyspnea, and wheezing
Target Organ(s):	Lung/Respiratory: Respiratory symptom: Cough, Respiratory symptom: Phlegm, Respiratory symptom: Dyspnea, Respiratory symptom: Wheezing
Asbestos Fiber Type(s):	Asbestos- Libby amphibole: 1318-09-8; Asbestos - Tremolite: 14567-73-8; Asbestos - Actinolite: 12172-67-7
Linked HERO ID(s):	3100838, 29839, 759132, 783513
HERO ID:	3100838

Domain	Metric		Rating	Comments
	Metric 8:	Reporting Bias	Medium	There are a number of findings reported at various points throughout this study. Where appropriate, standard errors and associated confidence intervals are reported, and in many instances, there are reports of the number of participants who fall within the respective categories. However, the confidence intervals and standard errors are not reported for every table and figure.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Medium	In the morbidity study, some of the analyses included covariate adjustment. For the respiratory symptoms examined, only dyspnea had covariates adjusted for, including smoking and age.
	Metric 10:	Covariate Characterization	Medium	There was no information presented pertaining to the methods for validating the assessment of potential confounders. However, there was no indication that the method had poor validity.
	Metric 11:	Co-exposure Counfounding	Low	Both studies conducted are examining asbestos exposure and health outcomes amongst vermiculite workers. However, it does not appear that the author is controlling for vermiculite exposure itself. While they mention that ”vermiculite has not been associated with significant health effects” there is still a potential for some impact of vermiculite dust on the workers (Amandus, 1986), and it may have been beneficial to control for.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	Medium	The study design implemented is appropriate for the research question being examined.
	Metric 13:	Statistical Power	Uninformative	When looking at the respiratory symptoms outcomes, it is noted by the author that ”the number of cases were small and statistical power was low” (Amandus, 1986). This presents some concern for the utility of results for these outcomes.
	Metric 14:	Reproducibility of Analyses	Medium	The description of the analysis is sufficient to understand how to conceptually reproduce the analysis with access to the analytical data.
	Metric 15:	Statistical Analysis	Low	While some statistical models were used, there was no description of the model assumptions present within this study. Assumptions for the regressions performed in the morbidity study were not reported. However, the method for calculating SMRs in the mortality analysis were described.

Additional Comments: It is important to note that this study was a dissertation. While the author examined both morbidity and mortality, some metrics were rated differently due to differences in outcome ascertainment, analysis etc. This particular outcome, respiratory symptoms, was rated as uninformative because of the self-reported nature of the symptoms. There were also some concerns about this outcome because of the number of cases and low statistical power.While the measurement exposure (M4) and/or exposure levels (M5) metrics are rated as medium upon review by both set of reviewers, the overall quality determination (OQD) is rated uninformative due to lack confidence on the outcome measurement.

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Study Citation:	Amandus, H. (1986). The morbidity and mortality of vermiculite miners and millers exposed to tremolite-actinolite. NIOSH(59):19861986.
Health Outcome:	Respiratory symptoms including cough, phlegm, dyspnea, and wheezing
Target Organ(s):	Lung/Respiratory: Respiratory symptom: Cough, Respiratory symptom: Phlegm, Respiratory symptom: Dyspnea, Respiratory symptom: Wheezing
Asbestos Fiber Type(s):	Asbestos- Libby amphibole: 1318-09-8; Asbestos - Tremolite: 14567-73-8; Asbestos - Actinolite: 12172-67-7
Linked HERO ID(s):	3100838, 29839, 759132, 783513
HERO ID:	3100838

Domain	Metric	Rating	Comments
Overall Quality Determination		**Uninformative**	

* No biomarkers were identified for this evaluation.

Study Citation:	Amandus, H. (1986). The morbidity and mortality of vermiculite miners and millers exposed to tremolite-actinolite. NIOSH(59):19861986.
Health Outcome:	Lung Cancer; digestive, respiratory cancer; Pleural Plaques; circulatory disease, NMRD
Target Organ(s):	Lung/Respiratory: Non-malignant respiratory disease (NMRD) mortality, Lung cancer, respiratory cancer, carcinoma trachea, bronchi, lung, small opacities, pleural thickening (plaques), pleural calcification; Cardiovascular: All diseases of the circulatory system; Mortality: Non-malignant respiratory disease (NMRD) mortality, All cause mortality, Respiratory cancer, carcinoma trachea, bronchi, lung; Gastrointestinal: Digestive cancer; Cancer/Carcinogenesis: Digestive cancer, Lung cancer, respiratory cancer, carcinoma trachea, bronchi, lung
Asbestos Fiber Type(s):	Asbestos- Libby amphibole: 1318-09-8; Asbestos - Tremolite: 14567-73-8; Asbestos - Actinolite: 12172-67-7
Linked HERO ID(s):	3100838, 29839, 759132, 783513
HERO ID:	3100838

Domain	Metric		Rating	Comments
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Low	This metric is rated low because the studies or any cited methods source do not explicitly mention the use of PCM or TEM (Amandus et al., 1988, 783513; Armstrong et al., 1988, 759132).This metric was also rated low for (Amandus & Wheeler, 1987, 29839), as the methods section or any cited source did not explicitly mention the use of PCM or TEM. However, one of the cited sources mentions TEM for mineralogical purposes, unrelated to the determination of exposure estimates (Mcdonald et al., 1986, 29964).
	Metric 5:	Exposure Levels	Medium	The range and distribution of exposure is sufficient to develop an adequate exposure-response estimate, and three or more levels of exposure are reported (Amandus et al., 1988, 783513; Armstrong et al., 1988, 759132; Amandus & Wheeler, 1987, 29839).

Additional Comments: This portion of the cohort was not fully evaluated because the methods section or any cited sources did not explicitly mention the use of PCM or TEM (Amandus et al., 1988, 783513; Armstrong et al., 1988, 759132).One of the cited sources mentions TEM for mineralogical purposes, unrelated to the determination of exposure estimates (Mcdonald et al., 1986, 29964).While the measurement of exposure metric (M4) methods used to quantify the exposure were not well defined, the exposure levels metric (M5) information reported was adequate to determine an exposure-response relationship.

** As described in Appendix B.2 of the *White Paper: Quantitative Approach to the Human Health Assessment for the Risk Evaluation for Asbestos Part 2: Supplemental Evaluation Including Legacy Uses and Associated Disposals of Asbestos*, to be considered as being informative for dose-response analysis, metrics 4 and 5 would need metric ratings of Medium or High. This reference did not satisfy this requirement; therefore data quality evaluation is presented for only for metrics 4 and 5.

Study Citation:	Andrion, A., Colombo, A., Mollo, F. (1982). Lung asbestos bodies and pleural plaques at autopsy. Ricerca in Clinica e in Laboratorio 12(3):461-468.
Health Outcome:	Pleural Plaques
Target Organ(s):	Lung/Respiratory: Pleural plaques
Asbestos Fiber Type(s):	Asbestos - Not specified: 1332-21-4
Linked HERO ID(s):	3083914, 3083599
HERO ID:	3083914

Domain		Metric	Rating	Comments
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Low	Both studies used asbestos bodies from autopsied lung tissue for measurements of exposure. Professional judgement was used to determine asbestos bodies. The parent study observed ”true asbestos bodies with well-defined morphological figures” (Andrion et al. 1982, HERO ID: 3083914). The linked study observed both coated fibres (asbestos bodies) and uncoated fibres and the concentration of asbestos was calculated by extrapolation and provided in number of fibres per gram of dry weight (Andrion et al. 1984, HERO ID: 3083599).
	Metric 5:	Exposure Levels	Medium	The parent study used asbestos bodies by number of asbestos bodies in 6.74mm. This was further grouped into 0=no bodies, I= 1-10 bodies, II=11-100 bodies, and III= over 100 bodies. (Andrion et al. 1982, HERO ID: 3083914). The linked study used both coated and uncoated fibres. Uncoated fibres are grouped by 0, 1-10,000, 10,001-50,000, and >50,000. Coated fibres are grouped by 0, 1-100, 101-1,000, and >1,000 (Andrion et al. 1984, HERO ID: 3083599).

Additional Comments: Overall, this cohort reviews asbestos bodies and pleural plaques from autopsies. The linked study (Andrion et al. 1984, HERO ID: 3083599) lacks statistical analyses, but the paret study (Andrion et al. 1982, HERO ID: 3083914) provides associations. While this cohort is ranked as a medium, it may better fit as a Low rating overall for its missing gaps in exposure assessment and limited analyses.

** As described in Appendix B.2 of the *White Paper: Quantitative Approach to the Human Health Assessment for the Risk Evaluation for Asbestos Part 2: Supplemental Evaluation Including Legacy Uses and Associated Disposals of Asbestos*, to be considered as being informative for dose-response analysis, metrics 4 and 5 would need metric ratings of Medium or High. This reference did not satisfy this requirement; therefore data quality evaluation is presented for only for metrics 4 and 5.

Study Citation:	Anttila, S., Karjalainen, A., Taikina-Aho, O., Kyyrönen, P., Vainio, H. (1993). Lung cancer in the lower lobe is associated with pulmonary asbestos fiber count and fiber size. Environmental Health Perspectives 101(2):166-170.		
Health Outcome:	Lung Cancer; Asbestosis		
Target Organ(s):	Cancer/Carcinogenesis: Lung cancer, including squamous cell carcinomas, adenocarcinomas, small cell carcinomas, large cell carcinomas, and adenosquamous carcinoma; Lung/Respiratory: Lung cancer		
Asbestos Fiber Type(s):	Asbestos - Anthophyllite: 17068-78-9; Asbestos - Crocidolite (riebeckite): 12001-28-4; Asbestos - Chrysotile (serpentine): 12001-29-5; Asbestos - Amosite (grunerite): 12172-73-5		
Linked HERO ID(s):	No linked references.		
HERO ID:	3081975		

Domain	Metric	Rating	Comments
Domain 2: Exposure Characterization			
	Metric 4: Measurement of Exposure	Low	Exposure to asbestos was determined to quantify concentration of asbestos fibers in lung tissue samples. Since an interview structure was utilized to determine general classifications of asbestos exposure, there is no information on air concentrations of asbestos.
	Metric 5: Exposure Levels	Low	There was no direct of asbestos fibers using monitoring . Asbestos exposure information was generated from asbestos fiber concentrations found in dried lung tissue samples from the study participants.

Additional Comments: As the QC reviewer, I also rate this study medium for several reasons. This study used a job exposure matrix to estimate the level of asbestos exposure into Definite Exposure, Probable Exposure, Possible Exposure, and Unlikely Exposure. The outcome of interest (lung cancer cases were confirmed by histological means). However, even though no direct air measurements were taken, the authors examined lung tissue samples of the participants to determine fibrosis, fiber type, etc. Those with signs of obstructive pneumonia were not included in the analysis. Table 3 includes information on the unadjusted and adjusted odds ratios for various factors and their relation to lower lobe tumors.Overall, information on the measurement of exposure metric (M4) to assess exposure was limited. Additionally, the exposure levels metric (M5) information reported was limited to determine exposure-response relationships.

* No biomarkers were identified for this evaluation.

** As described in Appendix B.2 of the *White Paper: Quantitative Approach to the Human Health Assessment for the Risk Evaluation for Asbestos Part 2: Supplemental Evaluation Including Legacy Uses and Associated Disposals of Asbestos*, to be considered as being informative for dose-response analysis, metrics 4 and 5 would need metric ratings of Medium or High. This reference did not satisfy this requirement; therefore data quality evaluation is presented for only for metrics 4 and 5.

Study Citation:	Arakawa, H., Kishimoto, T., Ashizawa, K., Kato, K., Okamoto, K., Honma, K., Hayashi, S., Akira, M. (2015). Asbestosis and other pulmonary fibrosis in asbestos-exposed workers: high-resolution CT features with pathological correlations. European Radiology 26(5):1485-1492.
Health Outcome:	Asbestosis
Target Organ(s):	Lung/Respiratory: Asbestosis (CT asbestos score)
Asbestos Fiber Type(s):	Asbestos - Not specified: 1332-21-4
Linked HERO ID(s):	No linked references.
HERO ID:	3077721

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Medium	Key elements of the study design were reported within this retrospective case study of a subset of possible asbestosis cases obtained from a Japanese nationwide hospital network that cares for asbestos workers. Of these cases (total number from hospital network not detailed), only those with a lobectomy or autopsy specimen (total: n=33, males: n=31, females: n=2; mean age at computed tomography (CT): 73 years) who underwent high-resolution chest CT between May 2000 and July 2011 were selected and enrolled for study. Of these, 30 cases underwent autopsy, and three cases had lobectomies for lung cancer. Only those images of patients in stable condition and without complications such as pneumonia or advanced lung cancer were evaluated. It is unclear if the exposure-outcome distribution of those selected is representative of the target population as the total number of possible asbestosis cases within the hospital network was not revealed, and only those cases with autopsy or pathology specimens, and potentially higher exposures or more disease, were selected for study. Authors noted the potential for selection bias.
	Metric 2:	Attrition	Low	Of the total hospital network possible asbestosis cases (number not detailed), only those with lobectomy or autopsy specimens, in stable conditions and without complications, were selected. The number of potential participants noted as possible asbestosis cases but without lobectomy or autopsy specimens was not detailed.
	Metric 3:	Comparison Group	Medium	Inclusion criteria and methods of participant selection were reported and all subjects were selected from the same eligible population within the same time frame. Demographic and other potentially relevant differences between subjects with differing levels of asbestos body counts were not detailed, however Table 1 notes that age and work period were not significantly different between asbestosis and non-asbestosis groups. It is unclear to what extent various aspects (such as healthy hire, healthy worker survivor) of the healthy worker effect might have been a factor in the cohort for study.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	High	Asbestos body counts were analyzed by transmission electron microscopy.
	Metric 5:	Exposure Levels	Medium	The range and distribution of asbestos body (AB) counts presented in Table 1 (AB mean (SD) for the Asbestosis group (n=15): 1,464,711 (1,974822); non-Asbestosis group (n=18): 98,745 (174,492)) is sufficient to develop an exposure response relationship. Correlation analyses utilized asbestos body counts as a continuous variable correlated with asbestosis scores.

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Study Citation:	Arakawa, H., Kishimoto, T., Ashizawa, K., Kato, K., Okamoto, K., Honma, K., Hayashi, S., Akira, M. (2015). Asbestosis and other pulmonary fibrosis in asbestos-exposed workers: high-resolution CT features with pathological correlations. European Radiology 26(5):1485-1492.
Health Outcome:	Asbestosis
Target Organ(s):	Lung/Respiratory: Asbestosis (CT asbestos score)
Asbestos Fiber Type(s):	Asbestos - Not specified: 1332-21-4
Linked HERO ID(s):	No linked references.
HERO ID:	3077721

Domain	Metric		Rating	Comments
	Metric 6:	Temporality	Medium	This study establishes appropriate temporality within occupational histories, but it is unclear if the interval between exposure and outcome is long enough for consideration of latency of the outcome for those with 10 years of exposure as working years ranged from 10 to 42 years (mean=24 years).
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Medium	Asbestosis: Outcomes of CT asbestosis score and pathological asbestosis score were investigated. CT images of cases were reviewed by two independent, experienced (over twenty years) radiologists aware of patient age and sex but blinded to pathological diagnoses and occupational histories, with disagreements resolved by a third experienced (over twenty years) radiologist. Pleural disease scores were averaged across pulmonary zones and the likelihood of asbestosis was designated for each case from a separate four-point scale: 0=not asbestosis, 1=possible asbestosis, 2=probably asbestosis, 3=definite asbestosis. Summation of the pleural disease and asbestosis likelihood scores provided the final CT-asbestosis score. Asbestosis diagnosis was made as in Akira et al., 2003 (HERO ID not available), and al-Jarad et al., (1992) (HERO ID not available). Authors noted CT images were obtained in the supine position with potential for difficulty in the analyses of ground-glass opacity and subpleural curvilinear lines. Radiologist inter-observer agreements were 4.9 and 1.2 for ground glass opacity and curvilinear lines by single determination standard deviation, respectively.
	Metric 8:	Reporting Bias	High	There were no concerns for selective reporting as all outcomes which were outlined within methods were also reported within the results. Correlations between asbestos body counts and CT asbestosis and pathological asbestosis scores were reported as correlation coefficients with corresponding p-values.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Low	Other than stratification of mean ages across asbestosis and non-asbestosis groups in Table 1, and the detail within the text regarding the total number of females (n=2), no adjustments for gender, age or race appear to have been made within analyses and the distribution of additional potentially relevant covariates and potential confounders was not reported.
	Metric 10:	Covariate Characterization	N/A	Covariates were not considered within final correlational analyses.

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Study Citation:	Arakawa, H., Kishimoto, T., Ashizawa, K., Kato, K., Okamoto, K., Honma, K., Hayashi, S., Akira, M. (2015). Asbestosis and other pulmonary fibrosis in asbestos-exposed workers: high-resolution CT features with pathological correlations. European Radiology 26(5):1485-1492.
Health Outcome:	Asbestosis
Target Organ(s):	Lung/Respiratory: Asbestosis (CT asbestos score)
Asbestos Fiber Type(s):	Asbestos - Not specified: 1332-21-4
Linked HERO ID(s):	No linked references.
HERO ID:	3077721

Domain	Metric		Rating	Comments
	Metric 11:	Co-exposure Counfounding	Low	The members of the cohort were workers with varying occupations. Occupational histories included: asbestos-manufacturing (n=9), shipyard workers (n=8), asbestos-spraying (n=4), boiler repair (n=2), insulation worker (n=2), plumbing worker (n=2) and others (n=5). Authors noted that non-asbestosis cases included workers exposed to asbestos as well as other kinds of dust, however additional details regarding these other kinds of dust were not provided and co-exposures were not addressed. Considerations for workers who might have initially left and worked elsewhere with additional exposures but eventually returned to asbestos work were not detailed. However, there was no evidence that there was an unbalanced provision of co-exposures among exposure groups.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	Medium	The study design was appropriate as an initial study to address the research aims. The correlations of asbestos body count and CT/pathological scores were evaluated with the Spearman rank correlation coefficient, however consideration for multivariate analyses was not detailed. A value of $p<0.05$ was considered significant. Additional analyses were detailed for the agreement of CT and pathological scores, calculated by weighted kappa statistics. The difference in CT scores between asbestosis and non-asbestosis cases was evaluated by a non-parametric test (IBM SPSS Statistics ver. 22, Tokyo, Japan).
	Metric 13:	Statistical Power	Medium	The number of participants (n=33 total with n=15 asbestosis and n=18 non-asbestosis cases) was minimal and described by the authors as small in number, but was adequate for Spearman rank correlation.
	Metric 14:	Reproducibility of Analyses	Medium	The description of analysis is sufficient to understand how to reproduce the analysis of the correlation between asbestos body count and CT/pathological scores.
	Metric 15:	Statistical Analysis	N/A	Model building was not utilized.
Domain 6: Other (if applicable) Considerations for Biomarker Selection and Measurement (Lakind et al. 2014)				
	Metric 16:	Use of Biomarker of Exposure	Low	Evidence was not detailed describing a relationship between asbestos body counts and external occupational exposure specific for this population.
	Metric 17:	Effect Biomarker	N/A	Biomarkers of effect were not assessed.
	Metric 18:	Method Sensitivity	Low	LOD/LOQ was not stated. The analytical method was noted to be transmission electron microscopy for asbestos body counts.
	Metric 19:	Biomarker Stability	Low	Lung specimen sample storage history and stability not detailed.
	Metric 20:	Sample Contamination	Medium	There is no information included regarding contamination.
	Metric 21:	Method Requirements	High	Transmission electron microscopy utilized to provide identification and quantitation of asbestos bodies.

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Study Citation:	Arakawa, H., Kishimoto, T., Ashizawa, K., Kato, K., Okamoto, K., Honma, K., Hayashi, S., Akira, M. (2015). Asbestosis and other pulmonary fibrosis in asbestos-exposed workers: high-resolution CT features with pathological correlations. European Radiology 26(5):1485-1492.
Health Outcome:	Asbestosis
Target Organ(s):	Lung/Respiratory: Asbestosis (CT asbestos score)
Asbestos Fiber Type(s):	Asbestos - Not specified: 1332-21-4
Linked HERO ID(s):	No linked references.
HERO ID:	3077721

Domain	Metric		Rating	Comments
	Metric 22:	Matrix Adjustment	N/A	Matrix adjustment is not required.

Additional Comments:	Cases of possible asbestosis were obtained from a Japanese nationwide hospital network that cares for asbestos workers in this retrospective case study. Of these cases (total number from hospital network not detailed), only those with a pathologic lobectomy or autopsy specimen (total: n=33, males: n=31, females: n=2; mean age at computed tomography (CT): 73 years) who underwent high-resolution chest CT between May 2000 and July 2011 were selected and enrolled for study. Of these, 30 cases underwent autopsy, and three cases had lobectomies for lung cancer. Only those images of patients in stable condition and without complications such as pneumonia or advanced lung cancer were evaluated. Outcomes of CT asbestosis score and pathological asbestosis score were investigated. The number of asbestos bodies, not the number of asbestos fibers, were counted by experienced technicians described as within participating institutions and utilizing transmission electron microscopy (TEM) asbestos counting methods as within Koyama et al., 1991 (HERO ID 709715). Occupational histories included: asbestos-manufacturing (n=9), shipyard workers (n=8), asbestos-spraying (n=4), boiler repair (n=2), insulation worker (n=2), plumbing worker (n=2) and others (n=5). Working years ranged from 10 to 42 years (mean=24 years). Asbestos body count positively correlated with CT likelihood of asbestosis (r=0.503, p=0.003), and with the pathological asbestosis score (r=0.637, p<0.001) (Figures 4 and 5). CT-asbestosis score and pathological asbestosis score also showed a significant positive correlation (r=0.656, p<0.001).

Overall Quality Determination — Medium

Study Citation:	Arakawa, H., Kishimoto, T., Ashizawa, K., Kato, K., Okamoto, K., Honma, K., Hayashi, S., Akira, M. (2015). Asbestosis and other pulmonary fibrosis in asbestos-exposed workers: high-resolution CT features with pathological correlations. European Radiology 26(5):1485-1492.			
Health Outcome:	Asbestosis			
Target Organ(s):	Lung/Respiratory: Asbestosis (pathological asbestos score)			
Asbestos Fiber Type(s):	Asbestos - Not specified: 1332-21-4			
Linked HERO ID(s):	No linked references.			
HERO ID:	3077721			
Domain		Metric	Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Medium	Key elements of the study design were reported within this retrospective case study of a subset of possible asbestosis cases obtained from a Japanese nationwide hospital network that cares for asbestos workers. Of these cases (total number from hospital network not detailed), only those with a lobectomy or autopsy specimen (total: n=33, males: n=31, females: n=2; mean age at computed tomography (CT): 73 years) who underwent high-resolution chest CT between May 2000 and July 2011 were selected and enrolled for study. Of these, 30 cases underwent autopsy, and three cases had lobectomies for lung cancer. Only those images of patients in stable condition and without complications such as pneumonia or advanced lung cancer were evaluated. It is unclear if the exposure-outcome distribution of those selected is representative of the target population as the total number of possible asbestosis cases within the hospital network was not revealed, and only those cases with autopsy or pathology specimens, and potentially higher exposures or more disease, were selected for study. Authors noted the potential for selection bias.
	Metric 2:	Attrition	Low	Of the total hospital network possible asbestosis cases (number not detailed), only those with lobectomy or autopsy specimens, in stable conditions and without complications, were selected. The number of potential participants noted as possible asbestosis cases but without lobectomy or autopsy specimens was not detailed.
	Metric 3:	Comparison Group	Medium	Inclusion criteria and methods of participant selection were reported and all subjects were selected from the same eligible population within the same time frame. Demographic and other potentially relevant differences between subjects with differing levels of asbestos body counts were not detailed, however Table 1 notes that age and work period were not significantly different between asbestosis and non-asbestosis groups. It is unclear to what extent various aspects (such as healthy hire, healthy worker survivor) of the healthy worker effect might have been a factor in the cohort for study.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	High	Asbestos body counts were analyzed by transmission electron microscopy.
	Metric 5:	Exposure Levels	Medium	The range and distribution of asbestos body (AB) counts presented in Table 1 (AB mean (SD) for the Asbestosis group (n=15): 1,464,711 (1,974822); non-Asbestosis group (n=18): 98,745 (174,492)) is sufficient to develop an exposure response relationship. Correlation analyses utilized asbestos body counts as a continuous variable correlated with asbestosis scores.

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Study Citation: Arakawa, H., Kishimoto, T., Ashizawa, K., Kato, K., Okamoto, K., Honma, K., Hayashi, S., Akira, M. (2015). Asbestosis and other pulmonary fibrosis in asbestos-exposed workers: high-resolution CT features with pathological correlations. European Radiology 26(5):1485-1492.
Health Outcome: Asbestosis
Target Organ(s): Lung/Respiratory: Asbestosis (pathological asbestos score)
Asbestos Fiber Type(s): Asbestos - Not specified: 1332-21-4
Linked HERO ID(s): No linked references.
HERO ID: 3077721

Domain	Metric		Rating	Comments
	Metric 6:	Temporality	Medium	This study establishes appropriate temporality within occupational histories, but it is unclear if the interval between exposure and outcome is long enough for consideration of latency of the outcome for those with 10 years of exposure as working years ranged from 10 to 42 years (mean=24 years).
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	High	Asbestosis: Outcomes of CT asbestosis score and pathological asbestosis score were investigated. Pathological asbestosis diagnoses of pulmonary tissues specimens from autopsy and lobectomy were made based upon asbestosis diagnostic criteria as in Roggli et al., 2010 (HERO ID 2587237) by two independent pulmonary pathologists blinded to case occupational history with pathological asbestosis diagnoses based upon a three-point scale: 0=fibrosis other than asbestosis, 1=possible asbestosis, 2=definite asbestosis. A pathological asbestosis score was obtained through the summation of the scores given by each pathologist.
	Metric 8:	Reporting Bias	High	There were no concerns for selective reporting as all outcomes which were outlined within methods were also reported within the results. Correlations between asbestos body counts and CT asbestosis and pathological asbestosis scores were reported as correlation coefficients with corresponding p-values.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Low	Other than stratification of mean ages across asbestosis and non-asbestosis groups in Table 1, and the detail within the text regarding the total number of females (n=2), no adjustments for gender, age or race appear to have been made within analyses and the distribution of additional potentially relevant covariates and potential confounders was not reported.
	Metric 10:	Covariate Characterization	N/A	Covariates were not considered within final correlational analyses.
	Metric 11:	Co-exposure Counfounding	Low	The members of the cohort were workers with varying occupations. Occupational histories included: asbestos-manufacturing (n=9), shipyard workers (n=8), asbestos-spraying (n=4), boiler repair (n=2), insulation worker (n=2), plumbing worker (n=2) and others (n=5). Authors noted that non-asbestosis cases included workers exposed to asbestos as well as other kinds of dust, however additional details regarding these other kinds of dust were not provided and co-exposures were not addressed. Considerations for workers who might have initially left and worked elsewhere with additional exposures but eventually returned to asbestos work were not detailed. However, there was no evidence that there was an unbalanced provision of co-exposures among exposure groups.
Domain 5: Analysis				

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Study Citation:	Arakawa, H., Kishimoto, T., Ashizawa, K., Kato, K., Okamoto, K., Honma, K., Hayashi, S., Akira, M. (2015). Asbestosis and other pulmonary fibrosis in asbestos-exposed workers: high-resolution CT features with pathological correlations. European Radiology 26(5):1485-1492.
Health Outcome:	Asbestosis
Target Organ(s):	Lung/Respiratory: Asbestosis (pathological asbestos score)
Asbestos Fiber Type(s):	Asbestos - Not specified: 1332-21-4
Linked HERO ID(s):	No linked references.
HERO ID:	3077721

Domain	Metric		Rating	Comments
	Metric 12:	Study Design and Methods	Medium	The study design was appropriate as an initial study to address the research aims. The correlations of asbestos body count and CT/pathological scores were evaluated with the Spearman rank correlation coefficient, however consideration for multivariate analyses was not detailed. A value of $p<0.05$ was considered significant. Additional analyses were detailed for the agreement of CT and pathological scores, calculated by weighted kappa statistics. The difference in CT scores between asbestosis and non-asbestosis cases was evaluated by a non-parametric test (IBM SPSS Statistics ver. 22, Tokyo, Japan).
	Metric 13:	Statistical Power	Medium	The number of participants (n=33 total with n=15 asbestosis and n=18 non-asbestosis cases) was minimal and described by the authors as small in number, but was adequate for Spearman rank correlation.
	Metric 14:	Reproducibility of Analyses	Medium	The description of analysis is sufficient to understand how to reproduce the analysis of the correlation between asbestos body count and CT/pathological scores.
	Metric 15:	Statistical Analysis	N/A	Model building was not utilized.
Domain 6: Other (if applicable) Considerations for Biomarker Selection and Measurement (Lakind et al. 2014)				
	Metric 16:	Use of Biomarker of Exposure	Low	Evidence was not detailed describing a relationship between asbestos body counts and external occupational exposure specific for this population.
	Metric 17:	Effect Biomarker	N/A	Biomarkers of effect were not assessed.
	Metric 18:	Method Sensitivity	Low	LOD/LOQ was not stated. The analytical method was noted to be transmission electron microscopy for asbestos body counts.
	Metric 19:	Biomarker Stability	Low	Lung specimen sample storage history and stability not detailed.
	Metric 20:	Sample Contamination	Medium	There is no information included regarding contamination.
	Metric 21:	Method Requirements	High	Transmission electron microscopy utilized to provide identification and quantitation of asbestos bodies.
	Metric 22:	Matrix Adjustment	N/A	Matrix adjustment is not required.

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Study Citation:	Arakawa, H., Kishimoto, T., Ashizawa, K., Kato, K., Okamoto, K., Honma, K., Hayashi, S., Akira, M. (2015). Asbestosis and other pulmonary fibrosis in asbestos-exposed workers: high-resolution CT features with pathological correlations. European Radiology 26(5):1485-1492.
Health Outcome:	Asbestosis
Target Organ(s):	Lung/Respiratory: Asbestosis (pathological asbestos score)
Asbestos Fiber Type(s):	Asbestos - Not specified: 1332-21-4
Linked HERO ID(s):	No linked references.
HERO ID:	3077721

Domain	Metric	Rating	Comments
Additional Comments:	Cases of possible asbestosis were obtained from a Japanese nationwide hospital network that cares for asbestos workers in this retrospective case study. Of these cases (total number from hospital network not detailed), only those with a pathologic lobectomy or autopsy specimen (total: n=33, males: n=31, females: n=2; mean age at computed tomography (CT): 73 years) who underwent high-resolution chest CT between May 2000 and July 2011 were selected and enrolled for study. Of these, 30 cases underwent autopsy, and three cases had lobectomies for lung cancer. Only those images of patients in stable condition and without complications such as pneumonia or advanced lung cancer were evaluated. Outcomes of CT asbestosis score and pathological asbestosis score were investigated. The number of asbestos bodies, not the number of asbestos fibers, were counted by experienced technicians described as within participating institutions and utilizing transmission electron microscopy (TEM) asbestos counting methods as within Koyama et al., 1991 (HERO ID 709715). Occupational histories included: asbestos-manufacturing (n=9), shipyard workers (n=8), asbestos-spraying (n=4), boiler repair (n=2), insulation worker (n=2), plumbing worker (n=2) and others (n=5). Working years ranged from 10 to 42 years (mean=24 years). Asbestos body count positively correlated with CT likelihood of asbestosis (r=0.503, p=0.003), and with the pathological asbestosis score (r=0.637, p<0.001) (Figures 4 and 5). CT-asbestosis score and pathological asbestosis score also showed a significant positive correlation (r=0.656, p<0.001).		

Overall Quality Determination — Medium

Study Citation:	Armstrong, B. K., de Klerk, N. H., Musk, A. W., Hobbs, M. S. (1988). Mortality in miners and millers of crocidolite in Western Australia. British Journal of Industrial Medicine 45(1):13-May.
Health Outcome:	Lung Cancer; Laryngeal Cancer; gastrointestinal, respiratory; infectious and parasitic diseases, mental disorders, accidents and injuries
Target Organ(s):	Gastrointestinal: Stomach cancer mortality, Neoplasms of the prostate mortality, Other digestive neoplasms mortality (not stomach, intestines, or pancreas), Neoplasms of the oesophagus mortality, Colorectal cancer mortality, Digestive diseases mortality, Neoplasms of intestines including rectum mortality, Neoplasms of pancreas mortality, Peptic ulceration mortality, Other digestive diseases mortality (not peptic ulceration or cirrhosis of the liver); nan: ; Cancer/Carcinogenesis: Lung cancer mortality, Stomach cancer mortality, Neoplasms of the prostate mortality, Lymphoma and myeloma mortality, Other digestive neoplasms mortality (not stomach, intestines, or pancreas), Neoplasms of the pancreas mortality, Neoplasms of the oesophagus mortality, Colorectal cancer mortality, Cancer of the larynx/pharynx mortality, All cancers mortality, Neoplasms of upper aerodigestive tract mortality, Neoplasms of intestines including rectum mortality, Neoplasms of larynx mortality, Neoplasms of trachea, bronchus, and lung, Other neoplasms mortality (not upper aerodigestive tract, oesophagus, gastrointestinal, larynx, trachea, bronchus, lung, mesothelioma, prostate, lymphoma, or myeloma); Lung/Respiratory: Lung cancer mortality, Pneumoconiosis mortality, Bronchitis and emphysema mortality, Respiratory diseases mortality, Tuberculosis mortality, Cancer of the larynx/pharynx mortality, Neoplasms of larynx mortality, Neoplasms of trachea, bronchus, and lung, Other respiratory disease mortality (not pneumoconiosis, bronchitis, or emphsyema); Mortality: Pneumoconiosis mortality, Bronchitis and emphysema mortality, Respiratory diseases mortality, Neoplasms of the prostate mortality, Lymphoma and myeloma mortality, Other digestive neoplasms mortality (not stomach, intestines, or pancreas), Neoplasms of the pancreas mortality, Neoplasms of the oesophagus mortality, Tuberculosis mortality, Colorectal cancer mortality, Liver cirrhosis mortality, Cardiovascular disease mortality, Lung cancer mortality, Stomach cancer mortality, Cancer of the larynx/pharynx mortality, All cancers mortality, All causes mortality, Mental disorders mortality, Nervous system and organ disease mortality, Infectious and parasitic diseases mortality, Digestive diseases mortality, Genitourinary diseases mortality, Other infectious and parasitic diseases (not Tuberculosis) mortality, Neoplasms of upper aerodigestive tract mortality, Neoplasms of intestines including rectum mortality, Neoplasms of larynx mortality, Neoplasms of trachea, bronchus, and lung, Other neoplasms mortality (not upper aerodigestive tract, oesophagus, gastrointestinal, larynx, trachea, bronchus, lung, mesothelioma, prostate, lymphoma, or myeloma), Alcoholism mortality, Other mental disorders mortality (non-alcoholism), Other respiratory disease mortality (not pneumoconiosis, bronchitis, or emphsyema), Peptic ulceration mortality, Other digestive diseases mortality (not peptic ulceration or cirrhosis of the liver); Hepatic/Liver: Liver cirrhosis mortality; Cardiovascular: Cardiovascular disease mortality; Neurological/Behavioral: Mental disorders mortality, Nervous system and organ disease mortality, Alcoholism mortality, Other mental disorders mortality (non-alcoholism); Renal/Kidney: Genitourinary diseases mortality; Immune/Hematological: Lymphoma and myeloma mortality
Asbestos Fiber Type(s):	Asbestos - Crocidolite (riebeckite): 12001-28-4
Linked HERO ID(s):	3083076, 6874474
HERO ID:	3083076

Domain	Metric		Rating	Comments
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Low	Dust concentration measurements were taken periodically at the mine and mill. A koniometer, which is a device used to estimate the amount of dust in the air, was utilized between 1948 and 1958. This only measured total dust per cubic centimeter (ppcc), and it had an upper limit of 1,000 ppcc. This limit was often exceeded. A survey was undertaken to determine the concentration of airborne crocidolite fibers greater than 5 microns in length in 1966. A Casella long running thermal precipitator was used to generate the data. A Casella gravimetric dust sampler and a Hexhelt were also used to estimate dust mass. No impingers or PCM/TEM were utilized in this study.This metric is rated low because the studies or any cited methods source do not explicitly mention the use of PCM or TEM (Armstrong et al., 1988, 3083076; Reid et al., 2018, 6874474).

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Study Citation:	Armstrong, B. K., de Klerk, N. H., Musk, A. W., Hobbs, M. S. (1988). Mortality in miners and millers of crocidolite in Western Australia. British Journal of Industrial Medicine 45(1):13-May.
Health Outcome:	Lung Cancer; Laryngeal Cancer; gastrointestinal, respiratory; infectious and parasitic diseases, mental disorders, accidents and injuries
Target Organ(s):	Gastrointestinal: Stomach cancer mortality, Neoplasms of the prostate mortality, Other digestive neoplasms mortality (not stomach, intestines, or pancreas), Neoplasms of the oesophagus mortality, Colorectal cancer mortality, Digestive diseases mortality, Neoplasms of intestines including rectum mortality, Neoplasms of pancreas mortality, Peptic ulceration mortality, Other digestive diseases mortality (not peptic ulceration or cirrhosis of the liver); nan: ; Cancer/Carcinogenesis: Lung cancer mortality, Stomach cancer mortality, Neoplasms of the prostate mortality, Lymphoma and myeloma mortality, Other digestive neoplasms mortality (not stomach, intestines, or pancreas), Neoplasms of the pancreas mortality, Neoplasms of the oesophagus mortality, Colorectal cancer mortality, Cancer of the larynx/pharynx mortality, All cancers mortality, Neoplasms of upper aerodigestive tract mortality, Neoplasms of intestines including rectum mortality, Neoplasms of larynx mortality, Neoplasms of trachea, bronchus, and lung, Other neoplasms mortality (not upper aerodigestive tract, oesophagus, gastrointestinal, larynx, trachea, bronchus, lung, mesothelioma, prostate, lymphoma, or myeloma); Lung/Respiratory: Lung cancer mortality, Pneumoconiosis mortality, Bronchitis and emphysema mortality, Respiratory diseases mortality, Tuberculosis mortality, Cancer of the larynx/pharynx mortality, Neoplasms of larynx mortality, Neoplasms of trachea, bronchus, and lung, Other respiratory disease mortality (not pneumoconiosis, bronchitis, or emphsyema); Mortality: Pneumoconiosis mortality, Bronchitis and emphysema mortality, Respiratory diseases mortality, Neoplasms of the prostate mortality, Lymphoma and myeloma mortality, Other digestive neoplasms mortality (not stomach, intestines, or pancreas), Neoplasms of the pancreas mortality, Neoplasms of the oesophagus mortality, Tuberculosis mortality, Colorectal cancer mortality, Liver cirrhosis mortality, Cardiovascular disease mortality, Lung cancer mortality, Stomach cancer mortality, Cancer of the larynx/pharynx mortality, All cancers mortality, All causes mortality, Mental disorders mortality, Nervous system and organ disease mortality, Infectious and parasitic diseases mortality, Digestive diseases mortality, Genitourinary diseases mortality, Other infectious and parasitic diseases (not Tuberculosis) mortality, Neoplasms of upper aerodigestive tract mortality, Neoplasms of intestines including rectum mortality, Neoplasms of larynx mortality, Neoplasms of trachea, bronchus, and lung, Other neoplasms mortality (not upper aerodigestive tract, oesophagus, gastrointestinal, larynx, trachea, bronchus, lung, mesothelioma, prostate, lymphoma, or myeloma), Alcoholism mortality, Other mental disorders mortality (non-alcoholism), Other respiratory disease mortality (not pneumoconiosis, bronchitis, or emphsyema), Peptic ulceration mortality, Other digestive diseases mortality (not peptic ulceration or cirrhosis of the liver); Hepatic/Liver: Liver cirrhosis mortality; Cardiovascular: Cardiovascular disease mortality; Neurological/Behavioral: Mental disorders mortality, Nervous system and organ disease mortality, Alcoholism mortality, Other mental disorders mortality (non-alcoholism); Renal/Kidney: Genitourinary diseases mortality; Immune/Hematological: Lymphoma and myeloma mortality
Asbestos Fiber Type(s):	Asbestos - Crocidolite (riebeckite): 12001-28-4
Linked HERO ID(s):	3083076, 6874474
HERO ID:	3083076

Domain	Metric		Rating	Comments
	Metric 5:	Exposure Levels	Medium	The figures included in the Armstrong et al., 1988, (HERO ID: 3083076) paper displays several mortality outcomes amongst the miners and millers at various exposure levels. They are split into groups as follows: <10 f/cc y, 10-100 f/cc y, and >100 f/cc y. They also include all exposures combined, which includes unknown exposures.The levels of exposure in the Reid et al. 2018 (HERO ID: 6874474) paper included <10 f/mL years, 10-50 f/mL years, and >50. These values allow for the development of an exposure-response estimate.

Additional Comments:	NOTE: This cohort was rated "Low" for Metric 4, and thus does not meet the criteria for usefulness for dose-response. Only outcome inventory, fiber types, and Metrics 4 and 5 received a full QC.There were several limitations in this paper. One of the primary concerns pertains to the use of an appropriate comparison group. The authors also did not discuss potential covariates to be included in the models, and the two different methods used to calculate SMRs may also introduce bias into the results.

* No biomarkers were identified for this evaluation.

** As described in Appendix B.2 of the *White Paper: Quantitative Approach to the Human Health Assessment for the Risk Evaluation for Asbestos Part 2: Supplemental Evaluation Including Legacy Uses and Associated Disposals of Asbestos*, to be considered as being informative for dose-response analysis, metrics 4 and 5 would need metric ratings of Medium or High. This reference did not satisfy this requirement; therefore data quality evaluation is presented for only for metrics 4 and 5.

Study Citation:	Bagatin, E., Neder, J. A., Nery, L. E., Terra-Filho, M., Kavakama, J., Castelo, A., Capelozzi, V., Sette, A., Kitamura, S., Favero, M., Moreira-Filho, D. C., Tavares, R., Peres, C., Becklake, M. R. (2005). Non-malignant consequences of decreasing asbestos exposure in the Brazil chrysotile mines and mills. Occupational and Environmental Medicine 62(6):381-389.
Health Outcome:	Pulmonary Function/Spirometry Results; Pleural Plaques
Target Organ(s):	Lung/Respiratory: FEV1, FVC, FEF, Dyspnea, Parenchymal abnormalities, Pleural and/or parenchymal abnormalities, Pleural plaques
Asbestos Fiber Type(s):	Asbestos - Tremolite: 14567-73-8; Asbestos - Chrysotile (serpentine): 12001-29-5
Linked HERO ID(s):	No linked references.
HERO ID:	2078960

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Medium	Cohort study, Ex-workers from a single asbestos mining and milling company who worked for the company for at least one year were invited to participate. Study population was separated into 3 groups whose working conditions improved over time: group I (1940–66, n = 180), group II (1967–76, n = 1317), and group III (1977–96, n = 2137). From the 6098 eligible subjects, 433 (7.1%) were found to bedead (148, 184, and 101 subjects for groups I, II, and III,respectively); 3634 of the remaining 5665 were actuallyexamined (64.1%). The rate of recruitment success variedbetween the different groups: group I=46.1% (180/390alive), group II=67.5% (1317/1950), and group III=64.2%(2137/3325) (table 1).
	Metric 2:	Attrition	Medium	121 lung function tests did not meet quality criteria and were not included in the study.
	Metric 3:	Comparison Group	Medium	The demographic and occupational variables differed significantly among the groups. Thus, group III subjects were younger and presented with a shorter latency than their counterparts of groups I and II (table 1). Higher cumulative exposure was also found in group I subjects compared to groups II and III. Subject numbers in group 1 n=180 compared to group 2 n=1317 and group 3 n=2137. Difference reported between exposure groups were controlled for.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Medium	Participants were split into three groups depending on when their exposure occurred. Group III had routine measurements of asbestos fibers, which were obtained by airborne samples from different areas of activity using a constant-flow sampler. A membrane filter was used to collect the fibers and the counting was done with a phase contrast microscope (PCM).
	Metric 5:	Exposure Levels	Medium	Tables 2 and 3 use binary exposure groups (i.e. less than 10 fibers/y/cc, or greater than or equal to 10 fibers/y/cc.) Tables 4 and 6 include a continuous measure of cumulative exposure (but this is not a robust analysis due to not considering confounders). The graphs in Figure 2 report three exposure levels (highest quartile, IQR, and lowest quartile).
	Metric 6:	Temporality	High	Latency differed across groups, however at the time of the present evaluation, more than half of group III workers already had a latency time of at least 20 years. Included in analysis was Group I (1940–66, n = 107), group II (1967–76, n = 930), and group III (1977–96, n = 713).

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Study Citation:	Bagatin, E., Neder, J. A., Nery, L. E., Terra-Filho, M., Kavakama, J., Castelo, A., Capelozzi, V., Sette, A., Kitamura, S., Favero, M., Moreira-Filho, D. C., Tavares, R., Peres, C., Becklake, M. R. (2005). Non-malignant consequences of decreasing asbestos exposure in the Brazil chrysotile mines and mills. Occupational and Environmental Medicine 62(6):381-389.
Health Outcome:	Pulmonary Function/Spirometry Results; Pleural Plaques
Target Organ(s):	Lung/Respiratory: FEV1, FVC, FEF, Dyspnea, Parenchymal abnormalities, Pleural and/or parenchymal abnormalities, Pleural plaques
Asbestos Fiber Type(s):	Asbestos - Tremolite: 14567-73-8; Asbestos - Chrysotile (serpentine): 12001-29-5
Linked HERO ID(s):	No linked references.
HERO ID:	2078960

Domain		Metric	Rating	Comments
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	High	Pulmonary Function/Spirometry Results: FVC1, FEF, FVC measured through spirometric tests, which were performed with a calibrated pneumo tacograph (Fleisch No. 3). The subjects completed at least three acceptable maximal forced expiratory manoeuvres: technical procedures, acceptability, and reproducibility criteria were those recommended by the American Thoracic Society.; Pleural Plaques: Standard high-kilovoltage, posteroanterior CRX were obtained, with radiographs classified by 3 chest physicians (2 B-readers and 1 A-reader) up to September 1999; after September 1999 one B-reader was replaced by a radiologist with 18 years' experience. Readers were blinded as to exposure status. Radiographs were interpreted using ILO standards; parenchymal opacities were reported if ILO reading was 1/0 or more. Profusion readings were reported as median values. Presence of pleural plaques also assessed.
	Metric 8:	Reporting Bias	High	The authors wanted to examine mortality but report that they were unable to due to a lack of reliability in death certificates. Additionally, the study reports information graphically but has point estimates reported in either the footnotes of graphs or in the text of the paper.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Low	Covariates included smoking, latency time, cumulative exposure. Sex and race were not adjusted for or analyzed.
	Metric 10:	Covariate Characterization	Medium	Collected via occupational interview.
	Metric 11:	Co-exposure Counfounding	Low	Co-exposure was not analyzed.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	Medium	The cohort uses a longitudinal design to study the long-term effects of asbestos exposure, using statistical models such as linear and logistic regression.
	Metric 13:	Statistical Power	Medium	This study included the following number of participants in each group: Group I (1940–66, n = 107), group II (1967–76, n = 930), and group III (1977–96, n = 713).
	Metric 14:	Reproducibility of Analyses	Medium	All analyses appear reproducible.
	Metric 15:	Statistical Analysis	Medium	The discussion of normality implies they did assess one of the assumptions for linear regression. A backward stepwise linear regression procedure was also used for analysing the relation of the spirometric variables to latency, cumulative exposure, smoking (pack-years), and radiographic abnormalities. Probability of type I error was established at 0.05 for all tests. Cumulative probability model in Figure 2

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Study Citation:	Bagatin, E., Neder, J. A., Nery, L. E., Terra-Filho, M., Kavakama, J., Castelo, A., Capelozzi, V., Sette, A., Kitamura, S., Favero, M., Moreira-Filho, D. C., Tavares, R., Peres, C., Becklake, M. R. (2005). Non-malignant consequences of decreasing asbestos exposure in the Brazil chrysotile mines and mills. Occupational and Environmental Medicine 62(6):381-389.		
Health Outcome:	Pulmonary Function/Spirometry Results; Pleural Plaques		
Target Organ(s):	Lung/Respiratory: FEV1, FVC, FEF, Dyspnea, Parenchymal abnormalities, Pleural and/or parenchymal abnormalities, Pleural plaques		
Asbestos Fiber Type(s):	Asbestos - Tremolite: 14567-73-8; Asbestos - Chrysotile (serpentine): 12001-29-5		
Linked HERO ID(s):	No linked references.		
HERO ID:	2078960		
Domain	Metric	Rating	Comments
Additional Comments:	A standardized occupational history was administered by interview, detailing the start and end of exposure, the specific workplace(s), and the estimated level of exposure (groups I and II) (Bagatin et al. 2004, HERO ID: 2078960). Groups I and II did not have routine systematic asbestos measurements, and thus a "subjective, logarithmic scale" was used to estimate indices of exposure based on fiber measurements before the development of routine measures. Participants self-identified their level of workplace dustiness as mild (0.3-3 fibers/cc), moderate (3-30 fibers/cc), or severe (more than 30 fibers/cc). Group I differed significantly in terms of size, latency, cumulative exposure and age. Dyspnea, wheezing, cough, phlegm were also assessed as was radiographic abnormalities (Bagatin et al. 2004, HERO ID: 2078960). Other study in other cohort revealed, however, that CXR compared to Thin-section CT was associated with false-positives for interstitial abnormalities and false-negatives for pleural plaques, regardless of the intensity of asbestos exposure (Terra-Filho et al. 2015, HERO ID: 3077807).		
Overall Quality Determination		**Medium**	

* No biomarkers were identified for this evaluation.

Study Citation:	Barbieri, P. G., Consonni, D., Somigliana, A. (2019). Relationship between pleural plaques prevalence and extension and biomarkers of cumulative asbestos dose. A necropsy study. La Medicina del Lavoro :353-362.		
Health Outcome:	Asbestosis; Pleural Plaques		
Target Organ(s):	Lung/Respiratory: Pleural plaques, Asbestosis		
Asbestos Fiber Type(s):	Asbestos - Amosite (grunerite): 12172-73-5; Asbestos - Crocidolite (riebeckite): 12001-28-4; Asbestos - Chrysotile (serpentine): 12001-29-5; Asbestos - Tremolite: 14567-73-8; Asbestos - Actinolite: 12172-67-7		
Linked HERO ID(s):	No linked references.		
HERO ID:	6861350		

Domain	Metric	Rating	Comments
Domain 2: Exposure Characterization			
	Metric 4: Measurement of Exposure	Low	The authors measured asbestos fibers in lung tissue of the subjects during necropsy, which represented a measure of cumulative exposure to asbestos over the lifetime. The authors did not collect primary or secondary data of asbestos fibers' concentration in the occupational exposure environment. The authors used SEM and what appears to be optical microscopy to quantify exposure, but this cannot be confirmed as the cited method is in Italian (Istituto Superiore di Sanità, 2017).
	Metric 5: Exposure Levels	Medium	The authors reported summary statistics representing four different levels of exposure associated with the pleural plaques' extension grades that are adequate for the development of an exposure-response relationship. (Table 1; millions of asbestos fibres and millions of amphibole fibres, per gram of dry lung tissue).

Additional Comments: The study authors may have had conflicts of interest in that they served as a consultants for victims' families in litigations concerning asbestos-related diseases.

** As described in Appendix B.2 of the *White Paper: Quantitative Approach to the Human Health Assessment for the Risk Evaluation for Asbestos Part 2: Supplemental Evaluation Including Legacy Uses and Associated Disposals of Asbestos*, to be considered as being informative for dose-response analysis, metrics 4 and 5 would need metric ratings of Medium or High. This reference did not satisfy this requirement; therefore data quality evaluation is presented for only for metrics 4 and 5.

Study Citation:	Beritić-Stahuljak, D., Valić, F., Zuskin, E. (1991). Relationship between cumulative occupational exposure to asbestos fibres and respiratory symptoms. Acta Medica Croatica 45(4-5):283-295.
Health Outcome:	Respiratory symptoms
Target Organ(s):	Lung/Respiratory: Respiratory symptom–chronic cough, Respiratory symptom–chronic phlegm, Respiratory symptom–chronic bronchitis, Respiratory symptom–dyspnea
Asbestos Fiber Type(s):	Asbestos - Not specified: 1332-21-4
Linked HERO ID(s):	No linked references.
HERO ID:	3082482

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Medium	This study examined the relationship between prevalent respiratory symptoms (chronic cough, chronic phlegm, chronic bronchitis, dyspnea) assessed through standardized interviews and asbestos exposure as represented by length of employment (years, range: 1-27 years), estimated cumulative exposure to total particles (particles/cc years), and estimated cumulative exposure to asbestos fibers (fibers/cc years) in asbestos workers (n=1127) engaged in asbestos mining, asbestos cement production, production of friction materials or the manufacture of asbestos textiles versus age-matched non-exposed controls (n=593).
	Metric 2:	Attrition	High	Characteristics, in terms of relevant variables of those possibly excluded due to missing outcome or exposure data, were not reported, however there was no indication that missing data or subject drop-out was an issue within this study.
	Metric 3:	Comparison Group	Medium	The control group (n=281) was described as having no known occupational exposure to airborne particles or irritant gases. Control subjects were described as age-matched (methods not specified) to asbestos male workers; however, text notes males and females were part of the exposed worker group (n=230 female nonsmoking asbestos workers). This study was restricted to employees working at the time of study and assessment of prevalent outcomes. It is unclear if healthy hire or healthy worker survivor effects were appreciable within this study which examined prevalent respiratory symptoms within a population with 1-27 years of employment exposure.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	High	Quantitative exposure measurements (1971-1974) of total airborne particulates and asbestos fibers were performed simultaneously during typical work cycles and were described in terms of equipment, procedures and referenced (Valic et al., 1988, foreign reference number 15 in text). Number of samples varied and time of sample collection ranged from 1 minute to three hours, depending on dust level. Asbestos exposure analytic methods utilized phase contrast illumination. Final estimated cumulative exposures calculations were based on mean measured concentrations measured during typical work cycles during all work shifts during two seasons, estimated duration of exposures, estimated weighted daily exposures for each typical work operation and complete work histories for each worker. Exposures in control subjects not detailed, however controls had no known occupational asbestos exposure.

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Study Citation: Beritić-Stahuljak, D., Valić, F., Zuskin, E. (1991). Relationship between cumulative occupational exposure to asbestos fibres and respiratory symptoms. Acta Medica Croatica 45(4-5):283-295.
Health Outcome: Respiratory symptoms
Target Organ(s): Lung/Respiratory: Respiratory symptom–chronic cough, Respiratory symptom–chronic phlegm, Respiratory symptom–chronic bronchitis, Respiratory symptom–dyspnea
Asbestos Fiber Type(s): Asbestos - Not specified: 1332-21-4
Linked HERO ID(s): No linked references.
HERO ID: 3082482

Domain	Metric		Rating	Comments
	Metric 5:	Exposure Levels	Medium	Measured (1971-1974) asbestos fiber concentrations (f/cc) were reported within Table 1 for each mine and factory work category and ranged from 0.3 – 62.0 f/cc for six categories of exposure. Summary measures of estimated cumulative exposures were detailed in Figure 1 footnote description of asbestos exposure categories and ranged from zero fibers/cc years to greater than 80 fibers/cc years. The range and distribution of exposure appeared adequate.
	Metric 6:	Temporality	Low	This study was restricted to employees working at the time of study and outcomes were those prevalent at time of assessment (dates of outcome assessment not provided). The temporality of exposure-outcome relationships is uncertain due to the cross-sectional nature of respiratory symptom outcome assessment within this study.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Medium	Other Non-Cancer Outcomes: Respiratory symptom outcomes of interest included prevalence of self-reported chronic cough, chronic phlegm, chronic bronchitis and dyspnea as assessed by standardized interview questionnaire, which was noted to be a modified form of the British Medical Research Council Questionnaire. Validation of outcomes was not reported, and results were participant reported, however there is no indication that methods had poor validity.
	Metric 8:	Reporting Bias	Medium	There were no concerns for selective reporting as all outcomes which were outlined within methods were also reported within the results. The results within Figure 1 were reported only as p-values for each level of exposure specified within figure footnotes, with details regarding number of participants, confidence intervals and standard errors lacking.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Medium	Controls were described as age-matched to male exposed workers. Text notes both male and female asbestos workers were included within analyses, however considerations for control of gender within analyses was lacking. Analyses within Tables 2-4 were restricted to those within categories of smokers and non-smokers. A distribution of demographic characteristics of exposed and control workers was presented.
	Metric 10:	Covariate Characterization	Medium	While the methods utilized to obtain and validate data regarding potential confounders were described only as obtained through interview, there is no indication that methods had poor validity and the interview methods were described as standardized.
	Metric 11:	Co-exposure Counfounding	Medium	Potential co-exposures somewhat considered by authors within assessment of total particles, however actual control of potential co-exposures potentially associated with increased experience of respiratory symptoms within a multivariate analyses was lacking.

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Study Citation:	Beritić-Stahuljak, D., Valić, F., Zuskin, E. (1991). Relationship between cumulative occupational exposure to asbestos fibres and respiratory symptoms. Acta Medica Croatica 45(4-5):283-295.
Health Outcome:	Respiratory symptoms
Target Organ(s):	Lung/Respiratory: Respiratory symptom–chronic cough, Respiratory symptom–chronic phlegm, Respiratory symptom–chronic bronchitis, Respiratory symptom–dyspnea
Asbestos Fiber Type(s):	Asbestos - Not specified: 1332-21-4
Linked HERO ID(s):	No linked references.
HERO ID:	3082482

Domain	Metric		Rating	Comments
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	Medium	Statistical analysis of the data within this study was not detailed within the text. Table 2 results for asbestos workers and controls indicate use of chi-square analyses for obtaining p-values, however statistical analyses for Figure 1 results are not detailed.
	Metric 13:	Statistical Power	Medium	The number of subjects (n=1127 asbestos workers, n=593 controls) appeared adequate for this analysis, although the number of subjects within each category of exposure within Figure 1 was not detailed.
	Metric 14:	Reproducibility of Analyses	Low	Statistical analysis methods were not reported and details such as rules for classification of smoking categories, consideration of outliers, transformation of continuous variables and methods for dealing with missing data were not detailed.
	Metric 15:	Statistical Analysis	Low	The description of statistical analysis was very brief and is only inferred from Table 2 as consisting of chi-square analyses.

Additional Comments: This study examined the relationship between prevalent respiratory symptoms (chronic cough, chronic phlegm, chronic bronchitis, dyspnea) assessed through standardized interviews and asbestos exposure as represented by length of employment (years, range: 1-27 years), estimated cumulative exposure to total particles (particles/cc years), and estimated cumulative exposure to asbestos fibers (fibers/cc years) in asbestos workers (n=1127) engaged in asbestos mining, asbestos cement production, production of friction materials or the manufacture of asbestos textiles versus age-matched non-exposed controls (n=593). Exposure was measured 1971-1974 and estimates of cumulative exposure were calculated utilizing these measurements as well as detailed complete work histories of each worker. Dates of assessment of respiratory outcomes through standardized interview questionnaire not specified. Results indicated a statistically significant relationship between prevalence of respiratory symptoms and duration of employment (Fig. 1A, $p<0.01$), total particles/cc years (Fig. 1B, $p<0.01$). The relationship between prevalence of respiratory symptoms and exposure expressed by measured asbestos fibers/cc years was not significant (Fig. 1C, $P>0.05$).

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation: Berry, G., Pooley, F., Gibbs, A., Harris, J., Mcdonald, J. (2009). Lung fiber burden in the Nottingham gas mask cohort. Inhalation Toxicology 21(2):168-172.
Health Outcome: mortality from other diseases and all cause mortality
Target Organ(s): Mortality: Other diseases, All cause mortality
Asbestos Fiber Type(s): Asbestos - Crocidolite (riebeckite): 12001-28-4
Linked HERO ID(s): No linked references.
HERO ID: 709467

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Medium	Key elements of study design were reported in this retrospective case study of a subset of the original Nottingham Gas Mask Cohort of n=1,154 mostly female employees who assembled military gas masks, 1940-1945, using filter pads containing 20% crocidolite asbestos. Within this cohort, a subset was selected of those with tissue samples. Lung tissue samples were obtained from 50 (77%) of the n=65 cases of mesothelioma, and n=20 deaths from other causes. Duration of employment was recorded in only 51 of the 70 deaths.
	Metric 2:	Attrition	Medium	Exclusions of subjects from the original cohort or analyses were adequately described for the cases (n=70) with lung tissue samples selected out of the original cohort (n=1,154) and those with employment duration data (n=-51 of n=70). Cause of death was not detailed for these exclusions for missing data.
	Metric 3:	Comparison Group	Medium	Inclusion criteria and methods of participant selection were reported. All included subjects came from the same original Nottingham cohort within the same time frame. It is unclear to what extent various aspects (healthy hire, healthy worker survivor, left truncation bias, exposure-dependent right censoring) of the healthy worker effect might have been a factor in the cohort for study.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	High	Crocidolite asbestos fiber levels per microgram of dried lung were analyzed by transmission electron microscopy.
	Metric 5:	Exposure Levels	Medium	The range and distribution of lung crocidolite fiber concentrations presented in Tables 1 and 2 by decade of death and categories (4 categories) of length (months) of exposure are sufficient to develop an exposure response relationship.
	Metric 6:	Temporality	High	The study establishes appropriate temporality and the interval between exposure and outcome is long enough for consideration of latency of the outcome. The period of possible exposure to crocidolite was noted to be September 1940 to March 1945 with follow-up for deaths through 1994.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	High	Other Non-Cancer Outcomes: ICD codes were not detailed within the main text, however data regarding deaths was described in the referenced original Nottingham cohort study by McDonald et al., 2006 (HERO ID 709504) and indicate use of ICD-9 as well as employment and pathological records for traced former workers with all deaths due to mesothelioma described as confirmed by pathology.

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Study Citation: Berry, G., Pooley, F., Gibbs, A., Harris, J., Mcdonald, J. (2009). Lung fiber burden in the Nottingham gas mask cohort. Inhalation Toxicology 21(2):168-172.
Health Outcome: mortality from other diseases and all cause mortality
Target Organ(s): Mortality: Other diseases, All cause mortality
Asbestos Fiber Type(s): Asbestos - Crocidolite (riebeckite): 12001-28-4
Linked HERO ID(s): No linked references.
HERO ID: 709467

Domain	Metric		Rating	Comments
	Metric 8:	Reporting Bias	High	There were no concerns for selective reporting as all outcomes which were outlined within methods were also reported within the results. Results for fiber concentrations within lungs were reported across year of death and cause of death categories within Table 1.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Low	Other than stratification of fiber concentration results across year and cause of death categories, no adjustments for gender, age or race appear to have been made and the distribution of primary covariates and potential confounders was not reported.
	Metric 10:	Covariate Characterization	Medium	The members of the cohort were workers at the Nottingham military gas mask factory 1940 through 1945. Although co-exposures were not addressed, there was no evidence that there was an unbalanced provision of co-exposures among exposure groups. Considerations for workers who might have initially left and worked elsewhere with additional exposures but eventually returned to the gas mask factory for study were not detailed. Authors noted that masks consisted of 20% crocidolite, but details regarding the remaining composition of masks were not provided.
	Metric 11:	Co-exposure Counfounding	Medium	The study design was appropriate to address the main objective of analyzing lung fiber burdens over time. The percentage of fibers longer than 6μm was analyzed by logistic regression with respect to year of death. Median geometric mean crocidolite fibers in lung tissue were presented in Table 1 for year of death categories and cause of death.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	Medium	The study design was appropriate to address the main objective of analyzing lung fiber burdens over time. The percentage of fibers longer than 6μm was analyzed by logistic regression with respect to year of death. Median geometric mean crocidolite fibers in lung tissue were presented in Table 1 for year of death categories and cause of death.
	Metric 13:	Statistical Power	Medium	The number of participants (n=70 total with n=51 with duration of employment data) was minimal for regression analyses, although additional covariates did not appear to have been considered within modeling.
	Metric 14:	Reproducibility of Analyses	Medium	The description of analysis is sufficient to understand how to generally reproduce the analyses. Transformation of exposure variables was described in detail. Imputation of exposures with zero values as one-half of the limit of detection was also detailed.
	Metric 15:	Statistical Analysis	Low	Model building was not described in terms of the reasoning for lack of considerations for potential confounders within models of the percentage of fibers longer than 6μm analyzed by logistic regression with respect to year of death.
Domain 6: Other (if applicable) Considerations for Biomarker Selection and Measurement (Lakind et al. 2014)				

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Study Citation:	Berry, G., Pooley, F., Gibbs, A., Harris, J., Mcdonald, J. (2009). Lung fiber burden in the Nottingham gas mask cohort. Inhalation Toxicology 21(2):168-172.
Health Outcome:	mortality from other diseases and all cause mortality
Target Organ(s):	Mortality: Other diseases, All cause mortality
Asbestos Fiber Type(s):	Asbestos - Crocidolite (riebeckite): 12001-28-4
Linked HERO ID(s):	No linked references.
HERO ID:	709467

Domain	Metric		Rating	Comments
	Metric 16:	Use of Biomarker of Exposure	Low	Evidence exists for a relationship between lung fiber concentrations and external exposure within models assessing the relationship between lung fiber concentrations and length of exposure in years, but there has been no assessment of accuracy and precision or none was reported.
	Metric 17:	Effect Biomarker	N/A	No biomarkers of effect were used.
	Metric 18:	Method Sensitivity	Medium	Authors noted, “For three zero values, half of the detection limit (0.005, 0.005, 0.05 fibers/μg) was substituted”. Analytical method utilized transmission electron microscopy.
	Metric 19:	Biomarker Stability	Low	Lung fiber sample storage history and stability not detailed.
	Metric 20:	Sample Contamination	Medium	There is no information included regarding contamination.
	Metric 21:	Method Requirements	High	Transmission electron microscopy utilized to provide identification and quantitation of lung fibers.
	Metric 22:	Matrix Adjustment	N/A	This study utilized a biomarker of exposure.

Additional Comments: This study focused upon post-mortem crocidolite lung fiber concentrations in a subset (n=70: n=50 mesothelioma and n=20 deaths from other causes) of the Nottingham Gas Mask cohort of n=1,154 employees with lung tissue samples who had worked 1940-1945 on the manufacture of military gas masks with filter pads containing 20% crocidolite and who were followed through 2003. Crocidolite asbestos fiber levels per microgram of dried lung were presented by decade of death and cause of death (Table 1), duration of exposure (Table 2), and the percentage of fibers longer than 6μm was analyzed with year of death by logistic regression (Figure 2). The crocidolite counts ranged from 0 to 1,949 (mean 234, median 47) fibers/μg.

Overall Quality Determination — Medium

Study Citation:	Bourgkard, E., Wild, P., Gonzalez, M., Févotte, J., Penven, E., Paris, C. (2013). Comparison of exposure assessment methods in a lung cancer case-control study: performance of a lifelong task-based questionnaire for asbestos and PAHs. Occupational and Environmental Medicine 70(12):884-891.
Health Outcome:	Lung Cancer
Target Organ(s):	Cancer/Carcinogenesis: Lung cancer; Lung/Respiratory: Lung cancer
Asbestos Fiber Type(s):	Asbestos - Not specified: 1332-21-4
Linked HERO ID(s):	No linked references.
HERO ID:	3078093

Domain	Metric		Rating	Comments
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Low	The study uses job-specific questionnaires (including JEM) to determine exposure; however, the authors are not clear whether the categories of exposure were based on PCM or TEM conversion factors. It appears that exposure was determined solely using professional judgement.This metric is rated low because the study or any cited methods source does not explicitly mention the use of PCM or TEM.
	Metric 5:	Exposure Levels	Low	The authors provide the range of exposures; however, the information is very limited. The distribution of exposures is only provided indirectly in comparing two of the different exposure methods (i.e., Table 2).

Additional Comments:	NOTE: This study would not have been evaluated fully under the current guidelines. Metric 4 was rated as low because there was no mention of PCM or TEM within the study or a cited methods source.

* No biomarkers were identified for this evaluation.

** As described in Appendix B.2 of the *White Paper: Quantitative Approach to the Human Health Assessment for the Risk Evaluation for Asbestos Part 2: Supplemental Evaluation Including Legacy Uses and Associated Disposals of Asbestos*, to be considered as being informative for dose-response analysis, metrics 4 and 5 would need metric ratings of Medium or High. This reference did not satisfy this requirement; therefore data quality evaluation is presented for only for metrics 4 and 5.

Study Citation:	Brims, F. J. H., Kong, K., Harris, E. J. A., Sodhi-Berry, N., Reid, A., Murray, C. P., Franklin, P. J., Musk, A. B., e Klerk, N. H. (2020). Pleural plaques and the risk of lung cancer in asbestos-exposed subjects. American Journal of Respiratory and Critical Care Medicine 201(1):57-62.
Health Outcome:	Lung Cancer; Ovarian Cancer; breast, cervical, corpus uterine, colorectal
Target Organ(s):	Reproductive/Developmental: Breast cancer, Ovarian cancer, Cervical cancer, Corpus uterine cancer; Cancer/Carcinogenesis: Cancer in the lung, trachea and bronchus, all cancers, Ovarian cancer, Breast cancer, Cervical cancer, Colorectal cancer, Corpus uterine cancer; Lung/Respiratory: Cancer in the lung, trachea and bronchus; Gastrointestinal: Colorectal cancer
Asbestos Fiber Type(s):	Asbestos - Crocidolite (riebeckite): 12001-28-4
Linked HERO ID(s):	733541, 709469, 3079298, 3520653, 3531364, 6868332
HERO ID:	6868332

Domain	Metric		Rating	Comments
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Low	This metric is rated Low because the study or any cited methods source does not explicitly mention the use of PCM or TEM. dust concentrations were measured using koniometer between 1948 and 1958. In 1966, fiber counting was done using a Casella long running thermal precipitator. Personal and fixed monitors were utilized in 1973. Additional measurements were taken in 1977, 1978, 1980, 1984, 1986, and 1992, using interpolation to estimate concentrations for years that surveys were not conducted. According to Hansen et al., 1997 2219991, all samples examined were analyzed using the standard membrane filter method. Some exceptions were surveys in 1984 and 1986 which used SEM, and in 1992 which used TEM. Although later surveys utilized TEM, the current study does not describe estimates in a way to know outcomes based on exposures measured from 1992 and after.
	Metric 5:	Exposure Levels	Medium	The distribution of exposure appears to be sufficient to develop an exposure-response estimate. Cumulative exposure was utiliized in statistical models.

Additional Comments: None

** As described in Appendix B.2 of the *White Paper: Quantitative Approach to the Human Health Assessment for the Risk Evaluation for Asbestos Part 2: Supplemental Evaluation Including Legacy Uses and Associated Disposals of Asbestos*, to be considered as being informative for dose-response analysis, metrics 4 and 5 would need metric ratings of Medium or High. This reference did not satisfy this requirement; therefore data quality evaluation is presented for only for metrics 4 and 5.

Study Citation:	Brown, D. P., Dement, J. M., Okun, A. (1994). Mortality patterns among female and male chrysotile asbestos textile workers. Journal of Occupational Medicine 36(8):882-888.
Health Outcome:	Pneumoconiosis and other respiratory disease mortality
Target Organ(s):	Lung/Respiratory: Pneumoconiosis and other respiratory disease mortality; Mortality: Pneumoconiosis and other respiratory disease mortality
Asbestos Fiber Type(s):	Asbestos - Chrysotile (serpentine): 12001-29-5
Linked HERO ID(s):	3081832, 66, 2238696, 6860087
HERO ID:	3081832

Domain		Metric	Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	High	The authors reference three previous studies of white male textile workers from a chrysotile asbestos plant in South Carolina (Dement et al., 1982, HEROID: 65; Dement et al., 1983, HEROID: 66; Dement et al., 1983, HEROID: 67). In the original analyses, the white male workers were required to be employed for at least one month between January 1, 1940-Decemeber 31, 1965. This study updates the cohort to include all workers who were employed at least one month, and follow-up vital status extended by 15 years, updating from 1975-1990. The authors discuss using death files from ”the Social Security Administration, the National Death Index, and the files of the Internal Revenue Service” (Brown et al., 1994, HEROID: 3081832). Black women employes were excluded due to the small number (n=19). Overall, the updated cohort included 3,022 workers (1,229 white women, 1,247 white men, and 546 black men).
	Metric 2:	Attrition	High	Authors note that 22.8% of white women from the plant were lost to follow-up as their vital status could not be confirmed. Authors found that most of these women were those employed for a shorter amount of time: ”54% worked less than 6 months, 17% worked between 6 months and 1 year, and 29% worked longer than 1 year”(Brown et al., 1994, HEROID: 3081832). Of the black men employed in the plant, 7.8% were lost to follow-up, and 1.5% of white men were lost to follow-up. Additionally, 11% of white women, 7.6% of black men, and 2.8% of white men were presumed dead, but their death certificates were not obtained. These workers were assumed alive in the analyses.
	Metric 3:	Comparison Group	High	The South Carolina death rate was used to calculate expected deaths and the SMRs. Additionally, outcomes are stratified by race/gender.
Domain 2: Exposure Characterization				

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Study Citation:	Brown, D. P., Dement, J. M., Okun, A. (1994). Mortality patterns among female and male chrysotile asbestos textile workers. Journal of Occupational Medicine 36(8):882-888.		
Health Outcome:	Pneumoconiosis and other respiratory disease mortality		
Target Organ(s):	Lung/Respiratory: Pneumoconiosis and other respiratory disease mortality; Mortality: Pneumoconiosis and other respiratory disease mortality		
Asbestos Fiber Type(s):	Asbestos - Chrysotile (serpentine): 12001-29-5		
Linked HERO ID(s):	3081832, 66, 2238696, 6860087		
HERO ID:	3081832		

Domain	Metric		Rating	Comments
	Metric 4:	Measurement of Exposure	Medium	Individual lifetime cumulative exposure to asbestos was estimated using data from Dement et al. (1983, HERO ID: 66), which clarifies that 5,952 environmental samples were used covering the period of 1930-1975 using impingers until 1965, impingers and membrane filter samples between 1965 and 1971, and membrane filter samples exclusively from 1971-1975. Another study from the same cohort, Richardson et al. (2018, HERO ID: 6860087) clarifies that the approach used phase-contrast microscopy (PCM) for fiber counting (as evidenced by the citation of Edwards and Lynch, 1968, HEROID: 783893). The impinger and membrane filter samples that were taken concurrently (n=1,106 pairs) were used to create conversion between the two types of data, resulting in a conversion factor of 2.9 fibers to one mpccf. Detailed job histories were also collected to calculate individual exposure estimates, which took into account the dust concentration for the job an individual worked at, the time spent in the job, and the number of jobs held. Data came from personnel records.
	Metric 5:	Exposure Levels	Medium	In SMR analysis, 7 different exposure levels are used which represent values of fibers/cm^3 days that range from <500 to >100,000.
	Metric 6:	Temporality	High	In the original study, workers had to be employed for at least one month at any time from January 1940- December 1975 (Dement et al., 1982, HEROID: 65; Dement et al., 1983, HEROID: 66; Dement et al., 1983, HEROID: 67). This study adds an additional 15 years of observation of mortality.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	High	Other Non-Cancer Outcomes: Authors used ICD-9 codes for pneumoconiosis and other respiratory diseases (470-478 and 949-519).
	Metric 8:	Reporting Bias	High	SMRs are reported in Table 5 for pneumoconiosis and other respiratory diseases, but confidence intervals are not provided. P-values of <0.05 and <0.01 are reported. Observed/expected mortality is also presented in Table 5
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Medium	SMRs are adjusted by race and sex, but authors did not consider smoking as a covariate.
	Metric 10:	Covariate Characterization	Medium	While not mentioned in this study, Dement et al. (1982, HEROID: 65) writes "detailed personnel records were first maintained beginning in approximately 1930. Therecord system has remained remarkably unchanged since that time. For each worker,an employment card was completed at initial employment giving name, date of birth,sex, race, social security number, marital status and address. This same card alsocontained the detailed work history giving exact dates of employment by plantdepartment and specific job. All information from these cards was entered onto acomputer data file."
	Metric 11:	Co-exposure Counfounding	Low	In an occupational setting, potential co-exposures are not discussed.

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Study Citation:	Brown, D. P., Dement, J. M., Okun, A. (1994). Mortality patterns among female and male chrysotile asbestos textile workers. Journal of Occupational Medicine 36(8):882-888.
Health Outcome:	Pneumoconiosis and other respiratory disease mortality
Target Organ(s):	Lung/Respiratory: Pneumoconiosis and other respiratory disease mortality; Mortality: Pneumoconiosis and other respiratory disease mortality
Asbestos Fiber Type(s):	Asbestos - Chrysotile (serpentine): 12001-29-5
Linked HERO ID(s):	3081832, 66, 2238696, 6860087
HERO ID:	3081832

Domain		Metric	Rating	Comments
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	Medium	The study uses appropriate methods for calculating SMRs.
	Metric 13:	Statistical Power	Medium	The sample size by sex and race is adequate to detect effect in the exposed worker's mortality. Authors excluded previously employed black women as the numbers were to calculate effect.
	Metric 14:	Reproducibility of Analyses	Medium	The methods are sufficient to conceptually reproduce this analysis, with reference to the original studies (Dement et al., 1982, HEROID: 65; Dement et al., 1983, HEROID: 66; Dement et al., 1983, HEROID: 67).
	Metric 15:	Statistical Analysis	Medium	Methods for calculating SMRs is transparent.

Additional Comments: This study is an extension of the retrospective cohort found in three studies (Dement et al., 1982, HEROID: 65; Dement et al., 1983, HEROID: 66; Dement et al., 1983, HEROID: 67). The authors add 15 years of observation and include white women and black men to the analysis, which was previously limited to white men. Overall, the study is well-designed but lacks covariates and adjustment for confounding for factors such as smoking.The measurement exposure (M4) and/or exposure levels (M5) metrics are rated as medium upon review by both set of reviewers. Also, the overall quality determination (OQD) is rated medium. Extraction has been completed and quality control reviewed.

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation:	Carel, R., Boffetta, P., Kauppinen, T., Teschke, K., Andersen, A., Jäppinen, P., Pearce, N., Rix, B. A., Bergeret, A., Coggon, D., Persson, B., Szadkowska-Stanczyk, I., Kielkowski, D., Henneberger, P., Kishi, R., Facchini, L. A., Sala, M., Colin, D., Kogevinas, M. (2002). Exposure to asbestos and lung and pleural cancer mortality among pulp and paper industry workers. Journal of Occupational and Environmental Medicine 44(6):579-584.
Health Outcome:	Lung Cancer; Pleural cancer
Target Organ(s):	Cancer/Carcinogenesis: Pleural cancer mortality, Lung cancer mortality; Lung/Respiratory: Lung cancer mortality, Pleural cancer mortality
Asbestos Fiber Type(s):	Asbestos - Not specified: 1332-21-4
Linked HERO ID(s):	No linked references.
HERO ID:	3080500

Domain	Metric		Rating	Comments
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Low	Exposure was estimated using a combination of job exposure matrices and available measurements. A total of 1024 measurements of asbestos levels were available, along with detailed information on processes and exposures in each department from industrial hygienists and engineers from each mill. Both were used by an international team of industrial hygienists to quantitatively estimate exposure, who developed mill-, department-, and time-specific assessments. Details on equipment used and measures from each mill were not provided. The likelihood of substantial exposure misclassification cannot be readily ascertained; there is no evidence suggesting differential error is likely.
	Metric 5:	Exposure Levels	Medium	Exposure concentrations were quantified in three levels as low (average ~ 0.001 fibers/cm3), medium (0.01 f/cc) and high (0.10 f/cc). Cumulative exposure in f/cc-years was then calculated by multiplying exposure intensity by the duration of exposure in years. A weighted cumulative exposure measure incorporated prevalence of exposure.

Additional Comments: This study analyzed associations between occupational asbestos exposure and lung and pleural cancer mortality in a 13-country cohort of 62,937 male pulp and paper workers employed for at least 1 year between 1945 and 1996. Exposure in this industry is predominantly from maintenance and repair work. Exposure estimates used available dust measures and paper mill-specific information on exposure probabilities in each department. In internal analyses, pleural but not lung cancer was significantly associated with ever exposure to asbestos, and non-significantly associated with higher years of exposure, years since first exposure, and cumulative exposure. Higher cumulative exposure was also non-significantly associated with increased risk of lung cancer (n=450 in the cohort). Only 24 pleural cancers were identified, 10 in subjects classified as unexposed although several worked in departments where exposure may occur. While there is no evidence of differential error, non-differential exposure misclassification may have attenuated associations. The authors also note that the mean follow up of 23.5 years may not have been sufficient to fully identify pleural cancers, which have an extremely long latency.Information on the measurement of exposure metric (M4) to assess exposure was limited and rated low. On the other hand, exposure levels metric (M5) information reported was adequate/rated medium to determine exposure-response relationships. The overall rating for this outcome/study is medium.

* No biomarkers were identified for this evaluation.

** As described in Appendix B.2 of the *White Paper: Quantitative Approach to the Human Health Assessment for the Risk Evaluation for Asbestos Part 2: Supplemental Evaluation Including Legacy Uses and Associated Disposals of Asbestos*, to be considered as being informative for dose-response analysis, metrics 4 and 5 would need metric ratings of Medium or High. This reference did not satisfy this requirement; therefore data quality evaluation is presented for only for metrics 4 and 5.

Study Citation:	Checkoway, H., Heyer, N. J., Demers, P. A., Gibbs, G. W. (1996). Reanalysis of mortality from lung cancer among diatomaceous earth industry workers, with consideration of potential confounding by asbestos exposure. Occupational and Environmental Medicine 53(9):645-647.			
Health Outcome:	Lung Cancer			
Target Organ(s):	Cancer/Carcinogenesis: lung cancer mortality; Lung/Respiratory: lung cancer mortality; Mortality: lung cancer mortality			
Asbestos Fiber Type(s):	Asbestos - Chrysotile (serpentine): 12001-29-5			
Linked HERO ID(s):	3081424, 4259501			
HERO ID:	3081424			
Domain	Metric		Rating	Comments
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Low	Both studies (Checkoway et al., 1996, HEROID: 3081424 and Checkoway et al., 1996, HEROID: 4259501) reference Gibbs and Checkoway, 1994, HEROID: 3653704 for exposure measurement information, which reports the use of midget impingers and membrane filter sampling only without discussion of conversion factors or the use of PCM or TEM methods, meriting a low rating. Gibbs and Checkoway, 1994 (HEROID: 3653704) specifically note the inability to account for dust or other fibers that were erroneously counted as asbestos fibers. In Gibbs and Checkoway, 1994, HEROID: 3653704, they do reference a NIOSH report, which could offer additional information, but this was not publicly available at the time of evaluation (NIOSH, 1977, ”Health hazard evaluation determination Report 77-2-404, Johns Manville Sales Corporation, Lompoc California”).
	Metric 5:	Exposure Levels	Medium	Both studies report four levels of exposure in their SMR analyses. Exposure groups in both studies include unexposed as the lowest group and >=6.8 fiber-years as the highest exposure group.
Additional Comments:	QC was not completed for metrics other than Metrics 4 and 5 because the study does not have sufficient exposure information to be useful for dose-response analysis.			

* No biomarkers were identified for this evaluation.

** As described in Appendix B.2 of the *White Paper: Quantitative Approach to the Human Health Assessment for the Risk Evaluation for Asbestos Part 2: Supplemental Evaluation Including Legacy Uses and Associated Disposals of Asbestos*, to be considered as being informative for dose-response analysis, metrics 4 and 5 would need metric ratings of Medium or High. This reference did not satisfy this requirement; therefore data quality evaluation is presented for only for metrics 4 and 5.

Study Citation:	Chiazze, L., Jr, Watkins, D. K., Fryar, C., Kozono, J. (1993). A case-control study of malignant and non-malignant respiratory disease among employees of a fiberglass manufacturing facility II Exposure assessment. Occupational and Environmental Medicine 50(8):717-725.
Health Outcome:	Lung Cancer; Non-malignant respiratory disease
Target Organ(s):	Lung/Respiratory: Lung cancer, Non-malignant respiratory disease mortality; Cancer/Carcinogenesis: Lung cancer; Mortality: Non-malignant respiratory disease mortality
Asbestos Fiber Type(s):	Asbestos - Not specified: 1332-21-4
Linked HERO ID(s):	No linked references.
HERO ID:	30090

Domain	Metric		Rating	Comments
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Low	This metric is rated Low because the study or any cited methods source does not explicitly mention the use of PCM or TEM. Final regression modeling results in Table 4 included cumulative exposure estimates to respirable fibers (fibers/mL), asbestos (fibers/mL), talc (fibers/mL), formaldehyde (ppm), respirable silica (mg/m^3), and asphalt fumes (mg/m^3). Estimates of daily exposure to each of the substances over a worker's entire working lifetime were formulated from personal (proxy) interview occupational history, detailed historical environmental reconstruction by year through engineering process history (1938-1987), historical department job code titles, process-specific chemical exposure analyses, industrial hygiene (IH) records (described as available from about 1970 onwards) and employee work histories. The engineering process history was compiled by four Owens-Corning Fiberglass engineers and audited by process division experts for validity. Assignment of department to process code was blinded to case and control status. Authors noted few IH records existed for early, pre-1970 processes and an exposure assessment committee of current and former Owens-Corning Fiberglass employees with knowledge of IH, current and historical plant processes was established to develop quantitative estimates of potential exposures to each substance for each process by assigning each process to one of four ranges of estimated potential exposure (eight-hour time weighted average (TWA) exposures specific to calendar time, Table 1). Cumulative exposure to each substance for these employees was developed for each employee as the product of the number of days in a process multiplied by the mid-point of the exposure range and summed over all processes. Authors did not discuss the potential for exposure misclassification within these methods, but the misclassification was likely non-differential.
	Metric 5:	Exposure Levels	Medium	The range and distribution of estimated exposure (Table 4, four categories for asbestos and three categories for talc estimated exposures) was sufficient to develop exposure-response estimates.

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Study Citation:	Chiazze, L., Jr, Watkins, D. K., Fryar, C., Kozono, J. (1993). A case-control study of malignant and non-malignant respiratory disease among employees of a fiberglass manufacturing facility II Exposure assessment. Occupational and Environmental Medicine 50(8):717-725.
Health Outcome:	Lung Cancer; Non-malignant respiratory disease
Target Organ(s):	Lung/Respiratory: Lung cancer, Non-malignant respiratory disease mortality; Cancer/Carcinogenesis: Lung cancer; Mortality: Non-malignant respiratory disease mortality
Asbestos Fiber Type(s):	Asbestos - Not specified: 1332-21-4
Linked HERO ID(s):	No linked references.
HERO ID:	30090

Domain	Metric	Rating	Comments
Additional Comments:	This occupational nested case-control study investigated the relationship between multiple exposures within cases of non-malignant (n=101) respiratory disease mortality and matched controls (n=183) obtained from the Thermal Insulation Manufacturer's Association (TIMA) historical cohort mortality study of production and maintenance workers employed at the Newark, Ohio fiberglass manufacturing plant for at least one year between 1 January 1940 and 31 December 1962 and followed up to the end of 1982. There is potential for Healthy Worker Survivor bias, indicated by results stratified by years of employment. For non-malignant respiratory disease, only smoking was statistically significant with OR = 2.637 (95% CI, 1.146-6.069). None of the exposure variables produced significant OR's but higher OR's were found for the higher ranked asbestos exposure levels.		

* No biomarkers were identified for this evaluation.

** As described in Appendix B.2 of the *White Paper: Quantitative Approach to the Human Health Assessment for the Risk Evaluation for Asbestos Part 2: Supplemental Evaluation Including Legacy Uses and Associated Disposals of Asbestos*, to be considered as being informative for dose-response analysis, metrics 4 and 5 would need metric ratings of Medium or High. This reference did not satisfy this requirement; therefore data quality evaluation is presented for only for metrics 4 and 5.

Study Citation:	Christensen, K. Y., Kopylev, L. (2012). Localized pleural thickening: smoking and exposure to Libby vermiculite. Journal of Exposure Science and Environmental Epidemiology 22(4):320-323.
Health Outcome:	Pleural Plaques; Pleural thickening
Target Organ(s):	Lung/Respiratory: Localized pleural thickening
Asbestos Fiber Type(s):	Asbestos- Libby amphibole: 1318-09-8
Linked HERO ID(s):	No linked references.
HERO ID:	1257859

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Medium	This study included workers from a Marysville, Ohio plant which used Libby amphibole asbestos. There was a study that examined pulmonary effects in 512 workers, conducted in 1980 (participation rates in Lockey et al., 1984 029685). The examination included physical exams, spirometry, and chest x-rays. Information on smoking, work, and exposure histories were collected. In 2002-2005, another follow-up study was conducted, and included 280 of the original individuals. They participated in interviews and received chest x-rays. The authors detail that they wanted to limit potential exposures in other occupational settings, so the total number of individuals included in the analysis was 118. They all began working in 1972 or later. The authors did not provide a robust description of the participation rate for this study, nor a comparison of participant characteristics or the prevalence of pleural thickening in included vs excluded subjects. However, there was no evidence of potential selection bias.
	Metric 2:	Attrition	Medium	To exclude potential error due to poorly measured occupational exposure prior to 1972, this analysis limited the sample to workers hired after 1972, including 118 (42.1%) of 280 workers included in a previous analysis of the same data (Rohs et al 2008, 709486). In contrast to the earlier study, this paper did not compare characteristics of this subset of participants vs. eligible living workers who were non-participants (e.g., age, exposure level, smoking status). The earlier study also conducted sensitivity analyses to assess the impact of attrition from the parent study (n=512) by adding the 151 eligible living non-participants (assuming they had no pleural changes) to the model; conclusions did not change. The potential impact of any attrition bias was not discussed here.
	Metric 3:	Comparison Group	Medium	Because of the nature of the analyses conducted in this study, subgroups were compared against each other (i.e., a within-cohort analysis). Smoking and nonsmoking groups were reported to be similar in age at x-ray and time from first exposure. However, further discussion about similarities between the two groups was somewhat limited.
Domain 2: Exposure Characterization				

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Study Citation: Christensen, K. Y., Kopylev, L. (2012). Localized pleural thickening: smoking and exposure to Libby vermiculite. Journal of Exposure Science and Environmental Epidemiology 22(4):320-323.
Health Outcome: Pleural Plaques; Pleural thickening
Target Organ(s): Lung/Respiratory: Localized pleural thickening
Asbestos Fiber Type(s): Asbestos- Libby amphibole: 1318-09-8
Linked HERO ID(s): No linked references.
HERO ID: 1257859

Domain	Metric		Rating	Comments
	Metric 4:	Measurement of Exposure	High	The authors detail that estimates of exposure through 2000 were developed through several methods, including fiber measurements when available, and estimated fiber concentrations. For this cohort, the most accurate exposure data comes from 1972 onward, because analytical measurements were used. According to the cited study (Rohs et al., 2008, ID: 709486), airborne fibers were collected on membrane filters. The Rohs et al. study cites another study in their methods section which details the use of transmission electron microscopy for exposure measurements, contributing to the high rating for this metric (Lockey et al., 1984, 29685). Prior to 1976, hygienists followed workers with a sampling device to gather information about various departments. Information on the year of hire and specific locations where individuals worked were used to determine a cumulative exposure, reported in fibers/cc-year.
	Metric 5:	Exposure Levels	Medium	The range and distribution of exposures presented in this study are sufficient to develop an exposure-response estimate. Table 1 presents the mean as 0.42, with a standard deviation of 0.77 fibers/cc-year. The range was reported as 0.001-5.51 fibers/cc-year.
	Metric 6:	Temporality	High	The interval between the exposure and the outcome is sufficiently long considering the latency period for asbestos exposure. Table 1 reports that the average time since first exposure was 28.2 years, with a standard deviation of 2.5 years. The range was reported as 23.2-32.6 years since first exposure.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	High	Pleural Plaques: See Other: Localized Pleural Thickening. From the manuscript: ”In the current International Labour Organization (ILO) classification, LPT includes both pleural plaques (focal areas of pleural thickening generally present at the parietal pleura, diaphragm or chest wall) and pleural thickening that does not involve blunting of the costophrenic angle between the rib cage and the diaphragm.”; Other Non-Cancer Outcomes: The authors detail that ”three board-certified radiologists blinded to any identifying information, independently classified the radiographs using the ILO classification system” (Christensen & Kopylev, 2012). The authors did not report the rate of agreement between readers, but this is a well-established method. The authors did highlight in the discussion section that one of the limitations of this study was a lack of BMI information for all participants. Some ”fat pads may be mistaken for pleural thickening” (Christensen & Kopylev, 2012).
	Metric 8:	Reporting Bias	Medium	The results were presented in the text and included details on model fitting and evaluation steps, p-values that informed decisions about variables included in the final model, model fit indices, and the benchmark dose (BMC) calculated using the final model. BMCs (the dose associated with a 10% increase in risk) were presented for the full sample, smokers, and non-smokers. However, coefficients from the models were not shown.

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Study Citation:	Christensen, K. Y., Kopylev, L. (2012). Localized pleural thickening: smoking and exposure to Libby vermiculite. Journal of Exposure Science and Environmental Epidemiology 22(4):320-323.
Health Outcome:	Pleural Plaques; Pleural thickening
Target Organ(s):	Lung/Respiratory: Localized pleural thickening
Asbestos Fiber Type(s):	Asbestos- Libby amphibole: 1318-09-8
Linked HERO ID(s):	No linked references.
HERO ID:	1257859

Domain	Metric		Rating	Comments
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	High	The authors considered numerous covariates in their analyses. Time from first exposure, age at x-ray, gender, and BMI were all considered for inclusion in the models; none reached significance. The ”covariates were evaluated according to the statistical significance of the covariate, and whether inclusion of the covariate improved model fit as assessed by the AIC” (Christensen & Kopylev, 2012). Smoking history was included in the final models, and interactions between smoking and asbestos exposure examined, in keeping with the study aim of evaluating the impact of smoking on the asbestos BMC for pleural thickening.
	Metric 10:	Covariate Characterization	Medium	There is no evidence to suggest poor validity of variables assessed as potential confounders . Confounders were characterized based on employee records, a screening exam, and either in-person or telephone interviews. The potential influence of missing data for BMI was considered in sensitivity analyses.
	Metric 11:	Co-exposure Counfounding	Medium	The authors did not discuss potential co-exposures within the occupational setting in this manuscript. However this issue was addressed in the manuscript analyzing the baseline cohort: Lockey et al 1984, 029685 reported that a careful evaluation did not identify any co-exposures that would cause pleural radiographic changes.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	Medium	The study design and methods employed were appropriate for the research question being examined. The candidate models used were provided, and the rationale for issues such as the variables included and exposure lags selected was given.
	Metric 13:	Statistical Power	Medium	The analysis sample included only 12 cases and 106 non-cases. Power may have been inadequate to detect statistically significant interactions.
	Metric 14:	Reproducibility of Analyses	Medium	A thorough description of the analyses performed is included in this study. The description is sufficient to be able to conceptually understand how to reproduce the analyses performed.
	Metric 15:	Statistical Analysis	Medium	The models included in this study are transparent, and it appears as though model assumptions have been met.

Additional Comments: Overall, the authors provided a lot of detail within this study, and they were explicit about the analyses and model fit criteria used. The quality of both exposure and outcome assessments was high, potential confounding was examined in depth, and there was lengthy follow-up. However, the small sample size limited statistical power and results were presented only as benchmark doses, without additionally providing model coefficients. In addition, the potential influence of any selection bias is uncertain: only 118 of the initial 512 workers in the cohort, and of the 431 alive at the time of X-rays, were included due to the stringent criteria needed to minimize exposure measurement error.

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Study Citation:	Christensen, K. Y., Kopylev, L. (2012). Localized pleural thickening: smoking and exposure to Libby vermiculite. Journal of Exposure Science and Environmental Epidemiology 22(4):320-323.
Health Outcome:	Pleural Plaques; Pleural thickening
Target Organ(s):	Lung/Respiratory: Localized pleural thickening
Asbestos Fiber Type(s):	Asbestos- Libby amphibole: 1318-09-8
Linked HERO ID(s):	No linked references.
HERO ID:	1257859

Domain	Metric	Rating	Comments
Overall Quality Determination		**Medium**	

* No biomarkers were identified for this evaluation.

Study Citation:	Churg, A., Vedal, S. (1994). Fiber burden and patterns of asbestos-related disease in workers with heavy mixed amosite and chrysotile exposure. American Journal of Respiratory and Critical Care Medicine 150(3):663-669.
Health Outcome:	Lung Cancer; Asbestosis; Pleural Plaques; Airway fibrosis
Target Organ(s):	Lung/Respiratory: Asbestosis, Airway fibrosis, pleural plaques, lung cancer; Cancer/Carcinogenesis: lung cancer
Asbestos Fiber Type(s):	Asbestos - Amosite (grunerite): 12172-73-5; Asbestos - Tremolite: 14567-73-8; Asbestos - Chrysotile (serpentine): 12001-29-5
Linked HERO ID(s):	No linked references.
HERO ID:	758904

Domain	Metric		Rating	Comments
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Low	Methods for fiber count included fiber morphology and fiber chemistry determined through energy-dispersive x-ray spectroscopy, followed by calculating fiber concentration using an algorithm that accounted for weight of lung tissue used in the study and number of grid squares. However, authors did not utilize PCM or TEM, thus warranting a low rating per the guidance.
	Metric 5:	Exposure Levels	Low	Actual measured exposure data were not available for the cases and are estimations based on historic data and calculations. Authors stated that exposure was not included in their models as they felt combining years of exposure with fiber burden did not make sense analytically nor is there a correlation between the two.

Additional Comments:	Authors stated crocidolite fibers were detected in a small number of cases but were excluded from analyses. Examining the association between chrysotile or tremolite with disease was not conducted due to low concentrations, but concentrations are reported.

* No biomarkers were identified for this evaluation.

** As described in Appendix B.2 of the *White Paper: Quantitative Approach to the Human Health Assessment for the Risk Evaluation for Asbestos Part 2: Supplemental Evaluation Including Legacy Uses and Associated Disposals of Asbestos*, to be considered as being informative for dose-response analysis, metrics 4 and 5 would need metric ratings of Medium or High. This reference did not satisfy this requirement; therefore data quality evaluation is presented for only for metrics 4 and 5.

Study Citation:	Churg, A., Wright, J. L., Vedal, S. (1993). Fiber burden and patterns of asbestos-related disease in chrysotile miners and millers. American Review of Respiratory Disease 148(1):25-31.
Health Outcome:	Lung Cancer; airway fibrosis
Target Organ(s):	Cancer/Carcinogenesis: Mesothelioma, lung cancer; Lung/Respiratory: Asbestosis, airway fibrosis, pleural plaques, lung cancer, mesothelioma
Asbestos Fiber Type(s):	Asbestos - Chrysotile (serpentine): 12001-29-5; Asbestos - Tremolite: 14567-73-8
Linked HERO ID(s):	No linked references.
HERO ID:	1481523

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Low	This study selected 300 autopsy lungs from workers in the Thetford Mines. The study included 94 lung samples from miners and millers were included because data was available. The selection criteria was not reported. Lack of information about the setting.
	Metric 2:	Attrition	Low	Only 94 out of 300 cases were included in analyses, over 2/3 of total subjects were lost due to data unavailability. No discussion about excluded subjects and their relationship with exposure or outcomes.
	Metric 3:	Comparison Group	Low	Comparison group was subjects without asbestos-related disease. The similarity of groups was not described and demographic information for subjects without asbestos related disease was not reported. There was very limited evidence indicated the groups were similar.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Medium	Fiber concentrations were measured using analytic electron microscopy. Summary statistics of exposure year and latency were reported. The nature of the study design determined exposure measured at only one time period.
	Metric 5:	Exposure Levels	Medium	The geometric means of asbestos concentration in cases by disease type and subjects without asbestos-related disease were reported. Fiber concentration was treated as continuous variable in multiple linear regression
	Metric 6:	Temporality	Medium	The latency and exposure years were obtained from occupational histories. The reported latency is sufficiently long. Uncertainty exists because exposure duration and latency data not available to everyone; exposure years available for 91 subjects; latency data available for 64 subjects.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Medium	Lung Cancer: Lung cancer samples were identified but not reported using ICD codes or confirmed by histological or cytological means.; Other Non-Cancer Outcomes: Airway fibrosis identified through autopsy lung samples, but no ICD code or validation process reported.
	Metric 8:	Reporting Bias	High	Mesothelioma findings reported in the abstract and results section. Number of cases and geometric mean of lung fiber burden were reported in table which allow extraction.
Domain 4: Potential Confounding / Variability Control				

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Study Citation: Churg, A., Wright, J. L., Vedal, S. (1993). Fiber burden and patterns of asbestos-related disease in chrysotile miners and millers. American Review of Respiratory Disease 148(1):25-31.
Health Outcome: Lung Cancer; airway fibrosis
Target Organ(s): Cancer/Carcinogenesis: Mesothelioma, lung cancer; Lung/Respiratory: Asbestosis, airway fibrosis, pleural plaques, lung cancer, mesothelioma
Asbestos Fiber Type(s): Asbestos - Chrysotile (serpentine): 12001-29-5; Asbestos - Tremolite: 14567-73-8
Linked HERO ID(s): No linked references.
HERO ID: 1481523

Domain	Metric		Rating	Comments
	Metric 9:	Covariate Adjustment	Low	The study mentioned covariates were adjusted but the age or smoking status were not adjusted in models, and their distribution was not reported between groups. The covariates controlled were concentration of another fiber and other disease.
	Metric 10:	Covariate Characterization	Low	Age and smoking status was checked for correlation with exposure concentration, but not controlled in models. In multiple linear regression models of asbestos and disease, concentration of another fiber and/or other asbestos related disease were sometimes controlled in the model.
	Metric 11:	Co-exposure Counfounding	Medium	Co-exposures other than asbestos that would likely bias the results were not likely to be present.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	Medium	The study design is appropriate for the research question. t-Tests and linear regression models were used to evaluate the association between fiber burden and asbestos related disease.
	Metric 13:	Statistical Power	Uninformative	The number of participants is small especially only n=6 subjects without asbestos related disease as reference group, which greatly limited the power of this study.
	Metric 14:	Reproducibility of Analyses	Medium	The description of the analysis is sufficient to understand how to conceptually reproduce the analysis with access to the analytic data.
	Metric 15:	Statistical Analysis	Medium	Statistical models and test method are transparent and appropriate

Additional Comments: None

Overall Quality Determination — Uninformative

* No biomarkers were identified for this evaluation.

Study Citation:	Churg, A., Wright, J. L., Vedal, S. (1993). Fiber burden and patterns of asbestos-related disease in chrysotile miners and millers. American Review of Respiratory Disease 148(1):25-31.
Health Outcome:	Asbestosis; Pleural Plaques
Target Organ(s):	Lung/Respiratory: Asbestosis, airway fibrosis, pleural plaques, lung cancer, mesothelioma; Cancer/Carcinogenesis: Mesothelioma, lung cancer
Asbestos Fiber Type(s):	Asbestos - Tremolite: 14567-73-8; Asbestos - Chrysotile (serpentine): 12001-29-5
Linked HERO ID(s):	No linked references.
HERO ID:	1481523

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Low	This study selected 300 autopsy lungs from workers in the Thetford Mines. The study included 94 lung samples from miners and millers were included because data was available. The selection criteria was not reported. Lack of information about the setting.
	Metric 2:	Attrition	Low	Only 94 out of 300 cases were included in analyses, over 2/3 of total subjects were lost due to data unavailability. No discussion about excluded subjects and their relationship with exposure or outcomes.
	Metric 3:	Comparison Group	Low	Comparison group was subjects without asbestos-related disease. The similarity of groups was not described and demographic information for subjects without asbestos related disease was not reported. There was very limited evidence indicated the groups were similar.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Medium	Fiber concentrations were measured using analytic electron microscopy. Summary statistics of exposure year and latency were reported. The nature of the study design determined exposure measured at only one time period.
	Metric 5:	Exposure Levels	Medium	The geometric means of asbestos concentration in cases by disease type and subjects without asbestos-related disease were reported. Fiber concentration was treated as continuous variable in multiple linear regression
	Metric 6:	Temporality	Medium	The latency and exposure years were obtained from occupational histories. The reported latency is sufficiently long. Uncertainty exists because exposure duration and latency data not available to everyone; exposure years available for 91 subjects; latency data available for 64 subjects.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Uninformative	Asbestosis: Asbestosis assessment method was not reported. No imaging diagnosis or validation or ICD code used.; Pleural Plaques: No established method usage reported for pleural plaques measurement. No ICD code or validation process reported.
	Metric 8:	Reporting Bias	High	Mesothelioma findings reported in the abstract and results section. Number of cases and geometric mean of lung fiber burden were reported in table which allow extraction.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Low	The study mentioned covariates were adjusted when apply but the age or smoking status were not adjusted in models, and their distribution was not reported between groups. The covariates controlled were concentration of another fiber and other disease.

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Study Citation: Churg, A., Wright, J. L., Vedal, S. (1993). Fiber burden and patterns of asbestos-related disease in chrysotile miners and millers. American Review of Respiratory Disease 148(1):25-31.

Health Outcome: Asbestosis; Pleural Plaques

Target Organ(s): Lung/Respiratory: Asbestosis, airway fibrosis, pleural plaques, lung cancer, mesothelioma; Cancer/Carcinogenesis: Mesothelioma, lung cancer

Asbestos Fiber Type(s): Asbestos - Tremolite: 14567-73-8; Asbestos - Chrysotile (serpentine): 12001-29-5

Linked HERO ID(s): No linked references.

HERO ID: 1481523

Domain	Metric		Rating	Comments
	Metric 10:	Covariate Characterization	Low	Age and smoking status only checked for correlation with exposure concentration, but not controlled in models. In multiple linear regression models of asbestos and disease, concentration of another fiber and/or other asbestos related disease were sometimes controlled in the model.
	Metric 11:	Co-exposure Counfounding	Medium	Co-exposures that other than asbestos that would likely bias the results were not likely to be present.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	Medium	The study design is appropriate for the research question. t-Tests and linear regression models were used to evaluate the association between fiber burden and asbestos related disease.
	Metric 13:	Statistical Power	Uninformative	The number of participants is small especially only n=6 subjects without asbestos related disease as reference group, which greatly limited the power of this study.
	Metric 14:	Reproducibility of Analyses	Medium	The description of the analysis is sufficient to understand how to conceptually reproduce the analysis with access to the analytic data.
	Metric 15:	Statistical Analysis	Medium	Statistical models and test method are transparent and appropriate

Additional Comments: Lack of information on outcome measurements and small reference group size drastically limited the study's confidence and ability to detect an effect.

Overall Quality Determination — Uninformative

* No biomarkers were identified for this evaluation.

Study Citation:	Clin, B., Thaon, I., Boulanger, M., Brochard, P., Chamming's, S., Gislard, A., Lacourt, A., Luc, A., Ogier, G., Paris, C. (2017). Cancer of the esophagus and asbestos exposure. American Journal of Industrial Medicine 60(11):968-975.			
Health Outcome:	esophageal cancer			
Target Organ(s):	Cancer/Carcinogenesis: Esophageal cancer mortality; Gastrointestinal: Esophageal cancer mortality; Mortality: Esophageal cancer mortality			
Asbestos Fiber Type(s):	Asbestos - Not specified: 1332-21-4			
Linked HERO ID(s):	No linked references.			
HERO ID:	6863220			
Domain		Metric	Rating	Comments
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Low	There is no detail regarding the measurement of exposure in this study, but a reference to Paris et al., 2009 (Paris et al., 2009, HEROID 758968). There, authors describe the use of a questionnaire and an a priori job-exposure matrix to calculate a cumulative exposure index. This paper and the paper by Paris et al., 2009 lack and detail of asbestos sample measurements or quantification.Authors describe using four classes for levels of exposure: "lowlevel (passive exposure), corresponding to a numerical value of "0.01equivalent fibers/mL"; low-intermediate, corresponding to a numericalvalue of"0.1 equivalent fibers/mL"; high-intermediate, corresponding toa numerical value of "1 equivalent fibers/mL"; and high exposure,corresponding to a numerical value of "10 equivalent fibers/mL" (Paris et al., 2009, HEROID 758968). A final cumulative exposure index was calculated as the sum of each job's four-level CEI for each subject.
	Metric 5:	Exposure Levels	Medium	Final models report 6 levels of exposure: unexposed, 0-3.3 f-y/mL, 3.3-13.5 f-y/ml, 13.6-32 f-y/ml, 32-64 f-y/ml, and >=64 f-y/ml. This data was calculated from cumulative exposure indices.
Additional Comments:	HEROID 6863220 was not evaluated for any metrics except Metric 4 and 5 and had no data extracted because it did not have sufficient exposure information to be useful for dose-response analysis.			

** As described in Appendix B.2 of the *White Paper: Quantitative Approach to the Human Health Assessment for the Risk Evaluation for Asbestos Part 2: Supplemental Evaluation Including Legacy Uses and Associated Disposals of Asbestos*, to be considered as being informative for dose-response analysis, metrics 4 and 5 would need metric ratings of Medium or High. This reference did not satisfy this requirement; therefore data quality evaluation is presented for only for metrics 4 and 5.

Study Citation:	Conforti, P. M., Kanarek, M. S., Jackson, L. A., Cooper, R. C., Murchio, J. C. (1981). Asbestos in drinking water and cancer in the San Francisco Bay area: 1969-1974 incidence. Journal of Clinical Epidemiology 34(5):211-224.
Health Outcome:	Lung Cancer; Ovarian Cancer
Target Organ(s):	Cancer/Carcinogenesis: Incidence of any cancer Incidence of 35 other system- and site-specific cancer outcomes, excluding skin and bone cancers:-Digestive cancers (tract, esophagus, stomach, small intestine, colon, rectum, digestive organs, liver, gall bladder, pancreas, retroperitoneum)-Respiratory cancers (larynx, trachea/bronchus/lung, pleura, lung small cell, lung squamous, lung adenocarcinoma)-Breast cancer-Female reproductive (cervix, corpus uteri, ovary)-Male reproductive (prostate, urinary)-Kidney, bladder, brain, thyroid, Hodgkin's disease, leukemia; Lung/Respiratory: Incidence of lung/respiratory cancer; Gastrointestinal: Incidence of gastrointestinal cancers; Hepatic/Liver: Incidence of liver cancer; Reproductive/Developmental: Incidence of male (prostate, urinary) and female (cervix, corpus uteri, ovary) reproductive cancersIncidence of breast cancer; nan:
Asbestos Fiber Type(s):	Asbestos - Chrysotile (serpentine): 12001-29-5
Linked HERO ID(s):	No linked references.
HERO ID:	60556

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Medium	This ecological analysis in the San Francisco-Oakland Metropolitan Statistical Area (SMSA) examined how standardized incidence ratios (SIRs) for cancer in 1969-1974 varied by level of chrysotile asbestos in residential water samples. Exposure was estimated and cases identified for all 722 census tracts in the SMSA (1970 population > 3 million). The SMSA is characterized by distinct water supply sources, some of which came from aquifers or reservoirs exposed to naturally occurring serpentine rock – the official state rock of California and the parent form of chrysotile asbestos. Water supply asbestos concentrations were estimated for 410 SMSA "super tracts" used to combine the tracts used in 1960 and 1970 censuses. Newly diagnosed cancers were obtained from surveys that comprehensively compiled data on cancers in the SMSA during the entire period, which included census tract information. Possible ecological study biases: Potential bias due to SES differences across super tracts was addressed by calculating SIRs cross-classified by median income or education as well as by exposure. The authors ensured that there were adequate numbers of tracts in each stratum (mostly n~50). Confounding due to super tract group differences in potential occupational exposure was addressed using models that adjusted for the percentage of construction, electrical and textile workers in each tract.
	Metric 2:	Attrition	Medium	As this study was cross-sectional and ecological, attrition was not a concern. The authors estimated the 1972 population – the midpoint of the period for which cancer incidence data were used – using available census data.
	Metric 3:	Comparison Group	High	Both the expected and observed cancer rates used to derive SIRs were calculated using the estimated 1972 SMSA population, ensuring comparability. Expected cancer incidence rates for the entire SMSA were calculated using an age, race (white vs non), and sex-specific population estimate for January 1972, extrapolated from 1960 and 1970 censuses. Observed cases were compiled in 5-year age groups for each super tract. These values were compared to the numbers of expected cancers based on the age, race, and sex population of that super tract.
Domain 2: Exposure Characterization				

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Study Citation:	Conforti, P. M., Kanarek, M. S., Jackson, L. A., Cooper, R. C., Murchio, J. C. (1981). Asbestos in drinking water and cancer in the San Francisco Bay area: 1969-1974 incidence. Journal of Clinical Epidemiology 34(5):211-224.
Health Outcome:	Lung Cancer; Ovarian Cancer
Target Organ(s):	Cancer/Carcinogenesis: Incidence of any cancer Incidence of 35 other system- and site-specific cancer outcomes, excluding skin and bone cancers:-Digestive cancers (tract, esophagus, stomach, small intestine, colon, rectum, digestive organs, liver, gall bladder, pancreas, retroperitoneum)-Respiratory cancers (larynx, trachea/bronchus/lung, pleura, lung small cell, lung squamous, lung adenocarcinoma)-Breast cancer-Female reproductive (cervix, corpus uteri, ovary)-Male reproductive (prostate, urinary)-Kidney, bladder, brain, thyroid, Hodgkin's disease, leukemia; Lung/Respiratory: Incidence of lung/respiratory cancer; Gastrointestinal: Incidence of gastrointestinal cancers; Hepatic/Liver: Incidence of liver cancer; Reproductive/Developmental: Incidence of male (prostate, urinary) and female (cervix, corpus uteri, ovary) reproductive cancersIncidence of breast cancer; nan:
Asbestos Fiber Type(s):	Asbestos - Chrysotile (serpentine): 12001-29-5
Linked HERO ID(s):	No linked references.
HERO ID:	60556

Domain	Metric		Rating	Comments
	Metric 4:	Measurement of Exposure	Medium	Exposure estimates used 353 water samples previously collected to represent the water distribution systems along with 19 additional samples (Kanarek et al 1980, RefID 60569). The mean of samples from each distribution area was assigned to all super tracts in that area. Exposure was assigned independently by personnel with no knowledge of cancer incidence across census tracts. In addition to household taps, analyses were made on raw and finished water at treatment plants and several stored historical samples to reflect exposure over 40 years. Water districts were subdivided to the extent possible by source, treatment process and/or pressure zones. Fibers were counted by filtering water through 0.45 μm filters and using TEM, with analysts blinded to the source of each sample and several samples analyzed in duplicate. When results were below detectable limits, the lowest detectable limit was used (usually 10^4 fibers/liter), vs a fraction such as half the detection limit. This approach likely inflated exposure estimates. Sources of measurement error that could not be addressed include the lack of information on residential drinking water intake, water intake from other sources (e.g., work, school), and use of bottled water or water filters (less common at the time than today). The authors did not mention the prevalence of asbestos cement pipes, or the prevalence households not connected to the public water supply. Possible ecological study biases: To evaluate risk of bias due to heterogeneity in drinking water asbestos concentrations within super tracts, the authors examined variability across random households within a selected tract, within a distribution system (from treatment plant to household tap), and at different times of day during high use. The authors described consistently finding very little variability. Secondly, potential bias due to population mobility (i.e., changes in residence and thus exposure) was examined in a sensitivity analysis limiting the sample to tracts in which more than 50% of the population aged >5y resided in the same household in 1965 and 1970.
	Metric 5:	Exposure Levels	Medium	The authors used 3 categories of exposure in most analyses, each including more than 100 super tracts. Multiple tracts had common water systems and identical fiber counts, resulting in gaps in the boundary values defining these categories.
	Metric 6:	Temporality	Medium	The study was cross-sectional, using predominantly recent measures of drinking water asbestos to characterize exposure. Given the long latency of many cancers, the authors report that they incorporated a few historical water samples to estimate past exposure, but no details were provided (number, timing, distribution, concentrations).
Domain 3: Outcome Assessment				

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Study Citation:	Conforti, P. M., Kanarek, M. S., Jackson, L. A., Cooper, R. C., Murchio, J. C. (1981). Asbestos in drinking water and cancer in the San Francisco Bay area: 1969-1974 incidence. Journal of Clinical Epidemiology 34(5):211-224.
Health Outcome:	Lung Cancer; Ovarian Cancer
Target Organ(s):	Cancer/Carcinogenesis: Incidence of any cancer Incidence of 35 other system- and site-specific cancer outcomes, excluding skin and bone cancers:-Digestive cancers (tract, esophagus, stomach, small intestine, colon, rectum, digestive organs, liver, gall bladder, pancreas, retroperitoneum)-Respiratory cancers (larynx, trachea/bronchus/lung, pleura, lung small cell, lung squamous, lung adenocarcinoma)-Breast cancer-Female reproductive (cervix, corpus uteri, ovary)-Male reproductive (prostate, urinary)-Kidney, bladder, brain, thyroid, Hodgkin's disease, leukemia; Lung/Respiratory: Incidence of lung/respiratory cancer; Gastrointestinal: Incidence of gastrointestinal cancers; Hepatic/Liver: Incidence of liver cancer; Reproductive/Developmental: Incidence of male (prostate, urinary) and female (cervix, corpus uteri, ovary) reproductive cancersIncidence of breast cancer; nan:
Asbestos Fiber Type(s):	Asbestos - Chrysotile (serpentine): 12001-29-5
Linked HERO ID(s):	No linked references.
HERO ID:	60556

Domain	Metric		Rating	Comments
	Metric 7:	Outcome Measurement or Characterization	High	Lung Cancer: The outcome database included 51,314 incidence cases obtained from a registry compiled by the San Francisco Bay Area Resource for Cancer Epidemiology (RCE). The registry included all newly diagnosed cancers collected for the Third National Cancer Survey (TNCS) 1969-1971 and subsequently for an RCE survey for 1972-1974 that collected comparable data. Over 90% of the cancers were microscopically confirmed. Codes for each cases included age, sex, race, body site, hospital, diagnosis method and date, and census tract. ICD 8 codes were used to classify cancers. However, the authors did not provide case counts. The number of cases available is relevant to evaluate the robustness of findings for very rare outcomes such as pleural cancer. Lung cancer: histological subtypes were assessed (lung small cell, squamous, and adenocarcinoma not otherwise specified).; Ovarian Cancer: See comments for all cancers shown for lung cancer.; Other Cancer(s): See comments for all cancers shown for lung cancer.
	Metric 8:	Reporting Bias	Low	The authors reported only statistically significant findings for most analyses. Consequently, SES-stratified SIRs, regression/correlation coefficients, and p-values are selectively available. In addition, most results were presented only for white men and women, but the authors stated that results for the total population were almost identical as the population was predominantly white.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Medium	Selected SIRs were cross-classified by asbestos exposure categories and median income or education. However, distributions of these variables across super tracts were not shown, nor was the extent to which they related to exposure described. Along with unadjusted correlations, multivariate regression models were used to examine how asbestos in water was associated with SIRs. These models adjusted for super tract medians for family income, education, percentage married, and proportion employed in industries with potential asbestos exposure. However, the authors were unable to adjust for the distribution of other known cancer risk factors (e.g., smoking, alcohol, physical activity, diet quality) which may vary by census tract.

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Study Citation:	Conforti, P. M., Kanarek, M. S., Jackson, L. A., Cooper, R. C., Murchio, J. C. (1981). Asbestos in drinking water and cancer in the San Francisco Bay area: 1969-1974 incidence. Journal of Clinical Epidemiology 34(5):211-224.
Health Outcome:	Lung Cancer; Ovarian Cancer
Target Organ(s):	Cancer/Carcinogenesis: Incidence of any cancer Incidence of 35 other system- and site-specific cancer outcomes, excluding skin and bone cancers:-Digestive cancers (tract, esophagus, stomach, small intestine, colon, rectum, digestive organs, liver, gall bladder, pancreas, retroperitoneum)-Respiratory cancers (larynx, trachea/bronchus/lung, pleura, lung small cell, lung squamous, lung adenocarcinoma)-Breast cancer-Female reproductive (cervix, corpus uteri, ovary)-Male reproductive (prostate, urinary)-Kidney, bladder, brain, thyroid, Hodgkin's disease, leukemia; Lung/Respiratory: Incidence of lung/respiratory cancer; Gastrointestinal: Incidence of gastrointestinal cancers; Hepatic/Liver: Incidence of liver cancer; Reproductive/Developmental: Incidence of male (prostate, urinary) and female (cervix, corpus uteri, ovary) reproductive cancersIncidence of breast cancer; nan:
Asbestos Fiber Type(s):	Asbestos - Chrysotile (serpentine): 12001-29-5
Linked HERO ID(s):	No linked references.
HERO ID:	60556

Domain	Metric		Rating	Comments
	Metric 10:	Covariate Characterization	Medium	It is uncertain to what extent adjusting for a variable defined using the estimated percentage of construction, electrical and textile workers in each super tract addressed any confounding by occupational exposure to asbestos. It is also uncertain to what extent any confounding by individual level SES is addressed using area level SES measures. SES may affect mobility and thus duration of exposure to water measured at current residence; the authors attempted to address this using a sensitivity analysis that limited the sample to persons remaining in the same census tract for 5y. However, 5 years is relatively short.
	Metric 11:	Co-exposure Counfounding	Low	Co-exposures to other pollutants, for example disinfectant by-products or other substances in the water supply (potential correlates of water quality), was not addressed.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	Medium	The primary analyses, which compared how SIRs varied across super tract groups with differing levels of drinking water asbestos, were appropriate to evaluate the study aims.
	Metric 13:	Statistical Power	Medium	The population included more than 3,000,000 individuals, and the study accrued more than 50,000 cases. However, no case numbers or confidence intervals were provided, making power for analyses involving rare cancers uncertain. Most super tracts would likely have had zero observed and expected cases for such outcomes.
	Metric 14:	Reproducibility of Analyses	Medium	Analyses are for the most part described adequately, but key details were at times lacking. For example, the authors present correlation coefficients between "asbestos values and cancer rates by site and sex for the white population". It is uncertain whether outcome variables are in fact incidence rates (vs standardized incidence ratios), and whether/how the rates used were adjusted. Additionally, the authors did not clearly specify whether the drinking water asbestos variable was categorized or used continuously (despite its highly non-normal distribution) in either correlations or regression models. Moreover, along with no case counts, the authors showed very few SIRs, which would make it difficult to ascertain the extent to which results were replicated.

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Study Citation:	Conforti, P. M., Kanarek, M. S., Jackson, L. A., Cooper, R. C., Murchio, J. C. (1981). Asbestos in drinking water and cancer in the San Francisco Bay area: 1969-1974 incidence. Journal of Clinical Epidemiology 34(5):211-224.
Health Outcome:	Lung Cancer; Ovarian Cancer
Target Organ(s):	Cancer/Carcinogenesis: Incidence of any cancer Incidence of 35 other system- and site-specific cancer outcomes, excluding skin and bone cancers:-Digestive cancers (tract, esophagus, stomach, small intestine, colon, rectum, digestive organs, liver, gall bladder, pancreas, retroperitoneum)-Respiratory cancers (larynx, trachea/bronchus/lung, pleura, lung small cell, lung squamous, lung adenocarcinoma)-Breast cancer-Female reproductive (cervix, corpus uteri, ovary)-Male reproductive (prostate, urinary)-Kidney, bladder, brain, thyroid, Hodgkin's disease, leukemia; Lung/Respiratory: Incidence of lung/respiratory cancer; Gastrointestinal: Incidence of gastrointestinal cancers; Hepatic/Liver: Incidence of liver cancer; Reproductive/Developmental: Incidence of male (prostate, urinary) and female (cervix, corpus uteri, ovary) reproductive cancersIncidence of breast cancer; nan:
Asbestos Fiber Type(s):	Asbestos - Chrysotile (serpentine): 12001-29-5
Linked HERO ID(s):	No linked references.
HERO ID:	60556

Domain	Metric		Rating	Comments
	Metric 15:	Statistical Analysis	Low	The authors described appropriate methods to calculate SIRs, accounting for age, race, and sex distributions. However, in addition to no case counts, the authors did not provide confidence intervals for the few SIR values shown. Particularly for very rare cancers, understanding the level of precision for these estimates is important. Another important concern is the use of Pearson's product moment correlations vs. a non-parametric method to characterize relationships with the non-normally distributed water asbestos variable (whether used continuously without transformation or categorized – which is unclear). Finally, the authors did not adequately describe the log-linear regression models they used to evaluate associations after accounting for confounding. Log-linear models are typically used for count/ordinal outcomes, and SIRs were continuous; particularly without specifying the link function it is unclear that regression models were used appropriately.The measurement exposure (M4) and/or exposure levels (M5) metrics are rated as medium upon review by both set of reviewers. Also, the overall quality determination (OQD) is rated medium. Extraction will be completed and quality control reviewed.

Additional Comments:	This ecologic study evaluated how standardized incidence ratios for cancers diagnosed in 1969-1974 varied across metropolitan San Francisco communities with differing levels of chrysotile asbestos – an issue due to natural occurrence - in residential drinking water. To address the limitations of ecological study designs, the authors incorporated adjustments and sensitivity analyses to address potential biases such as confounding due to area-level SES differences. A comprehensive cancer incidence registry that included census tract information was used, along with more than 350 water samples to characterize concentrations of asbestos in the drinking water of 410 census "super tracts". A minor concern is that exposure may have been overestimated by using the detection limit, rather than half of the detection limit, to impute values below quantification. The authors found that areas with higher drinking water asbestos consistently had higher standardized incidence ratios (SIRs) for digestive cancers in both men and women, but findings for some cancers were inconsistent. For example, Pearson's correlations with respiratory cancers (trachea, bronchus, lung) were significant only in men, while regression coefficients with these same cancers were significant only in women. Exposure was positively associated with pleural cancer in women using regression models but not correlations; negative associations between exposure and female reproductive cancers were significant only using correlations. Methodological issues such as using unadjusted Pearson correlations despite highly non-normal exposure data contributed to these inconsistencies. Neither case counts nor confidence intervals were provided for rare outcomes such as pleural cancers, making it difficult to fully interpret those results.The measurement exposure (M4) and/or exposure levels (M5) metrics are rated as medium upon review by both set of reviewers. Also, the overall quality determination (OQD) is rated medium. Extraction has been completed and quality control reviewed.

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Study Citation:	Conforti, P. M., Kanarek, M. S., Jackson, L. A., Cooper, R. C., Murchio, J. C. (1981). Asbestos in drinking water and cancer in the San Francisco Bay area: 1969-1974 incidence. Journal of Clinical Epidemiology 34(5):211-224.
Health Outcome:	Lung Cancer; Ovarian Cancer
Target Organ(s):	Cancer/Carcinogenesis: Incidence of any cancer Incidence of 35 other system- and site-specific cancer outcomes, excluding skin and bone cancers:-Digestive cancers (tract, esophagus, stomach, small intestine, colon, rectum, digestive organs, liver, gall bladder, pancreas, retroperitoneum)-Respiratory cancers (larynx, trachea/bronchus/lung, pleura, lung small cell, lung squamous, lung adenocarcinoma)-Breast cancer-Female reproductive (cervix, corpus uteri, ovary)-Male reproductive (prostate, urinary)-Kidney, bladder, brain, thyroid, Hodgkin's disease, leukemia; Lung/Respiratory: Incidence of lung/respiratory cancer; Gastrointestinal: Incidence of gastrointestinal cancers; Hepatic/Liver: Incidence of liver cancer; Reproductive/Developmental: Incidence of male (prostate, urinary) and female (cervix, corpus uteri, ovary) reproductive cancersIncidence of breast cancer; nan:
Asbestos Fiber Type(s):	Asbestos - Chrysotile (serpentine): 12001-29-5
Linked HERO ID(s):	No linked references.
HERO ID:	60556

Domain	Metric	Rating	Comments
Overall Quality Determination		**Medium**	

* No biomarkers were identified for this evaluation.

Study Citation:	Cookson, W. O., Musk, A. W., Glancy, J. J., de Klerk, N. H., Yin, R., Mele, R., Carr, N. G., Armstrong, B. K., Hobbs, M. S. (1985). Compensation, radiographic changes, and survival in applicants for asbestosis compensation. British Journal of Industrial Medicine 42(7):461-468.
Health Outcome:	mortality, radiographic profusions, pneumoconiosis
Target Organ(s):	Mortality: All causes mortality, Pneumoconiosis mortality, Bronchitis and emphysema mortality, Tuberculosis mortality, Other respiratory disease, Gastrointestinal cancer mortality, Other cancers mortality, Heart disease mortality, Other circulatory disease mortality, Respiratory neoplasms mortality; Lung/Respiratory: Profusion of radiographic opacities, Pneumoconiosis mortality, Bronchitis and emphysema mortality, Tuberculosis mortality, Other respiratory disease mortality, Respiratory neoplasms mortality; Cancer/Carcinogenesis: Gastrointestinal cancer mortality, Other cancer mortality, Respiratory neoplasms mortality; Gastrointestinal: Gastrointestinal cancer mortality; Cardiovascular: Heart disease mortality, Other circulatory disease mortality
Asbestos Fiber Type(s):	Asbestos - Crocidolite (riebeckite): 12001-28-4
Linked HERO ID(s):	No linked references.
HERO ID:	3083452

Domain		Metric	Rating	Comments
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Low	This metric is rated low because neither the study nor any cited methods sources explicitly mention the use of PCM or TEM to quantify asbestos fibers.
	Metric 5:	Exposure Levels	Medium	The distribution of exposure appears to be sufficient to develop an exposure-response estimate for profusion of radiographic opacities since it is assessed continuously. However, all other outcomes are assessed as "exposed" vs. "unexposed" and thus have a limited range of exposure.

Additional Comments: This study was not fully evaluated because metric 4 was rated as low, due to no explicit mention in the study or cited sources about the use of PCM or TEM.

* No biomarkers were identified for this evaluation.

** As described in Appendix B.2 of the *White Paper: Quantitative Approach to the Human Health Assessment for the Risk Evaluation for Asbestos Part 2: Supplemental Evaluation Including Legacy Uses and Associated Disposals of Asbestos*, to be considered as being informative for dose-response analysis, metrics 4 and 5 would need metric ratings of Medium or High. This reference did not satisfy this requirement; therefore data quality evaluation is presented for only for metrics 4 and 5.

Study Citation:	Cuccaro, F., Nannavecchia, A. M., Silvestri, S., Angelini, A., Coviello, V., Bisceglia, L., Magnani, C. (2019). Mortality for mesothelioma and lung cancer in a cohort of asbestos cement workers in BARI (Italy): Time related aspects of exposure. Journal of Occupational and Environmental Medicine 61(5):410-416.
Health Outcome:	Lung Cancer; "Even if the specific type of pneumoconiosis caused by exposure to asbestos is the, we decided to consider mortality for pneumoconiosis."
Target Organ(s):	Cancer/Carcinogenesis: Lung cancer mortality; Lung/Respiratory: Lung cancer mortality, Mortality from pneumoconiosis; Mortality: Cardiovascular disease, Pneumoconiosis, Lung cancer; Cardiovascular: Mortality from cardiovascular disease
Asbestos Fiber Type(s):	Asbestos - Chrysotile (serpentine): 12001-29-5; Asbestos - Crocidolite (riebeckite): 12001-28-4; Asbestos - Amosite (grunerite): 12172-73-5
Linked HERO ID(s):	No linked references.
HERO ID:	6867273

Domain	Metric		Rating	Comments
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Low	Between 1970 and 1974 several industrial hygiene investigations were carried out with measurement of the concentration of the airborne fibers (Coviello, et al., 2002, HERO ID 3080488). This metric is rated Low because authors in this paper do not explicitly cite use of PCM or TEM, and the cited methods paper (Coviello et al. 2002, 3080488) is not freely available or through HERO. PubMed also indicated that the article is in Italian.
	Metric 5:	Exposure Levels	Medium	The authors of this cohort study used an exposure index to evaluate individual cumulative exposure as proxy of asbestos dose, and reported 3 or more levels of exposure (3 tertiles).

Additional Comments:	QC was not completed for metrics other than Metrics 4 and 5 because the study does not have sufficient exposure information to be useful for dose-response analysis.Metric 4 is rated Low because authors in this paper do not explicitly cite use of PCM or TEM, and the cited methods paper (Coviello et al. 2002, 3080488) is not freely available. For Metric 5, this cohort study used an exposure index to evaluate individual cumulative exposure as proxy of asbestos dose and reported 3 or more levels of exposure (3 tertiles). Mesothelioma and other outcomes forms filled for Metrics 4 and 5 and evaluation stopped.

** As described in Appendix B.2 of the *White Paper: Quantitative Approach to the Human Health Assessment for the Risk Evaluation for Asbestos Part 2: Supplemental Evaluation Including Legacy Uses and Associated Disposals of Asbestos*, to be considered as being informative for dose-response analysis, metrics 4 and 5 would need metric ratings of Medium or High. This reference did not satisfy this requirement; therefore data quality evaluation is presented for only for metrics 4 and 5.

Study Citation:	Cullen, M. R., Lopez-Carrillo, L., Alli, B., Pace, P. E., Shalat, S. L., Baloyi, R. S. (1991). Chrysotile asbestos and health in Zimbabwe: II. Health status survey of active miners and millers. American Journal of Industrial Medicine 19(2):171-182.
Health Outcome:	Pulmonary Function/Spirometry Results; pleural disease
Target Organ(s):	Lung/Respiratory: FEV1, FVC, Pleural disease
Asbestos Fiber Type(s):	Asbestos - Chrysotile (serpentine): 12001-29-5
Linked HERO ID(s):	No linked references.
HERO ID:	2078970

Domain	Metric		Rating	Comments
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Medium	Concentration measurements were made in 1980 and were used to estimate exposures during that time. Exposure estimates prior to 1980 were calculated based on professional judgement.
	Metric 5:	Exposure Levels	Low	The authors reported two levels of exposure for FVCD (referent + 1 with 8 fibers/cc*years or more). For the X-ray abnormalities, the study presented the relationship between cumulative dose and radiographic category (0/1, 0/1, 1/0, 1/1) unadjusted for age in Chrysotile miners and millers.

Additional Comments: None

* No biomarkers were identified for this evaluation.

** As described in Appendix B.2 of the *White Paper: Quantitative Approach to the Human Health Assessment for the Risk Evaluation for Asbestos Part 2: Supplemental Evaluation Including Legacy Uses and Associated Disposals of Asbestos*, to be considered as being informative for dose-response analysis, metrics 4 and 5 would need metric ratings of Medium or High. This reference did not satisfy this requirement; therefore data quality evaluation is presented for only for metrics 4 and 5.

Study Citation:	Cvetanov, V., Karadžinska-Bislimovska, J., Vasevski, J., Ežova, N., Stikova, E. (1988). The relationship between asbestos bodies, serum immunoglobulin levels and X-ray changes in asbestos workers . Arhiv za Higijenu Rada i Toksikologiju 39(4):455-460.
Health Outcome:	Serum immunoglobulin levels
Target Organ(s):	Immune/Hematological: Serum immunoglobulin levels
Asbestos Fiber Type(s):	Asbestos - Not specified: 1332-21-4
Linked HERO ID(s):	No linked references.
HERO ID:	3082920

Domain	Metric		Rating	Comments
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Low	Exposure was directly measured and assessed using sputum samples taken from the workers. The asbestos bodies were counted using native microscopic slides. Additional information was not provided on the measurement of exposure.
	Metric 5:	Exposure Levels	Low	The range of exposure in the population is limited because the study reports the exposure using three categories: 1 to 5 asbestos bodies, 6 to 10 asbestos bodies, and over 10 asbestos bodies. One worker was cited to have over 20 asbestos bodies making it clear that the categories cannot adequately display the range and distribution.

Additional Comments: None

** As described in Appendix B.2 of the *White Paper: Quantitative Approach to the Human Health Assessment for the Risk Evaluation for Asbestos Part 2: Supplemental Evaluation Including Legacy Uses and Associated Disposals of Asbestos*, to be considered as being informative for dose-response analysis, metrics 4 and 5 would need metric ratings of Medium or High. This reference did not satisfy this requirement; therefore data quality evaluation is presented for only for metrics 4 and 5.

Study Citation:	Dahlqvist, M., Alexandersson, R., Hedenstierna, G. (1992). Lung function and exposure to asbestos among vehicle mechanics. American Journal of Industrial Medicine 22(1):59-68.
Health Outcome:	Pulmonary Function/Spirometry Results
Target Organ(s):	Lung/Respiratory: Forced vital capacity (FVC), Forced volume in 1 second (FEV1), FEV1 in percent of the largest vital capacity, Expiratory flow at 75% of FVC (MEF25), Residual volume (RV), Total lung capacity (TLC), Nitrogen breath wash-out, Carbon monoxide single breath wash-out, Closing volume (CV), Vital capacity (VC), Closing volume in percent of VC (CV%)
Asbestos Fiber Type(s):	Asbestos- Exposure reported as PCM or TEM (including conversion factors for dust)
Linked HERO ID(s):	No linked references.
HERO ID:	2248426

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Low	This Swedish cross-sectional study included currently employed 99 auto mechanics exposed to low levels of asbestos and 89 unexposed local controls. Only 101 of 259 (39%) exposed subjects (from the “Motor Health organization” register, selection process not described) were “approved to participate”. Inclusion criteria were age $\geq$40y, and $>$15y occupational asbestos exposure starting at least 20y prior. Selectivity is a concern given the absence of details on why they were excluded (primarily unspecified ”lung irritant” exposure), and how excluded candidates differed from those excluded. Importantly, excluding individuals with exposures common in mechanic workshops (ex. welding, paint, or varnish fumes) could yield a sample unrepresentative of the target population’s exposure-outcome distribution. Indeed, the authors noted in the discussion that healthy worker selectivity was a concern since “subjects who left their jobs as a consequence of lung disease were not included in the study”.
	Metric 2:	Attrition	Medium	There was a moderate loss of subjects. Two of the 101 exposed and 6 of the 89 unexposed individuals were excluded from the initial study sample (unspecified health disorders).
	Metric 3:	Comparison Group	Medium	The unexposed comparison group comprised of bus drivers and white-collar workers drawn from Motor Health and Stockholm traffic registers (no further details, Ns for each job not provided). Only 89 of 315 candidates (28%) were approved to participate (reasons not specified beyond stating many had past occupational exposure to lung irritants); the lack of details and comparisons with those included raises selectivity concerns. Comparability of this group with the exposed mechanics may also be suboptimal because: (i) current employment status is uncertain as participants were selected based on their “last job description”; (ii) age and duration of employment restrictions used for the exposed were not applied here. Other differences vs the exposed group which were not addressed include higher body weight despite similar height (BMI not calculated), and possible SES disparities.
Domain 2: Exposure Characterization				

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Study Citation:	Dahlqvist, M., Alexandersson, R., Hedenstierna, G. (1992). Lung function and exposure to asbestos among vehicle mechanics. American Journal of Industrial Medicine 22(1):59-68.
Health Outcome:	Pulmonary Function/Spirometry Results
Target Organ(s):	Lung/Respiratory: Forced vital capacity (FVC), Forced volume in 1 second (FEV1), FEV1 in percent of the largest vital capacity, Expiratory flow at 75% of FVC (MEF25), Residual volume (RV), Total lung capacity (TLC), Nitrogen breath wash-out, Carbon monoxide single breath wash-out, Closing volume (CV), Vital capacity (VC), Closing volume in percent of VC (CV%)
Asbestos Fiber Type(s):	Asbestos- Exposure reported as PCM or TEM (including conversion factors for dust)
Linked HERO ID(s):	No linked references.
HERO ID:	2248426

Domain	Metric		Rating	Comments
	Metric 4:	Measurement of Exposure	Medium	Exposure was estimated for 95 of the 99 exposed mechanics, who had worked in 386 places, using: fiber exposure measurement and analysis, reviews of earlier reports, questionnaires, and interviews. For fiber measures, no details were provided on: collection equipment; placement, duration or timing of sampling; data availability for past workplaces; or assumptions used in estimation (any published details in Swedish). Fiber counts were described as using phase contrast light microscope (PCM). Measurement error is a concern given the authors' report that asbestos dust from brakes – a major source of exposure – comprise very short fibers (<0.4 μm) not visible under these microscopes. They stated that concentrations were higher when analyzed using a STEM (scanning transmission electron microscope) microscope but did not state whether or how these STEM measures were used.
	Metric 5:	Exposure Levels	Medium	The range of exposure was low by design: work environments below the Swedish concentration limit of 0.2 fibers/ml. The median fiber concentration over the years evaluated was 0.08 (IQE 0.06-0.11) fibers/ml, and the median cumulative fiber dose 2.3 (IQR 1.5-3.6) fiber-years/ml (8-hour time weighted average). Exposure variables were analyzed continuously.
	Metric 6:	Temporality	Medium	Estimates accounting for past exposure were constructed (details not provided). Eligibility criteria for the exposed included a history of 15 years working in similar environments. Temporality is not a concern. However, as this study is cross-sectional, fiber measures obtained by the investigators to help derive exposure estimates would have been contemporaneous.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	High	Pulmonary Function/Spirometry Results: Dynamic and static spirometry, along with a carbon monoxide single breath wash-out and a nitrogen breath washout, were used to assess lung function. Measures derived included FVC, FEV1, FEV%, MEF25, closing volume percent (CV%) from the nitrogen washout, and transfer factor (TL-co) from the carbon monoxide washout. The authors cited references for the measures they derived and reported weekly calibration of equipment. Smokers were asked to refrain from smoking for 4 hours prior to testing. The authors did not, however, mention blinding testers to exposure group status.

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Study Citation: Dahlqvist, M., Alexandersson, R., Hedenstierna, G. (1992). Lung function and exposure to asbestos among vehicle mechanics. American Journal of Industrial Medicine 22(1):59-68.

Health Outcome: Pulmonary Function/Spirometry Results

Target Organ(s): Lung/Respiratory: Forced vital capacity (FVC), Forced volume in 1 second (FEV1), FEV1 in percent of the largest vital capacity, Expiratory flow at 75% of FVC (MEF25), Residual volume (RV), Total lung capacity (TLC), Nitrogen breath wash-out, Carbon monoxide single breath wash-out, Closing volume (CV), Vital capacity (VC), Closing volume in percent of VC (CV%)

Asbestos Fiber Type(s): Asbestos- Exposure reported as PCM or TEM (including conversion factors for dust)

Linked HERO ID(s): No linked references.

HERO ID: 2248426

Domain	Metric		Rating	Comments
	Metric 8:	Reporting Bias	Medium	Results (coefficients and SEs) from models analyzing how exposure status and other predictors related to all lung function measure were presented (Table III), though coefficients were not shown when non-significant. However, partial correlations relating increasing exposure to each lung function measure were presented only for the subgroup of mechanics also exposed to diesel exhaust (Table IV). The association between lung function and increasing exposure among all mechanics was shown only for CV% (Fig 1); the lack of a dose-response relationship with TLco was mentioned in the discussion. p-values, but not confidence intervals, were provided.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Medium	Models adjusted for age, height, never/ever smoking and pack-years for current smokers (not race or sex as participants were white males). Models did not adjust for body weight or BMI, or for socioeconomic factors.
	Metric 10:	Covariate Characterization	Medium	Questionnaires and detailed interviews were used to obtain information from participants, including potential co-exposures. Details on the structure and content of interviews and interviewer qualifications were not provided. Biomarkers were not used.
	Metric 11:	Co-exposure Counfounding	Medium	Diesel exhaust was included as a covariate in partial correlations associating asbestos exposure to lung function measures in a subgroup of workers. Exposure to ”lung irritant” co-exposures was an exclusion criterion.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	Medium	The authors appropriately used multivariable linear regression and partial correlations to analyze associations between asbestos exposure variables and lung function outcomes. Minimally or unadjusted associations were not shown. The paper reported using “appropriate transformations” if variables diverged from normality. ln-transformed asbestos exposure and diesel exhaust were noted in the results text. Testing of interactions between asbestos and smoking is mentioned in the discussion.
	Metric 13:	Statistical Power	Medium	The modest sample size (n=182), given the low range of exposure under study, might have undermined sensitivity. The analysis incorporating diesel exhaust, which was limited to auto mechanics with this exposure, was especially small (n=50). However, the use of continuous lung function outcome measures increased power.
	Metric 14:	Reproducibility of Analyses	Medium	Though few details were provided in the description of analyses, information presented in the tables facilitates reproducing results (variable coding is given, Ns and R-squared values are provided). However, the main results table presents coefficients only for variables with $p<0.05$ but does not state whether non-significant variables were included in the models.

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Study Citation:	Dahlqvist, M., Alexandersson, R., Hedenstierna, G. (1992). Lung function and exposure to asbestos among vehicle mechanics. American Journal of Industrial Medicine 22(1):59-68.
Health Outcome:	Pulmonary Function/Spirometry Results
Target Organ(s):	Lung/Respiratory: Forced vital capacity (FVC), Forced volume in 1 second (FEV1), FEV1 in percent of the largest vital capacity, Expiratory flow at 75% of FVC (MEF25), Residual volume (RV), Total lung capacity (TLC), Nitrogen breath wash-out, Carbon monoxide single breath wash-out, Closing volume (CV), Vital capacity (VC), Closing volume in percent of VC (CV%)
Asbestos Fiber Type(s):	Asbestos- Exposure reported as PCM or TEM (including conversion factors for dust)
Linked HERO ID(s):	No linked references.
HERO ID:	2248426

Domain	Metric	Rating	Comments
	Metric 15: Statistical Analysis	Low	The authors report appropriate models, correlations, and variable transformations. However, the analyses did not incorporate any methods aiming to reduce potential risk of "healthy worker effect" bias, which can be induced by "the selection of unhealthy people out of the workforce" (PMID: 17053019). The exposed population was restricted to persons sufficiently healthy to remain actively employed as mechanics after >15y, without comparable criteria for the unexposed group. Criteria such as the use of prevalent (but not past or incident) employees is a well-known risk for healthy worker effect. Strategies such as adjusting for employment status and duration could have helped to reduce risk of bias by comparing lung function among subgroups with comparably shorter- or longer-term employment durations – this was not done. Of note, "epidemiological studies of... non-fatal outcomes… are especially prone to bias through aspects of the healthy worker effect. The tendencies for sick workers to leave employment or transfer to less-exposed jobs are two very commonly observed phenomena in occupational morbidity studies" (PMID: 17053019).

Additional Comments: This study analyzed lung function among 99 auto mechanics exposed to low levels of asbestos (cumulative exposure 2.3 fiber-years/mL) vs. 89 unexposed white-collar workers and bus drivers with normal lung function. Though asbestos exposure was not associated with several outcomes including FEV1, exposure was associated with lower transfer factor (TLco from a CO washout) and with airway closure (CV% from a N washout), measures described as perhaps more sensitive to early lung function decline. There are, however, several concerns. First, 61% of exposed and 72% of unexposed candidate participants were excluded with few explanatory details. Exclusion of individuals with exposures very common in mechanic workshops (ex. welding or paint fumes) could yield an unrepresentative sample with limited generalizability. Second, limiting the exposed sample to mechanics actively employed for >15y, without comparable requirements that unexposed had similarly lengthy active employment, may have induced a healthy worker bias. Analyses did not adjust for potential confounding by employment status or duration, BMI, or SES. Finally, exposure may have been estimated with error as the thin fibers found in asbestos dust from automobile brakes are not captured by PCM. These issues may have affected validity of findings, potentially attenuating any association between exposure and lung function.

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation:	Dawson, A., Gibbs, A. R., Pooley, F. D., Griffiths, D. M., Hoy, J. (1993). Malignant mesothelioma in women. Thorax 48(3):269-274.
Health Outcome:	fibrosis in mesothelioma cases and controls
Target Organ(s):	Lung/Respiratory: Fibrosis
Asbestos Fiber Type(s):	Asbestos - Chrysotile (serpentine): 12001-29-5; Asbestos - Crocidolite (riebeckite): 12001-28-4; Asbestos - Tremolite: 14567-73-8; Asbestos - Amosite (grunerite): 12172-73-5
Linked HERO ID(s):	No linked references.
HERO ID:	718578

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Medium	Key elements of study design were reported. Participation is not likely biased and exposure-outcome distribution of participants is likely representative of those eligible for inclusion. However, the total number of patients, from which cases with post-mortem evaluations were chosen, with malignant mesothelioma but with no postmortem analyses records was not provided. Authors did acknowledged the potential non-representativeness of this population due to the patient-referred nature of cases which included wartime dockyard and gas mask workers known to have suffered from heavy asbestos exposure. All available pathological, occupational and lung fiber mineralogical data on n=177 female malignant mesothelioma cases from unspecified file records and unspecified geographic residential origin 1963-1990 were reviewed and compared with n=31 female controls from Exeter, Liverpool, Befast, Dublin, and Cardiff with post-mortem examinations and no known history of exposure to dusts and no mesothelioma or lung cancer. Source of data for controls not detailed but assumed to have been from the same files as cases.
	Metric 2:	Attrition	Medium	Missing information was noted for several subsets of outcome and exposure, and authors acknowledged the lack of completeness of exposure data, however it was unclear if this was related to exposure and/or outcome. The total number of participants with tumor tissue slides available (n=151) was a subset of the total number of mesothelioma cases (n=177). Tumor tissue slides were available for n=151 of a total of n=177 cases. Two cases of the total cases tested (n=103 of the n=151 with histologic slides available) were positive for carcinoembryonic antigen and were excluded from further analyses. Lung tissue fiber burden was examined by transmission electron microscopy for n=105 tumors of known sites (Table 2). Exposure classification according to Zielhuis et al., 1978 (HERO ID 6910362) data was available for n= 93 cases.

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Study Citation:	Dawson, A., Gibbs, A. R., Pooley, F. D., Griffiths, D. M., Hoy, J. (1993). Malignant mesothelioma in women. Thorax 48(3):269-274.
Health Outcome:	fibrosis in mesothelioma cases and controls
Target Organ(s):	Lung/Respiratory: Fibrosis
Asbestos Fiber Type(s):	Asbestos - Chrysotile (serpentine): 12001-29-5; Asbestos - Crocidolite (riebeckite): 12001-28-4; Asbestos - Tremolite: 14567-73-8; Asbestos - Amosite (grunerite): 12172-73-5
Linked HERO ID(s):	No linked references.
HERO ID:	718578

Domain	Metric		Rating	Comments
	Metric 3:	Comparison Group	Low	Inclusion criteria and methods of participant selection for cases and controls was reported. Geographic residential origin of controls, but not cases (other than one case from Antolia) was reported. Other than restriction of cases and controls to women and reporting the mean (range) age of n=102 malignant mesothelioma cases (60.5 years (18-89)) and n=31 controls (68.0 years (30-93)) for which age data was available, details regarding other potentially relevant demographic and occupational covariate differences between cases and controls were not considered. Statistical analyses of potential demographic or other relevant covariate differences between cases and controls was lacking, and multivariate statistical control for differences, particularly age, between groups was not detailed. It is unclear to what extent, if any, the healthy worker effect was involved within results including those cases classified within Table 4 as having direct occupational exposure in comparison with the population controls.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Medium	Methods used to quantify exposure were well defined, with sources of methods reported. Lung tissue fiber (106 fibers/g), fiber length and diameter analyses were assessed by Transmission Electron Microscopy (TEM) with energy dispersive x ray analysis using an "EDAX" machine according to the methods within Pooley et al., 1979 (HERO ID: 3084350). Asbestos exposure classification methods for cases only were conducted as in Zielhuis et al., HERO ID 6910362. Exposure to asbestos was classified for n=93 (of total n=177 cases) malignant mesothelioma cases according to Zielhuis18 into categories of (la) direct occupational exposure; (lb) indirect occupational exposure-for example, workers in the vicinity of asbestos contaminated work situations; (2) paraoccupational exposure-for example, the wives of men working with asbestos; (3) neighborhood exposure-for example, people living in the vicinity of asbestos mines or processing factories; (4) exposure in ambient air; and (5) no known exposure. Only n=74 (80% of the total n=93 cases with Zielhuis classified exposure history data of the total n=177 malignant mesothelioma cases) cases had a history of known exposure to asbestos. Zielhuis classification of potential historical exposure for controls was not detailed.
	Metric 5:	Exposure Levels	Medium	The range and distribution of exposure is sufficient to develop and exposure-response estimate. Table 3 reports lung fiber burden (x 10^6 fibers/g lung) across five fibrosis grade categories for n=116 mesothelioma cases.
	Metric 6:	Temporality	Low	The temporality of exposure and outcome is uncertain. This study reported cross-sectional analyses of the relationship between postmortem fibrosis and lung fiber burdens in mesothelioma cases and controls for which temporality cannot be established.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Medium	Other Non-Cancer Outcomes: Fibrosis was assessed and graded for n=152 mesothelioma cases and n=31 controls according to Hinson et al., 1973 (HERO ID 3101627).

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Study Citation:	Dawson, A., Gibbs, A. R., Pooley, F. D., Griffiths, D. M., Hoy, J. (1993). Malignant mesothelioma in women. Thorax 48(3):269-274.
Health Outcome:	fibrosis in mesothelioma cases and controls
Target Organ(s):	Lung/Respiratory: Fibrosis
Asbestos Fiber Type(s):	Asbestos - Chrysotile (serpentine): 12001-29-5; Asbestos - Crocidolite (riebeckite): 12001-28-4; Asbestos - Tremolite: 14567-73-8; Asbestos - Amosite (grunerite): 12172-73-5
Linked HERO ID(s):	No linked references.
HERO ID:	718578

Domain	Metric		Rating	Comments
	Metric 8:	Reporting Bias	Medium	There were no concerns for selective reporting. No formal statistical analyses between cases and controls was conducted, and no effect estimates were reported however lung fiber concentration burdens as geometric means (range) were reported across categories of fibrosis grade in Table 3.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Low	Analyses were restricted to female cases and controls. Additional statistical control for potentially relevant demographic or other variables was not conducted.
	Metric 10:	Covariate Characterization	Low	Source of covariate data (age only) was not directly stated, nor validated, but assumed to have been obtained from the files from which patient data were obtained.
	Metric 11:	Co-exposure Counfounding	Low	The patient population under study included mesothelioma case workers in Table 4 to have had direct and indirect occupational exposure, however potential confounding due to co-exposures was not reported as considered.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	Medium	The study method chosen was appropriate for the cross-sectional data available.
	Metric 13:	Statistical Power	Medium	The number of cases and controls are generally adequate to detect an effect in the overall population, however it is unclear if the number of cases in fibrosis grade subgroups would be adequate. Authors acknowledged the inadequacy of the sample size for analyses of fiber types on outcomes of interest.
	Metric 14:	Reproducibility of Analyses	Medium	The description of analysis is sufficient to understand how to conceptually reproduce the data within the presented tables, although raw data was not reported.
	Metric 15:	Statistical Analysis	N/A	This study did not utilize multivariate statistical modeling methods.

Additional Comments: This study reported cross-sectional results of postmortem fibrosis and lung fiber burdens from an initial total population of n=177 female malignant mesothelioma cases 1963-1990 (geographic origin not detailed) and n=31 female controls from Exeter, Liverpool, Belfast, Dublin, and Cardiff with no initially known exposure history to dusts and no mesothelioma or lung cancer. Mesothelioma cases (n=102 of total n=177) with age data were described as being of mean (range) age 60.5 years (18-89 years) with n=31 controls aged 68 years (30-93 years).

Overall Quality Determination — Low

* No biomarkers were identified for this evaluation.

Study Citation:	de Klerk, N. H., Armstrong, B. K., Musk, A. W., Hobbs, M. S. T. (1989). Cancer mortality in relation to measures of occupational exposure to crocidolite at Wittenoom Gorge in Western Australia. British Journal of Industrial Medicine 46(8):529-536.
Health Outcome:	Lung Cancer; Laryngeal Cancer; stomach cancer
Target Organ(s):	Lung/Respiratory: Mortality from cancer of the trachea, bronchus, and lung, Lung cancer incidence; Cancer/Carcinogenesis: Lung cancer incidence, Upper aerodigestive cancer (lip, tongue, pharynx, larynx), Mortality from cancer of the stomach, Mortality from cancer of the trachea, bronchus, and lung; Gastrointestinal: Lower aerodigestive cancer (oesophagus, stomach, colon/rectum), Upper aerodigestive cancer (lip, tongue, pharynx, larynx) - incidence, Mortality from cancer of the stomach; Mortality: Upper aerodigestive cancer (lip, tongue, pharynx, larynx) - mortality, Mortality from cancer of the trachea, bronchus, and lung, Mortality from cancer of the stomach
Asbestos Fiber Type(s):	Asbestos - Crocidolite (riebeckite): 12001-28-4
Linked HERO ID(s):	783917, 3079799, 3080174
HERO ID:	783917

Domain	Metric		Rating	Comments
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Low	This metric is rated low because Klerk et al. 1989 783917, Reid et al. 2006 3079799, and Reid et al. 2004 3080174 relied on historic dust measures (konimeters, thermal precipitators) without documenting the use of appropriate conversions. These papers cited the single time point membrane filter PCM fiber concentration measures that were taken in 1966, shortly before the facility closed (publication not available in HERO or other online sources, Major 1968 entitled the First Australian Pneumoconiosis Conference). However, they did not mention or cite a dust-to-fiber conversion factor, and no such factors were identified in the literature. Concerns regarding the validity and utility of occupational exposure measures used in Wittenoom studies have been expressed by the industrial hygienist responsible for the membrane filter measures (e.g., Rogers and Major 2002 HEROID 3080506).
	Metric 5:	Exposure Levels	Medium	The distribution of exposure provided in de Klerk et al 783917 appears to be sufficient to develop an exposure-response estimate. Cumulative exposure was used in analyses either as a continuous variable or in 4 categories. As noted above, however, there are important concerns remain regarding the validity of exposure estimates.

Additional Comments: Klerk et al. 1989 783917, Reid et al. 2006 3079799, and Reid et al. 2004 3080174 were not evaluated for any metrics except Metric 4 and 5 and had no data extracted because they did not have sufficient exposure information to be useful for dose-response analysis.

** As described in Appendix B.2 of the *White Paper: Quantitative Approach to the Human Health Assessment for the Risk Evaluation for Asbestos Part 2: Supplemental Evaluation Including Legacy Uses and Associated Disposals of Asbestos*, to be considered as being informative for dose-response analysis, metrics 4 and 5 would need metric ratings of Medium or High. This reference did not satisfy this requirement; therefore data quality evaluation is presented for only for metrics 4 and 5.

Study Citation:	de Klerk, N. H., Cookson, W. O., Musk, A. W., Armstrong, B. K., Glancy, J. J. (1989). Natural history of pleural thickening after exposure to crocidolite. British Journal of Industrial Medicine 46(7):461-467.			
Health Outcome:	Pleural Plaques			
Target Organ(s):	Lung/Respiratory: Diffuse pleural thickening			
Asbestos Fiber Type(s):	Asbestos - Crocidolite (riebeckite): 12001-28-4			
Linked HERO ID(s):	No linked references.			
HERO ID:	3082741			

Domain	Metric		Rating	Comments
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Low	The method of quantifying/counting fibers was not specified by the authors. They only indicated that measurements had been taken "in a survey of the industry undertaken on behalf of the Mines Department of Western Australia in 1966." The cited source is not freely available at this time (Major, 1968, Proceedings of the first Australian Pneumoconiosis Conference).
	Metric 5:	Exposure Levels	Medium	The authors reported four levels of exposure: expressed as "intensity of exposure" in fibers/cc (Table 4). They also reported 5 levels of "cumulative exposure" (Table 5)

Additional Comments: None

* No biomarkers were identified for this evaluation.

** As described in Appendix B.2 of the *White Paper: Quantitative Approach to the Human Health Assessment for the Risk Evaluation for Asbestos Part 2: Supplemental Evaluation Including Legacy Uses and Associated Disposals of Asbestos*, to be considered as being informative for dose-response analysis, metrics 4 and 5 would need metric ratings of Medium or High. This reference did not satisfy this requirement; therefore data quality evaluation is presented for only for metrics 4 and 5.

Study Citation:	de Klerk, N. H., Musk, A. W., Armstrong, B. K., Hobbs, M. S. (1991). Smoking, exposure to crocidolite, and the incidence of lung cancer and asbestosis. British Journal of Industrial Medicine 48(6):412-417.			
Health Outcome:	Lung Cancer; Asbestosis			
Target Organ(s):	Lung/Respiratory: Asbestosis, Lung cancer; Cancer/Carcinogenesis: Lung cancer			
Asbestos Fiber Type(s):	Asbestos - Crocidolite (riebeckite): 12001-28-4			
Linked HERO ID(s):	No linked references.			
HERO ID:	3082378			

Domain	Metric		Rating	Comments
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Low	The authors did not use PCM or TEM to quantify fibers. “A survey of airborne respirable fibres of crocidolite greater than 5um in length was carried out at various work sites at Wittenoom in 1966. These measurements were used to obtain estimates of fibre concentrations for all 87 job categories in the various worksites.” This survey was supplemented by subjective ranking of the degree of dustiness ”provided by an ex-superintendent of operations at Wittenoom, and verified by the industrial hygienist who conducted the 1966 survey.”
	Metric 5:	Exposure Levels	Low	Mean cumulative exposure (f/ml-years) was 71 for cases, and 23 for controls for asbestosis (Table 4), reporting only 2 levels of exposure. Subjects could be controls for more than one case and some cases could be control for other earlier cases (e.g., controls may have been exposed and/or at risk for asbestosis/lung cancer).

Additional Comments: QC was not completed for metrics other than Metrics 4 and 5 because the study does not have sufficient exposure information to be useful for dose-response analysis.Asbestosis was not assessed for all subjects thoroughly (only through death certificates or through reported workers compensation claims). Wittenoom cohort the diagnosis of asbestosis for compensation purposes the of death is or as cause closely related to the degree of crocidolite to exposure but not to smoking habits. Although study mentions 2400 men were included in the cohort, it appears that the cases and controls considered for asbestosis were pulled from a larger cohort (N=2713).

* No biomarkers were identified for this evaluation.

** As described in Appendix B.2 of the *White Paper: Quantitative Approach to the Human Health Assessment for the Risk Evaluation for Asbestos Part 2: Supplemental Evaluation Including Legacy Uses and Associated Disposals of Asbestos*, to be considered as being informative for dose-response analysis, metrics 4 and 5 would need metric ratings of Medium or High. This reference did not satisfy this requirement; therefore data quality evaluation is presented for only for metrics 4 and 5.

Study Citation:	de Klerk, N. H., Musk, A. W., Cookson, W. O., Glancy, J. J., Hobbs, M. S. (1993). Radiographic abnormalities and mortality in subjects with exposure to crocidolite. British Journal of Industrial Medicine 50(10):902-906.
Health Outcome:	Lung Cancer; Stomach cancer, other unspecified cancer; Asbestosis
Target Organ(s):	Lung/Respiratory: Lung cancer mortality, mesothelioma mortality, pneumoconiosis mortality; Cancer/Carcinogenesis: Lung cancer mortality
Asbestos Fiber Type(s):	Asbestos - Crocidolite (riebeckite): 12001-28-4
Linked HERO ID(s):	No linked references.
HERO ID:	3081932

Domain	Metric		Rating	Comments
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Low	Study reports that estimates of crocidolite from Wittenoom Gorge were collected from existing industry records of fibre. The exact tool utilized to measure the asbestos is not mentioned, but methods state that fibers in the air >5mu in length from 1966 were used to create cumulative exposure measures. However, the calculation for cumulative exposure measures was not mentioned.
	Metric 5:	Exposure Levels	Low	The study only reported geometric means of asbestos exposure in terms of cumulative exposure (f/ml-years), intensity (f/ml), and duration (days). There is no range and distribution of exposure.

Additional Comments: For the year of the study and the 5 different case-control analyses conducted, I agree with the rating. There are some discrepancies, such as how the asbestos was measured and exposures to various forms of asbestos which were not regarded.

* No biomarkers were identified for this evaluation.

** As described in Appendix B.2 of the *White Paper: Quantitative Approach to the Human Health Assessment for the Risk Evaluation for Asbestos Part 2: Supplemental Evaluation Including Legacy Uses and Associated Disposals of Asbestos*, to be considered as being informative for dose-response analysis, metrics 4 and 5 would need metric ratings of Medium or High. This reference did not satisfy this requirement; therefore data quality evaluation is presented for only for metrics 4 and 5.

Study Citation:	de Klerk, N. H., Musk, A. W., Cookson, W. O., Glancy, J. J., Hobbs, M. S. (1993). Radiographic abnormalities and mortality in subjects with exposure to crocidolite. British Journal of Industrial Medicine 50(10):902-906.
Health Outcome:	Pneumoconiosis, asbestosis, and all other causes
Target Organ(s):	Other causes: Classified as all other causes of death (excluding malignant mesothelioma, lung cancer, stomach cancer, other cancer, and pneumoconiosis)
Asbestos Fiber Type(s):	Asbestos - Crocidolite (riebeckite): 12001-28-4
Linked HERO ID(s):	No linked references.
HERO ID:	3081932

Domain	Metric		Rating	Comments
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Low	Study reports that estimates of crocidolite from Wittenoom Gorge were collected from existing industry records of fibre. The exact tool utilized to measure the asbestos is not mentioned, but methods state that fibers in the air >5mu in length from 1966 were used to create cumulative exposure measures. However, the calculation for cumulative exposure measures was not mentioned.
	Metric 5:	Exposure Levels	Low	The study only reported geometric means of asbestos exposure in terms of cumulative exposure (f/ml-years), intensity (f/ml), and duration (days). There is no range and distribution of exposure.

Additional Comments: For the year of the study and the 5 different case-control analyses conducted, I agree with the rating. There are some discrepancies, such as how the asbestos was measured and exposures to various forms of asbestos which were not regarded.

* No biomarkers were identified for this evaluation.

** As described in Appendix B.2 of the *White Paper: Quantitative Approach to the Human Health Assessment for the Risk Evaluation for Asbestos Part 2: Supplemental Evaluation Including Legacy Uses and Associated Disposals of Asbestos*, to be considered as being informative for dose-response analysis, metrics 4 and 5 would need metric ratings of Medium or High. This reference did not satisfy this requirement; therefore data quality evaluation is presented for only for metrics 4 and 5.

Study Citation:	de Klerk, N. H., Musk, A. W., Eccles, J. L., Hansen, J., Hobbs, M. S. (1996). Exposure to crocidolite and the incidence of different histological types of lung cancer. Occupational and Environmental Medicine 53(3):157-159.
Health Outcome:	Lung Cancer
Target Organ(s):	Cancer/Carcinogenesis: Squamous cell carcinoma, Adenocarcinoma, Undifferentiated large cell cancer, Small cell cancer, All lung cancer; Lung/Respiratory: Squamous cell carcinoma, Adenocarcinoma, Undifferentiated large cell cancer, Small cell cancer, All lung cancer
Asbestos Fiber Type(s):	Asbestos - Crocidolite (riebeckite): 12001-28-4
Linked HERO ID(s):	No linked references.
HERO ID:	3081494

Domain	Metric		Rating	Comments
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Low	Authors do not describe how exposure was measured. Instead, measurements from a different study were referenced for this paper (Armstrong, et al., 1988). The introduction states that the median duration of employment (four months) and medium cumulative exposure (six f/mL-y). They authors do not explain how the research in Armstrong et al., 1988 measured this exposure.
	Metric 5:	Exposure Levels	Medium	The provided values from Armstrong, et al., 1988 seem sufficient to the analysis in this paper. Duration since exposure to crocidolite is distributed by years:0-20 y, 21-25 y,26-30 y, and >31 y

Additional Comments:	Overall, this study did a good job in adjusting for smoking and providing various types of lung cancer following past exposure to crocidolite. The study has some inconsistencies in how exposure was measured, only referencing a past study. Additionally, women were excluded from this study when included in the original survey, and authors do not explain why.Overall, information on the measurement of exposure metric (M4) to assess exposure was limited. However, the exposure levels metric (M5) information reported was adequate to determine exposure-response relationships. The overall quality determination (OQD) for this study is rated medium.

* No biomarkers were identified for this evaluation.

** As described in Appendix B.2 of the *White Paper: Quantitative Approach to the Human Health Assessment for the Risk Evaluation for Asbestos Part 2: Supplemental Evaluation Including Legacy Uses and Associated Disposals of Asbestos*, to be considered as being informative for dose-response analysis, metrics 4 and 5 would need metric ratings of Medium or High. This reference did not satisfy this requirement; therefore data quality evaluation is presented for only for metrics 4 and 5.

Study Citation:	Dement, J. M. (1980). Estimation of dose and evaluation of dose-response in a retrospective cohort mortality study of chrysotile asbestos textile workers. Doctoral Dissertation:1-259.
Health Outcome:	Lung Cancer; Digestive system cancer; All cause mortality, diseases of the circulatory system mortality, other nonmalignant respiratory diseases mortality
Target Organ(s):	Mortality: All cause mortality, Diseases of the circulatory system mortality, Nonmalignant respiratory diseases (NMRD) mortality, Lung cancer mortality, Digestive system cancer mortality; Lung/Respiratory: Nonmalignant respiratory disease (NMRD) mortality, Lung cancer mortality; Cardiovascular: Diseases of the circulatory system mortality; Cancer/Carcinogenesis: Lung cancer mortality, Digestive system cancer mortality; Gastrointestinal: Digestive system cancer mortality
Asbestos Fiber Type(s):	Asbestos - Chrysotile (serpentine): 12001-29-5
Linked HERO ID(s):	No linked references.
HERO ID:	6884448

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Medium	A retrospective cohort design was used for this study. Inclusion in the cohort was limited to the male employees who had worked in the asbestos plant for 6 months or more, and at least one month of that must have taken place between January 1, 1940 and December 31, 1965. It is important to note that the 1965 deadline was used to provide a latency of 10 years for participants. The authors reported that a total of 768 white males and 372 black males were included in the final cohort, however only white males were used for the dose-response analysis. Some individuals were excluded for various reasons including: lacking sufficient demographic data (8 individuals), and two individuals were identified as war deaths, and were thus removed from the analysis once their employment was terminated. The eight individuals excluded for a lack of demographic information were not believed to introduce bias because they ”demonstrated no unusual characteristics such as employment in specific departments or jobs or a racial composition different from the remainder of the cohort.” A United States Public Health Service study was conducted at the plant in 1968, and all employee records were microfilmed. These records contained detailed information on demographic data, the employment history, which was coded based on the job functions performed. This coding scheme helped with determining fiber exposures. While some details are presented pertaining to participant selection, information about participation rates at the various steps would be beneficial.
	Metric 2:	Attrition	High	Of the 768 white males originally identified for this cohort. all of them were included in final analyses. Several participants had an unknown vital status as of December 31, 1975 (n=22) - however, for those participants it was assumed that they were still alive to ensure that they could still be used for analysis.

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Study Citation:	Dement, J. M. (1980). Estimation of dose and evaluation of dose-response in a retrospective cohort mortality study of chrysotile asbestos textile workers. Doctoral Dissertation:1-259.
Health Outcome:	Lung Cancer; Digestive system cancer; All cause mortality, diseases of the circulatory system mortality, other nonmalignant respiratory diseases mortality
Target Organ(s):	Mortality: All cause mortality, Diseases of the circulatory system mortality, Nonmalignant respiratory diseases (NMRD) mortality, Lung cancer mortality, Digestive system cancer mortality; Lung/Respiratory: Nonmalignant respiratory disease (NMRD) mortality, Lung cancer mortality; Cardiovascular: Diseases of the circulatory system mortality; Cancer/Carcinogenesis: Lung cancer mortality, Digestive system cancer mortality; Gastrointestinal: Digestive system cancer mortality
Asbestos Fiber Type(s):	Asbestos - Chrysotile (serpentine): 12001-29-5
Linked HERO ID(s):	No linked references.
HERO ID:	6884448

Domain	Metric		Rating	Comments
	Metric 3:	Comparison Group	Medium	For the standardized mortality ratio analysis conducted in this study, the expected number of deaths were determined using ”cause-specific death rates for the total United States to the person-years at risk of dying.” The authors specify that the number of expected deaths were standardized for sex, age, race, and calendar time. The period of follow-up for this study incorporated a time period when the Fifth through Eighth Revisions of the International Lists of Diseases and Causes of Death were being used. ”Death rates specific to the 89 Seventh Revision death groups were calculated form yearly tallies of deaths and census data.” U.S. deaths from 1940-1975 were obtained from the ”Vital Statistics of the United States,” which was published yearly. The author mentioned that they considered determining the expected death rates from counties surrounding the county in which the plant was located. However, this was rejected because a shipyard industry was present, which has been associated with potential asbestos exposure. This was compounded by the potential increase in lung cancer and other health outcomes resulting from asbestos plant workers, especially from the time when records were not as well-maintained. It was also mentioned that the smoking rates among white cohort members was nearly identical to the U.S. population. There is some potential concern for healthy worker bias due to the comparison of an occupational population to the general population, but this is not expected to have a substantial impact on the results of the study.
Domain 2: Exposure Characterization				

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Study Citation:	Dement, J. M. (1980). Estimation of dose and evaluation of dose-response in a retrospective cohort mortality study of chrysotile asbestos textile workers. Doctoral Dissertation:1-259.		
Health Outcome:	Lung Cancer; Digestive system cancer; All cause mortality, diseases of the circulatory system mortality, other nonmalignant respiratory diseases mortality		
Target Organ(s):	Mortality: All cause mortality, Diseases of the circulatory system mortality, Nonmalignant respiratory diseases (NMRD) mortality, Lung cancer mortality, Digestive system cancer mortality; Lung/Respiratory: Nonmalignant respiratory disease (NMRD) mortality, Lung cancer mortality; Cardiovascular: Diseases of the circulatory system mortality; Cancer/Carcinogenesis: Lung cancer mortality, Digestive system cancer mortality; Gastrointestinal: Digestive system cancer mortality		
Asbestos Fiber Type(s):	Asbestos - Chrysotile (serpentine): 12001-29-5		
Linked HERO ID(s):	No linked references.		
HERO ID:	6884448		

Domain	Metric		Rating	Comments
	Metric 4:	Measurement of Exposure	High	Due to the number of years that this plant was operational, there was a plethora of exposure data available from a number of sources, including the company's insurance carrier, the State Board of Health, the U.S. Public Health Service, and a sampling program that was run by the company itself. It is noted that "prior to 1965 all samples were of the impinger type; from 1965 until 1971 membrane filter samples were also taken. In 1971, the impinger method was abandoned and the membrane filter method used exclusively." Impinger samples were reported to be collected at the worker's "breathing level" and "operators were followed when there was considerable movement." Membrane filter samples were collected via battery operated pumps worn by the workers being sampled. When the midget impinger methods were utilized, a bright field optical microscope was used to count the asbestos particles, at a magnification of 100x. All concentrations calculated using this method were reported in millions of particles per cubic foot of air (MPPCF). When using the membrane filter method, phase contrast optical microscopy was used, at a magnification of 400-450x. Paired sample analysis was used to compare the impinger data to the membrane filter data, resulting in a conversion ratio of 3.0 generally and 8.0 for all activities related to fiber preparation, for final measurements presented in fibers/cc. Cumulative fiber exposure for individual workers was calculated by using detailed work histories and location-specific and job-specific estimates of fiber exposure.
	Metric 5:	Exposure Levels	Medium	The authors report 4 levels of exposure in their SMR analysis to evaluate dose-response relationships. Estimates of exposure are reported in fiber/cc days. The lowest comparator group represents exposures less than $<$10,000 fiber/cc days, while the highest comparator group represents exposures between 100,000-200,000 fiber/cc days.
	Metric 6:	Temporality	Medium	The author mentions that the cutoff for follow-up, in 1965, was selected to allow for a minimum latency of 10 years. The metric was rated as medium because of this indication from the author, although there were some individuals enrolled who had a longer latency period, including intervals of 10-19, 20-29, and greater than or equal to 30. However, summary statistics regarding latency are not provided, preventing a determination of the average latency for the cohort.
Domain 3: Outcome Assessment				

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Study Citation:	Dement, J. M. (1980). Estimation of dose and evaluation of dose-response in a retrospective cohort mortality study of chrysotile asbestos textile workers. Doctoral Dissertation:1-259.
Health Outcome:	Lung Cancer; Digestive system cancer; All cause mortality, diseases of the circulatory system mortality, other nonmalignant respiratory diseases mortality
Target Organ(s):	Mortality: All cause mortality, Diseases of the circulatory system mortality, Nonmalignant respiratory diseases (NMRD) mortality, Lung cancer mortality, Digestive system cancer mortality; Lung/Respiratory: Nonmalignant respiratory disease (NMRD) mortality, Lung cancer mortality; Cardiovascular: Diseases of the circulatory system mortality; Cancer/Carcinogenesis: Lung cancer mortality, Digestive system cancer mortality; Gastrointestinal: Digestive system cancer mortality
Asbestos Fiber Type(s):	Asbestos - Chrysotile (serpentine): 12001-29-5
Linked HERO ID(s):	No linked references.
HERO ID:	6884448

Domain	Metric		Rating	Comments
	Metric 7:	Outcome Measurement or Characterization	High	Lung Cancer: The authors examined death certificates to determine cause-specific mortality. Requests for these certificates were submitted through the state vital statistics offices. Also, ”the entire death index (1935-1979) for the state in which the plant was located was searched in an attempt to locate certificates missed by searches conducted by state personnel.” The follow-up period for this study incorporated a few different versions of the International Lists of Diseases and Causes of Death, including the Fifth through Eighth Revisions. A nosologist coded all of the death certificates according to the ICDA revision that was being used at the time of the participants death. and were then grouped into ”89 death categories based on the Seventh Revision for purposes of standardization.” This was reported as ICDA 7th codes 162 and 163 for lung cancer.; Other Cancer(s): (Digestive System Cancer) The authors examined death certificates to determine cause-specific mortality. Requests for these certificates were submitted through the state vital statistics offices. Also, ”the entire death index (1935-1979) for the state in which the plant was located was searched in an attempt to locate certificates missed by searches conducted by state personnel.” The follow-up period for this study incorporated a few different versions of the International Lists of Diseases and Causes of Death, including the Fifth through Eighth Revisions. A nosologist coded all of the death certificates according to the ICDA revision that was being used at the time of the participants death. and were then grouped into ”89 death categories based on the Seventh Revision for purposes of standardization.” This was reported as ICDA 7th codes 150-159 for digestive system cancer.; Other Non-Cancer Outcomes: (All-cause mortality; Diseases of the Circulatory System, Other Nonmalignant Respiratory Diseases) The authors examined death certificates to determine cause-specific mortality. Requests for these certificates were submitted through the state vital statistics offices. Also, ”the entire death index (1935-1979) for the state in which the plant was located was searched in an attempt to locate certificates missed by searches conducted by state personnel.” The follow-up period for this study incorporated a few different versions of the International Lists of Diseases and Causes of Death, including the Fifth through Eighth Revisions. A nosologist coded all of the death certificates according to the ICDA revision that was being used at the time of the participants death. and were then grouped into ”89 death categories based on the Seventh Revision for purposes of standardization.” This was reported as ICDA 7th codes 400-468 for diseases of the circulatory system and 510-527 for other nonmalignant respiratory diseases.

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Study Citation: Dement, J. M. (1980). Estimation of dose and evaluation of dose-response in a retrospective cohort mortality study of chrysotile asbestos textile workers. Doctoral Dissertation:1-259.

Health Outcome: Lung Cancer; Digestive system cancer; All cause mortality, diseases of the circulatory system mortality, other nonmalignant respiratory diseases mortality

Target Organ(s): Mortality: All cause mortality, Diseases of the circulatory system mortality, Nonmalignant respiratory diseases (NMRD) mortality, Lung cancer mortality, Digestive system cancer mortality; Lung/Respiratory: Nonmalignant respiratory disease (NMRD) mortality, Lung cancer mortality; Cardiovascular: Diseases of the circulatory system mortality; Cancer/Carcinogenesis: Lung cancer mortality, Digestive system cancer mortality; Gastrointestinal: Digestive system cancer mortality

Asbestos Fiber Type(s): Asbestos - Chrysotile (serpentine): 12001-29-5

Linked HERO ID(s): No linked references.

HERO ID: 6884448

Domain	Metric		Rating	Comments
	Metric 8:	Reporting Bias	Medium	SMRs are reported with both observed numbers of deaths and expected numbers of deaths, along with indicators of statistical significance. Some outcomes are used in an analysis of binary exposure (exposed vs. unexposed) but are then not used in dose-response analysis. It is not explained why they were not analyzed for dose-response data. SMRs for lung cancer and other nonmalignant respiratory diseases were also plotted via least squares based on the Poisson distribution, and 95% confidence intervals are presented, although the exact effect estimates from that analysis are only presented graphically with no reporting of regression coefficients.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Medium	Age, race, sex, and calendar time period were adjusted for via the calculation of standardized mortality rates based on those criteria.
	Metric 10:	Covariate Characterization	Medium	The author did not discuss the tools used to assess potential confounders among study participants. However, because this was an occupational study, it can be assumed that personnel records were used to obtain covariate data. Comparison population covariates (via standardized mortality rates) were pulled from "Vital Statistics of the United States."
	Metric 11:	Co-exposure Counfounding	Medium	The author details in Chapter 2 that over the years of operation, various expansions took place to allow for the production of rubber goods. It is important to note that many of the asbestos textile productions took place in specific buildings. While this might have presented a situation in which individuals were exposed to asbestos and various materials involved in the creation of rubber products, this does not appear to be the case. It was reported that "a departmental seniority system limited employee transfer between rubber and textile departments." The separation of production facilities on the plant grounds seems to be useful in limited potential exposures to substances other than asbestos.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	Medium	The retrospective cohort design implemented by the author was appropriate for the research question being examined. The calculation of SMRs is an appropriate method for assessing the potential association between asbestos exposure and general or cause-specific mortality.
	Metric 13:	Statistical Power	Medium	While there was no explicit discussion of the power for their calculations, the number of participants analyzed (n=768) is adequate to detect an effect in the exposed population.

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Study Citation: Dement, J. M. (1980). Estimation of dose and evaluation of dose-response in a retrospective cohort mortality study of chrysotile asbestos textile workers. Doctoral Dissertation:1-259.

Health Outcome: Lung Cancer; Digestive system cancer; All cause mortality, diseases of the circulatory system mortality, other nonmalignant respiratory diseases mortality

Target Organ(s): Mortality: All cause mortality, Diseases of the circulatory system mortality, Nonmalignant respiratory diseases (NMRD) mortality, Lung cancer mortality, Digestive system cancer mortality; Lung/Respiratory: Nonmalignant respiratory disease (NMRD) mortality, Lung cancer mortality; Cardiovascular: Diseases of the circulatory system mortality; Cancer/Carcinogenesis: Lung cancer mortality, Digestive system cancer mortality; Gastrointestinal: Digestive system cancer mortality

Asbestos Fiber Type(s): Asbestos - Chrysotile (serpentine): 12001-29-5

Linked HERO ID(s): No linked references.

HERO ID: 6884448

Domain	Metric		Rating	Comments
	Metric 14:	Reproducibility of Analyses	Medium	The authors clearly describe their methods; thus, it would be possible to recreate their findings if given access to the analytic data.
	Metric 15:	Statistical Analysis	Medium	The method the authors report for the calculation of SMRs is transparent and well-documented. There are less details provided for their use of a Poisson distribution and they do not describe model assumptions, but it is reasonable to assume that model assumptions were met.

Additional Comments: It is important to note that this study is a dissertation. The author provides extensive detail pertaining to the history of the plant, along with information about engineering controls and how exposure data was collected over the years. Section 5 and 6 are the most relevant, discussing the mortality study and dose-response analysis, respectively. There were some limitations noted for this study, including the information pertaining to participant selection. Information about participation rates and a total number of employees would have been beneficial. This study also had some strengths, including the author's discussion about limiting potential co-exposures from the rubber production at the plant, as well as their explanation about using broader U.S. death rates as a comparison for SMR analysis because of characteristics of the surrounding counties. The separate mortality and dose-response analyses were a benefit of this study, as the author is able to report results for various relationships between asbestos exposure and health outcomes.

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation:	Dement, J. M. (1980). Estimation of dose and evaluation of dose-response in a retrospective cohort mortality study of chrysotile asbestos textile workers. Doctoral Dissertation:1-259.
Health Outcome:	all cancers except lung and digestive; all non-cancer outcomes
Target Organ(s):	Mortality: All cause mortality, Diseases of the circulatory system mortality, Diseases of the central nervous system mortality, Tuberculosis mortality, Nonmalignant respiratory diseases (NMRD) mortality, Acute upper respiratory infection mortality, Influenza mortality, Pneumonia mortality, Bronchitis mortality, Other respiratory diseases mortality, All other known causes mortality, All malignant neoplasms mortality, Trachea, bronchus & lung neoplasms mortality, Other and unspecified sites neoplasms mortality, Digestive system neoplasms mortality; Lung/Respiratory: Nonmalignant respiratory disease (NMRD) mortality, Acute upper respiratory infection mortality, Influenza mortality, Pneumonia mortality, Bronchitis mortality, Other respiratory diseases mortality, Tuberculosis mortality, Trachea, bronchus & lung neoplasms mortality; Neurological/Behavioral: Diseases of the central nervous system mortality; Cardiovascular: Diseases of the circulatory system mortality; Cancer/Carcinogenesis: All malignant neoplasms mortality, Digestive system neoplasms mortality, Trachea, bronchus & lung neoplasms mortality, Other and unspecified sites neoplasms mortality; Gastrointestinal: Digestive system neoplasms mortality
Asbestos Fiber Type(s):	Asbestos - Chrysotile (serpentine): 12001-29-5
Linked HERO ID(s):	No linked references.
HERO ID:	6884448

Domain	Metric		Rating	Comments
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	High	Due to the number of years that this plant was operational, there was a plethora of exposure data available from a number of sources, including the company's insurance carrier, the State Board of Health, the U.S. Public Health Service, and a sampling program that was run by the company itself. It is noted that "prior to 1965 all samples were of the impinger type; from 1965 until 1971 membrane filter samples were also taken. In 1971, the impinger method was abandoned and the membrane filter method used exclusively." Impinger samples were reported to be collected at the worker's "breathing level" and "operators were followed when there was considerable movement." Membrane filter samples were collected via battery operated pumps worn by the workers being sampled. When the midget impinger methods were utilized, a bright field optical microscope was used to count the asbestos particles, at a magnification of 100x. All concentrations calculated using this method were reported in millions of particles per cubic foot of air (MPPCF). When using the membrane filter method, phase contrast optical microscopy was used, at a magnification of 400-450x. Paired sample analysis was used to compare the impinger data to the membrane filter data, resulting in a conversion ratio of 3.0 generally and 8.0 for all activities related to fiber preparation, for final measurements presented in fibers/cc. Cumulative fiber exposure for individual workers was calculated by using detailed work histories and location-specific and job-specific estimates of fiber exposure.
	Metric 5:	Exposure Levels	Low	All outcomes inventoried in this form are evaluated using an exposed vs. unexposed exposure comparison.

Additional Comments: The outcome data represented here is not suitable for dose-response assessment due to a low rating for Metric 5

** As described in Appendix B.2 of the *White Paper: Quantitative Approach to the Human Health Assessment for the Risk Evaluation for Asbestos Part 2: Supplemental Evaluation Including Legacy Uses and Associated Disposals of Asbestos*, to be considered as being informative for dose-response analysis, metrics 4 and 5 would need metric ratings of Medium or High. This reference did not satisfy this requirement; therefore data quality evaluation is presented for only for metrics 4 and 5.

Study Citation:	Dement, J. M., Harris, R. L., Jr, Symons, M. J., Shy, C. M. (1983). Exposures and mortality among chrysotile asbestos workers: Part II: Mortality. American Journal of Industrial Medicine 4(3):421-433.
Health Outcome:	Asbestosis; Mortality from non-malignant respiratory disease, mortality from circulatory system disease
Target Organ(s):	Lung/Respiratory: Asbestosis or pulmonary fibrosis as underlying causes of mortality, Non-malignant respiratory disease mortality (non-infectious); Mortality: All-cause mortality, Non-malignant respiratory disease mortality (non-infectious), Asbestosis or pulmonary fibrosis as underlying causes of mortality, Circulatory system mortality; Cardiovascular: Circulatory system mortality
Asbestos Fiber Type(s):	Asbestos - Chrysotile (serpentine): 12001-29-5
Linked HERO ID(s):	No linked references.
HERO ID:	67

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	High	The cohort comprised 1,261 white males employed $\geq$1 month at a chrysotile asbestos textile factory in South Carolina between 1940 an 1965, with vital status ascertained through December 1975. Personnel records were maintained starting in 1930 – 10 years prior to this study – with similar information collected since that time. Selection bias should be limited since the study included a diverse sample of workers with both long and very short employment duration and varying dates of initial employment.
	Metric 2:	Attrition	High	The cohort included all records that met eligibility criteria. Vital status was ascertained for all but 26 (2.1%) members of the cohort.
	Metric 3:	Comparison Group	High	SMRs were calculated using the total US white male population to define the number of expected overall and cause-specific deaths. "The number of expected deaths, standardized for sex, age, race and calendar time, were calculated by application of cause-specific death rates for the total United States to the person-years at risk of dying. Death rates specific to the 89... death groups were calculated from yearly tallies of deaths and census data." The US population referent was used because of very high mortality rates in the county where the plant was located (75% higher than US white males), making the general population a more suitable referent. The high rate may be due in part to a large shipyard industry in the county (potential source of asbestos exposure). Mortality was also elevated in neighboring counties.
Domain 2: Exposure Characterization				

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Study Citation:	Dement, J. M., Harris, R. L., Jr, Symons, M. J., Shy, C. M. (1983). Exposures and mortality among chrysotile asbestos workers: Part II: Mortality. American Journal of Industrial Medicine 4(3):421-433.
Health Outcome:	Asbestosis; Mortality from non-malignant respiratory disease, mortality from circulatory system disease
Target Organ(s):	Lung/Respiratory: Asbestosis or pulmonary fibrosis as underlying causes of mortality, Non-malignant respiratory disease mortality (non-infectious); Mortality: All-cause mortality, Non-malignant respiratory disease mortality (non-infectious), Asbestosis or pulmonary fibrosis as underlying causes of mortality, Circulatory system mortality; Cardiovascular: Circulatory system mortality
Asbestos Fiber Type(s):	Asbestos - Chrysotile (serpentine): 12001-29-5
Linked HERO ID(s):	No linked references.
HERO ID:	67

Domain	Metric		Rating	Comments
	Metric 4:	Measurement of Exposure	Medium	Cumulative exposure estimates used detailed work histories and air sampling data; time exposed in each job and fiber conversions may be over-estimates as detailed below. Individual exposure was obtained by summing the product of average concentrations for each job at that time by the duration spent in that job. Time worked in each job/exposure zone was estimated in days based on the difference in dates of job changes. This method did not eliminate weekends and holidays, and did not account for overtime, both of which introduced some measurement error. Estimated fiber concentrations, expressed as fibers > 5 μm per cubic center (i.e., milliliter), were derived using a total of 5,952 dust samples collected between 1930 and 1975 by the company, insurance carrier, state health board and US public health service. Samples were collected by impinger prior to 1965, by impinger and membrane filter from 1965-1971, and from 1971 onward by membrane filter. Pre-1930 exposures were assigned the values measured prior to implementation of controls. Conversion of dust measures to estimated fiber concentrations using concurrent impinger - membrane filter samples (120 in 1965 from the US Public Health service, 968 from plant operations in 1968-71). No significant differences in conversions were detected by calendar time or plant operation: mean conversions were 7.8 fibers/cc per MPPCF for fiber preparation, and 2.5 fibers per MPPCF for other operations. However, this study used conversion factors of 8 for fiber preparation and 3 for other operations, described as "conservatively high conversion values".
	Metric 5:	Exposure Levels	Medium	Several analyses (overall and cause-specific SMRs, incidence density for respiratory outcomes) used 5 categories of cumulative exposure in fibers/cc-days (<1,000; 1,000-10,000; 10,000-40,000; 40,000-100,000; and >100,000). In addition, some analyses were stratified by exposure characterized using 4 categories of either years since initial employment (<10, 10-19, 20-29, ≥30 years) or total years employed (same categories).
	Metric 6:	Temporality	High	The maximum follow up was >35 years (1940 to 1975, some employed prior to 1940), and the minimum 10 years (1965-1975). With a total of 33,141 person years at risk among 1,261 members, the mean follow-up was likely about 26 years. Additionally, analyses of dose-response rates for respiratory outcomes were limited to men with 15 or more years latency.
Domain 3: Outcome Assessment				

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Study Citation:	Dement, J. M., Harris, R. L., Jr, Symons, M. J., Shy, C. M. (1983). Exposures and mortality among chrysotile asbestos workers: Part II: Mortality. American Journal of Industrial Medicine 4(3):421-433.
Health Outcome:	Asbestosis; Mortality from non-malignant respiratory disease, mortality from circulatory system disease
Target Organ(s):	Lung/Respiratory: Asbestosis or pulmonary fibrosis as underlying causes of mortality, Non-malignant respiratory disease mortality (non-infectious); Mortality: All-cause mortality, Non-malignant respiratory disease mortality (non-infectious), Asbestosis or pulmonary fibrosis as underlying causes of mortality, Circulatory system mortality; Cardiovascular: Circulatory system mortality
Asbestos Fiber Type(s):	Asbestos - Chrysotile (serpentine): 12001-29-5
Linked HERO ID(s):	No linked references.
HERO ID:	67

Domain	Metric		Rating	Comments
	Metric 7:	Outcome Measurement or Characterization	Medium	Asbestosis: Death certificates were coded by a qualified nosologist, using ICD 7 codes 510-527 (523 and 527 are pneumoconioses) to identify non-infectious non-malignant respiratory disease, which included asbestosis/pulmonary fibrosis (combined) as underlying causes of disease (including among cardiovascular deaths). Overall, asbestosis or pulmonary fibrosis were specified as the cause in 17 of 24 cases of non-infectious, non-malignant respiratory disease. All of these cases had 15 or more years of latency since first exposure. It was not feasible in this study design to obtain other information (e.g., medical records) to confirm diagnoses reported on death certificates. Combining asbestosis and pulmonary fibrosis limits specificity. However, asbestosis may have been under-diagnosed/classified as pulmonary fibrosis.; Other Non-Cancer Outcomes: The outcomes evaluated included all-cause mortality, mortality from other (non-infectious) non-malignant respiratory disease (ONMRD), and circulatory system mortality, and lung cancer mortality. The 24 deaths from other non-malignant respiratory disease (ONMRD) included asbestosis. Asbestosis or pulmonary fibrosis were underlying causes of 17 of these deaths (6 identified by examining contributory causes for the 105 individuals with cardiovascular mortality). Vital status through 1975 was ascertained for all but 26 (2.1%) of the 1,261 cohort members. Multiple sources were used, including the Social Security Administration (SSA), IRS, USPS, drivers' license records, and state vital statistics offices, along with telephone listings, property, and voter records, among others. Of 308 deaths, all but 17 death certificates were obtained. Death certificates (which spanned ICD versions 5 to 8) were coded in 89 categories by a nosologist and standardized using ICD 7 codes. Cause unknown was assigned for the 17 known deaths for which no certificate was available.
	Metric 8:	Reporting Bias	Medium	Numbers of expected and observed deaths were presented for all SMR analyses. However, SMRs did not include confidence intervals. Confidence intervals and the person-years at risk denominator were reported for the incidence density of respiratory outcomes, which was reported by cumulative exposure category. The authors did not report the methods used for statistical significance testing.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Medium	SMRs accounted for age, sex, race, and calendar period. Smoking data was only available for cohort members who completed a respiratory symptom questionnaire in 1964 and 1971 as part of a public health service study. However, the authors illustrated that available estimates for current, past, and non-smoking for the cohort were extremely similar to those for US white males in 1965. Incidence density analyses did not report covariate adjustments. However, the study was limited to white males and incidence density accounts for person-time.

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Study Citation: Dement, J. M., Harris, R. L., Jr, Symons, M. J., Shy, C. M. (1983). Exposures and mortality among chrysotile asbestos workers: Part II: Mortality. American Journal of Industrial Medicine 4(3):421-433.

Health Outcome: Asbestosis; Mortality from non-malignant respiratory disease, mortality from circulatory system disease

Target Organ(s): Lung/Respiratory: Asbestosis or pulmonary fibrosis as underlying causes of mortality, Non-malignant respiratory disease mortality (non-infectious); Mortality: All-cause mortality, Non-malignant respiratory disease mortality (non-infectious), Asbestosis or pulmonary fibrosis as underlying causes of mortality, Circulatory system mortality; Cardiovascular: Circulatory system mortality

Asbestos Fiber Type(s): Asbestos - Chrysotile (serpentine): 12001-29-5

Linked HERO ID(s): No linked references.

HERO ID: 67

Domain	Metric		Rating	Comments
	Metric 10:	Covariate Characterization	Medium	Data came primarily from personnel records and death certificates.
	Metric 11:	Co-exposure Counfounding	Medium	Co-exposures (e.g., from earlier or subsequent work) were not taken into account. Silica or other occupational exposures may have contributed to risk of deaths coded pulmonary fibroses. However, there is no direct evidence that co-exposures might have confounded the findings.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	Medium	Methods were appropriate. SMRs were calculated using a life-table method (reference is cited) and Poisson regression was used to estimate incidence density.
	Metric 13:	Statistical Power	Medium	There were 308 deaths overall, including 24 from other non-malignant respiratory diseases (22 with 15+ years latency). Of the 22, 17 deaths had codes for asbestosis and pulmonary fibrosis as primary or underlying causes of death. Sparse numbers are not unusual for outcomes such as asbestosis.
	Metric 14:	Reproducibility of Analyses	Medium	The analyses presented should be readily reproducible as analyses were described and cell sizes presented in adequate detail.
	Metric 15:	Statistical Analysis	Medium	The authors explained their rationale and methods in sufficient detail and methods were appropriate. For SMRs, few confounders besides smoking are typically considered.

Additional Comments: This study analyzed mortality in a cohort of 1,261 white males employed ≥1 month at a chrysotile asbestos textile factory in South Carolina between 1940 and 1965, followed through 1975. Vital status (98%) and cause of death (94%) ascertainment were nearly complete. Use of a dynamic cohort of individuals employed at any time during a 25-year period reduced the likelihood of healthy worker survivor bias. Exposure was estimated using historical air samples, applying dust-to-fiber conversion estimates for early years; methods may have over-estimated exposure. Based on person-years among participants with >15 years of follow-up and converting cumulative exposure-days to years (÷365), about 61% of the cohort had exposures >27.4 fiber/mL-years [10,000 fiber/cc-days]; 7% had exposures >109.6 fiber/mL-years [40,000 fiber/cc-years]. SMRs for non-malignant respiratory disease (excluding infectious) increased from 362 to 2500 over 5 categories of increasing cumulative exposure. Incidence density for asbestos or pulmonary fibrosis mortality also increased from 0.32/1000 person years to 15.98/1000 person-years with increasing exposure. SMRs were also stratified by years employed and years since initial employment categories. SMRs for lung cancer increased from 140 to 1818 over 5 categories of increasing cumulative exposure. Limitations include that asbestosis and pulmonary fibrosis were combined; it is not possible to ascertain if some cases might be fibroses attributable to other occupational exposures. Although smoking adjustments were not possible, limited data suggested that smoking history in the cohort closely resembled the US white male population.

Overall Quality Determination — Medium

* No biomarkers were identified for this evaluation.

Study Citation:	Dement, J. M., Harris, R. L., Jr, Symons, M. J., Shy, C. M. (1983). Exposures and mortality among chrysotile asbestos workers: Part II: Mortality. American Journal of Industrial Medicine 4(3):421-433.
Health Outcome:	Lung Cancer; digestive system cancer
Target Organ(s):	Lung/Respiratory: Lung cancer mortality; Cancer/Carcinogenesis: Lung cancer mortality, Digestive system cancer mortality; Mortality: Lung cancer mortality, Digestive system cancer mortality; Gastrointestinal: Digestive system cancer mortality
Asbestos Fiber Type(s):	Asbestos - Chrysotile (serpentine): 12001-29-5
Linked HERO ID(s):	No linked references.
HERO ID:	67

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	High	The cohort comprised 1,261 white males employed $\geq$1 month at a chrysotile asbestos textile factory in South Carolina between 1940 an 1965, with vital status ascertained through December 1975. Personnel records were maintained starting in 1930 – 10 years prior to this study – with similar information collected since that time. Selection bias should be limited since the study included a diverse sample of workers with both long and very short employment duration and varying dates of initial employment.
	Metric 2:	Attrition	High	The cohort included all records that met eligibility criteria. Vital status was ascertained for all but 26 (2.1%) members of the cohort.
	Metric 3:	Comparison Group	High	SMRs were calculated using the total US white male population to define the number of expected overall and cause-specific deaths. "The number of expected deaths, standardized for sex, age, race and calendar time, were calculated by application of cause-specific death rates for the total United States to the person-years at risk of dying. Death rates specific to the 89... death groups were calculated from yearly tallies of deaths and census data." The US population referent was used because of very high mortality rates in the county where the plant was located (75% higher than US white males), making the general population a more suitable referent. The high rate may be due in part to a large shipyard industry in the county (potential source of asbestos exposure). Mortality was also elevated in neighboring counties.
Domain 2: Exposure Characterization				

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Study Citation:	Dement, J. M., Harris, R. L., Jr, Symons, M. J., Shy, C. M. (1983). Exposures and mortality among chrysotile asbestos workers: Part II: Mortality. American Journal of Industrial Medicine 4(3):421-433.
Health Outcome:	Lung Cancer; digestive system cancer
Target Organ(s):	Lung/Respiratory: Lung cancer mortality; Cancer/Carcinogenesis: Lung cancer mortality, Digestive system cancer mortality; Mortality: Lung cancer mortality, Digestive system cancer mortality; Gastrointestinal: Digestive system cancer mortality
Asbestos Fiber Type(s):	Asbestos - Chrysotile (serpentine): 12001-29-5
Linked HERO ID(s):	No linked references.
HERO ID:	67

Domain	Metric		Rating	Comments
	Metric 4:	Measurement of Exposure	Medium	Cumulative exposure estimates used detailed work histories and air sampling data; time exposed in each job and fiber conversions may be over-estimates as detailed below. Individual exposure was obtained by summing the product of average concentrations for each job at that time by the duration spent in that job. Time worked in each job/exposure zone was estimated in days based on the difference in dates of job changes. This method did not eliminate weekends and holidays, and did not account for overtime, both of which introduced some measurement error. Estimated fiber concentrations, expressed as fibers > 5 μm per cubic center (i.e., milliliter), were derived using a total of 5,952 dust samples collected between 1930 and 1975 by the company, insurance carrier, state health board and US public health service. Samples were collected by impinger prior to 1965, by impinger and membrane filter from 1965-1971, and from 1971 onward by membrane filter. Pre-1930 exposures were assigned the values measured prior to implementation of controls. Conversion of dust measures to estimated fiber concentrations using concurrent impinger - membrane filter samples (120 in 1965 from the US Public Health service, 968 from plant operations in 1968-71). No significant differences in conversions were detected by calendar time or plant operation: mean conversions were 7.8 fibers/cc per MPPCF for fiber preparation, and 2.5 fibers per MPPCF for other operations. However, this study used conversion factors of 8 for fiber preparation and 3 for other operations, described as "conservatively high conversion values".
	Metric 5:	Exposure Levels	Medium	Several analyses (overall and cause-specific SMRs, incidence density for respiratory outcomes) used 5 categories of cumulative exposure in fibers/cc-days (<1,000; 1,000-10,000; 10,000-40,000; 40,000-100,000; and >100,000). In addition, some analyses were stratified by exposure characterized using 4 categories of either years since initial employment (<10, 10-19, 20-29, ≥30 years) or total years employed (same categories).
	Metric 6:	Temporality	High	The maximum follow up was >35 years (1940 to 1975, some employed prior to 1940), and the minimum 10 years (1965-1975). With a total of 33,141 person years at risk among 1,261 members, the mean follow-up was likely about 26 years. Additionally, analyses of dose-response rates for respiratory outcomes were limited to men with 15 or more years latency.
Domain 3: Outcome Assessment				

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Study Citation:	Dement, J. M., Harris, R. L., Jr, Symons, M. J., Shy, C. M. (1983). Exposures and mortality among chrysotile asbestos workers: Part II: Mortality. American Journal of Industrial Medicine 4(3):421-433.
Health Outcome:	Lung Cancer; digestive system cancer
Target Organ(s):	Lung/Respiratory: Lung cancer mortality; Cancer/Carcinogenesis: Lung cancer mortality, Digestive system cancer mortality; Mortality: Lung cancer mortality, Digestive system cancer mortality; Gastrointestinal: Digestive system cancer mortality
Asbestos Fiber Type(s):	Asbestos - Chrysotile (serpentine): 12001-29-5
Linked HERO ID(s):	No linked references.
HERO ID:	67

Domain	Metric		Rating	Comments
	Metric 7:	Outcome Measurement or Characterization	High	Lung Cancer: Lung cancer mortality was assessed on death certificates by a nosologist using the ICD revision that was in use at the time of death (which spanned ICD versions 5 to 8). Cause of death was coded into 89 categories standardized to ICD-7 for analysis. Lung cancer mortality was defined as a 3-digit ICD-7 code of 162 or 163.; Other Cancer(s): Digestive system cancer mortality was assessed on death certificates by a nosologist using the ICD revision that was in use at the time of death (which spanned ICD versions 5 to 8). Cause of death was coded into 89 categories standardized to ICD-7 for analysis. Digestive system cancer mortality was defined as a 3-digit ICD-7 code of 150-159.
	Metric 8:	Reporting Bias	Medium	Numbers of expected and observed deaths were presented for all SMR analyses. However, SMRs did not include confidence intervals. Confidence intervals and the person-years at risk denominator were reported for the incidence density of respiratory outcomes, which was reported by cumulative exposure category. The authors did not report the methods used for statistical significance testing.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Medium	SMRs accounted for age, sex, race, and calendar period. Smoking data was only available for cohort members who completed a respiratory symptom questionnaire in 1964 and 1971 as part of a public health service study. However, the authors illustrated that available estimates for current, past, and non-smoking for the cohort were extremely similar to those for US white males in 1965. Incidence density analyses did not report covariate adjustments. However, the study was limited to white males and incidence density accounts for person-time.
	Metric 10:	Covariate Characterization	Medium	Data came primarily from personnel records and death certificates.
	Metric 11:	Co-exposure Counfounding	Medium	Co-exposures (e.g., from earlier or subsequent work) were not taken into account. Silica or other occupational exposures may have contributed to risk of deaths coded pulmonary fibroses. However, there is no direct evidence that co-exposures might have confounded the findings.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	Medium	Methods were appropriate. SMRs were calculated using a life-table method (reference is cited) and Poisson regression was used to estimate incidence density.
	Metric 13:	Statistical Power	Medium	There were 308 deaths overall, including 24 from other non-malignant respiratory diseases (22 with 15+ years latency). Of the 22, 17 deaths had codes for asbestosis and pulmonary fibrosis as primary or underlying causes of death. Sparse numbers are not unusual for outcomes such as asbestosis.

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Study Citation: Dement, J. M., Harris, R. L., Jr, Symons, M. J., Shy, C. M. (1983). Exposures and mortality among chrysotile asbestos workers: Part II: Mortality. American Journal of Industrial Medicine 4(3):421-433.

Health Outcome: Lung Cancer; digestive system cancer

Target Organ(s): Lung/Respiratory: Lung cancer mortality; Cancer/Carcinogenesis: Lung cancer mortality, Digestive system cancer mortality; Mortality: Lung cancer mortality, Digestive system cancer mortality; Gastrointestinal: Digestive system cancer mortality

Asbestos Fiber Type(s): Asbestos - Chrysotile (serpentine): 12001-29-5

Linked HERO ID(s): No linked references.

HERO ID: 67

Domain	Metric		Rating	Comments
	Metric 14:	Reproducibility of Analyses	Medium	The analyses presented should be readily reproducible as analyses were described and cell sizes presented in adequate detail.
	Metric 15:	Statistical Analysis	Medium	The authors explained their rationale and methods in sufficient detail and methods were appropriate. For SMRs, few confounders besides smoking are typically considered.

Additional Comments: This study analyzed mortality in a cohort of 1,261 white males employed ≥1 month at a chrysotile asbestos textile factory in South Carolina between 1940 and 1965, followed through 1975. Vital status (98%) and cause of death (94%) ascertainment were nearly complete. Use of a dynamic cohort of individuals employed at any time during a 25-year period reduced the likelihood of healthy worker survivor bias. Exposure was estimated using historical air samples, applying dust-to-fiber conversion estimates for early years; methods may have over-estimated exposure. Based on person-years among participants with >15 years of follow-up and converting cumulative exposure-days to years (÷365), about 61% of the cohort had exposures >27.4 fiber/mL-years [10,000 fiber/cc-days]; 7% had exposures >109.6 fiber/mL-years [40,000 fiber/cc-years]. SMRs for non-malignant respiratory disease (excluding infectious) increased from 362 to 2500 over 5 categories of increasing cumulative exposure. Incidence density for asbestos or pulmonary fibrosis mortality also increased from 0.32/1000 person years to 15.98/1000 person-years with increasing exposure. SMRs were also stratified by years employed and years since initial employment categories. SMRs for lung cancer increased from 140 to 1818 over 5 categories of increasing cumulative exposure. Limitations include that asbestosis and pulmonary fibrosis were combined; it is not possible to ascertain if some cases might be fibroses attributable to other occupational exposures. Although smoking adjustments were not possible, limited data suggested that smoking history in the cohort closely resembled the US white male population.

Overall Quality Determination — Medium

* No biomarkers were identified for this evaluation.

Study Citation: Deng, Q., Wang, X., Wang, M., Lan, Y. (2012). Exposure-response relationship between chrysotile exposure and mortality from lung cancer and asbestosis. Occupational and Environmental Medicine 69(2):81-86.
Health Outcome: Asbestosis
Target Organ(s): Lung/Respiratory: Asbestosis mortality
Asbestos Fiber Type(s): Asbestos - Chrysotile (serpentine): 12001-29-5
Linked HERO ID(s): 2573093, 3520560
HERO ID: 2573093

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Medium	This fixed cohort comprised 586 male workers at an asbestos plant in Chongqing, China employed in 1972 and followed through December 2006. The plant used chrysotile asbestos to manufacture textiles, rubber plate and cement. This fixed cohort excluded workers not employed for $\geq$ 1 year at baseline and did not include either former workers or new workers employed after 1972. These exclusions might induce the risk of healthy worker survivor bias, shifting associations toward the null (e.g., Arrighi & Picciotto, 1996, HEROID 79805). Mean (SD) length of employment in the cohort was 25.4 (8.3) years. Very long-term workers with low attrition likely over-represent those individuals least vulnerable to adverse effects and to have accumulated high exposure. In contrast, employees who may have self-selected out of employment after a shorter duration due to poor health/symptoms are likely to be both under-represented in the cohort, and to contribute person-time primarily to low exposure.
	Metric 2:	Attrition	High	Overall, only 49 workers – 7.7% of the 635 men employed at the factory in 1972 – were excluded at baseline because they had worked for less than 1 year (shorter-term employees). In addition, 73 workers in the cohort were lost to follow-up, but job histories and vital records were available from records.
	Metric 3:	Comparison Group	Medium	Analyses used workers in the same cohort with lower exposure as the comparison group. This approach reduces healthy worker hire bias but may not address healthy worker survivor bias related to attrition. Because the cohort was fixed, lower exposure is primarily a consequence of a relatively shorter employment duration: the comparison group may over-represent individuals who stopped work due to poor health. To address this issue, the authors incorporated exposure lag times, a method recommended to account for disease latency and help reduce healthy worker survivor bias by reducing reliance on the participants with the shortest exposures. However, the effectiveness of applying this approach cannot be ascertained (e.g., Arrighi & Picciotto, 1996 79805).
Domain 2: Exposure Characterization				

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Study Citation:	Deng, Q., Wang, X., Wang, M., Lan, Y. (2012). Exposure-response relationship between chrysotile exposure and mortality from lung cancer and asbestosis. Occupational and Environmental Medicine 69(2):81-86.
Health Outcome:	Asbestosis
Target Organ(s):	Lung/Respiratory: Asbestosis mortality
Asbestos Fiber Type(s):	Asbestos - Chrysotile (serpentine): 12001-29-5
Linked HERO ID(s):	2573093, 3520560
HERO ID:	2573093

Domain	Metric		Rating	Comments
	Metric 4:	Measurement of Exposure	Medium	Despite limitations (e.g., infrequent measures with sampling every 4 years), exposure was estimated based on substantial quantitative data: a total of 556 measures, 223 using fiber counting with PCM. Estimated exposure intensity in this Chinese study was considerably higher than in numerous studies in Western countries. Air monitoring data from plant records was used for 1955-1970; the authors did not describe methods, equipment, or frequency for this period. Exposure was measured every four years at the area level (breathing zones) from 1970 to 2006 using a membrane filter (missing details e.g., on # hours). Paired dust and fiber concentrations (n=90) collected in 1999, 2002 and 2006 in each of the 7 factory workshops were used to develop a linear model to convert dust measures to estimated fiber concentrations. No details were provided e.g., on goodness-of-fit, or how measured and estimated fiber concentrations were combined for 1970-1994. Work areas were grouped into 4 categories based on work processes and dust/fiber concentrations, with cumulative exposure for individuals estimated by summing the relevant concentration multiplied by duration. Exposure status in the cohort was updated annually after baseline.
	Metric 5:	Exposure Levels	Medium	Cumulative exposure was analyzed using a continuous fiber/mL-year variable.
	Metric 6:	Temporality	High	The follow-up time of 35 years was adequate for analyses of asbestosis. The authors stated that none of the workers had a diagnosis of cardiopulmonary disease at baseline (details not provided on any health examinations). All deaths from asbestosis occurred 10+ years after first exposure, the great majority after 15+ years.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	High	Asbestosis: Vital status and cause of death were obtained from death certificates and a municipal hospital death registry, with ICD codes used to classify outcomes. Total mortality was high (n=226 deaths). Asbestosis (n=37 cases) was determined by a special panel based on criteria that included a job history confirming occupational exposure, positive radiographic findings, and clinical signs and symptoms, as established by the 1986 Chinese Diagnosis Criteria of Pneumoconiosis by Radiograph. "Death from asbestosis was broadened to include asbestosis and any asbestosis complications, such as cor pulmonale." Ascertainment of vital status involved annual follow-up at the plant and with families (97%).
	Metric 8:	Reporting Bias	Medium	The study presented results that included descriptive data on numbers and causes of death stratified by smoking, fiber-to-dust conversions, and associations using alternative model specifications. However, the authors did not present the distribution of deaths over time or describe the number of deaths included when different exposure lag times were applied in their analyses.

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Study Citation:	Deng, Q., Wang, X., Wang, M., Lan, Y. (2012). Exposure-response relationship between chrysotile exposure and mortality from lung cancer and asbestosis. Occupational and Environmental Medicine 69(2):81-86.
Health Outcome:	Asbestosis
Target Organ(s):	Lung/Respiratory: Asbestosis mortality
Asbestos Fiber Type(s):	Asbestos - Chrysotile (serpentine): 12001-29-5
Linked HERO ID(s):	2573093, 3520560
HERO ID:	2573093

Domain	Metric		Rating	Comments
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Medium	Models adjusted for age, calendar time and smoking status. The article stated that the majority of workers retired during the follow-up period; however, analyses did not account for employment status changes as recommended (Arrighi & Picciotto, 1996 79805). Changes in employment status related to symptoms might be a confounder.
	Metric 10:	Covariate Characterization	Medium	Questionnaires, employment records and interviews with employees, family members and coworkers were used to characterize covariates (e.g., smoking habits, job changes) for both living and deceased workers.
	Metric 11:	Co-exposure Counfounding	Medium	The study did not evaluate any co-exposures, but co-exposure confounding is unlikely for asbestosis.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	Medium	The study compared associations using alternative models based on varying possible exposure-response relationship. Models adjusted for potential confounders that included calendar time and smoking, and incorporated exposure lag times in an effort to address both disease latency and potential healthy worker survivor bias. As noted earlier models did not adjust for employment status. NOTE: The online supplementary materials that provided more details on these alternative models were requested but not yet available at the time of this evaluation.
	Metric 13:	Statistical Power	Medium	There were 226 deaths in the cohort of 568 men, including 37 from asbestosis. Power to detect interactions (tested with smoking) was likely limited given the small number of cases and moderate overall sample size. Indeed, one model specification failed to converge for asbestosis.
	Metric 14:	Reproducibility of Analyses	Medium	The analyses presented are likely to be reproducible given the substantial detail provided on model specifications. NOTE: Reproducibility of results in online supplementary materials has not been evaluated as they are not yet available.
	Metric 15:	Statistical Analysis	Medium	The authors explained the rationale for their statistical methods used and covariates examined. For example, they described the alternative model forms examined, discussed interactions tested, and explained the use of exposure lagging.

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Study Citation:	Deng, Q., Wang, X., Wang, M., Lan, Y. (2012). Exposure-response relationship between chrysotile exposure and mortality from lung cancer and asbestosis. Occupational and Environmental Medicine 69(2):81-86.		
Health Outcome:	Asbestosis		
Target Organ(s):	Lung/Respiratory: Asbestosis mortality		
Asbestos Fiber Type(s):	Asbestos - Chrysotile (serpentine): 12001-29-5		
Linked HERO ID(s):	2573093, 3520560		
HERO ID:	2573093		

Domain	Metric	Rating	Comments
Additional Comments:	This study evaluated the association between chrysotile asbestos exposure and mortality from asbestosis. The population comprised a fixed cohort of 586 workers employed for ≥1 year at a Chinese asbestos textile factory in 1972, followed to 2006. Neither former workers nor individuals employed after 1972 were not included. High exposure concentrations (attributed to legislation and management delays) and lengthy employment duration resulted in higher cumulative exposure (126.1 f-y/mL) than in Western studies of chrysotile textile workers (e.g., 17.1 f/mL-year in a North Carolina study, Loomis et al 2009). However, details on early exposure measurement methods were not provided, and monitoring was infrequent throughout the study. Mortality (n=226 total) included 37 deaths from asbestosis. The authors evaluated alternative model forms and reported significant associations with asbestosis mortality: the relative risk was 10.4 for 40 years of exposure to 1 f/mL of asbestos. Lung cancer mortality was also analyzed and the association with cumulative asbestos exposure described as significant (additional details in online supplement not yet available). Given the use of a fixed cohort, healthy worker survivor bias could have shifted associations towards the null. Low exposure may over-represent individuals selected out of employment duration due in part to poorer health, while the more highly exposed long-term workers may over-represent less vulnerable “survivors”. The authors incorporated exposure lags of up to 10 years to help address this bias (Arrighi & Picciotto, 1996 79805), but effectiveness is uncertain. NOTE: Online supplementary materials that included parameter estimates of key models not yet available.The measurement exposure (M4) and/or exposure levels (M5) metrics are rated as medium upon review by both set of reviewers. Also, the overall quality determination (OQD) is rated medium. Extraction has been completed and quality control reviewed.		

Overall Quality Determination — Medium

* No biomarkers were identified for this evaluation.

Study Citation:	Dunning, K. K., Adjei, S., Levin, L., Rohs, A. M., Hilbert, T., Borton, E., Kapil, V., Rice, C., Lemasters, G. K., Lockey, J. E. (2012). Mesothelioma associated with commercial use of vermiculite containing Libby amphibole. Journal of Occupational and Environmental Medicine 54(11):1359-1363.
Health Outcome:	Lung Cancer
Target Organ(s):	Mortality: Mortality from cancer of trachea, bronchus, or lung; Cancer/Carcinogenesis: Mortality from cancer of trachea, bronchus, or lung; Lung/Respiratory: Mortality from cancer of trachea, bronchus, or lung
Asbestos Fiber Type(s):	Asbestos- Libby amphibole: 1318-09-8; Asbestos - Not specified: 1332-21-4; Asbestos - Winchite: 12425-92-2; Asbestos- Richterite: 17068-76-7; Asbestos - Tremolite: 14567-73-8
Linked HERO ID(s):	No linked references.
HERO ID:	1066036

Domain		Metric	Rating	Comments
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Low	Analyses use cumulative fiber exposure. Additional details about exposure measurement are reported in Lockey et al., 1984, HEROID 29685. Samples were collected via membrane filters either by following an employee with a sampler (from 1972-1976) or by breathing zone sampling (after 1976). Authors note that exposure of fiber was defined as "particles with a length greater than 5 um, a diameter less than 3 um, and an aspect ratio of 3:1 or greater". Thus, fiber type was unknown, and samples likely included fibers other than asbestos. Samples were reviewed through polarized light microscopy, scanning electron microscopy, and TEM. Indexes were created for each department within the facility. Study authors used work histories reported by workers in 1980 to calculate the cumulative fiber exposure level for each employee. Previous estimates were revised to include additional data related to exposure collected in 2010, such as adjustments for vermiculite source and changes in duration of work by season (Borton et al., 2012, HEROID 1066035). Borton et al. also estimated exposures from 1957-1971 using estimates from 1972 with adjustments for dustier historical conditions. This study also reported comparisons between personal and area samples and found approximately equal means and ranges.
	Metric 5:	Exposure Levels	Medium	For SMR and SRR analyses of lung cancer, exposure is presented in three groups based on cumulative fiber exposure estimates. Authors note the possibility that associations were not observed due to the low exposure levels among the study population, which raises some concern about the influence of the exposure distribution on the ability to detect an effect.

Additional Comments: QC was not completed for metrics other than Metrics 4 and 5 because the study does not have sufficient exposure information to be useful for dose-response analysis.This retrospective occupational cohort study examined the association between asbestos exposure and all cancer mortality among workers mining and milling contaminated vermiculite. There were no major concerns with the study, aside from limited exposure distributions among the study population and concerns about fibrous co-exposures that were not characterized or quantified. Since these workers were exposed to fibers that were not asbestos, it can be assumed that these exposures influenced the observed outcomes, but they were not characterized. The approach for exposure measurement and statistical analysis was strong, and there were no concerns about selection bias resulting from population recruitment approaches.

* No biomarkers were identified for this evaluation.

** As described in Appendix B.2 of the *White Paper: Quantitative Approach to the Human Health Assessment for the Risk Evaluation for Asbestos Part 2: Supplemental Evaluation Including Legacy Uses and Associated Disposals of Asbestos*, to be considered as being informative for dose-response analysis, metrics 4 and 5 would need metric ratings of Medium or High. This reference did not satisfy this requirement; therefore data quality evaluation is presented for only for metrics 4 and 5.

Study Citation:	Dunning, K. K., Adjei, S., Levin, L., Rohs, A. M., Hilbert, T., Borton, E., Kapil, V., Rice, C., Lemasters, G. K., Lockey, J. E. (2012). Mesothelioma associated with commercial use of vermiculite containing Libby amphibole. Journal of Occupational and Environmental Medicine 54(11):1359-1363.
Health Outcome:	All cancer mortality
Target Organ(s):	Cancer/Carcinogenesis: All cancer mortality; Mortality: All cancer mortality
Asbestos Fiber Type(s):	Asbestos- Libby amphibole: 1318-09-8; Asbestos - Not specified: 1332-21-4; Asbestos - Winchite: 12425-92-2; Asbestos- Richterite: 17068-76-7; Asbestos - Tremolite: 14567-73-8
Linked HERO ID(s):	No linked references.
HERO ID:	1066036

Domain	Metric		Rating	Comments
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Low	Analyses use cumulative fiber exposure. Additional details about exposure measurement are reported in Lockey et al., 1984, HEROID 29685. Samples were collected via membrane filters either by following an employee with a sampler (from 1972-1976) or by breathing zone sampling (after 1976). Authors note that exposure of fiber was defined as "particles with a length greater than 5 um, a diameter less than 3 um, and an aspect ratio of 3:1 or greater". Thus, fiber type was unknown, and samples likely included fibers other than asbestos. Samples were reviewed through polarized light microscopy, scanning electron microscopy, and TEM. Indexes were created for each department within the facility. Study authors used work histories reported by workers in 1980 to calculate the cumulative fiber exposure level for each employee. Previous estimates were revised to include additional data related to exposure collected in 2010, such as adjustments for vermiculite source and changes in duration of work by season (Borton et al., 2012, HEROID 1066035). Borton et al. also estimated exposures from 1957-1971 using estimates from 1972 with adjustments for dustier historical conditions. This study also reported comparisons between personal and area samples and found approximately equal means and ranges.
	Metric 5:	Exposure Levels	Medium	For SMR and SRR analyses of all cancer mortality, exposure is presented in three groups based on cumulative fiber exposure estimates. Authors note the possibility that associations were not observed due to the low exposure levels among the study population, which raises some concern about the influence of the exposure distribution on the ability to detect an effect.

Additional Comments:	QC was not completed for metric other than Metrics 4 and 5 because the study does not have sufficient exposure information to be useful for dose-response analysis.This retrospective occupational cohort study examined the association between asbestos exposure and all cancer mortality among workers mining and milling contaminated vermiculite. There were no major concerns with the study, aside from limited exposure distributions among the study population and concerns about fibrous co-exposures that were not characterized or quantified. Since these workers were exposed to fibers that were not asbestos, it can be assumed that these exposures influenced the observed outcomes, but they were not characterized. The approach for exposure measurement and statistical analysis was strong, and there were no concerns about selection bias resulting from population recruitment approaches.

* No biomarkers were identified for this evaluation.

** As described in Appendix B.2 of the *White Paper: Quantitative Approach to the Human Health Assessment for the Risk Evaluation for Asbestos Part 2: Supplemental Evaluation Including Legacy Uses and Associated Disposals of Asbestos*, to be considered as being informative for dose-response analysis, metrics 4 and 5 would need metric ratings of Medium or High. This reference did not satisfy this requirement; therefore data quality evaluation is presented for only for metrics 4 and 5.

Study Citation:	Dunning, K. K., Adjei, S., Levin, L., Rohs, A. M., Hilbert, T., Borton, E., Kapil, V., Rice, C., Lemasters, G. K., Lockey, J. E. (2012). Mesothelioma associated with commercial use of vermiculite containing Libby amphibole. Journal of Occupational and Environmental Medicine 54(11):1359-1363.
Health Outcome:	All cause mortality
Target Organ(s):	Mortality: All cause mortality
Asbestos Fiber Type(s):	Asbestos- Libby amphibole: 1318-09-8; Asbestos - Not specified: 1332-21-4; Asbestos - Winchite: 12425-92-2; Asbestos- Richterite: 17068-76-7; Asbestos - Tremolite: 14567-73-8
Linked HERO ID(s):	No linked references.
HERO ID:	1066036

Domain	Metric		Rating	Comments
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Low	Analyses use cumulative fiber exposure. Additional details about exposure measurement are reported in Lockey et al., 1984, HEROID 29685. Samples were collected via membrane filters either by following an employee with a sampler (from 1972-1976) or by breathing zone sampling (after 1976). Authors note that exposure of fiber was defined as "particles with a length greater than 5 um, a diameter less than 3 um, and an aspect ratio of 3:1 or greater". Thus, fiber type was unknown, and samples likely included fibers other than asbestos. Samples were reviewed through polarized light microscopy, scanning electron microscopy, and TEM. Indexes were created for each department within the facility. Study authors used work histories reported by workers in 1980 to calculate the cumulative fiber exposure level for each employee. Previous estimates were revised to include additional data related to exposure collected in 2010, such as adjustments for vermiculite source and changes in duration of work by season (Borton et al., 2012, HEROID 1066035). Borton et al. also estimated exposures from 1957-1971 using estimates from 1972 with adjustments for dustier historical conditions. This study also reported comparisons between personal and area samples and found approximately equal means and ranges.
	Metric 5:	Exposure Levels	Low	For SMR analyses of all-cause mortality, exposure is presented in two groups only (exposed workers and unexposed US general population). Authors note the possibility that associations were not observed due to the low exposure levels among the study population, which raises some concern about the influence of the exposure distribution on the ability to detect an effect.

Additional Comments:	QC was not completed for metrics other than Metrics 4 and 5 because the study does not have sufficient exposure information to be useful for dose-response analysis.This retrospective occupational cohort study examined the association between asbestos exposure and all cause mortality among workers mining and milling contaminated vermiculite. There were no major concerns with the study, aside from limited exposure distributions among the study population and concerns about fibrous co-exposures that were not characterized or quantified. Since these workers were exposed to fibers that were not asbestos, it can be assumed that these exposures influenced the observed outcomes, but they were not characterized. The approach for exposure measurement and statistical analysis was strong, and there were no concerns about selection bias resulting from population recruitment approaches.

* No biomarkers were identified for this evaluation.

** As described in Appendix B.2 of the *White Paper: Quantitative Approach to the Human Health Assessment for the Risk Evaluation for Asbestos Part 2: Supplemental Evaluation Including Legacy Uses and Associated Disposals of Asbestos*, to be considered as being informative for dose-response analysis, metrics 4 and 5 would need metric ratings of Medium or High. This reference did not satisfy this requirement; therefore data quality evaluation is presented for only for metrics 4 and 5.

Study Citation:	Dunning, K. K., Adjei, S., Levin, L., Rohs, A. M., Hilbert, T., Borton, E., Kapil, V., Rice, C., Lemasters, G. K., Lockey, J. E. (2012). Mesothelioma associated with commercial use of vermiculite containing Libby amphibole. Journal of Occupational and Environmental Medicine 54(11):1359-1363.
Health Outcome:	Chronic obstructive pulmonary disease
Target Organ(s):	Mortality: Mortality from chronic obstructive pulmonary disease; Lung/Respiratory: Mortality from chronic obstructive pulmonary disease
Asbestos Fiber Type(s):	Asbestos- Libby amphibole: 1318-09-8; Asbestos - Not specified: 1332-21-4; Asbestos - Winchite: 12425-92-2; Asbestos- Richterite: 17068-76-7; Asbestos - Tremolite: 14567-73-8
Linked HERO ID(s):	No linked references.
HERO ID:	1066036

Domain	Metric		Rating	Comments
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Low	Analyses use cumulative fiber exposure. Additional details about exposure measurement are reported in Lockey et al., 1984, HEROID 29685. Samples were collected via membrane filters either by following an employee with a sampler (from 1972-1976) or by breathing zone sampling (after 1976). Authors note that exposure of fiber was defined as "particles with a length greater than 5 um, a diameter less than 3 um, and an aspect ratio of 3:1 or greater". Thus, fiber type was unknown, and samples likely included fibers other than asbestos. Samples were reviewed through polarized light microscopy, scanning electron microscopy, and TEM. Indexes were created for each department within the facility. Study authors used work histories reported by workers in 1980 to calculate the cumulative fiber exposure level for each employee. Previous estimates were revised to include additional data related to exposure collected in 2010, such as adjustments for vermiculite source and changes in duration of work by season (Borton et al., 2012, HEROID 1066035). Borton et al. also estimated exposures from 1957-1971 using estimates from 1972 with adjustments for dustier historical conditions. This study also reported comparisons between personal and area samples and found approximately equal means and ranges.
	Metric 5:	Exposure Levels	Low	For SMR analyses of chronic obstructive pulmonary disease, exposure is presented in two groups only (exposed workers vs. unexposed general population). Authors note the possibility that associations were not observed due to the low exposure levels among the study population, which raises some concern about the influence of the exposure distribution on the ability to detect an effect.

Additional Comments: QC was not completed for metrics other than Metrics 4 and 5 because the study does not have sufficient exposure information to be useful for dose-response analysis.This retrospective occupational cohort study examined the association between asbestos exposure and chronic obstructive pulmonary disease mortality among workers mining and milling contaminated vermiculite. There were concerns about the limited number of observed chronic obstructive pulmonary disease cases in the study population (n=8) and the ability to detect an effect with a cohort of this sample size. Additionally, there were concerns with the lack of consideration of co-exposures and the limited exposure distributions among the study population. Otherwise, the approach for exposure measurement and statistical analysis was strong, and there were no concerns about selection bias resulting from population recruitment approaches.

* No biomarkers were identified for this evaluation.

** As described in Appendix B.2 of the *White Paper: Quantitative Approach to the Human Health Assessment for the Risk Evaluation for Asbestos Part 2: Supplemental Evaluation Including Legacy Uses and Associated Disposals of Asbestos*, to be considered as being informative for dose-response analysis, metrics 4 and 5 would need metric ratings of Medium or High. This reference did not satisfy this requirement; therefore data quality evaluation is presented for only for metrics 4 and 5.

Study Citation:	Dunning, K. K., Adjei, S., Levin, L., Rohs, A. M., Hilbert, T., Borton, E., Kapil, V., Rice, C., Lemasters, G. K., Lockey, J. E. (2012). Mesothelioma associated with commercial use of vermiculite containing Libby amphibole. Journal of Occupational and Environmental Medicine 54(11):1359-1363.
Health Outcome:	Asbestosis
Target Organ(s):	Mortality: Asbestosis mortality; Lung/Respiratory: Asbestosis mortality
Asbestos Fiber Type(s):	Asbestos- Libby amphibole: 1318-09-8; Asbestos - Not specified: 1332-21-4; Asbestos - Winchite: 12425-92-2; Asbestos- Richterite: 17068-76-7; Asbestos - Tremolite: 14567-73-8
Linked HERO ID(s):	No linked references.
HERO ID:	1066036

Domain	Metric		Rating	Comments
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Low	Analyses use cumulative fiber exposure. Additional details about exposure measurement are reported in Lockey et al., 1984, HEROID 29685. Samples were collected via membrane filters either by following an employee with a sampler (from 1972-1976) or by breathing zone sampling (after 1976). Authors note that exposure of fiber was defined as ”particles with a length greater than 5 um, a diameter less than 3 um, and an aspect ratio of 3:1 or greater”. Thus, fiber type was unknown, and samples likely included fibers other than asbestos. Samples were reviewed through polarized light microscopy, scanning electron microscopy, and TEM. Indexes were created for each department within the facility. Study authors used work histories reported by workers in 1980 to calculate the cumulative fiber exposure level for each employee. Previous estimates were revised to include additional data related to exposure collected in 2010, such as adjustments for vermiculite source and changes in duration of work by season (Borton et al., 2012, HEROID 1066035). Borton et al. also estimated exposures from 1957-1971 using estimates from 1972 with adjustments for dustier historical conditions. This study also reported comparisons between personal and area samples and found approximately equal means and ranges.
	Metric 5:	Exposure Levels	Low	For SMR analyses of asbestosis, exposure is presented in two groups only (exposed workers vs. unexposed general population). Authors note the possibility that associations were not observed due to the low exposure levels among the study population, which raises some concern about the influence of the exposure distribution on the ability to detect an effect.

Additional Comments:	QC was not completed for metrics other than Metrics 4 and 5 because the study does not have sufficient exposure information to be useful for dose-response analysis.This retrospective occupational cohort study examined the association between asbestos exposure and asbestosis mortality among workers mining and milling contaminated vermiculite. There were concerns about the limited number of observed asbestosis cases in the study population (n=1) and the ability to detect an effect with a cohort of this sample size. Additionally, there were limited exposure distributions among the study population. Otherwise, the approach for exposure measurement and statistical analysis was strong, and there were no concerns about selection bias resulting from population recruitment approaches.

* No biomarkers were identified for this evaluation.

** As described in Appendix B.2 of the *White Paper: Quantitative Approach to the Human Health Assessment for the Risk Evaluation for Asbestos Part 2: Supplemental Evaluation Including Legacy Uses and Associated Disposals of Asbestos*, to be considered as being informative for dose-response analysis, metrics 4 and 5 would need metric ratings of Medium or High. This reference did not satisfy this requirement; therefore data quality evaluation is presented for only for metrics 4 and 5.

Study Citation:	Dunning, K. K., Adjei, S., Levin, L., Rohs, A. M., Hilbert, T., Borton, E., Kapil, V., Rice, C., Lemasters, G. K., Lockey, J. E. (2012). Mesothelioma associated with commercial use of vermiculite containing Libby amphibole. Journal of Occupational and Environmental Medicine 54(11):1359-1363.
Health Outcome:	Other respiratory disease
Target Organ(s):	Mortality: Mortality from other respiratory disease; Lung/Respiratory: Mortality from other respiratory disease
Asbestos Fiber Type(s):	Asbestos- Libby amphibole: 1318-09-8; Asbestos - Not specified: 1332-21-4; Asbestos - Winchite: 12425-92-2; Asbestos- Richterite: 17068-76-7; Asbestos - Tremolite: 14567-73-8
Linked HERO ID(s):	No linked references.
HERO ID:	1066036

Domain	Metric		Rating	Comments
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Low	Analyses use cumulative fiber exposure. Additional details about exposure measurement are reported in Lockey et al., 1984, HEROID 29685. Samples were collected via membrane filters either by following an employee with a sampler (from 1972-1976) or by breathing zone sampling (after 1976). Authors note that exposure of fiber was defined as ”particles with a length greater than 5 um, a diameter less than 3 um, and an aspect ratio of 3:1 or greater”. Thus, fiber type was unknown, and samples likely included fibers other than asbestos. Samples were reviewed through polarized light microscopy, scanning electron microscopy, and TEM. Indexes were created for each department within the facility. Study authors used work histories reported by workers in 1980 to calculate the cumulative fiber exposure level for each employee. Previous estimates were revised to include additional data related to exposure collected in 2010, such as adjustments for vermiculite source and changes in duration of work by season (Borton et al., 2012, HEROID 1066035). Borton et al. also estimated exposures from 1957-1971 using estimates from 1972 with adjustments for dustier historical conditions. This study also reported comparisons between personal and area samples and found approximately equal means and ranges.
	Metric 5:	Exposure Levels	Low	For SMR analyses of other respiratory diseases, exposure is presented in two groups only (exposed workers vs. unexposed general population). Authors note the possibility that associations were not observed due to the low exposure levels among the study population, which raises some concern about the influence of the exposure distribution on the ability to detect an effect.

Additional Comments:	QC was not completed for metrics other than Metrics 4 and 5 because the study does not have sufficient exposure information to be useful for dose-response analysis.This retrospective occupational cohort study examined the association between asbestos exposure and other respiratory disease mortality among workers mining and milling contaminated vermiculite. There were concerns about the limited number of deaths from respiratory diseases in the study population (n=2) and the ability to detect an effect with a cohort of this sample size. Additionally, there were concerns with the lack of consideration of co-exposures and the limited exposure distributions among the study population. Otherwise, the approach for exposure measurement and statistical analysis was strong, and there were no concerns about selection bias resulting from population recruitment approaches.

* No biomarkers were identified for this evaluation.

** As described in Appendix B.2 of the *White Paper: Quantitative Approach to the Human Health Assessment for the Risk Evaluation for Asbestos Part 2: Supplemental Evaluation Including Legacy Uses and Associated Disposals of Asbestos*, to be considered as being informative for dose-response analysis, metrics 4 and 5 would need metric ratings of Medium or High. This reference did not satisfy this requirement; therefore data quality evaluation is presented for only for metrics 4 and 5.

Study Citation:	Dunning, K. K., Adjei, S., Levin, L., Rohs, A. M., Hilbert, T., Borton, E., Kapil, V., Rice, C., Lemasters, G. K., Lockey, J. E. (2012). Mesothelioma associated with commercial use of vermiculite containing Libby amphibole. Journal of Occupational and Environmental Medicine 54(11):1359-1363.
Health Outcome:	Cancer of the digestive system and peritoneum
Target Organ(s):	Mortality: Mortality from cancer of the digestive system and peritoneum; Cancer/Carcinogenesis: Mortality from cancer of the digestive system and peritoneum; Gastrointestinal: Mortality from cancer of the digestive system and peritoneum
Asbestos Fiber Type(s):	Asbestos- Libby amphibole: 1318-09-8; Asbestos - Not specified: 1332-21-4; Asbestos - Winchite: 12425-92-2; Asbestos- Richterite: 17068-76-7; Asbestos - Tremolite: 14567-73-8
Linked HERO ID(s):	No linked references.
HERO ID:	1066036

Domain	Metric		Rating	Comments
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Low	Analyses use cumulative fiber exposure. Additional details about exposure measurement are reported in Lockey et al., 1984, HEROID 29685. Samples were collected via membrane filters either by following an employee with a sampler (from 1972-1976) or by breathing zone sampling (after 1976). Authors note that exposure of fiber was defined as "particles with a length greater than 5 um, a diameter less than 3 um, and an aspect ratio of 3:1 or greater". Thus, fiber type was unknown, and samples likely included fibers other than asbestos. Samples were reviewed through polarized light microscopy, scanning electron microscopy, and TEM. Indexes were created for each department within the facility. Study authors used work histories reported by workers in 1980 to calculate the cumulative fiber exposure level for each employee. Previous estimates were revised to include additional data related to exposure collected in 2010, such as adjustments for vermiculite source and changes in duration of work by season (Borton et al., 2012, HEROID 1066035). Borton et al. also estimated exposures from 1957-1971 using estimates from 1972 with adjustments for dustier historical conditions. This study also reported comparisons between personal and area samples and found approximately equal means and ranges.
	Metric 5:	Exposure Levels	Medium	For SMR and SRR analyses of digestive cancers, exposure is presented in three groups based on cumulative fiber exposure estimates. Authors note the possibility that associations were not observed due to the low exposure levels among the study population, which raises some concern about the influence of the exposure distribution on the ability to detect an effect.

Additional Comments:	QC was not completed for metrics other than Metrics 4 and 5 because the study does not have sufficient exposure information to be useful for dose-response analysis.This retrospective occupational cohort study examined the association between asbestos exposure and digestive and peritoneum cancer mortality among workers mining and milling contaminated vermiculite. There were no major concerns with the study, aside from the low number of cases, the limited exposure distributions among the study population and concerns about fibrous co-exposures that were not characterized or quantified. Since these workers were exposed to fibers that were not asbestos, it can be assumed that these exposures influenced the observed outcomes, but they were not characterized. The approach for exposure measurement and statistical analysis was strong, and there were no concerns about selection bias resulting from population recruitment approaches.

* No biomarkers were identified for this evaluation.

** As described in Appendix B.2 of the *White Paper: Quantitative Approach to the Human Health Assessment for the Risk Evaluation for Asbestos Part 2: Supplemental Evaluation Including Legacy Uses and Associated Disposals of Asbestos*, to be considered as being informative for dose-response analysis, metrics 4 and 5 would need metric ratings of Medium or High. This reference did not satisfy this requirement; therefore data quality evaluation is presented for only for metrics 4 and 5.

Study Citation:	e La Provôté, S., Desoubeaux, N., Paris, C., Letourneux, M., Raffaelli, C., Galateau-Salle, F., Gignoux, M., Launoy, G. (2002). Incidence of digestive cancers and occupational exposure to asbestos. European Journal of Cancer Prevention 11(6):523-528.
Health Outcome:	All digestive cancers
Target Organ(s):	Cancer/Carcinogenesis: All digestive cancers; Gastrointestinal: All digestive cancers
Asbestos Fiber Type(s):	Asbestos - Chrysotile (serpentine): 12001-29-5; Asbestos - Crocidolite (riebeckite): 12001-28-4
Linked HERO ID(s):	3520580, 3077730, 3078903, 3520549
HERO ID:	3520580

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Medium	Clin et al. 2011, HERO ID: 3078903 analyzed the risk of cancers among salaried and retired workers (men and women) from an asbestos reprocessing plant (textiles and friction materials) in the Calvados department in Normandy, France. Eligibility was based on: (i) working at the plant for at least 1 year; (ii) being alive in 1978 when the regional cancer registry was established; (iii) having resided in Calvados during at least part of the 1978 to 1995 initial follow-up period, with known vital status (de la Provote et al al. 2002, HERO ID: 3520580). As noted by Clin et al. 2011, HERO ID: 3078903, "... since one of our inclusion criteria was that subjects had to be alive in 1978, there may be a selection bias related to the 'healthy worker effect'." Including retired workers, however, would have helped to reduce this bias. The number of workers who did not meet eligibility criteria was not provided; it is unknown whether a large number of workers of similar age and employment duration as those in the cohort had cancer diagnoses prior to 1978, which could bias results. The factories had operated using asbestos in various capacities since 1928. All cancer cases from 1978 to 1996 were included, resulting in 1820 subjects (1454 men).
	Metric 2:	Attrition	High	De la Provote et al al. 2002, HERO ID: 3520580 reported that 152 subjects (8.4%) had missing vital status at the end of 1995 and were excluded from analysis. It is unclear why vital status was missing, but given the relatively small share of subjects and that it would not be expected to be related exposure and outcome make this a limited concern for bias.
	Metric 3:	Comparison Group	Medium	In calculating relative risk for cancers, workers with varying concentrations of exposures were compared amongst each other. There is no indication that groups were similar, but there is no indication of healthy worker effect.
Domain 2: Exposure Characterization				

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Study Citation:	e La Provôté, S., Desoubeaux, N., Paris, C., Letourneux, M., Raffaelli, C., Galateau-Salle, F., Gignoux, M., Launoy, G. (2002). Incidence of digestive cancers and occupational exposure to asbestos. European Journal of Cancer Prevention 11(6):523-528.
Health Outcome:	All digestive cancers
Target Organ(s):	Cancer/Carcinogenesis: All digestive cancers; Gastrointestinal: All digestive cancers
Asbestos Fiber Type(s):	Asbestos - Chrysotile (serpentine): 12001-29-5; Asbestos - Crocidolite (riebeckite): 12001-28-4
Linked HERO ID(s):	3520580, 3077730, 3078903, 3520549
HERO ID:	3520580

Domain	Metric		Rating	Comments
	Metric 4:	Measurement of Exposure	Medium	Exposure estimates were assigned to individuals based on job functions and timing/duration of employment and fiber count measures. As described by de la Provote et al. 2002, HERO ID: 3520580, fiber counts were measured at different locations in the plant as follows: (i) 1973 -1995 data were collected by Casella pumps on a membrane filter, with PCM (phase-contrast light microscopy) counts of fibers longer than 5µ m, less than 3µ m in diameter, with a length/diameter ratio greater than 3; (ii) 1960-1974 data were collected on soluble filters by an ARM (Avy–Raillere–Martin) apparatus, with light microscopy fiber counts as particles per liter of air; and (iii) estimates prior to 1959/1960 were based on production reports for 1939-1945 [50% of 1960 levels], linearly extrapolated to 1960. Date cutoffs differed slightly across manuscripts [e.g. ARM started in 1959 vs 1960 according to Clin et al. 2011, HERO ID: 3078903]. Side-by-side Casella vs. ARM method measures in 1974 were used to develop a conversion factor for the different methods. A cumulative exposure index (CEI) for the entire career (fibers/mL * year) was calculated as the sum of exposure * duration for each job position. A mean exposure concentration (MEC), also referred to as averaged exposure (AEL) was also calculated and expressed in fibers/mL). Clin et al. 2009, HERO ID: 3520549 and Boulanger et al. 2017, HERO ID: 3077730 explain these same methods but in lesser detail. Clin et al. 2011, HERO ID: 3078903 uses CEI and AEL exposure categories with a 10-year lag to account for latency.
	Metric 5:	Exposure Levels	Medium	To estimate cancer risk, only de la Provote et al. 2002, HERO ID: 3520580 categorized asbestos exposure variables using >=3 ordinal levels. Of note is that only mean cumulative exposure, not cumulative exposure index values were used in adjusted models.In Clin et al. 2009, HERO ID: 3520549 and Boulanger et al. 2015, HERO ID: 307773, SIRs are only calculated using 2 exposure categories of cumulative exposure, such as exposed/unexposed or <= vs > 80 fibers/mL-year, all of which merit a Low rating for this metric. Because of this, Clin et al. 2009, HERO ID: 3520549 and Boulanger et al. 2015, HERO ID: 307773 are only evaluated for metrics 4 and 5 in this entry.
	Metric 6:	Temporality	High	De la Provote et al. 2002, HERO ID: 3520580 shows that 69% of workers had at least 10 years at work, and 50% had >= 20 years.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Uninformative	Other Cancer(s): The outcome is a combination of all digestive cancers, thus meriting an uninformative rating.
	Metric 8:	Reporting Bias	High	De la Provote et al. 2002, HERO ID: 3520580 reported findings in the abstract, results, and discussion sections adequately, where confidence intervals are provided for relative risk estimates. P-values and numbers of cases were also presented in detail.

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Study Citation: e La Provôté, S., Desoubeaux, N., Paris, C., Letourneux, M., Raffaelli, C., Galateau-Salle, F., Gignoux, M., Launoy, G. (2002). Incidence of digestive cancers and occupational exposure to asbestos. European Journal of Cancer Prevention 11(6):523-528.
Health Outcome: All digestive cancers
Target Organ(s): Cancer/Carcinogenesis: All digestive cancers; Gastrointestinal: All digestive cancers
Asbestos Fiber Type(s): Asbestos - Chrysotile (serpentine): 12001-29-5; Asbestos - Crocidolite (riebeckite): 12001-28-4
Linked HERO ID(s): 3520580, 3077730, 3078903, 3520549
HERO ID: 3520580

Domain	Metric		Rating	Comments
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Low	De la Provote et al. 2002, HERO ID: 3520580 adjusted models for age at recruitment, latency (time dependent) and years at the company, but not sex. Data on smoking were not available. Race was not discussed, although it is likely that the population was largely white.
	Metric 10:	Covariate Characterization	Medium	Information on covariates was obtained from the company's occupational health department records.
	Metric 11:	Co-exposure Counfounding	Low	There was no discussion of coexposures at these factories.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	Medium	De la Provote et al. 2002, HERO ID: 3520580 used a Cox hazard model to analyze the dose-response relationship of occupational asbestos exposure (mean cumulative exposure only) and risk of digestive cancer.
	Metric 13:	Statistical Power	Medium	De la Provote et al. 2002, HERO ID: 3520580 likely has adequate power to detect an association (total n=1820, n cases=56).
	Metric 14:	Reproducibility of Analyses	Medium	The descriptions of analyses are clear and sufficiently well-written to conceptually reproduce analyses.
	Metric 15:	Statistical Analysis	Medium	The authors describe appropriate methods and note that the assumption of proportional hazards was checked graphically.

Additional Comments: Note that only De la Provote et al. 2002, HERO ID: 3520580 was evaluated for all metrics. The only outcome evaluated here is all digestive cancers. In Clin et al. 2009, HERO ID: 3520549 and Boulanger et al. 2015, HERO ID: 307773, SIRs are only calculated using 2 exposure categories of cumulative exposure, such as exposed/unexposed or <= vs > 80 fibers/mL-year, meaning these studies were not evaluated for this outcome.

Overall Quality Determination — Uninformative

* No biomarkers were identified for this evaluation.

Study Citation:	e La Provôté, S., Desoubeaux, N., Paris, C., Letourneux, M., Raffaelli, C., Galateau-Salle, F., Gignoux, M., Launoy, G. (2002). Incidence of digestive cancers and occupational exposure to asbestos. European Journal of Cancer Prevention 11(6):523-528.
Health Outcome:	Lung Cancer; colorectal, prostate, skin cancer, ear/nose/throat (ENT) cancer, bladder and kidney cancer, esophageal cancer, female genital tract cancer
Target Organ(s):	Gastrointestinal: Colon-rectum cancer, Esophagus cancer; Cancer/Carcinogenesis: Colon-rectum cancer, Esophagus cancer, Prostate cancer, Skin cancer (excluding basal cell tumors), Ear nose throat (ENT) cancer, Bladder and kidney cancer, Female genital tract cancer, Lung cancer; Reproductive/Developmental: Prostate cancer, Female genital tract cancer; Skin/Connective Tissue: Skin cancer (excluding basal cell tumors); nan: ; Renal/Kidney: Bladder and kidney cancer; Lung/Respiratory: Lung cancer
Asbestos Fiber Type(s):	Asbestos - Chrysotile (serpentine): 12001-29-5; Asbestos - Crocidolite (riebeckite): 12001-28-4
Linked HERO ID(s):	3520580, 3077730, 3078903, 3520549
HERO ID:	3520580

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Medium	Clin et al. 2011, HERO ID: 3078903 analyzed the risk of cancers among salaried and retired workers (men and women) from an asbestos reprocessing plant (textiles and friction materials) in the Calvados department in Normandy, France. Eligibility was based on: (i) working at the plant for at least 1 year; (ii) being alive in 1978 when the regional cancer registry was established; (iii) having resided in Calvados during at least part of the 1978 to 1995 initial follow-up period, with known vital status (de la Provote et al al. 2002, HERO ID: 3520580). As noted by Clin et al. 2011, HERO ID: 3078903, "... since one of our inclusion criteria was that subjects had to be alive in 1978, there may be a selection bias related to the 'healthy worker effect'." Including retired workers, however, would have helped to reduce this bias. The number of workers who did not meet eligibility criteria was not provided; it is unknown whether a large number of workers of similar age and employment duration as those in the cohort had cancer diagnoses prior to 1978, which could bias results. The factories had operated using asbestos in various capacities since 1928. All cancer cases from 1978 to 2004 were included, resulting in 2024 subjects (1604 men).
	Metric 2:	Attrition	High	Clin et al. 2011, HERO ID: 3078903 reported that 107 subjects (5.3%) had missing vital status at the end of 2004 and were excluded from analysis. It is unclear why vital status was missing, but given the relatively small share of subjects and that it would not be expected to be related exposure and outcome make this a limited concern for bias.
	Metric 3:	Comparison Group	Medium	In calculating relative risk for cancers, workers with varying concentrations of exposures were compared amongst each other. There is no indication that groups were similar, but there is no indication of healthy worker effect.
Domain 2: Exposure Characterization				

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Study Citation:	e La Provôté, S., Desoubeaux, N., Paris, C., Letourneux, M., Raffaelli, C., Galateau-Salle, F., Gignoux, M., Launoy, G. (2002). Incidence of digestive cancers and occupational exposure to asbestos. European Journal of Cancer Prevention 11(6):523-528.
Health Outcome:	Lung Cancer; colorectal, prostate, skin cancer, ear/nose/throat (ENT) cancer, bladder and kidney cancer, esophageal cancer, female genital tract cancer
Target Organ(s):	Gastrointestinal: Colon-rectum cancer, Esophagus cancer; Cancer/Carcinogenesis: Colon-rectum cancer, Esophagus cancer, Prostate cancer, Skin cancer (excluding basal cell tumors), Ear nose throat (ENT) cancer, Bladder and kidney cancer, Female genital tract cancer, Lung cancer; Reproductive/Developmental: Prostate cancer, Female genital tract cancer; Skin/Connective Tissue: Skin cancer (excluding basal cell tumors); nan: ; Renal/Kidney: Bladder and kidney cancer; Lung/Respiratory: Lung cancer
Asbestos Fiber Type(s):	Asbestos - Chrysotile (serpentine): 12001-29-5; Asbestos - Crocidolite (riebeckite): 12001-28-4
Linked HERO ID(s):	3520580, 3077730, 3078903, 3520549
HERO ID:	3520580

Domain	Metric		Rating	Comments
	Metric 4:	Measurement of Exposure	Medium	Exposure estimates were assigned to individuals based on job functions and timing/duration of employment and fiber count measures. As described by de la Provote et al. 2002, HERO ID: 3520580, fiber counts were measured at different locations in the plant as follows: (i) 1973 -1995 data were collected by Casella pumps on a membrane filter, with PCM (phase-contrast light microscopy) counts of fibers longer than 5μ m, less than 3μ m in diameter, with a length/diameter ratio greater than 3; (ii) 1960-1974 data were collected on soluble filters by an ARM (Avy–Raillere–Martin) apparatus, with light microscopy fiber counts as particles per liter of air; and (iii) estimates prior to 1959/1960 were based on production reports for 1939-1945 [50% of 1960 levels], linearly extrapolated to 1960. Date cutoffs differed slightly across manuscripts [e.g. ARM started in 1959 vs 1960 according to Clin et al. 2011, HERO ID: 3078903]. Side-by-side Casella vs. ARM method measures in 1974 were used to develop a conversion factor for the different methods. A cumulative exposure index (CEI) for the entire career (fibers/mL * year) was calculated as the sum of exposure * duration for each job position. A mean exposure concentration (MEC), also referred to as averaged exposure (AEL) was also calculated and expressed in fibers/mL). Clin et al. 2009, HERO ID: 3520549 and Boulanger et al. 2017, HERO ID: 3077730 explain these same methods but in lesser detail. Clin et al. 2011, HERO ID: 3078903 uses CEI and AEL exposure categories with a 10-year lag to account for latency.
	Metric 5:	Exposure Levels	Medium	To estimate cancer risk, only Clin et al. 2011, HERO ID: 3078903 categorized asbestos exposure variables using 3 ordinal levels.In Clin et al. 2009, HERO ID: 3520549 and Boulanger et al. 2015, HERO ID: 307773, SIRs are only calculated using 2 exposure categories of cumulative exposure, such as exposed/unexposed or <= vs > 80 fibers/mL-year, all of which merit a Low rating for this metric. In de la Provote et al. 2002, HERO ID: 3520580, only the "All digestive cancers" outcomes in analyzed with more than dichotomous exposure categories, but is evaluated in a different entry because the outcome is rated differently. All other outcomes in that study have dichotomous exposure categories. Because of this, de la Provote et al. 2002, HERO ID: 3520580, Clin et al. 2009, HERO ID: 3520549, and Boulanger et al. 2015, HERO ID: 307773, are only evaluated for metrics 4 and 5 in this entry.
	Metric 6:	Temporality	High	While Clin et al. 2011, HERO ID: 3078903 gives limited detail on temporality, de la Provote et al. 2002, HERO ID: 3520580 shows that 69% of workers had at least 10 years at work, and 50% had >= 20 years.
Domain 3: Outcome Assessment				

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Study Citation:	e La Provôté, S., Desoubeaux, N., Paris, C., Letourneux, M., Raffaelli, C., Galateau-Salle, F., Gignoux, M., Launoy, G. (2002). Incidence of digestive cancers and occupational exposure to asbestos. European Journal of Cancer Prevention 11(6):523-528.
Health Outcome:	Lung Cancer; colorectal, prostate, skin cancer, ear/nose/throat (ENT) cancer, bladder and kidney cancer, esophageal cancer, female genital tract cancer
Target Organ(s):	Gastrointestinal: Colon-rectum cancer, Esophagus cancer; Cancer/Carcinogenesis: Colon-rectum cancer, Esophagus cancer, Prostate cancer, Skin cancer (excluding basal cell tumors), Ear nose throat (ENT) cancer, Bladder and kidney cancer, Female genital tract cancer, Lung cancer; Reproductive/Developmental: Prostate cancer, Female genital tract cancer; Skin/Connective Tissue: Skin cancer (excluding basal cell tumors); nan: ; Renal/Kidney: Bladder and kidney cancer; Lung/Respiratory: Lung cancer
Asbestos Fiber Type(s):	Asbestos - Chrysotile (serpentine): 12001-29-5; Asbestos - Crocidolite (riebeckite): 12001-28-4
Linked HERO ID(s):	3520580, 3077730, 3078903, 3520549
HERO ID:	3520580

Domain	Metric		Rating	Comments
	Metric 7:	Outcome Measurement or Characterization	High	Lung Cancer: In Clin et al. 2011, HERO ID: 3078903, lung cancer incidence outcomes were characterized by histology in a cancer registry: ”The incidence of cancer was accordingly estimated for each anatomical cancer site (ICD-O 3 coding). Only primary cancers were taken into account in our study, secondary cancer sites having been excluded. No subjects presented with secondary cancer at the same site. For subjects presenting with primary cancers at different anatomical sites, each cancer was considered independently in our analysis.” ”The table in the online supplementary appendix lists (ICD-O 3 codes) the number of observed cancers for the entire cohort site by site and separately for each sex, together with latency (time to diagnosis since first exposure) and age at diagnosis.” At the time of evaluation, the supplemental material was not freely available and thus cannot be taken into account. However, because cases were diagnosed with histologies, this metric is rated High.; Other Cancer(s): In Clin et al. 2011, HERO ID: 3078903, lung cancer incidence outcomes were characterized by histology in a cancer registry: ”The incidence of cancer was accordingly estimated for each anatomical cancer site (ICD-O 3 coding). Only primary cancers were taken into account in our study, secondary cancer sites having been excluded. No subjects presented with secondary cancer at the same site. For subjects presenting with primary cancers at different anatomical sites, each cancer was considered independently in our analysis.” ”The table in the online supplementary appendix lists (ICD-O 3 codes) the number of observed cancers for the entire cohort site by site and separately for each sex, together with latency (time to diagnosis since first exposure) and age at diagnosis.” At the time of evaluation, the supplemental material was not freely available and thus cannot be taken into account. However, because cases were diagnosed with histologies, this metric is rated High.
	Metric 8:	Reporting Bias	High	Clin et al. 2011, HERO ID: 3078903 reported findings in the abstract, results, and discussion sections adequately, where confidence intervals are provided for relative risk estimates. P-values and numbers of cases were also presented in detail.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	High	Clin et al. 2011, HERO ID: 3078903 adjusted models by sex and age (time dependent). Data on smoking were not available. Race was not discussed, although it is likely that the population was largely white.
	Metric 10:	Covariate Characterization	Medium	Information on covariates was obtained from the company’s occupational health department records.
	Metric 11:	Co-exposure Counfounding	Low	There was no discussion of coexposures at these factories.

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Study Citation:	e La Provôté, S., Desoubeaux, N., Paris, C., Letourneux, M., Raffaelli, C., Galateau-Salle, F., Gignoux, M., Launoy, G. (2002). Incidence of digestive cancers and occupational exposure to asbestos. European Journal of Cancer Prevention 11(6):523-528.
Health Outcome:	Lung Cancer; colorectal, prostate, skin cancer, ear/nose/throat (ENT) cancer, bladder and kidney cancer, esophageal cancer, female genital tract cancer
Target Organ(s):	Gastrointestinal: Colon-rectum cancer, Esophagus cancer; Cancer/Carcinogenesis: Colon-rectum cancer, Esophagus cancer, Prostate cancer, Skin cancer (excluding basal cell tumors), Ear nose throat (ENT) cancer, Bladder and kidney cancer, Female genital tract cancer, Lung cancer; Reproductive/Developmental: Prostate cancer, Female genital tract cancer; Skin/Connective Tissue: Skin cancer (excluding basal cell tumors); nan: ; Renal/Kidney: Bladder and kidney cancer; Lung/Respiratory: Lung cancer
Asbestos Fiber Type(s):	Asbestos - Chrysotile (serpentine): 12001-29-5; Asbestos - Crocidolite (riebeckite): 12001-28-4
Linked HERO ID(s):	3520580, 3077730, 3078903, 3520549
HERO ID:	3520580

Domain	Metric		Rating	Comments
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	Medium	Clin et al. 2011, HERO ID: 3078903 used a Cox hazard model to analyze the dose-response relationship of occupational asbestos exposure and risk of cancer.
	Metric 13:	Statistical Power	Medium	Clin et al. 2011, HERO ID: 3078903 likely has adequate power to detect an association (total n=2024), with the cancer having the fewest cases being for female genital tract cancer (n=15).
	Metric 14:	Reproducibility of Analyses	Medium	The descriptions of analyses are clear and sufficiently well-written to conceptually reproduce analyses.
	Metric 15:	Statistical Analysis	Medium	The authors describe appropriate methods, including using exposure lags, categorizing exposure to avoid assumptions of linearity, and examining alternative time scales in Cox models.

Additional Comments: Note that for de la Provote et al. 2002, HERO ID: 3520580, Clin et al. 2009, HERO ID: 3520549 and Boulanger et al. 2015, HERO ID: 307773, SIRs are only calculated using 2 exposure categories of cumulative exposure, such as exposed/unexposed or <= vs > 80 fibers/mL-year, all of which merit a Low rating for this metric. Because of this, de la Provote et al. 2002, HERO ID: 3520580, Clin et al. 2009, HERO ID: 3520549, and Boulanger et al. 2015, HERO ID: 307773 are only evaluated for metrics 4 and 5, and QC was not performed for any other metrics. Only Clin et al. 2011, HERO ID: 3078903 was evaluated for all metrics. The only outcomes evaluated here are lung, colorectal, prostate, skin, ear/nose/throat (ENT), bladder and kidney, esophageal, female genital tract cancers.

Overall Quality Determination **Medium**

* No biomarkers were identified for this evaluation.

Study Citation:	Ehrlich, R., Lilis, R., Chan, E., Nicholson, W. J., Selikoff, I. J. (1992). Long term radiological effects of short term exposure to amosite asbestos among factory workers. British Journal of Industrial Medicine 49(4):268-275.		
Health Outcome:	Asbestosis		
Target Organ(s):	Lung/Respiratory: parenchymal abnormality, pleural abnormality		
Asbestos Fiber Type(s):	Asbestos - Amosite (grunerite): 12172-73-5		
Linked HERO ID(s):	No linked references.		
HERO ID:	709723		

Domain	Metric		Rating	Comments
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Low	Exposure was estimated on professional judgement by using information on job tile and duration of service for each subject. The fibre count estimates were used to derive the average fibre concentration and cumulative exposure for each subject.
	Metric 5:	Exposure Levels	Low	Range of exposure in the population is limited. The estimated counts ranged from 5 fibres/ml among office workers, to 120 fibres/ml among disintegrator operators.

Additional Comments: This is an occupational study with no appropriate mention of the comparison group. It looks for parenchymal and pleural abnormalities and asbestosis among factory workers.Overall, the measurement of exposure metric (M4) methods used to quantify the exposure were not well defined. Additionally, the exposure levels metric (M5) information reported was not adequate to determine an exposure-response relationship.

* No biomarkers were identified for this evaluation.

** As described in Appendix B.2 of the *White Paper: Quantitative Approach to the Human Health Assessment for the Risk Evaluation for Asbestos Part 2: Supplemental Evaluation Including Legacy Uses and Associated Disposals of Asbestos*, to be considered as being informative for dose-response analysis, metrics 4 and 5 would need metric ratings of Medium or High. This reference did not satisfy this requirement; therefore data quality evaluation is presented for only for metrics 4 and 5.

Study Citation:	Eisenhawer, C., Felten, M. K., Tamm, M., Das, M., Kraus, T. (2014). Radiological surveillance of formerly asbestos-exposed power industry workers: rates and risk factors of benign changes on chest X-ray and MDCT. Journal of Occupational Medicine and Toxicology 9:18.		
Health Outcome:	Asbestosis; Pleural Plaques; Diffuse pleural thickening, parenchymal or pleural changes		
Target Organ(s):	Lung/Respiratory: Asbestosis, Pleural plaques, Diffuse pleural thickening, Parenchymal or pleural changes		
Asbestos Fiber Type(s):	Asbestos - Not specified: 1332-21-4		
Linked HERO ID(s):	3077968, 2584064		
HERO ID:	3077968		

Domain	Metric	Rating	Comments
Domain 2: Exposure Characterization			
	Metric 4: Measurement of Exposure	Low	This study or any cited methods source does not explicitly mention the use of PCM or TEM.Individual cumulative exposure level was determined by self-reported job history and periods of exposure using a computer program based on ambient air monitoring data of asbestos concentration, recall bias is likely to be present. The measurement and quantifying methods were not specified. There is little information about exposure measurement and mainly based on professional judgement. Exposure misclassification is likely to exist according to the exposure measurement methods.Study cites another paper (Felten et al., 2010, 2584064) that discusses ambient asbestos measuring techniques with no indication of the use of PCM/TEM to measure fibers: "The ambient monitoring data used in the report covered a period of four decades from the beginning of the 1950s until 1990. In the 1970s, the original technique of konimetrical measurements was gradually replaced with membrane filter techniques applying a defined airflow. Both methods were not specific for asbestos fibres. That deficit was overcome by combining membranous filtering systems with the microscopical count of fibres."
	Metric 5: Exposure Levels	Medium	The distribution of cumulative exposure level is sufficient to develop an exposure-outcome estimate. The study used 3 levels of exposure.

Additional Comments: The main concern of this group of studies is exposure measurement, which is based on computer program and self-reported work history, could introduce exposure misclassification to the analysis. In addition, high attrition plus missing exposure values could impact the accuracy of the results.

* No biomarkers were identified for this evaluation.

** As described in Appendix B.2 of the *White Paper: Quantitative Approach to the Human Health Assessment for the Risk Evaluation for Asbestos Part 2: Supplemental Evaluation Including Legacy Uses and Associated Disposals of Asbestos*, to be considered as being informative for dose-response analysis, metrics 4 and 5 would need metric ratings of Medium or High. This reference did not satisfy this requirement; therefore data quality evaluation is presented for only for metrics 4 and 5.

Study Citation:	Elci, O. C., Akpinar-Elci, M., Blair, A., Dosemeci, M. (2002). Occupational dust exposure and the risk of laryngeal cancer in Turkey. Scandinavian Journal of Work, Environment and Health 28(4):278-284.
Health Outcome:	Laryngeal Cancer; Supraglottic cancer, glottic cancer, other cancers
Target Organ(s):	Throat: All laryngeal cancers, Supraglottic cancer, Glottic cancer; Cancer/Carcinogenesis: Supraglottic cancer, All laryngeal cancers, Other cancers, Glottic cancer
Asbestos Fiber Type(s):	Asbestos - Not specified: 1332-21-4
Linked HERO ID(s):	No linked references.
HERO ID:	3080472

Domain	Metric		Rating	Comments
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Uninformative	This is marked as uninformative because there were no quantitative measure or estimate of exposure. Study does not discuss any use of fibre measurements. Authors discuss using a job-exposure matrix but provide no quantitative measures for this.
	Metric 5:	Exposure Levels	Medium	Job matrix exposure levels are provided by exposure intensity (low, medium, and high) and exposure probability levels (low, medium, and high).

Additional Comments: This study not evaluated for any metrics except Metric 4 and 5 and had no data extracted because it did not have sufficient exposure information to be useful for dose-response analysis.Overall, The Measurement of Exposure Metric 4 (M4) is Uninformative for this Study.

** As described in Appendix B.2 of the *White Paper: Quantitative Approach to the Human Health Assessment for the Risk Evaluation for Asbestos Part 2: Supplemental Evaluation Including Legacy Uses and Associated Disposals of Asbestos*, to be considered as being informative for dose-response analysis, metrics 4 and 5 would need metric ratings of Medium or High. This reference did not satisfy this requirement; therefore data quality evaluation is presented for only for metrics 4 and 5.

Study Citation:	Farioli, A., Straif, K., Brandi, G., Curti, S., Kjaerheim, K., Martinsen, J. I., Sparen, P., Tryggvadottir, L., Weiderpass, E., Biasco, G. (2018). Occupational exposure to asbestos and risk of cholangiocarcinoma: a population-based case-control study in four Nordic countries. Occupational and Environmental Medicine 75(3):191-198.
Health Outcome:	Cholangiocarcinoma
Target Organ(s):	Cancer/Carcinogenesis: Cholangiocarcinoma, Intrahepatic cholangiocarcinoma, Extrahepatic cholangiocarcinoma; Hepatic/Liver: Cholangiocarcinoma, Intrahepatic cholangiocarcinoma, Extrahepatic cholangiocarcinoma
Asbestos Fiber Type(s):	Asbestos - Not specified: 1332-21-4
Linked HERO ID(s):	5029590, 6875563
HERO ID:	5029590

Domain		Metric	Rating	Comments
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Low	This metric is rated low because the study or any cited methods sources do not explicitly mention the use of PCM or TEM (Farioli et al., 2018, 5029590). Exposure in this study was estimated using a generic job-exposure matrix that was specifically developed for this cohort, but did not include personal measurements based on PCM or TEM (Kauppinen et al., 2009, 699236).
	Metric 5:	Exposure Levels	Medium	A range of exposure levels are reported within the paper. The levels of maximum intensity of exposure reported include 0 f/mL, <0.11 f/mL, 0.11-0.79 f/mL, >/=0.80 f/mL (Farioli et al., 2018, 5029590). In Farioli et al. (2017, 5029590), the study reports cumulative exposure split into groups of 0 f/mL x years, 0.1-4.9 f/mL x years, 5.0-9.9 f/mL x years, 10.0-14.0 f/mL x years, and greater than or equal to 15.0 f/mL x years.

Additional Comments:	This study was not fully evaluated because metric 4 was rated as low. Neither this study nor any cited sources papers explicitly mentioned the use of PCM or TEM.

** As described in Appendix B.2 of the *White Paper: Quantitative Approach to the Human Health Assessment for the Risk Evaluation for Asbestos Part 2: Supplemental Evaluation Including Legacy Uses and Associated Disposals of Asbestos*, to be considered as being informative for dose-response analysis, metrics 4 and 5 would need metric ratings of Medium or High. This reference did not satisfy this requirement; therefore data quality evaluation is presented for only for metrics 4 and 5.

Study Citation:	Finkelstein, M. (1986). Pulmonary function in asbestos cement workers: a dose-response study. British Journal of Industrial Medicine 43(6):406-413.
Health Outcome:	Pulmonary Function/Spirometry Results
Target Organ(s):	Lung/Respiratory: FVC, FEV1, FEV1/FVC, FVC%, FEV1%, TLC, DLCO (mL/min/mmHg), DLCO (% predicted), KCO (mL/min/mmHg)
Asbestos Fiber Type(s):	Asbestos - Not specified: 1332-21-4
Linked HERO ID(s):	No linked references.
HERO ID:	2248137

Domain		Metric	Rating	Comments
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Low	Exposure was measured using personal membrane filters. Authors assumed a fixed proportion of workplace air concentrations deposited in the lungs of each subject, and each year's accumulation was weighted by residence time in lung tissue. Asbestos dosages were calculated as fibers/mL*years squared (y^2). Authors note that exposure assessment methods involved extrapolation, and that cumulative exposure values had been previously estimated to within a factor of 3-5.
	Metric 5:	Exposure Levels	Medium	Exposure distribution is not explicitly reported in text or table format, but is indicated by scatterplot (Figure 2). Asbestos doses (f/mL*y^2) appeared to vary from <500 to nearly 8,000. Exposure was assessed as a continuous, quantitative variable.

Additional Comments: None

* No biomarkers were identified for this evaluation.

** As described in Appendix B.2 of the *White Paper: Quantitative Approach to the Human Health Assessment for the Risk Evaluation for Asbestos Part 2: Supplemental Evaluation Including Legacy Uses and Associated Disposals of Asbestos*, to be considered as being informative for dose-response analysis, metrics 4 and 5 would need metric ratings of Medium or High. This reference did not satisfy this requirement; therefore data quality evaluation is presented for only for metrics 4 and 5.

Study Citation:	Finkelstein, M. M. (1997). Radiographic asbestosis is not a prerequisite for asbestos-associated lung cancer in Ontario asbestos-cement workers. American Journal of Industrial Medicine 32(4):341-348.
Health Outcome:	Lung Cancer
Target Organ(s):	Cancer/Carcinogenesis: lung cancer mortality; Lung/Respiratory: lung cancer mortality; Mortality: lung cancer mortality
Asbestos Fiber Type(s):	Asbestos - Chrysotile (serpentine): 12001-29-5; Asbestos - Crocidolite (riebeckite): 12001-28-4
Linked HERO ID(s):	No linked references.
HERO ID:	3081283

Domain	Metric		Rating	Comments
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Low	Authors state that estimates of exposure were calculated through the use of a ”model that extrapolated measurements made by the personal membrane filter” and did not utilize PCM or TEM. There appears to be a contradiction in time in that the personal membrane filters was utilized by the industrial in 1969 (21 years after the plant opened in 1948). The cohort includes workers hired prior to 1960 so it is unclear what exposure data was used for workers who had worked for there before 1969.
	Metric 5:	Exposure Levels	Medium	Estimates of 18-year cumulative exposure since first exposure is provided in Table 2 and Figure 1 in fiber-years/ml for 5 groups.

Additional Comments: Majority of analyses were conducted to assess the lung cancer risk among those with and without asbestosis.

* No biomarkers were identified for this evaluation.

** As described in Appendix B.2 of the *White Paper: Quantitative Approach to the Human Health Assessment for the Risk Evaluation for Asbestos Part 2: Supplemental Evaluation Including Legacy Uses and Associated Disposals of Asbestos*, to be considered as being informative for dose-response analysis, metrics 4 and 5 would need metric ratings of Medium or High. This reference did not satisfy this requirement; therefore data quality evaluation is presented for only for metrics 4 and 5.

Study Citation:	Finkelstein, M. M. (1997). Radiographic asbestosis is not a prerequisite for asbestos-associated lung cancer in Ontario asbestos-cement workers. American Journal of Industrial Medicine 32(4):341-348.
Health Outcome:	digestive
Target Organ(s):	Cancer/Carcinogenesis: digestive cancer mortality; Gastrointestinal: digestive cancer mortality; Mortality: digestive cancer mortality
Asbestos Fiber Type(s):	Asbestos - Chrysotile (serpentine): 12001-29-5; Asbestos - Crocidolite (riebeckite): 12001-28-4
Linked HERO ID(s):	No linked references.
HERO ID:	3081283

Domain	Metric		Rating	Comments
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Low	Authors state that estimates of exposure were calculated through the use of a ”model that extrapolated measurements made by the personal membrane filter” and did not utilize PCM or TEM. There appears to be a contradiction in time in that the personal membrane filters was utilized by the industrial in 1969 (21 years after the plant opened in 1948). The cohort includes workers hired prior to 1960 so it is unclear what exposure data was used for workers who had worked there before 1969.
	Metric 5:	Exposure Levels	Medium	Estimates of 18-year cumulative exposure since first exposure is provided in Table 2 and Figure 1 in fiber-years/ml for 5 groups.

Additional Comments: None

* No biomarkers were identified for this evaluation.

** As described in Appendix B.2 of the *White Paper: Quantitative Approach to the Human Health Assessment for the Risk Evaluation for Asbestos Part 2: Supplemental Evaluation Including Legacy Uses and Associated Disposals of Asbestos*, to be considered as being informative for dose-response analysis, metrics 4 and 5 would need metric ratings of Medium or High. This reference did not satisfy this requirement; therefore data quality evaluation is presented for only for metrics 4 and 5.

Study Citation:	Finkelstein, M. M. (1997). Radiographic asbestosis is not a prerequisite for asbestos-associated lung cancer in Ontario asbestos-cement workers. American Journal of Industrial Medicine 32(4):341-348.
Health Outcome:	circulatory disease, respiratory disease, pneumoconiosis
Target Organ(s):	Mortality: all causes mortality, all malignancies mortality, respiratory disease mortality, pneumoconiosis mortality, Pleural mesothelioma mortality, circulatory disease mortality; Cardiovascular: circulatory disease mortality; Lung/Respiratory: respiratory disease mortality, pneumoconiosis mortality, Pleural mesothelioma mortality
Asbestos Fiber Type(s):	Asbestos - Chrysotile (serpentine): 12001-29-5; Asbestos - Crocidolite (riebeckite): 12001-28-4
Linked HERO ID(s):	No linked references.
HERO ID:	3081283

Domain	Metric		Rating	Comments
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Low	Authors state that estimates of exposure were calculated through the use of a "model that extrapolated measurements made by the personal membrane filter" and did not utilize PCM or TEM. There appears to be a contradiction in time in that the personal membrane filters was utilized by the industrial in 1969 (21 years after the plant opened in 1948). The cohort includes workers hired prior to 1960 so it is unclear what exposure data was used for workers who had worked for there before 1969.
	Metric 5:	Exposure Levels	Medium	Estimates of 18-year cumulative exposure since first exposure is provided in Table 2 and Figure 1 in fiber-year/ml for 5 groups.

Additional Comments: While pleural mesothelioma is a reported outcome for Table 1, it did not seem to warrant a standalone data evaluation due to the lack of available findings.

* No biomarkers were identified for this evaluation.

** As described in Appendix B.2 of the *White Paper: Quantitative Approach to the Human Health Assessment for the Risk Evaluation for Asbestos Part 2: Supplemental Evaluation Including Legacy Uses and Associated Disposals of Asbestos*, to be considered as being informative for dose-response analysis, metrics 4 and 5 would need metric ratings of Medium or High. This reference did not satisfy this requirement; therefore data quality evaluation is presented for only for metrics 4 and 5.

Study Citation: Finkelstein, M. M. (1984). Mortality among employees of an Ontario asbestos-cement factory. American Review of Respiratory Disease 129(5):754-761.
Health Outcome: overall mortality, non-malignant respiratory disease mortality, and ischemic heart disease mortality
Target Organ(s): Mortality: overall mortality, non-malignant respiratory disease mortality, ischemic heart disease mortality; Lung/Respiratory: non-malignant respiratory disease mortality; Cardiovascular: ischemic heart disease mortality
Asbestos Fiber Type(s): Asbestos - Chrysotile (serpentine): 12001-29-5; Asbestos - Crocidolite (riebeckite): 12001-28-4
Linked HERO ID(s): No linked references.
HERO ID: 3083612

Domain	Metric		Rating	Comments
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Low	This metric is rated Low because the study or any cited methods source does not explicitly mention the use of PCM or TEM. The estimated average cumulative exposure of the production workers was about 60 fiber-years/mL (chrysotile and crocidolite). The estimated mean cumulative exposure within the board shop, in which chrysotile was the sole asbestos type utilized, was 39 f-y/mL. Air sampling data from government, insurance and company hygienists initiated in late 1969 were utilized along with company employment records to classify each production worker (n=186) according to estimated annual cumulative asbestos exposure as described within Finkelstein et al., 1983 (HERO ID 3100548), which also referenced Finkelstein, 1982 (HERO ID 76). Microscopic method of fiber analysis (PCM or TEM) was not detailed in main or referenced text. Air sampling data was obtained from only later factory years (late 1969 onward) and was not representative of earlier years, although assumptions for exposure levels for those earlier years were supported by impinger area sampling data. Air sampling data from government, insurance and company hygienists initiated in late 1969 were utilized along with company employment records to classify each production worker (n=186) according to estimated annual cumulative asbestos exposure as described within Finkelstein et al., 1983 (HERO ID 3100548) and Finkelstein, 1982 (HERO ID 76). Eighteen-year cumulative exposures were calculated for the production workers (Table 7) by combining work histories and exposure estimates, with job-related exposures multiplied by the time spent at each job and summed over the 18 years from first exposure. Workers were assigned to an exposure category according to their 18-year exposure totals. Exposures were assumed to have been unchanged from 1962 to 1970, to have been 30% higher from 1955 to 1961, and to have been twice as high from 1948 to 1954, with assumptions supported by impinger area sampling performed 1949 through the 1960's. Raw materials in the production worker pipe manufacturing process included cement, silica and both chrysotile and crocidolite asbestos, while the asbestos cement board production utilized chrysotile asbestos only. Comparison control workers were primarily within the rock wool/fiberglass insulation production area, although authors noted it was possible for employees to be assigned to the pipe shop for brief clean-up duties, or re-assigned from non-asbestos to asbestos work areas, such that some control workers were exposed as well. Exposures for maintenance workers were not calculated due to inadequate data.
	Metric 5:	Exposure Levels	Medium	The range and distribution of asbestos exposure in Table 7 presented across five exposure categories ranging from <=30 fiber-years/ML through >150 fiber-years/mL for production workers is sufficient to develop an exposure-response estimate.

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Study Citation:	Finkelstein, M. M. (1984). Mortality among employees of an Ontario asbestos-cement factory. American Review of Respiratory Disease 129(5):754-761.
Health Outcome:	overall mortality, non-malignant respiratory disease mortality, and ischemic heart disease mortality
Target Organ(s):	Mortality: overall mortality, non-malignant respiratory disease mortality, ischemic heart disease mortality; Lung/Respiratory: non-malignant respiratory disease mortality; Cardiovascular: ischemic heart disease mortality
Asbestos Fiber Type(s):	Asbestos - Chrysotile (serpentine): 12001-29-5; Asbestos - Crocidolite (riebeckite): 12001-28-4
Linked HERO ID(s):	No linked references.
HERO ID:	3083612

Domain	Metric	Rating	Comments
Additional Comments:	QC was not completed for metrics other than Metrics 4 and 5 because the study does not have sufficient exposure information to be useful for dose-response analysis.NOTE: This study would not be fully evaluated under the current guidelines. This is due to the low rating for metric 4, as no PCM or TEM was mentioned in the study or a cited source.Within this retrospective cohort study, mortality among asbestos exposed (n=535, production and maintenance workers) and control (n=205) male employees (total n=740) of an asbestos cement pipe manufacturing factory with a minimum of one year employment who had been hired prior to 1960 was compared with mortality of the Ontario, Canada male general population over a period of 10 to 34 years of follow-up. Workers were divided into three groups for study: production workers involved in asbestos cement pipe manufacture, maintenance workers, and those involved in rock wool and fiberglass insulation or other minimal exposure areas who were classified as non-exposed controls. Factory production of asbestos cement pipe in one shed and rock wool (later fiberglass) insulation in another shed began in 1948, and asbestos cement board was produced in a separate building from 1955 to 1970. Air sampling data from government, insurance and company hygienists initiated in late 1969 were utilized along with company employment records to classify each production worker (n=186) according to estimated annual cumulative asbestos exposure. Air sampling data was obtained from only later factory years (late 1969 onward) and was not representative of earlier years, although assumptions for exposure levels for those earlier years were supported by impinger area sampling data. In the period 20 years from first exposure, the production workers had a standardized mortality ratio of 181 for all causes of death, 320 for non-malignant respiratory disease, and 58 for ischemic heart disease.		

* No biomarkers were identified for this evaluation.

** As described in Appendix B.2 of the *White Paper: Quantitative Approach to the Human Health Assessment for the Risk Evaluation for Asbestos Part 2: Supplemental Evaluation Including Legacy Uses and Associated Disposals of Asbestos*, to be considered as being informative for dose-response analysis, metrics 4 and 5 would need metric ratings of Medium or High. This reference did not satisfy this requirement; therefore data quality evaluation is presented for only for metrics 4 and 5.

Study Citation:	Finkelstein, M. M. (1984). Mortality among employees of an Ontario asbestos-cement factory. American Review of Respiratory Disease 129(5):754-761.
Health Outcome:	Lung Cancer; gastrointestinal cancer
Target Organ(s):	Lung/Respiratory: Lung cancer mortality; Cancer/Carcinogenesis: Lung cancer mortality, Gastrointestinal cancer; Mortality: Lung cancer mortality, Gastrointestinal cancer; Gastrointestinal: Gastrointestinal cancer
Asbestos Fiber Type(s):	Asbestos - Chrysotile (serpentine): 12001-29-5; Asbestos - Crocidolite (riebeckite): 12001-28-4
Linked HERO ID(s):	No linked references.
HERO ID:	3083612

Domain	Metric		Rating	Comments
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Low	This metric is rated Low because the study or any cited methods source does not explicitly mention the use of PCM or TEM.The estimated average cumulative exposure of the production workers was about 60 fiber-years/mL (chrysotile and crocidolite). The estimated mean cumulative exposure within the board shop, in which chrysotile was the sole asbestos type utilized, was 39 f-y/mL. Air sampling data from government, insurance and company hygienists initiated in late 1969 were utilized along with company employment records to classify each production worker (n=186) according to estimated annual cumulative asbestos exposure as described within Finkelstein et al., 1983 (HERO ID 3100548), which also referenced Finkelstein, 1982 (HERO ID 76). Microscopic method of fiber analysis (PCM or TEM) was not detailed in main or referenced text. Air sampling data was obtained from only later factory years (late 1969 onward) and was not representative of earlier years, although assumptions for exposure levels for those earlier years were supported by impinger area sampling data. Air sampling data from government, insurance and company hygienists initiated in late 1969 were utilized along with company employment records to classify each production worker (n=186) according to estimated annual cumulative asbestos exposure as described within Finkelstein et al., 1983 (HERO ID 3100548) and Finkelstein, 1982 (HERO ID 76). Eighteen-year cumulative exposures were calculated for the production workers (Table 7) by combining work histories and exposure estimates, with job-related exposures multiplied by the time spent at each job and summed over the 18 years from first exposure. Workers were assigned to an exposure category according to their 18-year exposure totals. Exposures were assumed to have been unchanged from 1962 to 1970, to have been 30% higher from 1955 to 1961, and to have been twice as high from 1948 to 1954, with assumptions supported by impinger area sampling performed 1949 through the 1960's. Raw materials in the production worker pipe manufacturing process included cement, silica and both chrysotile and crocidolite asbestos, while the asbestos cement board production utilized chrysotile asbestos only. Comparison control workers were primarily within the rock wool/fiberglass insulation production area, although authors noted it was possible for employees to be assigned to the pipe shop for brief clean-up duties, or re-assigned from non-asbestos to asbestos work areas, such that some control workers were exposed as well. Exposures for maintenance workers were not calculated due to inadequate data.
	Metric 5:	Exposure Levels	Medium	The range and distribution of asbestos exposure in Table 7 presented across five exposure categories ranging from <=30 fiber-years/ML through >150 fiber-years/mL for production workers is sufficient to develop an exposure-response estimate.

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Study Citation:	Finkelstein, M. M. (1984). Mortality among employees of an Ontario asbestos-cement factory. American Review of Respiratory Disease 129(5):754-761.
Health Outcome:	Lung Cancer; gastrointestinal cancer
Target Organ(s):	Lung/Respiratory: Lung cancer mortality; Cancer/Carcinogenesis: Lung cancer mortality, Gastrointestinal cancer; Mortality: Lung cancer mortality, Gastrointestinal cancer; Gastrointestinal: Gastrointestinal cancer
Asbestos Fiber Type(s):	Asbestos - Chrysotile (serpentine): 12001-29-5; Asbestos - Crocidolite (riebeckite): 12001-28-4
Linked HERO ID(s):	No linked references.
HERO ID:	3083612

Domain	Metric	Rating	Comments
Additional Comments:	QC was not completed for metrics other than Metrics 4 and 5 because the study does not have sufficient exposure information to be useful for dose-response analysis.NOTE: this study was not evaluated for any metrics except Metric 4 and 5 and had no data extracted because it did not have sufficient exposure information to be useful for dose-response analysis. Within this retrospective cohort study, mortality among asbestos exposed (n=535, production and maintenance workers) and control (n=205) male employees (total n=740) of an asbestos cement pipe manufacturing factory with a minimum of one year employment who had been hired prior to 1960 was compared with mortality of the Ontario, Canada male general population over a period of 10 to 34 years of follow-up. Workers were divided into three groups for study: production workers involved in asbestos cement pipe manufacture, maintenance workers, and those involved in rock wool and fiberglass insulation or other minimal exposure areas who were classified as non-exposed controls. Factory production of asbestos cement pipe in one shed and rock wool (later fiberglass) insulation in another shed began in 1948, and asbestos cement board was produced in a separate building from 1955 to 1970. Air sampling data from government, insurance and company hygienists initiated in late 1969 were utilized along with company employment records to classify each production worker (n=186) according to estimated annual cumulative asbestos exposure. Air sampling data was obtained from only later factory years (late 1969 onward) and was not representative of earlier years, although assumptions for exposure levels for those earlier years were supported by impinger area sampling data. In the period 20 years from first exposure, the production workers had a standardized mortality ratio of 181 for all causes of death, 320 for non-malignant respiratory disease, and 58 for ischemic heart disease.		

* No biomarkers were identified for this evaluation.

** As described in Appendix B.2 of the *White Paper: Quantitative Approach to the Human Health Assessment for the Risk Evaluation for Asbestos Part 2: Supplemental Evaluation Including Legacy Uses and Associated Disposals of Asbestos*, to be considered as being informative for dose-response analysis, metrics 4 and 5 would need metric ratings of Medium or High. This reference did not satisfy this requirement; therefore data quality evaluation is presented for only for metrics 4 and 5.

Study Citation:	Finkelstein, M. M. (1983). Mortality among long-term employees of an Ontario (Canada) asbestos-cement factory. British Journal of Industrial Medicine 40(2):138-144.
Health Outcome:	Lung Cancer
Target Organ(s):	Mortality: Lung cancer mortality; Cancer/Carcinogenesis: Lung cancer mortality; Lung/Respiratory: Lung cancer mortality
Asbestos Fiber Type(s):	Asbestos - Chrysotile (serpentine): 12001-29-5; Asbestos - Crocidolite (riebeckite): 12001-28-4
Linked HERO ID(s):	No linked references.
HERO ID:	3100548

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Medium	Key elements of the study design were reported within this retrospective cohort study of long-term male workers in which n=339 male asbestos workers hired prior to 1960 and employed by the same company in Ontario, Canada for at least nine years were followed until 31 October 1980 for mortality outcomes of interest. An additional n=11 men (3.2% of the total) could not be properly classified from their work histories as production, maintenance or rock wool/fiberglass workers and were excluded from the current analysis. Participants were identified from company records of all hourly and salaried employees who had worked at the plant of interest. Employees were excluded if they did not work for at least nine years to account for the long latency of asbestos-related diseases and difficulties of tracing short-term employees. There is no evidence to suggest inclusion or exclusion from the sample differed significantly by outcome or exposure status.
	Metric 2:	Attrition	Low	Official death certificates were obtained for all men who had died. However, a total of five (2.7%) of the n=186 production workers, three (5.5%) of the n=55 maintenance workers and five (5.7%) of the n=87 unexposed or minimally exposed workers were unable to be traced for mortality outcomes and were assumed still alive for analysis. A group of 55 maintenance workers were originally included, but later excluded as the study reported that it ”was not thought possible to estimate exposures for the maintenance men.”

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Study Citation:	Finkelstein, M. M. (1983). Mortality among long-term employees of an Ontario (Canada) asbestos-cement factory. British Journal of Industrial Medicine 40(2):138-144.
Health Outcome:	Lung Cancer
Target Organ(s):	Mortality: Lung cancer mortality; Cancer/Carcinogenesis: Lung cancer mortality; Lung/Respiratory: Lung cancer mortality
Asbestos Fiber Type(s):	Asbestos - Chrysotile (serpentine): 12001-29-5; Asbestos - Crocidolite (riebeckite): 12001-28-4
Linked HERO ID(s):	No linked references.
HERO ID:	3100548

Domain	Metric		Rating	Comments
	Metric 3:	Comparison Group	Medium	Inclusion criteria and methods of participant selection were reported. Workers within the rock wool/fiber glass operations (n=87) were classified as minimally exposed, had mortality described as similar to the general male Ontario population and were utilized as the comparison control workers. SMR analyses results utilized the age and calendar specific mortality experience of the male Ontario general population as a comparison group for expected mortality rates. The mean age at the start of exposure or employment was described as similar between the exposed and general populations. Comparison control workers were primarily within the rock wool/fiberglass insulation production area, although the author of the current study noted in another publication (Finkelstein et al., 1983, HERO ID 3083612) of workers in the same factory that it was possible for employees to be assigned to the pipe shop for brief clean-up duties, or re-assigned from non-asbestos to asbestos work areas, such that some control workers may have been exposed as well. There is potential for healthy worker effect in terms of left truncation bias, as the cohort for the current study was restricted to workers with at least nine years of employment, such that all workers had to survive for at least nine years to be included. However, Table 2 SMR results for non-malignant respiratory disease indicate no evidence of healthy worker effect in terms of the healthy hire or healthy worker survivor effect.

Domain 2: Exposure Characterization

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Study Citation:	Finkelstein, M. M. (1983). Mortality among long-term employees of an Ontario (Canada) asbestos-cement factory. British Journal of Industrial Medicine 40(2):138-144.
Health Outcome:	Lung Cancer
Target Organ(s):	Mortality: Lung cancer mortality; Cancer/Carcinogenesis: Lung cancer mortality; Lung/Respiratory: Lung cancer mortality
Asbestos Fiber Type(s):	Asbestos - Chrysotile (serpentine): 12001-29-5; Asbestos - Crocidolite (riebeckite): 12001-28-4
Linked HERO ID(s):	No linked references.
HERO ID:	3100548

Domain	Metric		Rating	Comments
	Metric 4:	Measurement of Exposure	Medium	The microscopic method (PCM or TEM) of analysis of air sampling data reported in Table 1 with outcome mortality rates was not detailed. The average estimated cumulative exposure among production workers was reported for three groups of production workers of 62 men each as 44 f-y/ml, 92 f-y/ml, and 180 f-y/mL (chrysotile and crocidolite). Groups were created on the basis of ranking 18-year cumulative exposures. Air sampling data from government, insurance and company hygienists initiated in late 1969 was utilized along with company employment records to classify each production worker's exposure, however production within the plant began in 1948 and measured exposures for periods 1948-1970 were lacking and assumed as related to the quantitative measurements made beginning in 1969. Exposures for maintenance workers was described as not calculated due to inadequate data. Estimated cumulative exposure for only the first 18 years of employment was utilized such that for men employed less than 18 years this parameter was used and for men employed more than 18 years, the potential exposures after 18 years were excluded. Exposures were assumed to have been unchanged from 1962 to 1970, to have been 30% higher from 1955 to 1961, and to have been twice as high from 1948 to 1954, with assumptions supported by impinger area sampling performed 1949 through the 1960's. Based on subsequent discussion and review of additional information, the rating was adjusted based on impinger data was collected and personal membrane sampling was conducted beginning in late 1969 and detailed employment records were used to construct exposure histories.
	Metric 5:	Exposure Levels	Medium	The range and distribution of estimated exposures is reported within Table 1 for production workers as 8 to 420 fiber-years/mL. Table 1 provides the mortality rates for production workers across three groups of exposure categories.
	Metric 6:	Temporality	High	The study presents an appropriate temporality and the interval between exposure and outcome is appropriate considering the latency of disease. Workers were required to have been hired before 1960 and were followed up until 1980, ensuring at least 20 years of follow-up for the cohort
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	High	Lung Cancer: ICD code 162 was utilized for lung cancer outcomes on official death certificates for all men who had died. Additional clinical, pathological and necropsy reports were available for n=44 of the n=58 deaths among production workers and are used in analyses of exposure duration, but not of exposure concentration.
	Metric 8:	Reporting Bias	Medium	There were no concerns for selective reporting. SMR's in Table 2 and mortality rates across age and time since first exposure groups per man years in production workers in Table 3 were reported as single values, with no measures of variation or confidence intervals. Confidence intervals for specific outcomes were reported within the text.

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Study Citation:	Finkelstein, M. M. (1983). Mortality among long-term employees of an Ontario (Canada) asbestos-cement factory. British Journal of Industrial Medicine 40(2):138-144.
Health Outcome:	Lung Cancer
Target Organ(s):	Mortality: Lung cancer mortality; Cancer/Carcinogenesis: Lung cancer mortality; Lung/Respiratory: Lung cancer mortality
Asbestos Fiber Type(s):	Asbestos - Chrysotile (serpentine): 12001-29-5; Asbestos - Crocidolite (riebeckite): 12001-28-4
Linked HERO ID(s):	No linked references.
HERO ID:	3100548

Domain	Metric		Rating	Comments
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Medium	Other than stratification for years since first exposure and age, no additional adjustments or consideration for differences between exposed and non-exposed groups regarding distributions of relevant covariates were detailed. The cohort for study was restricted to males. The authors mention that information for smoking was available for 70% of the cohort, but this information is not used in statistical analyses. The authors state that data was available for 17 of 20 men who had died of lung cancer: 1 never smoked, 2 had quit for 10 or more years, and 14 were smokers. Based on subsequent discussion and review of additional information, the rating was adjusted based on stratification by age and only males being included in the study.
	Metric 10:	Covariate Characterization	Medium	Finkelstein, 1982 provides evidence of detailed personnel files use for TSFE, age, job history, etc.
	Metric 11:	Co-exposure Counfounding	Medium	For lung cancer, there was no evidence of co-exposure or unbalanced provision of co-exposures.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	Medium	The study design was appropriate as an early study to address the research aims. Two types of comparisons were performed, internal and external. Table 2 SMR results were obtained through external comparisons by applying the Ontario general population mortality rates as reference and presented for production, maintenance and control workers. Table 3 mortality rate results were presented for production workers stratified across age and years since first exposure groups. Tests for trend were not reported.
	Metric 13:	Statistical Power	Medium	The number of participants was adequate, however formal statistical comparisons between exposed and non-exposed workers, or across time since first exposure groups, were not presented. SMR results in Table 2 were reported for the n=328 workers, while results in Table 3 were reported only for the n=186 production workers.
	Metric 14:	Reproducibility of Analyses	Medium	The data are presented in Table 1 that were used used in the 1986 analysis. Reporting errors are present in Table 2, but these data are not used in the 1986 analysis.
	Metric 15:	Statistical Analysis	Medium	Model building was not conducted. The construction of SMRs appears appropriate.

Additional Comments: This was an occupational retrospective cohort study reporting SMRs of long-term male workers in which n=339 male asbestos workers hired prior to 1960 and employed by the same company in Ontario, Canada for at least nine years were followed until 31 October 1980 for mortality outcomes of interest. Concerns included the assumption that workers unable to be traced for mortality outcomes were still alive at the end of follow-up, with no sensitivity analyses conducted to examine results with and without these workers. Lung cancer mortality was obtained utilizing pre-ICD 10 coding. Exposure concentrations are provided for three groups of exposure in relation to a reference population of Ontario men by outcome - however, no statistical analysis is done to compare mortality using exposure concentration data, limiting the study's usefulness for dose-response analysis.

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Study Citation:	Finkelstein, M. M. (1983). Mortality among long-term employees of an Ontario (Canada) asbestos-cement factory. British Journal of Industrial Medicine 40(2):138-144.
Health Outcome:	Lung Cancer
Target Organ(s):	Mortality: Lung cancer mortality; Cancer/Carcinogenesis: Lung cancer mortality; Lung/Respiratory: Lung cancer mortality
Asbestos Fiber Type(s):	Asbestos - Chrysotile (serpentine): 12001-29-5; Asbestos - Crocidolite (riebeckite): 12001-28-4
Linked HERO ID(s):	No linked references.
HERO ID:	3100548

Domain	Metric	Rating	Comments
Overall Quality Determination		**Medium**	

* No biomarkers were identified for this evaluation.

Study Citation:	Finkelstein, M. M. (1983). Mortality among long-term employees of an Ontario (Canada) asbestos-cement factory. British Journal of Industrial Medicine 40(2):138-144.
Health Outcome:	gastrointestinal cancer mortality; all-cause mortality, non-malignant respiratory disease mortality, ischemic heart disease mortality
Target Organ(s):	Mortality: All causes mortality, All malignancies mortality, Gastrointestinal cancer mortality, Non-malignant respiratory disease mortality, Ischemic heart disease mortality; Cancer/Carcinogenesis: All malignancies mortality, Gastrointestinal cancer mortality; Gastrointestinal: Gastrointestinal cancer mortality; Lung/Respiratory: Non-malignant respiratory disease mortality; Cardiovascular: Ischemic heart disease mortality
Asbestos Fiber Type(s):	Asbestos - Chrysotile (serpentine): 12001-29-5; Asbestos - Crocidolite (riebeckite): 12001-28-4
Linked HERO ID(s):	No linked references.
HERO ID:	3100548

Domain		Metric	Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Medium	Key elements of the study design were reported within this retrospective cohort study of long-term male workers in which n=339 male asbestos workers hired prior to 1960 and employed by the same company in Ontario, Canada for at least nine years were followed until 31 October 1980 for mortality outcomes of interest. An additional n=11 men (3.2% of the total) could not be properly classified from their work histories as production, maintenance or rock wool/fiberglass workers and were excluded from the current analysis. Participants were identified from company records of all hourly and salaried employees who had worked at the plant of interest. Employees were excluded if they did not work for at least nine years to account for the long latency of asbestos-related diseases and difficulties of tracing short-term employees. There is no evidence to suggest inclusion or exclusion from the sample differed significantly by outcome or exposure status.
	Metric 2:	Attrition	Low	Official death certificates were obtained for all men who had died. However, a total of five (2.7%) of the n=186 production workers, three (5.5%) of the n=55 maintenance workers and five (5.7%) of the n=87 unexposed or minimally exposed workers were unable to be traced for mortality outcomes and were assumed still alive for analysis. A group of 55 maintenance workers were originally included, but later excluded as the study reported that it "was not thought possible to estimate exposures for the maintenance men."

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Study Citation: Finkelstein, M. M. (1983). Mortality among long-term employees of an Ontario (Canada) asbestos-cement factory. British Journal of Industrial Medicine 40(2):138-144.
Health Outcome: gastrointestinal cancer mortality; all-cause mortality, non-malignant respiratory disease mortality, ischemic heart disease mortality
Target Organ(s): Mortality: All causes mortality, All malignancies mortality, Gastrointestinal cancer mortality, Non-malignant respiratory disease mortality, Ischemic heart disease mortality; Cancer/Carcinogenesis: All malignancies mortality, Gastrointestinal cancer mortality; Gastrointestinal: Gastrointestinal cancer mortality; Lung/Respiratory: Non-malignant respiratory disease mortality; Cardiovascular: Ischemic heart disease mortality
Asbestos Fiber Type(s): Asbestos - Chrysotile (serpentine): 12001-29-5; Asbestos - Crocidolite (riebeckite): 12001-28-4
Linked HERO ID(s): No linked references.
HERO ID: 3100548

Domain	Metric		Rating	Comments
	Metric 3:	Comparison Group	Medium	Inclusion criteria and methods of participant selection were reported. Workers within the rock wool/fiber glass operations (n=87) were classified as minimally exposed, had mortality described as similar to the general male Ontario population and were utilized as the comparison control workers. SMR analyses results utilized the age and calendar specific mortality experience of the male Ontario general population as a comparison group for expected mortality rates. The mean age at the start of exposure or employment was described as similar between the exposed and general populations. Comparison control workers were primarily within the rock wool/fiberglass insulation production area, although the author of the current study noted in another publication (Finkelstein et al., 1983, HERO ID 3083612) of workers in the same factory that it was possible for employees to be assigned to the pipe shop for brief clean-up duties, or re-assigned from non-asbestos to asbestos work areas, such that some control workers may have been exposed as well. There is potential for healthy worker effect in terms of left truncation bias, as the cohort for the current study was restricted to workers with at least nine years of employment, such that all workers had to survive for at least nine years to be included. However, Table 2 SMR results for non-malignant respiratory disease indicate no evidence of healthy worker effect in terms of the healthy hire or healthy worker survivor effect.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Low	The microscopic method (PCM or TEM) of analysis of air sampling data reported in Table 1 with outcome mortality rates was not detailed. The average estimated cumulative exposure among production workers was reported for three groups of production workers of 62 men each as 44 f-y/ml, 92 f-y/ml, and 180 f-y/mL (chrysotile and crocidolite). Groups were created on the basis of ranking 18-year cumulative exposures. Air sampling data from government, insurance and company hygienists initiated in late 1969 was utilized along with company employment records to classify each production worker's exposure, however production within the plant began in 1948 and measured exposures for periods 1948-1970 were lacking and assumed as related to the quantitative measurements made beginning in 1969. Exposures for maintenance workers was described as not calculated due to inadequate data. Estimated cumulative exposure for only the first 18 years of employment was utilized such that for men employed less than 18 years this parameter was used and for men employed more than 18 years, the potential exposures after 18 years were excluded. Exposures were assumed to have been unchanged from 1962 to 1970, to have been 30% higher from 1955 to 1961, and to have been twice as high from 1948 to 1954, with assumptions supported by impinger area sampling performed 1949 through the 1960's.

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Study Citation:	Finkelstein, M. M. (1983). Mortality among long-term employees of an Ontario (Canada) asbestos-cement factory. British Journal of Industrial Medicine 40(2):138-144.
Health Outcome:	gastrointestinal cancer mortality; all-cause mortality, non-malignant respiratory disease mortality, ischemic heart disease mortality
Target Organ(s):	Mortality: All causes mortality, All malignancies mortality, Gastrointestinal cancer mortality, Non-malignant respiratory disease mortality, Ischemic heart disease mortality; Cancer/Carcinogenesis: All malignancies mortality, Gastrointestinal cancer mortality; Gastrointestinal: Gastrointestinal cancer mortality; Lung/Respiratory: Non-malignant respiratory disease mortality; Cardiovascular: Ischemic heart disease mortality
Asbestos Fiber Type(s):	Asbestos - Chrysotile (serpentine): 12001-29-5; Asbestos - Crocidolite (riebeckite): 12001-28-4
Linked HERO ID(s):	No linked references.
HERO ID:	3100548

Domain	Metric		Rating	Comments
	Metric 5:	Exposure Levels	Medium	The range and distribution of estimated exposures is reported within Table 1 for production workers as 8 to 420 fiber-years/mL. Table 1 provides the mortality rates for production workers across three groups of exposure categories.
	Metric 6:	Temporality	High	The study presents an appropriate temporality and the interval between exposure and outcome is appropriate considering the latency of disease. Workers were required to have been hired before 1960 and were followed up until 1980, ensuring at least 20 years of follow-up for the cohort.

Domain 3: Outcome Assessment

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Study Citation:	Finkelstein, M. M. (1983). Mortality among long-term employees of an Ontario (Canada) asbestos-cement factory. British Journal of Industrial Medicine 40(2):138-144.
Health Outcome:	gastrointestinal cancer mortality; all-cause mortality, non-malignant respiratory disease mortality, ischemic heart disease mortality
Target Organ(s):	Mortality: All causes mortality, All malignancies mortality, Gastrointestinal cancer mortality, Non-malignant respiratory disease mortality, Ischemic heart disease mortality; Cancer/Carcinogenesis: All malignancies mortality, Gastrointestinal cancer mortality; Gastrointestinal: Gastrointestinal cancer mortality; Lung/Respiratory: Non-malignant respiratory disease mortality; Cardiovascular: Ischemic heart disease mortality
Asbestos Fiber Type(s):	Asbestos - Chrysotile (serpentine): 12001-29-5; Asbestos - Crocidolite (riebeckite): 12001-28-4
Linked HERO ID(s):	No linked references.
HERO ID:	3100548

Domain	Metric		Rating	Comments
	Metric 7:	Outcome Measurement or Characterization	Medium	Other Cancer(s): Follow-up for mortality was described as conducted by a local trace supplemented by a mortality search performed by Statistics Canada. Mortality rates from mesothelioma, lung cancer, gastrointestinal cancer, and all malignancies deaths were assessed in production workers and compared with the Ontario general population rates in Table 1 (no ICD codes reported). Mortality rates in Table 2 from all-cause mortality, all malignancies (ICD codes 140-209), lung cancer (ICD code 162), mesothelioma (ICD codes 163, 158, 228), gastrointestinal cancer (ICD codes 150-154), non-malignant respiratory disease (ICD codes 460-519) and ischemic heart disease (ICD codes 410-414) deaths were reported for production workers, production plus maintenance workers and control workers. Official death certificates were obtained for all men who had died. For those production workers (n=5), maintenance workers (n=3) and control workers (n=5) who were untraceable, authors assumed these workers were still alive at the end of follow-up, 31 October 1980. Additional clinical, pathological and necropsy reports were available for n=44 of the n=58 deaths among production workers and are used in analyses of exposure duration, but not of exposure concentration.; Other Non-Cancer Outcomes: Follow-up for mortality was described as conducted by a local trace supplemented by a mortality search performed by Statistics Canada. Mortality rates from mesothelioma, lung cancer, gastrointestinal cancer, and all malignancies deaths were assessed in production workers and compared with the Ontario general population rates in Table 1 (no ICD codes reported). Mortality rates in Table 2 from all-cause mortality, all malignancies (ICD codes 140-209), lung cancer (ICD code 162), mesothelioma (ICD codes 163, 158, 228), gastrointestinal cancer (ICD codes 150-154), non-malignant respiratory disease (ICD codes 460-519) and ischemic heart disease (ICD codes 410-414) deaths were reported for production workers, production plus maintenance workers and control workers. Official death certificates were obtained for all men who had died. For those production workers (n=5), maintenance workers (n=3) and control workers (n=5) who were untraceable, authors assumed these workers were still alive at the end of follow-up, 31 October 1980. Additional clinical, pathological and necropsy reports were available for n=44 of the n=58 deaths among production workers and are used in analyses of exposure duration, but not of exposure concentration.
	Metric 8:	Reporting Bias	Medium	There were no concerns for selective reporting. SMRs in Table 2 and mortality rates across age and time since first exposure groups per man years in production workers in Table 3 were reported as single values, with no measures of variation or confidence intervals. Confidence intervals for specific outcomes were reported within the text.

Domain 4: Potential Confounding / Variability Control

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Study Citation: Finkelstein, M. M. (1983). Mortality among long-term employees of an Ontario (Canada) asbestos-cement factory. British Journal of Industrial Medicine 40(2):138-144.
Health Outcome: gastrointestinal cancer mortality; all-cause mortality, non-malignant respiratory disease mortality, ischemic heart disease mortality
Target Organ(s): Mortality: All causes mortality, All malignancies mortality, Gastrointestinal cancer mortality, Non-malignant respiratory disease mortality, Ischemic heart disease mortality; Cancer/Carcinogenesis: All malignancies mortality, Gastrointestinal cancer mortality; Gastrointestinal: Gastrointestinal cancer mortality; Lung/Respiratory: Non-malignant respiratory disease mortality; Cardiovascular: Ischemic heart disease mortality
Asbestos Fiber Type(s): Asbestos - Chrysotile (serpentine): 12001-29-5; Asbestos - Crocidolite (riebeckite): 12001-28-4
Linked HERO ID(s): No linked references.
HERO ID: 3100548

Domain	Metric		Rating	Comments
	Metric 9:	Covariate Adjustment	Low	Other than stratification for years since first exposure and age, no additional adjustments or consideration for differences between exposed and non-exposed groups regarding distributions of relevant covariates were detailed. The cohort for study was restricted to males. The authors mention that information for smoking was available for 70% of the cohort, but this information is not used in statistical analyses. .
	Metric 10:	Covariate Characterization	Low	Although not specified within this occupational study, it is assumed that personnel files were utilized to obtain age and time since first employed/exposed data.
	Metric 11:	Co-exposure Counfounding	Low	The members of the cohort were employees of an Ontario asbestos cement pipe manufacturing factory classified as production, maintenance and factory control workers. In addition to chrysotile and crocidolite asbestos, authors noted production of asbestos cement pipe included exposures to cement and silica, which were not accounted for. Considerations for workers who might have initially left and worked elsewhere with additional exposures but eventually returned to asbestos work were not detailed. However, there was no evidence that there was an unbalanced provision of co-exposures among exposure groups.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	Medium	The study design was appropriate as an early study to address the research aims. Two types of comparisons were performed, internal and external. Table 2 SMR results were obtained through external comparisons by applying the Ontario general population mortality rates as reference and presented for production, maintenance and control workers. Table 3 mortality rate results were presented for production workers stratified across age and years since first exposure groups. Tests for trend were not reported.
	Metric 13:	Statistical Power	Medium	The number of participants was adequate, however formal statistical comparisons between exposed and non-exposed workers, or across time since first exposure groups, were not presented. SMR results in Table 2 were reported for the n=328 workers, while results in Table 3 were reported only for the n=186 production workers.
	Metric 14:	Reproducibility of Analyses	Low	The only table presenting results and exposures was Table 1, which reported mortality rates across each exposure group (A, B and C) and estimated mean and range of exposures within each exposure group. However, no formal statistical analysis was conducted to examine the statistical differences between the less exposed (Group A) and more exposed (Group C) groups. The description of this, as well as SMR results in Table 2 and mortality rates in production workers in Table 3 is generally sufficient to understand. Some of Table 2 observed / expected (SMR) results were unclear, as with the non-malignant respiratory disease SMR for production workers within the 15-19 years since first exposure group, where the observed mortality was 1, the expected was 0.4, but the reported SMR is 1.0, rather than 2.5.

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Study Citation:	Finkelstein, M. M. (1983). Mortality among long-term employees of an Ontario (Canada) asbestos-cement factory. British Journal of Industrial Medicine 40(2):138-144.
Health Outcome:	gastrointestinal cancer mortality; all-cause mortality, non-malignant respiratory disease mortality, ischemic heart disease mortality
Target Organ(s):	Mortality: All causes mortality, All malignancies mortality, Gastrointestinal cancer mortality, Non-malignant respiratory disease mortality, Ischemic heart disease mortality; Cancer/Carcinogenesis: All malignancies mortality, Gastrointestinal cancer mortality; Gastrointestinal: Gastrointestinal cancer mortality; Lung/Respiratory: Non-malignant respiratory disease mortality; Cardiovascular: Ischemic heart disease mortality
Asbestos Fiber Type(s):	Asbestos - Chrysotile (serpentine): 12001-29-5; Asbestos - Crocidolite (riebeckite): 12001-28-4
Linked HERO ID(s):	No linked references.
HERO ID:	3100548

Domain	Metric		Rating	Comments
	Metric 15:	Statistical Analysis	Medium	Model building was not conducted. The construction of SMRs appears appropriate.

Additional Comments: This was an occupational retrospective cohort study reporting SMRs of long-term male workers in which n=339 male asbestos workers hired prior to 1960 and employed by the same company in Ontario, Canada for at least nine years were followed until 31 October 1980 for mortality outcomes of interest. Concerns included the assumption that workers unable to be traced for mortality outcomes were still alive at the end of follow-up, with no sensitivity analyses conducted to examine results with and without these workers. Mesothelioma mortality was obtained utilizing pre-ICD 10 coding. Exposure concentrations are provided for three groups of exposure in relation to a reference population of Ontario men by outcome - however, no statistical analysis is done to compare mortality using exposure concentration data, limiting the study's usefulness for dose-response analysis.

Overall Quality Determination — Low

* No biomarkers were identified for this evaluation.

Study Citation:	Finkelstein, M. M. (1985). A study of dose-response relationships for asbestos associated disease. British Journal of Industrial Medicine 42(5):319-325.
Health Outcome:	small opacities, pleural thickening
Target Organ(s):	Lung/Respiratory: Small opacities >=1/0, Pleural thickening >=A, Small opacities >=1/1, Small opacities >=1/2, Pleural thickening >=B, Small opacities >=0/1
Asbestos Fiber Type(s):	Asbestos - Crocidolite (riebeckite): 12001-28-4; Asbestos - Chrysotile (serpentine): 12001-29-5
Linked HERO ID(s):	No linked references.
HERO ID:	709685

Domain	Metric		Rating	Comments
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Low	This metric is rated Low because the study or any cited methods source does not explicitly mention the use of PCM or TEM.Air sampling was conducted by different entities including the government, the asbestos cement company, and insurance hygienists (Finkelstein, 1982, HEROID: 76). Measurements were primarily made through impinger area sampling (Finkelstein, 1982, HEROID: 76). In 1969, personal membrane filters were used (Finkelstein, 1982, HEROID: 76). Because of the infrequent consistency of reporting exposure, extrapolations were needed for missing time frames (Finkelstein, 1982, HEROID: 76).Authors described the following for calculation expose and dose estimation: "Cumulative exposures were calculated for each man by summing annual exposures accumulated during the first 18 years from the start of exposure. Asbestos dosages were calculated by assuming that a fixed proportion of the workplace air concentrations were deposited in the lungs, and each year's accumulation was weighted by the residence time in lung tissue (the formulas used are given in the appendix). Cumulative exposures had been estimated to be accurate to within a factor of 3 to 5."
	Metric 5:	Exposure Levels	Medium	The distribution of exposure appears to be sufficient to develop an exposure-response estimate. Cumulative exposure (f-y/ml) and dose (f/ml*yr-squared) for calculating cumulative risk were utilized in statistical models. Range or other measure distribution is not present in this paper, however Figures 1 and 2 show values ranging from 0-6,000 fibers/mL x year^2.

Additional Comments: Finkelstein, 1982, HEROID: 76 reported the dominant asbestos fibers were crocidolite and chrysotile. QCer may want to review Metric 9 to ensure appropriate rating. QC was not completed for metrics other than Metrics 4 and 5 because the study does not have sufficient exposure information to be useful for dose-response analysis.

* No biomarkers were identified for this evaluation.

** As described in Appendix B.2 of the *White Paper: Quantitative Approach to the Human Health Assessment for the Risk Evaluation for Asbestos Part 2: Supplemental Evaluation Including Legacy Uses and Associated Disposals of Asbestos*, to be considered as being informative for dose-response analysis, metrics 4 and 5 would need metric ratings of Medium or High. This reference did not satisfy this requirement; therefore data quality evaluation is presented for only for metrics 4 and 5.

Study Citation:	Finkelstein, M. M. (1982). Asbestosis in long-term employees of an Ontario asbestos-cement factory. American Review of Respiratory Disease 125(5):496-501.
Health Outcome:	Asbestosis
Target Organ(s):	Lung/Respiratory: Asbestosis
Asbestos Fiber Type(s):	Asbestos - Crocidolite (riebeckite): 12001-28-4; Asbestos - Chrysotile (serpentine): 12001-29-5
Linked HERO ID(s):	No linked references.
HERO ID:	76

Domain	Metric		Rating	Comments
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Low	This metric is rated Low because the study or any cited methods source does not explicitly mention the use of PCM or TEM. Samples were collected using impingers and membrane filters.
	Metric 5:	Exposure Levels	Medium	The authors reported the incidence of certified asbestosis as a function of time and exposure to asbestos. Authors utilize a continuous measure of exposure in the 18th year from initial exposure to create 6 ordinal categories.

Additional Comments:	QC was not completed for metrics other than Metrics 4 and 5 because the study does not have sufficient exposure information to be useful for dose-response analysis. The method of fiber quantification was not mentioned or cited, resulting in Low rating for Metric 4.

* No biomarkers were identified for this evaluation.

** As described in Appendix B.2 of the *White Paper: Quantitative Approach to the Human Health Assessment for the Risk Evaluation for Asbestos Part 2: Supplemental Evaluation Including Legacy Uses and Associated Disposals of Asbestos*, to be considered as being informative for dose-response analysis, metrics 4 and 5 would need metric ratings of Medium or High. This reference did not satisfy this requirement; therefore data quality evaluation is presented for only for metrics 4 and 5.

Study Citation:	Finkelstein, M. M., Vingilis, J. J. (1984). Radiographic abnormalities among asbestos-cement workers. An exposure-response study. American Review of Respiratory Disease 129(1):17-22.
Health Outcome:	Small irregular opacities on radiograph; bilateral pleural thickening on raidograph
Target Organ(s):	Lung/Respiratory: Small irregular opacities on radiograph, Bilateral pleural thickening
Asbestos Fiber Type(s):	Asbestos - Chrysotile (serpentine): 12001-29-5; Asbestos - Crocidolite (riebeckite): 12001-28-4
Linked HERO ID(s):	No linked references.
HERO ID:	3083654

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	High	Subjects included 181 asbestos-cement male workers hired prior to 1960 and who were employed for 9 years or more at the factory (in Ontario) and who worked at least 12 months in asbestos exposure.
	Metric 2:	Attrition	Medium	Excluded participants was 5 subjects ”who had died before or shortly after 18 years from first exposure and who had not had a recent film”. Men who were lost to follow up were mentioned, but details on the number lost to follow up was not included.
	Metric 3:	Comparison Group	Medium	There is only indirect evidence stated by authors without description of methods that groups are similar. ”To investigate the influence of age and smoking habits on risk, the cohort was stratified for exposure by the method described by Breslow (Breslow, 1979). These include estimation of the survival curve, nonparametric tests to compare several survival curves, tests for trend, and regression analysis.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	High	”Cumulative exposures to asbestos were calculated using a model that extrapolated measurements made by the personal membrane filter, a method that came into use 21 years after the plant opened... calculates estimated to be accurate to within a factor of 3 to 5.” Earlier report on this cohort was referenced (Finkelstein, 1982).
	Metric 5:	Exposure Levels	Medium	Results of the 5 exposure groups/ exposure-response model were adequate (in f-y/ml: A=0-49.9 (n=32); B=50-99.9 (n=68); C=100-149.9 (n=41); D=150-199.9 (n=25); E=>=200 (n=15).)
	Metric 6:	Temporality	High	The study presents an appropriate temporality between exposure and outcome (radiograph taken 18 or more years since first exposure).
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Medium	Other Non-Cancer Outcomes: Chest radiographs (postanterior projections) were taken annually as part of the routine medical surveillance. ICD-10CA codes were not mentioned.
	Metric 8:	Reporting Bias	Medium	Number of exposed workers by category clearly outlined in exposure-response analysis, for smokers and non-smokers (Table 2).
Domain 4: Potential Confounding / Variability Control				

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Study Citation:	Finkelstein, M. M., Vingilis, J. J. (1984). Radiographic abnormalities among asbestos-cement workers. An exposure-response study. American Review of Respiratory Disease 129(1):17-22.
Health Outcome:	Small irregular opacities on radiograph; bilateral pleural thickening on raidograph
Target Organ(s):	Lung/Respiratory: Small irregular opacities on radiograph, Bilateral pleural thickening
Asbestos Fiber Type(s):	Asbestos - Chrysotile (serpentine): 12001-29-5; Asbestos - Crocidolite (riebeckite): 12001-28-4
Linked HERO ID(s):	No linked references.
HERO ID:	3083654

Domain	Metric		Rating	Comments
	Metric 9:	Covariate Adjustment	Medium	Stratification by age and smoking were mentioned, however methods not explicitly clear on which stratification method was used from reference to the study by Breslow on Statistical methods for censored survival data.
	Metric 10:	Covariate Characterization	Low	Occupational study, it can be assumed that personnel records were used to obtain covariate data, not otherwise mentioned.
	Metric 11:	Co-exposure Counfounding	Medium	The authors mentioned co-exposure to silica which the study team ”attempted no analysis” since quantitative measures for silica did not exist and ”nor could we investigate possible interaction between silica and asbestos.”
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	Medium	Cohort design was appropriate for the exposure-response study. Methods for variable stratification /regression analysis are difficult to determine.
	Metric 13:	Statistical Power	Medium	The number of participants are adequate to detect an effect in the exposed population. 181 men, separated into 5 exposure groups (A=32, B=68, C=41, D=25, E=15)
	Metric 14:	Reproducibility of Analyses	Low	The description of the analysis is insufficient to understand what has been done and to be reproducible. Other papers are referenced for methods and mortality data, but not entirely clear as to what methodology was used.
	Metric 15:	Statistical Analysis	Medium	”Life-table analyses were performed using a computer program” and ”risk was assessed by calculating the 32-year cumulative probability of developing ’certified asbestosis”’ and ”relative risk was calculated by assuming that if exposure were irrelevant to risk of developing an abnormality, then at each examination the abnormalities would be distributed among the exposure categories solely on the basis of the proportion of the population at risk to be found in each category (the expected number). The expected numbers were summed over the follow-up interval, and the number of abnormalities actually observed in each exposure group was compared with the total expected. This approach allowed statistical testing for equality of the ”survival” distributions and for trend with exposure” (Thomas et al., HERO ID 196727 ; Breslow, 1979).

Additional Comments: Studied the development of small irregular opacities and bilateral pleural thickening on radiograph in longitudinal cohort study of 181 asbestos and silica-exposed male cement factory workers in Ontario. Co-exposure to silica not measured/analyzed but mentioned. Methods for stratifying by age and smoking status not clearly outlined. Mortality data included and referenced from another earlier cohort, but not included in extraction as study did not appear to be producing new results.

Overall Quality Determination — Medium

* No biomarkers were identified for this evaluation.

Study Citation:	Gamble, J. F., Fellner, W., Dimeo, M. J. (1979). An epidemiologic study of a group of talc workers. American Review of Respiratory Disease 119(5):741-753.
Health Outcome:	Pulmonary Function/Spirometry Results
Target Organ(s):	Lung/Respiratory: FEV1
Asbestos Fiber Type(s):	Asbestos - Tremolite: 14567-73-8; Asbestos - Anthophyllite: 17068-78-9
Linked HERO ID(s):	No linked references.
HERO ID:	29531

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Medium	This cross-sectional study examined the relationship between pulmonary function and exposures to talc containing anthophyllite and tremolite fibers in talc workers (n=93) versus potash miners (n=1,077) and versus synthetic textile workers. A total of n=121 workers (78% of the n=156 total miller and miner work force) participated, however results were restricted to the n=93 males who had only worked at the talc mine and mill under study. Participation rates were noted as similar across different work areas. Participants and non-participants were noted to have had similar average exposure duration in years (10.2 years for participants, 10.5 years for non-participants). Selection process and participation rates for potash and synthetic textile comparison group worker data not detailed.
	Metric 2:	Attrition	Medium	Talc millers and miner participants not working at the talc mine and mill under study (n=28) were excluded, however sensitivity analyses revealed similar results when all 121 participants of the original n=156 male talc workforce were included in the analyses. Comparison population consisted of n=1,077 potash mine workers and synthetic textile workers (Table 10), however details on any exclusions involved in the creation of the comparison populations not detailed. Missing data not detailed for talc miners or comparison populations.
	Metric 3:	Comparison Group	Medium	Demographics between talc workers and potash workers noted as comparable with a few exceptions for those with less than 15 years employment (non-smoking talc workers were younger than potash workers, smoking talc workers smoked more than potash workers) and for those with more than 15 years of exposure (potash non-smokers and ex-smokers were slightly older than talc workers and smoking talc workers smoked less daily but had more overall pack-years than potash workers). However, workers in each population were grouped into or adjusted for categories of similar age, smoking and duration of mining employment for stratified and regression analyses. Uncertainty regarding potential healthy worker effects as prevalent hires comprised the available population for study. Further uncertainty in utilizing potash workers and synthetic textile workers as comparison groups with the potential for asbestos fibers within potash mines, as well as the potential for pulmonary function changes in workers exposed to synthetic fibers.
Domain 2: Exposure Characterization				

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Study Citation:	Gamble, J. F., Fellner, W., Dimeo, M. J. (1979). An epidemiologic study of a group of talc workers. American Review of Respiratory Disease 119(5):741-753.			
Health Outcome:	Pulmonary Function/Spirometry Results			
Target Organ(s):	Lung/Respiratory: FEV1			
Asbestos Fiber Type(s):	Asbestos - Tremolite: 14567-73-8; Asbestos - Anthophyllite: 17068-78-9			
Linked HERO ID(s):	No linked references.			
HERO ID:	29531			
Domain	Metric		Rating	Comments
	Metric 4:	Measurement of Exposure	Medium	Personal air samples were collected from miners and millers to determine the time-weighted average (TWA) exposure to respirable dust, free silica, and asbestos fibers. Sampling methods described in terms of sampling equipment, procedures and study site characteristics for talc miners, with sampling equipment and procedures described for potash miner exposures. Analytic methodology described in terms of instrumentation (electron microscopy on a random sample) and standard (NIOSH phase contrast counting technique) methods for talc miners and in terms of instrumentation (for total dust, percent free silica, NO2, but not area total respirable particulate sampling) for potash miners. Estimated personal exposure to respirable particulates in potash miners was calculated from averaged proportions of total particulate from area sampling within each potash mine. Cumulative exposure for talc and potash miners described as calculated from personal sampling and summation of historical time in each job. Uncertainty regarding cumulative exposure estimates as text notes no fiber sampling was done before 1970, exposures for each job were not well documented, representativeness of samples described as “unknown” and estimates of cumulative exposures described as “probably lower than actual cumulative exposures”.
	Metric 5:	Exposure Levels	Medium	Distribution of asbestos fiber exposure presented within Table 2 by age group and adequate for analyses. Table 8 presented regression results utilizing estimated cumulative fiber exposure calculated from historical exposures as continuous independent variables predicting mean percent of predicted pulmonary function and changes in predicted pulmonary function. Other analyses presented results across talc versus potash and textile worker groups as exposed versus non-exposed categories without incorporation of measured or estimated cumulative exposures within models (Table 7).
	Metric 6:	Temporality	Medium	Uncertainty regarding temporality due to cross-sectional nature of study, however text notes average duration of exposure to talc was 10.2 years. Range of employment duration not specified. Unclear number of years required for appearance of some pulmonary function outcomes of interest.
Domain 3: Outcome Assessment				

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Study Citation:	Gamble, J. F., Fellner, W., Dimeo, M. J. (1979). An epidemiologic study of a group of talc workers. American Review of Respiratory Disease 119(5):741-753.
Health Outcome:	Pulmonary Function/Spirometry Results
Target Organ(s):	Lung/Respiratory: FEV1
Asbestos Fiber Type(s):	Asbestos - Tremolite: 14567-73-8; Asbestos - Anthophyllite: 17068-78-9
Linked HERO ID(s):	No linked references.
HERO ID:	29531

Domain	Metric		Rating	Comments
	Metric 7:	Outcome Measurement or Characterization	Medium	Pulmonary Function/Spirometry Results: Pulmonary function outcomes of interest included FEV1, FVC, FEV1/FVC%, Vmax50, Vmax75, pulmonary symptoms (cough, phlegm, hemoptysis, dyspnea >= grade 2, pleural calcification, pneumoconiosis (opacities) and pleural thickening). Text notes use of respiratory questionnaire by the Medical Research Council for smoking and total work data, however it is unclear if this questionnaire was also utilized for obtaining data for pulmonary symptom outcomes. Pleural thickening, opacities and calcification outcomes would have been obtainable from the standard posteroanterior chest roentgenograms read independently without knowledge of age, occupation and smoking history by three “B” readers using ILO standard schemes. Pulmonary function outcomes obtained utilizing standard spirometry methods.
	Metric 8:	Reporting Bias	Medium	No substantial concerns for selective reporting, although text noted blood samples collected from talc workers for analyses of antinuclear antibodies and rheumatoid factor which do not seem to have been analyzed, however these were not included as outcomes of interest within original study objectives.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	High	Results reported as adjusted utilizing stratification and multivariate regression. Final multivariate analysis (Table 6) adjusted for age, height, and smoking status. Additional analyses (Table 8) adjusted for years of employment. Study restricted to males. Distribution of covariates presented for talc and potash workers presented within Table 5.
	Metric 10:	Covariate Characterization	Medium	Data regarding potential confounders seems to have been collected within the Medical Research Council respiratory questionnaire, however it is unclear as source for independent variable data not detailed directly in text.
	Metric 11:	Co-exposure Counfounding	Low	Final analyses presented results without adjusting for co-exposures potentially relevant to pulmonary function outcomes, such as silica.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	Medium	Study utilized stratification and multivariate regression for analyses of cross-sectional data for lung function outcomes. Unclear amount of asbestos exposure in comparison group potash workers. Unclear effect of utilizing synthetic textile workers as comparison group, with their potential for increased risks of fiber exposure-related decreased pulmonary function.
	Metric 13:	Statistical Power	Medium	Number of subjects adequate and reported as n=93 male talc miners and millers compared with n=1,077 potash miners. Uncertainty regarding the number of comparison group textile workers (Table 10).

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Study Citation:	Gamble, J. F., Fellner, W., Dimeo, M. J. (1979). An epidemiologic study of a group of talc workers. American Review of Respiratory Disease 119(5):741-753.
Health Outcome:	Pulmonary Function/Spirometry Results
Target Organ(s):	Lung/Respiratory: FEV1
Asbestos Fiber Type(s):	Asbestos - Tremolite: 14567-73-8; Asbestos - Anthophyllite: 17068-78-9
Linked HERO ID(s):	No linked references.
HERO ID:	29531

Domain	Metric		Rating	Comments
	Metric 14:	Reproducibility of Analyses	Medium	Statistical analyses reported as multivariate regression, however details of analyses unclear for regression in terms of handling of missing data, consideration of outliers, transformation of continuous variables and model assumptions.
	Metric 15:	Statistical Analysis	Low	Description of analysis brief with assumptions lacking.

Additional Comments: The relationship between pulmonary function (FEV1, FVC, FEV1/FVC%, Vmax50, Vmax75, pulmonary symptoms, pleural calcification, pneumoconiosis, pleural thickening) and exposures to talc containing anthophyllite and tremolite fibers in talc workers (n=93) versus potash miners (n=1,077) and synthetic textile workers (Table 10) was examined in this cross-sectional study. Results indicated increased respiratory symptoms, radiographic abnormalities and decreased pulmonary function among these talc miners and millers with some findings noted as related to dose and duration of exposure.The measurement exposure (M4) and/or exposure levels (M5) metrics are rated as medium upon review by both set of reviewers. Also, the overall quality determination (OQD) is rated medium. Extraction has been completed and quality control reviewed.

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation:	Gamble, J. F., Fellner, W., Dimeo, M. J. (1979). An epidemiologic study of a group of talc workers. American Review of Respiratory Disease 119(5):741-753.
Health Outcome:	Pulmonary Function/Spirometry Results
Target Organ(s):	Lung/Respiratory: FVC
Asbestos Fiber Type(s):	Asbestos - Tremolite: 14567-73-8; Asbestos - Anthophyllite: 17068-78-9
Linked HERO ID(s):	No linked references.
HERO ID:	29531

Domain		Metric	Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Medium	The relationship between pulmonary function and exposures to talc containing anthophyllite and tremolite fibers in talc workers (n=93) versus potash miners (n=1,077) and versus synthetic textile workers (Table 10) was examined in this cross-sectional study. A total of n=121 workers (78% of the n=156 total miller and miner work force) participated, however results were restricted to the n=93 males who had only worked at the talc mine and mill under study. Participation rates were noted as similar across different work areas. Participants and non-participants were noted to have had similar average exposure duration in years (10.2 years for participants, 10.5 years for non-participants). Selection process and participation rates for potash and synthetic textile comparison group worker data not detailed.
	Metric 2:	Attrition	Medium	Talc millers and miner participants not working at the talc mine and mill under study (n=28) were excluded, however sensitivity analyses revealed similar results when all 121 participants of the original n=156 male talc workforce were included in the analyses. Comparison population consisted of n=1,077 potash mine workers and synthetic textile workers (Table 10), however details on any exclusions involved in the creation of the comparison populations not detailed. Missing data not detailed for talc miners or comparison populations.
	Metric 3:	Comparison Group	Medium	Demographics between talc workers and potash workers noted as comparable with a few exceptions for those with less than 15 years employment (non-smoking talc workers were younger than potash workers, smoking talc workers smoked more than potash workers) and for those with more than 15 years of exposure (potash non-smokers and ex-smokers were slightly older than talc workers and smoking talc workers smoked less daily but had more overall pack-years than potash workers). However, workers in each population were grouped into or adjusted for categories of similar age, smoking and duration of mining employment for stratified and regression analyses. Uncertainty regarding potential healthy worker effects as prevalent hires comprised the available population for study. Further uncertainty in utilizing potash workers and synthetic textile workers as comparison groups with the potential for asbestos fibers within potash mines, as well as the potential for pulmonary function changes in workers exposed to synthetic fibers.
Domain 2: Exposure Characterization				

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Study Citation:	Gamble, J. F., Fellner, W., Dimeo, M. J. (1979). An epidemiologic study of a group of talc workers. American Review of Respiratory Disease 119(5):741-753.
Health Outcome:	Pulmonary Function/Spirometry Results
Target Organ(s):	Lung/Respiratory: FVC
Asbestos Fiber Type(s):	Asbestos - Tremolite: 14567-73-8; Asbestos - Anthophyllite: 17068-78-9
Linked HERO ID(s):	No linked references.
HERO ID:	29531

Domain	Metric		Rating	Comments
	Metric 4:	Measurement of Exposure	Medium	Personal air samples were collected from miners and millers to determine the time-weighted average (TWA) exposure to respirable dust, free silica, and asbestos fibers. Sampling methods described in terms of sampling equipment, procedures and study site characteristics for talc miners, with sampling equipment and procedures described for potash miner exposures. Analytic methodology described in terms of instrumentation (electron microscopy on a random sample) and standard (NIOSH phase contrast counting technique) methods for talc miners and in terms of instrumentation (for total dust, percent free silica, NO2, but not area total respirable particulate sampling) for potash miners. Estimated personal exposure to respirable particulates in potash miners was calculated from averaged proportions of total particulate from area sampling within each potash mine. Cumulative exposure for talc and potash miners described as calculated from personal sampling and summation of historical time in each job. Uncertainty regarding cumulative exposure estimates as text notes no fiber sampling was done before 1970, exposures for each job were not well documented, representativeness of samples described as “unknown” and estimates of cumulative exposures described as “probably lower than actual cumulative exposures”.
	Metric 5:	Exposure Levels	Medium	Distribution of asbestos fiber exposure presented within Table 2 by age group and adequate for analyses. Table 8 presented regression results utilizing estimated cumulative fiber exposure calculated from historical exposures as continuous independent variables predicting mean percent of predicted pulmonary function and changes in predicted pulmonary function. Other analyses presented results across talc versus potash and textile worker groups as exposed versus non-exposed categories without incorporation of measured or estimated cumulative exposures within models (Table 7).
	Metric 6:	Temporality	Medium	Uncertainty regarding temporality due to cross-sectional nature of study, however text notes average duration of exposure to talc was 10.2 years. Range of employment duration not specified. Unclear number of years required for appearance of some pulmonary function outcomes of interest.
Domain 3: Outcome Assessment				

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Study Citation:	Gamble, J. F., Fellner, W., Dimeo, M. J. (1979). An epidemiologic study of a group of talc workers. American Review of Respiratory Disease 119(5):741-753.
Health Outcome:	Pulmonary Function/Spirometry Results
Target Organ(s):	Lung/Respiratory: FVC
Asbestos Fiber Type(s):	Asbestos - Tremolite: 14567-73-8; Asbestos - Anthophyllite: 17068-78-9
Linked HERO ID(s):	No linked references.
HERO ID:	29531

Domain	Metric		Rating	Comments
	Metric 7:	Outcome Measurement or Characterization	Medium	Pulmonary Function/Spirometry Results: Pulmonary function outcomes of interest included FEV1, FVC, FEV1/FVC%, Vmax50, Vmax75, pulmonary symptoms (cough, phlegm, hemoptysis, dyspnea >= grade 2, pleural calcification, pneumoconiosis (opacities) and pleural thickening). Text notes use of respiratory questionnaire by the Medical Research Council for smoking and total work data, however it is unclear if this questionnaire was also utilized for obtaining data for pulmonary symptom outcomes. Pleural thickening, opacities and calcification outcomes would have been obtainable from the standard posteroanterior chest roentgenograms read independently without knowledge of age, occupation and smoking history by three "B" readers using ILO standard schemes. Pulmonary function outcomes obtained utilizing standard spirometry methods.
	Metric 8:	Reporting Bias	Medium	No substantial concerns for selective reporting, although text noted blood samples collected from talc workers for analyses of antinuclear antibodies and rheumatoid factor which do not seem to have been analyzed, however these were not included as outcomes of interest within original study objectives.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	High	Results reported as adjusted utilizing stratification and multivariate regression. Final multivariate analysis (Table 6) adjusted for age, height, and smoking status. Additional analyses (Table 8) adjusted for years of employment. Study restricted to males. Distribution of covariates presented for talc and potash workers presented within Table 5.
	Metric 10:	Covariate Characterization	Medium	Data regarding potential confounders seems to have been collected within the Medical Research Council respiratory questionnaire, however it is unclear as source for independent variable data not detailed directly in text.
	Metric 11:	Co-exposure Counfounding	Low	Final analyses presented results without adjusting for co-exposures potentially relevant to pulmonary function outcomes, such as silica.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	Medium	Study utilized stratification and multivariate regression for analyses of cross-sectional data for lung function outcomes. Unclear amount of asbestos exposure in comparison group potash workers. Unclear effect of utilizing synthetic textile workers as comparison group, with their potential for increased risks of fiber exposure-related decreased pulmonary function.
	Metric 13:	Statistical Power	Medium	Number of subjects adequate and reported as n=93 male talc miners and millers compared with n=1,077 potash miners. Uncertainty regarding the number of comparison group textile workers (Table 10).

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Study Citation:	Gamble, J. F., Fellner, W., Dimeo, M. J. (1979). An epidemiologic study of a group of talc workers. American Review of Respiratory Disease 119(5):741-753.
Health Outcome:	Pulmonary Function/Spirometry Results
Target Organ(s):	Lung/Respiratory: FVC
Asbestos Fiber Type(s):	Asbestos - Tremolite: 14567-73-8; Asbestos - Anthophyllite: 17068-78-9
Linked HERO ID(s):	No linked references.
HERO ID:	29531

Domain	Metric		Rating	Comments
	Metric 14:	Reproducibility of Analyses	Medium	Statistical analyses reported as multivariate regression, however details of analyses unclear for regression in terms of handling of missing data, consideration of outliers, transformation of continuous variables and model assumptions.
	Metric 15:	Statistical Analysis	Low	Description of analysis brief with assumptions lacking.

Additional Comments: The relationship between pulmonary function (FEV1, FVC, FEV1/FVC%, Vmax50, Vmax75, pulmonary symptoms, pleural calcification, pneumonoconiosis, pleural thickening) and exposures to talc containing anthophyllite and tremolite fibers in talc workers (n=93) versus potash miners (n=1,077) and synthetic textile workers (Table 10) was examined in this cross-sectional study. Results indicated increased respiratory symptoms, radiographic abnormalities and decreased pulmonary function among these talc miners and millers with some findings noted as related to dose and duration of exposure.The measurement exposure (M4) and/or exposure levels (M5) metrics are rated as medium upon review by both set of reviewers. Also, the overall quality determination (OQD) is rated medium. Extraction has been completed and quality control reviewed.

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation:	Gamble, J. F., Fellner, W., Dimeo, M. J. (1979). An epidemiologic study of a group of talc workers. American Review of Respiratory Disease 119(5):741-753.
Health Outcome:	Pulmonary Function/Spirometry Results
Target Organ(s):	Lung/Respiratory: FEV1%
Asbestos Fiber Type(s):	Asbestos - Tremolite: 14567-73-8; Asbestos - Anthophyllite: 17068-78-9
Linked HERO ID(s):	No linked references.
HERO ID:	29531

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Medium	The relationship between pulmonary function and exposures to talc containing anthophyllite and tremolite fibers in talc workers (n=93) versus potash miners (n=1,077) and versus synthetic textile workers (Table 10) was examined in this cross-sectional study. A total of n=121 workers (78% of the n=156 total miller and miner work force) participated, however results were restricted to the n=93 males who had only worked at the talc mine and mill under study. Participation rates were noted as similar across different work areas. Participants and non-participants were noted to have had similar average exposure duration in years (10.2 years for participants, 10.5 years for non-participants). Selection process and participation rates for potash and synthetic textile comparison group worker data not detailed.
	Metric 2:	Attrition	Medium	Talc millers and miner participants not working at the talc mine and mill under study (n=28) were excluded, however sensitivity analyses revealed similar results when all 121 participants of the original n=156 male talc workforce were included in the analyses. Comparison population consisted of n=1,077 potash mine workers and synthetic textile workers (Table 10), however details on any exclusions involved in the creation of the comparison populations not detailed. Missing data not detailed for talc miners or comparison populations.
	Metric 3:	Comparison Group	Medium	Demographics between talc workers and potash workers noted as comparable with a few exceptions for those with less than 15 years employment (non-smoking talc workers were younger than potash workers, smoking talc workers smoked more than potash workers) and for those with more than 15 years of exposure (potash non-smokers and ex-smokers were slightly older than talc workers and smoking talc workers smoked less daily but had more overall pack-years than potash workers). However, workers in each population were grouped into or adjusted for categories of similar age, smoking and duration of mining employment for stratified and regression analyses. Uncertainty regarding potential healthy worker effects as prevalent hires comprised the available population for study. Further uncertainty in utilizing potash workers and synthetic textile workers as comparison groups with the potential for asbestos fibers within potash mines, as well as the potential for pulmonary function changes in workers exposed to synthetic fibers.
Domain 2: Exposure Characterization				

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Study Citation:	Gamble, J. F., Fellner, W., Dimeo, M. J. (1979). An epidemiologic study of a group of talc workers. American Review of Respiratory Disease 119(5):741-753.
Health Outcome:	Pulmonary Function/Spirometry Results
Target Organ(s):	Lung/Respiratory: FEV1%
Asbestos Fiber Type(s):	Asbestos - Tremolite: 14567-73-8; Asbestos - Anthophyllite: 17068-78-9
Linked HERO ID(s):	No linked references.
HERO ID:	29531

Domain	Metric		Rating	Comments
	Metric 4:	Measurement of Exposure	Medium	Personal air samples were collected from miners and millers to determine the time-weighted average (TWA) exposure to respirable dust, free silica, and asbestos fibers. Sampling methods described in terms of sampling equipment, procedures and study site characteristics for talc miners, with sampling equipment and procedures described for potash miner exposures. Analytic methodology described in terms of instrumentation (electron microscopy on a random sample) and standard (NIOSH phase contrast counting technique) methods for talc miners and in terms of instrumentation (for total dust, percent free silica, NO2, but not area total respirable particulate sampling) for potash miners. Estimated personal exposure to respirable particulates in potash miners was calculated from averaged proportions of total particulate from area sampling within each potash mine. Cumulative exposure for talc and potash miners described as calculated from personal sampling and summation of historical time in each job. Uncertainty regarding cumulative exposure estimates as text notes no fiber sampling was done before 1970, exposures for each job were not well documented, representativeness of samples described as "unknown" and estimates of cumulative exposures described as "probably lower than actual cumulative exposures".
	Metric 5:	Exposure Levels	Medium	Distribution of asbestos fiber exposure presented within Table 2 by age group and adequate for analyses. Table 8 presented regression results utilizing estimated cumulative fiber exposure calculated from historical exposures as continuous independent variables predicting mean percent of predicted pulmonary function and changes in predicted pulmonary function. Other analyses presented results across talc versus potash and textile worker groups as exposed versus non-exposed categories without incorporation of measured or estimated cumulative exposures within models (Table 7).
	Metric 6:	Temporality	Medium	Uncertainty regarding temporality due to cross-sectional nature of study, however text notes average duration of exposure to talc was 10.2 years. Range of employment duration not specified. Unclear number of years required for appearance of some pulmonary function outcomes of interest.
Domain 3: Outcome Assessment				

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Study Citation:	Gamble, J. F., Fellner, W., Dimeo, M. J. (1979). An epidemiologic study of a group of talc workers. American Review of Respiratory Disease 119(5):741-753.
Health Outcome:	Pulmonary Function/Spirometry Results
Target Organ(s):	Lung/Respiratory: FEV1%
Asbestos Fiber Type(s):	Asbestos - Tremolite: 14567-73-8; Asbestos - Anthophyllite: 17068-78-9
Linked HERO ID(s):	No linked references.
HERO ID:	29531

Domain	Metric		Rating	Comments
	Metric 7:	Outcome Measurement or Characterization	Medium	Pulmonary Function/Spirometry Results: Pulmonary function outcomes of interest included FEV1, FVC, FEV1/FVC%, Vmax50, Vmax75, pulmonary symptoms (cough, phlegm, hemoptysis, dyspnea >= grade 2, pleural calcification, pneumoconiosis (opacities) and pleural thickening). Text notes use of respiratory questionnaire by the Medical Research Council for smoking and total work data, however it is unclear if this questionnaire was also utilized for obtaining data for pulmonary symptom outcomes. Pleural thickening, opacities and calcification outcomes would have been obtainable from the standard posteroanterior chest roentgenograms read independently without knowledge of age, occupation and smoking history by three “B” readers using ILO standard schemes. Pulmonary function outcomes obtained utilizing standard spirometry methods.
	Metric 8:	Reporting Bias	Medium	No substantial concerns for selective reporting, although text noted blood samples collected from talc workers for analyses of antinuclear antibodies and rheumatoid factor which do not seem to have been analyzed, however these were not included as outcomes of interest within original study objectives.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	High	Results reported as adjusted utilizing stratification and multivariate regression. Final multivariate analysis (Table 6) adjusted for age, height, and smoking status. Additional analyses (Table 8) adjusted for years of employment. Study restricted to males. Distribution of covariates presented for talc and potash workers presented within Table 5.
	Metric 10:	Covariate Characterization	Medium	Data regarding potential confounders seems to have been collected within the Medical Research Council respiratory questionnaire, however it is unclear as source for independent variable data not detailed directly in text.
	Metric 11:	Co-exposure Counfounding	Low	Final analyses presented results without adjusting for co-exposures potentially relevant to pulmonary function outcomes, such as silica.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	Medium	Study utilized stratification and multivariate regression for analyses of cross-sectional data for lung function outcomes. Unclear amount of asbestos exposure in comparison group potash workers. Unclear effect of utilizing synthetic textile workers as comparison group, with their potential for increased risks of fiber exposure-related decreased pulmonary function.
	Metric 13:	Statistical Power	Medium	Number of subjects adequate and reported as n=93 male talc miners and millers compared with n=1,077 potash miners. Uncertainty regarding the number of comparison group textile workers (Table 10).

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Study Citation:	Gamble, J. F., Fellner, W., Dimeo, M. J. (1979). An epidemiologic study of a group of talc workers. American Review of Respiratory Disease 119(5):741-753.
Health Outcome:	Pulmonary Function/Spirometry Results
Target Organ(s):	Lung/Respiratory: FEV1%
Asbestos Fiber Type(s):	Asbestos - Tremolite: 14567-73-8; Asbestos - Anthophyllite: 17068-78-9
Linked HERO ID(s):	No linked references.
HERO ID:	29531

Domain	Metric		Rating	Comments
	Metric 14:	Reproducibility of Analyses	Medium	Statistical analyses reported as multivariate regression, however details of analyses unclear for regression in terms of handling of missing data, consideration of outliers, transformation of continuous variables and model assumptions.
	Metric 15:	Statistical Analysis	Low	Description of analysis brief with assumptions lacking.

Additional Comments: The relationship between pulmonary function (FEV1, FVC, FEV1/FVC%, Vmax50, Vmax75, pulmonary symptoms, pleural calcification, pneumonoconiosis, pleural thickening) and exposures to talc containing anthophyllite and tremolite fibers in talc workers (n=93) versus potash miners (n=1,077) and synthetic textile workers (Table 10) was examined in this cross-sectional study. Results indicated increased respiratory symptoms, radiographic abnormalities and decreased pulmonary function among these talc miners and millers with some findings noted as related to dose and duration of exposure.The measurement exposure (M4) and/or exposure levels (M5) metrics are rated as medium upon review by both set of reviewers. Also, the overall quality determination (OQD) is rated medium. Extraction has been completed and quality control reviewed.

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation:	Gamble, J. F., Fellner, W., Dimeo, M. J. (1979). An epidemiologic study of a group of talc workers. American Review of Respiratory Disease 119(5):741-753.
Health Outcome:	Pulmonary Function/Spirometry Results
Target Organ(s):	Lung/Respiratory: Vmax50
Asbestos Fiber Type(s):	Asbestos - Tremolite: 14567-73-8; Asbestos - Anthophyllite: 17068-78-9
Linked HERO ID(s):	No linked references.
HERO ID:	29531

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Medium	The relationship between pulmonary function and exposures to talc containing anthophyllite and tremolite fibers in talc workers (n=93) versus potash miners (n=1,077) and versus synthetic textile workers (Table 10) was examined in this cross-sectional study. A total of n=121 workers (78% of the n=156 total miller and miner work force) participated, however results were restricted to the n=93 males who had only worked at the talc mine and mill under study. Participation rates were noted as similar across different work areas. Participants and non-participants were noted to have had similar average exposure duration in years (10.2 years for participants, 10.5 years for non-participants). Selection process and participation rates for potash and synthetic textile comparison group worker data not detailed.
	Metric 2:	Attrition	Medium	Talc millers and miner participants not working at the talc mine and mill under study (n=28) were excluded, however sensitivity analyses revealed similar results when all 121 participants of the original n=156 male talc workforce were included in the analyses. Comparison population consisted of n=1,077 potash mine workers and synthetic textile workers (Table 10), however details on any exclusions involved in the creation of the comparison populations not detailed. Missing data not detailed for talc miners or comparison populations.
	Metric 3:	Comparison Group	Medium	Demographics between talc workers and potash workers noted as comparable with a few exceptions for those with less than 15 years employment (non-smoking talc workers were younger than potash workers, smoking talc workers smoked more than potash workers) and for those with more than 15 years of exposure (potash non-smokers and ex-smokers were slightly older than talc workers and smoking talc workers smoked less daily but had more overall pack-years than potash workers). However, workers in each population were grouped into or adjusted for categories of similar age, smoking and duration of mining employment for stratified and regression analyses. Uncertainty regarding potential healthy worker effects as prevalent hires comprised the available population for study. Further uncertainty in utilizing potash workers and synthetic textile workers as comparison groups with the potential for asbestos fibers within potash mines, as well as the potential for pulmonary function changes in workers exposed to synthetic fibers.
Domain 2: Exposure Characterization				

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Study Citation:	Gamble, J. F., Fellner, W., Dimeo, M. J. (1979). An epidemiologic study of a group of talc workers. American Review of Respiratory Disease 119(5):741-753.
Health Outcome:	Pulmonary Function/Spirometry Results
Target Organ(s):	Lung/Respiratory: Vmax50
Asbestos Fiber Type(s):	Asbestos - Tremolite: 14567-73-8; Asbestos - Anthophyllite: 17068-78-9
Linked HERO ID(s):	No linked references.
HERO ID:	29531

Domain	Metric		Rating	Comments
	Metric 4:	Measurement of Exposure	Medium	Personal air samples were collected from miners and millers to determine the time-weighted average (TWA) exposure to respirable dust, free silica, and asbestos fibers. Sampling methods described in terms of sampling equipment, procedures and study site characteristics for talc miners, with sampling equipment and procedures described for potash miner exposures. Analytic methodology described in terms of instrumentation (electron microscopy on a random sample) and standard (NIOSH phase contrast counting technique) methods for talc miners and in terms of instrumentation (for total dust, percent free silica, NO2, but not area total respirable particulate sampling) for potash miners. Estimated personal exposure to respirable particulates in potash miners was calculated from averaged proportions of total particulate from area sampling within each potash mine. Cumulative exposure for talc and potash miners described as calculated from personal sampling and summation of historical time in each job. Uncertainty regarding cumulative exposure estimates as text notes no fiber sampling was done before 1970, exposures for each job were not well documented, representativeness of samples described as "unknown" and estimates of cumulative exposures described as "probably lower than actual cumulative exposures".
	Metric 5:	Exposure Levels	Medium	Distribution of asbestos fiber exposure presented within Table 2 by age group and adequate for analyses. Table 8 presented regression results utilizing estimated cumulative fiber exposure calculated from historical exposures as continuous independent variables predicting mean percent of predicted pulmonary function and changes in predicted pulmonary function. Other analyses presented results across talc versus potash and textile worker groups as exposed versus non-exposed categories without incorporation of measured or estimated cumulative exposures within models (Table 7).
	Metric 6:	Temporality	Medium	Uncertainty regarding temporality due to cross-sectional nature of study, however text notes average duration of exposure to talc was 10.2 years. Range of employment duration not specified. Unclear number of years required for appearance of some pulmonary function outcomes of interest.
Domain 3: Outcome Assessment				

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Study Citation:	Gamble, J. F., Fellner, W., Dimeo, M. J. (1979). An epidemiologic study of a group of talc workers. American Review of Respiratory Disease 119(5):741-753.
Health Outcome:	Pulmonary Function/Spirometry Results
Target Organ(s):	Lung/Respiratory: Vmax50
Asbestos Fiber Type(s):	Asbestos - Tremolite: 14567-73-8; Asbestos - Anthophyllite: 17068-78-9
Linked HERO ID(s):	No linked references.
HERO ID:	29531

Domain	Metric		Rating	Comments
	Metric 7:	Outcome Measurement or Characterization	Medium	Pulmonary Function/Spirometry Results: Pulmonary function outcomes of interest included FEV1, FVC, FEV1/FVC%, Vmax50, Vmax75, pulmonary symptoms (cough, phlegm, hemoptysis, dyspnea >= grade 2, pleural calcification, pneumoconiosis (opacities) and pleural thickening). Text notes use of respiratory questionnaire by the Medical Research Council for smoking and total work data, however it is unclear if this questionnaire was also utilized for obtaining data for pulmonary symptom outcomes. Pleural thickening, opacities and calcification outcomes would have been obtainable from the standard posteroanterior chest roentgenograms read independently without knowledge of age, occupation and smoking history by three "B" readers using ILO standard schemes. Pulmonary function outcomes obtained utilizing standard spirometry methods.
	Metric 8:	Reporting Bias	Medium	No substantial concerns for selective reporting, although text noted blood samples collected from talc workers for analyses of antinuclear antibodies and rheumatoid factor which do not seem to have been analyzed, however these were not included as outcomes of interest within original study objectives.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	High	Results reported as adjusted utilizing stratification and multivariate regression. Final multivariate analysis (Table 6) adjusted for age, height, and smoking status. Additional analyses (Table 8) adjusted for years of employment. Study restricted to males. Distribution of covariates presented for talc and potash workers presented within Table 5.
	Metric 10:	Covariate Characterization	Medium	Data regarding potential confounders seems to have been collected within the Medical Research Council respiratory questionnaire, however it is unclear as source for independent variable data not detailed directly in text.
	Metric 11:	Co-exposure Counfounding	Low	Final analyses presented results without adjusting for co-exposures potentially relevant to pulmonary function outcomes, such as silica.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	Medium	Study utilized stratification and multivariate regression for analyses of cross-sectional data for lung function outcomes. Unclear amount of asbestos exposure in comparison group potash workers. Unclear effect of utilizing synthetic textile workers as comparison group, with their potential for increased risks of fiber exposure-related decreased pulmonary function.
	Metric 13:	Statistical Power	Medium	Number of subjects adequate and reported as n=93 male talc miners and millers compared with n=1,077 potash miners. Uncertainty regarding the number of comparison group textile workers (Table 10).

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Study Citation:	Gamble, J. F., Fellner, W., Dimeo, M. J. (1979). An epidemiologic study of a group of talc workers. American Review of Respiratory Disease 119(5):741-753.
Health Outcome:	Pulmonary Function/Spirometry Results
Target Organ(s):	Lung/Respiratory: Vmax50
Asbestos Fiber Type(s):	Asbestos - Tremolite: 14567-73-8; Asbestos - Anthophyllite: 17068-78-9
Linked HERO ID(s):	No linked references.
HERO ID:	29531

Domain	Metric		Rating	Comments
	Metric 14:	Reproducibility of Analyses	Medium	Statistical analyses reported as multivariate regression, however details of analyses unclear for regression in terms of handling of missing data, consideration of outliers, transformation of continuous variables and model assumptions.
	Metric 15:	Statistical Analysis	Low	Description of analysis brief with assumptions lacking.

Additional Comments: The relationship between pulmonary function (FEV1, FVC, FEV1/FVC%, Vmax50, Vmax75, pulmonary symptoms, pleural calcification, pneumonoconiosis, pleural thickening) and exposures to talc containing anthophyllite and tremolite fibers in talc workers (n=93) versus potash miners (n=1,077) and synthetic textile workers (Table 10) was examined in this cross-sectional study. Results indicated increased respiratory symptoms, radiographic abnormalities and decreased pulmonary function among these talc miners and millers with some findings noted as related to dose and duration of exposure.The measurement exposure (M4) and/or exposure levels (M5) metrics are rated as medium upon review by both set of reviewers. Also, the overall quality determination (OQD) is rated medium. Extraction has been completed and quality control reviewed.

Overall Quality Determination — Medium

* No biomarkers were identified for this evaluation.

Study Citation:	Gamble, J. F., Fellner, W., Dimeo, M. J. (1979). An epidemiologic study of a group of talc workers. American Review of Respiratory Disease 119(5):741-753.
Health Outcome:	Pulmonary Function/Spirometry Results
Target Organ(s):	Lung/Respiratory: VMax75
Asbestos Fiber Type(s):	Asbestos - Tremolite: 14567-73-8; Asbestos - Anthophyllite: 17068-78-9
Linked HERO ID(s):	No linked references.
HERO ID:	29531

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Medium	The relationship between pulmonary function and exposures to talc containing anthophyllite and tremolite fibers in talc workers (n=93) versus potash miners (n=1,077) and versus synthetic textile workers (Table 10) was examined in this cross-sectional study. A total of n=121 workers (78% of the n=156 total miller and miner work force) participated, however results were restricted to the n=93 males who had only worked at the talc mine and mill under study. Participation rates were noted as similar across different work areas. Participants and non-participants were noted to have had similar average exposure duration in years (10.2 years for participants, 10.5 years for non-participants). Selection process and participation rates for potash and synthetic textile comparison group worker data not detailed.
	Metric 2:	Attrition	Medium	Talc millers and miner participants not working at the talc mine and mill under study (n=28) were excluded, however sensitivity analyses revealed similar results when all 121 participants of the original n=156 male talc workforce were included in the analyses. Comparison population consisted of n=1,077 potash mine workers and synthetic textile workers (Table 10), however details on any exclusions involved in the creation of the comparison populations not detailed. Missing data not detailed for talc miners or comparison populations.
	Metric 3:	Comparison Group	Medium	Demographics between talc workers and potash workers noted as comparable with a few exceptions for those with less than 15 years employment (non-smoking talc workers were younger than potash workers, smoking talc workers smoked more than potash workers) and for those with more than 15 years of exposure (potash non-smokers and ex-smokers were slightly older than talc workers and smoking talc workers smoked less daily but had more overall pack-years than potash workers). However, workers in each population were grouped into or adjusted for categories of similar age, smoking and duration of mining employment for stratified and regression analyses. Uncertainty regarding potential healthy worker effects as prevalent hires comprised the available population for study. Further uncertainty in utilizing potash workers and synthetic textile workers as comparison groups with the potential for asbestos fibers within potash mines, as well as the potential for pulmonary function changes in workers exposed to synthetic fibers.
Domain 2: Exposure Characterization				

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Study Citation:	Gamble, J. F., Fellner, W., Dimeo, M. J. (1979). An epidemiologic study of a group of talc workers. American Review of Respiratory Disease 119(5):741-753.
Health Outcome:	Pulmonary Function/Spirometry Results
Target Organ(s):	Lung/Respiratory: VMax75
Asbestos Fiber Type(s):	Asbestos - Tremolite: 14567-73-8; Asbestos - Anthophyllite: 17068-78-9
Linked HERO ID(s):	No linked references.
HERO ID:	29531

Domain	Metric		Rating	Comments
	Metric 4:	Measurement of Exposure	Medium	Personal air samples were collected from miners and millers to determine the time-weighted average (TWA) exposure to respirable dust, free silica, and asbestos fibers. Sampling methods described in terms of sampling equipment, procedures and study site characteristics for talc miners, with sampling equipment and procedures described for potash miner exposures. Analytic methodology described in terms of instrumentation (electron microscopy on a random sample) and standard (NIOSH phase contrast counting technique) methods for talc miners and in terms of instrumentation (for total dust, percent free silica, NO2, but not area total respirable particulate sampling) for potash miners. Estimated personal exposure to respirable particulates in potash miners was calculated from averaged proportions of total particulate from area sampling within each potash mine. Cumulative exposure for talc and potash miners described as calculated from personal sampling and summation of historical time in each job. Uncertainty regarding cumulative exposure estimates as text notes no fiber sampling was done before 1970, exposures for each job were not well documented, representativeness of samples described as "unknown" and estimates of cumulative exposures described as "probably lower than actual cumulative exposures".
	Metric 5:	Exposure Levels	Medium	Distribution of asbestos fiber exposure presented within Table 2 by age group and adequate for analyses. Table 8 presented regression results utilizing estimated cumulative fiber exposure calculated from historical exposures as continuous independent variables predicting mean percent of predicted pulmonary function and changes in predicted pulmonary function. Other analyses presented results across talc versus potash and textile worker groups as exposed versus non-exposed categories without incorporation of measured or estimated cumulative exposures within models (Table 7).
	Metric 6:	Temporality	Medium	Uncertainty regarding temporality due to cross-sectional nature of study, however text notes average duration of exposure to talc was 10.2 years. Range of employment duration not specified. Unclear number of years required for appearance of some pulmonary function outcomes of interest.
Domain 3: Outcome Assessment				

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Study Citation: Gamble, J. F., Fellner, W., Dimeo, M. J. (1979). An epidemiologic study of a group of talc workers. American Review of Respiratory Disease 119(5):741-753.
Health Outcome: Pulmonary Function/Spirometry Results
Target Organ(s): Lung/Respiratory: VMax75
Asbestos Fiber Type(s): Asbestos - Tremolite: 14567-73-8; Asbestos - Anthophyllite: 17068-78-9
Linked HERO ID(s): No linked references.
HERO ID: 29531

Domain	Metric		Rating	Comments
	Metric 7:	Outcome Measurement or Characterization	Medium	Pulmonary Function/Spirometry Results: Pulmonary function outcomes of interest included FEV1, FVC, FEV1/FVC%, Vmax50, Vmax75, pulmonary symptoms (cough, phlegm, hemoptysis, dyspnea >= grade 2, pleural calcification, pneumoconiosis (opacities) and pleural thickening). Text notes use of respiratory questionnaire by the Medical Research Council for smoking and total work data, however it is unclear if this questionnaire was also utilized for obtaining data for pulmonary symptom outcomes. Pleural thickening, opacities and calcification outcomes would have been obtainable from the standard posteroanterior chest roentgenograms read independently without knowledge of age, occupation and smoking history by three "B" readers using ILO standard schemes. Pulmonary function outcomes obtained utilizing standard spirometry methods.
	Metric 8:	Reporting Bias	Medium	No substantial concerns for selective reporting, although text noted blood samples collected from talc workers for analyses of antinuclear antibodies and rheumatoid factor which do not seem to have been analyzed, however these were not included as outcomes of interest within original study objectives.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	High	Results reported as adjusted utilizing stratification and multivariate regression. Final multivariate analysis (Table 6) adjusted for age, height, and smoking status. Additional analyses (Table 8) adjusted for years of employment. Study restricted to males. Distribution of covariates presented for talc and potash workers presented within Table 5.
	Metric 10:	Covariate Characterization	Medium	Data regarding potential confounders seems to have been collected within the Medical Research Council respiratory questionnaire, however it is unclear as source for independent variable data not detailed directly in text.
	Metric 11:	Co-exposure Counfounding	Low	Final analyses presented results without adjusting for co-exposures potentially relevant to pulmonary function outcomes, such as silica.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	Medium	Study utilized stratification and multivariate regression for analyses of cross-sectional data for lung function outcomes. Unclear amount of asbestos exposure in comparison group potash workers. Unclear effect of utilizing synthetic textile workers as comparison group, with their potential for increased risks of fiber exposure-related decreased pulmonary function.
	Metric 13:	Statistical Power	Medium	Number of subjects adequate and reported as n=93 male talc miners and millers compared with n=1,077 potash miners. Uncertainty regarding the number of comparison group textile workers (Table 10).

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Study Citation:	Gamble, J. F., Fellner, W., Dimeo, M. J. (1979). An epidemiologic study of a group of talc workers. American Review of Respiratory Disease 119(5):741-753.
Health Outcome:	Pulmonary Function/Spirometry Results
Target Organ(s):	Lung/Respiratory: VMax75
Asbestos Fiber Type(s):	Asbestos - Tremolite: 14567-73-8; Asbestos - Anthophyllite: 17068-78-9
Linked HERO ID(s):	No linked references.
HERO ID:	29531

Domain	Metric		Rating	Comments
	Metric 14:	Reproducibility of Analyses	Medium	Statistical analyses reported as multivariate regression, however details of analyses unclear for regression in terms of handling of missing data, consideration of outliers, transformation of continuous variables and model assumptions.
	Metric 15:	Statistical Analysis	Low	Description of analysis brief with assumptions lacking.

Additional Comments: The relationship between pulmonary function (FEV1, FVC, FEV1/FVC%, Vmax50, Vmax75, pulmonary symptoms, pleural calcification, pneumonoconiosis, pleural thickening) and exposures to talc containing anthophyllite and tremolite fibers in talc workers (n=93) versus potash miners (n=1,077) and synthetic textile workers (Table 10) was examined in this cross-sectional study. Results indicated increased respiratory symptoms, radiographic abnormalities and decreased pulmonary function among these talc miners and millers with some findings noted as related to dose and duration of exposure.The measurement exposure (M4) and/or exposure levels (M5) metrics are rated as medium upon review by both set of reviewers. Also, the overall quality determination (OQD) is rated medium. Extraction has been completed and quality control reviewed.

Overall Quality Determination — Medium

* No biomarkers were identified for this evaluation.

Study Citation:	Gamble, J. F., Fellner, W., Dimeo, M. J. (1979). An epidemiologic study of a group of talc workers. American Review of Respiratory Disease 119(5):741-753.
Health Outcome:	Pleural Plaques
Target Organ(s):	Lung/Respiratory: Pleural thickening, Pleural calcification, Irregular opacities, Rounded opacities
Asbestos Fiber Type(s):	Asbestos - Tremolite: 14567-73-8; Asbestos - Anthophyllite: 17068-78-9
Linked HERO ID(s):	No linked references.
HERO ID:	29531

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Medium	This cross-sectional study examined the relationship between pulmonary function and exposures to talc containing anthophyllite and tremolite fibers in talc workers (n=93) versus potash miners (n=1,077) and versus synthetic textile workers. A total of n=121 workers (78% of the n=156 total miller and miner work force) participated, however results were restricted to the n=93 males who had only worked at the talc mine and mill under study. Participation rates were noted as similar across different work areas. Participants and non-participants were noted to have had similar average exposure duration in years (10.2 years for participants, 10.5 years for non-participants). Selection process and participation rates for potash and synthetic textile comparison group worker data not detailed.
	Metric 2:	Attrition	Medium	Talc millers and miner participants not working at the talc mine and mill under study (n=28) were excluded, however sensitivity analyses revealed similar results when all 121 participants of the original n=156 male talc workforce were included in the analyses. Comparison population consisted of n=1,077 potash mine workers and synthetic textile workers (Table 10), however details on any exclusions involved in the creation of the comparison populations not detailed. Missing data not detailed for talc miners or comparison populations.
	Metric 3:	Comparison Group	Medium	Demographics between talc workers and potash workers noted as comparable with a few exceptions for those with less than 15 years employment (non-smoking talc workers were younger than potash workers, smoking talc workers smoked more than potash workers) and for those with more than 15 years of exposure (potash non-smokers and ex-smokers were slightly older than talc workers and smoking talc workers smoked less daily but had more overall pack-years than potash workers). However, workers in each population were grouped into or adjusted for categories of similar age, smoking and duration of mining employment for stratified and regression analyses. Uncertainty regarding potential healthy worker effects as prevalent hires comprised the available population for study. Further uncertainty in utilizing potash workers and synthetic textile workers as comparison groups with the potential for asbestos fibers within potash mines, as well as the potential for pulmonary function changes in workers exposed to synthetic fibers.
Domain 2: Exposure Characterization				

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Study Citation:	Gamble, J. F., Fellner, W., Dimeo, M. J. (1979). An epidemiologic study of a group of talc workers. American Review of Respiratory Disease 119(5):741-753.
Health Outcome:	Pleural Plaques
Target Organ(s):	Lung/Respiratory: Pleural thickening, Pleural calcification, Irregular opacities, Rounded opacities
Asbestos Fiber Type(s):	Asbestos - Tremolite: 14567-73-8; Asbestos - Anthophyllite: 17068-78-9
Linked HERO ID(s):	No linked references.
HERO ID:	29531

Domain	Metric		Rating	Comments
	Metric 4:	Measurement of Exposure	Medium	Personal air samples were collected from miners and millers to determine the time-weighted average (TWA) exposure to respirable dust, free silica, and asbestos fibers. Sampling methods described in terms of sampling equipment, procedures and study site characteristics for talc miners, with sampling equipment and procedures described for potash miner exposures. Analytic methodology described in terms of instrumentation (electron microscopy on a random sample) and standard (NIOSH phase contrast counting technique) methods for talc miners and in terms of instrumentation (for total dust, percent free silica, NO2, but not area total respirable particulate sampling) for potash miners. Estimated personal exposure to respirable particulates in potash miners was calculated from averaged proportions of total particulate from area sampling within each potash mine. Cumulative exposure for talc and potash miners described as calculated from personal sampling and summation of historical time in each job. Uncertainty regarding cumulative exposure estimates as text notes no fiber sampling was done before 1970, exposures for each job were not well documented, representativeness of samples described as "unknown" and estimates of cumulative exposures described as "probably lower than actual cumulative exposures".
	Metric 5:	Exposure Levels	Medium	Distribution of asbestos fiber exposure presented within Table 2 by age group and adequate for analyses. Table 8 presented regression results utilizing estimated cumulative fiber exposure calculated from historical exposures as continuous independent variables predicting mean percent of predicted pulmonary function and changes in predicted pulmonary function. Other analyses presented results across talc versus potash and textile worker groups as exposed versus non-exposed categories without incorporation of measured or estimated cumulative exposures within models (Table 7).
	Metric 6:	Temporality	Medium	Uncertainty regarding temporality due to cross-sectional nature of study, however text notes average duration of exposure to talc was 10.2 years. Range of employment duration not specified. Unclear number of years required for appearance of some pulmonary function outcomes of interest.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	High	Pleural Plaques: Chest roentgenograms were examined by three "B" readers according to the ILO U/C 1971 scheme. Each film was read independently, and the readers were blinded to the age, occupation, and smoking history of the individuals the roentgenograms belonged to. The median value from the three readings was included and utilized for analyses. It is important to note that authors only examined prevalence of pleural findings, such as in Tables 3 and 4.

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Asbestos Fiber Type(s):	Asbestos - Tremolite: 14567-73-8; Asbestos - Anthophyllite: 17068-78-9
Linked HERO ID(s):	No linked references.
HERO ID:	29531

Domain	Metric		Rating	Comments
	Metric 8:	Reporting Bias	Medium	No substantial concerns for selective reporting, although text noted blood samples collected from talc workers for analyses of antinuclear antibodies and rheumatoid factor which do not seem to have been analyzed, however these were not included as outcomes of interest within original study objectives.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	High	Results reported as adjusted utilizing stratification and multivariate regression. Final multivariate analysis (Table 6) adjusted for age, height, and smoking status. Additional analyses (Table 8) adjusted for years of employment. Study restricted to males. Distribution of covariates presented for talc and potash workers presented within Table 5.
	Metric 10:	Covariate Characterization	Medium	Data regarding potential confounders seems to have been collected within the Medical Research Council respiratory questionnaire, however it is unclear as source for independent variable data not detailed directly in text.
	Metric 11:	Co-exposure Counfounding	Low	Final analyses presented results without adjusting for co-exposures potentially relevant to pulmonary function outcomes, such as silica.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	Medium	Study utilized stratification and multivariate regression for analyses of cross-sectional data for lung function outcomes. Unclear amount of asbestos exposure in comparison group potash workers. Unclear effect of utilizing synthetic textile workers as comparison group, with their potential for increased risks of fiber exposure-related decreased pulmonary function.
	Metric 13:	Statistical Power	Medium	Number of subjects adequate and reported as n=93 male talc miners and millers compared with n=1,077 potash miners. Uncertainty regarding the number of comparison group textile workers (Table 10).
	Metric 14:	Reproducibility of Analyses	Medium	Statistical analyses reported as multivariate regression, however details of analyses unclear for regression in terms of handling of missing data, consideration of outliers, transformation of continuous variables and model assumptions.
	Metric 15:	Statistical Analysis	Low	Description of analysis brief with assumptions lacking.

Additional Comments:	The relationship between pulmonary function (FEV1, FVC, FEV1/FVC%, Vmax50, Vmax75, pulmonary symptoms, pleural calcification, pneumoconiosis, pleural thickening) and exposures to talc containing anthophyllite and tremolite fibers in talc workers (n=93) versus potash miners (n=1,077) and synthetic textile workers (Table 10) was examined in this cross-sectional study. Results indicated increased respiratory symptoms, radiographic abnormalities and decreased pulmonary function among these talc miners and millers with some findings noted as related to dose and duration of exposure.

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Asbestos Fiber Type(s):	Asbestos - Tremolite: 14567-73-8; Asbestos - Anthophyllite: 17068-78-9
Linked HERO ID(s):	No linked references.
HERO ID:	29531

Domain	Metric	Rating	Comments
Overall Quality Determination		**Medium**	

* No biomarkers were identified for this evaluation.

Study Citation:	Gardner, M. J., Winter, P. D., Pannett, B., Powell, C. A. (1986). Follow up study of workers manufacturing chrysotile asbestos cement products. British Journal of Industrial Medicine 43(11):726-732.
Health Outcome:	Lung Cancer; All malignant neoplasms, other sites; Asbestosis; All other causes, circulatory disease, respiratory disease, accidents poisoning and violence, other causes, all causes
Target Organ(s):	Lung/Respiratory: Asbestosis; Cancer/Carcinogenesis: Lung cancer, All malignant neoplasms; Mortality: All other causes, circulatory diseases, respiratory diseases, accidents poisoning and violence, other causes, all cause
Asbestos Fiber Type(s):	Asbestos - Chrysotile (serpentine): 12001-29-5
Linked HERO ID(s):	No linked references.
HERO ID:	3083223

Domain		Metric	Rating	Comments
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Low	Atmospheric fibre concentrations were made during period 1968-82 by company and were assigned codes to job ittles to reflect levels of probable exposure (table 2). Over 70% of readings are based on use of personal samplers. ”For the period before 1968 it would be reasonable to assume that levels were higher because of less extensive exhaust ventilation and more direct handling of raw asbestos”.
	Metric 5:	Exposure Levels	Low	”Since 10=970 fibre levels have generally bene low with mean levels under 1 f/ml throughout factory. Only a few exposures over 2f/ml have been recorded and most measured concentrations have been under 0.5f/ml.”

Additional Comments: Cohort study, 2167 subjects employed between 1941-1983 at asbestos cement factory in England. One death from mesothelioma (pleural in the study cohort during the follow-up period. A death, for which the underlying cause was reported as cancer of the lung mentioned as asbestosis as an associated condition. Metric 4 and 5 were low for both mesothelioma and other outcomes, so stopped evaluating. Mention of ”small amount of amosite during four months in 1976,” but not further analyzed.Overall, information on the measurement of exposure metric (M4) to assess exposure was limited. Additionally, the exposure levels metric (M5) information reported was limited to determine an exposure-response relationships.

** As described in Appendix B.2 of the *White Paper: Quantitative Approach to the Human Health Assessment for the Risk Evaluation for Asbestos Part 2: Supplemental Evaluation Including Legacy Uses and Associated Disposals of Asbestos*, to be considered as being informative for dose-response analysis, metrics 4 and 5 would need metric ratings of Medium or High. This reference did not satisfy this requirement; therefore data quality evaluation is presented for only for metrics 4 and 5.

Study Citation:	Gautam, A. K., Yunus, M., Rahman, A., Reddy, S. S. (2003). Environmental monitoring of asbestos products manufacturing units–a case study. Indian Journal of Environmental Health 45(4):289-292.			
Health Outcome:	Pulmonary Function/Spirometry Results			
Target Organ(s):	Lung/Respiratory: VC, FVC, FEV1, %FEV1/FVC, Peak Expiratory Flow Rate (PEFR), Forced Expiratory Flow Rate (FEF2-12), Maximum Mid Expiratory Flow Rate (MEF25-75%)			
Asbestos Fiber Type(s):	Asbestos - Not specified: 1332-21-4			
Linked HERO ID(s):	No linked references.			
HERO ID:	3080098			
Domain	Metric		Rating	Comments
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Medium	The authors described how the measurements were taken and the use of PCM to count asbestos fibers, but do not provide details about the sampling procedure or detailed quantitative estimates of exposure.
	Metric 5:	Exposure Levels	Low	The range of exposure in the study's population is limited based on the data reported on Figure 2.
Additional Comments:	None			

* No biomarkers were identified for this evaluation.

** As described in Appendix B.2 of the *White Paper: Quantitative Approach to the Human Health Assessment for the Risk Evaluation for Asbestos Part 2: Supplemental Evaluation Including Legacy Uses and Associated Disposals of Asbestos*, to be considered as being informative for dose-response analysis, metrics 4 and 5 would need metric ratings of Medium or High. This reference did not satisfy this requirement; therefore data quality evaluation is presented for only for metrics 4 and 5.

Study Citation:	Gilham, C., Rake, C., Burdett, G., Nicholson, A. G., Davison, L., Franchini, A., Carpenter, J., Hodgson, J., Darnton, A., Peto, J. (2015). Pleural mesothelioma and lung cancer risks in relation to occupational history and asbestos lung burden. Occupational and Environmental Medicine 73(5):290-299.
Health Outcome:	Lung Cancer
Target Organ(s):	Cancer/Carcinogenesis: Lung cancer cases and lung cancer mortality; Lung/Respiratory: Lung cancer cases and lung cancer mortality; Mortality: Lung cancer cases and lung cancer mortality
Asbestos Fiber Type(s):	Asbestos - Amosite (grunerite): 12172-73-5; Asbestos - Crocidolite (riebeckite): 12001-28-4; Asbestos - Chrysotile (serpentine): 12001-29-5; Asbestos - Not specified: 1332-21-4; Asbestos - Tremolite: 14567-73-8; Asbestos - Anthophyllite: 17068-78-9
Linked HERO ID(s):	No linked references.
HERO ID:	3077660

Domain	Metric	Rating	Comments
Domain 1: Study Participation			
	Metric 1: Participant Selection	Low	This study built on a case-control study referred to as the MALCS study (Rake et al., 2009, HERO ID 733522), which included mesothelioma patients and population controls. Telephone interviews of 622 mesothelioma patients and 1420 population controls in England, Wales, and Scotland were conducted between 2001 and 2006 as part of the MALCS study. Additionally, 420 patients with resected lung cancer born since 1940 were interviewed in the present study as controls for the mesothelioma patients as part of the present study (Gilham et al., 2015, HERO ID 3077660), though the dates of these interviews were not specified.Lung cancer patients were identified by ”chest physicians, lung cancer nurse specialists, and Hospital Episode Statistics (HES) notifications” from 170 hospitals throughout Britain ”Gilman et al., 2015, 3077660). Out of 420 lung cancer patients who were interviewed, 406 (96%) provided consent for resected tissue to be analyzed.The lung cancer patients were selected to be a control group for the analysis of mesothelioma patients because ”resected lung cancers provide the only adequate national source of lung samples in people who can be identified systematically, are available for interview and have an age distribution similar to mesothelioma. Only a small proportion of all lung cancers are caused by asbestos, so the asbestos lung burdens of this national sample are reasonably representative of the general population except for a few per cent with very high burdens.”The analysis of lung samples in the present paper was conducted on mesothelioma patients and lung cancer patients, but not the population controls from the MALCS study.Whereas reasons for exclusion were reported for the mesothelioma patients in the MALCS publication (Gilham et al., 2015, HERO ID 3077660), the present study (Gilham et al., 2015, HERO ID 3077660) did not report detailed inclusion and exclusion criteria for lung cancer cases, and did not report the number of lung cancer patients who were contacted but declined to be interviewed. Of those who were interviewed, ”written informed consent was obtained from 346 (77%) patients with mesothelioma and their next of kin for postmortem samples to be analyzed and from 406 (96%) patients with lung cancer for analysis of resected tissue.”Lifetime excess lung cancer and SMR risks standardized to British males born in 1945 were also determined.Thus, the paper did not report some relevant information about selection criteria.

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Linked HERO ID(s):	No linked references.
HERO ID:	3077660

Domain	Metric		Rating	Comments
	Metric 2:	Attrition	Medium	The authors reported that "written informed consent was obtained from 346 (77%) patients with mesothelioma and their next of kin for postmortem samples to be analyzed and from 406 (96%) patients with lung cancer for analysis of resected tissue." The use of postmortem samples for mesothelioma patients indicates that the analyses could not include samples from mesothelioma patients who were still alive. The use of resected tissue for lung cancer patients implies that the lung cancer patients may have been alive at the time of sample collection. The authors reported that samples were analyzed as they became available, such that transmission electron microscopy (TEM) was performed on 133 mesothelioma samples and 262 lung cancer samples. All of the analyzed samples were from patients born since 1940, with the exception of 11 female mesothelioma patients born between 1925-1939, who were excluded from most of the analyses. Thus, lung samples were analyzed for 133/346 (38%) of the mesothelioma patients and 262/406 (65%) of the lung cancer patients for whom consent was obtained. Thus, there was at least moderate exclusion from the analysis sample of lung cancer patients.
	Metric 3:	Comparison Group	Low	For the main analyses there was no control group for lung cancer because lung cancer cases were included as a control group for mesothelioma cases. The paper also included additional analyses of SMR, in which the comparison group was all British men born in 1945.The authors reported that "the lifetime risk (probability of dying by age 90) was calculated actuarially in each lung burden category assuming current (2013) UK rates for all other causes of death. These lifetime risks were standardized to the projected probabilities of dying by age 90 for mesothelioma (0.86%) and lung cancer (4.67%) of all British men born in 1945." SMRs in each lung burden category were determined "for the cohort of British men whose central date of birth is the beginning of 1945, (The median date of birth of our mesothelioma cases was September 1944.)"The SMR analyses were restricted to males, but the birth years of cases were not restricted to the one year (1945) of birth of the comparison group. Race was not mentioned in the paper.
Domain 2: Exposure Characterization				

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Study Citation:	Gilham, C., Rake, C., Burdett, G., Nicholson, A. G., Davison, L., Franchini, A., Carpenter, J., Hodgson, J., Darnton, A., Peto, J. (2015). Pleural mesothelioma and lung cancer risks in relation to occupational history and asbestos lung burden. Occupational and Environmental Medicine 73(5):290-299.
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Target Organ(s):	Cancer/Carcinogenesis: Lung cancer cases and lung cancer mortality; Lung/Respiratory: Lung cancer cases and lung cancer mortality; Mortality: Lung cancer cases and lung cancer mortality
Asbestos Fiber Type(s):	Asbestos - Amosite (grunerite): 12172-73-5; Asbestos - Crocidolite (riebeckite): 12001-28-4; Asbestos - Chrysotile (serpentine): 12001-29-5; Asbestos - Not specified: 1332-21-4; Asbestos - Tremolite: 14567-73-8; Asbestos - Anthophyllite: 17068-78-9
Linked HERO ID(s):	No linked references.
HERO ID:	3077660

Domain	Metric		Rating	Comments
	Metric 4:	Measurement of Exposure	Medium	Lifetime occupational history was obtained from telephone interviews of 622 mesothelioma patients, 1420 population controls, and 420 patients with resected lung cancer. Then "job titles were assigned to Standard Occupational Classification 1990 (SOC 90) and Standard Industrial Classification 1992 (SIC 92) codes and grouped into main job categories" (Gilham et al., 2015, 733522). The authors reported that "subjects were assigned to the highest-ranking occupation they had worked in irrespective of duration". Thus, although lifetime work history was obtained, the assignment of occupation was based on only a portion of this history.Transmission electron microscopy (TEM) was used to analyze 133 post-mortem lung tissue samples from a subset of the mesothelioma patients and 262 resected lung tissue samples from a subset of the lung cancer patients. The authors reported that "lung samples were anonymized and sent to the Health and Safety Laboratory (HSL) for TEM counting of asbestos fibers longer than 5 um."Lung tissue samples were analyzed as they became available. Because tissue samples, but not environmental samples, were analyzed, the samples were only analyzed at one time point for each individual, but this time point is representative of cumulative asbestos lung fiber burden.
	Metric 5:	Exposure Levels	Medium	The range and distribution of exposure was sufficient to develop an exposure-response estimate. The asbestos fiber burden in lung tissue was grouped into six categories for the analyses of SMR.
	Metric 6:	Temporality	Low	This study analyzed resected tissue from lung cancer patients. It is unclear whether all of the resected tissue samples were from lung cancer patients who were alive or whether some of the samples were obtained post-mortem. Regardless, the lung tissue samples were taken after the diagnosis of lung cancer. Thus, the exposure measurement was obtained after the outcome measurement. Therefore, the temporality of exposure and outcome is uncertain.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Medium	Lung Cancer: The authors state that lung cancer cases were "identified through chest physicians, lung cancer nurse specialists and Hospital Episode Statistics (HES)" from 170 hospitals throughout Britain (Gilham et al., 2015, HERO ID 733522). However, the paper did not specify whether the cases were confirmed by histological or cytological means, and did not specify ICD codes.
	Metric 8:	Reporting Bias	Medium	Although lung cancer SMRs were reported, associated confidence intervals were not reported.
Domain 4: Potential Confounding / Variability Control				

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Linked HERO ID(s):	No linked references.
HERO ID:	3077660

Domain		Metric	Rating	Comments
	Metric 9:	Covariate Adjustment	Low	The SMR analyses were restricted to males. SMR were standardized to the population of British males born in 1945, but the lung cancer cases were not restricted by birth year. Race was not mentioned in the paper.
	Metric 10:	Covariate Characterization	Medium	Although the authors did not discuss whether the questionnaires used to interview participants were validated, there is no evidence to suggest any concerns about the validity of the method. It is unlikely that the participants would have incorrectly reported sex or age.
	Metric 11:	Co-exposure Counfounding	Low	Potential co-exposures were not addressed.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	Medium	The main research question addressed the association between asbestos lung burden and mesothelioma. The main study design and methods are uninformative for lung cancer because lung cancer cases were used as a control group for mesothelioma cases. Thus, the main study design is not appropriate for assessing the association between asbestos exposure and lung cancer.However, the study also assessed lifetime excess lung cancer risk and lung cancer SMRs for asbestos fiber burden categories standardized to the population of British males born in 1945, which is an appropriate statistical method for assessing the association between asbestos exposure and lung cancer mortality.
	Metric 13:	Statistical Power	Medium	Although the authors did not provide an explicit discussion of power, and did not provide p-values or confidence intervals for some of the results, there appears to be a sufficient number of lung cancer cases for analyses of SMR by asbestos fiber burden category.
	Metric 14:	Reproducibility of Analyses	Medium	The analyses were described in sufficient detail in the paper and in ”Appendix 1: Statistical Methods” (Gilham et al., 2015, 3077660).
	Metric 15:	Statistical Analysis	Medium	Although some details could have been explained better, the methods for calculating the SMRs were sufficiently transparent.
Domain 6: Other (if applicable) Considerations for Biomarker Selection and Measurement (Lakind et al. 2014)				

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Linked HERO ID(s):	No linked references.
HERO ID:	3077660

Domain	Metric		Rating	Comments
	Metric 16:	Use of Biomarker of Exposure	High	This study asbestos used fiber concentrations in lung tissue samples as a biomarker of asbestos exposure, which has a clear relationship with target dose. Transmission electron microscopy (TEM) was used to measure this biomarker. In the lung cancer and mesothelioma lung tissue samples assessed in this study, 75% of the counted fibers were amosite, 18% were crocidolite, 1.9% were chrysotile, 1 % were tremolite, 2 % were anthophyllite, 0.6% were actinolite, and 1.7% were uncharacterized amphiboles. Thus, several different fiber types were identified in this study because TEM can distinguish between fiber types, thus determining specific biomarkers of exposure (fiber concentrations in lung tissue) for each specific fiber type.
	Metric 17:	Effect Biomarker	N/A	The only biomarkers assessed were biomarkers of exposure. Biomarkers of effect were not assessed.
	Metric 18:	Method Sensitivity	Medium	As described in Appendix 2, the analytical sensitivity for fiber counts was 0.01 million fibers per dry gram. Only 2.8% of all samples, and 9/262 lung cancer samples, did not achieve this sensitivity due to low fiber concentrations and high amounts of other particles. The sensitivity was later increased to 0.003 mf/g by using newer equipment for a selected subgroup of samples.
	Metric 19:	Biomarker Stability	Low	All lung tissue samples were sent to a pathology laboratory in Leeds for an initial assessment and preparation and then were sent to the Health and Safety Laboratory (HSL) for TEM analysis. Specific preparation for storage and transport was not detailed, though it was mentioned that blocks were waxed and de-waxed. The authors did not specifically discuss the stability of the biomarker.
	Metric 20:	Sample Contamination	High	The authors detail that “new disposable containers and filtration equipment were used for each sample to avoid cross-contamination and a process blank was run with each batch of analyses” (Gilham et al., 2015, 3077660)
	Metric 21:	Method Requirements	High	The use of transmission electron microscopy (TEM) enabled appropriate identification and quantification of asbestos fibers in the samples.
	Metric 22:	Matrix Adjustment	N/A	Matrix adjustment is not required for assessment of this biomarker.

Additional Comments:	The main study design and methods are uninformative for lung cancer because lung cancer cases were used as a control group for mesothelioma cases. The study also assessed lifetime excess lung cancer risk and standardized mortality ratios (SMR) for lung cancer standardized to all British men born in 1945, which may be informative, but there are several concerns about the potential usefulness of this study for assessing the association between asbestos exposure and lung cancer. A strength is that researchers utilized transmission electron microscopy (TEM) to determine asbestos concentrations in resected tissue samples from lung cancer patients. Concerns include insufficient details reported for participant selection, outcome measurement, and participant characteristics including age and race.

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Study Citation:	Gilham, C., Rake, C., Burdett, G., Nicholson, A. G., Davison, L., Franchini, A., Carpenter, J., Hodgson, J., Darnton, A., Peto, J. (2015). Pleural mesothelioma and lung cancer risks in relation to occupational history and asbestos lung burden. Occupational and Environmental Medicine 73(5):290-299.
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Linked HERO ID(s):	No linked references.
HERO ID:	3077660

Domain	Metric	Rating	Comments
Overall Quality Determination		**Low**	

Study Citation:	Green, F. H. Y., Harley, R., Vallyathan, V., Althouse, R., Fick, G., Dement, J., Mitha, R., Pooley, F. (1997). Exposure and mineralogical correlates of pulmonary fibrosis in chrysotile asbestos workers. Occupational and Environmental Medicine 54(8):549-559.
Health Outcome:	Lung Cancer; Asbestosis
Target Organ(s):	Lung/Respiratory: asbestosis (pathological pulmonary fibrosis grade), lung cancer, asbestosis mortality, lung cancer mortality; Cancer/Carcinogenesis: lung cancer, lung cancer mortality; Mortality: asbestosis mortality, lung cancer mortality
Asbestos Fiber Type(s):	Asbestos - Chrysotile (serpentine): 12001-29-5; Asbestos - Crocidolite (riebeckite): 12001-28-4; Asbestos - Tremolite: 14567-73-8; Asbestos - Amosite (grunerite): 12172-73-5; Asbestos - Anthophyllite: 17068-78-9
Linked HERO ID(s):	7837, 709498, 3081241
HERO ID:	7837

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Medium	This retrospective cohort study included employees of a Charleston, South Carolina asbestos packing material and asbestos textile producing plant. As described in Green et al. 1997 (RefID 7837), eligible participants included all employees employed in textile production for at least one month (men) or six months (women) in the plant between 01 January 1940 and 31 December 1965 who were followed up until 31 December 1975. A total of n=3744 employees were identified, with n=874 deaths. Necropsy records were obtained for only n=87 (10%) of these deaths, for which pathological material was available for only n=59. Exclusion of five asbestos workers due to major confounding diseases of chemotherapy fibrosis (n=2) and radiation fibrosis (n=3) left a total of n=54 asbestos workers for analysis (Green et al, 1997, 7837). Non-asbestos control workers with available necropsy data were only described as matched to asbestos workers in terms of age of death, sex, hospital of death, and year of death. Of the n=38 initially identified controls, n=4 controls were excluded due to sarcoidosis (n=1), radiation fibrosis (n=1), tuberculosis (n=1), and scleroderma (n=1), leaving only n=34 matched controls for analyses. Lung tissue suitable for mineralogical fiber analysis was only available for n=39 former asbestos workers and n=31 non-exposed controls, however authors noted no significant differences in demographic profile or exposure history between the whole cohort of asbestos workers and the subgroup with mineralogical fiber data (Green et al., 1997, 7837). Due to the small number of asbestos workers with eligible necropsy data (n=87, or 10%) out of the total number of deaths (n=874) from the original population, as well as the number of eligible non-exposed controls (n=34), it is unclear if the exposure-outcome distribution of participants is representative of that of the target population (Green et al., 1997, RefID 7837). Key elements of study design are also reported for Stayner et al., 1997, RefID 3081241 and Hein et al., 2007, RefID 709498 for employees at the same asbestos plant employed at least one month between 1940 and 1975. However, follow-up for RefID 3081241 was extended up to 31 December 1990 and included an additional n=546 non-white men, n=1,229 white women, and n=19 non-white women. Follow-up for RefID 709498 was extended through 2001 for a total of 3,072 workers which included white and non-white males, white and non-white female workers as well as additional n=29 workers previously excluded but for whom updated demographic information was obtained.

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Study Citation:	Green, F. H. Y., Harley, R., Vallyathan, V., Althouse, R., Fick, G., Dement, J., Mitha, R., Pooley, F. (1997). Exposure and mineralogical correlates of pulmonary fibrosis in chrysotile asbestos workers. Occupational and Environmental Medicine 54(8):549-559.
Health Outcome:	Lung Cancer; Asbestosis
Target Organ(s):	Lung/Respiratory: asbestosis (pathological pulmonary fibrosis grade), lung cancer, asbestosis mortality, lung cancer mortality; Cancer/Carcinogenesis: lung cancer, lung cancer mortality; Mortality: asbestosis mortality, lung cancer mortality
Asbestos Fiber Type(s):	Asbestos - Chrysotile (serpentine): 12001-29-5; Asbestos - Crocidolite (riebeckite): 12001-28-4; Asbestos - Tremolite: 14567-73-8; Asbestos - Amosite (grunerite): 12172-73-5; Asbestos - Anthophyllite: 17068-78-9
Linked HERO ID(s):	7837, 709498, 3081241
HERO ID:	7837

Domain	Metric		Rating	Comments
	Metric 2:	Attrition	Medium	The text noted that for the outcome of fibrosis score, slides consisting predominantly of tumor, bronchus, lymph nodes, abscess or infarct were excluded, but the number of excluded slides was not detailed and any additional loss to follow-up or missing data for outcome or exposure was not detailed for RefID 7837. Loss to follow-up and missing data for outcome or exposure was not detailed within RefID 3081241. For RefID 709498, authors noted nearly 10% of the cohort was considered lost to follow-up, mostly because of high rates of loss to follow-up among females and n=120 workers known to be dead as of 31 December 2001 were missing cause of death information with an additional 426 workers who died or were lost to follow-up before 1 January 1960 excluded from analyses using South Carolina referent rates because rates were not available before 1960.
	Metric 3:	Comparison Group	Medium	Although a formal statistical evaluation of differences in baseline characteristics of cases and controls was not conducted and reasons for choice of matching and potential confounding variables were not explicitly stated within RefID 7837 and RefID 3081241, all analyses between asbestos workers and non-exposed matched controls were adjusted for matching variables of age at death, sex, hospital at death, and year of death for RefID 7837, and for age, sex, race and calendar time for RefID 3081241. Mortality results for SMR analyses within RefID 709498 were not stratified for any additional covariates, however results from Poisson analyses were adjusted for sex, race, age and calendar-year.
Domain 2: Exposure Characterization				

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Study Citation:	Green, F. H. Y., Harley, R., Vallyathan, V., Althouse, R., Fick, G., Dement, J., Mitha, R., Pooley, F. (1997). Exposure and mineralogical correlates of pulmonary fibrosis in chrysotile asbestos workers. Occupational and Environmental Medicine 54(8):549-559.
Health Outcome:	Lung Cancer; Asbestosis
Target Organ(s):	Lung/Respiratory: asbestosis (pathological pulmonary fibrosis grade), lung cancer, asbestosis mortality, lung cancer mortality; Cancer/Carcinogenesis: lung cancer, lung cancer mortality; Mortality: asbestosis mortality, lung cancer mortality
Asbestos Fiber Type(s):	Asbestos - Chrysotile (serpentine): 12001-29-5; Asbestos - Crocidolite (riebeckite): 12001-28-4; Asbestos - Tremolite: 14567-73-8; Asbestos - Amosite (grunerite): 12172-73-5; Asbestos - Anthophyllite: 17068-78-9
Linked HERO ID(s):	7837, 709498, 3081241
HERO ID:	7837

Domain	Metric		Rating	Comments
	Metric 4:	Measurement of Exposure	Medium	Exposure was summarized by estimated cumulative asbestos exposures, reported lung fiber concentrations, and asbestos bodies in RefID 7837, and by estimated cumulative chrysotile asbestos exposures within RefID 3081241 and RefID 709498. Exposure data was not available for each worker and exposures were estimated in RefID 7837, RefID 3081241 and RefID 709498 as detailed within Dement et al., 1983 (HERO ID 66) and described within the main text as utilizing a job coding scheme for each worker which used detailed job histories and 5,952 industrial hygiene plant dust sampling (conversion factor to fiber exposure details provided) results from the plant under study covering the period 1930-1975. HERO ID 66 noted that all known industrial hygiene data were collected utilizing midget impingers by the company insurance carrier, the State Board of Health, the U.S. Public Health Service, and the Company sampling program. Impinger dust concentrations were converted to fiber concentrations utilizing the reported conversion factors. Concurrent paired sampling was utilized to assess possible differences in conversion factors over time. Cumulative lifetime time weighted average exposure for each worker was described as calculated by multiplying estimates of exposure for each job held by the time spent in each job (fibers > 5 µm/mL3 x years in job = fiber-years. Estimations of exposure included considerations for engineering controls and historical textile production process changes. Authors within referenced HERO ID 66 noted the potential for exposure misclassification but asserted that it would be nondifferential as exposures for both diseased and non-diseased individuals were calculated in the same manner. Other than noting that controls were never employees of the one plant under study and concentrations of mullite were statistically significantly greater in lungs of non-exposed controls than in asbestos workers, no assessment of “non-exposed” control occupational exposure history was noted in 7837. Total lung asbestos fibers (fibers x 106/g dry lung) were also reported within 7837 and lung tissue fiber mineralogical analyses was conducted according to methods within Pooley et al., 1979 (HERO ID: 3084350) utilizing transmission electron microscopy. Asbestos bodies in 7837 were graded by independently by three pathologists utilizing light microscopy and a scale reported by Wagner et al., 1982 (HERO ID: 3083948).
	Metric 5:	Exposure Levels	Medium	The range and distribution of estimated exposure is sufficient to develop exposure-response estimates within RefID 7837, RefID 3081241 and RefID 709498. Estimates of lifetime cumulative, peak and average exposure medians and quartiles are detailed within Table 2 (and within referenced HERO ID 66 Tables IV-XII by textile production area) of Ref ID 709498. Exposure summaries within RefID 3081241 were referenced (HERO ID 66), but reported in main text for estimated cumulative exposures in Table 1 of RefID 709498. Cumulative lifetime exposure estimates in a log scale were utilized for regression analyses within RefID 7837, as continuous estimated cumulative exposures within RefID 3081241 and RefID 709498.

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Study Citation:	Green, F. H. Y., Harley, R., Vallyathan, V., Althouse, R., Fick, G., Dement, J., Mitha, R., Pooley, F. (1997). Exposure and mineralogical correlates of pulmonary fibrosis in chrysotile asbestos workers. Occupational and Environmental Medicine 54(8):549-559.
Health Outcome:	Lung Cancer; Asbestosis
Target Organ(s):	Lung/Respiratory: asbestosis (pathological pulmonary fibrosis grade), lung cancer, asbestosis mortality, lung cancer mortality; Cancer/Carcinogenesis: lung cancer, lung cancer mortality; Mortality: asbestosis mortality, lung cancer mortality
Asbestos Fiber Type(s):	Asbestos - Chrysotile (serpentine): 12001-29-5; Asbestos - Crocidolite (riebeckite): 12001-28-4; Asbestos - Tremolite: 14567-73-8; Asbestos - Amosite (grunerite): 12172-73-5; Asbestos - Anthophyllite: 17068-78-9
Linked HERO ID(s):	7837, 709498, 3081241
HERO ID:	7837

Domain	Metric		Rating	Comments
	Metric 6:	Temporality	Medium	Eligible participants were followed up until 31 December 1975 in RefID 7837, but it is unclear if follow-up was sufficient for those who began work in the later years of study as those hired around 1965 would have only been followed for approximately ten years and Table 1 of main text indicates dates of death range from 1964-1975. Follow-up for RefID 3081241 was extended through 1990, and follow-up for RefID 709498 was extended through 2001.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Medium	Lung Cancer: In RefID 7837, both workers and control subjects for whom necropsy lung tissue samples were evaluated for pulmonary fibrosis were additionally classified based on lung cancer status; the methods for doing so are not stated.; Asbestosis: In RefID 7837, deaths were identified from hospital records, death certificates, and state records. The extent of pulmonary fibrosis (referred to as ”pulmonary fibrosis (asbestosis)”) in necropsy samples was graded according to criteria established by a joint National Institute for Occupational Safety and Health (NIOSH) and College of American Pathologists (CAP) Committee. The fibrosis scores for all slides from each case were reviewed by three pathologists blinded to exposure status independently, averaged to give an overall fibrosis score, only slides with recognizable lung parenchyma were graded and those slides with predominantly tumor, bronchus, lymph notes abscess or infarct were excluded. Pairwise reproducibility between pathologists in RefID 7837 was assessed and for fibrosis severity was 71% for exact agreement and 98% for agreement to ± one category and average pairwise reproducibility within pathologists for severity was 53% for exact agreement and 96% for agreement to one category. For RefID 3081241, deaths due to asbestosis were identified on death certificates using ICD codes. Asbestosis deaths were identified using a multiple cause of death approach that included a review of all death certificate fields as in Steenland et al., 1992 (HERO ID not available). A broad definition was used that included both deaths from asbestosis (ICD-9 501) and pneumoconiosis (ICD-9 505).For RefID 709498, deaths due to asbestosis were identified using ICD codes in the National Death Index (via NDI Plus); codes used in the definition of asbestosis are not provided but the methods are stated to be the same as in prior studies of this cohort.

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Study Citation: Green, F. H. Y., Harley, R., Vallyathan, V., Althouse, R., Fick, G., Dement, J., Mitha, R., Pooley, F. (1997). Exposure and mineralogical correlates of pulmonary fibrosis in chrysotile asbestos workers. Occupational and Environmental Medicine 54(8):549-559.

Health Outcome: Lung Cancer; Asbestosis

Target Organ(s): Lung/Respiratory: asbestosis (pathological pulmonary fibrosis grade), lung cancer, asbestosis mortality, lung cancer mortality; Cancer/Carcinogenesis: lung cancer, lung cancer mortality; Mortality: asbestosis mortality, lung cancer mortality

Asbestos Fiber Type(s): Asbestos - Chrysotile (serpentine): 12001-29-5; Asbestos - Crocidolite (riebeckite): 12001-28-4; Asbestos - Tremolite: 14567-73-8; Asbestos - Amosite (grunerite): 12172-73-5; Asbestos - Anthophyllite: 17068-78-9

Linked HERO ID(s): 7837, 709498, 3081241

HERO ID: 7837

Domain	Metric		Rating	Comments
	Metric 8:	Reporting Bias	Medium	There were no concerns for selective reporting as all outcomes which were outlined within methods were also reported within the results for RefID 7837, RefID 3081241 and RefID 709498. For RefID 7837, regression equation and correlation results from the text and Figures 2 and 3 were summarized for the relationship between estimated cumulative lifetime exposure, concentrations of lung fibers lung burden of asbestos and lung fibrosis scores for asbestos textile workers. Results for RefID 7837 pleural plaques were only reported within text as the proportion (percentage) of pleural plaque cases in asbestos exposed workers versus non-exposed controls.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Medium	Final regression analyses in RefID 7837 were adjusted for age and sex for the outcome of lung fibrosis score however it is unclear if all regression analyses results included these covariates. All analyses between asbestos workers and non-exposed matched controls in RefID 7837 were adjusted for matching variables of age at death, sex, hospital at death, and year of death. Data regarding smoking status was not available, however authors noted smoking history from a 1964 Public Health survey of the plant seemed similar to the general population and it was surmised that there would not be significant differences in smoking status between exposed workers and non-exposed controls. all analyses were adjusted for age, sex, race and calendar time for RefID 3081241. Mortality results for SMR analyses within RefID 709498 were not stratified for any additional covariates, however results from Poisson analyses were adjusted for sex, race, age and calendar-year.
	Metric 10:	Covariate Characterization	Medium	While the methods in RefID 7837 utilized to obtain and validate data regarding potential confounders were described only as obtained through computerized hospital records, there is no indication that methods had poor validity. Methods for obtaining confounder data within RefID 3081241 and RefID 709498 were not detailed, but assumed to be obtained through similar hospital and national vital status records.
	Metric 11:	Co-exposure Counfounding	Medium	Potential co-exposures to non-asbestos mullite, rutile and iron were considered within analyses of fibrosis (Figure 3D) in RefID 7837. Assessment of potential co-exposures in analyses within non-exposed controls in RefID 7837 was not detailed, although authors noted that concentrations of mullite were statistically significantly greater in lungs of non-exposed controls than in asbestos workers. Considerations of non-asbestos fibers within RefID 3081241 and RefID 709498 was not detailed.
Domain 5: Analysis				

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Study Citation: Green, F. H. Y., Harley, R., Vallyathan, V., Althouse, R., Fick, G., Dement, J., Mitha, R., Pooley, F. (1997). Exposure and mineralogical correlates of pulmonary fibrosis in chrysotile asbestos workers. Occupational and Environmental Medicine 54(8):549-559.
Health Outcome: Lung Cancer; Asbestosis
Target Organ(s): Lung/Respiratory: asbestosis (pathological pulmonary fibrosis grade), lung cancer, asbestosis mortality, lung cancer mortality; Cancer/Carcinogenesis: lung cancer, lung cancer mortality; Mortality: asbestosis mortality, lung cancer mortality
Asbestos Fiber Type(s): Asbestos - Chrysotile (serpentine): 12001-29-5; Asbestos - Crocidolite (riebeckite): 12001-28-4; Asbestos - Tremolite: 14567-73-8; Asbestos - Amosite (grunerite): 12172-73-5; Asbestos - Anthophyllite: 17068-78-9
Linked HERO ID(s): 7837, 709498, 3081241
HERO ID: 7837

Domain	Metric		Rating	Comments
	Metric 12:	Study Design and Methods	Medium	Multivariate linear regression was utilized for analysis of the relationship between estimated occupational asbestos exposure and fibrosis score in RefID 7837. Authors several regression models in RefID 7837, including addition of a quadratic term for exposure and exploration of a threshold effect of exposure on lung fibrosis, were developed, however results were not detailed and authors noted the model was not precise enough to determine a minimal or threshold level of exposure that would produce asbestosis. Analyses within RefID 3081241 utilized Poisson regression and restricted cubic spline models, while RefID 709498 focused upon SMR, Poisson and cubic spline models.
	Metric 13:	Statistical Power	Medium	It is likely the number of subjects (n=54 total; n=44 male asbestos workers, n=10 female asbestos workers) was inadequate in RefID 7837 for analyses of fibrosis scores with estimated exposures in asbestos workers only, or lung fiber content in asbestos and non-asbestos workers (n=39 asbestos workers and n=31 non-exposed controls), particularly within results of multivariate analyses. Authors in RefID 7837 noted the lack of statistical power was largely due to the small number of cases with low and intermediate levels of exposure. The number of subjects within RefID 3081241 (n=1,848) and RefID 709498 (n=3,072) was adequate.
	Metric 14:	Reproducibility of Analyses	Medium	Details were provided for exposure assessment within HERO ID 66 for RefID 7837, RefID 3081241 and RefID 709498. Detailed statistical analysis methods for RefID 7837 were reported, however details such as rules for transformation of continuous variables of age, assessment of non-linearity and missing data, other than smoking status, were not detailed. The statistical analyses for RefID 3081241 and RefID 709498 were described including variables within the analyses.
	Metric 15:	Statistical Analysis	Medium	The description of statistical analysis was fairly detailed in RefID 7837, RefID 3081241 and RefID 709498, however model details regarding consideration of non-linear effects within reported exploration of quadratic exposure covariates and threshold effects of exposure on lung fibrosis were reported in RefID 7837 but not in detail.
Domain 6: Other (if applicable) Considerations for Biomarker Selection and Measurement (Lakind et al. 2014)				
	Metric 16:	Use of Biomarker of Exposure	High	Total lung asbestos fiber content in RefID 7837 was noted to have a highly significant correlation with estimated cumulative asbestos exposure (Figure 1 and text). Additional analyses indicated similar correlations with specific asbestos fiber types within lung tissue. The mean number of asbestos bodies on tissue sections in RefID 7837 was strongly associated with lifetime cumulative exposure ($P < 0.01$), total amphibole ($P < 0.01$), and total chrysotile fibers ($P < 0.05$) in the lung.
	Metric 17:	Effect Biomarker	N/A	N/A. RefID 7837 reports a biomarker of exposure.
	Metric 18:	Method Sensitivity	Low	LOD/LOQ values were not stated in RefID 7837.
	Metric 19:	Biomarker Stability	Low	Storage history of samples not detailed in RefID 7837.

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Study Citation:	Green, F. H. Y., Harley, R., Vallyathan, V., Althouse, R., Fick, G., Dement, J., Mitha, R., Pooley, F. (1997). Exposure and mineralogical correlates of pulmonary fibrosis in chrysotile asbestos workers. Occupational and Environmental Medicine 54(8):549-559.
Health Outcome:	Lung Cancer; Asbestosis
Target Organ(s):	Lung/Respiratory: asbestosis (pathological pulmonary fibrosis grade), lung cancer, asbestosis mortality, lung cancer mortality; Cancer/Carcinogenesis: lung cancer, lung cancer mortality; Mortality: asbestosis mortality, lung cancer mortality
Asbestos Fiber Type(s):	Asbestos - Chrysotile (serpentine): 12001-29-5; Asbestos - Crocidolite (riebeckite): 12001-28-4; Asbestos - Tremolite: 14567-73-8; Asbestos - Amosite (grunerite): 12172-73-5; Asbestos - Anthophyllite: 17068-78-9
Linked HERO ID(s):	7837, 709498, 3081241
HERO ID:	7837

Domain	Metric		Rating	Comments
	Metric 20:	Sample Contamination	Medium	Contamination information was not detailed in RefID 7837.
	Metric 21:	Method Requirements	Medium	Transmission electron microscopy instrumentation within RefID 7837 methods provides unambiguous identification and quantitation of the biomarker, however text noted analysis of samples from different unspecified sites yielded moderate variability in fiber counts, but the proportions by fiber type were described as relatively constant. Asbestos bodies in RefID 7837 were graded by independently by three pathologists utilizing light microscopy and a scale reported by Wagner et al., 1982 (HERO ID: 3083948).
	Metric 22:	Matrix Adjustment	N/A	N/A. RefID 7837 reports biomarker of exposure data.

Additional Comments: RefIDs 3081241 and 709498 report n=3 cases of mesothelioma, but authors in RefID 3081241 noted it was not possible to model this outcome due to the low number of cases, and RefID 709498 did not include mesothelioma within SMR analyses outcomes. Pleural plaques were noted as an outcome in the text of RefID 7837, but only reported as prevalent with lung cancer and not presented within results tables or analyzed with respect to levels of asbestos exposure.RefID 709498 reported SMRs for a wide range of cancer and non-cancer outcomes in Table 2, but did not analyze these outcomes with respect to levels of asbestos exposure.

Overall Quality Determination — Medium

Study Citation:	Gustavsson, P., Jakobsson, R., Johansson, H., Lewin, F., Norell, S., Rutkvist, L. E. (1998). Occupational exposures and squamous cell carcinoma of the oral cavity, pharynx, larynx, and oesophagus: A case-control study in Sweden. Occupational and Environmental Medicine 55(6):393-400.
Health Outcome:	Laryngeal Cancer; oral cavity, pharynx, oesophagus, larynx , all sites (including head and neck)
Target Organ(s):	Cancer/Carcinogenesis: cancer in all sites, cancer in larynx, cancer in oesophagus, cancer in pharynx, cancer in oral cavity; Lung/Respiratory: cancer in larynx, cancer in pharynx; Gastrointestinal: cancer in oesophagus, cancer in oral cavity; head and neck: cancer in all sites
Asbestos Fiber Type(s):	Asbestos - Not specified: 1332-21-4
Linked HERO ID(s):	No linked references.
HERO ID:	626459

Domain	Metric		Rating	Comments
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Uninformative	Neither PCM nor TEM were used for measuring exposure. The study measures asbestos exposure and other selected exposures using occupational codes from the Swedish standard classification of occupations, NYK 1983, which were inputted by a blinded occupational hygienist. However, it appears that occupational history was collected via interview which may be subject to recall bias and, thus, exposure misclassification. Authors also stated “The classification of occupational exposures was based on occupational histories, and could not account for variation in the exposure that was not reflected in the job titles or description of work tasks in the interviews. It is probable that there is imprecision in the classification of the intensity of occupational exposures, even if the histories were obtained directly from the men rather than from surrogates.”
	Metric 5:	Exposure Levels	Low	Although cumulative exposure appeared to be collected for asbestos, levels of exposure were separated into quartiles with no identification of the distribution of cumulative dose (see Table 3). Additionally, Table 4 shows asbestos exposure treated as a dichotomized variable. Authors also stated it was “not feasible to calculate dose-response in terms of fibre concentrations or fibre-years from the data in its present form. Dose estimations were based on quantitative assessments of the intensity of the exposure (annual average fibre concentration) as well as the probability of exposure.”

Additional Comments:	Some target organs were categorized as either GI or respiratory. However, it might be worth considering them as overlapping since the authors stated they were investigating ” aetiological factors for cancer of the upper aerodigestive tract.” Data were not extracted as the study was deemed uninformative in Metric 4.

* No biomarkers were identified for this evaluation.

** As described in Appendix B.2 of the *White Paper: Quantitative Approach to the Human Health Assessment for the Risk Evaluation for Asbestos Part 2: Supplemental Evaluation Including Legacy Uses and Associated Disposals of Asbestos*, to be considered as being informative for dose-response analysis, metrics 4 and 5 would need metric ratings of Medium or High. This reference did not satisfy this requirement; therefore data quality evaluation is presented for only for metrics 4 and 5.

Study Citation:	Hagmar, L., Akesson, B., Nielsen, J., Andersson, C., Linden, K., Attewell, R., Moller, T. (1990). Mortality and cancer morbidity in workers exposed to low levels of vinyl chloride monomer at a polyvinyl chloride processing plant. American Journal of Industrial Medicine 17(5):553-565.
Health Outcome:	Lung Cancer; Laryngeal Cancer
Target Organ(s):	Cancer/Carcinogenesis: malignant tumor mortality, gastrointestinal tumor mortality, respiratory tumor mortality, gastrointestinal tract tumor morbidity, Liver and bile duct tumor morbidity, Respiratory tract tumor morbidity, nose and sinus tumor morbidity, larynx tumor morbidity, lung tumor morbidity, prostate tumor morbidity, All cancer morbidity, Brain tumor morbidity; Cardiovascular: cardiovascular disease mortality, ischemic heart disease mortality; Lung/Respiratory: bronchitis, emphysema, asthma mortality, respiratory tumor mortality, Respiratory tract tumor morbidity, nose and sinus tumor morbidity, larynx tumor morbidity, lung tumor morbidity; Gastrointestinal: gastrointestinal disease mortality, gastrointestinal tumor mortality, gastrointestinal tract tumor morbidity; Renal/Kidney: urinary tract disease mortality; Mortality: mortality from violence, All cause, gastrointestinal disease mortality, urinary tract disease mortality, bronchitis, emphysema, asthma mortality, ischemic heart disease mortality, cardiovascular disease mortality, malignant tumor mortality, gastrointestinal tumor mortality, respiratory tumor mortality; Hepatic/Liver: Liver and bile duct tumor morbidity; Reproductive/Developmental: prostate tumor morbidity; Neurological/Behavioral: Brain tumor morbidity
Asbestos Fiber Type(s):	Asbestos - Chrysotile (serpentine): 12001-29-5
Linked HERO ID(s):	No linked references.
HERO ID:	675185

Domain		Metric	Rating	Comments
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Low	Measurement of exposure was not mentioned using a combination of midget impinger, PCM, or TEM, and conversion factors were not determined.Estimates of asbestos exposure were obtained from breathing zone samples conducted in 1971. Details on the sampling method were minimal. Other time periods were not sampled, but industrial hygienists estimated job- and department-specific . Time-weighted averages were assumed to be 40% lower after 1969 compared to prior years. Cumulative exposure was determined by adding years of exposure.
	Metric 5:	Exposure Levels	Medium	The mean exposure level among highly exposed workers was 1-3 fibers/ml, that among moderately exposed workers was >0.1-0.5 fibers/ml, and that among workers exposed to low levels was up to 0.1 fibers/ml. These measurements were performed for 108 hours in 1971. The study showed a relationship between three cumulative exposure levels and SMR/SSMR of the respiratory tract, pleura of the lung, and all sites.

Additional Comments: This study utilized an occupational cohort in Sweden to examine rates of tumor mortality and morbidity. There was some concern regarding details of exposure characterization, and the presence of other potential chemical hazards (e.g., VCM and plasticizers). Results indicated increased risk of mortality, which was more apparent in 10-yr latency models.

* No biomarkers were identified for this evaluation.

** As described in Appendix B.2 of the *White Paper: Quantitative Approach to the Human Health Assessment for the Risk Evaluation for Asbestos Part 2: Supplemental Evaluation Including Legacy Uses and Associated Disposals of Asbestos*, to be considered as being informative for dose-response analysis, metrics 4 and 5 would need metric ratings of Medium or High. This reference did not satisfy this requirement; therefore data quality evaluation is presented for only for metrics 4 and 5.

Study Citation:	Hall, A., Kromhout, H., Schüz, J., Peters, S., Portengen, L., Vermeulen, R., Agudo, A., Ahrens, W., Boffetta, P., Brennan, P. (2020). Laryngeal cancer risks in workers exposed to lung carcinogens: Exposure-effect analyses using a quantitative job exposure matrix. Epidemiology 31(1):145-154.
Health Outcome:	Laryngeal Cancer
Target Organ(s):	Cancer/Carcinogenesis: Laryngeal cancer; Lung/Respiratory: Laryngeal cancer
Asbestos Fiber Type(s):	Asbestos - Not specified: 1332-21-4
Linked HERO ID(s):	No linked references.
HERO ID:	6775698

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Medium	Subjects were male and female cases with diagnosed laryngeal cancer and drawn from the International Head and Neck Cancer Epidemiology (INHANCE) Consortium, described as a “global collaboration established in 2004 among research groups currently or recently conducting large molecular epidemiologic studies of head and neck cancer.” Subjects represented five INHANCE studies with occupational histories coded to the International Standard Classification of Occupations (ISCO)-68, representing individuals from Western Europe, Latin America, France, and Germany. Descriptive characteristics of subjects are provided in Table 1. All subjects identified as blue-collar workers. For studies to be included in this analysis, they needed to have a recruitment protocol for cases and controls, and structured questionnaires to capture information on demographic factors, occupational history, tumor characteristics, alcohol consumption, and tobacco use. The authors report that most studies were hospital based. Available information indicates a low risk of selection bias as to which groups were included in the present analysis.The final analytic sample consisted of 2256 laryngeal cancer cases (203 females; 2035 males) and 7857 controls (1604 females, 6263 males).
	Metric 2:	Attrition	Medium	There was moderate subject loss in the study. Participation rates across the five studies ranged from 80%-96% and 62%-86% for cases and controls, respectively. However, exposure and outcome data remain largely complete. Exclusion of subjects were also adequately addressed, as 213 cases and 471 controls were excluded from the final analytical sample due to missing data on sex, age, occupational history, tobacco smoking, and alcohol use. There is no evidence that this missingness is a significant source of bias.
	Metric 3:	Comparison Group	High	Controls in the study were subject to the same inclusion and exclusion criteria as cases. Additionally, controls were frequency-matched to cases based on factors such as age, sex, and regional factors. However, in statistical analysis different exposure groups were compared to each other rather than comparing cases to controls in logistic regression analyses. Adjustment factors in those models included which study they originated from, age, alcohol intake, and tobacco smoking. Results are also presented as stratified by sex, thus allowing for an appropriate controlling for differences in exposure groups. Difference in descriptive characteristics between cases and controls are also presented in Table 1.
Domain 2: Exposure Characterization				

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Study Citation:	Hall, A., Kromhout, H., Schüz, J., Peters, S., Portengen, L., Vermeulen, R., Agudo, A., Ahrens, W., Boffetta, P., Brennan, P. (2020). Laryngeal cancer risks in workers exposed to lung carcinogens: Exposure-effect analyses using a quantitative job exposure matrix. Epidemiology 31(1):145-154.
Health Outcome:	Laryngeal Cancer
Target Organ(s):	Cancer/Carcinogenesis: Laryngeal cancer; Lung/Respiratory: Laryngeal cancer
Asbestos Fiber Type(s):	Asbestos - Not specified: 1332-21-4
Linked HERO ID(s):	No linked references.
HERO ID:	6775698

Domain	Metric		Rating	Comments
	Metric 4:	Measurement of Exposure	Medium	Assessment of measures were completed using a SYN-JEM which used empirical models using individual personal measurements of occupational exposures from European countries and Canada. Data represented measurements taken between the 1970s and 2009. For linear mixed-effect modeling, 27,958 measurements were recorded for asbestos (expressed in f/ml) and represented measurements that had a job code available and a sampling duration between 60-600 minutes. Random effects terms in modeling included region/country and job title, while fixed effects included measurement year, sampling duration, and prior exposure rating that was based on a general population JEM. Predictions provided an estimated annual mean exposure for a given job and region/country for asbestos.According to Peters et al., 2016 (HERO ID: 3531308), asbestos fiber concentrations were measured using PCM in over 95% of samples. One caveat is that measurements conducted in Germany were predominantly (99%) done using electron microscopy, which may make data from German participants (10% of cases and 11% of controls) somewhat biased relative to the rest of the participants. Additionally, there is some risk for exposure misclassification when using JEMs since all individuals in a given job category are given the same exposure measurement.
	Metric 5:	Exposure Levels	Medium	The distribution of exposure appears to be sufficient to develop an exposure-response estimate. Cumulative exposure was calculated and stratified by diameter and length. <50th, 50–75th, 75–90th, and >90th percentiles were used to stratify cumulative exposure. Because of the small sample size for females, the median exposure in controls was used as the "cut-point" for categories of cumulative exposure.
	Metric 6:	Temporality	Medium	The authors report that the duration of exposure ranged from less than 10 years to greater than 30 years, with a somewhat even distribution. The study appears to establish appropriate temporality between exposure and outcome, but it's unclear if this applied for all subjects. Data on time since first exposure is not discussed; however, the study applied "exposure lags of 10 and 20 years before diagnosis and interview to all agents and metrics" in sensitivity analyses.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	High	Laryngeal Cancer: Laryngeal cancer status was ascertained in the original studies included in this analysis using ICD-10 classification codes: C32.0-C32.3 and C32.8-C32.9.
	Metric 8:	Reporting Bias	High	All results seem to be reported in all aspects of the report. The authors provided sufficient explanation for difference in methodology between male and female participants. Effect estimates report confidence intervals. Footnotes are provided for additional clarification on analyses. Links to supplemental results tables are available.

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Study Citation:	Hall, A., Kromhout, H., Schüz, J., Peters, S., Portengen, L., Vermeulen, R., Agudo, A., Ahrens, W., Boffetta, P., Brennan, P. (2020). Laryngeal cancer risks in workers exposed to lung carcinogens: Exposure-effect analyses using a quantitative job exposure matrix. Epidemiology 31(1):145-154.
Health Outcome:	Laryngeal Cancer
Target Organ(s):	Cancer/Carcinogenesis: Laryngeal cancer; Lung/Respiratory: Laryngeal cancer
Asbestos Fiber Type(s):	Asbestos - Not specified: 1332-21-4
Linked HERO ID(s):	No linked references.
HERO ID:	6775698

Domain	Metric		Rating	Comments
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Medium	Appropriate adjustments were made to account for potential confounding in final analyses. In Model 1, the study adjusted for participant age and study. In Model 2, they further adjusted for tobacco smoking and alcohol consumption which are well-known risk factors for laryngeal cancer. There is no adjustment for socioeconomic status, and it is not explicitly clear why all covariates were chosen.
	Metric 10:	Covariate Characterization	Medium	As an occupational study, it can be assumed that covariate data was collected from personnel records.
	Metric 11:	Co-exposure Counfounding	Low	Co-exposures were not assessed in this study. Authors also recognized that potential co-exposure to other carcinogenic agents can influence the precision of being able to identify the agents of interest in the study as risk factors for laryngeal cancer.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	Medium	The study design chosen was appropriate for the research question. Logistic regression models were utilized in this case-control study.
	Metric 13:	Statistical Power	Medium	2256 cases and 7857 controls were analyzed in this study. Sample sizes for female participants tended to be smaller than males, but authors specified appropriate changes in methodology to account for this. This included structuring percentile categories of cumulative exposure based on the median exposure in controls as the cut-point and using a continuous log-transformed pack-years variable to represent adjustment for tobacco smoking.
	Metric 14:	Reproducibility of Analyses	Medium	Methods and analyses were described sufficiently enough for reproducibility.
	Metric 15:	Statistical Analysis	Medium	Methods for calculating risk estimates are clear. The authors report the results of logistic regression and there is no reason to suspect assumptions were not met.

Additional Comments: This study assessed the association between several carcinogenic agents (including asbestos) and the risk of laryngeal cancer. For asbestos, it should be noted that measurements conducted in Germany were predominantly (99%) done using electron microscopy (Peters et al., 2016 3531308). However, the paper does not report statistically significant results.

Overall Quality Determination — Medium

* No biomarkers were identified for this evaluation.

Study Citation:	Hansen, J., de Klerk, N. H., Musk, A. W., Hobbs, M. S. T. (1998). Environmental exposure to crocidolite and mesothelioma: Exposure-response relationships. American Journal of Respiratory and Critical Care Medicine 157(1):69-75.
Health Outcome:	Lung Cancer; Ovarian Cancer; Leukemia, colorectal cancer, digestive system cancers; Signs/symptoms ill defined mortality, nervous system mortality
Target Organ(s):	Lung/Respiratory: Lung cancer mortalityLung cancer incidenceRespiratory system mortalityMesothelioma incidenceMesothelioma mortality; Cancer/Carcinogenesis: Mesothelioma incidenceMesothelioma mortalityLung cancer incidenceLung cancer mortalityCancer incidence, all and specific types (SIRs for exposed/gen pop, no dose-reponse)Cancer mortality, all and specific types (SMRs for exposed/gen pop, no dose-response); Mortality: Mesothelioma mortalityLung cancer mortalityAll-cause mortality (SMR for exposed/gen pop, no dose-response)Respiratory system mortality (SMR for exposed/gen pop, no dose-response)Digestive system mortality (SMR for exposed/gen pop, no dose-response)Signs/symptoms ill-defined (SMR for exposed/gen pop, no dose-response)Nervous system mortality (SMR, no dose-response); nan:
Asbestos Fiber Type(s):	Asbestos - Crocidolite (riebeckite): 12001-28-4
Linked HERO ID(s):	709618, 709466, 709501, 2088306, 6869529
HERO ID:	709618

Domain	Metric		Rating	Comments
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Medium	Exposure estimates for Wittenoom residents used intensities of 1.0 f/mL for 1943-1957 (old mill), 0.5 f/mL for 1958-1966 (new mill – mining ended), and declining values interpolated to 0.01 f/mL in 1992 (see Hansen et al. 1997, HERO ID 2219991). These values were based on measures of fibers > 5 µm that began in 1966 using a Casella thermal precipitator and PCM, cited as 0.5 f/mL (Armstrong et al. 1988, 3083076; Rogers et al. 2001, 3080506). Earlier measures (1948-1966) were limited to dust collected by konimeter; pre-1958 intensity was extrapolated based on estimates that the new mill halved exposure (Hansen et al. 1997, 2219991; Rogers et al. 2002, 3080506). Subsequent fiber measures were collected from personal and/or fixed monitors in 1973 (median 0.22 f/mL), 1977, and 1978 using PCM counts; in 1984 and 1986 using scanning electron microscopy (SEM); and in 1992 using TEM. Concerns include the limited number, location, and quality of samples, as well as use of less precise SEM counts. Cumulative exposure was calculated based on duration of residence, assuming 24 h a day, 7 d a week exposure, estimated with varying degrees of error and likely differing by mesothelioma case status. Duration estimated used available data as follows: (i) mesothelioma registry data; (ii) questionnaire responses; (iii) worker employment dates for relatives; (iv) family member questionnaires; (v) records at hospitals, schools, etc; and finally (vi) a value of 6 months if still unknown. Details were not provided on the proportion estimated using methods with increasing error. Another source of error includes the lack of information on specific locations and activities that would affect individual exposure (having lived with and/or likely washed the clothes of an asbestos worker were estimated). The most recent publication indicated that cumulative exposure data was missing for about 5% of the sample (Reid et al. 2018, 6869529).
	Metric 5:	Exposure Levels	Low	SMR and SIR analyses did not examine whether these rates varied over levels of exposure. Lung cancer associations reported in Reid et al. 2008, 709466 used continuous f/mL-years for cumulative exposure.

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Study Citation:	Hansen, J., de Klerk, N. H., Musk, A. W., Hobbs, M. S. T. (1998). Environmental exposure to crocidolite and mesothelioma: Exposure-response relationships. American Journal of Respiratory and Critical Care Medicine 157(1):69-75.		
Health Outcome:	Lung Cancer; Ovarian Cancer; Leukemia, colorectal cancer, digestive system cancers; Signs/symptoms ill defined mortality, nervous system mortality		
Target Organ(s):	Lung/Respiratory: Lung cancer mortalityLung cancer incidenceRespiratory system mortalityMesothelioma incidenceMesothelioma mortality; Cancer/Carcinogenesis: Mesothelioma incidenceMesothelioma mortalityLung cancer incidenceLung cancer mortalityCancer incidence, all and specific types (SIRs for exposed/gen pop, no dose-reponse)Cancer mortality, all and specific types (SMRs for exposed/gen pop, no dose-response); Mortality: Mesothelioma mortalityLung cancer mortalityAll-cause mortality (SMR for exposed/gen pop, no dose-response)Respiratory system mortality (SMR for exposed/gen pop, no dose-response)Digestive system mortality (SMR for exposed/gen pop, no dose-response)Signs/symptoms ill-defined (SMR for exposed/gen pop, no dose-response)Nervous system mortality (SMR, no dose-response); nan:		
Asbestos Fiber Type(s):	Asbestos - Crocidolite (riebeckite): 12001-28-4		
Linked HERO ID(s):	709618, 709466, 709501, 2088306, 6869529		
HERO ID:	709618		
Domain	Metric	Rating	Comments
Additional Comments:	These studies analyzed >5,000 individuals who had lived in Wittenoom, Australia for ≥1 month from 1943-1993 to evaluate associations between residential asbestos exposure and (i) mesothelioma (all studies); (ii) mortality in women and persons exposed as children (Reid et al. 2008, 709466; Reid et al., 2012 2088306), and (iii) cancer incidence (Reid et al. 2012, 2088306). The cohort excluded asbestos workers. In the most recent study geometric mean (IQR) cumulative exposure was 3.02 (1.4-7.70) f/mL-years in children and 2.05 (0.90-5.75) f/mL-years in adults. SMRs for residents exposed as children were significantly higher for all causes, all neoplasms, mesothelioma, and the nervous system in males, but not for lung cancer (Reid et al. 2012, 2088306). Cancer SIRs for childhood exposure were significant for mesothelioma, and for leukemia in males (Reid et al. 2012, 2088306). Among women, SMRs but not HRs for lung cancer were significant (Reid et al. 2008, 709466). SMRs in women were also significant for pneumoconiosis, but there were only 2 cases. SMRs for both female childhood exposure and for women were large (>4) and significant for "symptoms/signed ill-defined". Key concerns include exposure measurement error, particularly prior to 1966 when mining ceased: a single value was extrapolated to the entire period as no fiber measures were taken. There is potential for differential measurement error by mesothelioma case status, since much more detailed occupational and residential history information was available for cases. In contrast, duration of residence - used to calculate exposure - was estimated from limited public records for about half of the cohort who did not return mailed questionnaires. There was also ~20% loss to follow-up. This was addressed in some of the cohort papers by comparing different assumptions on the status of these subjects. Several SMRs/SIRs calculated using alternate assumptions were inconsistent, significant only with the censoring method that would tend to over-estimate effects.The measurement exposure (M4) metric is rated medium and exposure levels (M5) metric is rated as low upon review by both set of reviewers. Also, the overall quality determination (OQD) is rated medium. Extraction has been completed and quality control reviewed.		

* No biomarkers were identified for this evaluation.

** As described in Appendix B.2 of the *White Paper: Quantitative Approach to the Human Health Assessment for the Risk Evaluation for Asbestos Part 2: Supplemental Evaluation Including Legacy Uses and Associated Disposals of Asbestos*, to be considered as being informative for dose-response analysis, metrics 4 and 5 would need metric ratings of Medium or High. This reference did not satisfy this requirement; therefore data quality evaluation is presented for only for metrics 4 and 5.

Study Citation:	Haque, A. K., Vrazel, D. M., Burau, K. D., Cooper, S. P., Downs, T. (1996). Is there transplacental transfer of asbestos? A study of 40 stillborn infants. Pediatric Pathology & Laboratory Medicine 16(6):877-892.
Health Outcome:	stillbirth, placental pathology, fetal diseases, fetal masceration, gestational age
Target Organ(s):	Mortality: stillbirth, placental pathology, fetal diseases, fetal masceration; Reproductive/Developmental: stillbirth, placental pathology, fetal diseases, fetal masceration, gestational age
Asbestos Fiber Type(s):	Asbestos - Chrysotile (serpentine): 12001-29-5; Asbestos - Tremolite: 14567-73-8; Asbestos - Crocidolite (riebeckite): 12001-28-4; Asbestos - Actinolite: 12172-67-7; Asbestos - Anthophyllite: 17068-78-9
Linked HERO ID(s):	No linked references.
HERO ID:	709626

Domain	Metric		Rating	Comments
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Medium	Exposure was measured at a single time period (autopsy for stillbirth, birth for healthy infants) via transmission electron microscopy (JOEL 100CX and Philips 525M). Energy dispersive x-ray analysis was paired with selected area diffraction analyses to identify asbestos fibers. For stillbirths, fiber burden was measured in lung, liver, placenta, and skeletal muscle tissue, while fiber burden was measured in placental tissue only from healthy live births. Before analysis, NC pore filters were measured to identify the background levels of asbestos. Exposure was measured at a single time period but can be reasonably assumed to represent fetal exposure. Samples with calculated levels <=30,000 fibers/g were assigned a value of 0 for analyses.
	Metric 5:	Exposure Levels	Low	PRIMARY EVALUATION STOPPED AFTER METRIC 5 WAS RATED LOW****Only two asbestos exposure levels are used in analyses of stillbirth infants. Analyses use the presence or absence of fibers for their exposure levels. Mean fiber levels are compared for stillbirth infants and healthy liveborn infants (report p-value for significant difference).

Additional Comments:	This study provided vague descriptions of statistical analyses which made it difficult to understand the results reported. Additionally, the study had a small sample size with limited numbers of health live born infants and still births, limiting the likely sensitivity of analyses. The crude nature of statistical analyses (Fisher's test and chi-square tests) prevented the consideration of confounders, though it appeared that the demographic variables differed among the study population. Metric 10 received an NA rating, as covariates were not included in the analyses.

** As described in Appendix B.2 of the *White Paper: Quantitative Approach to the Human Health Assessment for the Risk Evaluation for Asbestos Part 2: Supplemental Evaluation Including Legacy Uses and Associated Disposals of Asbestos*, to be considered as being informative for dose-response analysis, metrics 4 and 5 would need metric ratings of Medium or High. This reference did not satisfy this requirement; therefore data quality evaluation is presented for only for metrics 4 and 5.

Study Citation:	Harless, K. W., Watanabe, S., Renzetti, A. D., Jr (1978). The acute effects of chrysotile asbestos exposure on lung function. Environmental Research 16(1-3):360-372.
Health Outcome:	Pulmonary Function/Spirometry Results
Target Organ(s):	Lung/Respiratory: FVC, FEV1, FEF(25-75%), FRC
Asbestos Fiber Type(s):	Asbestos - Chrysotile (serpentine): 12001-29-5
Linked HERO ID(s):	No linked references.
HERO ID:	3084436

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	High	The authors provided sufficient details about the setting and study participants (n=23).
	Metric 2:	Attrition	Low	There was moderate subject loss (30% of all those evaluated in the initial visit) from the study, but outcome and exposure data were largely complete.
	Metric 3:	Comparison Group	Low	The study only had an exposed group of participants and provided details about the setting, suggesting the participants were similar. The authors did not include a clear inclusion or exclusion criteria.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Medium	The asbestos samples were not taken during regular operations or during the exposure of the study participants. The sampling occurred after job closure using an OSHA method, but it was not described in detail.
	Metric 5:	Exposure Levels	Medium	The range of exposure is sufficient, albeit the measurements were taken during simulated activities.
	Metric 6:	Temporality	Low	Temporality is established, but it is unclear whether there is adequate follow-up for consideration of latency as spirometric measurements were taken within months of their last exposure day.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	High	Pulmonary Function/Spirometry Results: The outcome was assessed using well established methods that include standardized spirometric measurements (e.g., FEV1, FVC).
	Metric 8:	Reporting Bias	Medium	The authors reported all results outlined in the methods section.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Medium	The authors collected additional data on covariates e.g., age, weight, but they did not use these data for adjustment in e.g., correlation analyses (not conducted).
	Metric 10:	Covariate Characterization	Medium	Data on potential confounders (excluding co-exposures) were collected, assuming accurate personnel files were used.
	Metric 11:	Co-exposure Counfounding	Medium	The authors collected data on co-exposures i.e., tobacco smoke, and analyzed the study results comparing smokers to nonsmokers and light smokers.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	Medium	The authors used descriptive statistics to report their incidence findings.

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Study Citation: Harless, K. W., Watanabe, S., Renzetti, A. D., Jr (1978). The acute effects of chrysotile asbestos exposure on lung function. Environmental Research 16(1-3):360-372.
Health Outcome: Pulmonary Function/Spirometry Results
Target Organ(s): Lung/Respiratory: FVC, FEV1, FEF(25-75%), FRC
Asbestos Fiber Type(s): Asbestos - Chrysotile (serpentine): 12001-29-5
Linked HERO ID(s): No linked references.
HERO ID: 3084436

Domain	Metric		Rating	Comments
	Metric 13:	Statistical Power	Medium	While the sample size is low (n=16 participants who provided complete data), the occupational setting and outcome measurements seem adequate to detect an effect in them.
	Metric 14:	Reproducibility of Analyses	Medium	The description of the analysis is sufficient to reproduce the analysis conducted by the authors.
	Metric 15:	Statistical Analysis	Medium	The use of descriptive statistics for this small study seems appropriate for the analysis that was conducted.

Additional Comments: None

Overall Quality Determination — Medium

* No biomarkers were identified for this evaluation.

Study Citation:	Henderson, V. L., Enterline, P. E. (1979). Asbestos exposure: Factors associated with excess cancer and respiratory disease mortality. Annals of the New York Academy of Sciences 330(ED.):117-126.
Health Outcome:	Lung Cancer; cancer mortality, digestive cancer, all other cancer mortality; Asbestosis; stroke mortality, heart disease mortality, pneumoconiosis and pulmonary fibrosis mortality, all other cause mortality
Target Organ(s):	Mortality: all cause mortality, cancer (140-205) mortality, digestive cancer (150-159) mortality, respiratory cancer (162-163) mortality, all other cancer mortality, stroke (330-334) mortality, heart disease (400-443) mortality, respiratory disease (470-527) mortality, pneumoconiosis and pulmonary fibrosis (523-525) mortality, asbestosis (523.2) mortality, all other cause mortality; Cancer/Carcinogenesis: cancer (140-205) mortality, digestive cancer (150-159) mortality, respiratory cancer (162-163) mortality, all other cancer mortality; Gastrointestinal: digestive cancer (150-159) mortality; Lung/Respiratory: respiratory cancer (162-163) mortality, respiratory disease (470-527) mortality, pneumoconiosis and pulmonary fibrosis (523-525) mortality, asbestosis (523.2) mortality; Cardiovascular: stroke (330-334) mortality, heart disease (400-443) mortality
Asbestos Fiber Type(s):	Asbestos - Amosite (grunerite): 12172-73-5; Asbestos - Chrysotile (serpentine): 12001-29-5; Asbestos - Crocidolite (riebeckite): 12001-28-4
Linked HERO ID(s):	No linked references.
HERO ID:	101

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Medium	Key elements of study design were reported within this retrospective cohort study of n=1075 male asbestos workers who retired 1941-1967 with a pension from work within U.S. asbestos manufacturing facilities and were followed for mortality outcomes during the years 1941-1973. The retirees included those who retired normally at age 65, those who retired before age 65 for personal reasons but lived to age 65, and those who retired prior to age 65 due to a disability but also lived to age 65. The U.S. white male population was used as a comparison population for standardized mortality ratio (SMR) analyses. This study was an update to a previous study which only followed the original cohort of this population (originally n=1,348 men) through December 31, 1969. Of this original cohort of n=1,348 men, a total of n=273 employed only in Canada had to be excluded as the current study deaths 1970-1973 through social security records. The distribution of these exclusions with respect to exposure and outcomes was not detailed.
	Metric 2:	Attrition	Medium	Of the 781 deaths identified, death certificates were obtained for 749 individuals, and authors noted exclusion of those with missing death certificates from analyses. No detail regarding exposure or outcomes for these individuals was provided. Estimated cumulative dust exposure was complete and described as calculated for each cohort member.
	Metric 3:	Comparison Group	High	Inclusion criteria and methods of participant selection were detailed. For SMR analyses, the use of U.S. white males living at the same age and time periods was chosen as a comparison population. This study was restricted to males.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Medium	Section 3.9.12 of the 1986 assessment describes the application of a conversion factor based on a study in a factory making asbestos cement pipes and sheets.
	Metric 5:	Exposure Levels	Medium	Fiber concentrations for 5 different exposure groups are presented in Section 3.9.12 of the 1986 assessment.
	Metric 6:	Temporality	High	The study presents an appropriate temporality and the interval between exposure and outcome is appropriate considering the latency of disease. The cohort was followed for mortality 1941-1973. The average length of employment was 25 years.

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Study Citation:	Henderson, V. L., Enterline, P. E. (1979). Asbestos exposure: Factors associated with excess cancer and respiratory disease mortality. Annals of the New York Academy of Sciences 330(ED.):117-126.
Health Outcome:	Lung Cancer; cancer mortality, digestive cancer, all other cancer mortality; Asbestosis; stroke mortality, heart disease mortality, pneumoconiosis and pulmonary fibrosis mortality, all other cause mortality
Target Organ(s):	Mortality: all cause mortality, cancer (140-205) mortality, digestive cancer (150-159) mortality, respiratory cancer (162-163) mortality, all other cancer mortality, stroke (330-334) mortality, heart disease (400-443) mortality, respiratory disease (470-527) mortality, pneumoconiosis and pulmonary fibrosis (523-525) mortality, asbestosis (523.2) mortality, all other cause mortality; Cancer/Carcinogenesis: cancer (140-205) mortality, digestive cancer (150-159) mortality, respiratory cancer (162-163) mortality, all other cancer mortality; Gastrointestinal: digestive cancer (150-159) mortality; Lung/Respiratory: respiratory cancer (162-163) mortality, respiratory disease (470-527) mortality, pneumoconiosis and pulmonary fibrosis (523-525) mortality, asbestosis (523.2) mortality; Cardiovascular: stroke (330-334) mortality, heart disease (400-443) mortality
Asbestos Fiber Type(s):	Asbestos - Amosite (grunerite): 12172-73-5; Asbestos - Chrysotile (serpentine): 12001-29-5; Asbestos - Crocidolite (riebeckite): 12001-28-4
Linked HERO ID(s):	No linked references.
HERO ID:	101

Domain		Metric	Rating	Comments
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	High	Lung Cancer: Mortality data was coded by a qualified nosologist using codes in ICD-7. Lung cancer was coded as 162-163.; Other Cancer(s): Mortality data was coded by a qualified nosologist using codes in ICD-7, including any cancer (140-205) and digestive cancer (150-159).; Asbestosis: Mortality data was coded by a qualified nosologist using codes in ICD-7. Asbestosis was coded as 523.2.; Other Non-Cancer Outcomes: Mortality data was coded by a qualified nosologist using codes in ICD-7, including stroke (330-334), heart disease (400-443), respiratory disease (470-527), and pneumoconiosis and pulmonary fibrosis (523-525).
	Metric 8:	Reporting Bias	High	There were no concerns for selective reporting, with outcome counts reported in most results and 95% CIs for some.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Medium	Other than stratification for total estimated dust exposure, department in which most of the worker's life was spent, type of asbestos, and periods of follow-up, no additional adjustments or consideration for differences between exposed and comparison groups regarding distributions of relevant covariates were detailed. The cohort for study and the comparison population for SMR analyses was restricted to white males.
	Metric 10:	Covariate Characterization	Medium	Although not specified within this occupational study, it is assumed that personnel files were utilized to obtain department, asbestos type, and years of follow-up data.
	Metric 11:	Co-exposure Counfounding	Medium	Authors noted the potential for silica exposure within production of asbestos cement pipe and asbestos cement shingles. Analyses did not account for these exposures, however authors noted no indication of unbalanced provision of these exposures across study groups.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	Medium	The study design was appropriate. Table 3 presented predicted SMR's, derived from linear regression from dose-response data, as well as observed SMR's for respiratory (lung) cancer.
	Metric 13:	Statistical Power	Medium	The number of participants (n=1075) was adequate to detect an association.
	Metric 14:	Reproducibility of Analyses	Medium	The description of SMR analyses and formation of rates for the comparison population was presented in detail and generally sufficient to reproduce.

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Study Citation:	Henderson, V. L., Enterline, P. E. (1979). Asbestos exposure: Factors associated with excess cancer and respiratory disease mortality. Annals of the New York Academy of Sciences 330(ED.):117-126.
Health Outcome:	Lung Cancer; cancer mortality, digestive cancer, all other cancer mortality; Asbestosis; stroke mortality, heart disease mortality, pneumoconiosis and pulmonary fibrosis mortality, all other cause mortality
Target Organ(s):	Mortality: all cause mortality, cancer (140-205) mortality, digestive cancer (150-159) mortality, respiratory cancer (162-163) mortality, all other cancer mortality, stroke (330-334) mortality, heart disease (400-443) mortality, respiratory disease (470-527) mortality, pneumoconiosis and pulmonary fibrosis (523-525) mortality, asbestosis (523.2) mortality, all other cause mortality; Cancer/Carcinogenesis: cancer (140-205) mortality, digestive cancer (150-159) mortality, respiratory cancer (162-163) mortality, all other cancer mortality; Gastrointestinal: digestive cancer (150-159) mortality; Lung/Respiratory: respiratory cancer (162-163) mortality, respiratory disease (470-527) mortality, pneumoconiosis and pulmonary fibrosis (523-525) mortality, asbestosis (523.2) mortality; Cardiovascular: stroke (330-334) mortality, heart disease (400-443) mortality
Asbestos Fiber Type(s):	Asbestos - Amosite (grunerite): 12172-73-5; Asbestos - Chrysotile (serpentine): 12001-29-5; Asbestos - Crocidolite (riebeckite): 12001-28-4
Linked HERO ID(s):	No linked references.
HERO ID:	101

Domain	Metric		Rating	Comments
	Metric 15:	Statistical Analysis	Medium	The method for calculating SMRs is transparent and no assumptions need to be met.

Additional Comments:	This study summarized the mortality experience of a cohort of 1075 men who attained age 65 years and retired with pensions from work in a U.S. asbestos company during the period of 1941-1967 and was followed for deaths through 1973. Mortality was compared with the general U. S. white male population within various SMR analyses. Exposure was only estimated for each worker as cumulative asbestos dust mppc-years and no measure of asbestos fiber concentration was presented.

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation:	Hirsch, A., Di Menza, L., Dorbon, F., Carre, A., Bignon, J. (1980). Diaphragmatic straightness in 302 asbestos-exposed patients. IARC Scientific Publications no. 30 (30):523-526.			
Health Outcome:	Pulmonary Function/Spirometry Results; Pleural Plaques; diaphragmatic straightness, fibrosis, bronchoalveolar cells			
Target Organ(s):	Lung/Respiratory: Diaphragmatic straightness, Pleural thickening, Pleural calcification, Fibrosis			
Asbestos Fiber Type(s):	Asbestos - Not specified: 1332-21-4			
Linked HERO ID(s):	No linked references.			
HERO ID:	3084255			

Domain	Metric		Rating	Comments
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Low	In this cohort, most groups had information on asbestos exposure generated through the examination of ferruginous bodies counted in sputum or broncho-alveolar lavage fluid samples (Hirsch et al., 1980, 3084255). A surgeon also examined the parietal pleura in the costal and diaphragmatic regions. Specifics on how things were measured not provided.
	Metric 5:	Exposure Levels	Low	Exposure was categorized into definite, moderate, suspected, and absent. Quantitative levels were not provided, very little information on actual exposure, however, they reported 3 or more levels of exposure

Additional Comments: There wasn't anything relevant to dose response for extraction.

* No biomarkers were identified for this evaluation.

** As described in Appendix B.2 of the *White Paper: Quantitative Approach to the Human Health Assessment for the Risk Evaluation for Asbestos Part 2: Supplemental Evaluation Including Legacy Uses and Associated Disposals of Asbestos*, to be considered as being informative for dose-response analysis, metrics 4 and 5 would need metric ratings of Medium or High. This reference did not satisfy this requirement; therefore data quality evaluation is presented for only for metrics 4 and 5.

Study Citation:	Howe, H. L., Wolfgang, P. E., Burnett, W. S., Nasca, P. C., Youngblood, L. (1989). Cancer incidence following exposure to drinking water with asbestos leachate. Public Health Reports 104(3):251-256.
Health Outcome:	Lung Cancer; Ovarian Cancer; Buccal, stomach, colon, rectum, liver, pancreas, melanoma, breast, uterus, cervix, prostate, testis, bladder, kidney, brain, thyroid, lymphoma, leukemia
Target Organ(s):	Cancer/Carcinogenesis: Standardized incidence ratios (SIR) of buccal cancer, Standardized incidence ratios (SIR) of stomach cancer, Standardized incidence ratios (SIR) of colon cancer, Standardized incidence ratios (SIR) of rectum cancer, Standardized incidence ratios (SIR) of liver cancer, Standardized incidence ratios (SIR) of pancreas cancer, Standardized incidence ratios (SIR) of lung cancer, Standardized incidence ratios (SIR) of melanoma, Standardized incidence ratios (SIR) of breast cancer, Standardized incidence ratios (SIR) of uterus cancer, Standardized incidence ratios (SIR) of cervix cancer, Standardized incidence ratios (SIR) of ovary cancer, Standardized incidence ratios (SIR) of prostate cancer, Standardized incidence ratios (SIR) of testis cancer, Standardized incidence ratios (SIR) of bladder cancer, Standardized incidence ratios (SIR) of kidney cancer, Standardized incidence ratios (SIR) of brain cancer, Standardized incidence ratios (SIR) of thyroid cancer, Standardized incidence ratios (SIR) of lymphoma, Standardized incidence ratios (SIR) of leukemia; Gastrointestinal: Standardized incidence ratios (SIR) of buccal cancer, Standardized incidence ratios (SIR) of stomach cancer, Standardized incidence ratios (SIR) of colon cancer, Standardized incidence ratios (SIR) of rectum cancer, Standardized incidence ratios (SIR) of pancreas cancer; Hepatic/Liver: Standardized incidence ratios (SIR) of liver cancer; Lung/Respiratory: Standardized incidence ratios (SIR) of lung cancer; Skin/Connective Tissue: Standardized incidence ratios (SIR) of melanoma; Reproductive/Developmental: Standardized incidence ratios (SIR) of breast cancer, Standardized incidence ratios (SIR) of uterus cancer, Standardized incidence ratios (SIR) of cervix cancer, Standardized incidence ratios (SIR) of ovary cancer, Standardized incidence ratios (SIR) of prostate cancer, Standardized incidence ratios (SIR) of testis cancer; Renal/Kidney: Standardized incidence ratios (SIR) of bladder cancer, Standardized incidence ratios (SIR) of kidney cancer; Neurological/Behavioral: Standardized incidence ratios (SIR) of brain cancer; Thyroid: Standardized incidence ratios (SIR) of thyroid cancer; Immune/Hematological: Standardized incidence ratios (SIR) of lymphoma, Standardized incidence ratios (SIR) of leukemia
Asbestos Fiber Type(s):	Asbestos - Not specified: 1332-21-4
Linked HERO ID(s):	No linked references.
HERO ID:	3082764

Domain	Metric		Rating	Comments
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Uninformative	The methods used to quantify the exposure were not well defined, and detailed methods of exposure assessment were not reported.
	Metric 5:	Exposure Levels	Uninformative	The limited exposure data (only concentrations of 5 samples) that were reported are not adequate to determine an exposure-response relationship between asbestos fibers in drinking water and the different cancers evaluated in the study population.

Additional Comments: Overall, the measurement of exposure metric (M4) methods used to quantify the exposure were not well defined. Additionally, the exposure levels metric (M5) information reported was not adequate to determine an exposure-response relationship.

** As described in Appendix B.2 of the *White Paper: Quantitative Approach to the Human Health Assessment for the Risk Evaluation for Asbestos Part 2: Supplemental Evaluation Including Legacy Uses and Associated Disposals of Asbestos*, to be considered as being informative for dose-response analysis, metrics 4 and 5 would need metric ratings of Medium or High. This reference did not satisfy this requirement; therefore data quality evaluation is presented for only for metrics 4 and 5.

Study Citation:	Huang, J. Q. (1990). A study on the dose-response relationship between asbestos exposure level and asbestosis among workers in a Chinese chrysotile product factory. Biomedical and Environmental Sciences 3(1):90-98.
Health Outcome:	Asbestosis
Target Organ(s):	Lung/Respiratory: asbestosis
Asbestos Fiber Type(s):	Asbestos - Chrysotile (serpentine): 12001-29-5
Linked HERO ID(s):	No linked references.
HERO ID:	3082611

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Medium	Of the total 1059 workers (including retirees) at a Shanghai suburb chrysotile product factory founded in 1958, 824 had been exposed to asbestos; all were employed prior to 1980 for at least 3 years. Employees were identified and information obtained from factory records. Including retirees as well as current workers in the target population of workers reduced the likelihood of healthy worker bias.
	Metric 2:	Attrition	Medium	Of the 824 employees 48 (5.8%) could not be followed up “for various reasons”; the study sample therefore included 776 workers with complete records. In addition, of the total of 277 workers diagnosed with asbestosis, 259 cases (93.5%) had complete occupational histories and were included in analyses examining the dose-response relationship with exposure. Despite some losses, attrition was low, with no evidence of bias.
	Metric 3:	Comparison Group	Low	Participant characteristics were not provided for the study population; it is therefore not possible to evaluate to what extent associations might be confounded by factors such as age or gender. In addition, the authors noted that in the study population “[a] portion of the workers had been exposed to asbestos before this factory was founded in the early 1950s”. The percentage of workers with unquantified prior exposure was not shown, and analyses excluding these individuals to assess their influence on results were not included. This issue can undermine the validity of analyses aiming to compare the risk of asbestosis across levels of exposure.
Domain 2: Exposure Characterization				

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Study Citation:	Huang, J. Q. (1990). A study on the dose-response relationship between asbestos exposure level and asbestosis among workers in a Chinese chrysotile product factory. Biomedical and Environmental Sciences 3(1):90-98.
Health Outcome:	Asbestosis
Target Organ(s):	Lung/Respiratory: asbestosis
Asbestos Fiber Type(s):	Asbestos - Chrysotile (serpentine): 12001-29-5
Linked HERO ID(s):	No linked references.
HERO ID:	3082611

Domain	Metric		Rating	Comments
	Metric 4:	Measurement of Exposure	Medium	Quantitative measures of dust levels for different workplaces in the factory were collected from the facility records: "[t]he dust concentration of every workplace during the subject's employment was retrieved from the factory's dust monitoring records." Protocols (e.g., personal vs area sampling, number of hours) used historically were not described. Exposure in the facility was measured using Chinese-made membrane filters and gravimetry, which the authors report were rates as suitable by the Asbestos Institute of Canada. Paired dust-fiber samples were measured for 18 location-job function groups; 7-26 samples were collected for each of these groups. Historical gravimetry (dust) measures were converted to fiber concentrations using side by side sampling and linear regression-derived conversion factors. Sampling protocols for the paired samples were not described, but concentrations are shown for areas and specific job functions (e.g., braiding round rope, braiding cubic rope); this suggests some personal samples may have been collected. The fiber counting method cited was PCM [AIA (1979) Reference Method for the Determination of Airborne Asbestos Fibre Concentrations at Workplaces by Light Microscopy (Membrane Filter Method)]. Asbestos exposure for each worker was calculated using occupational history and fiber concentrations estimated for that period. Since details on the sampling methods are lacking, the domain has received a medium rating.
	Metric 5:	Exposure Levels	Medium	Prevalence of asbestosis is reported cumulative exposure categorized in 8 levels, representing a wide range of both high and low levels of exposure. The range of exposure in the reference category was 0 to 99 f/ml-years, and thus included workers with large disparities in exposure.
	Metric 6:	Temporality	Medium	Sequencing in this retrospective cohort was appropriate. The distribution of employment dates was not presented, but the timing of initial exposure was described for the 101 asbestosis cases in the lowest exposure category. For 88 of these cases, exposure began prior to 1958, i.e. 24 years prior to the end of cumulative exposure estimation in 1982. While the proportion of the sample with adequate vs inadequate follow-up is unknown, there is also no evidence that follow-up time was inadequate for a large proportion of the sample.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Medium	Asbestosis: Asbestosis was identified by the Pneumoconiosis Diagnostic Panel of Shanghai via chest x-rays. The panel used the "original Chinese standard system". Authors note that this system has been compared with the ILO system, but the evaluator could not access the cited study. As a comparison with the ILO coding system is not available, the domain was rated medium.

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Study Citation: Huang, J. Q. (1990). A study on the dose-response relationship between asbestos exposure level and asbestosis among workers in a Chinese chrysotile product factory. Biomedical and Environmental Sciences 3(1):90-98.
Health Outcome: Asbestosis
Target Organ(s): Lung/Respiratory: asbestosis
Asbestos Fiber Type(s): Asbestos - Chrysotile (serpentine): 12001-29-5
Linked HERO ID(s): No linked references.
HERO ID: 3082611

Domain	Metric		Rating	Comments
	Metric 8:	Reporting Bias	Medium	Numbers of employees in each exposure group and number of diagnosed cases are reported. The authors present coefficients from a regression model as well as a life table analysis. Methods used for the latter were not detailed, and the reference cited was in Chinese. It is uncertain whether the life table analysis method used was similar to the NIOSH Life Table Analysis System (LTAS) approach, in which estimates may be standardized for variables such as age, sex, race and calendar year.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Medium	No covariates were included in the regression model. However, there is no evidence to suggest important differences by case status in the distribution of variables that might have been considered (e.g., age or smoking history). Substantial confounding is not likely an important issue for this association; many studies report little or no confounding of associations between asbestos exposure and asbestosis (e.g., Paris et al 2009, HERO ID: 758968).
	Metric 10:	Covariate Characterization	Medium	All variables were characterized from employment records; it is not certain whether age adjustments were incorporated in the life table analysis.
	Metric 11:	Co-exposure Counfounding	Medium	Asbestosis is explicitly linked to asbestos fibers and co-exposures are not an important concern if disease ascertainment is adequate. In addition, the study was set in a Chinese asbestos textile and friction material manufacturing facility, a setting where important co-exposures are unlikely.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	Medium	The retrospective cohort study design was appropriate to examine the exposure-outcome relationship in this occupational setting.
	Metric 13:	Statistical Power	Medium	The number of participants (n=776) was adequate to detect an effect in the study population.
	Metric 14:	Reproducibility of Analyses	Medium	Results of the regression model are readily reproducible. Without access to the methods reference, however, reproduction of the life table analysis might be difficult.
	Metric 15:	Statistical Analysis	Medium	The authors presented results of “a linear regression model with the prevalence in logit vs logarithm of the dose (f-y)”, i.e. a logit model for asbestosis using a continuous log-transformed asbestos exposure variable. Life table analyses were also used to analyze the exposure-outcome association.

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Study Citation:	Huang, J. Q. (1990). A study on the dose-response relationship between asbestos exposure level and asbestosis among workers in a Chinese chrysotile product factory. Biomedical and Environmental Sciences 3(1):90-98.
Health Outcome:	Asbestosis
Target Organ(s):	Lung/Respiratory: asbestosis
Asbestos Fiber Type(s):	Asbestos - Chrysotile (serpentine): 12001-29-5
Linked HERO ID(s):	No linked references.
HERO ID:	3082611

Domain	Metric	Rating	Comments
Additional Comments:	This study examined the association between cumulative asbestos exposure and asbestosis in a Chinese factory manufacturing asbestos textile and friction materials using chrysotile fiber. Participant selection, exposure measurement at the current facility, and outcome ascertainment appeared to be appropriate, although details on sampling protocols were lacking (e.g., area vs personal samples, duration). Prior exposure to asbestos was reportedly an issue for an unknown proportion of the sample; cumulative exposure could not be properly estimated for these individuals, as study information came solely from factory records. The extent to which this issue undermined the validity of results cannot be determined.		

Overall Quality Determination — Medium

* No biomarkers were identified for this evaluation.

Study Citation:	Hughes, J. M., Weill, H. (1991). Asbestosis as a precursor of asbestos related lung cancer: Results of a prospective mortality study. British Journal of Industrial Medicine 48(4):229-233.
Health Outcome:	Lung Cancer; respiratory cancer mortality, larynx cancer mortality, buccal/pharynx cancer mortality, digestive cancer mortality, bladder/kidney cancer mortality, lymphatic cancer mortality, miscellaneous cancer mortality, residual cancer mortality
Target Organ(s):	Cancer/Carcinogenesis: All malignancies mortality, Respiratory cancer mortality, Larynx cancer mortality, Buccal/pharynx cancer mortality, Digestive cancer mortality, Bladder and kidney cancer mortality, Lymphatic cancer mortality, Miscellaneous cancer mortality, Residual cancer mortality; Mortality: All malignancies mortality, Respiratory cancer mortality, Larynx cancer mortality, Buccal/pharynx cancer mortality, Digestive cancer mortality, Bladder and kidney cancer mortality, Lymphatic cancer mortality, Miscellaneous cancer mortality, Residual cancer mortality; Lung/Respiratory: Respiratory cancer mortality, Larynx cancer mortality; Gastrointestinal: Buccal/pharynx cancer mortality, Digestive cancer mortality; Renal/Kidney: Bladder and kidney cancer mortality; Immune/Hematological: Lymphatic cancer mortality
Asbestos Fiber Type(s):	Asbestos - Chrysotile (serpentine): 12001-29-5; Asbestos - Crocidolite (riebeckite): 12001-28-4
Linked HERO ID(s):	No linked references.
HERO ID:	2223821

Domain	Metric		Rating	Comments
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Low	This outcome is rated Low due to the lack of PCM or TEM being used in the study.Authors refer to a different study for all information regarding to exposure to asbestos (Hughes et al. 1987, 3583332) That paper notes that air sampling data was collected by a mix of the government, industry, and insurance companies with a midget impinger (recorded in millions of particles per cubic foot(mppcf)). This was done from the 1950s-1960s. Membrane filter sampling (measured in fibers per milliliter) was also noted to have been carried out starting in 1969. Authors note that because of the employment population occurring from 1940-1950, all exposure estimates were converted into mppcf. These air sampling data in combination with job history data were used to estimate cumulative exposure.
	Metric 5:	Exposure Levels	Low	SMRs for cancer do not provide results by levels of exposure. Authors only provide categorical cumulative exposure levels for small opacities (<25, 25-99, 100-149, and >=150 mppcf-y) and for lung cancer (<51, 51-85, 86-121, 122-169, and >=170 mppcf-y).

Additional Comments: Overall, this study is well-designed and references most methods to a previous paper (Hughes et al. 1987, 3583332).Note that the cancerous health outcomes were not evaluated for any metrics except Metric 4 and 5 and had no data extracted because they did not have sufficient exposure information to be useful for dose-response analysis.

** As described in Appendix B.2 of the *White Paper: Quantitative Approach to the Human Health Assessment for the Risk Evaluation for Asbestos Part 2: Supplemental Evaluation Including Legacy Uses and Associated Disposals of Asbestos*, to be considered as being informative for dose-response analysis, metrics 4 and 5 would need metric ratings of Medium or High. This reference did not satisfy this requirement; therefore data quality evaluation is presented for only for metrics 4 and 5.

Study Citation:	Hughes, J. M., Weill, H. (1991). Asbestosis as a precursor of asbestos related lung cancer: Results of a prospective mortality study. British Journal of Industrial Medicine 48(4):229-233.
Health Outcome:	cardiovascular mortality, non-malignant respiratory disease mortality, external causes mortality, pneumoconiosis mortality
Target Organ(s):	Mortality: All-cause mortality, Cardiovascular mortality, Non-malignant respiratory diseases mortality, Pneumoconiosis mortality, External causes mortality, Residual mortality; Cardiovascular: Cardiovascular mortality; Lung/Respiratory: Non-malignant respiratory diseases mortality, Pneumoconiosis mortality
Asbestos Fiber Type(s):	Asbestos - Chrysotile (serpentine): 12001-29-5; Asbestos - Crocidolite (riebeckite): 12001-28-4
Linked HERO ID(s):	No linked references.
HERO ID:	2223821

Domain	Metric		Rating	Comments
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Low	This outcome is rated Low due to the lack of PCM or TEM being used in the study.Authors refer to a different study for all information regarding to exposure to asbestos (Hughes et al. 1987, 3583332) That paper notes that air sampling data was collected by a mix of the government, industry, and insurance companies with a midget impinger (recorded in millions of particles per cubic foot(mppcf)). This was done from the 1950s-1960s. Membrane filter sampling (measured in fibers per milliliter) was also noted to have been carried out starting in 1969. Authors note that because of the employment population occurring from 1940-1950, all exposure estimates were converted into mppcf. These air sampling data in combination with job history data were used to estimate cumulative exposure.
	Metric 5:	Exposure Levels	Low	SMRs for cancer do not provide results by levels of exposure. Authors only provide categorical cumulative exposure levels for small opacities (<25, 25-99, 100-149, and >=150 mppcf-y) and for lung cancer (<51, 51-85, 86-121, 122-169, and >=170 mppcf-y).

Additional Comments:	Overall, this study is well-designed and references most methods to a previous paper (Hughes et al. 1987, 3583332).Note that the cancerous health outcomes were not evaluated for any metrics except Metric 4 and 5 and had no data extracted because they did not have sufficient exposure information to be useful for dose-response analysis.

** As described in Appendix B.2 of the *White Paper: Quantitative Approach to the Human Health Assessment for the Risk Evaluation for Asbestos Part 2: Supplemental Evaluation Including Legacy Uses and Associated Disposals of Asbestos*, to be considered as being informative for dose-response analysis, metrics 4 and 5 would need metric ratings of Medium or High. This reference did not satisfy this requirement; therefore data quality evaluation is presented for only for metrics 4 and 5.

Study Citation:	Hughes, J. M., Weill, H. (1991). Asbestosis as a precursor of asbestos related lung cancer: Results of a prospective mortality study. British Journal of Industrial Medicine 48(4):229-233.
Health Outcome:	Pleural Plaques; small opacities
Target Organ(s):	Lung/Respiratory: Small opacities mortality, Pleural plaques mortality; Mortality: Small opacities mortality, Pleural plaques mortality
Asbestos Fiber Type(s):	Asbestos - Chrysotile (serpentine): 12001-29-5; Asbestos - Crocidolite (riebeckite): 12001-28-4
Linked HERO ID(s):	No linked references.
HERO ID:	2223821

Domain	Metric		Rating	Comments
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Low	This outcome is rated Low due to the lack of PCM or TEM being used in the study.Authors refer to a different study for all information regarding to exposure to asbestos (Hughes et al. 1987, 3583332) That paper notes that air sampling data was collected by a mix of the government, industry, and insurance companies with a midget impinger (recorded in millions of particles per cubic foot(mppcf)). This was done from the 1950s-1960s. Membrane filter sampling (measured in fibers per milliliter) was also noted to have been carried out starting in 1969. Authors note that because of the employment population occurring from 1940-1950, all exposure estimates were converted into mppcf. These air sampling data in combination with job history data were used to estimate cumulative exposure.
	Metric 5:	Exposure Levels	Medium	Table 1 presents categorical cumulative exposure levels (<25, 25-99, 100-149, and >=150 mppcf-y) paired with percentages of each group with normal and abnormal small opacities.

Additional Comments: The purpose of this paper was to determine whether asbestos workers with small opacities had a higher risk of developing lung cancer, so it was not completely focused on the relationship between asbestos exposure and pleural plaques, however the information collected for the purposes of answering this question can be extracted to approach answering this other question. Table 1 contains a comparison between cumulative asbestos exposure groups and percentage of the groups with >=1/0 and %0/1 small opacities. The SMR analysis for small opacities does not compare groups by exposure concentration.Note: QC was not completed for metrics other than metric 4 and metric 5 because the data are not amenable for dose-response modeling due to metric 4 being rated low.

* No biomarkers were identified for this evaluation.

** As described in Appendix B.2 of the *White Paper: Quantitative Approach to the Human Health Assessment for the Risk Evaluation for Asbestos Part 2: Supplemental Evaluation Including Legacy Uses and Associated Disposals of Asbestos*, to be considered as being informative for dose-response analysis, metrics 4 and 5 would need metric ratings of Medium or High. This reference did not satisfy this requirement; therefore data quality evaluation is presented for only for metrics 4 and 5.

Study Citation:	Hughes, J. M., Weill, H., Hammad, Y. Y. (1987). Mortality of workers employed in two asbestos cement manufacturing plants. Occupational and Environmental Medicine 44(3):161-174.
Health Outcome:	Laryngeal Cancer; All, digestive, kidney or bladder, lymphatic, buccal, pharynx, and prostate
Target Organ(s):	Cancer/Carcinogenesis: All malignancies mortality, Respiratory cancer mortality, Digestive cancer mortality, Kidney or bladder cancer mortality, Lymphatic cancer mortality, Residual cancer mortality (includes larynx, buccal, pharynx, and prostate cancer); Mortality: All malignancies mortality, Respiratory cancer mortality, Digestive cancer mortality, Kidney or bladder cancer mortality, Lymphatic cancer mortality, Residual cancer mortality (includes larynx, buccal, pharynx, and prostate cancer), Pneumoconiosis mortality; Lung/Respiratory: Respiratory cancer mortality, Pneumoconiosis mortality; Gastrointestinal: Digestive cancer mortality; Renal/Kidney: Kidney or bladder cancer mortality; Immune/Hematological: Lymphatic cancer mortality; larynx, buccal, pharynx, and prostate cancer): Residual cancer mortality (includes larynx, buccal, pharynx, and prostate cancer)
Asbestos Fiber Type(s):	Asbestos - Chrysotile (serpentine): 12001-29-5; Asbestos - Amosite (grunerite): 12172-73-5; Asbestos - Crocidolite (riebeckite): 12001-28-4
Linked HERO ID(s):	No linked references.
HERO ID:	281

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Medium	Study participants included male workers (n = 6,931) from two asbestos cement factory plants in New Orleans, LA, USA. Participants were identified by abstracting all job records on file in the two plants in 1970. Participants included those hired after 1942 (plant 1) or 1937 (plant 2) who worked at least one month prior to 1970 and had a valid social security number. Employees hired before these dates were excluded due to concerns about record keeping, which introduces the potential for healthy worker bias (n=167). While the authors do note differences between the two plant populations (age at employment, race, and location of plant) and analyses do not include adjustments (SMR), the results are presented separately for each plant, minimizing concerns for bias in the results. The authors attempted to validate their employment identification by obtaining copies of Social Security Administration quarterly reporting forms for three years of operation. They found that of the 1291 employees listed on those forms, 95.6% were included in the study population. This analysis was not able to be performed on the plant 1 participants. Overall this indicates a high level of participation, and there is no reason to suspect that missingness would be related to exposure and outcome.
	Metric 2:	Attrition	Medium	Participants were followed through 1982 or to age 80, whichever was earlier, with only a 4% loss to follow up rate. While information about the treatment of missing subjects is not included, the extremely low attrition rate minimizes concerns about treatment of these subjects introducing bias to the overall results. The authors do note that tracing was more successful among those employed for more than year (97.7%) compared to other workers (95.1%). However, this is not significant relative to the total amount of participants who were successfully traced. Of the participants who were able to be traced and identified as dead (n=2,143), death certificates to confirm cause of death were obtained in 94% of cases. For the remaining 6%, causes of death were ”allocated to categories of cause of death in the same proportion as those with certificates.” While this is overall a low rate of missing outcome data an adequate way of addressing missingness, there is some potential for bias of the true outcome data for the 6% without death certificates.

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Study Citation:	Hughes, J. M., Weill, H., Hammad, Y. Y. (1987). Mortality of workers employed in two asbestos cement manufacturing plants. Occupational and Environmental Medicine 44(3):161-174.
Health Outcome:	Laryngeal Cancer; All, digestive, kidney or bladder, lymphatic, buccal, pharynx, and prostate
Target Organ(s):	Cancer/Carcinogenesis: All malignancies mortality, Respiratory cancer mortality, Digestive cancer mortality, Kidney or bladder cancer mortality, Lymphatic cancer mortality, Residual cancer mortality (includes larynx, buccal, pharynx, and prostate cancer); Mortality: All malignancies mortality, Respiratory cancer mortality, Digestive cancer mortality, Kidney or bladder cancer mortality, Lymphatic cancer mortality, Residual cancer mortality (includes larynx, buccal, pharynx, and prostate cancer), Pneumoconiosis mortality; Lung/Respiratory: Respiratory cancer mortality, Pneumoconiosis mortality; Gastrointestinal: Digestive cancer mortality; Renal/Kidney: Kidney or bladder cancer mortality; Immune/Hematological: Lymphatic cancer mortality; larynx, buccal, pharynx, and prostate cancer): Residual cancer mortality (includes larynx, buccal, pharynx, and prostate cancer)
Asbestos Fiber Type(s):	Asbestos - Chrysotile (serpentine): 12001-29-5; Asbestos - Amosite (grunerite): 12172-73-5; Asbestos - Crocidolite (riebeckite): 12001-28-4
Linked HERO ID(s):	No linked references.
HERO ID:	281

Domain	Metric		Rating	Comments
	Metric 3:	Comparison Group	Medium	SMRs were reported to be adjusted for age (three categories for age at hire) and race (black and white). However, these are only mentioned qualitatively in the text, as the authors report ”No effect of these factors was observed.” The sample was limited to only men. Rates from the Louisiana general population were used as the referent values, which could introduce bias considering the employed population introduces the healthy worker effect. Comparisons to the general United States population are also briefly mentioned in the Results, but are a secondary analysis.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Medium	Factory measurements of fiber levels were taken using midget impingers from 1952-1969. After 1969, membrane filter sampling was conducted for the remaining samples. Job categories were used to relate quantitative measures to person-years of exposure in order to establish a cumulative exposure measure. Anecdotal information was used to group different jobs. For each category of jobs, the mean of the quantitative fiber measures was assigned to all individuals. The authors report a conversion factor of 1.4 f/ml = 1 mppcf. Their citation for this conversion factor is Hammad et al. 1979, HERO ID: 91), which explains their use of paired samples of dust and fiber concentrations. Hammad et al. 1979 cites NIOSH publication HSM72-10267 for their method of counting fibers, which is specified to have been conducted using PCM.
	Metric 5:	Exposure Levels	Medium	Five levels of exposure are reported as ranges of cumulative asbestos exposure. The levels appear to be adequate to develop exposure-response estimates.
	Metric 6:	Temporality	High	Measurement of outcomes occurred at least 20 years following the initial exposure. Additionally, authors note that exposure measures 10-15 years prior to the outcome were disregarded in the analyses. This follow-up period is adequate to establish temporality and considers latency periods for cancer-related outcomes.
Domain 3: Outcome Assessment				

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Study Citation:	Hughes, J. M., Weill, H., Hammad, Y. Y. (1987). Mortality of workers employed in two asbestos cement manufacturing plants. Occupational and Environmental Medicine 44(3):161-174.
Health Outcome:	Laryngeal Cancer; All, digestive, kidney or bladder, lymphatic, buccal, pharynx, and prostate
Target Organ(s):	Cancer/Carcinogenesis: All malignancies mortality, Respiratory cancer mortality, Digestive cancer mortality, Kidney or bladder cancer mortality, Lymphatic cancer mortality, Residual cancer mortality (includes larynx, buccal, pharynx, and prostate cancer); Mortality: All malignancies mortality, Respiratory cancer mortality, Digestive cancer mortality, Kidney or bladder cancer mortality, Lymphatic cancer mortality, Residual cancer mortality (includes larynx, buccal, pharynx, and prostate cancer), Pneumoconiosis mortality; Lung/Respiratory: Respiratory cancer mortality, Pneumoconiosis mortality; Gastrointestinal: Digestive cancer mortality; Renal/Kidney: Kidney or bladder cancer mortality; Immune/Hematological: Lymphatic cancer mortality; larynx, buccal, pharynx, and prostate cancer): Residual cancer mortality (includes larynx, buccal, pharynx, and prostate cancer)
Asbestos Fiber Type(s):	Asbestos - Chrysotile (serpentine): 12001-29-5; Asbestos - Amosite (grunerite): 12172-73-5; Asbestos - Crocidolite (riebeckite): 12001-28-4
Linked HERO ID(s):	No linked references.
HERO ID:	281

Domain	Metric		Rating	Comments
	Metric 7:	Outcome Measurement or Characterization	Medium	Laryngeal Cancer: Deaths were identified in 96% of the population with vital status tracing with the help of federal, state and local agencies. Of the 2143 who were identified as dead, death certificates were able to be obtained in 94% of cases. For the remaining 6%, causes of death were ”allocated to categories of cause of death in the same proportion as those with certificates.” Death certificates were coded to ICD-8 codes by a nosolgist.ICD-8 code 161 was used to identify laryngeal cancer.; Other Cancer(s): Deaths were identified in 96% of the population with vital status tracing with the help of federal, state and local agencies. Of the 2143 who were identified as dead, death certificates were able to be obtained in 94% of cases. For the remaining 6%, causes of death were ”allocated to categories of cause of death in the same proportion as those with certificates.” Death certificates were coded to ICD-8 codes by a nosolgist.ICD-8 codes 140-209 were used to determine all malignancies.ICD-8 codes 162-163 were used to determine respiratory malignancies.ICD-8 codes 150-159 were used to determine digestive malignancies.ICD-8 codes 188 and 189 were used to determine kidney/bladder malignancies.ICD-8 codes 200-209 were used to determine lymphatic malignancies.; Other Non-Cancer Outcomes: Deaths were identified in 96% of the population with vital status tracing with the help of federal, state and local agencies. Of the 2143 who were identified as dead, death certificates were able to be obtained in 94% of cases. For the remaining 6%, causes of death were ”allocated to categories of cause of death in the same proportion as those with certificates.” Death certificates were coded to ICD-8 codes by a nosolgist.ICD-8 code 515 was used to determine pneumoconiosis
	Metric 8:	Reporting Bias	Medium	SMRs are reported, but a measure of variance is not included. The number of observed and expected deaths for each plant are reported in a separate table.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Medium	Authors report that age and race stratified results did not show differences from the unstratified results. The study population was restricted to males, which effectively controls for sex in the study.
	Metric 10:	Covariate Characterization	Medium	While not explicitly stated, it is appropriate to assume that age, race, and sex information was collected from personnel records at the two factories.
	Metric 11:	Co-exposure Counfounding	Medium	While the study does not explicitly discuss the consideration of co-exposures, the occupational settings appear restricted to asbestos cement production, thus minimizing concerns about other chemicals encountered in the factories.

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Study Citation:	Hughes, J. M., Weill, H., Hammad, Y. Y. (1987). Mortality of workers employed in two asbestos cement manufacturing plants. Occupational and Environmental Medicine 44(3):161-174.
Health Outcome:	Laryngeal Cancer; All, digestive, kidney or bladder, lymphatic, buccal, pharynx, and prostate
Target Organ(s):	Cancer/Carcinogenesis: All malignancies mortality, Respiratory cancer mortality, Digestive cancer mortality, Kidney or bladder cancer mortality, Lymphatic cancer mortality, Residual cancer mortality (includes larynx, buccal, pharynx, and prostate cancer); Mortality: All malignancies mortality, Respiratory cancer mortality, Digestive cancer mortality, Kidney or bladder cancer mortality, Lymphatic cancer mortality, Residual cancer mortality (includes larynx, buccal, pharynx, and prostate cancer), Pneumoconiosis mortality; Lung/Respiratory: Respiratory cancer mortality, Pneumoconiosis mortality; Gastrointestinal: Digestive cancer mortality; Renal/Kidney: Kidney or bladder cancer mortality; Immune/Hematological: Lymphatic cancer mortality; larynx, buccal, pharynx, and prostate cancer): Residual cancer mortality (includes larynx, buccal, pharynx, and prostate cancer)
Asbestos Fiber Type(s):	Asbestos - Chrysotile (serpentine): 12001-29-5; Asbestos - Amosite (grunerite): 12172-73-5; Asbestos - Crocidolite (riebeckite): 12001-28-4
Linked HERO ID(s):	No linked references.
HERO ID:	281

Domain	Metric		Rating	Comments
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	Medium	The cohort study design and SMR analyses were appropriate to assess associations between asbestos exposure and cancer outcomes. The use of linear regression models to estimate the dose-response effect on lung cancer is also an appropriate model.
	Metric 13:	Statistical Power	Medium	The study population size is adequate to detect an effect in the exposed population. Some subgroups have a lower number of cases, but this does not introduce major concerns about the power of the analyses.
	Metric 14:	Reproducibility of Analyses	Medium	Authors report that mortality was compared using standardized mortality ratios and that dose-response relationships were evaluated using weighted least squares regressions. Enough conceptual information is reported to reproduce the analyses.
	Metric 15:	Statistical Analysis	Medium	The authors transparently report their use of SMR calculations, which does not have specific model assumptions that would be expected to be violated in this study.

Additional Comments: This retrospective occupational cohort study examined lung cancer mortality SMRs among male workers from two asbestos cement factories. While the study had an adequate sample size, consideration of exposure, approach to outcome ascertainment, and follow-up time, the assignment of cause of death based on proportions of causes on available death certificates introduces potential outcome misclassification.

Overall Quality Determination — Medium

* No biomarkers were identified for this evaluation.

Study Citation:	Hughes, J. M., Weill, H., Hammad, Y. Y. (1987). Mortality of workers employed in two asbestos cement manufacturing plants. Occupational and Environmental Medicine 44(3):161-174.
Health Outcome:	Laryngeal Cancer
Target Organ(s):	Mortality: Larynx malignancies mortality, Buccal/pharynx malignancies mortality, Prostate malignancies mortality, Bladder malignancies mortality, Kidney malignancies mortality, Cardiovascular malignancies mortality, Influenza, pneumonia, bronchitis, emphysema, and asthma mortality, Oesophagus malignancies mortality, Stomach malignancies mortality, Colon, rectum malignancies mortality, Other digestive malignancies (not oesophagus, stomach, colon, or rectum) mortality; Cancer/Carcinogenesis: Larynx malignancies mortality, Buccal/pharynx malignancies mortality, Prostate malignancies mortality, Bladder malignancies mortality, Kidney malignancies mortality, Cardiovascular malignancies mortality, Oesophagus malignancies mortality, Stomach malignancies mortality, Colon, rectum malignancies mortality, Other digestive malignancies (not oesophagus, stomach, colon, or rectum) mortality; Lung/Respiratory: Larynx malignancies mortality, Influenza, pneumonia, bronchitis, emphysema, and asthma mortality; Buccal: Buccal/pharynx malignancies mortality; Gastrointestinal: Prostate malignancies mortality, Oesophagus malignancies mortality, Stomach malignancies mortality, Colon, rectum malignancies mortality, Other digestive malignancies (not oesophagus, stomach, colon, or rectum) mortality; Renal/Kidney: Bladder malignancies mortality, Kidney malignancies mortality; Cardiovascular: Cardiovascular malignancies mortality
Asbestos Fiber Type(s):	Asbestos - Chrysotile (serpentine): 12001-29-5; Asbestos - Amosite (grunerite): 12172-73-5; Asbestos - Crocidolite (riebeckite): 12001-28-4
Linked HERO ID(s):	No linked references.
HERO ID:	281

Domain	Metric		Rating	Comments
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Medium	Factory measurements of fiber levels were taken using midget impingers from 1952-1969. After 1969, membrane filter sampling was conducted for the remaining samples. Job categories were used to relate quantitative measures to person-years of exposure in order to establish a cumulative exposure measure. Anecdotal information was used to group different jobs. For each category of jobs, the mean of the quantitative fiber measures was assigned to all individuals. The authors report a conversion factor of 1.4 f/ml = 1 mppcf. Their citation for this conversion factor is Hammad et al. 1979, HERO ID: 91), which explains their use of paired samples of dust and fiber concentrations. Hammad et al. 1979 cites NIOSH publication HSM72-10267 for their method of counting fibers, which is specified to have been conducted using PCM.
	Metric 5:	Exposure Levels	Low	Analyses for these outcomes are only presented as "exposed vs, unexposed."

Additional Comments: These outcomes were rated "Low" for Metric 5, and thus did not meet the criteria for usefulness in dose-response analysis.

** As described in Appendix B.2 of the *White Paper: Quantitative Approach to the Human Health Assessment for the Risk Evaluation for Asbestos Part 2: Supplemental Evaluation Including Legacy Uses and Associated Disposals of Asbestos*, to be considered as being informative for dose-response analysis, metrics 4 and 5 would need metric ratings of Medium or High. This reference did not satisfy this requirement; therefore data quality evaluation is presented for only for metrics 4 and 5.

Study Citation:	Hughes, J. M., Weill, H., Hammad, Y. Y. (1987). MORTALITY OF WORKERS EMPLOYED IN 2 ASBESTOS CEMENT MANUFACTURING PLANTS. British Journal of Industrial Medicine 44(3):161-174.
Health Outcome:	Mortality (all cause, various causes)
Target Organ(s):	Mortality: All cause mortality; Cardiovascular: Cardiovascular mortality; Cancer/Carcinogenesis: Cancer mortality; Lung/Respiratory: Respiratory mortality (influenza, pneumonia, bronchitis, emphysema, asthma)Lung cancer mortality
Asbestos Fiber Type(s):	Asbestos - Chrysotile (serpentine): 12001-29-5; Asbestos - Crocidolite (riebeckite): 12001-28-4
Linked HERO ID(s):	No linked references.
HERO ID:	3583332

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Low	This study on mortality among male workers at two asbestos cement manufacturing plants in New Orleans. Overall, there were 6931 employed for at least one month prior to 1970, according to job records, with mortality ascertained through 1982 or age 80 (whichever came first). However, analyses were restricted to the 5492 (79%) employees with >20 years since initial exposure (rationale not completely clear; see exposure). As a result, the data analyzed represented only 477 of 886 (53.8%) deaths at plant 1, and 874 of 1257 (69.5%) deaths at plant 2 (Table 4 vs. Table 5). The authors did not discuss differences in causes of death among those included vs. excluded or note that the large proportion excluded could have introduced bias. Other aspects of participant selection were good. A small number of workers employed prior to comprehensive record-keeping dates (n=167 employed before 1942 or 1937) were also excluded; limited information on early workers meant these workers might be a "survivor population". The sample included workers with variable hire dates (61% and 74% of workers at plants 1 and 2 respectively < 1950 vs. 1950-69) and employment duration (60.8% and 60.6% at plants 1 and 2 employed <= 1 year, 19.3% and 19.6 employed >5 years).
	Metric 2:	Attrition	High	Tracing and mortality ascertainment were high. The estimated rates of inclusion were ~ 95.6% enrolled based on plant 2 social security information, and mortality ascertainment > 96%.
	Metric 3:	Comparison Group	Medium	This study calculated SMRs based on Louisiana mortality rates (preferable to US rates given the higher mortality in that state). Nonetheless, as noted in the occupational epidemiology literature (e.g., Chowdhury et al 2017 PMID: 29391741; McMichael 1976 HEROID 73484), use of general population referents to calculate SMRs often induces a healthy worker effect bias given that the working population is healthier than the general population. Use of internal referents (i.e. within-cohort analyses), or a comparable occupational population, are more appropriate approaches that reduce bias.
Domain 2: Exposure Characterization				

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Study Citation:	Hughes, J. M., Weill, H., Hammad, Y. Y. (1987). MORTALITY OF WORKERS EMPLOYED IN 2 ASBESTOS CEMENT MANUFACTURING PLANTS. British Journal of Industrial Medicine 44(3):161-174.
Health Outcome:	Mortality (all cause, various causes)
Target Organ(s):	Mortality: All cause mortality; Cardiovascular: Cardiovascular mortality; Cancer/Carcinogenesis: Cancer mortality; Lung/Respiratory: Respiratory mortality (influenza, pneumonia, bronchitis, emphysema, asthma)Lung cancer mortality
Asbestos Fiber Type(s):	Asbestos - Chrysotile (serpentine): 12001-29-5; Asbestos - Crocidolite (riebeckite): 12001-28-4
Linked HERO ID(s):	No linked references.
HERO ID:	3583332

Domain	Metric		Rating	Comments
	Metric 4:	Measurement of Exposure	Medium	Workers in these factories were exposed to both asbestos fibers and free silica dust (see other manuscripts on this population e.g. Weill et al 1977, HEROID 3084634; Weill et al 1975 HEROID 2079035). Both plants used chrysotile asbestos; some plant 2 workers were also exposed to crocidolite. The measures analyzed were total dust concentrations from impinger air sampling, updated in this study using additional samples (reducing extrapolation based on anecdotal data), totaling 100 at plant 1 and 1664 at plant 2 from 1952 to 1969, at which point membrane filter sampling began. Cumulative exposure multiplied the mean of available dust measures for each job title (area and type of work) by duration, excluding outliers ("In calculating this mean very high measurements found to be statistical outliers based on a lognormal distribution were first recoded to be equal to the highest non-outlying value"). Concern: It appears that recent exposures (>1970) were omitted. The authors stated "In analysing risk … (20 or more years after initial exposure) each person contributed person-years to the cumulative exposure category attained ten years previously. In this way relatively recent exposures (10-15 years previously) were disregarded in determining exposure category for each worker." A conversion factor was provided to estimate dust mppcf measures as asbestos (f/mL) equivalents: "Based on data collected in one of these plants, the best factor for converting mppcf to f/ml will be assumed to be 1.4 f/mL = 1 mppcf." This factor was the mean of dust-to-fibers >5 µm ratio derived from impinger-filter pairs operated in 20- to 60-minute intervals in five "dust zones" (Hammad et al 1979, HEROID 91). Concern: Ratios for individual dust zones varied, ranging from 0.63 to 2.5, which led the authors to conclude in 1979 that "no one conversion factor can be used for all areas of this type of operation".
	Metric 5:	Exposure Levels	Medium	SMRs were calculated using 5 categories of employment duration that ranged from a few months to >15 years (different values for each plant), and using 5 categories of cumulative exposure (<c to >= 100 mppcf).
	Metric 6:	Temporality	Medium	Exposure was estimated retrospectively, and analyses included only employees with >20 years since first exposure. Temporality was appropriate. However, the authors did not adequately justify a 20-year latency or acknowledge that estimated latency time for some outcomes are shorter.
Domain 3: Outcome Assessment				

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Study Citation:	Hughes, J. M., Weill, H., Hammad, Y. Y. (1987). MORTALITY OF WORKERS EMPLOYED IN 2 ASBESTOS CEMENT MANUFACTURING PLANTS. British Journal of Industrial Medicine 44(3):161-174.			
Health Outcome:	Mortality (all cause, various causes)			
Target Organ(s):	Mortality: All cause mortality; Cardiovascular: Cardiovascular mortality; Cancer/Carcinogenesis: Cancer mortality; Lung/Respiratory: Respiratory mortality (influenza, pneumonia, bronchitis, emphysema, asthma)Lung cancer mortality			
Asbestos Fiber Type(s):	Asbestos - Chrysotile (serpentine): 12001-29-5; Asbestos - Crocidolite (riebeckite): 12001-28-4			
Linked HERO ID(s):	No linked references.			
HERO ID:	3583332			
Domain	Metric		Rating	Comments
	Metric 7:	Outcome Measurement or Characterization	Low	Other Non-Cancer Outcomes: Death certificates available for 94% of the 2143 total deaths were coded in categories by a nosologist; ICD codes were provided with detailed codes for malignancies and pneumoconiosis. However, other causes were categorized in ways that limited utility. All cardiovascular mortality was combined (vs. ischemic, cerebrovascular, pulmonary heart disease [e.g. see asbestos-CVD analyses in Harding et al 2012 HEROID 2564917]); respiratory mortality combined infectious and non-infectious causes (influenza, pneumonia, bronchitis, emphysema, asthma); other broad categories were “external” (ICD codes for injuries, poisoning) and unspecified “residual (n=190)” causes. Some misclassification is likely: the authors stated that “deaths for which certificates were not obtained were allocated to categories of causes of death in the same proportion as those with certificates.”
	Metric 8:	Reporting Bias	Low	The authors presented analyses stratified by exposure and employment duration categories only for all-cause mortality and selected malignancies, where they demonstrated how SMRs varied with greater exposure. Similar analyses were not reported for other outcomes. The authors used linear regression models to analyze dose-response trends in SMRs only for lung cancer (i.e., selectively). Only mesothelioma was analyzed using logistic regression and within-cohort comparisons. As noted earlier, the authors also failed to analyze deaths that occurred fewer than 20 years since first exposure, with no discussion of potential bias.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Medium	The manuscript stated “[s]tandardised mortality ratio (SMR) analyses were carried out using a computer program written in Britain (J Peto).” The authors describe using local county-based death rates as a reference due to small numbers for age specific, race specific and cause specific rates, suggesting that their SMR calculations incorporated these factors. SMRs were not adjusted for smoking.
	Metric 10:	Covariate Characterization	Medium	Age and race were obtained from job records.
	Metric 11:	Co-exposure Counfounding	Low	Co-exposure to silica, discussed elsewhere by the authors, was not taken into account in this manuscript. Possible prior or subsequent exposure to asbestos from other sources was also not discussed.
Domain 5: Analysis				

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Study Citation: Hughes, J. M., Weill, H., Hammad, Y. Y. (1987). MORTALITY OF WORKERS EMPLOYED IN 2 ASBESTOS CEMENT MANUFACTURING PLANTS. British Journal of Industrial Medicine 44(3):161-174.

Health Outcome: Mortality (all cause, various causes)

Target Organ(s): Mortality: All cause mortality; Cardiovascular: Cardiovascular mortality; Cancer/Carcinogenesis: Cancer mortality; Lung/Respiratory: Respiratory mortality (influenza, pneumonia, bronchitis, emphysema, asthma)Lung cancer mortality

Asbestos Fiber Type(s): Asbestos - Chrysotile (serpentine): 12001-29-5; Asbestos - Crocidolite (riebeckite): 12001-28-4

Linked HERO ID(s): No linked references.

HERO ID: 3583332

Domain	Metric		Rating	Comments
	Metric 12:	Study Design and Methods	Medium	The use of SMRs in occupational epidemiology is widely accepted in spite of concerns regarding the use of general population mortality rates as a referent for relatively healthier worker populations. Adjustments have been suggested to address this limitation including the calculation of relative SMRs as applied by Waggoner et al 2010 in the Agricultural Health Study (PMID: 21084556): "we define the relative SMR (rSMR) as the ratio of the cause-specific SMR to the SMR for all other causes, omitting the cause of interest (i.e., rSMRx ¼ SMRx/SMRnot x)" That study found an SMR of 0.61 and an rSMR of 1.20 for all cancers. Other studies (e.g. Hwang et al 2021 PMID: 34525505) report similarly that deriving rSMRs can provide additional insights over SMRs alone. In addition to SMRs, a linear regression model ("an iteratively weighted least squares regression line") was fit to examine the dose-response trend between exposure category and odds of lung cancer. Details such as confirmation of age and race adjustments were not given. A logistic regression model was also used to analyze employment duration category and odds of mesothelioma (details lacking).
	Metric 13:	Statistical Power	Medium	The analyses of nearly 5500 workers included 1,351 deaths from all causes.
	Metric 14:	Reproducibility of Analyses	Medium	Tables present both observed and expected deaths in detail, making SMR results readily reproducible. The authors also adequately explained their application of the dust-to-fiber conversion factor. However, details on the models used were lacking.
	Metric 15:	Statistical Analysis	Low	SMR methods were not described in detail, tables present observed and expected cell sizes, and the text mentions considering age and race specific numbers for cause of death.

Additional Comments: This paper analyzed mortality in a subset of workers from 2 asbestos cement factories. There were numerous concerns that undermine validity including: selectively analyaing deaths that occurred >20 years after 1st exposure; analyzing primarily total dust measures and applying a summary conversion factor of uncertain precision and validity; using a general population referent to calculate SMRs with no additional adjustments or efforts to take into account possible effects of healthy worker effect bias. Analyses of the 10 mesotheliomas identified were not evaluated.NOTE: This study would not be fully evaluated under the current guidelines. This is due to the low rating for metric 4, as no PCM or TEM was mentioned in the study or a cited source.

Overall Quality Determination Low

* No biomarkers were identified for this evaluation.

Study Citation:	Ilar, A., Klareskog, L., Saevarsdottir, S., Wiebert, P., Askling, J., Gustavsson, P., Alfredsson, L. (2019). Occupational exposure to asbestos and silica and risk of developing rheumatoid arthritis: findings from a Swedish population-based case-control study. 5(2):e000978.
Health Outcome:	Rheumatoid Arthritis
Target Organ(s):	Immune/Hematological: Rheumatoid Arthritis
Asbestos Fiber Type(s):	Asbestos - Not specified: 1332-21-4
Linked HERO ID(s):	No linked references.
HERO ID:	6869216

Domain	Metric		Rating	Comments
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Low	Asbestos exposure was defined as occupational, inhalable exposure to any form of asbestos or asbestos-containing material. Silica exposure was defined as occupational exposure to respirable (aerodynamic diameter less than 5 µm) crystalline silica-containing dusts (for example, granite). A detailed job exposure matrix (JEM) containing historical exposure estimates was constructed for each study participant's occupational title. Occupational titles were obtained through the Swedish Population and Housing Censuses which were conducted every fifth year and described as containing data from questionnaires and various registries. For this study, occupational titles were available from the Population and Housing Censuses carried out in 1960, 1970, 1975, 1980 and 1990. Methods of occupational exposure measurement assessment (PCM or TEM) and proportion of occupational history with historic measurements were not detailed, however the JEM contained exposure estimates for the time periods 1955-1964, 1965-1972, 1973-1977, 1978-1984, and 1985-1995, as well as intensity level and probability of exposure for asbestos and silica for each occupation. Only workers with at least 50 percent probability of being exposed according to the JEM were considered exposed, and it is unclear to what extent this might have been responsible for the exclusion of subjects with low exposure but similar chance for development of RA outcome due to the understanding that single asbestos fibers may cause significant inflammation and subsequent disease. It is unclear if all changes in job title were captured within the censuses conducted every five years and utilized for this study.This metric is rated low because the study or any cited methods source does not explicitly mention the use of PCM or TEM.
	Metric 5:	Exposure Levels	Low	Median estimated asbestos exposure (Table 2) was noted as 0.10 fiber/cm3 for men, and 0.02 fiber/cm3 for women. Details on the range and distribution of estimated exposure was lacking, and analyses utilized comparisons between workers ever versus never exposed to asbestos, however some analyses (Table 4) utilized considerations for number of exposed occupations (one – five occupations) within analyses.

Additional Comments:	This study examined occupational exposure to asbestos and silica with risk of developing rheumatoid arthritis (RA) within a Swedish population-based case-control study.Results indicated male workers exposed to asbestos had higher risks of seropositive RA and seronegative RA compared with workers classified as non-exposed, with risks highest among workers exposed to asbestos from 1970, before a national ban was introduced. The highest risk estimates were among smoking workers for seropositive RA, regardless of whether these workers had been exposed to asbestos or not.NOTE: This study would not be reviewed in full under the current guidelines because of the low rating in metric 4.

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Study Citation:	Ilar, A., Klareskog, L., Saevarsdottir, S., Wiebert, P., Askling, J., Gustavsson, P., Alfredsson, L. (2019). Occupational exposure to asbestos and silica and risk of developing rheumatoid arthritis: findings from a Swedish population-based case-control study. 5(2):e000978.
Health Outcome:	Rheumatoid Arthritis
Target Organ(s):	Immune/Hematological: Rheumatoid Arthritis
Asbestos Fiber Type(s):	Asbestos - Not specified: 1332-21-4
Linked HERO ID(s):	No linked references.
HERO ID:	6869216

Domain	Metric	Rating	Comments

* No biomarkers were identified for this evaluation.

** As described in Appendix B.2 of the *White Paper: Quantitative Approach to the Human Health Assessment for the Risk Evaluation for Asbestos Part 2: Supplemental Evaluation Including Legacy Uses and Associated Disposals of Asbestos*, to be considered as being informative for dose-response analysis, metrics 4 and 5 would need metric ratings of Medium or High. This reference did not satisfy this requirement; therefore data quality evaluation is presented for only for metrics 4 and 5.

Study Citation:	Johnson, W. M., Lemen, R. A., Hurst, G. A., Spiegel, R. M., Liu, F. H. (1982). Respiratory morbidity among workers in an amosite asbestos insulation plant. Journal of Occupational Medicine 24(12):994-999.			
Health Outcome:	Asbestosis; Pulmonary Function/Spirometry Results			
Target Organ(s):	Lung/Respiratory: Asbestosis, Pulmonary function (FEV, FVC)			
Asbestos Fiber Type(s):	Asbestos - Amosite (grunerite): 12172-73-5			
Linked HERO ID(s):	No linked references.			
HERO ID:	3083873			
Domain		Metric	Rating	Comments
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Medium	The authors used years of exposure in five-year categories as a proxy for cumulative asbestos exposure. Fiber concentrations in different locations at the plant were also measured using personal breathing zone sampling; these concentration measures were not used to estimate exposure levels of individual participants. Sampling equipment and methods were not detailed; the manuscript states that PCM was used to count fibers greater than 5 μm in length using the OSHA standard methods. Measures were obtained in 1967, 1970 and 1971. Mean concentrations were shown, and varied considerably in different areas of the plant, particularly in earlier years.
	Metric 5:	Exposure Levels	Low	The exposure measure used for analysis was duration of employment, in categories that ranged from 1-4 to >15 years of employment. Duration of employment alone may imprecisely classify cumulative exposure given the wide variation in intensity of exposures at different locations in the plant (Table 1).
Additional Comments:	This cross-sectional study described the prevalence of 5 asbestosis symptoms among 50 workers at an amosite asbestos insulation plant in East Texas. Workers included had been employed for at least one year and were currently employed at the time of the study in 1971. The plant had been under study by public health agencies and closed shortly after this study. Limiting the study to current workers, particularly since health risks were known, may have induced some degree of healthy worker effect (HWE) bias in the form of employment changes among more susceptible workers. In fact, the paper documented very high turnover among 850 workers. Based on multiple symptoms, the study identified possible asbestosis in 7 of the 18 workers who had >=10 years of employment. In the sample as a whole, symptoms including measures of lung function tended to worsen with longer duration of employment. However, there was an uptick in lung function among workers who remained employed for 15 years or more. Results were stratified by race, but there were too few black workers to meaningfully assess trends. Overall, the small sample size, potential HWE, and use of employment duration alone to classify exposure are limitations.			

* No biomarkers were identified for this evaluation.

** As described in Appendix B.2 of the *White Paper: Quantitative Approach to the Human Health Assessment for the Risk Evaluation for Asbestos Part 2: Supplemental Evaluation Including Legacy Uses and Associated Disposals of Asbestos*, to be considered as being informative for dose-response analysis, metrics 4 and 5 would need metric ratings of Medium or High. This reference did not satisfy this requirement; therefore data quality evaluation is presented for only for metrics 4 and 5.

Study Citation:	Järvholm, B., Larsson, S., Hagberg, S., Olling, S., Ryd, W., Torén, K. (1993). Quantitative importance of asbestos as a cause of lung cancer in a Swedish industrial city: A case-referent study. European Respiratory Journal 6(9):1271-1275.
Health Outcome:	Lung Cancer
Target Organ(s):	Cancer/Carcinogenesis: Lung cancer; Lung/Respiratory: Lung cancer
Asbestos Fiber Type(s):	Asbestos - Not specified: 1332-21-4
Linked HERO ID(s):	No linked references.
HERO ID:	3081928

Domain	Metric		Rating	Comments
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Low	Exposure was based on a questionnaire with the patients and referents focused on asbestos exposure and different occupational exposures; that information was used by trained occupational hygienists to categorize cumulative asbestos exposure.This metric is rated low because the study or any cited methods sources do not explicitly mention the use of PCM or TEM.
	Metric 5:	Exposure Levels	Low	Low. The study reports the estimated cumulative doses of asbestos (>25 fibre-year/mL, 1-24 fibre-years/mL, 0.05 - 0.9 fibre-years/mL, and <0.05 fibre-years/mL) along with the number of cases and referents in each category of exposure. However, this does not adequately represent a continuous range and distribution.

Additional Comments: Based upon the current guidance, this study would not be evaluated fully because of the metric 4 rating. This study, and any cited methods sources, did not mention the use of PCM or TEM.

* No biomarkers were identified for this evaluation.

** As described in Appendix B.2 of the *White Paper: Quantitative Approach to the Human Health Assessment for the Risk Evaluation for Asbestos Part 2: Supplemental Evaluation Including Legacy Uses and Associated Disposals of Asbestos*, to be considered as being informative for dose-response analysis, metrics 4 and 5 would need metric ratings of Medium or High. This reference did not satisfy this requirement; therefore data quality evaluation is presented for only for metrics 4 and 5.

Study Citation:	Karjalainen, A., Anttila, S., Vanhala, E., Vainio, H. (1994). Asbestos exposure and the risk of lung cancer in a general urban population. Scandinavian Journal of Work, Environment and Health 20(4):243-250.			
Health Outcome:	Lung Cancer			
Target Organ(s):	Cancer/Carcinogenesis: lung cancer; Lung/Respiratory: lung cancer			
Asbestos Fiber Type(s):	Asbestos - Anthophyllite: 17068-78-9; Asbestos - Crocidolite (riebeckite): 12001-28-4			
Linked HERO ID(s):	No linked references.			
HERO ID:	3081833			
Domain	Metric		Rating	Comments
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Low	Asbestos exposure (10^6 f/g) was defined by scanning electron microscopic analysis of pulmonary tissue of cases and referents.
	Metric 5:	Exposure Levels	Medium	The range and distribution of exposure (Table 2) is sufficient to develop exposure-response estimates. Multivariate logistic regression models incorporated three categories (<1.0 x 10^6 f/g, 1.0-4.99 x 10^6 f/g, and >=5.0 x 10^6 f/g).
Additional Comments:	Karjalainen et al., 1994 (HERO ID 3081833) was not QC evaluated for any metrics except Metric 4 and 5 as it did not have sufficient exposure information to be useful for dose-response analysis.Overall, information on the measurement of exposure metric (M4) to assess exposure was limited or rated low (asbestos exposure was defined by SEM analysis of lung tissue of cases and referents). The exposure levels metric (M5) information reported was adequate to determine exposure-response relationships.			

** As described in Appendix B.2 of the *White Paper: Quantitative Approach to the Human Health Assessment for the Risk Evaluation for Asbestos Part 2: Supplemental Evaluation Including Legacy Uses and Associated Disposals of Asbestos*, to be considered as being informative for dose-response analysis, metrics 4 and 5 would need metric ratings of Medium or High. This reference did not satisfy this requirement; therefore data quality evaluation is presented for only for metrics 4 and 5.

Study Citation:	Karjalainen, A., Karhunen, P. J., Lalu, K., Penttilä, A., Vanhala, E., Kyyrönen, P., Tossavainen, A. (1994). Pleural plaques and exposure to mineral fibres in a male urban necropsy population. Occupational and Environmental Medicine 51(7):456-460.
Health Outcome:	Pleural Plaques
Target Organ(s):	Lung/Respiratory: Pleural plaques
Asbestos Fiber Type(s):	Asbestos - Anthophyllite: 17068-78-9; Asbestos - Crocidolite (riebeckite): 12001-28-4; Asbestos - Amosite (grunerite): 12172-73-5
Linked HERO ID(s):	No linked references.
HERO ID:	3081814

Domain	Metric		Rating	Comments
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Low	Occupational exposure was classified according to four groups: Probable exposure, possible exposure, unlikely exposure, and unknown exposure. Individuals were grouped according to the last occupation indicated on the necropsy records. The Nordic Classification of Occupations was used to code the probability of exposure. One important note pertains to the unknown exposure group, because this was for individuals who did not have information on occupation and may have been listed as ”retired.” The researchers also collected lung tissue samples so that they could conduct a fiber analysis with an electron microscope. The procedure had an analytical sensitivity of ~0.07 million fibers per gram (f/g). The authors did not specify the use of PCM or TEM and mentioned detecting chrysotile fibes with scanning electron microscopy.
	Metric 5:	Exposure Levels	Medium	This metric is rated as medium because in Table 2, the authors present three levels of exposure based on the concentration of asbestos fibers found in lung tissue samples. These levels are reported in million f/g, and include: <0.1, 0.1-0.99, and >1.0.

Additional Comments: None

** As described in Appendix B.2 of the *White Paper: Quantitative Approach to the Human Health Assessment for the Risk Evaluation for Asbestos Part 2: Supplemental Evaluation Including Legacy Uses and Associated Disposals of Asbestos*, to be considered as being informative for dose-response analysis, metrics 4 and 5 would need metric ratings of Medium or High. This reference did not satisfy this requirement; therefore data quality evaluation is presented for only for metrics 4 and 5.

Study Citation:	Kishimoto, T., Gemba, K., Fujimoto, N., Onishi, K., Usami, I., Mizuhashi, K., Kimura, K. (2010). Clinical study of asbestos-related lung cancer in Japan with special reference to occupational history. Cancer Science 101(5):1194-1198.
Health Outcome:	Lung Cancer
Target Organ(s):	Cancer/Carcinogenesis: Lung cancer; Lung/Respiratory: Lung cancer
Asbestos Fiber Type(s):	Asbestos - Not specified: 1332-21-4
Linked HERO ID(s):	No linked references.
HERO ID:	3079077

Domain	Metric		Rating	Comments
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Medium	The number of asbestos particles in the lung were assessed using PCM.
	Metric 5:	Exposure Levels	Low	The study only reports the number of asbestos particle using categories of exposure (i.e., 1,000 - 4,999; 5,000 - 9,999) using a bar graph. The distribution information is limited.

Additional Comments:	Note added 1/5/23 by Nathan Lothrop (ICF) - this study was reviewed and initially was part of a cohort, but upon further review determined it was not. In process, it was noticed authors did a basic descriptive analysis of asbestosis.

** As described in Appendix B.2 of the *White Paper: Quantitative Approach to the Human Health Assessment for the Risk Evaluation for Asbestos Part 2: Supplemental Evaluation Including Legacy Uses and Associated Disposals of Asbestos*, to be considered as being informative for dose-response analysis, metrics 4 and 5 would need metric ratings of Medium or High. This reference did not satisfy this requirement; therefore data quality evaluation is presented for only for metrics 4 and 5.

Study Citation:	Kishimoto, T., Ono, T., Okada, K., Ito, H. (1989). Relationship between number of asbestos bodies in autopsy lung and pleural plaques on chest X-ray film. Chest 95(3):549-552.
Health Outcome:	Pleural Plaques
Target Organ(s):	Lung/Respiratory: Pleural plaques
Asbestos Fiber Type(s):	Asbestos - Not specified: 1332-21-4
Linked HERO ID(s):	No linked references.
HERO ID:	3082790

Domain	Metric		Rating	Comments
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Low	Five gram samples of lung tissue were collected and lysed from the autopsied individuals. Light microscopy was used to determine the number of asbestos bodies present in the prepared samples. An occupational history was collected for the 71 cases with >500 asbestos bodies in their samples, but there were no quantitative measurements provided for those locations.
	Metric 5:	Exposure Levels	Medium	This metric was rated as ”medium” because they displayed three different ranges of exposure based on the type of plaque found by the x-ray readers. For plaques of type IIIB, there were 960 +/- 104 asbestos bodies, for type IV there were 32,560 +/- 31,346, and for type V there were 42,841 +/- 10,981. This information is also presented in Figure 3.

Additional Comments:	This study focused on the relationship between the asbestos bodies in lung samples and pleural plaques. They did not provide any discussions of confounders that may be present in this study, and there was mention that this study cannot examine the relationship between time since first exposure and pleural plaques/asbestos bodies because of a lack of asbestos exposure history for some participants. They did provide information on the range of asbestos bodies found in the various groupings of pleural plaque determinations, but they had a wide variance within the groups. There are some qualitative statements made in this study, such as ”the cases with clear pleural plaques on chest x-ray film had many more asbestos bodies than unclear cases” (Kishimoto et al., 1989).

** As described in Appendix B.2 of the *White Paper: Quantitative Approach to the Human Health Assessment for the Risk Evaluation for Asbestos Part 2: Supplemental Evaluation Including Legacy Uses and Associated Disposals of Asbestos*, to be considered as being informative for dose-response analysis, metrics 4 and 5 would need metric ratings of Medium or High. This reference did not satisfy this requirement; therefore data quality evaluation is presented for only for metrics 4 and 5.

Study Citation:	Knox, J. F., Holmes, S., Doll, R., Hill, I. D. (1968). Mortality from lung cancer and other causes among workers in an asbestos textile factory. Occupational and Environmental Medicine 25(4):293-303.
Health Outcome:	Lung Cancer; other neoplasms; Pulmonary Function/Spirometry Results; disease of the circulatory system mortality, diseases of the respiratory system mortality
Target Organ(s):	Mortality: cancer of the lung or pleura mortality, other neoplasms mortality, diseases of the circulatory system mortality, diseases of the respiratory system mortality, all other causes mortality, all cause mortality; Lung/Respiratory: cancer of the lung or pleura mortality, diseases of the respiratory system mortality, Forced expiratory volume (FEV), Forced vital capacity (FVC), Total lung capacity (TLC); Cancer/Carcinogenesis: cancer of the lung or pleura mortality, other neoplasms mortality; Cardiovascular: diseases of the circulatory system mortality
Asbestos Fiber Type(s):	Asbestos - Crocidolite (riebeckite): 12001-28-4; Asbestos - Chrysotile (serpentine): 12001-29-5
Linked HERO ID(s):	115, 46
HERO ID:	115

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	High	Key elements of study design are reported for Knox et al., 1968 (HERO ID 000115) and Berry et al., 1979 (HERO ID 00046). Knox et al., 1968 included men and women employed in scheduled areas (defined as parts of the factory to which 1931 regulations which controlled asbestos dust exposure for the asbestos industry were applied by 1933) for more than 20 years at any time since the asbestos textile factory opened in England. Men and women who were employed for more than 10 years were also included if they were first employed on or after January 1, 1933. A total of n=878 workers were available for this study with follow-up over 50 years from 1916 through the end of June 1966. Table 1 detailed the numbers of men (Groups 1-4) and women (Group 5 only) within categories of period of exposure (Groups 1-3: 20 males with or more years of exposure; Group 4: men with 10-19 years exposure; Group 5: women with 10 or more years of exposure) in scheduled areas and duration of exposure before 1933. Berry et al., 1979 included n=379 men who had worked at the same asbestos textile factory in England for at least 10 years and extended follow-up for 6.5 years beyond that of Knox et al., 1968. Exclusions within Berry et al., 1979 were made for n=12 men who had also worked at a subsidiary asbestos factory for several years where the asbestos dust concentrations were unknown, as well as n=1 worker for whom a job history could not be constructed, leaving the n=379 men for the final analysis.

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Study Citation:	Knox, J. F., Holmes, S., Doll, R., Hill, I. D. (1968). Mortality from lung cancer and other causes among workers in an asbestos textile factory. Occupational and Environmental Medicine 25(4):293-303.
Health Outcome:	Lung Cancer; other neoplasms; Pulmonary Function/Spirometry Results; disease of the circulatory system mortality, diseases of the respiratory system mortality
Target Organ(s):	Mortality: cancer of the lung or pleura mortality, other neoplasms mortality, diseases of the circulatory system mortality, diseases of the respiratory system mortality, all other causes mortality, all cause mortality; Lung/Respiratory: cancer of the lung or pleura mortality, diseases of the respiratory system mortality, Forced expiratory volume (FEV), Forced vital capacity (FVC), Total lung capacity (TLC); Cancer/Carcinogenesis: cancer of the lung or pleura mortality, other neoplasms mortality; Cardiovascular: diseases of the circulatory system mortality
Asbestos Fiber Type(s):	Asbestos - Crocidolite (riebeckite): 12001-28-4; Asbestos - Chrysotile (serpentine): 12001-29-5
Linked HERO ID(s):	115, 46
HERO ID:	115

Domain	Metric		Rating	Comments
	Metric 2:	Attrition	Medium	Outcome and exposure data were relatively complete for Knox et al., 1968 and Berry et al., 1979. For Knox et al., Other than one man and one woman who could not be traced, all other subjects were described as successfully traced. Death certificates were obtained for all deaths but one, described as occurring abroad. Authors noted that three instances of lung cancer were discovered post mortem that were not mentioned on death certificates and these deaths were not attributed to lung cancer. Asbestos dust quantitative sampling data was not available prior to 1951, and quantitative measures of asbestos fiber counts were not available until 1961 (Table I). Missing covariate information was not detailed, although authors noted follow-up was facilitated by the restriction of the main study to workers with more than 20 years exposure who would have been provided pensions and thus were still in company personnel files. Berry et al., 1979 extended the Knox et al., 1968 study to include n=89 men who had completed 10 years of service between 30 June 1966 and 31 December 1972, as well as men who had left the factory after 30 June 1966. Authors in Berry et al., 1979 noted 93% of the men in the study had been medically examined or had a chest radiograph since 1969 or within three years of death as the men working in scheduled occupations have periodic medical examinations by a Pneumoconiosis Medical Panel under the Prescribed Diseases Regulations of the National Insurance (Industrial Injuries) Act of 1946 and workers were given chest radiographs every three years from 1951 until 1967 and every year since then. Berry et al., 1979 noted information on asbestosis certification was complete up to 1975 for all men, including those who had left the factory. For Berry et al., 1979, because pulmonary function tests were not introduced until 1967 and were carried out every two years, these data were available for only n=311 or 82% of the men in this study.

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Study Citation:	Knox, J. F., Holmes, S., Doll, R., Hill, I. D. (1968). Mortality from lung cancer and other causes among workers in an asbestos textile factory. Occupational and Environmental Medicine 25(4):293-303.
Health Outcome:	Lung Cancer; other neoplasms; Pulmonary Function/Spirometry Results; disease of the circulatory system mortality, diseases of the respiratory system mortality
Target Organ(s):	Mortality: cancer of the lung or pleura mortality, other neoplasms mortality, diseases of the circulatory system mortality, diseases of the respiratory system mortality, all other causes mortality, all cause mortality; Lung/Respiratory: cancer of the lung or pleura mortality, diseases of the respiratory system mortality, Forced expiratory volume (FEV), Forced vital capacity (FVC), Total lung capacity (TLC); Cancer/Carcinogenesis: cancer of the lung or pleura mortality, other neoplasms mortality; Cardiovascular: diseases of the circulatory system mortality
Asbestos Fiber Type(s):	Asbestos - Crocidolite (riebeckite): 12001-28-4; Asbestos - Chrysotile (serpentine): 12001-29-5
Linked HERO ID(s):	115, 46
HERO ID:	115

Domain	Metric		Rating	Comments
	Metric 3:	Comparison Group	Medium	Inclusion criteria and methods of subject selection were reported for Knox et al., 1968 (HERO ID 000115) and Berry et al., 1979 (HERO ID 00046). For Knox et al., 1968, results were reported as observed and expected deaths for each outcome category, facilitating the calculation of Standardized Mortality Ratios (SMRs). Results in Table III were reported stratified by designated Groups (1-5), which would have controlled for sex as all Groups 1-4 were men only and Group 5 was only women, but were not stratified by age. Additional analyses within subsequent tables IV, V and VI were standardized for, or stratified by, age, but only Table IV was standardized by age and stratified by Groups restricting to males and thus controlled for gender and age. Choice of reference population was reported as the general population for expected deaths within Table III, and as the internal worker population for expected deaths within Tables IV, V and VI. There is potential and evidence for the Healthy Worker Effect (HWE) within results where the ratio of observed total deaths versus expected deaths was <=1.0, including results in Table III within some designated exposure period Group strata for cancer of the lung or pleura, other neoplasms, disease of the respiratory system, all other causes, and all causes. Substantial potential for the HWE is noted for the Table III results for cancer outcomes where ratios of reported observed versus expected deaths would be <=1.0 as the general population was used as the referent for expected deaths in Table III and smoking was not controlled for. Additional potential for HWE may be noted for Table IV with an internal worker population was used as the referent for non-cancer outcomes with lower observed versus expected deaths within some exposure group strata. Berry et al., 1979 inclusion criteria and participation were reported. Differences in baseline characteristics within the population were considered as potential confounding variables in regression models–pulmonary function indices and cumulative asbestos exposure regression models in Table 5 included age and height, but not smoking, and were restricted to males first employed after 1950. The relationship between percentage developing crepitations, possible asbestosis and certified asbestosis for men first employed after 1950 presented in Figure 4 of Berry et al., 1979 were described as obtained by life table methods.
Domain 2: Exposure Characterization				

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Study Citation:	Knox, J. F., Holmes, S., Doll, R., Hill, I. D. (1968). Mortality from lung cancer and other causes among workers in an asbestos textile factory. Occupational and Environmental Medicine 25(4):293-303.
Health Outcome:	Lung Cancer; other neoplasms; Pulmonary Function/Spirometry Results; disease of the circulatory system mortality, diseases of the respiratory system mortality
Target Organ(s):	Mortality: cancer of the lung or pleura mortality, other neoplasms mortality, diseases of the circulatory system mortality, diseases of the respiratory system mortality, all other causes mortality, all cause mortality; Lung/Respiratory: cancer of the lung or pleura mortality, diseases of the respiratory system mortality, Forced expiratory volume (FEV), Forced vital capacity (FVC), Total lung capacity (TLC); Cancer/Carcinogenesis: cancer of the lung or pleura mortality, other neoplasms mortality; Cardiovascular: diseases of the circulatory system mortality
Asbestos Fiber Type(s):	Asbestos - Crocidolite (riebeckite): 12001-28-4; Asbestos - Chrysotile (serpentine): 12001-29-5
Linked HERO ID(s):	115, 46
HERO ID:	115

Domain	Metric		Rating	Comments
	Metric 4:	Measurement of Exposure	Medium	For Knox et al., 1968 quantitative measures of asbestos fiber levels were available only after 1961, and dust sampling results were only available after 1951, however workers were followed up for outcomes beginning in 1916. Table I reports average exposure sampling results from routine dust (particles per c.c.; 1952, 1960) sampling using the Casella Thermal Precipitator with analysis at a magnification of x 1,000, and fiber (fibers per c.c.; 1961, 1966) sampling using the Long Running Thermal Precipitator (magnification of x 500 with fibers 5-100 microns long and whose length was between 5 and 100 microns) or Cellulose Membrane sampler. Although Phase Contrast Microscopy (PCM) was not specified, the magnifications detailed indicate compatibility with this standard. Authors noted substantial changes in asbestos dust levels following introduction of asbestos industry control standards in 1931. Cumulative exposure to asbestos in Berry et al., 1979 for analyses restricted to men employed after 1950 was described as estimated from quantitative asbestos fiber sampling conducted beginning in 1961, with the counts for 1951-1955 taken as those of 1961 multiplied by the ratio of 1952 to 1960 thermal precipitator measurements, and the counts for 1956-1960 assumed as the same as 1961-1965 as there were no dust measurements prior to 1950.
	Metric 5:	Exposure Levels	Medium	The range and distribution of exposure (Table I in both Knox et al., 1968 and Berry et al., 1979) is sufficient to develop exposure-response estimates. Mortality was analyzed as observed and expected deaths, but was stratified for periods of exposure in Knox et al., 1968.
	Metric 6:	Temporality	High	The study establishes temporality by inclusion of workers with more than 20 (and more than 10 years in Berry et al., 1979 and some analyses in Knox et al., 1968) years of exposure and presentation of results (Table VI in Knox et al., 1968) stratified across categories of years after completing twenty years of employment.
Domain 3: Outcome Assessment				

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Health Outcome:	Lung Cancer; other neoplasms; Pulmonary Function/Spirometry Results; disease of the circulatory system mortality, diseases of the respiratory system mortality
Target Organ(s):	Mortality: cancer of the lung or pleura mortality, other neoplasms mortality, diseases of the circulatory system mortality, diseases of the respiratory system mortality, all other causes mortality, all cause mortality; Lung/Respiratory: cancer of the lung or pleura mortality, diseases of the respiratory system mortality, Forced expiratory volume (FEV), Forced vital capacity (FVC), Total lung capacity (TLC); Cancer/Carcinogenesis: cancer of the lung or pleura mortality, other neoplasms mortality; Cardiovascular: diseases of the circulatory system mortality
Asbestos Fiber Type(s):	Asbestos - Crocidolite (riebeckite): 12001-28-4; Asbestos - Chrysotile (serpentine): 12001-29-5
Linked HERO ID(s):	115, 46
HERO ID:	115

Domain	Metric		Rating	Comments
	Metric 7:	Outcome Measurement or Characterization	Medium	Lung Cancer: For Knox et al., 1968, mortality outcomes for workers followed up from 1916 through 1966 included cancer of the lung or pleura (ICD codes 162, 163), other neoplasms (ICD codes 140-239, except 162 and 163), diseases of the circulatory system (ICD codes 400-468), diseases of the respiratory system (ICD codes 470-527), all other causes, and all causes (Table III), with Tables IV, V, and VI focusing on lung cancer deaths (ICD codes 162, 163). ICD codes were provided in Table III. Deaths were described as assessed for all deaths but one (occurring abroad) through cause provided on death certificate using the method of classification in use by the Registrar-General at the relevant period, with ICD codes provided, and according to the best information obtainable from all sources, although validation through histologic or cytologic means was not described. For Berry et al., 1979, pulmonary function test results for FEV1, FVC, TLC and TL, as well as diagnoses of crepitations, and possible asbestosis were obtained from records in the factory's medical department (ICD codes were not detailed in text). Pneumoconiosis Medical Panel records were obtained for data regarding asbestosis certification.; Other Cancer(s): For Knox et al., 1968, mortality outcomes for workers followed up from 1916 through 1966 included cancer of the lung or pleura (ICD codes 162, 163), other neoplasms (ICD codes 140-239, except 162 and 163), diseases of the circulatory system (ICD codes 400-468), diseases of the respiratory system (ICD codes 470-527), all other causes, and all causes (Table III), with Tables IV, V, and VI focusing on lung cancer deaths (ICD codes 162, 163). ICD codes were provided in Table III. Deaths were described as assessed for all deaths but one (occurring abroad) through cause provided on death certificate using the method of classification in use by the Registrar-General at the relevant period, with ICD codes provided, and according to the best information obtainable from all sources, although validation through histologic or cytologic means was not described. For Berry et al., 1979, pulmonary function test results for FEV1, FVC, TLC and TL, as well as diagnoses of crepitations, and possible asbestosis were obtained from records in the factory's medical department (ICD codes were not detailed in text). Pneumoconiosis Medical Panel records were obtained for data regarding asbestosis certification.; Pulmonary Function/Spirometry Results: For Knox et al., 1968, mortality outcomes for workers followed up from 1916 through 1966 included cancer of the lung or pleura (ICD codes 162, 163), other neoplasms (ICD codes 140-239, except 162 and 163), diseases of the circulatory system (ICD codes 400-468), diseases of the respiratory system (ICD codes 470-527), all other causes, and all causes (Table III), with Tables IV, V, and VI focusing on lung cancer deaths (ICD codes 162, 163). ICD codes were provided in Table III. Deaths were described as assessed for all deaths but one (occurring abroad) through cause provided on death certificate using the method of classification in use by the Registrar-General at the relevant period, with ICD codes provided, and according to the best information obtainable from all sources, although validation through histologic or cytologic means was not described. For Berry et al., 1979, pulmonary function test results for FEV1, FVC, TLC and TL, as well as diagnoses of crepitations, and possible asbestosis were obtained from records in the

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Study Citation:	Knox, J. F., Holmes, S., Doll, R., Hill, I. D. (1968). Mortality from lung cancer and other causes among workers in an asbestos textile factory. Occupational and Environmental Medicine 25(4):293-303.
Health Outcome:	Lung Cancer; other neoplasms; Pulmonary Function/Spirometry Results; disease of the circulatory system mortality, diseases of the respiratory system mortality
Target Organ(s):	Mortality: cancer of the lung or pleura mortality, other neoplasms mortality, diseases of the circulatory system mortality, diseases of the respiratory system mortality, all other causes mortality, all cause mortality; Lung/Respiratory: cancer of the lung or pleura mortality, diseases of the respiratory system mortality, Forced expiratory volume (FEV), Forced vital capacity (FVC), Total lung capacity (TLC); Cancer/Carcinogenesis: cancer of the lung or pleura mortality, other neoplasms mortality; Cardiovascular: diseases of the circulatory system mortality
Asbestos Fiber Type(s):	Asbestos - Crocidolite (riebeckite): 12001-28-4; Asbestos - Chrysotile (serpentine): 12001-29-5
Linked HERO ID(s):	115, 46
HERO ID:	115

Domain	Metric		Rating	Comments
	Metric 8:	Reporting Bias	Medium	There were no concerns in Knox et al., 1968 or Berry et al., 1979 for selective reporting as all outcomes which were outlined within methods were also reported within the results. Observed and expected deaths were reported in tables as single values, rather than ratios or SMRs for Knox et al., 1968, and regression results were reported as coefficients (standard errors) for pulmonary function in Berry et al., 1979.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Medium	Final results for Knox et al., 1968 were reported in tables of observed and expected deaths with no adjustments for sex, however results in Table III were stratified by designated exposure Group, which was males only for Groups 1-4 and females only for Group 5. Additional tables IV, V and VI reported results standardized for age, period of exposure Group, and time since completing 20 years exposure. Smoking status, especially for the lung cancer analyses with the general population as referent in Table III, was not considered. Berry et al., 1979 pulmonary function indices and cumulative asbestos exposure regression models in Table 5 included age and height, and were restricted to males first employed after 1950. The relationship between percentage developing crepitations, possible asbestosis and certified asbestosis for men first employed after 1950 presented in Figure 4 of Berry et al., 1979 were described as only as obtained by life table methods.
	Metric 10:	Covariate Characterization	Medium	Covariates were described as assessed using data from personnel files, with no method of validation for both Knox et al., 1968 and Berry et al., 1979.
	Metric 11:	Co-exposure Counfounding	Medium	The members of the Knox et al., 1968 and Berry et al., 1979 cohorts for the main analyses were workers with at least 20 years (10 years for Berry et al., 1979) of exposure at an asbestos textile plant with no evidence of an unbalanced provision of co-exposures among exposure groups.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	Medium	The study design in Knox et al., 1968 was appropriate as a preliminary step to address research questions on outcomes of interest. Results were reported as observed and expected deaths across gender and exposure period strata. Berry et al., 1979 included n=379 men who had worked at the same asbestos textile factory in England for at least 10 years, with follow-up extended and analyses conducted utilizing multivariate regression and life table methods.

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Study Citation: Knox, J. F., Holmes, S., Doll, R., Hill, I. D. (1968). Mortality from lung cancer and other causes among workers in an asbestos textile factory. Occupational and Environmental Medicine 25(4):293-303.

Health Outcome: Lung Cancer; other neoplasms; Pulmonary Function/Spirometry Results; disease of the circulatory system mortality, diseases of the respiratory system mortality

Target Organ(s): Mortality: cancer of the lung or pleura mortality, other neoplasms mortality, diseases of the circulatory system mortality, diseases of the respiratory system mortality, all other causes mortality, all cause mortality; Lung/Respiratory: cancer of the lung or pleura mortality, diseases of the respiratory system mortality, Forced expiratory volume (FEV), Forced vital capacity (FVC), Total lung capacity (TLC); Cancer/Carcinogenesis: cancer of the lung or pleura mortality, other neoplasms mortality; Cardiovascular: diseases of the circulatory system mortality

Asbestos Fiber Type(s): Asbestos - Crocidolite (riebeckite): 12001-28-4; Asbestos - Chrysotile (serpentine): 12001-29-5

Linked HERO ID(s): 115, 46

HERO ID: 115

Domain	Metric		Rating	Comments
	Metric 13:	Statistical Power	Medium	A total of n=878 workers were available for the Knox et al., 1968 study of observed mortality with follow-up over 50 years from 1916 through the end of June 1966. A total of n=379 men were utilized for the final analyses within Berry et al., 1979.
	Metric 14:	Reproducibility of Analyses	Medium	The methods utilized to estimate summarized exposures, as well as statistical analyses, were described in a way that would facilitate general reproducibility in Knox et al., 1968 and Berry et al., 1979.
	Metric 15:	Statistical Analysis	Medium	N/A. for Knox et al., 1968. Medium for Berry et al., 1979 where methods utilized to estimate regression coefficients were generally adequately described, although procedures for outliers and missing data were not detailed. Multiple sensitivity models were produced within Berry et al., 1979.

Additional Comments: These retrospective cohort studies investigated mortality from lung cancer and other causes (Knox et al., 1968) as well as pulmonary function and asbestosis (Berry et al., 1979) in workers with at least 10 years of work in an asbestos textile factory in England. Results in Knox et al., 1968 indicated highly significant increased mortality when compared with the general population for lung cancer, respiratory diseases and circulatory diseases associated with asbestosis for men exposed for 10 or more years before 1933, but decreased mortality for those working greater than twenty years since 1933 for diseases of the circulatory and respiratory system, and no change in mortality with the internal worker population as comparison for any cause of death for workers with 20 years of work. Results in Berry et al., 1979 indicated forced expiratory volume (FEV) and forced vital capacity (FVC), but not total lung capacity (TLC), declined significantly with cumulative asbestos exposure for men first employed after 1950, and the relationship between exposure and 1% prevalence of crepitations, possible asbestosis and certified asbestosis were detailed.

Overall Quality Determination — Medium

* No biomarkers were identified for this evaluation.

Study Citation:	Konen, T., Johnson, J. E., Lindgren, P., Williams, A. (2019). Cancer incidence and mortality associated with non-occupational and low dose exposure to Libby vermiculite in Minnesota. Environmental Research 175(Elsevier):449-456.
Health Outcome:	Lung Cancer; All cancers; Asbestosis; COPD, NMRD, All causes of death
Target Organ(s):	Lung/Respiratory: Asbestosis mortality, COPD mortality, Non-malignant respiratory disease (NMRD) mortality, All Respiratory Cancer mortality, Lung Cancer mortality; Mortality: Mortality from asbestosis, Mortality from COPD, Mortality from NMRD, All respiratory cancer mortality, Lung Cancer mortality, All causes mortality, All Cancer Mortality; Cancer/Carcinogenesis: All respiratory cancer mortality, Lung Cancer mortality, All Cancer Mortality; All causes: All causes mortality
Asbestos Fiber Type(s):	Asbestos- Libby amphibole: 1318-09-8
Linked HERO ID(s):	No linked references.
HERO ID:	6866465

Domain	Metric		Rating	Comments
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Low	Asbestos exposure was estimated, and no quantitative measurements were taken. The authors reported that the exposure estimates were calculated ”based on total months of residency (duration) and addresses in the study area and using results of modeled ambient asbestos concentration levels during three different time periods during plant operations (1938-1989).”
	Metric 5:	Exposure Levels	Medium	The range of exposure was adequate to create an exposure-response estimate. The study’s analyses included 3 exposed groups (<50th percentile, 50th - 75th percentile, and >75th percentile).

Additional Comments:	METRIC 4 IS RATED AS LOW. EVALUATION FOR THIS STUDY WAS ALREADY IN PROGRESS, BUT AFTER LEARNING OF NEW GUIDANCE (ABOUT METRICS 4/5) ON 1.27.23, STOPPED EVALUATIONInformation on the measurement of exposure metric (M4) to assess exposure is limited (low rating) as no quantitative measurements were taken. However, the exposure levels metric (M5) information reported is sufficient to determine exposure-response relationships.

* No biomarkers were identified for this evaluation.

** As described in Appendix B.2 of the *White Paper: Quantitative Approach to the Human Health Assessment for the Risk Evaluation for Asbestos Part 2: Supplemental Evaluation Including Legacy Uses and Associated Disposals of Asbestos*, to be considered as being informative for dose-response analysis, metrics 4 and 5 would need metric ratings of Medium or High. This reference did not satisfy this requirement; therefore data quality evaluation is presented for only for metrics 4 and 5.

Study Citation:	Kumagai, S., Kurumatani, N., Tsuda, T., Yorifuji, T., Suzuki, E. (2010). Increased risk of lung cancer mortality among residents near an asbestos product manufacturing plant. International Journal of Occupational and Environmental Health 16(3):268-278.
Health Outcome:	Lung Cancer; All body systems; All body system
Target Organ(s):	Mortality: All causes, Infections (ICD10 - A,B), Neoplasm mortality (ICD 10 - C, D00-D48), Malignant neoplasm mortality (ICD 10 - C00-C97), Lip, oral cavity, and pharynx neoplasm mortality (ICD 10 - C00-C14), Oesophagus neoplasm mortality (ICD10 - C15), Stomach neoplasm mortality (ICD10 - C16), Colon and rectum neoplasm mortality (ICD10 C18-C20), Liver neoplasm mortality (ICD10 - C22), Gallbladder and biliary tract neoplasm mortality (ICD10-C23-C24), Pancreas neoplasm mortality (ICD10 - C25), Lung and trachea excluding cases with occupational asbestos exposure, neoplasm mortality (ICD10 - C33-C34), Lung and trachea excluding cases with occupational asbestos and silica exposure, neoplasm mortality (ICD10 - C33-C34), Skin neoplasm mortality (ICD10 - C43-44), Breast neoplasm mortality (ICD10 - C50), Uterus neoplasm mortality (ICD10 - C53-C55), Prostate neoplasm mortality (ICD10 - C61), Bladder neoplasm mortality (ICD10 - C67), Central nervous system neoplasm mortality (ICD10 - C70-C72, C75.1-C75.3), Leukemia mortality (ICD10 - C91-C95), Other malignant neoplasm mortality, Endocrine mortality (ICD10 - E), Nervous system mortality (ICD10 - G), Circulatory system mortality (ICD10 - I), Respiratory system mortality (ICD10 - J), Digestive system mortality (ICD10 - K), Musculoskeletal system mortality (ICD10 - M), Genitourinary system mortality (ICD10 - N); Cancer/Carcinogenesis: Neoplasm mortality (ICD 10 - C, D00-D48), Malignant neoplasm mortality (ICD 10 - C00-C97), Lip, oral cavity, and pharynx neoplasm mortality (ICD 10 - C00-C14), Oesophagus neoplasm mortality (ICD10 - C15), Stomach neoplasm mortality (ICD10 - C16), Colon and rectum neoplasm mortality (ICD10 C18-C20), Liver neoplasm mortality (ICD10 - C22), Gallbladder and biliary tract neoplasm mortality (ICD10-C23-C24), Pancreas neoplasm mortality (ICD10 - C25), Lung and trachea excluding cases with occupational asbestos exposure, neoplasm mortality (ICD10 - C33-C34), Lung and trachea excluding cases with occupational asbestos and silica exposure, neoplasm mortality (ICD10 - C33-C34), Skin neoplasm mortality (ICD10 - C43-44), Breast neoplasm mortality (ICD10 - C50), Uterus neoplasm mortality (ICD10 - C53-C55), Prostate neoplasm mortality (ICD10 - C61), Bladder neoplasm mortality (ICD10 - C67), Central nervous system neoplasm mortality (ICD10 - C70-C72, C75.1-C75.3), Leukemia mortality (ICD10 - C91-C95), Other malignant neoplasm mortality; Dermal: Lip, oral cavity, and pharynx neoplasm mortality (ICD 10 - C00-C14); Gastrointestinal: Oesophagus neoplasm mortality (ICD10 - C15), Stomach neoplasm mortality (ICD10 - C16), Colon and rectum neoplasm mortality (ICD10 C18-C20), Gallbladder and biliary tract neoplasm mortality (ICD10-C23-C24), Pancreas neoplasm mortality (ICD10 - C25), Digestive system mortality (ICD10 - K); Hepatic/Liver: Liver neoplasm mortality (ICD10 - C22); Lung/Respiratory: Lung and trachea excluding cases with occupational asbestos exposure, neoplasm mortality (ICD10 - C33-C34), Lung and trachea excluding cases with occupational asbestos and silica exposure, neoplasm mortality (ICD10 - C33-C34), Respiratory system mortality (ICD10 - J); Skin/Connective Tissue: Skin neoplasm mortality (ICD10 - C43-44); Reproductive/Developmental: Breast neoplasm mortality (ICD10 - C50), Uterus neoplasm mortality (ICD10 - C53-C55), Prostate neoplasm mortality (ICD10 - C61), Genitourinary system mortality (ICD10 - N); Renal/Kidney: Bladder neoplasm mortality (ICD10 - C67), Genitourinary system mortality (ICD10 - N); Neurological/Behavioral: Central nervous system neoplasm mortality (ICD10 - C70-C72, C75.1-C75.3), Nervous system mortality (ICD10 - G); Circulatory system: Leukemia mortality (ICD10 - C91-C95), Circulatory system mortality (ICD10 - I); Thyroid: Endocrine mortality (ICD10 - E); Musculoskeletal: Musculoskeletal system mortality (ICD10 - M)
Asbestos Fiber Type(s):	Asbestos - Not specified: 1332-21-4
Linked HERO ID(s):	2583283, 3541492
HERO ID:	2583283

Domain	Metric	Rating	Comments
Domain 2: Exposure Characterization			

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Study Citation:	Kumagai, S., Kurumatani, N., Tsuda, T., Yorifuji, T., Suzuki, E. (2010). Increased risk of lung cancer mortality among residents near an asbestos product manufacturing plant. International Journal of Occupational and Environmental Health 16(3):268-278.
Health Outcome:	Lung Cancer; All body systems; All body system
Target Organ(s):	Mortality: All causes, Infections (ICD10 - A,B), Neoplasm mortality (ICD 10 - C, D00-D48), Malignant neoplasm mortality (ICD 10 - C00-C97), Lip, oral cavity, and pharynx neoplasm mortality (ICD 10 - C00-C14), Oesophagus neoplasm mortality (ICD10 - C15), Stomach neoplasm mortality (ICD10 - C16), Colon and rectum neoplasm mortality (ICD10 C18-C20), Liver neoplasm mortality (ICD10 - C22), Gallbladder and biliary tract neoplasm mortality (ICD10-C23-C24), Pancreas neoplasm mortality (ICD10 - C25), Lung and trachea excluding cases with occupational asbestos exposure, neoplasm mortality (ICD10 - C33-C34), Lung and trachea excluding cases with occupational asbestos and silica exposure, neoplasm mortality (ICD10 - C33-C34), Skin neoplasm mortality (ICD10 - C43-44), Breast neoplasm mortality (ICD10 - C50), Uterus neoplasm mortality (ICD10 - C53-C55), Prostate neoplasm mortality (ICD10 - C61), Bladder neoplasm mortality (ICD10 - C67), Central nervous system neoplasm mortality (ICD10 - C70-C72, C75.1-C75.3), Leukemia mortality (ICD10 - C91-C95), Other malignant neoplasm mortality, Endocrine mortality (ICD10 - E), Nervous system mortality (ICD10 - G), Circulatory system mortality (ICD10 - I), Respiratory system mortality (ICD10 - J), Digestive system mortality (ICD10 - K), Musculoskeletal system mortality (ICD10 - M), Genitourinary system mortality (ICD10 - N); Cancer/Carcinogenesis: Neoplasm mortality (ICD 10 - C, D00-D48), Malignant neoplasm mortality (ICD 10 - C00-C97), Lip, oral cavity, and pharynx neoplasm mortality (ICD 10 - C00-C14), Oesophagus neoplasm mortality (ICD10 - C15), Stomach neoplasm mortality (ICD10 - C16), Colon and rectum neoplasm mortality (ICD10 C18-C20), Liver neoplasm mortality (ICD10 - C22), Gallbladder and biliary tract neoplasm mortality (ICD10-C23-C24), Pancreas neoplasm mortality (ICD10 - C25), Lung and trachea excluding cases with occupational asbestos exposure, neoplasm mortality (ICD10 - C33-C34), Lung and trachea excluding cases with occupational asbestos and silica exposure, neoplasm mortality (ICD10 - C33-C34), Skin neoplasm mortality (ICD10 - C43-44), Breast neoplasm mortality (ICD10 - C50), Uterus neoplasm mortality (ICD10 - C53-C55), Prostate neoplasm mortality (ICD10 - C61), Bladder neoplasm mortality (ICD10 - C67), Central nervous system neoplasm mortality (ICD10 - C70-C72, C75.1-C75.3), Leukemia mortality (ICD10 - C91-C95), Other malignant neoplasm mortality; Dermal: Lip, oral cavity, and pharynx neoplasm mortality (ICD 10 - C00-C14); Gastrointestinal: Oesophagus neoplasm mortality (ICD10 - C15), Stomach neoplasm mortality (ICD10 - C16), Colon and rectum neoplasm mortality (ICD10 C18-C20), Gallbladder and biliary tract neoplasm mortality (ICD10-C23-C24), Pancreas neoplasm mortality (ICD10 - C25), Digestive system mortality (ICD10 - K); Hepatic/Liver: Liver neoplasm mortality (ICD10 - C22); Lung/Respiratory: Lung and trachea excluding cases with occupational asbestos exposure, neoplasm mortality (ICD10 - C33-C34), Lung and trachea excluding cases with occupational asbestos and silica exposure, neoplasm mortality (ICD10 - C33-C34), Respiratory system mortality (ICD10 - J); Skin/Connective Tissue: Skin neoplasm mortality (ICD10 - C43-44); Reproductive/Developmental: Breast neoplasm mortality (ICD10 - C50), Uterus neoplasm mortality (ICD10 - C53-C55), Prostate neoplasm mortality (ICD10 - C61), Genitourinary system mortality (ICD10 - N); Renal/Kidney: Bladder neoplasm mortality (ICD10 - C67), Genitourinary system mortality (ICD10 - N); Neurological/Behavioral: Central nervous system neoplasm mortality (ICD10 - C70-C72, C75.1-C75.3), Nervous system mortality (ICD10 - G); Circulatory system: Leukemia mortality (ICD10 - C91-C95), Circulatory system mortality (ICD10 - I); Thyroid: Endocrine mortality (ICD10 - E); Musculoskeletal: Musculoskeletal system mortality (ICD10 - M)
Asbestos Fiber Type(s):	Asbestos - Not specified: 1332-21-4
Linked HERO ID(s):	2583283, 3541492
HERO ID:	2583283

Domain	Metric		Rating	Comments
	Metric 4:	Measurement of Exposure	Low	Exposure was not directly measured using a quantitative method. Instead, the authors estimated relative asbestos concentrations using meteorological parameters and asbestos emission data. The assumptions and methodology were described in the paper. However, exposure misclassification is likely to be present since no direct measurements using well-established methods.Note: responses to other metrics beyond 4 and 5 were not QC'ed because metric 4 was rated low.
	Metric 5:	Exposure Levels	Medium	Subjects were categorized into 4 exposure levels according to their estimated exposure level. The range and distribution of exposure is sufficient to detect an effect.

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Study Citation:	Kumagai, S., Kurumatani, N., Tsuda, T., Yorifuji, T., Suzuki, E. (2010). Increased risk of lung cancer mortality among residents near an asbestos product manufacturing plant. International Journal of Occupational and Environmental Health 16(3):268-278.
Health Outcome:	Lung Cancer; All body systems; All body system
Target Organ(s):	Mortality: All causes, Infections (ICD10 - A,B), Neoplasm mortality (ICD 10 - C, D00-D48), Malignant neoplasm mortality (ICD 10 - C00-C97), Lip, oral cavity, and pharynx neoplasm mortality (ICD 10 - C00-C14), Oesophagus neoplasm mortality (ICD10 - C15), Stomach neoplasm mortality (ICD10 - C16), Colon and rectum neoplasm mortality (ICD10 C18-C20), Liver neoplasm mortality (ICD10 - C22), Gallbladder and biliary tract neoplasm mortality (ICD10-C23-C24), Pancreas neoplasm mortality (ICD10 - C25), Lung and trachea excluding cases with occupational asbestos exposure, neoplasm mortality (ICD10 - C33-C34), Lung and trachea excluding cases with occupational asbestos and silica exposure, neoplasm mortality (ICD10 - C33-C34), Skin neoplasm mortality (ICD10 - C43-44), Breast neoplasm mortality (ICD10 - C50), Uterus neoplasm mortality (ICD10 - C53-C55), Prostate neoplasm mortality (ICD10 - C61), Bladder neoplasm mortality (ICD10 - C67), Central nervous system neoplasm mortality (ICD10 - C70-C72, C75.1-C75.3), Leukemia mortality (ICD10 - C91-C95), Other malignant neoplasm mortality, Endocrine mortality (ICD10 - E), Nervous system mortality (ICD10 - G), Circulatory system mortality (ICD10 - I), Respiratory system mortality (ICD10 - J), Digestive system mortality (ICD10 - K), Musculoskeletal system mortality (ICD10 - M), Genitourinary system mortality (ICD10 - N); Cancer/Carcinogenesis: Neoplasm mortality (ICD 10 - C, D00-D48), Malignant neoplasm mortality (ICD 10 - C00-C97), Lip, oral cavity, and pharynx neoplasm mortality (ICD 10 - C00-C14), Oesophagus neoplasm mortality (ICD10 - C15), Stomach neoplasm mortality (ICD10 - C16), Colon and rectum neoplasm mortality (ICD10 C18-C20), Liver neoplasm mortality (ICD10 - C22), Gallbladder and biliary tract neoplasm mortality (ICD10-C23-C24), Pancreas neoplasm mortality (ICD10 - C25), Lung and trachea excluding cases with occupational asbestos exposure, neoplasm mortality (ICD10 - C33-C34), Lung and trachea excluding cases with occupational asbestos and silica exposure, neoplasm mortality (ICD10 - C33-C34), Skin neoplasm mortality (ICD10 - C43-44), Breast neoplasm mortality (ICD10 - C50), Uterus neoplasm mortality (ICD10 - C53-C55), Prostate neoplasm mortality (ICD10 - C61), Bladder neoplasm mortality (ICD10 - C67), Central nervous system neoplasm mortality (ICD10 - C70-C72, C75.1-C75.3), Leukemia mortality (ICD10 - C91-C95), Other malignant neoplasm mortality; Dermal: Lip, oral cavity, and pharynx neoplasm mortality (ICD 10 - C00-C14); Gastrointestinal: Oesophagus neoplasm mortality (ICD10 - C15), Stomach neoplasm mortality (ICD10 - C16), Colon and rectum neoplasm mortality (ICD10 C18-C20), Gallbladder and biliary tract neoplasm mortality (ICD10-C23-C24), Pancreas neoplasm mortality (ICD10 - C25), Digestive system mortality (ICD10 - K); Hepatic/Liver: Liver neoplasm mortality (ICD10 - C22); Lung/Respiratory: Lung and trachea excluding cases with occupational asbestos exposure, neoplasm mortality (ICD10 - C33-C34), Lung and trachea excluding cases with occupational asbestos and silica exposure, neoplasm mortality (ICD10 - C33-C34), Respiratory system mortality (ICD10 - J); Skin/Connective Tissue: Skin neoplasm mortality (ICD10 - C43-44); Reproductive/Developmental: Breast neoplasm mortality (ICD10 - C50), Uterus neoplasm mortality (ICD10 - C53-C55), Prostate neoplasm mortality (ICD10 - C61), Genitourinary system mortality (ICD10 - N); Renal/Kidney: Bladder neoplasm mortality (ICD10 - C67), Genitourinary system mortality (ICD10 - N); Neurological/Behavioral: Central nervous system neoplasm mortality (ICD10 - C70-C72, C75.1-C75.3), Nervous system mortality (ICD10 - G); Circulatory system: Leukemia mortality (ICD10 - C91-C95), Circulatory system mortality (ICD10 - I); Thyroid: Endocrine mortality (ICD10 - E); Musculoskeletal: Musculoskeletal system mortality (ICD10 - M)
Asbestos Fiber Type(s):	Asbestos - Not specified: 1332-21-4
Linked HERO ID(s):	2583283, 3541492
HERO ID:	2583283

Domain	Metric	Rating	Comments
Additional Comments:	The major concern of this study is no direct measurement of exposure, so potential exposure misclassification is likely to be present. Other part of the study such as population selection and outcome measurements were appropriate and sufficiently described.Lung cancer SMR was assessed but not evaluated here according to instruction from EPA.		

* No biomarkers were identified for this evaluation.

** As described in Appendix B.2 of the *White Paper: Quantitative Approach to the Human Health Assessment for the Risk Evaluation for Asbestos Part 2: Supplemental Evaluation Including Legacy Uses and Associated Disposals of Asbestos*, to be considered as being informative for dose-response analysis, metrics 4 and 5 would need metric ratings of Medium or High. This reference did not satisfy this requirement; therefore data quality evaluation is presented for only for metrics 4 and 5.

Study Citation:	Lacquet, L. M., van der Linden, L., Lepoutre, J. (1980). Roentgenographic lung changes, asbestosis and mortality in a Belgian asbestos-cement factory. IARC Scientific Publications -30:783-793.
Health Outcome:	Lung Cancer; gastrointestinal cancer, nervous cancer, lymphoid and haematopoietic cancer, other cancer, not specified cancer; Asbestosis; external cause, cerebro-cardiovascular cancer, respiratory, gastrointestinal, other, unknow or poorly specified cause
Target Organ(s):	Lung/Respiratory: Asbestosis, Respiratory cancer mortality, Respiratory non-malignant mortality; Mortality: All cause mortality, Respiratory cancer mortality, Gastrointestinal cancer mortality, External cause mortality, Unknown of poorly specified cause mortality, Malignant cause mortality, Cerebro-cardiovascular non-malignant mortality, Respiratory non-malignant mortality, Gastrointestinal non-malignant mortality, Other non-malignant mortality, Nervous cancer mortality, Lymphoid and haematopoietic cancer mortality, Other cancer mortality, Not specified cancer mortality, All cancers mortality; Cancer/Carcinogenesis: Respiratory cancer mortality, Gastrointestinal cancer mortality, Malignant cause mortality, Nervous cancer mortality, Lymphoid and haematopoietic cancer mortality, Other cancer mortality, Not specified cancer mortality, All cancers mortality; Gastrointestinal: Gastrointestinal cancer mortality, Gastrointestinal non-malignant mortality; Cardiovascular: Cerebro-cardiovascular non-malignant mortality; Other non-malignant mortality: Other non-malignant mortality; Neurological/Behavioral: Nervous cancer mortality; Immune/Hematological: Lymphoid and haematopoietic cancer mortality; Other cancer mortality: Other cancer mortality; Not specified cancer mortality: Not specified cancer mortality
Asbestos Fiber Type(s):	Asbestos - Chrysotile (serpentine): 12001-29-5; Asbestos - Crocidolite (riebeckite): 12001-28-4; Asbestos - Amosite (grunerite): 12172-73-5
Linked HERO ID(s):	No linked references.
HERO ID:	3084226

Domain		Metric	Rating	Comments
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Low	This metric is rated low because neither PCM nor TEM were explicitly mentioned as a method for fiber quantification. Fiber measurements from 1970-1976 were obtained with filter-membrane methods. This was specified as static sampling during peak installation activities in Van Cleemput et al., 2000 783706. Measurements prior to 1970 were estimated using a formula that assumed dust concentrations followed a logistic decay, but no apparent use of conversion factors.
	Metric 5:	Exposure Levels	Low	The range and distribution of exposure was sufficient to develop and exposure-response estimate. The cohort study reported up to 7 levels of exposure (number varied between analyses), with estimates ranging from 0 to 3200 fiber-years. However, most analyses have only dichotomous exposures, with the sole exception of respiratory and gastrointestinal cancer (table 8).

Additional Comments:	QC was not completed for metrics other than Metrics 4 and 5 because the study does not have sufficient exposure information to be useful for dose-response analysis.

* No biomarkers were identified for this evaluation.

** As described in Appendix B.2 of the *White Paper: Quantitative Approach to the Human Health Assessment for the Risk Evaluation for Asbestos Part 2: Supplemental Evaluation Including Legacy Uses and Associated Disposals of Asbestos*, to be considered as being informative for dose-response analysis, metrics 4 and 5 would need metric ratings of Medium or High. This reference did not satisfy this requirement; therefore data quality evaluation is presented for only for metrics 4 and 5.

Study Citation: Larson, T. C., Antao, V. C., Bove, F. J. (2010). Vermiculite worker mortality: Estimated effects of occupational exposure to Libby amphibole. Journal of Occupational and Environmental Medicine 52(5):555-560.

Health Outcome: Lung Cancer; digestive system cancer; non-malignant respiratory disease, cardiovascular disease

Target Organ(s): Mortality: cardiovascular disease, digestive system cancer, Lung cancer, Asbestosis, non-malignant respiratory disease; Cardiovascular: cardiovascular disease; Cancer/Carcinogenesis: Lung cancer, digestive system cancer; Gastrointestinal: digestive system cancer; Lung/Respiratory: non-malignant respiratory disease, Lung cancer, Asbestosis

Asbestos Fiber Type(s): Asbestos- Libby amphibole: 1318-09-8

Linked HERO ID(s): 709497, 709457, 711560, 2238712

HERO ID: 711560

Domain	Metric		Rating	Comments
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Low	This metric is rated Low because the study or any cited methods source does not explicitly mention the use of PCM or TEM to develop quantitative estimates of exposure.
	Metric 5:	Exposure Levels	Medium	The distribution of exposure appears to be sufficient to develop an exposure-response estimate. Cumulative exposure was utilized in dose-response calculations and were represented in four levels: <1.4 f/cc-y, 1.4 to <8.6 f/cc-y, 8.6 to <44.0 f/cc-y, and >=44.0 f/cc-y.

Additional Comments: QC was not completed for metrics other than Metrics 4 and 5 because the study does not have sufficient exposure information to be useful for dose-response analysis. Metric 4 had a low level of confidence because the authors do not mention using PCM or TEM to develop quantitative estimates of exposure.

** As described in Appendix B.2 of the *White Paper: Quantitative Approach to the Human Health Assessment for the Risk Evaluation for Asbestos Part 2: Supplemental Evaluation Including Legacy Uses and Associated Disposals of Asbestos*, to be considered as being informative for dose-response analysis, metrics 4 and 5 would need metric ratings of Medium or High. This reference did not satisfy this requirement; therefore data quality evaluation is presented for only for metrics 4 and 5.

Study Citation:	Larson, T. C., Antao, V. C., Bove, F. J., Cusack, C. (2012). Association between cumulative fiber exposure and respiratory outcomes among Libby vermiculite workers. Journal of Occupational and Environmental Medicine 54(1):56-63.
Health Outcome:	Pulmonary Function/Spirometry Results; Pleural Plaques
Target Organ(s):	Lung/Respiratory: Radiographic lung changes: diffuse or localized pleural thickening, parenchymal abnormalities. Respiratory symptoms: restrictive spirometry, dyspnea/shortness of breath, excess cough, chronic bronchitis.
Asbestos Fiber Type(s):	Asbestos- Libby amphibole: 1318-09-8; Asbestos - Winchite: 12425-92-2; Asbestos- Richterite: 17068-76-7; Asbestos - Tremolite: 14567-73-8; Asbestos - Actinolite: 12172-67-7
Linked HERO ID(s):	No linked references.
HERO ID:	1005289

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Low	Larson et al., 2012 1005289 analyzed data from 336 participants in a 2000-2001 ATSDR community screening in Libby, MT who identified themselves as having worked at the vermiculite mine. The screening included volunteers who had lived, worked, or played in Libby for at least 6 months prior to 1991. The sample had fewer years since first exposure (29 vs 48 years), lower cumulative fiber exposure (CFE), and more years employed vs others in a complete registry of mine workers (>700 deceased workers not excluded for that comparison). Concerns: Self-selection bias is an important concern since voluntary participation is potentially related to both exposure and health status. Along with losses due to mortality (healthy worker survivor effect), morbidity may have affected interest in or ability to participate in the screening. As the authors noted, "workers with greater cumulative exposure may have already been diagnosed with asbestos-related health outcomes and opted not to participate." Only 18% of the eligible population participated in the study.
	Metric 2:	Attrition	Low	Attrition was high relative to the target sample of more than 900 workers still alive, according to mortality studies conducted by the authors at about the same time (see Larson et al. 2010, 711560). Sensitivity analyses to evaluate the potential influence of non-participants were not discussed. Loss to follow-up after enrollment was not an issue as the study was cross-sectional, and 336 of 370 (91%) of the self-selected screening participants who reported working at mine were matched to company records.
	Metric 3:	Comparison Group	Low	This study compared workers within the cohort with higher vs. lower exposure. Self-selection is a major concern, as noted above. For the comparison group, individuals with lower exposure may have been more motivated to participate in the screening if they had symptoms potentially linked to their work and had not yet been diagnosed with a related condition.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Medium	This metric is rated medium because the Larson et al., 2012 1005289 study mentions the use of PCM for analysis of personal air sampling data for all areas of the vermiculite operation. Larson et al., 2012 1005289 estimated retrospective cumulative fiber exposure (CFE) through 1980 using the methods described in the NIOSH cohort (Armstrong et al., 709456). Exposure after 1980 was incorporated using updated job history data collected by ATSDR (details not provided).

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Study Citation:	Larson, T. C., Antao, V. C., Bove, F. J., Cusack, C. (2012). Association between cumulative fiber exposure and respiratory outcomes among Libby vermiculite workers. Journal of Occupational and Environmental Medicine 54(1):56-63.
Health Outcome:	Pulmonary Function/Spirometry Results; Pleural Plaques
Target Organ(s):	Lung/Respiratory: Radiographic lung changes: diffuse or localized pleural thickening, parenchymal abnormalities. Respiratory symptoms: restrictive spirometry, dyspnea/shortness of breath, excess cough, chronic bronchitis.
Asbestos Fiber Type(s):	Asbestos- Libby amphibole: 1318-09-8; Asbestos - Winchite: 12425-92-2; Asbestos- Richterite: 17068-76-7; Asbestos - Tremolite: 14567-73-8; Asbestos - Actinolite: 12172-67-7
Linked HERO ID(s):	No linked references.
HERO ID:	1005289

Domain	Metric		Rating	Comments
	Metric 5:	Exposure Levels	Medium	Analyses used either CFE quartiles (<0.4, 0.4-3.5, 3.6-15.7, or >=15.7 f/cc-years) or a continuous CFE measure, which was modeled used restricted cubic splines to allow for non-linear associations.
	Metric 6:	Temporality	High	Sequencing was appropriate as exposure was estimated retrospectively in Larson et al., 2012 1005289. The median (IQR) follow-up time since date of hire was 29.4 (25.6–39.3) years, which was adequate for asbestos-related radiographic changes to occur.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	High	Pulmonary Function/Spirometry Results: Spirometry testing was conducted by a qualified technician used American Thoracic Society guidelines and published references for predicted values. Spirometry was defined as restrictive, obstructive, mixed, and normal based on lower limits of normal (LLN) cutoffs, with restrictive defined as FEV1/FVC < LLN. 16% had restrictive spirometry, 11% obstructive, and 4% mixed.; Pleural Plaques: In Larson et al., 2012 1005289, posterior-anterior chest radiographs taken in accordance with NIOSH guidelines were read by two primary readers using the 1980 ILO classification. A third reader did an independent reading in case of disagreements. The radiographic changes were classified as the presence or absence of parenchymal abnormalities, localized pleural abnormalities, and diffuse pleural thickening. No information about whether the B readers were blinded to exposure status was included.
	Metric 8:	Reporting Bias	High	Results were presented for all stated aims.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	High	Multivariable analyses adjusted for age. The authors also evaluated confounding by employment before 1974 (exposure estimates prior to that time were less valid and exposure was higher), smoking, sex, and BMI. Covariates ultimately included in models were selected empirically based on changes of 10% or more in the odds ratio of the exposure-response association with their inclusion.
	Metric 10:	Covariate Characterization	Medium	Employment records were used in this study; other studies reported some errors in recorded smoking history (Rohs et al 2007, 709486). BMI was measured as part of the community screening.
	Metric 11:	Co-exposure Counfounding	Medium	Subsequent occupational exposure to commercial asbestos was considered in a sensitivity analysis. However, community/residential exposure was not taken into account.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	Medium	Appropriate analyses were used. In addition to descriptive tabulations, logistic regression models were used with adjustment for potential confounders.

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Study Citation:	Larson, T. C., Antao, V. C., Bove, F. J., Cusack, C. (2012). Association between cumulative fiber exposure and respiratory outcomes among Libby vermiculite workers. Journal of Occupational and Environmental Medicine 54(1):56-63.
Health Outcome:	Pulmonary Function/Spirometry Results; Pleural Plaques
Target Organ(s):	Lung/Respiratory: Radiographic lung changes: diffuse or localized pleural thickening, parenchymal abnormalities. Respiratory symptoms: restrictive spirometry, dyspnea/shortness of breath, excess cough, chronic bronchitis.
Asbestos Fiber Type(s):	Asbestos- Libby amphibole: 1318-09-8; Asbestos - Winchite: 12425-92-2; Asbestos- Richterite: 17068-76-7; Asbestos - Tremolite: 14567-73-8; Asbestos - Actinolite: 12172-67-7
Linked HERO ID(s):	No linked references.
HERO ID:	1005289

Domain	Metric		Rating	Comments
	Metric 13:	Statistical Power	Medium	The number of cases was adequate for localized pleural thickening (n=117). However, few cases had diffuse pleural thickening (n=18); parenchymal abnormalities (n=18); and restrictive lung function (n=45) – statistical power was likely limited for these outcomes.
	Metric 14:	Reproducibility of Analyses	Medium	Methods used were described clearly, and results tables included cell sizes for numbers of cases.
	Metric 15:	Statistical Analysis	Medium	Methods were appropriate, and the authors explained their rationale for the methods they used (e.g., splines used to increase power and examine non-linearities; 10% change-in-estimate used to identify confounders). Model fit was examined.

Additional Comments: This analysis of radiologic lung changes and spirometry-based lung function among Libby vermiculite mine workers by Larson et al., 2012 1005289 had a long follow-up time (median 29.4 years). Self-selection bias is a major concern: a voluntary community screening was the source of study participants. This bias may explain the weak or null associations observed despite the long follow-up. As the authors noted, the prevalence of lung changes at higher levels of exposure was lower than expected; this would occur if more highly exposed individuals who already had lung diagnoses were not interested in or able to participate (i.e., suggestive of bias). Overall, they authors found a high (46%) prevalence of pleural abnormalities (n=154 or 35% localized pleural thickening, n=18 or 5% diffuse pleural thickening, n=74 or 22% pleural calcification); 18 or 5% had parenchymal abnormalities. The prevalence of restrictive lung function was low. Although associations were weak and largely non-significant, the trend, particularly in spline models, was for generally positive associations with increasing CFE. For some outcomes, however, the magnitude of association declined at the highest levels of exposure (again consistent with self-selection bias). Despite major concerns regarding self-selection bias, the high prevalence of lung changes at relatively low exposure observed in this study is noteworthy.

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation:	Larson, T. C., Antao, V. C., Bove, F. J., Cusack, C. (2012). Association between cumulative fiber exposure and respiratory outcomes among Libby vermiculite workers. Journal of Occupational and Environmental Medicine 54(1):56-63.
Health Outcome:	Dyspnea/shortness of breath, excess cough, chronic bronchitis
Target Organ(s):	Lung/Respiratory: Radiographic lung changes: diffuse or localized pleural thickening, parenchymal abnormalities. Respiratory symptoms: restrictive spirometry, dyspnea/shortness of breath, excess cough, chronic bronchitis.
Asbestos Fiber Type(s):	Asbestos- Libby amphibole: 1318-09-8; Asbestos - Winchite: 12425-92-2; Asbestos- Richterite: 17068-76-7; Asbestos - Tremolite: 14567-73-8; Asbestos - Actinolite: 12172-67-7
Linked HERO ID(s):	No linked references.
HERO ID:	1005289

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Low	Larson et al., 2012 1005289 analyzed data from 336 participants in a 2000-2001 ATSDR community screening in Libby, MT who identified themselves as having worked at the vermiculite mine. The screening included volunteers who had lived, worked, or played in Libby for at least 6 months prior to 1991. The sample had fewer years since first exposure (29 vs 48 years), lower cumulative fiber exposure (CFE), and more years employed vs others in a complete registry of mine workers (>700 deceased workers not excluded for that comparison). Concerns: Self-selection bias is an important concern since voluntary participation is potentially related to both exposure and health status. Along with losses due to mortality (healthy worker survivor effect), morbidity may have affected interest in or ability to participate in the screening. As the authors noted, "workers with greater cumulative exposure may have already been diagnosed with asbestos-related health outcomes and opted not to participate." Only 18% of the eligible population participated in the study.
	Metric 2:	Attrition	Low	Attrition was high relative to the target sample of more than 900 workers still alive, according to mortality studies conducted by the authors at about the same time (see Larson et al. 2010, 711560). Sensitivity analyses to evaluate the potential influence of non-participants were not discussed. Loss to follow-up after enrollment was not an issue as the study was cross-sectional, and 336 of 370 (91%) of the self-selected screening participants who reported working at mine were matched to company records.
	Metric 3:	Comparison Group	Low	This study compared workers within the cohort with higher vs. lower exposure. Self-selection is a major concern, as noted above. For the comparison group, individuals with lower exposure may have been more motivated to participate in the screening if they had symptoms potentially linked to their work and had not yet been diagnosed with a related condition.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Medium	This metric is rated medium because the Larson et al., 2012 1005289 study mentions the use of PCM for analysis of personal air sampling data for all areas of the vermiculite operation. Larson et al., 2012 1005289 estimated retrospective cumulative fiber exposure (CFE) through 1980 using the methods described in the NIOSH cohort (Armstrong et al., 709456). Exposure after 1980 was incorporated using updated job history data collected by ATSDR (details not provided).
	Metric 5:	Exposure Levels	Medium	Analyses used either CFE quartiles (<0.4, 0.4-3.5, 3.6-15.7, or >=15.7 f/cc-years) or a continuous CFE measure, which was modeled used restricted cubic splines to allow for non-linear associations.

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Study Citation: Larson, T. C., Antao, V. C., Bove, F. J., Cusack, C. (2012). Association between cumulative fiber exposure and respiratory outcomes among Libby vermiculite workers. Journal of Occupational and Environmental Medicine 54(1):56-63.

Health Outcome: Dyspnea/shortness of breath, excess cough, chronic bronchitis

Target Organ(s): Lung/Respiratory: Radiographic lung changes: diffuse or localized pleural thickening, parenchymal abnormalities. Respiratory symptoms: restrictive spirometry, dyspnea/shortness of breath, excess cough, chronic bronchitis.

Asbestos Fiber Type(s): Asbestos- Libby amphibole: 1318-09-8; Asbestos - Winchite: 12425-92-2; Asbestos- Richterite: 17068-76-7; Asbestos - Tremolite: 14567-73-8; Asbestos - Actinolite: 12172-67-7

Linked HERO ID(s): No linked references.

HERO ID: 1005289

Domain	Metric		Rating	Comments
	Metric 6:	Temporality	High	Sequencing was appropriate as exposure was estimated retrospectively in Larson et al., 2012 1005289. The median (IQR) follow-up time since date of hire was 29.4 (25.6–39.3) years, which was adequate for asbestos-related radiographic changes to occur.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Low	Other Non-Cancer Outcomes: Outcomes were self-reported without confirmation by a clinician. A questionnaire was used to identify respiratory symptoms; the manuscript does not state whether they adapted or used items from validated questionnaires. The following three respiratory symptoms were analyzed: (i) dyspnea, defined as shortness of breath "when walking up a slight hill or when hurrying on level ground") = 66 or 20%; (ii) excess cough, defined as having a cough "on most days [at least 4 days of the week]" = 49 or 15%; and (iii) chronic bronchitis, defined as both excess cough and excess phlegm [coughing up phlegm "for at least 3 months of the year for the past 2 years"] = 26 or 8%. The authors stated that "[a]s part of the definition of these respiratory symptoms and conditions, we excluded workers with radiographic abnormalities consistent with pneumoconiosis or restrictive spirometry."
	Metric 8:	Reporting Bias	High	Results were presented for all stated aims.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	High	Multivariable analyses adjusted for age. The authors also evaluated confounding by employment before 1974 (exposure estimates prior to that time were less valid and exposure was higher), smoking, sex, and BMI. Covariates ultimately included in models were selected empirically based on changes of 10% or more in the odds ratio of the exposure-response association with their inclusion.
	Metric 10:	Covariate Characterization	Medium	Employment records were used in this study; other studies reported some errors in recorded smoking history (Rohs et al 2007, 709486). BMI was measured as part of the community screening.
	Metric 11:	Co-exposure Counfounding	Medium	Subsequent occupational exposure to commercial asbestos was considered in a sensitivity analysis. However, community/residential exposure was not taken into account.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	Medium	Appropriate analyses were used. In addition to descriptive tabulations, logistic regression models were used with adjustment for potential confounders
	Metric 13:	Statistical Power	Medium	The number of cases was adequate for respiratory outcomes.
	Metric 14:	Reproducibility of Analyses	Medium	Methods used were described clearly, and results tables included cell sizes for numbers of cases.

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Study Citation:	Larson, T. C., Antao, V. C., Bove, F. J., Cusack, C. (2012). Association between cumulative fiber exposure and respiratory outcomes among Libby vermiculite workers. Journal of Occupational and Environmental Medicine 54(1):56-63.
Health Outcome:	Dyspnea/shortness of breath, excess cough, chronic bronchitis
Target Organ(s):	Lung/Respiratory: Radiographic lung changes: diffuse or localized pleural thickening, parenchymal abnormalities. Respiratory symptoms: restrictive spirometry, dyspnea/shortness of breath, excess cough, chronic bronchitis.
Asbestos Fiber Type(s):	Asbestos- Libby amphibole: 1318-09-8; Asbestos - Winchite: 12425-92-2; Asbestos- Richterite: 17068-76-7; Asbestos - Tremolite: 14567-73-8; Asbestos - Actinolite: 12172-67-7
Linked HERO ID(s):	No linked references.
HERO ID:	1005289

Domain	Metric		Rating	Comments
	Metric 15:	Statistical Analysis	Medium	Methods were appropriate, and the authors explained their rationale for the methods they used (e.g., splines used to increase power and examine non-linearities; 10% change-in-estimate used to identify confounders). Model fit was examined.

Additional Comments: Self-selection bias is a major concern, as discussed in the evaluation of radiologic lung change and spirometry outcomes. For respiratory symptoms, an additional concern is reliance exclusively on self-report without physician validation. It was also not fully clear whether participants with radiologic lung changes - but without the respiratory symptom of interest - were included in or excluded from the referent population used for estimating associations (i.e., was the referent group limited to healthy workers?).

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation:	Larson, T., Meyer, C., Kapil, V., Gurney, J., Tarver, R., Black, C., Lockey, J. (2010). Workers with Libby amphibole exposure: retrospective identification and progression of radiographic changes. Radiology 255(3):924-933.
Health Outcome:	Pleural Plaques
Target Organ(s):	Lung/Respiratory: Progression of radiographic lung changes.
Asbestos Fiber Type(s):	Asbestos - Tremolite: 14567-73-8; Asbestos- Richterite: 17068-76-7; Asbestos - Winchite: 12425-92-2; Asbestos- Libby amphibole: 1318-09-8
Linked HERO ID(s):	No linked references.
HERO ID:	709456

Domain		Metric	Rating	Comments
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Medium	Cumulative fiber exposure was estimated retrospectively using available historic fiber measures; PCM counts were used when membrane filter measures were initiated in 1974. Earlier measures included few measures from limited areas and used instruments such as midget impingers. Measurement error is a concern especially before 1974. Employment records were used to calculate individual exposure. Methods were detailed elsewhere (Amandus et al 1987 PMID: 3028135).
	Metric 5:	Exposure Levels	Low	Distributions of participants or the prevalence of progressive lung changes was not presented by category of cumulative fiber exposure. The cumulative fiber exposure (CFE) variable used in logistic regression models was not specified, and results were not shown. However, mean CFE was shown for the full sample and for subgroups with different types of radiographic lung changes.

Additional Comments: The association between cumulative fiber exposure and odds of progressive lung abnormalities was not presented as it was not statistically significant. Concerns regarding sample selectivity may have influenced this finding. Although the association between progression and fiber exposure was not presented, this study provides very useful information on patterns of progression of radiographic lung changes, including the median latency time for progression to occur.

* No biomarkers were identified for this evaluation.

** As described in Appendix B.2 of the *White Paper: Quantitative Approach to the Human Health Assessment for the Risk Evaluation for Asbestos Part 2: Supplemental Evaluation Including Legacy Uses and Associated Disposals of Asbestos*, to be considered as being informative for dose-response analysis, metrics 4 and 5 would need metric ratings of Medium or High. This reference did not satisfy this requirement; therefore data quality evaluation is presented for only for metrics 4 and 5.

Study Citation:	Liddell, F. D., Gibbs, G. W., Mcdonald, J. C. (1982). Radiological changes and fibre exposure in chrysotile workers aged 60-69 years at Thetford Mines. Annals of Occupational Hygiene 26(1-4):889-898.
Health Outcome:	Pleural Plaques
Target Organ(s):	Lung/Respiratory: small opacities, pleural changes
Asbestos Fiber Type(s):	Asbestos - Chrysotile (serpentine): 12001-29-5
Linked HERO ID(s):	3083980, 3083580
HERO ID:	3083980

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Medium	Liddel et al. RefID 3083980: Study population included all male Thetford Mines employees born 1891-1920 who had 20+ years of employment at the facility and were aged 60+ in November 1966 (when radiographs were taken) or at termination of their last job, if earlier (n=515).Cordier et al. RefID 3083580: Study population included male Thetford Mines employees beginning employment between 1954-1969 with 5+ years cumulative exposure, excluding those who works 6+ months at another asbestos factory and/or 1+ years at another asbestos mine (n=394).Inclusion/exclusion criteria for both studies were generally appropriate. Key elements of study population were reported in sufficient detail.
	Metric 2:	Attrition	Medium	Outcome assessment and exposure monitoring were both conducted onsite at the facility for all active employees, so missing outcome information is not a large concern. Subjects were included in both studies retroactively after both exposure and outcome status had been measured. Exclusion criteria were adequately documented and appropriate. No direct evidence of substantial bias by attrition.
	Metric 3:	Comparison Group	Medium	Comparison structure was appropriate. For both studies, all subjects were employees at the facility. Outcome status(es) were compared across multiple quantitative exposure level bins. Requirements for duration of employment/exposure (20+ years experience for Liddel et al.; 5+ years cumulative exposure for Cordier et al.) may have introduced healthy worker effect.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Medium	Liddel et al:Exposure was consistently assessed quantitatively. Asbestos fibers were using midget impingers and fiber/dust ratios were calculated for each main and sub-area of the facility. Individual exposures were calculated based on job histories collected via questionnaire by outcome-blinded researchers in 1977. Cumulative and average fiber exposures were calculated using formulas from Gibbs and Lachance (1972).Cordier et al:Exposure was consistently assessed quantitatively. Asbestos fibers were measured using midget impingers from 1958-1976 and using membrane filters from 1976 onward. Cumulative exposures for individuals were calculated using a job matrix and Gibbs procedure. Due to incomplete monitoring data, cumulative exposure was only calculated for 7 job locations.Both studies note likely incompletion of exposure monitoring data.

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Study Citation: Liddell, F. D., Gibbs, G. W., Mcdonald, J. C. (1982). Radiological changes and fibre exposure in chrysotile workers aged 60-69 years at Thetford Mines. Annals of Occupational Hygiene 26(1-4):889-898.
Health Outcome: Pleural Plaques
Target Organ(s): Lung/Respiratory: small opacities, pleural changes
Asbestos Fiber Type(s): Asbestos - Chrysotile (serpentine): 12001-29-5
Linked HERO ID(s): 3083980, 3083580
HERO ID: 3083980

Domain	Metric		Rating	Comments
	Metric 5:	Exposure Levels	Medium	Liddel et al:Number of workers in each average fiber concentration category are reported, stratified by gross service years (Table 1). Average fiber concentration ranged from <=10 f/mL to >75 f/mL.Cordier et al:Number of workers in each cumulative exposure category are reported (<30 f/cc*yr: 42 workers; 30-89 f/cc*yr: 155 workers; >=90 f/cc*yr: 134 workers). In both studies, observed exposure ranges are adequate to determine an exposure-response relationship.
	Metric 6:	Temporality	Low	Liddel et al:Outcomes were measured via the most recent chest radiograph for each subject prior to 1966. Subjects were required to have 20+ years of service at the mine before 1966 to be eligible for inclusion. Cordier et al:Timing of outcome measurement is somewhat vague (chest radiographs were assembled beginning in 1975 and each subject's most recent radiograph was used, but the year of measurement is not reported). Subjects were required to have begun employment between 1954-1969 and have 5+ years of cumulative exposure at the time of outcome assessment. There is some overlap in exposure assessment and outcome assessment window, but because exposure index was estimated based on year-accurate measurements, temporality could be established.For both studies, temporality is established between exposure and outcome but the latency window is not clear or necessarily consistent among subjects. A shorter latency window is less concerning for the outcomes of interest (small opacities of the lung, plural changes) than for a cancer outcome.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Medium	Pleural Plaques: Liddel et al:Most recent radiograph for each employee prior to 1966 was read in 3 stages by an international group of 6 readers using the IUCC/Cincinnati classification. Films were then randomly divided into 30 equal sets and each reader read 5 sets, providing 1 reading for each film. The 6 readers worked separately and independently and were blinded to age, work history, and other personal details of subjects. Readers were involved in development of classifications.Cordier et al:Annual chest radiographs for asbestos mine workers in this geographic area were compiled beginning in 1975. The most recent chest radiograph for each man still working in the mine (through 1980) was used. Each radiograph was read by 5 readers according to the ILO U/C 1980 classification. Readers were all radiologists and pulmonary physicians experienced in reading pneumoconiosis and certified by NIOSH. Readers worked independently and received films in random order. Readers were blinded to occupation or exposure status of subjects.Equipment details for chest radiographs are not reported, but reading classification materials are included and there is no direct evidence of mis-measurement.
	Metric 8:	Reporting Bias	Medium	Results for all anticipated analyses are included in the paper.
Domain 4: Potential Confounding / Variability Control				

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Study Citation:	Liddell, F. D., Gibbs, G. W., Mcdonald, J. C. (1982). Radiological changes and fibre exposure in chrysotile workers aged 60-69 years at Thetford Mines. Annals of Occupational Hygiene 26(1-4):889-898.
Health Outcome:	Pleural Plaques
Target Organ(s):	Lung/Respiratory: small opacities, pleural changes
Asbestos Fiber Type(s):	Asbestos - Chrysotile (serpentine): 12001-29-5
Linked HERO ID(s):	3083980, 3083580
HERO ID:	3083980

Domain	Metric		Rating	Comments
	Metric 9:	Covariate Adjustment	Medium	Both papers were restricted to male employees only. Liddel et al. accounted for age by calculating cumulative and average exposure indexes standardized to "by 45 years of age." Cordier et al. accounted for age by including it as an independent variable in multivariate analyses. Both papers included stratified analyses by dichotomized smoking. Length and timing of employment were considered through calculation of exposure indexes. Neither paper discusses additional covariates such as race/ethnicity or SES.
	Metric 10:	Covariate Characterization	Medium	Covariate information was collected from interviews (Liddel et al.) or medical records (Cordier et al.). No direct evidence of misclassification.
	Metric 11:	Co-exposure Counfounding	Medium	No direct evidence that co-exposures were likely to be present.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	Medium	Both studies compared prevalence of small irregular opacities and pleural changes across ordinal cumulative and average exposure bins. Liddel et al. used a modified least squares analysis (X^2 values reported) and Cordier et al. used a multivariate analysis that included age, smoking and exposure as independent terms (p-values discussed in text). Both analytical approaches were generally appropriate for the subject matter, if not overly robust.
	Metric 13:	Statistical Power	Medium	Sample size and observed exposure ranges are adequate to detect present relationships in both studies.
	Metric 14:	Reproducibility of Analyses	Low	Descriptions of analytical methods are lacking and could not be easily reproduced (e.g., type of multivariate analysis performed and comparison statistic calculated are not reported in Cordier et al.).
	Metric 15:	Statistical Analysis	Low	Liddel et al. used a modified least square analysis and Cordier et al., used an unidentified "multivariate analysis" to characterize differences in prevalence of outcomes across exposure groups. There is not direct evidence that these methods were inappropriate, but full information is lacking.

Additional Comments: None

Overall Quality Determination — Medium

* No biomarkers were identified for this evaluation.

Study Citation:	Liddell, F. D., Thomas, D. C., Gibbs, G. W., McDonald, J. C. (1984). Fibre exposure and mortality from pneumoconiosis, respiratory and abdominal malignancies in chrysotile production in Quebec, 1926-75. Annals of the Academy of Medicine, Singapore 13(2 Suppl.):340-344.
Health Outcome:	Lung Cancer; Laryngeal Cancer; cancer of the esophagus and stomach, cancer of the colon and rectum, other abdominal cancers; pneumoconiosis
Target Organ(s):	Lung/Respiratory: death from pneumoconiosis, death from lung cancer, death from cancer of larynx; Mortality: death from pneumoconiosis, death from lung cancer, death from cancer of larynx, death from cancer of oesophagus and stomach, death from cancer of colon and rectum, death from other abdominal cancers; Cancer/Carcinogenesis: death from lung cancer, death from cancer of larynx, death from cancer of oesophagus and stomach, death from cancer of colon and rectum, death from other abdominal cancers; Gastrointestinal: death from cancer of oesophagus and stomach, death from cancer of colon and rectum; Abdomen: death from other abdominal cancers
Asbestos Fiber Type(s):	Asbestos - Chrysotile (serpentine): 12001-29-5
Linked HERO ID(s):	No linked references.
HERO ID:	3083620

Domain		Metric	Rating	Comments
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Low	This metric is rated Low because authors in this paper do not explicitly cite use of PCM or TEM. Authors suggest that side-by-side measurements of dust and fiber were made to develop a conversion factor, but there is no detail on microscopy methods. The methods paper cited is Gibbs and Lachance, 1972, HEROID: 3580825, but this does not clarify fiber counting methods. Methods of sample collection included midget impinger dust counts measured between 1949 and 1976 and membrane filters between 1969 and 1976. Conversion factors were utilized but were based on other studies to convert mpcf to f-ml. Exposure data was examined for both cases and referents and came from exposure work histories. For measurements prior to 1949, estimates were based off of interviews from long-service employees which could introduce recall bias.
	Metric 5:	Exposure Levels	Medium	Four levels of exposure are provided in the analyses in (f/ml)*y. Mean exposure was 828.3 (f/ml)*y.

Additional Comments:	QC was not completed for metrics other than Metrics 4 and 5 because the study does not have sufficient exposure information to be useful for dose-response analysis.

* No biomarkers were identified for this evaluation.

** As described in Appendix B.2 of the *White Paper: Quantitative Approach to the Human Health Assessment for the Risk Evaluation for Asbestos Part 2: Supplemental Evaluation Including Legacy Uses and Associated Disposals of Asbestos*, to be considered as being informative for dose-response analysis, metrics 4 and 5 would need metric ratings of Medium or High. This reference did not satisfy this requirement; therefore data quality evaluation is presented for only for metrics 4 and 5.

Study Citation:	Lin, S., Wang, X., Yu, I. T., Yano, E., Courtice, M., Qiu, H., Wang, M. (2012). Cause-specific mortality in relation to chrysotile-asbestos exposure in a Chinese cohort. Journal of Thoracic Oncology 7(7):1109-1114.
Health Outcome:	Lung Cancer; all cancer mortality, GI cancer mortality; all cause mortality, non-malignant respiratory disease mortality
Target Organ(s):	Gastrointestinal: GI cancer mortality; Cancer/Carcinogenesis: GI cancer mortality, lung cancer mortality, all cancer mortality; Mortality: GI cancer mortality, lung cancer mortality, all cancer mortality, all cause mortality, non-malignant respiratory disease mortality; Lung/Respiratory: lung cancer mortality, non-malignant respiratory disease mortality
Asbestos Fiber Type(s):	Asbestos - Chrysotile (serpentine): 12001-29-5
Linked HERO ID(s):	3078595, 3078782
HERO ID:	3078595

Domain	Metric		Rating	Comments
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Low	In both Lin et al., 2012 (HERO ID 3078595) and Wang et al., 2012 (HERO ID 3078782) worker job titles or workshops are utilized as surrogates for exposure within categories of final SMR results (Lin et al., 2012) and Cox models (Wang et al., 2012). In Lin et al., 2012 (HERO ID 3078595), SMR results were only presented across low, medium and high exposure categories based on exposure measurements conducted only in 2002, with only references to the Wang et al., 2012 (HERO ID 3078782) study. In Wang et al., 2012, authors reference the 2002 measurements made using TEM (referencing a study by Yano et al., 2001 with title ”Longitudinal study of the mortality of lung cancer in chrysotile workers”, which does not exist and may be a misprint or has been replaced by Yano et al., 2001, HERO ID 3080569, entitled ”Cancer Mortality among Workers Exposed to Amphibole-free ChrysotileAsbestos” and found in the same journal).It was not until 2016 when Courtice et al., 2016 (HERO ID 3520560) was conducted with the specific purpose of estimating cumulative fiber exposures in this Chinese asbestos factory worker cohort that exposure from historical dust measures and PCM-analyzed sampling was combined within a formal analysis. In this study they note about the studies at hand: ”In the published studies, however, workers’ job titles or workshops were used as surrogates for exposure. This could have led to potential exposure misclassification and over- or underestimation of the associations. These studies did not consider quantitative estimates of individual exposures, with which one can test hypotheses concerning quantitative exposure–response relationships. The purpose of the present study is to estimate cumulative fiber exposures in this Chinese asbestos factory worker cohort and determine the exposure–response relationships with lung cancer mortality...” (page 370).
	Metric 5:	Exposure Levels	Medium	The range and distribution of exposures summarized within Table 1 of Wang et al., 2012 (HERO ID 3079792) was adequate to develop an exposure response estimate, however these were summary measures for only the year 2002 for a cohort follow-up for outcomes for 37 years. These 2002 measures were only briefly summarized as median levels within the text of in Lin et al., 2012 (HERO ID 3078595).

Additional Comments:	Lin et al., 2012 (HERO ID 3078595) and Wang et al., 2012 (HERO ID 3078782) studied n=577 workers from a chrysotile asbestos textile plant in China, 1972-2008. Both Lin et al., 2012 (HERO ID 3078595) and Wang et al., 2012 (HERO ID 3078782) were not evaluated for any metrics except Metric 4 and 5 as they did not have sufficient exposure information to be useful for dose-response analysis.

** As described in Appendix B.2 of the *White Paper: Quantitative Approach to the Human Health Assessment for the Risk Evaluation for Asbestos Part 2: Supplemental Evaluation Including Legacy Uses and Associated Disposals of Asbestos*, to be considered as being informative for dose-response analysis, metrics 4 and 5 would need metric ratings of Medium or High. This reference did not satisfy this requirement; therefore data quality evaluation is presented for only for metrics 4 and 5.

Study Citation:	Lockey, J. E., Brooks, S. M., Jarabek, A. M., Khoury, P. R., Mckay, R. T., Carson, A., Morrison, J. A., Wiot, J. F., Spitz, H. B. (1984). Pulmonary changes after exposure to vermiculite contaminated with fibrous tremolite. American Review of Respiratory Disease 129(6):952-958.
Health Outcome:	Pulmonary Function/Spirometry Results; Pleural Plaques; Pleural pain; asbestosis symptoms (dyspnea, rales, nail clubbing)
Target Organ(s):	Lung/Respiratory: Dyspnea and pleural painLung function (spirometry, CO diffusing capacity)Rales (lung crackles)Nail clubbing
Asbestos Fiber Type(s):	Asbestos - Tremolite: 14567-73-8; Asbestos - Winchite: 12425-92-2; Asbestos- Richterite: 17068-76-7; Asbestos- Libby amphibole: 1318-09-8
Linked HERO ID(s):	No linked references.
HERO ID:	29685

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Medium	Lockey et al. 1984, 029685 is a retrospective cohort and cross-sectional study of 512 workers conducted in 1980 at a facility that processed Libby vermiculite contaminated with tremolite as an inert carrier. All vermiculite-exposed employees and a group of unexposed workers from the same plant were included (480 males, 32 females; 496 white) and stratified into three exposure groups. Group III/high exposure (n=194, 37.8%) which included vermiculite expanders and plant maintenance workers) was older and had longer duration of employment than the other groups. Concerns: No specific evidence of bias but studying only current employees risks some HWE as susceptible exposed individuals may have had a higher probability to transfer or leave.
	Metric 2:	Attrition	High	Of 530 workers asked to participate, 512 (97%) were included.
	Metric 3:	Comparison Group	Medium	The comparison group comprised workers in the cohort with lower vermiculite exposure. Other exposures were similar to those among the exposed group (particularly for chemical workers in group II). The younger age and shorter duration of work in the comparison vs. exposed group may warrant assessment of confounding.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Medium	Retrospective cumulative fiber exposure (CFE) was characterized using detailed job histories and available fiber counts. Membrane filter samples and PCM was used, counting particles > 5μm in length, <9 μm in diameter, and aspect ratio of 3:1. Concerns: (i) Exposure monitoring was initiated only in 1972; extrapolations to earlier years may be underestimates as no data were available. Protocols were refined over time: measures prior to 1976, when personal breathing zone sampling began, may be less accurate. (ii) Lack of information on extensive overtime worked may underestimate and/or misclassify exposures assigned to individuals. In addition, specific fiber types were not characterized at that time.
	Metric 5:	Exposure Levels	Medium	Three exposure groups were compared, either as CFE (<1, 1-10 and >10 fibers/mL-year) or based on work groups (I, II and III). Mean exposure in these groups further stratified by smoking ranged from 0.35 to 7.55 fibers/mL-year.
	Metric 6:	Temporality	Medium	Sequencing was appropriate. However, mean follow-up (6.6 to 13.3 years by work type and smoking groups) was below the 20+ years estimated for some asbestos-associated lung changes to occur. Only 48 employees were employed for ≥20 years.
Domain 3: Outcome Assessment				

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Study Citation: Lockey, J. E., Brooks, S. M., Jarabek, A. M., Khoury, P. R., Mckay, R. T., Carson, A., Morrison, J. A., Wiot, J. F., Spitz, H. B. (1984). Pulmonary changes after exposure to vermiculite contaminated with fibrous tremolite. American Review of Respiratory Disease 129(6):952-958.
Health Outcome: Pulmonary Function/Spirometry Results; Pleural Plaques; Pleural pain; asbestosis symptoms (dyspnea, rales, nail clubbing)
Target Organ(s): Lung/Respiratory: Dyspnea and pleural painLung function (spirometry, CO diffusing capacity)Rales (lung crackles)Nail clubbing
Asbestos Fiber Type(s): Asbestos - Tremolite: 14567-73-8; Asbestos - Winchite: 12425-92-2; Asbestos- Richterite: 17068-76-7; Asbestos- Libby amphibole: 1318-09-8
Linked HERO ID(s): No linked references.
HERO ID: 29685

Domain	Metric		Rating	Comments
	Metric 7:	Outcome Measurement or Characterization	High	Pulmonary Function/Spirometry Results: Lung function: spirometry and CO diffusing capacity. Assessed by trained staff using ATS criteria and published reference. Measures were repeated if participants had a respiratory infection in the previous 3 weeks or had smoked in the past hour.; Pleural Plaques: Radiographic lung changes (observed in n=22): Chest radiographs were evaluated by two board-certified readers with no knowledge of exposure using modified 1971 ILO criteria. A third reader resolved any lack of consensus, and x-rays were retaken if necessary. Costophrenic angle blunting included separately vs combined with diffuse pleural thickening as in later studies.; Other Non-Cancer Outcomes: (1) Dyspnea: The American Thoracic Society (ATS) questionnaire was modified to ask about pleuritic chest pain (reporting an evaluation by physician). (2) Rales and nail clubbing: A physical exam including breath measures in 4 locations was conducted.
	Metric 8:	Reporting Bias	Medium	The study presented results for all aims and frequently showed details such as numbers of cases and non-cases by exposure category. However, some results were presented only in figures without population numbers.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Medium	Most associations were presented as unadjusted descriptive data, but confounding was also considered. To address confounding, Lockey et al 029685: (i) provided an age-matched case-control comparison of mean CFE for lung change outcomes; (ii) showed pleuritic chest pain prevalence stratified by smoking history as well as asbestos exposure; and (iii) reported results of discriminant analysis accounting for age and smoking for some associations.
	Metric 10:	Covariate Characterization	Medium	Questionnaires and employment records were used.
	Metric 11:	Co-exposure Counfounding	Medium	Lockey et al, RefID 029685 reported that a "careful review of all chemical and physical agents "did not identify any co-exposures at the plant that would be associated with pleural radiographic changes. They also reported that "the study and control populations were evenly matched for exposure history except for the presence or absence of exposure to vermiculite".
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	Medium	Appropriate analyses were used for all studies. Lockey et al, RefID 029685 used discriminant analysis for categorical analysis of covariance for continuous measures. The statistical significance of differences in exposure for age-matched case-control pairs was also evaluated using alternative tests given that the N was small (paired t-tests and non-parametric Wilcoxon rank tests applied).

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Study Citation: Lockey, J. E., Brooks, S. M., Jarabek, A. M., Khoury, P. R., Mckay, R. T., Carson, A., Morrison, J. A., Wiot, J. F., Spitz, H. B. (1984). Pulmonary changes after exposure to vermiculite contaminated with fibrous tremolite. American Review of Respiratory Disease 129(6):952-958.

Health Outcome: Pulmonary Function/Spirometry Results; Pleural Plaques; Pleural pain; asbestosis symptoms (dyspnea, rales, nail clubbing)

Target Organ(s): Lung/Respiratory: Dyspnea and pleural painLung function (spirometry, CO diffusing capacity)Rales (lung crackles)Nail clubbing

Asbestos Fiber Type(s): Asbestos - Tremolite: 14567-73-8; Asbestos - Winchite: 12425-92-2; Asbestos- Richterite: 17068-76-7; Asbestos- Libby amphibole: 1318-09-8

Linked HERO ID(s): No linked references.

HERO ID: 29685

Domain	Metric		Rating	Comments
	Metric 13:	Statistical Power	Medium	The overall N (512) was adequate, but power was limited because the prevalence of lung radiographic changes was low in this first study, in which duration since first exposure was short. Only 2.2% of the sample had significant pleural or parenchymal changes, and 2.2% had costophrenic blunting only.
	Metric 14:	Reproducibility of Analyses	Medium	The analyses presented are reproducible, sufficient detail was provided.
	Metric 15:	Statistical Analysis	Medium	The authors explained the rationale for the statistical methods used (discriminant analysis, ANCOVA, age-matched case-control comparisons) and for the covariates examined (age, smoking). Non-parametric tests were used when Ns were small. It is unclear whether they examined whether transformations to improve linearity or reduce skewness of the cumulative fiber exposure variable would have better met model assumptions.

Additional Comments: This 1980 cohort begins a series of studies on 501 workers from facility that had been processing asbestos-contaminated vermiculite since 1957. The low level of asbestos exposure at the plant was associated with radiographic lung changes, dyspnea, and pleuritic chest pain, but not lung function, rales, or finger clubbing. The 8h time-weighted average exposure among the most exposed workers was 1.5 fibers/mL through 1973 and thereafter 0.375 fibers/mL. Cumulative fiber exposure (CFE) was >10 fibers/mL-years in 9.6% of workers; 10.7% had a 20+-year work duration. Only 22 (4.4%) workers had radiographic lung changes at this time point: prevalence was 2.8%, 3.9% and 5.8% in the low, medium, and high exposure groups. Concerns: (1) Enrolling only current workers limited employment duration and time since first exposure. HWE is possible if susceptible employees were more likely to change jobs over time. Indeed, only 4 of the 7 workers with previously documented benign pleural effusions were enrolled in this study. (2) Misclassification of historic fiber exposure is likely as exposure measurement began only in 1972 and no information on considerable overtime hours was included.Note: Libby ore was later found to contain winchite and richterite along with tremolite.

Overall Quality Determination — Medium

* No biomarkers were identified for this evaluation.

Study Citation:	Loomis, D., Dement, J. M., Elliott, L., Richardson, D., Kuempel, E. D., Stayner, L. (2012). Increased lung cancer mortality among chrysotile asbestos textile workers is more strongly associated with exposure to long thin fibres. Occupational and Environmental Medicine 69(8):564-568.
Health Outcome:	Lung Cancer
Target Organ(s):	Lung/Respiratory: lung cancer mortality; Mortality: lung cancer mortality; Cancer/Carcinogenesis: lung cancer mortality
Asbestos Fiber Type(s):	Asbestos - Chrysotile (serpentine): 12001-29-5; Asbestos - Amosite (grunerite): 12172-73-5; Asbestos - Crocidolite (riebeckite): 12001-28-4
Linked HERO ID(s):	No linked references.
HERO ID:	1257856

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Medium	The study included pooled data from cohorts of people who were employed at any of four textile mills in North Carolina (from 1950 - 1973) and South Carolina (from 1940-1965). This pooled study population included 3717 men and 2419 women. To be included in this study, participants needed to have worked at least 30 days in textile production departments. Recruitment methods are described in previous publications. Additional demographic information such as race, gender, and duration of employment is provided in Elliott et al. 2012 HERO ID: 1247861 (Table 1). Available information does not indicate substantial risk of selection bias.
	Metric 2:	Attrition	High	Elliott et al. 2012 HERO ID: 1247861 stated that loss to follow-up was approximately 7% and that 5% of deaths had an undetermined cause, but this proportion of subjects would not have significantly biased the exposure-outcome relationship.
	Metric 3:	Comparison Group	High	All participants were textile workers from North Carolina and South Carolina who were included based on the same participant selection criteria. Differences in demographic characteristics were considered as potential confounders and were adjusted for in statistical models.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Medium	TEM was used to estimate the distributions of fibers for combinations of plant and department in categories defined by diameter and length, using a stratified random sample of historical dust samples collected from the study plants. The samples were collected from 1964-1971, which is only a small portion of the exposure period. The authors acknowledge this limitation but note that methods of operation did not change during the study period. Poisson regression modelling was used to estimate adjustment factors for each length-diameter category, which were applied to a matrix of "fiber concentrations estimated by the standard PCM method to generate fiber size-specific estimates of exposure". Estimated exposures to fibers were linked to occupational histories to assign individual cumulative exposure in fiber-years/ml.
	Metric 5:	Exposure Levels	Medium	The range and distribution of exposure appear to be sufficient to develop an exposure-response estimate. The distribution of fibers was classified into four diameter-based categories and six length-based categories. Cumulative exposure was estimated as a continuous variable.

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Study Citation: Loomis, D., Dement, J. M., Elliott, L., Richardson, D., Kuempel, E. D., Stayner, L. (2012). Increased lung cancer mortality among chrysotile asbestos textile workers is more strongly associated with exposure to long thin fibres. Occupational and Environmental Medicine 69(8):564-568.
Health Outcome: Lung Cancer
Target Organ(s): Lung/Respiratory: lung cancer mortality; Mortality: lung cancer mortality; Cancer/Carcinogenesis: lung cancer mortality
Asbestos Fiber Type(s): Asbestos - Chrysotile (serpentine): 12001-29-5; Asbestos - Amosite (grunerite): 12172-73-5; Asbestos - Crocidolite (riebeckite): 12001-28-4
Linked HERO ID(s): No linked references.
HERO ID: 1257856

Domain	Metric		Rating	Comments
	Metric 6:	Temporality	High	The exposure precedes the outcome of lung cancer mortality. Participants were followed for vital status until December 31, 2001 and December 31, 2003 for South Carolina and North Carolina workers, respectively. These dates provide more than 15 years of follow-up after the employment end dates of 1973 and 1965, respectively. However, individuals who died of other causes might not have survived long enough to develop lung cancer.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Medium	Lung Cancer: The authors stated ”Causes of death, including underlying cause, immediate causes and other significant conditions, were coded to the International Classification of Diseases in effect at the time of the death.”
	Metric 8:	Reporting Bias	High	Effect estimates are reported with standard errors.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	High	Appropriate adjustments were made to account for potential confounding in the analyses. Models adjusted for age, sex, race, and calendar time.
	Metric 10:	Covariate Characterization	High	Elliott et al. 2012 1247861 stated that occupational histories stemmed from “several sources, including employers’ personnel records, records microfilmed by the USA Public Health Service during the 1960s and records of a state occupational health programme.” Thus, it is likely that covariate data were obtained from these valid sources.
	Metric 11:	Co-exposure Counfounding	Medium	Although co-exposures were not directly assessed in this study, the authors stated that any variation in the strength of the association between asbestos fiber exposure and lung cancer mortality is unlikely to be attributed to co-exposures. The authors stated that mineral oils used for dust control were the only notable co-exposure, but that previous studies indicated that mineral oil exposure was not a confounder of the association between asbestos and lung cancer.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	Medium	The study design chosen was appropriate for the research question. Poisson regression models were utilized in this cohort study.
	Metric 13:	Statistical Power	Medium	The sample size was large enough to detect an association. Statistically significant results were found.
	Metric 14:	Reproducibility of Analyses	Medium	Methods and analyses were described sufficiently to be reproducible.
	Metric 15:	Statistical Analysis	Medium	Methods for calculating risk estimates are clear and model assumptions appear to be met.

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Study Citation:	Loomis, D., Dement, J. M., Elliott, L., Richardson, D., Kuempel, E. D., Stayner, L. (2012). Increased lung cancer mortality among chrysotile asbestos textile workers is more strongly associated with exposure to long thin fibres. Occupational and Environmental Medicine 69(8):564-568.
Health Outcome:	Lung Cancer
Target Organ(s):	Lung/Respiratory: lung cancer mortality; Mortality: lung cancer mortality; Cancer/Carcinogenesis: lung cancer mortality
Asbestos Fiber Type(s):	Asbestos - Chrysotile (serpentine): 12001-29-5; Asbestos - Amosite (grunerite): 12172-73-5; Asbestos - Crocidolite (riebeckite): 12001-28-4
Linked HERO ID(s):	No linked references.
HERO ID:	1257856

Domain	Metric	Rating	Comments
Additional Comments:	The main fiber type in this study is chrysotile, but one plant processed limited amounts of amosite between 1973-1976 and one plant used limited amounts of crocidolite from the 1950s - 1975. This study assessed cohorts from North Carolina and South Carolina that have been assessed in previous publications. This study assessed the association between fiber dimensions (diameter and length) and lung cancer mortality. The study found that cumulative exposures to total fibers and to fibers in every length and diameter category were significantly associated with lung cancer mortality, and the association was stronger for long and thin fibers. The exposure estimation methods are the main limitation of the study, including that the TEM-based exposure estimates were based on historical sampling that had occurred only for a small portion of the study period.		

Overall Quality Determination High

* No biomarkers were identified for this evaluation.

Study Citation:	Loomis, D., Richardson, D. B., Elliott, L. (2019). Quantitative relationships of exposure to chrysotile asbestos and mesothelioma mortality. American Journal of Industrial Medicine 62(6):471-477.
Health Outcome:	Pleural cancer
Target Organ(s):	Cancer/Carcinogenesis: Mortality from pleural cancer and mesothelioma combined (deaths coded as either mesothelioma or cancer of the pleura); Lung/Respiratory: Mortality from pleural cancer and mesothelioma combined (deaths coded as either mesothelioma or cancer of the pleura); Mortality: Mortality from pleural cancer and mesothelioma combined (deaths coded as either mesothelioma or cancer of the pleura)
Asbestos Fiber Type(s):	Asbestos - Chrysotile (serpentine): 12001-29-5
Linked HERO ID(s):	No linked references.
HERO ID:	5160027

Domain		Metric	Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	High	This paper was evaluated for mesothelioma as part of the North Carolina cohort in the Asbestos Part 1 risk evaluation. The criteria for High are met for pleural cancer, because as described in Asbestos Part 1 "Setting and methods of case ascertainment were reported in (Loomis et al., 2009), p. 535-536. Participant selection and inclusion/exclusion criteria varied by study and analysis. Although there were 4 plants in the cohort, exposure data were available only for three of the four, so exposure-response analyses were limited to these three plants. Original selection criteria reported in (Loomis et al., 2009) p 536 (participants had to work at least 1 day between 1950 and 1973) and p 539 (participants excluded due to missing data). (Elliott et al., 2012) evaluated a subset of the cohort that worked >30 days during the same time frame. b. Selection in or out of the study was based on 1) employment in production job during designated time frame and b) availability of necessary data (birth and hire dates; work history; vital status). These criteria are unlikely to result in biased subject participation."
	Metric 2:	Attrition	Medium	This paper was evaluated for mesothelioma as part of the North Carolina cohort in the Asbestos Part 1 risk evaluation. The criteria for Medium are met for pleural cancer, because as described in Asbestos Part 1 "Attrition/missing data exclusions were reported in ((SRC, 2019a) p. 1), ((Loomis et al., 2009) p. 539) and (Elliott et al., 2012) pg 386. The original cohort was 5770 persons; 373 workers at plant 2 were excluded due to lack of exposure data at this plant, 1596 were excluded due to incomplete work histories (at department level) or non-production jobs ((Loomis et al., 2009) p. 539). Final cohort for exposure-response analyses was 3803. Vital status was unknown for 241 of the 3803 (6%) cohort members (suggesting moderate loss to follow up). The subgroup evaluated in (Elliott et al., 2012) consisted of 3082 subjects (excluded persons who worked <30 days); the proportion for whom vital status was missing was not reported for the subgroup."

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Study Citation:	Loomis, D., Richardson, D. B., Elliott, L. (2019). Quantitative relationships of exposure to chrysotile asbestos and mesothelioma mortality. American Journal of Industrial Medicine 62(6):471-477.
Health Outcome:	Pleural cancer
Target Organ(s):	Cancer/Carcinogenesis: Mortality from pleural cancer and mesothelioma combined (deaths coded as either mesothelioma or cancer of the pleura); Lung/Respiratory: Mortality from pleural cancer and mesothelioma combined (deaths coded as either mesothelioma or cancer of the pleura); Mortality: Mortality from pleural cancer and mesothelioma combined (deaths coded as either mesothelioma or cancer of the pleura)
Asbestos Fiber Type(s):	Asbestos - Chrysotile (serpentine): 12001-29-5
Linked HERO ID(s):	No linked references.
HERO ID:	5160027

Domain	Metric		Rating	Comments
	Metric 3:	Comparison Group	High	This paper was evaluated for mesothelioma as part of the North Carolina cohort in the Asbestos Part 1 risk evaluation and was rated as not applicable for mesothelioma. Key elements of the study design for the North Carolina cohort study are reported in Loomis et al., 2009, HERO ID 1257856. Men and women employed for at least one day between 1950 - 1973 in three North Carolina textile mills were included in the present study. A fourth smaller plant that did not process raw fibers was excluded from the present study due to a lack of adequate exposure data. Differences in demographic characteristics were considered as potential confounders and were adjusted for in statistical models.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Medium	This paper was evaluated for mesothelioma as part of the North Carolina cohort in the Asbestos Part 1 risk evaluation. The criteria for Medium are met for pleural cancer, because as described in Asbestos Part 1 "(SRC, 2019a) reports air concentrations and exposure duration by interval of TSFE. Air samples were available for 3 plants covering period from 1935 to 1986 (459 <1950; 1674 from 1950-1969, and 1287 from 1970 forward; (Loomis et al., 2009), p. 536). Measurements used impinger before 1964 and PCM thereafter; paired and concurrent samples between 1964 and 1971 were used to relate impinger to PCM-equivalent concentrations. Air samples were not collected yearly, so mean PCM-equivalent concentrations were estimated by plant, department, job, and time period using multivariate mixed models ((Loomis et al., 2009), p. 536). Individual cumulative exposure assessed using the modeled concentrations and JEM ((Loomis et al., 2009) p 536); details of JEM reported in (Dement et al., 2008)."
	Metric 5:	Exposure Levels	Medium	This paper was evaluated for mesothelioma as part of the North Carolina cohort in the Asbestos Part 1 risk evaluation. The criteria for Medium are met for pleural cancer, because as described in Asbestos Part 1 "(SRC, 2019a) reports air concentrations and exposure durations by interval of TSFE." The authors of the present study note that the study includes "extensive individual exposure estimates, which facilitate a range of exposure-response analyses."
	Metric 6:	Temporality	High	This paper was evaluated for mesothelioma as part of the North Carolina cohort in the Asbestos Part 1 risk evaluation. The criteria for High are met for pleural cancer, because as described in Asbestos Part 1 "Temporality was established (exposure preceded death). (SRC, 2019a) reports cases by interval of TSFE ranging up to 72 years since first exposure."
Domain 3: Outcome Assessment				

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Study Citation:	Loomis, D., Richardson, D. B., Elliott, L. (2019). Quantitative relationships of exposure to chrysotile asbestos and mesothelioma mortality. American Journal of Industrial Medicine 62(6):471-477.
Health Outcome:	Pleural cancer
Target Organ(s):	Cancer/Carcinogenesis: Mortality from pleural cancer and mesothelioma combined (deaths coded as either mesothelioma or cancer of the pleura); Lung/Respiratory: Mortality from pleural cancer and mesothelioma combined (deaths coded as either mesothelioma or cancer of the pleura); Mortality: Mortality from pleural cancer and mesothelioma combined (deaths coded as either mesothelioma or cancer of the pleura)
Asbestos Fiber Type(s):	Asbestos - Chrysotile (serpentine): 12001-29-5
Linked HERO ID(s):	No linked references.
HERO ID:	5160027

Domain	Metric		Rating	Comments
	Metric 7:	Outcome Measurement or Characterization	High	Other Cancer(s): This paper was evaluated for mesothelioma as part of the North Carolina cohort in the Asbestos Part 1 risk evaluation, and was rated as High for mesothelioma with a note that the ”High rating applies to cases assessed with ICD10. For some analyses, the authors pooled these cases with cases coded to cancer of the pleura in ICDs 6-9, which is not considered a reliable measure of mesothelioma outcome. (SRC, 2019a) reports cases assessed with ICD10 by interval of TSFE”. As described in the present study, vital status of the cohort was ascertained using searches of the National Death Index (NDI) and other sources. Cause of death information was coded to the 9th or 10th revision of the ICD for information obtained from NDI-plus and to the ICD in force at the time of death for deaths before 1979. This paper ”fit models for the outcome of pleural cancer combined with mesothelioma (including deaths coded as either mesothelioma or cancer of the pleura), as well as for the outcome of mesothelioma (including only deaths with ICD-10 codes for mesothelioma) in the subcohort of workers who survived until at least 1999”. Thus, the present study includes proper consideration of the coding for pleural cancer and mesothelioma.
	Metric 8:	Reporting Bias	High	This paper was evaluated for mesothelioma as part of the North Carolina cohort in the Asbestos Part 1 risk evaluation. The criteria for High are met for pleural cancer, because as described in Asbestos Part 1 ”(SRC, 2019a) provides mesothelioma cases and person-years at risk by interval of TSFE, including separate reporting of those assessed by ICD10. Mesothelioma cases (with detail of those assessed by ICD10) reported by employment duration in Table 4 of (Loomis et al., 2009) (2 coded cases with 5-10 years employment and 1 coded case each with 10-20 and 20-30 years employment). SMR with CI reported in Table 3 (Loomis et al., 2009). and in (SRC, 2019a) . (Loomis et al., 2009) reports number in cohort, total PY of follow-up, and median duration employment. In (Elliott et al., 2012), Table 1 reports cohort characteristics including age at entry, age at first employment, person years at risk, cumulative exposures, for the subset of workers who were employed at least 30 days (by NC plant and for the whole NC cohort).”
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	High	This paper was evaluated for mesothelioma as part of the North Carolina cohort in the Asbestos Part 1 risk evaluation. The cohort was not rated for mesothelioma for this metric.In the present study, ”all models were adjusted for age at risk (continuous) and race (white or nonwhite)”. The authors reported that ”adjustment for gender had little impact on any model and was omitted from” the final models. Thus, explicit considerations were made for potential confounders.

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Study Citation:	Loomis, D., Richardson, D. B., Elliott, L. (2019). Quantitative relationships of exposure to chrysotile asbestos and mesothelioma mortality. American Journal of Industrial Medicine 62(6):471-477.
Health Outcome:	Pleural cancer
Target Organ(s):	Cancer/Carcinogenesis: Mortality from pleural cancer and mesothelioma combined (deaths coded as either mesothelioma or cancer of the pleura); Lung/Respiratory: Mortality from pleural cancer and mesothelioma combined (deaths coded as either mesothelioma or cancer of the pleura); Mortality: Mortality from pleural cancer and mesothelioma combined (deaths coded as either mesothelioma or cancer of the pleura)
Asbestos Fiber Type(s):	Asbestos - Chrysotile (serpentine): 12001-29-5
Linked HERO ID(s):	No linked references.
HERO ID:	5160027

Domain	Metric		Rating	Comments
	Metric 10:	Covariate Characterization	High	This paper was evaluated for mesothelioma as part of the North Carolina cohort in the Asbestos Part 1 risk evaluation. The cohort was not rated for mesothelioma for this metric.A previous paper from this cohort, Elliott et al. 2012 1247861, stated that occupational histories stemmed from “several sources, including employers’ personnel records, records microfilmed by the USA Public Health Service during the 1960s and records of a state occupational health program.” Thus, it is likely that covariate data were obtained from these valid sources.
	Metric 11:	Co-exposure Counfounding	Low	This paper was evaluated for mesothelioma as part of the North Carolina cohort in the Asbestos Part 1 risk evaluation. The cohort was not rated for mesothelioma for this metric because potential co-exposure confounding is generally not a concern for mesothelioma because there are few potential confounders of the association between asbestos and mesothelioma. In a previous publication from this cohort (Loomis et al. 2012, HERO ID 1257856), The authors stated that mineral oils used for dust control were the only notable co-exposure. It is unclear whether mineral oils are a potential confounder of the association between asbestos exposure and pleural cancer. But in the present study, potential co-exposures were not discussed.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	Medium	This paper was evaluated for mesothelioma as part of the North Carolina cohort in the Asbestos Part 1 risk evaluation. The retrospective cohort design was appropriate to address the research question. The present study used Poisson regression modeling to estimate relationships between asbestos exposure and mortality from pleural cancer and mesothelioma. Thus, the present paper used an appropriate statistical method to address the research question.
	Metric 13:	Statistical Power	Medium	This paper was evaluated for mesothelioma as part of the North Carolina cohort in the Asbestos Part 1 risk evaluation. The cohort was not rated for mesothelioma for this metric. The present analyses included 5397 workers included in analysis, which is a sufficiently large sample size. Although pleural cancer and mesothelioma are rare outcomes, which may have resulted in reduced precision in this study, there was sufficient power to detect an association, as evidenced by the findings of statistically significant associations between asbestos exposure and all pleural cancer (including mesothelioma).
	Metric 14:	Reproducibility of Analyses	Medium	This paper was evaluated for mesothelioma as part of the North Carolina cohort in the Asbestos Part 1 risk evaluation. The cohort was not rated for mesothelioma for this metric in Asbestos Part 1, but it was noted that ”(SRC, 2019a) provides individual data elements allowing independent analysis.” The description of the analysis in the present paper is sufficient to understand how to conceptually reproduce the analysis with access to the analytic data.

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Study Citation:	Loomis, D., Richardson, D. B., Elliott, L. (2019). Quantitative relationships of exposure to chrysotile asbestos and mesothelioma mortality. American Journal of Industrial Medicine 62(6):471-477.
Health Outcome:	Pleural cancer
Target Organ(s):	Cancer/Carcinogenesis: Mortality from pleural cancer and mesothelioma combined (deaths coded as either mesothelioma or cancer of the pleura); Lung/Respiratory: Mortality from pleural cancer and mesothelioma combined (deaths coded as either mesothelioma or cancer of the pleura); Mortality: Mortality from pleural cancer and mesothelioma combined (deaths coded as either mesothelioma or cancer of the pleura)
Asbestos Fiber Type(s):	Asbestos - Chrysotile (serpentine): 12001-29-5
Linked HERO ID(s):	No linked references.
HERO ID:	5160027

Domain	Metric	Rating	Comments
	Metric 15: Statistical Analysis	Medium	This paper was evaluated for mesothelioma as part of the North Carolina cohort in the Asbestos Part 1 risk evaluation. The cohort was not rated for mesothelioma for this metric in Asbestos Part 1. The model for calculating the risk estimates in the present paper is sufficiently transparent.

Additional Comments: This study assessed the outcomes of pleural cancer and mesothelioma. This study was evaluated for mesothelioma as part of the North Carolina cohort in Asbestos Part 1. Therefore an evaluation form for the specific outcome of mesothelioma was not included in this evaluation. This evaluation is for the broader category of pleural cancer, which includes mesothelioma. In Asbestos Part 1, this cohort was rated as High quality for mesothelioma. In this particular study, models were fit ”for the outcome of pleural cancer combined with mesothelioma (including deaths coded as either mesothelioma or cancer of the pleura), as well as for the outcome of mesothelioma (including only deaths with ICD-10 codes for mesothelioma) in the subcohort of workers who survived until at least 1999.” This study assessed associations of mesothelioma and pleural cancer with exposure duration, time since first exposure (TSFE) and cumulative fiber exposure. In addition to fitting Poisson regression models, this study also evaluated a mesothelioma risk model that was developed in the 1980s and used by the EPA and OSHA. This study has several strengths. The authors noted that the study includes ”extensive individual exposure estimates, which facilitate a range of exposure-response analyses.” The main limitations noted by the authors were reduced precision due to the small number of informative deaths, and concerns about the quality of outcome assessment for mesothelioma. The latter concern was addressed in part by the assessment of pleural cancer together with mesothelioma, and the assessment of mesothelioma only as identified by ICD-10. Thus, this study may provide useful dose-response information for pleural cancer and mesothelioma, though most of this information has been captured in the Asbestos Part 1 assessment of mesothelioma.

Overall Quality Determination High

* No biomarkers were identified for this evaluation.

Study Citation:	Loyola, R. C., Carneiro, A. P., Silveira, A. M., La Rocca, P., Nascimento, M. S., Chaves, R. H. (2010). Respiratory effects from industrial talc exposure among former mining workers. Revista de Saude Publica 44(3):541-547.
Health Outcome:	Pulmonary Function/Spirometry Results; Pleural Plaques
Target Organ(s):	Lung/Respiratory: Radiological abnormalities of the pulmonary parenchyma, FVC, FEV1
Asbestos Fiber Type(s):	Asbestos - Actinolite: 12172-67-7; Asbestos - Tremolite: 14567-73-8
Linked HERO ID(s):	No linked references.
HERO ID:	2247973

Domain	Metric		Rating	Comments
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Low	Exposure to asbestos was measured via exposure to talc. The study reports that the Regional Work and Employment Superintendency of Minas Gerais State (SRTE/MG) had been monitoring the mining company since 1993, and in 2000 mineral samples were collected and analyzed to confirm asbestos contaminated talc. Exposure score were created from ”qualitative information on the environment and working conditions” obtained from company experts, and these scores were computed into an index for cumulative exposure to talc by multiplying the exposure score by the length of time in years of exposure for each work position. Due to the lack of details regarding how asbestos fibers within talc were quantified, it is likely that there is exposure misclassification.
	Metric 5:	Exposure Levels	Medium	Exposure was modeled continuously in statistical analyses. The cumulative talc exposure index ranges from 0 to 100, which is likely large enough to allow for sufficient contrast.

Additional Comments: This study was not fully evaluated because metric 4 was rated as low, due to no explicit mention in the study or cited sources about the use of PCM or TEM.

* No biomarkers were identified for this evaluation.

** As described in Appendix B.2 of the *White Paper: Quantitative Approach to the Human Health Assessment for the Risk Evaluation for Asbestos Part 2: Supplemental Evaluation Including Legacy Uses and Associated Disposals of Asbestos*, to be considered as being informative for dose-response analysis, metrics 4 and 5 would need metric ratings of Medium or High. This reference did not satisfy this requirement; therefore data quality evaluation is presented for only for metrics 4 and 5.

Study Citation:	Luberto, F., Ferrante, D., Silvestri, S., Angelini, A., Cuccaro, F., Nannavecchia, A. M., Oddone, E., Vicentini, M., Barone-Adesi, F., Cena, T. (2019). Cumulative asbestos exposure and mortality from asbestos related diseases in a pooled analysis of 21 asbestos cement cohorts in Italy. Environmental Health: A Global Access Science Source 18(1):71.
Health Outcome:	Lung Cancer; Ovarian Cancer; Laryngeal Cancer; stomach, colon, rectum, peritoneum, pleura, liver, pancreas, uterus, kidney, bladder, lip, oral cavity, pharynx, esophagus, small intestine; Asbestosis; psychiatric diseases, neurological dieases, cardiovascular disease, bronchitis, emphysema, asthma, accidents, and violence, genitourinary diseases, other pneumoconioses
Target Organ(s):	Gastrointestinal: malignant neoplasm stomach mortality, malignant neoplasm colon mortality, malignant neoplasm rectum mortality, malignant neoplasm peritoneum mortality, digestive disease mortality, malignant neoplasm esophagus mortality, malignant neoplasm digestive organs (including peritoneum) mortality, malignant neoplasm small intestine mortality; Cancer/Carcinogenesis: malignant neoplasm stomach mortality, malignant neoplasm colon mortality, malignant neoplasm rectum mortality, malignant neoplasm peritoneum mortality, malignant neoplasm respiratory organs mortality, malignant neoplasm larynx mortality, malignant neoplasm lung mortality, malignant neoplasm pleura mortality, malignant neoplasm ovary mortality, malignant neoplasm lip, oral cavity, and pharynx mortality, malignant neoplasm esophagus mortality, malignant neoplasm digestive organs (including peritoneum) mortality, malignant neoplasm small intestine mortality, malignant neoplasm liver and intrahepatic bile ducts mortality, malignant neoplasm nose and paranasal sinuses mortality, malignant neoplasm prostate mortality, malignant neoplasm bladder mortality, malignant neoplasm eye and nervous system mortality, malignant neoplasm uterus mortality, malignant neoplasm ovaries mortality, Malignant neoplasm mortality, Leukemia and lymphoma mortality, Malignant neoplasm unspecified site mortality; Mortality: malignant neoplasm stomach mortality, malignant neoplasm colon mortality, malignant neoplasm rectum mortality, malignant neoplasm peritoneum mortality, malignant neoplasm respiratory organs mortality, malignant neoplasm larynx mortality, malignant neoplasm lung mortality, malignant neoplasm pleura mortality, Respiratory diseases mortality, Bronchitis, emphysema, asthma mortality, asbestosis mortality, cardiovascular disease mortality, digestive disease mortality, accidental and violent mortality, malignant neoplasm ovary mortality, malignant neoplasm lip, oral cavity, and pharynx mortality, malignant neoplasm esophagus mortality, malignant neoplasm digestive organs (including peritoneum) mortality, malignant neoplasm small intestine mortality, malignant neoplasm liver and intrahepatic bile ducts mortality, malignant neoplasm nose and paranasal sinuses mortality, malignant neoplasm prostate mortality, malignant neoplasm bladder mortality, malignant neoplasm kidney mortality, malignant neoplasm eye and nervous system mortality, psychiatric diseases mortality, neurological diseases mortality, ischemic heart diseases mortality, myocardial infarction mortality, malignant neoplasm uterus mortality, malignant neoplasm ovaries mortality, All causes mortality, Malignant neoplasm mortality, Unknown causes mortality, Leukemia and lymphoma mortality, Malignant neoplasm unspecified site mortality, Genitourinary diseases mortality, Other pneumoconioses mortality, Poorly specified causes mortality; Lung/Respiratory: malignant neoplasm respiratory organs mortality, malignant neoplasm larynx mortality, malignant neoplasm lung mortality, malignant neoplasm pleura mortality, Respiratory diseases mortality, Bronchitis, emphysema, asthma mortality, asbestosis mortality, malignant neoplasm nose and paranasal sinuses mortality, Other pneumoconioses mortality; Cardiovascular: cardiovascular disease mortality, ischemic heart diseases mortality, myocardial infarction mortality; unspecified: accidental and violent mortality; Reproductive/Developmental: malignant neoplasm ovary mortality, malignant neoplasm prostate mortality, malignant neoplasm uterus mortality, malignant neoplasm ovaries mortality, Genitourinary diseases mortality; Head/face: malignant neoplasm lip, oral cavity, and pharynx mortality; Hepatic/Liver: malignant neoplasm liver and intrahepatic bile ducts mortality; Renal/Kidney: malignant neoplasm bladder mortality, malignant neoplasm kidney mortality; Neurological/Behavioral: malignant neoplasm eye and nervous system mortality, psychiatric diseases mortality, neurological diseases mortality; circulatory: Leukemia and lymphoma mortality
Asbestos Fiber Type(s):	Asbestos - Amosite (grunerite): 12172-73-5; Asbestos - Chrysotile (serpentine): 12001-29-5; Asbestos - Crocidolite (riebeckite): 12001-28-4
Linked HERO ID(s):	6868486, 7460047
HERO ID:	6868486

Domain	Metric	Rating	Comments
Domain 2: Exposure Characterization			

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Study Citation:	Luberto, F., Ferrante, D., Silvestri, S., Angelini, A., Cuccaro, F., Nannavecchia, A. M., Oddone, E., Vicentini, M., Barone-Adesi, F., Cena, T. (2019). Cumulative asbestos exposure and mortality from asbestos related diseases in a pooled analysis of 21 asbestos cement cohorts in Italy. Environmental Health: A Global Access Science Source 18(1):71.
Health Outcome:	Lung Cancer; Ovarian Cancer; Laryngeal Cancer; stomach, colon, rectum, peritoneum, pleura, liver, pancreas, uterus, kidney, bladder, lip, oral cavity, pharynx, esophagus, small intestine; Asbestosis; psychiatric diseases, neurological dieases, cardiovascular disease, bronchitis, emphysema, asthma, accidents, and violence, genitourinary diseases, other pneumoconioses
Target Organ(s):	Gastrointestinal: malignant neoplasm stomach mortality, malignant neoplasm colon mortality, malignant neoplasm rectum mortality, malignant neoplasm peritoneum mortality, digestive disease mortality, malignant neoplasm esophagus mortality, malignant neoplasm digestive organs (including peritoneum) mortality, malignant neoplasm small intestine mortality; Cancer/Carcinogenesis: malignant neoplasm stomach mortality, malignant neoplasm colon mortality, malignant neoplasm rectum mortality, malignant neoplasm peritoneum mortality, malignant neoplasm respiratory organs mortality, malignant neoplasm larynx mortality, malignant neoplasm lung mortality, malignant neoplasm pleura mortality, malignant neoplasm ovary mortality, malignant neoplasm lip, oral cavity, and pharynx mortality, malignant neoplasm esophagus mortality, malignant neoplasm digestive organs (including peritoneum) mortality, malignant neoplasm small intestine mortality, malignant neoplasm liver and intrahepatic bile ducts mortality, malignant neoplasm nose and paranasal sinuses mortality, malignant neoplasm prostate mortality, malignant neoplasm bladder mortality, malignant neoplasm eye and nervous system mortality, malignant neoplasm uterus mortality, malignant neoplasm ovaries mortality, Malignant neoplasm mortality, Leukemia and lymphoma mortality, Malignant neoplasm unspecified site mortality; Mortality: malignant neoplasm stomach mortality, malignant neoplasm colon mortality, malignant neoplasm rectum mortality, malignant neoplasm peritoneum mortality, malignant neoplasm respiratory organs mortality, malignant neoplasm larynx mortality, malignant neoplasm lung mortality, malignant neoplasm pleura mortality, Respiratory diseases mortality, Bronchitis, emphysema, asthma mortality, asbestosis mortality, cardiovascular disease mortality, digestive disease mortality, accidental and violent mortality, malignant neoplasm ovary mortality, malignant neoplasm lip, oral cavity, and pharynx mortality, malignant neoplasm esophagus mortality, malignant neoplasm digestive organs (including peritoneum) mortality, malignant neoplasm small intestine mortality, malignant neoplasm liver and intrahepatic bile ducts mortality, malignant neoplasm nose and paranasal sinuses mortality, malignant neoplasm prostate mortality, malignant neoplasm bladder mortality, malignant neoplasm kidney mortality, malignant neoplasm eye and nervous system mortality, psychiatric diseases mortality, neurological diseases mortality, ischemic heart diseases mortality, myocardial infarction mortality, malignant neoplasm uterus mortality, malignant neoplasm ovaries mortality, All causes mortality, Malignant neoplasm mortality, Unknown causes mortality, Leukemia and lymphoma mortality, Malignant neoplasm unspecified site mortality, Genitourinary diseases mortality, Other pneumoconioses mortality, Poorly specified causes mortality; Lung/Respiratory: malignant neoplasm respiratory organs mortality, malignant neoplasm larynx mortality, malignant neoplasm lung mortality, malignant neoplasm pleura mortality, Respiratory diseases mortality, Bronchitis, emphysema, asthma mortality, asbestosis mortality, malignant neoplasm nose and paranasal sinuses mortality, Other pneumoconioses mortality; Cardiovascular: cardiovascular disease mortality, ischemic heart diseases mortality, myocardial infarction mortality; unspecified: accidental and violent mortality; Reproductive/Developmental: malignant neoplasm ovary mortality, malignant neoplasm prostate mortality, malignant neoplasm uterus mortality, malignant neoplasm ovaries mortality, Genitourinary diseases mortality; Head/face: malignant neoplasm lip, oral cavity, and pharynx mortality; Hepatic/Liver: malignant neoplasm liver and intrahepatic bile ducts mortality; Renal/Kidney: malignant neoplasm bladder mortality, malignant neoplasm kidney mortality; Neurological/Behavioral: malignant neoplasm eye and nervous system mortality, psychiatric diseases mortality, neurological diseases mortality; circulatory: Leukemia and lymphoma mortality
Asbestos Fiber Type(s):	Asbestos - Amosite (grunerite): 12172-73-5; Asbestos - Chrysotile (serpentine): 12001-29-5; Asbestos - Crocidolite (riebeckite): 12001-28-4
Linked HERO ID(s):	6868486, 7460047
HERO ID:	6868486

Domain	Metric		Rating	Comments
	Metric 4:	Measurement of Exposure	Low	This metric is rated Low because neither study explicitly mentions the use of PCM or TEM. In Luberto et al., 2019, HERO ID 6868486, there is no mention of microscopy of citation of methods paper that would give details. In Magnani et al., 2020, HERO ID 7460047, authors mention optical microscopy: ”The experts estimated for each plant and year the proportion of exposed workers, the percentage of time in asbestos exposing tasks and the minimum and maximumconcentrations of asbestos airborne fibres (f/ml, from data measured in optical microscopy), for direct and indirect exposure separately.” In addition, both studies rely heavily on expert judgment to develop exposure estimates.

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Study Citation: Luberto, F., Ferrante, D., Silvestri, S., Angelini, A., Cuccaro, F., Nannavecchia, A. M., Oddone, E., Vicentini, M., Barone-Adesi, F., Cena, T. (2019). Cumulative asbestos exposure and mortality from asbestos related diseases in a pooled analysis of 21 asbestos cement cohorts in Italy. Environmental Health: A Global Access Science Source 18(1):71.

Health Outcome: Lung Cancer; Ovarian Cancer; Laryngeal Cancer; stomach, colon, rectum, peritoneum, pleura, liver, pancreas, uterus, kidney, bladder, lip, oral cavity, pharynx, esophagus, small intestine; Asbestosis; psychiatric diseases, neurological dieases, cardiovascular disease, bronchitis, emphysema, asthma, accidents, and violence, genitourinary diseases, other pneumoconioses

Target Organ(s): Gastrointestinal: malignant neoplasm stomach mortality, malignant neoplasm colon mortality, malignant neoplasm rectum mortality, malignant neoplasm peritoneum mortality, digestive disease mortality, malignant neoplasm esophagus mortality, malignant neoplasm digestive organs (including peritoneum) mortality, malignant neoplasm small intestine mortality; Cancer/Carcinogenesis: malignant neoplasm stomach mortality, malignant neoplasm colon mortality, malignant neoplasm rectum mortality, malignant neoplasm peritoneum mortality, malignant neoplasm respiratory organs mortality, malignant neoplasm larynx mortality, malignant neoplasm lung mortality, malignant neoplasm pleura mortality, malignant neoplasm ovary mortality, malignant neoplasm lip, oral cavity, and pharynx mortality, malignant neoplasm esophagus mortality, malignant neoplasm digestive organs (including peritoneum) mortality, malignant neoplasm small intestine mortality, malignant neoplasm liver and intrahepatic bile ducts mortality, malignant neoplasm nose and paranasal sinuses mortality, malignant neoplasm prostate mortality, malignant neoplasm bladder mortality, malignant neoplasm eye and nervous system mortality, malignant neoplasm uterus mortality, malignant neoplasm ovaries mortality, Malignant neoplasm mortality, Leukemia and lymphoma mortality, Malignant neoplasm unspecified site mortality; Mortality: malignant neoplasm stomach mortality, malignant neoplasm colon mortality, malignant neoplasm rectum mortality, malignant neoplasm peritoneum mortality, malignant neoplasm respiratory organs mortality, malignant neoplasm larynx mortality, malignant neoplasm lung mortality, malignant neoplasm pleura mortality, Respiratory diseases mortality, Bronchitis, emphysema, asthma mortality, asbestosis mortality, cardiovascular disease mortality, digestive disease mortality, accidental and violent mortality, malignant neoplasm ovary mortality, malignant neoplasm lip, oral cavity, and pharynx mortality, malignant neoplasm esophagus mortality, malignant neoplasm digestive organs (including peritoneum) mortality, malignant neoplasm small intestine mortality, malignant neoplasm liver and intrahepatic bile ducts mortality, malignant neoplasm nose and paranasal sinuses mortality, malignant neoplasm prostate mortality, malignant neoplasm bladder mortality, malignant neoplasm kidney mortality, malignant neoplasm eye and nervous system mortality, psychiatric diseases mortality, neurological diseases mortality, ischemic heart diseases mortality, myocardial infarction mortality, malignant neoplasm uterus mortality, malignant neoplasm ovaries mortality, All causes mortality, Malignant neoplasm mortality, Unknown causes mortality, Leukemia and lymphoma mortality, Malignant neoplasm unspecified site mortality, Genitourinary diseases mortality, Other pneumoconioses mortality, Poorly specified causes mortality; Lung/Respiratory: malignant neoplasm respiratory organs mortality, malignant neoplasm larynx mortality, malignant neoplasm lung mortality, malignant neoplasm pleura mortality, Respiratory diseases mortality, Bronchitis, emphysema, asthma mortality, asbestosis mortality, malignant neoplasm nose and paranasal sinuses mortality, Other pneumoconioses mortality; Cardiovascular: cardiovascular disease mortality, ischemic heart diseases mortality, myocardial infarction mortality; unspecified: accidental and violent mortality; Reproductive/Developmental: malignant neoplasm ovary mortality, malignant neoplasm prostate mortality, malignant neoplasm uterus mortality, malignant neoplasm ovaries mortality, Genitourinary diseases mortality; Head/face: malignant neoplasm lip, oral cavity, and pharynx mortality; Hepatic/Liver: malignant neoplasm liver and intrahepatic bile ducts mortality; Renal/Kidney: malignant neoplasm bladder mortality, malignant neoplasm kidney mortality; Neurological/Behavioral: malignant neoplasm eye and nervous system mortality, psychiatric diseases mortality, neurological diseases mortality; circulatory: Leukemia and lymphoma mortality

Asbestos Fiber Type(s): Asbestos - Amosite (grunerite): 12172-73-5; Asbestos - Chrysotile (serpentine): 12001-29-5; Asbestos - Crocidolite (riebeckite): 12001-28-4

Linked HERO ID(s): 6868486, 7460047

HERO ID: 6868486

Domain	Metric		Rating	Comments
	Metric 5:	Exposure Levels	Medium	The range and distribution of exposure is sufficient to develop an exposure-response estimate and the included analyses are stratified by three levels of exposure (Luberto et al., 2019, HERO ID 6868486). In Magnani et al., 2020, HERO ID 7460047, there are only 2 exposure categories for SMR analyses.

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Study Citation:	Luberto, F., Ferrante, D., Silvestri, S., Angelini, A., Cuccaro, F., Nannavecchia, A. M., Oddone, E., Vicentini, M., Barone-Adesi, F., Cena, T. (2019). Cumulative asbestos exposure and mortality from asbestos related diseases in a pooled analysis of 21 asbestos cement cohorts in Italy. Environmental Health: A Global Access Science Source 18(1):71.
Health Outcome:	Lung Cancer; Ovarian Cancer; Laryngeal Cancer; stomach, colon, rectum, peritoneum, pleura, liver, pancreas, uterus, kidney, bladder, lip, oral cavity, pharynx, esophagus, small intestine; Asbestosis; psychiatric diseases, neurological dieases, cardiovascular disease, bronchitis, emphysema, asthma, accidents, and violence, genitourinary diseases, other pneumoconioses
Target Organ(s):	Gastrointestinal: malignant neoplasm stomach mortality, malignant neoplasm colon mortality, malignant neoplasm rectum mortality, malignant neoplasm peritoneum mortality, digestive disease mortality, malignant neoplasm esophagus mortality, malignant neoplasm digestive organs (including peritoneum) mortality, malignant neoplasm small intestine mortality; Cancer/Carcinogenesis: malignant neoplasm stomach mortality, malignant neoplasm colon mortality, malignant neoplasm rectum mortality, malignant neoplasm peritoneum mortality, malignant neoplasm respiratory organs mortality, malignant neoplasm larynx mortality, malignant neoplasm lung mortality, malignant neoplasm pleura mortality, malignant neoplasm ovary mortality, malignant neoplasm lip, oral cavity, and pharynx mortality, malignant neoplasm esophagus mortality, malignant neoplasm digestive organs (including peritoneum) mortality, malignant neoplasm small intestine mortality, malignant neoplasm liver and intrahepatic bile ducts mortality, malignant neoplasm nose and paranasal sinuses mortality, malignant neoplasm prostate mortality, malignant neoplasm bladder mortality, malignant neoplasm eye and nervous system mortality, malignant neoplasm uterus mortality, malignant neoplasm ovaries mortality, Malignant neoplasm mortality, Leukemia and lymphoma mortality, Malignant neoplasm unspecified site mortality; Mortality: malignant neoplasm stomach mortality, malignant neoplasm colon mortality, malignant neoplasm rectum mortality, malignant neoplasm peritoneum mortality, malignant neoplasm respiratory organs mortality, malignant neoplasm larynx mortality, malignant neoplasm lung mortality, malignant neoplasm pleura mortality, Respiratory diseases mortality, Bronchitis, emphysema, asthma mortality, asbestosis mortality, cardiovascular disease mortality, digestive disease mortality, accidental and violent mortality, malignant neoplasm ovary mortality, malignant neoplasm lip, oral cavity, and pharynx mortality, malignant neoplasm esophagus mortality, malignant neoplasm digestive organs (including peritoneum) mortality, malignant neoplasm small intestine mortality, malignant neoplasm liver and intrahepatic bile ducts mortality, malignant neoplasm nose and paranasal sinuses mortality, malignant neoplasm prostate mortality, malignant neoplasm bladder mortality, malignant neoplasm kidney mortality, malignant neoplasm eye and nervous system mortality, psychiatric diseases mortality, neurological diseases mortality, ischemic heart diseases mortality, myocardial infarction mortality, malignant neoplasm uterus mortality, malignant neoplasm ovaries mortality, All causes mortality, Malignant neoplasm mortality, Unknown causes mortality, Leukemia and lymphoma mortality, Malignant neoplasm unspecified site mortality, Genitourinary diseases mortality, Other pneumoconioses mortality, Poorly specified causes mortality; Lung/Respiratory: malignant neoplasm respiratory organs mortality, malignant neoplasm larynx mortality, malignant neoplasm lung mortality, malignant neoplasm pleura mortality, Respiratory diseases mortality, Bronchitis, emphysema, asthma mortality, asbestosis mortality, malignant neoplasm nose and paranasal sinuses mortality, Other pneumoconioses mortality; Cardiovascular: cardiovascular disease mortality, ischemic heart diseases mortality, myocardial infarction mortality; unspecified: accidental and violent mortality; Reproductive/Developmental: malignant neoplasm ovary mortality, malignant neoplasm prostate mortality, malignant neoplasm uterus mortality, malignant neoplasm ovaries mortality, Genitourinary diseases mortality; Head/face: malignant neoplasm lip, oral cavity, and pharynx mortality; Hepatic/Liver: malignant neoplasm liver and intrahepatic bile ducts mortality; Renal/Kidney: malignant neoplasm bladder mortality, malignant neoplasm kidney mortality; Neurological/Behavioral: malignant neoplasm eye and nervous system mortality, psychiatric diseases mortality, neurological diseases mortality; circulatory: Leukemia and lymphoma mortality
Asbestos Fiber Type(s):	Asbestos - Amosite (grunerite): 12172-73-5; Asbestos - Chrysotile (serpentine): 12001-29-5; Asbestos - Crocidolite (riebeckite): 12001-28-4
Linked HERO ID(s):	6868486, 7460047
HERO ID:	6868486

Domain	Metric	Rating	Comments
Additional Comments:	HEROIDs 7460047 and 6868486 were not QC'd for any metrics except 4 and 5 and had no data extracted because they did not have sufficient information to confirm the use of TEM or PCM and thus did not have sufficient information to be useful for dose-response analysis.		

** As described in Appendix B.2 of the *White Paper: Quantitative Approach to the Human Health Assessment for the Risk Evaluation for Asbestos Part 2: Supplemental Evaluation Including Legacy Uses and Associated Disposals of Asbestos*, to be considered as being informative for dose-response analysis, metrics 4 and 5 would need metric ratings of Medium or High. This reference did not satisfy this requirement; therefore data quality evaluation is presented for only for metrics 4 and 5.

Study Citation:	Matrat, M., Guida, F., Cénée, S., Févotte, J., Carton, M., Cyr, D., Menvielle, G., Paget-Bailly, S., Radoï, L., Schmaus, A., Bara, S., Velten, M., Luce, D., Stücker, I., The Icare Study Group, I. (2015). Occupational Exposure to Diesel Motor Exhaust and Lung Cancer: A Dose-Response Relationship Hidden by Asbestos Exposure Adjustment? The ICARE Study. Journal of Cancer Epidemiology 2015:879302.
Health Outcome:	Lung Cancer
Target Organ(s):	Lung/Respiratory: Lung cancer; Cancer/Carcinogenesis: Lung cancer
Asbestos Fiber Type(s):	Asbestos - Not specified: 1332-21-4
Linked HERO ID(s):	3077711, 6748863
HERO ID:	3077711

Domain		Metric	Rating	Comments
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Low	This metric is rated Low because the studies or any cited methods source do not explicitly mention the use of PCM or TEM. Exposure for workers was assigned by a JEM described in Févotte et al. 2011 (HERO ID: 2571088). However, the methods there do not descibe how the exact JEM used in the present cohort was created, and do not cite any sources providing data on sampling or quantification methods. The only sources cited for details are in French and thus were not able to be evaluated by the EPA QC team.
	Metric 5:	Exposure Levels	Medium	The distribution of exposure appears to be sufficient to develop an exposure-response estimate. Cumulative exposure was calculated in Matrat et al., 2015 307711 . Lévêque et al., 2018 6748863 measured the association based on a "1 fiber/ml difference in the annual average daily intensity each year of the specific exposure time-window."

Additional Comments: Matrat et al., 2015 307711 and Lévêque et al., 2018 6748863 were not evaluated for any metrics except Metric 4 and 5 and had no data extracted because they did not have sufficient exposure information to be useful for dose-response analysis.

** As described in Appendix B.2 of the *White Paper: Quantitative Approach to the Human Health Assessment for the Risk Evaluation for Asbestos Part 2: Supplemental Evaluation Including Legacy Uses and Associated Disposals of Asbestos*, to be considered as being informative for dose-response analysis, metrics 4 and 5 would need metric ratings of Medium or High. This reference did not satisfy this requirement; therefore data quality evaluation is presented for only for metrics 4 and 5.

Study Citation:	Matrat, M., Pairon, J. C., Paolillo, A. G., Joly, N., Iwatsubo, Y., Orlowski, E., Letourneux, M., Ameille, J. (2004). Asbestos exposure and radiological abnormalities among maintenance and custodian workers in buildings with friable asbestos-containing materials. International Archives of Occupational and Environmental Health 77(5):307-312.
Health Outcome:	Circumscribed pleural thickening, diffuse pleural thickening, Pleural thickening , small opacity profusions
Target Organ(s):	Lung/Respiratory: Pleural thickening, Small opacities profusion, Circumscribed pleural thickening, Diffuse pleural thickening
Asbestos Fiber Type(s):	Asbestos - Not specified: 1332-21-4
Linked HERO ID(s):	No linked references.
HERO ID:	3080192

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Medium	Key elements of the study design are described in the Matrat et al., 2004 study (Matrat et al. 2004, HERO ID: 3080192) which measures asbestos exposure and radiological abnormalities in male and female maintenance workers. Male and female participants (n=336) of (Matrat et al. 2004, HERO ID: 3080192) were aged an average of 44.1 +/- 7.5 and latency began at less than or equal to 15 years since exposure, 16-22 years, and greater than 22 years. Study participants complete a standardized questionnaire regarding their work history, types of asbestos containing materials (ACMs), and other work-related questions. All participants were volunteers.
	Metric 2:	Attrition	High	Studu functioned on a voluntary basis. (Matrat et al. 2004, HERO ID: 3080192) described that 80% of eligible subjects participated, and that some subject loss occurred due to poor quality x-ray imaging and previous asbestos exposure from other activities.
	Metric 3:	Comparison Group	High	95 controls who were male workers in a public hospital with no known asbestos exposures participated in the parent study (Matrat et al. 2004, HERO ID: 3080192). These controls also received chest radiographs, same as the exposure group.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Medium	Matrat et al. referenced their measurements of exposure from the French Evalutil database for specific occupational exposures to find fibre concentrations to estimate the intensity and to create a cumulative exposure index (Matrat et al. 2004, HERO ID: 3080192). An article for the French Evalutil database describes all data from before 2012 as using studies which followed the standards of the time, expertise, and that most air samples were taken with ”membrane filters and analyzed by phase-contrast optical microscopy (PCOM)” (Orlowski et al. 2015, HERO ID: 3089885).
	Metric 5:	Exposure Levels	Medium	Matrat et al. reports a referent group and exposure group distributed by latency or cumulative exposure index (f/mL*years) (Matrat et al. 2004, HERO ID: 3080192).
	Metric 6:	Temporality	High	Matrat et al. reports latency as <=15 years, 16-22 years, and >22 years, which is adequate for the health outcomes evaluated (Matrat et al. 2004, HERO ID: 3080192).
Domain 3: Outcome Assessment				

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Study Citation:	Matrat, M., Pairon, J. C., Paolillo, A. G., Joly, N., Iwatsubo, Y., Orlowski, E., Letourneux, M., Ameille, J. (2004). Asbestos exposure and radiological abnormalities among maintenance and custodian workers in buildings with friable asbestos-containing materials. International Archives of Occupational and Environmental Health 77(5):307-312.
Health Outcome:	Circumscribed pleural thickening, diffuse pleural thickening, Pleural thickening , small opacity profusions
Target Organ(s):	Lung/Respiratory: Pleural thickening, Small opacities profusion, Circumscribed pleural thickening, Diffuse pleural thickening
Asbestos Fiber Type(s):	Asbestos - Not specified: 1332-21-4
Linked HERO ID(s):	No linked references.
HERO ID:	3080192

Domain	Metric		Rating	Comments
	Metric 7:	Outcome Measurement or Characterization	High	Other Non-Cancer Outcomes: Pleural thickening(s): Matrat et al. reports that all chest radiographs were "classified independently by three expereicned readers according to the International Labour Office (ILO) 1980" in random order. This includes profusions of small opacities, circumscribed pleural thickening, and diffuse pleural thickening (Matrat et al. 2004, HERO ID: 3080192).
	Metric 8:	Reporting Bias	High	Findings are appropriately reported (Matrat et al. 2004, HERO ID: 3080192) and extraction is possible. Confidence intervals of 95% are reported where multivariate logistic regression analysis was completed in the exposed groups for an adjusted odds ratio.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Medium	For the multiple logistic regression in (Matrat et al. 2004, HERO ID: 3080192), three models are created to analyze the exposure group. Model A measures by latency with age, BMI and tobacco smoking; Model B measures duration of asbestos exposure by age, BMI and tobacco smoking; and Model C measures cumulative exposure index by age, BMI and tobacco smoking.
	Metric 10:	Covariate Characterization	Medium	(Matrat et al. 2004, HERO ID: 3080192) report using a standardized questionnaire to collect information on volunteers regarding their work history, including areas where they worked, detailed list of tasks, duration (years), frequency (number of days a year and number of hours a day) where exposure occurred.The authors only mentioned that detailed information was obtained on tobacco consumption and height and weight were measured to calculate BMI, but they did not describe the information source.
	Metric 11:	Co-exposure Counfounding	Low	In an occupational setting, potential co-exposures are not discussed. This is relevant for (Matrat et al. 2004, HERO ID: 3080192).
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	Medium	(Matrat et al. 2004, HERO ID: 3080192) used an appropriate study design to address the research question with a multivariate logistic regression.
	Metric 13:	Statistical Power	Medium	The number of participants was adequate to detect an effect in the exposure group.
	Metric 14:	Reproducibility of Analyses	Medium	(Matrat et al. 2004, HERO ID: 3080192) provided adequate methodology to understand how to conceptually reproduce analyses.
	Metric 15:	Statistical Analysis	Medium	(Matrat et al. 2004, HERO ID: 3080192) provided transparent methods for the multivariate logistic regression, organized by three models (A, B, and C) and provided the covariates used in each analysis.

Additional Comments: None

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Study Citation:	Matrat, M., Pairon, J. C., Paolillo, A. G., Joly, N., Iwatsubo, Y., Orlowski, E., Letourneux, M., Ameille, J. (2004). Asbestos exposure and radiological abnormalities among maintenance and custodian workers in buildings with friable asbestos-containing materials. International Archives of Occupational and Environmental Health 77(5):307-312.
Health Outcome:	Circumscribed pleural thickening, diffuse pleural thickening, Pleural thickening , small opacity profusions
Target Organ(s):	Lung/Respiratory: Pleural thickening, Small opacities profusion, Circumscribed pleural thickening, Diffuse pleural thickening
Asbestos Fiber Type(s):	Asbestos - Not specified: 1332-21-4
Linked HERO ID(s):	No linked references.
HERO ID:	3080192

Domain	Metric	Rating	Comments
Overall Quality Determination		**Medium**	

* No biomarkers were identified for this evaluation.

Study Citation:	McCredie, M., Stewart, J. H. (1993). Risk factors for kidney cancer in New South Wales. IV. Occupation. British Journal of Industrial Medicine 50(4):349-354.
Health Outcome:	Renal cell and renal pelvic cancer (kidney cancer)
Target Organ(s):	Cancer/Carcinogenesis: Renal cell cancer, Renal pelvic cancer; Renal/Kidney: Renal cell cancer, Renal pelvic cancer
Asbestos Fiber Type(s):	Asbestos - Not specified: 1332-21-4
Linked HERO ID(s):	No linked references.
HERO ID:	630760

Domain	Metric		Rating	Comments
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Low	Measures of exposure were generated using professional judgment based on responses to the interviews and questionnaires administered. Because there were no quantitative measures of asbestos exposure, this metric was rated as uninformative. However, there could be some utility for this study qualitatively.This metric is rated low because the study or any cited methods sources does not use PCM or TEM.
	Metric 5:	Exposure Levels	Low	Because the authors used professional judgment and responses to questionnaires to determine asbestos exposure, individuals were only ranked as exposed or unexposed.

Additional Comments: There are several limitations of this study that are important to note. For one, there were no quantitative measures of exposure to asbestos. The information gathered through the self-report interviews may also be questionable, as even the authors highlight that there was no validation of the exposures reported. This could introduce a certain level of bias to the results. While asbestos was one of the exposures examined, it was not the sole focus of this study.NOTE: Based on the new guidance, this study would not have been evaluated past metric 4 and 5. There was no mention within the study or cited sources that mentioned the use of PCM or TEM.

* No biomarkers were identified for this evaluation.

** As described in Appendix B.2 of the *White Paper: Quantitative Approach to the Human Health Assessment for the Risk Evaluation for Asbestos Part 2: Supplemental Evaluation Including Legacy Uses and Associated Disposals of Asbestos*, to be considered as being informative for dose-response analysis, metrics 4 and 5 would need metric ratings of Medium or High. This reference did not satisfy this requirement; therefore data quality evaluation is presented for only for metrics 4 and 5.

Study Citation:	Mcdonald, J. C., Mcdonald, A. D. (1997). Chrysotile, tremolite and carcinogenicity. Annals of Occupational Hygiene 41(6):699-705.
Health Outcome:	Lung Cancer; Laryngeal Cancer; stomach, colon and rectum
Target Organ(s):	Cancer/Carcinogenesis: Lung cancer mortality, Laryngeal cancer mortality, Stomach cancer mortality, Colorectal cancer mortality; Lung/Respiratory: Lung cancer mortality, Laryngeal cancer mortality; Mortality: Lung cancer mortality, Laryngeal cancer mortality, Stomach cancer mortality, Colorectal cancer mortality; Gastrointestinal: Stomach cancer mortality, Colorectal cancer mortality
Asbestos Fiber Type(s):	Asbestos - Chrysotile (serpentine): 12001-29-5; Asbestos - Tremolite: 14567-73-8
Linked HERO ID(s):	No linked references.
HERO ID:	7836

Domain	Metric		Rating	Comments
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Uninformative	Details on exposure measurement methods were not reported in the present reference or cited references (HERO ID 3081408 and 3651098). Men were compared by years of employment.
	Metric 5:	Exposure Levels	Medium	Participants were compared using logistic regression, suggesting a continuous measure of exposure (years of employment).

Additional Comments: This study used a large occupational cohort to create a case-control study for several cancer types. Individuals were followed for a long period of time (potentially >25 years). Some concerns included lack of description of exposure measurement in the current study and cited studies. Other minor concerns included potential missing personnel records and lack of detail for outcome assessment (e.g., ICD codes used and/or case confirmation).

* No biomarkers were identified for this evaluation.

** As described in Appendix B.2 of the *White Paper: Quantitative Approach to the Human Health Assessment for the Risk Evaluation for Asbestos Part 2: Supplemental Evaluation Including Legacy Uses and Associated Disposals of Asbestos*, to be considered as being informative for dose-response analysis, metrics 4 and 5 would need metric ratings of Medium or High. This reference did not satisfy this requirement; therefore data quality evaluation is presented for only for metrics 4 and 5.

Study Citation:	Mcdonald, J. C., Mcdonald, A. D., Armstrong, B., Sebastien, P. (1986). Cohort study of mortality of vermiculite miners exposed to tremolite. Occupational and Environmental Medicine 43(7):436-444.
Health Outcome:	Lung Cancer; all causes mortality, pneumoconiosis mortality, non-malignant respiratory disease mortality
Target Organ(s):	Cancer/Carcinogenesis: respiratory cancer mortality; Lung/Respiratory: respiratory cancer mortality, pneumoconiosis mortality, non-malignant respiratory disease mortality; Mortality: all cause mortality, pneumoconiosis mortality, respiratory cancer mortality, non-malignant respiratory disease mortality
Asbestos Fiber Type(s):	Asbestos - Tremolite: 14567-73-8; Asbestos- Libby amphibole: 1318-09-8
Linked HERO ID(s):	29964, 709547, 709695
HERO ID:	29964

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Medium	Description of study setting was provided, and other elements including inclusion criteria and case ascertainment, primarily from McDonald et al. 1986, HERO ID: 29964, with McDonald and Armstrong 2003, HERO ID: 709547 giving a briefer version of the info. The study population includes male workers from a Libby mining company who have been hired before 1963. In total, 406 males worked at the site for at least one net year were included, 12 of which were employed before 1940. No other description of additional inclusion or exclusion criteria. There is limited information on subjects not included or participation rate, which introduces potential for selection bias.
	Metric 2:	Attrition	High	In McDonald et al. 1986, HERO ID: 29964, at the end of the follow-up period (July 1st, 1983), 226 were alive and 165 were dead. 14 men were found alive on 1981 but subsequent status was not available. In total, vital status of 405 out of 406 men included in this study were traced. Death certificates were obtained for 163 of the 165 deceased. In McDonald and Armstrong 2003, HERO ID: 709547, at the end of the follow-up period (July 1st, 1983), the remaining 241 (vs 240 in McDonald et al. 1986, HERO ID: 29964) known to be alive at the end of the 1983 follow up period were traced via the National Death Index to 1998, where another 120 were confirmed dead.There is little loss to follow up.
	Metric 3:	Comparison Group	Medium	In McDonald et al. 1986, HERO ID: 29964 case-referent analyses, "controls for each case were chosen as men surviving beyond the age of death of the case, who had been born and had started work at Libby mine within three years of the case."In McDonald and Armstrong 2003, HERO ID: 709547, comparison was made among other workers. Age and sex were considered in the analyses.Thus, there is only indirect evidence that groups are not similar to each other.
Domain 2: Exposure Characterization				

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Study Citation:	Mcdonald, J. C., Mcdonald, A. D., Armstrong, B., Sebastien, P. (1986). Cohort study of mortality of vermiculite miners exposed to tremolite. Occupational and Environmental Medicine 43(7):436-444.
Health Outcome:	Lung Cancer; all causes mortality, pneumoconiosis mortality, non-malignant respiratory disease mortality
Target Organ(s):	Cancer/Carcinogenesis: respiratory cancer mortality; Lung/Respiratory: respiratory cancer mortality, pneumoconiosis mortality, non-malignant respiratory disease mortality; Mortality: all cause mortality, pneumoconiosis mortality, respiratory cancer mortality, non-malignant respiratory disease mortality
Asbestos Fiber Type(s):	Asbestos - Tremolite: 14567-73-8; Asbestos- Libby amphibole: 1318-09-8
Linked HERO ID(s):	29964, 709547, 709695
HERO ID:	29964

Domain	Metric		Rating	Comments
	Metric 4:	Measurement of Exposure	Medium	Details on exposure assessment are primarily from McDonald et al. 1986, HERO ID: 29964, with McDonald and Armstrong 2003, HERO ID: 709547 citing this paper. The measurement of exposure (a mix of personal and area) changed during the study period but was ultimately based employment records and quantitative estimates of exposure using a combination of midget impingers and PCM (cited as optical microscopy while referencing Walton 1982, HERO ID: 29649, which clarifies it as phase contrast optical microscopy) for a portion of participant's work history of exposure, requiring extrapolation for earlier years. Air samples were collected using midget impinger before 1970 and using membrane filters after 1970. Samples before 1970 only measured dust concentrations without conversion factors. Limited amount of samples were collected before 1965, and the measurements were much higher after 1975 when the company introduced a systematic air sampling program. Authors assumed that fiber exposure measures made before 1965 (engineering controls installed at this point to reduce dust/fiber levels), were a fraction of those measured afterwards. Authors further note: "For the other operation locations fiber measurements were available only for the recent periods. When the data were considered inadequate to describe past conditions, because of changes in process or control practice, arbitrary correction factors were applied. This was done after discussion with the company's representatives and especially with a previous manager who had spent almost all his career with Libby and who had extensive knowledge of the operations.""Samples were taken until 1982. Cumulative exposure levels were calculated based on job histories, operation locations, and estimated average fiber concentrations.In McDonald and Armstrong 2003, HERO ID: 709547, they used three different indices for exposure: "...(A) average intensity over first five years of employment (f/ml); (B) cumulative exposure (f/ml.y); and (C) residence weighted cumulative exposure, for which each year's exposure is weighted according to the number of years since it was experienced (f/ml.y)."
	Metric 5:	Exposure Levels	Medium	In McDonald et al. 1986, HERO ID: 29964, cumulative continuous exposure levels were used for case-referent analyses. In McDonald and Armstrong 2003, HERO ID: 709547, both continuous and categorical exposure levels were used in Poisson regression analyses. Dichotomous exposure SMR analyses in both papers merit a Low rating.
	Metric 6:	Temporality	High	The follow-up period is greater than 20 years in this cohort for >2/3 of deaths (as shown in McDonald et al. 1986, HERO ID: 29964), suggesting there is sufficient consideration of latency for a range of outcomes. The temporality is established and exposure occurred before outcome.
Domain 3: Outcome Assessment				

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Study Citation: Mcdonald, J. C., Mcdonald, A. D., Armstrong, B., Sebastien, P. (1986). Cohort study of mortality of vermiculite miners exposed to tremolite. Occupational and Environmental Medicine 43(7):436-444.
Health Outcome: Lung Cancer; all causes mortality, pneumoconiosis mortality, non-malignant respiratory disease mortality
Target Organ(s): Cancer/Carcinogenesis: respiratory cancer mortality; Lung/Respiratory: respiratory cancer mortality, pneumoconiosis mortality, non-malignant respiratory disease mortality; Mortality: all cause mortality, pneumoconiosis mortality, respiratory cancer mortality, non-malignant respiratory disease mortality
Asbestos Fiber Type(s): Asbestos - Tremolite: 14567-73-8; Asbestos- Libby amphibole: 1318-09-8
Linked HERO ID(s): 29964, 709547, 709695
HERO ID: 29964

Domain	Metric		Rating	Comments
	Metric 7:	Outcome Measurement or Characterization	High	Lung Cancer: In McDonald et al. 1986, HERO ID: 29964, the cases were ascertained from death certificates and underlying cause of death was coded by a single qualified nosologist according to ICD-8 codes (160-163). In McDonald and Armstrong 2003, HERO ID: 709547, the additional deaths were coded by State nosologists in ICD-9 (160-165).; Other Non-Cancer Outcomes: In McDonald et al. 1986, HERO ID: 29964, the cases were ascertained from death certificates and underlying cause of death was coded by a single qualified nosologist according to ICD-8 codes: pneumoconiosis (515). In McDonald and Armstrong 2003, HERO ID: 709547, the additional deaths were coded by State nosologists in ICD-9: non-malignant respiratory disease (010-018, 460-519) and all causes mortality (codes not specified but are implicit).
	Metric 8:	Reporting Bias	High	Findings of the study were reported in abstract and results. Analyses show relative risk with 95% CI (McDonald et al. 1986, HERO ID: 29964, McDonald and Armstrong 2003, HERO ID: 709547). McDonald and Armstrong 2003, HERO ID: 709547 also reports a p-trend. Reporting bias is not likely to be introduced.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Medium	For case-referent analysis, age, sex, and date of hire were matched (McDonald et al. 1986, HERO ID: 29964), while in McDonald and Armstrong 2003, HERO ID: 709547, there is no covariate adjustment, except for sex and race. Smoking is not addressed.
	Metric 10:	Covariate Characterization	Medium	The source of covariates were not described but likely collected from employment records.
	Metric 11:	Co-exposure Counfounding	Low	There is no discussion of coexposures in these occupational studies.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	Medium	The case-referent and Poisson analyses were appropriate method to evaluate the exposure-outcome associations.
	Metric 13:	Statistical Power	Medium	Both studies likely have the statistical power to detect true associations, however there are often more deaths in the latter study. The only exception may be pneumoconiosis, which may be underpowered. Counts are as follows: for lung cancer (McDonald et al. 1986, HERO ID: 29964, n=23; McDonald and Armstrong 2003, HERO ID: 709547, n=44); pneumoconiosis (McDonald et al. 1986, HERO ID: 29964, n=8); non-malignant respiratory disease (McDonald and Armstrong 2003, HERO ID: 709547, n=51); all causes of death (McDonald and Armstrong 2003, HERO ID: 709547, n=285).
	Metric 14:	Reproducibility of Analyses	Medium	The descriptions of the methods and analyses are sufficient and conceptually reproducible.
	Metric 15:	Statistical Analysis	Medium	Descriptions of case-referent and Poisson models are clear.

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Study Citation:	Mcdonald, J. C., Mcdonald, A. D., Armstrong, B., Sebastien, P. (1986). Cohort study of mortality of vermiculite miners exposed to tremolite. Occupational and Environmental Medicine 43(7):436-444.
Health Outcome:	Lung Cancer; all causes mortality, pneumoconiosis mortality, non-malignant respiratory disease mortality
Target Organ(s):	Cancer/Carcinogenesis: respiratory cancer mortality; Lung/Respiratory: respiratory cancer mortality, pneumoconiosis mortality, non-malignant respiratory disease mortality; Mortality: all cause mortality, pneumoconiosis mortality, respiratory cancer mortality, non-malignant respiratory disease mortality
Asbestos Fiber Type(s):	Asbestos - Tremolite: 14567-73-8; Asbestos- Libby amphibole: 1318-09-8
Linked HERO ID(s):	29964, 709547, 709695
HERO ID:	29964

Domain	Metric	Rating	Comments
Additional Comments:	Note that only outcomes with a rating higher than Low for Metric 5 were evaluated and QC'd. Many outcomes that only are analyzed by SMR (a dichotomous exposure characterization) are thus not QC'd.This is a cohort of 2 studies (McDonald et al. 1986, HERO ID: 29964, McDonald and Armstrong 2003, HERO ID: 709547), with latter being a follow-up on the same cohort of workers in a Libby asbestos mine, with more deaths added for analyses. Of note is that lung cancer shares slightly different ICD codings, however they are also from different ICDs (8 vs 9) but share the same total deaths, suggesting that this difference has no impact.		

Overall Quality Determination **Medium**

* No biomarkers were identified for this evaluation.

Study Citation:	Mcdonald, J. C., Mcdonald, A. D., Sebastien, P., Moy, K. (1988). Health of vermiculite miners exposed to trace amounts of fibrous tremolite. Occupational and Environmental Medicine 45(9):630-634.
Health Outcome:	Mortality from abdominal cancer, Mortality from other cancers; Mortality from circulatory disease, mortality from non-malignant respiratory disease, all cause mortality
Target Organ(s):	Mortality: Mortality from circulatory disease (ICD 390-458), Mortality from non-malignant respiratory disease (ICD 460-519), All causes mortality, Mortality from respiratory cancer (ICD 160-163), mortality from abdominal cancer (ICD 150-159), and mortality from other cancers (140-149, 160, 164-208); Cardiovascular: Mortality from circulatory disease (ICD 390-458); Lung/Respiratory: Mortality from non-malignant respiratory disease (ICD 460-519); Cancer/Carcinogenesis: Mortality from respiratory cancer (ICD 160-163), mortality from abdominal cancer (ICD 150-159), and mortality from other cancers (140-149, 160, 164-208); Gastrointestinal: Mortality from abdominal cancer (ICD 150-159); Other cancer sites (not specified): Mortality from respiratory cancer (ICD 160-163), mortality from abdominal cancer (ICD 150-159), and mortality from other cancers (140-149, 160, 164-208)
Asbestos Fiber Type(s):	Asbestos - Tremolite: 14567-73-8; Asbestos - Actinolite: 12172-67-7; Asbestos - Anthophyllite: 17068-78-9
Linked HERO ID(s):	No linked references.
HERO ID:	29998

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Medium	The study comprised 194 men employed by the company in South Carolina for 6 months or more who were hired before 1971. Criteria for inclusion in the cohort were stated: all men who met the criteria were included. Exclusion criteria and other demographic characteristics were unclear. Some key elements of the study design were not present but available information indicates a low risk of selection bias
	Metric 2:	Attrition	High	The study reported that the vital status of 189 men out of 194 men were obtained through local inquiries. The remaining 5 men were traced only through social security files.
	Metric 3:	Comparison Group	Low	”The mortality of the cohort was compared with that of white and black men in the US using the person-years at risk method to compute the expected number of deaths and hence standardized mortality ratios (SMRs).” SMR analysis adjusted for race but not age. Workers are compared to an inappropriate general population, not a working population.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Medium	From 1969-1984, the company and Mine Safety and Health Administration took fiber samples using personal and area measures in different work zones. No fiber counting is explicitly stated for sampling in this period, and no comparison is made between company and MSHA samples. From 1985-1986, the study took dust samples and quantified asbestos fibers using PCM and ATEM. ATEM is not defined in the study.
	Metric 5:	Exposure Levels	Medium	Mean concentrations of airborne fibers were reported in Table 1 and 2. Estimates of exposure intensity (expressed through f/cc) by zones and calendar years were reported in Table 3 which were continuous measure. Exposure estimates were stratified by wet and dry zones.
	Metric 6:	Temporality	High	The study presents an appropriate temporality between exposure and outcome. The follow up was at least 15 years for the participants.
Domain 3: Outcome Assessment				

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Study Citation:	Mcdonald, J. C., Mcdonald, A. D., Sebastien, P., Moy, K. (1988). Health of vermiculite miners exposed to trace amounts of fibrous tremolite. Occupational and Environmental Medicine 45(9):630-634.
Health Outcome:	Mortality from abdominal cancer, Mortality from other cancers; Mortality from circulatory disease, mortality from non-malignant respiratory disease, all cause mortality
Target Organ(s):	Mortality: Mortality from circulatory disease (ICD 390-458), Mortality from non-malignant respiratory disease (ICD 460-519), All causes mortality, Mortality from respiratory cancer (ICD 160-163), mortality from abdominal cancer (ICD 150-159), and mortality from other cancers (140-149, 160, 164-208); Cardiovascular: Mortality from circulatory disease (ICD 390-458); Lung/Respiratory: Mortality from non-malignant respiratory disease (ICD 460-519); Cancer/Carcinogenesis: Mortality from respiratory cancer (ICD 160-163), mortality from abdominal cancer (ICD 150-159), and mortality from other cancers (140-149, 160, 164-208); Gastrointestinal: Mortality from abdominal cancer (ICD 150-159); Other cancer sites (not specified): Mortality from respiratory cancer (ICD 160-163), mortality from abdominal cancer (ICD 150-159), and mortality from other cancers (140-149, 160, 164-208)
Asbestos Fiber Type(s):	Asbestos - Tremolite: 14567-73-8; Asbestos - Actinolite: 12172-67-7; Asbestos - Anthophyllite: 17068-78-9
Linked HERO ID(s):	No linked references.
HERO ID:	29998

Domain	Metric		Rating	Comments
	Metric 7:	Outcome Measurement or Characterization	High	Other Cancer(s): Mortality was characterized by registered causes of death, which were coded according to the 8th revision of the International Classification of Diseases (ICD) by a nosologist. Mortality from "other cancers" corresponded to codes 140-149, 160, 164-208.; Other Non-Cancer Outcomes: Mortality was characterized by registered causes of death, which were coded according to the 8th revision of the International Classification of Diseases (ICD). Mortality from circulatory disease corresponded to ICD 390-458. Mortality from respiratory disease corresponded to ICD 460-519. Radiologic examination were assessed using ILO 1980 classification.
	Metric 8:	Reporting Bias	High	Outcomes were outlined in all sections of the report. For SMR analyses, all relevant findings were presented.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Low	SMRs were reported. The authors stratified by race, but did not adjust for age.
	Metric 10:	Covariate Characterization	Medium	The study used personnel files which were assumed to be accurate.
	Metric 11:	Co-exposure Counfounding	Low	The study was in an occupational setting with no discussion of co-exposures.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	Medium	The study design and method, SMR analyses in an occupational cohort, were appropriate.
	Metric 13:	Statistical Power	Medium	The number of participants (n=194) was adequate to detect an effect in the exposed population.
	Metric 14:	Reproducibility of Analyses	Medium	The authors provided sufficient details to reproduce the analysis.
	Metric 15:	Statistical Analysis	Medium	The study conducted SMR analysis, which has no explicit assumptions to be met.

Additional Comments: Radiographic outcomes are shown (Table 8) but not analyzed.

Overall Quality Determination — Medium

* No biomarkers were identified for this evaluation.

Study Citation:	Mcdonald, J. C., Mcdonald, A. D., Sebastien, P., Moy, K. (1988). Health of vermiculite miners exposed to trace amounts of fibrous tremolite. Occupational and Environmental Medicine 45(9):630-634.
Health Outcome:	Lung Cancer
Target Organ(s):	Cancer/Carcinogenesis: Mortality from respiratory cancer (ICD 160-163), mortality from abdominal cancer (ICD 150-159), and mortality from other cancers (140-149, 160, 164-208); Mortality: Mortality from respiratory cancer (ICD 160-163), mortality from abdominal cancer (ICD 150-159), and mortality from other cancers (140-149, 160, 164-208)
Asbestos Fiber Type(s):	Asbestos - Tremolite: 14567-73-8; Asbestos - Actinolite: 12172-67-7; Asbestos - Anthophyllite: 17068-78-9
Linked HERO ID(s):	No linked references.
HERO ID:	29998

Domain		Metric	Rating	Comments
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Low	From 1969-1984, the company and Mine Safety and Health Administration took fiber samples using personal and area measures in different work zones. No fiber counting is explicitly stated for sampling in this period, and no comparison is made between company and MSHA samples. From 1985-1986, the study took dust samples and quantified asbestos fibers using PCM and ATEM. ATEM is not defined in the study.
	Metric 5:	Exposure Levels	Medium	Mean concentrations of airborne fibers were reported in Table 1 and 2. Estimates of exposure intensity (expressed through f/cc) by zones and calendar years were reported in Table 3 which were continuous measure. Exposure estimates were stratified by wet and dry zones.

Additional Comments: Radiographic outcomes are shown (Table 8) but not analyzed. Lung cancer is not assessed separately from respiratory cancer outcomes, meriting an uninformative rating for this health outcome.

* No biomarkers were identified for this evaluation.

** As described in Appendix B.2 of the *White Paper: Quantitative Approach to the Human Health Assessment for the Risk Evaluation for Asbestos Part 2: Supplemental Evaluation Including Legacy Uses and Associated Disposals of Asbestos*, to be considered as being informative for dose-response analysis, metrics 4 and 5 would need metric ratings of Medium or High. This reference did not satisfy this requirement; therefore data quality evaluation is presented for only for metrics 4 and 5.

Study Citation:	Mcdonald, J. C., Sebastien, P., Armstrong, B. (1986). Radiological survey of past and present vermiculite miners exposed to tremolite. British Journal of Industrial Medicine 43(7):445-449.
Health Outcome:	small opacities, pleural thickening of chest wall
Target Organ(s):	Lung/Respiratory: small opacities, pleural thickening
Asbestos Fiber Type(s):	Asbestos - Tremolite: 14567-73-8
Linked HERO ID(s):	29964, 709547, 709695
HERO ID:	709695

Domain	Metric		Rating	Comments
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Low	Neither PCM or TEM was mentioned to be used to develop quantitative estimates of exposure. The authors stated: ”The mean airborne fibre concentrations for each location operation, year by year, were estimated from all available midget impinger and membrane filter measurements”
	Metric 5:	Exposure Levels	Medium	The range and distribution of cumulative exposure is sufficient to develop an exposure-response estimate. Five exposure levels were reported as groups (<10, 10<=20, 20<=I00, 100<=200, and >=200 fibers/ml year).

Additional Comments:	QC was not completed for metrics other than Metrics 4 and 5 because the study does not have sufficient exposure information to be useful for dose-response analysis. Metric 4 was deemed low because the authors did not indicate if exposure measurements were done with PCM or TEM.

* No biomarkers were identified for this evaluation.

** As described in Appendix B.2 of the *White Paper: Quantitative Approach to the Human Health Assessment for the Risk Evaluation for Asbestos Part 2: Supplemental Evaluation Including Legacy Uses and Associated Disposals of Asbestos*, to be considered as being informative for dose-response analysis, metrics 4 and 5 would need metric ratings of Medium or High. This reference did not satisfy this requirement; therefore data quality evaluation is presented for only for metrics 4 and 5.

Study Citation:	Mcelvenny, D. M., van Tongeren, M., Turner, M. C., Benke, G., Figuerola, J., Fleming, S., Hours, M., Kincl, L., Krewski, D., Mclean, D., Parent, M. É., Richardson, L., Schlehofer, B., Schlaefer, K., Sadetzki, S., Schüz, J., Siemiatycki, J., Cardis, E. (2018). The INTEROCC case-control study: risk of meningioma and occupational exposure to selected combustion products, dusts and other chemical agents. Occupational and Environmental Medicine 75(1):22-Dec.
Health Outcome:	Meningioma
Target Organ(s):	Cancer/Carcinogenesis: Meningioma
Asbestos Fiber Type(s):	Asbestos - Not specified: 1332-21-4
Linked HERO ID(s):	No linked references.
HERO ID:	4165644

Domain		Metric	Rating	Comments
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Low	Exposure was estimated using a job-exposure matrix; however, it is uncertain whether PCM or TEM were used to construct the job-exposure matrix. The paper referenced with more details (van Tongeren et al., 2013, HERO ID: 4142033) only mentions the calculation of weighted means based on occupational codes.This study or any cited methods source does not explicitly mention the use of PCM or TEM.
	Metric 5:	Exposure Levels	Low	The study reports the mean cumulative exposure between cases and controls overall and then stratified by sex; the range of exposure in the population is limited to the means. There are no other summary statistics provided for exposure.

Additional Comments: NOTE: This study would not be fully evaluated under the current guidelines. Metrics 4 and 5 were rated low due to a limited range of exposure and no mention of the use of PCM or TEM for the determination of asbestos exposure.

* No biomarkers were identified for this evaluation.

** As described in Appendix B.2 of the *White Paper: Quantitative Approach to the Human Health Assessment for the Risk Evaluation for Asbestos Part 2: Supplemental Evaluation Including Legacy Uses and Associated Disposals of Asbestos*, to be considered as being informative for dose-response analysis, metrics 4 and 5 would need metric ratings of Medium or High. This reference did not satisfy this requirement; therefore data quality evaluation is presented for only for metrics 4 and 5.

Study Citation:	Menegozzo, S., Comba, P., Ferrante, D., De Santis, M., Gorini, G., Izzo, F., Magnani, C., Pirastu, R., Simonetti, A., Tùnesi, S., Menegozzo, M. (2011). Mortality study in an asbestos cement factory in Naples, Italy. Annali dell'Istituto superiore di sanità 47(3):296-304.		
Health Outcome:	Lung Cancer		
Target Organ(s):	Lung/Respiratory: malignant neoplasms respiratory tract (160-165) mortality, malignant neoplasms larynx (161) mortality, malignant neoplasms lung (162) mortality, Respiratory diseases (460-519) mortality; Mortality: malignant neoplasms respiratory tract (160-165) mortality, malignant neoplasms larynx (161) mortality, malignant neoplasms lung (162) mortality, malignant neoplasms pleura (163) mortality; Cancer/Carcinogenesis: malignant neoplasms respiratory tract (160-165) mortality, malignant neoplasms larynx (161) mortality, malignant neoplasms lung (162) mortality, malignant neoplasms pleura (163) mortality		
Asbestos Fiber Type(s):	Asbestos - Amosite (grunerite): 12172-73-5; Asbestos - Crocidolite (riebeckite): 12001-28-4; Asbestos - Chrysotile (serpentine): 12001-29-5		
Linked HERO ID(s):	No linked references.		
HERO ID:	3078781		

Domain	Metric		Rating	Comments
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Low	This metric is rated Low because the study or any cited methods source does not explicitly mention the use of PCM or TEM.Authors provided a detailed history of asbestos work in the plant, but methodology of exposure measurement is limited. Generic dust measures were available from the 1960s and in 1979, 64 airborne asbestos fiber samplings were available (crocidolite specific). No information is provided regarding how measures were taken.
	Metric 5:	Exposure Levels	Medium	Study cohort includes workers hired from 1950-1986 and follow-up is from 1965-2005. Even though the environmental airborne generic asbestos fiber and crocidolite sampling in different areas in 1979, this study only presented "duration of exposure" that can be used as a surrogate of exposure assessment for several diseases and to determine exposure-response relationships.

Additional Comments:	NOTE: This study would not be fully evaluated under the current guidelines. This is due to the low rating for metric 4, as no PCM or TEM was mentioned in the study or a cited source.This study provides a comprehensive analysis of SMRs from workers in the Bagnoli factory cohort. Overall, the study describes metrics well, but lacks proper covariables and excluded smoking in their analyses. There is very little information regarding the measurements of asbestos dusts within the factory, with no mention of what tools were used or measures for non-crocidolite asbestos exposures.

* No biomarkers were identified for this evaluation.

** As described in Appendix B.2 of the *White Paper: Quantitative Approach to the Human Health Assessment for the Risk Evaluation for Asbestos Part 2: Supplemental Evaluation Including Legacy Uses and Associated Disposals of Asbestos*, to be considered as being informative for dose-response analysis, metrics 4 and 5 would need metric ratings of Medium or High. This reference did not satisfy this requirement; therefore data quality evaluation is presented for only for metrics 4 and 5.

Study Citation:	Menegozzo, S., Comba, P., Ferrante, D., De Santis, M., Gorini, G., Izzo, F., Magnani, C., Pirastu, R., Simonetti, A., Tùnesi, S., Menegozzo, M. (2011). Mortality study in an asbestos cement factory in Naples, Italy. Annali dell'Istituto superiore di sanità 47(3):296-304.
Health Outcome:	Asbestosis; Respiratory diseases, bronchitis, emphysema, asthma, pneumoconiosis
Target Organ(s):	Mortality: Asbestosis (501) mortality, Pneumoconiosi (500-505) mortality, Bronchitis, emphysema, asthma (490-493) mortality, Respiratory diseases (460-519) mortality; Lung/Respiratory: Asbestosis (501) mortality, Pneumoconiosi (500-505) mortality, Bronchitis, emphysema, asthma (490-493) mortality, Respiratory diseases (460-519) mortality
Asbestos Fiber Type(s):	Asbestos - Amosite (grunerite): 12172-73-5; Asbestos - Crocidolite (riebeckite): 12001-28-4; Asbestos - Chrysotile (serpentine): 12001-29-5
Linked HERO ID(s):	No linked references.
HERO ID:	3078781

Domain	Metric		Rating	Comments
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Low	This metric is rated Low because the study or any cited methods source does not explicitly mention the use of PCM or TEM. Authors provided a detailed history of asbestos work in the plant, but methodology of exposure measurement is limited. Generic dust measures were available from the 1960s and in 1979, 64 airborne asbestos fiber samplings were available (crocidolite specific). No information is provided regarding how measures were taken.
	Metric 5:	Exposure Levels	Medium	The study cohort includes workers hired from 1950-1986, and follow-up is from 1965-2005. Even though the environmental airborne generic asbestos fiber and crocidolite sampling in different areas in 1979, this study only presented "duration of exposure" that can be used as a surrogate of exposure assessment for several diseases and to determine exposure-response relationships.
Additional Comments:	NOTE: This study would not be fully evaluated under the current guidelines. This is due to the low rating for metric 4, as no PCM or TEM was mentioned in the study or a cited source.This study provides a comprehensive analysis of SMRs from workers in the Bagnoli factory cohort. Overall, the study describes metrics well, but lacks proper covariables and excluded smoking in their analyses. There is very little information regarding the measurements of asbestos dusts within the factory, with no mention of what tools were used or measures for non-crocidolite asbestos exposures.			

* No biomarkers were identified for this evaluation.

** As described in Appendix B.2 of the *White Paper: Quantitative Approach to the Human Health Assessment for the Risk Evaluation for Asbestos Part 2: Supplemental Evaluation Including Legacy Uses and Associated Disposals of Asbestos*, to be considered as being informative for dose-response analysis, metrics 4 and 5 would need metric ratings of Medium or High. This reference did not satisfy this requirement; therefore data quality evaluation is presented for only for metrics 4 and 5.

Study Citation:	Menegozzo, S., Comba, P., Ferrante, D., De Santis, M., Gorini, G., Izzo, F., Magnani, C., Pirastu, R., Simonetti, A., Tùnesi, S., Menegozzo, M. (2011). Mortality study in an asbestos cement factory in Naples, Italy. Annali dell'Istituto superiore di sanità 47(3):296-304.
Health Outcome:	malignant neoplasms of digestive organs and peritoneum, malignant neoplasms stomach, malignant neoplasm intesntine and rectum; digestive system disease,
Target Organ(s):	Cancer/Carcinogenesis: malignant neoplasms intestine and rectum (152-154) mortality, malignant neoplasms digestive organs and peritoneum (150-159) mortality, malignant neoplasms stomach (151) mortality, malignant neoplasms rectum (154) mortality; Gastrointestinal: malignant neoplasms digestive organs and peritoneum (150-159) mortality, malignant neoplasms stomach (151) mortality, malignant neoplasms rectum (154) mortality, Digestive system disease (520-579) mortality, malignant neoplasms intestine and rectum (152-154) mortality; Mortality: malignant neoplasms digestive organs and peritoneum (150-159) mortality, malignant neoplasms stomach (151) mortality, malignant neoplasms intestine and rectum (152-154) mortality, malignant neoplasms rectum (154) mortality, Digestive system disease (520-579) mortality
Asbestos Fiber Type(s):	Asbestos - Amosite (grunerite): 12172-73-5; Asbestos - Crocidolite (riebeckite): 12001-28-4; Asbestos - Chrysotile (serpentine): 12001-29-5
Linked HERO ID(s):	No linked references.
HERO ID:	3078781

Domain	Metric		Rating	Comments
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Low	This metric is rated Low because the study or any cited methods source does not explicitly mention the use of PCM or TEM. Authors provided a detailed history of asbestos work in the plant, but methodology of exposure measurement is limited. Generic dust measures were available from the 1960s and in 1979, 64 airborne asbestos fiber samplings were available (crocidolite specific). No information is provided regarding how measures were taken.
	Metric 5:	Exposure Levels	Medium	The study cohort includes workers hired from 1950-1986, and follow-up is from 1965-2005. Even though the environmental airborne generic asbestos fiber and crocidolite sampling in different areas in 1979, this study only presented "duration of exposure" that can be used as a surrogate of exposure assessment for several diseases and to determine exposure-response relationships.

Additional Comments:	NOTE: This study would not be fully evaluated under the current guidelines. This is due to the low rating for metric 4, as no PCM or TEM was mentioned in the study or a cited source. This study provides a comprehensive analysis of SMRs from workers in the Bagnoli factory cohort. Overall, the study describes metrics well, but lacks proper covariables and excluded smoking in their analyses. There is very little information regarding the measurements of asbestos dusts within the factory, with no mention of what tools were used or measures for non-crocidolite asbestos exposures.

* No biomarkers were identified for this evaluation.

** As described in Appendix B.2 of the *White Paper: Quantitative Approach to the Human Health Assessment for the Risk Evaluation for Asbestos Part 2: Supplemental Evaluation Including Legacy Uses and Associated Disposals of Asbestos*, to be considered as being informative for dose-response analysis, metrics 4 and 5 would need metric ratings of Medium or High. This reference did not satisfy this requirement; therefore data quality evaluation is presented for only for metrics 4 and 5.

Study Citation:	Menegozzo, S., Comba, P., Ferrante, D., De Santis, M., Gorini, G., Izzo, F., Magnani, C., Pirastu, R., Simonetti, A., Tùnesi, S., Menegozzo, M. (2011). Mortality study in an asbestos cement factory in Naples, Italy. Annali dell'Istituto superiore di sanità 47(3):296-304.
Health Outcome:	malignant neoplasms (genitourinary, bladder); genitourinary diseases
Target Organ(s):	Renal/Kidney: malignant neoplasms genitourinary (179-189) mortality, malignant neoplasms bladder (188) mortality, Genitourinary disease (580-629) mortality; Mortality: malignant neoplasms genitourinary (179-189) mortality, malignant neoplasms bladder (188) mortality, Genitourinary disease (580-629) mortality; Cancer/Carcinogenesis: malignant neoplasms genitourinary (179-189) mortality, malignant neoplasms bladder (188) mortality
Asbestos Fiber Type(s):	Asbestos - Amosite (grunerite): 12172-73-5; Asbestos - Crocidolite (riebeckite): 12001-28-4; Asbestos - Chrysotile (serpentine): 12001-29-5
Linked HERO ID(s):	No linked references.
HERO ID:	3078781

Domain	Metric		Rating	Comments
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Low	This metric is rated Low because the study or any cited methods source does not explicitly mention the use of PCM or TEM. Authors provided a detailed history of asbestos work in the plant, but methodology of exposure measurement is limited. Generic dust measures were available from the 1960s and in 1979, 64 airborne asbestos fiber samplings were available (crocidolite specific). No information is provided regarding how measures were taken.
	Metric 5:	Exposure Levels	Medium	The study cohort includes workers hired from 1950-1986, and follow-up is from 1965-2005. Even though the environmental airborne generic asbestos fiber and crocidolite sampling in different areas in 1979, this study only presented "duration of exposure" that can be used as a surrogate of exposure assessment for several diseases and to determine exposure-response relationships.

Additional Comments:	NOTE: This study would not be fully evaluated under the current guidelines. This is due to the low rating for metric 4, as no PCM or TEM was mentioned in the study or a cited source.This study provides a comprehensive analysis of SMRs from workers in the Bagnoli factory cohort. Overall, the study describes metrics well, but lacks proper covariables and excluded smoking in their analyses. There is very little information regarding the measurements of asbestos dusts within the factory, with no mention of what tools were used or measures for non-crocidolite asbestos exposures.

* No biomarkers were identified for this evaluation.

** As described in Appendix B.2 of the *White Paper: Quantitative Approach to the Human Health Assessment for the Risk Evaluation for Asbestos Part 2: Supplemental Evaluation Including Legacy Uses and Associated Disposals of Asbestos*, to be considered as being informative for dose-response analysis, metrics 4 and 5 would need metric ratings of Medium or High. This reference did not satisfy this requirement; therefore data quality evaluation is presented for only for metrics 4 and 5.

Study Citation:	Menegozzo, S., Comba, P., Ferrante, D., De Santis, M., Gorini, G., Izzo, F., Magnani, C., Pirastu, R., Simonetti, A., Tùnesi, S., Menegozzo, M. (2011). Mortality study in an asbestos cement factory in Naples, Italy. Annali dell'Istituto superiore di sanità 47(3):296-304.
Health Outcome:	malignant neoplasms (nervous system))
Target Organ(s):	Neurological/Behavioral: malignant neoplasms nervous system (190-192) mortality; Mortality: malignant neoplasms nervous system (190-192) mortality; Cancer/Carcinogenesis: malignant neoplasms nervous system (190-192) mortality
Asbestos Fiber Type(s):	Asbestos - Amosite (grunerite): 12172-73-5; Asbestos - Crocidolite (riebeckite): 12001-28-4; Asbestos - Chrysotile (serpentine): 12001-29-5
Linked HERO ID(s):	No linked references.
HERO ID:	3078781

Domain	Metric		Rating	Comments
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Low	This metric is rated Low because the study or any cited methods source does not explicitly mention the use of PCM or TEM. Authors provided a detailed history of asbestos work in the plant, but methodology of exposure measurement is limited. Generic dust measures were available from the 1960s and in 1979, 64 airborne asbestos fiber samplings were available (crocidolite specific). No information is provided regarding how measures were taken.
	Metric 5:	Exposure Levels	Medium	The study cohort includes workers hired from 1950-1986, and follow-up is from 1965-2005. Even though the environmental airborne generic asbestos fiber and crocidolite sampling in different areas in 1979, this study only presented "duration of exposure" that can be used as a surrogate of exposure assessment for several diseases and to determine exposure-response relationships.

Additional Comments: NOTE: This study would not be fully evaluated under the current guidelines. This is due to the low rating for metric 4, as no PCM or TEM was mentioned in the study or a cited source.This study provides a comprehensive analysis of SMRs from workers in the Bagnoli factory cohort. Overall, the study describes metrics well, but lacks proper covariables and excluded smoking in their analyses. There is very little information regarding the measurements of asbestos dusts within the factory, with no mention of what tools were used or measures for non-crocidolite asbestos exposures.

* No biomarkers were identified for this evaluation.

** As described in Appendix B.2 of the *White Paper: Quantitative Approach to the Human Health Assessment for the Risk Evaluation for Asbestos Part 2: Supplemental Evaluation Including Legacy Uses and Associated Disposals of Asbestos*, to be considered as being informative for dose-response analysis, metrics 4 and 5 would need metric ratings of Medium or High. This reference did not satisfy this requirement; therefore data quality evaluation is presented for only for metrics 4 and 5.

Study Citation:	Menegozzo, S., Comba, P., Ferrante, D., De Santis, M., Gorini, G., Izzo, F., Magnani, C., Pirastu, R., Simonetti, A., Tùnesi, S., Menegozzo, M. (2011). Mortality study in an asbestos cement factory in Naples, Italy. Annali dell'Istituto superiore di sanità 47(3):296-304.
Health Outcome:	malignant neoplasms lynphohematopoietic system
Target Organ(s):	Immune/Hematological: malignant neoplasms lynphohematopoietic system (200-208) mortality; Mortality: malignant neoplasms lynphohematopoietic system (200-208) mortality; Cancer/Carcinogenesis: malignant neoplasms lynphohematopoietic system (200-208) mortality
Asbestos Fiber Type(s):	Asbestos - Amosite (grunerite): 12172-73-5; Asbestos - Crocidolite (riebeckite): 12001-28-4; Asbestos - Chrysotile (serpentine): 12001-29-5
Linked HERO ID(s):	No linked references.
HERO ID:	3078781

Domain	Metric		Rating	Comments
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Low	This metric is rated Low because the study or any cited methods source does not explicitly mention the use of PCM or TEM. Authors provided a detailed history of asbestos work in the plant, but methodology of exposure measurement is limited. Generic dust measures were available from the 1960s and in 1979, 64 airborne asbestos fiber samplings were available (crocidolite specific). No information is provided regarding how measures were taken.
	Metric 5:	Exposure Levels	Medium	The study cohort includes workers hired from 1950-1986, and follow-up is from 1965-2005. Even though the environmental airborne generic asbestos fiber and crocidolite sampling in different areas in 1979, this study only presented "duration of exposure" that can be used as a surrogate of exposure assessment for several diseases and to determine exposure-response relationships.

Additional Comments: NOTE: This study would not be fully evaluated under the current guidelines. This is due to the low rating for metric 4, as no PCM or TEM was mentioned in the study or a cited source.This study provides a comprehensive analysis of SMRs from workers in the Bagnoli factory cohort. Overall, the study describes metrics well, but lacks proper covariables and excluded smoking in their analyses. There is very little information regarding the measurements of asbestos dusts within the factory, with no mention of what tools were used or measures for non-crocidolite asbestos exposures.

* No biomarkers were identified for this evaluation.

** As described in Appendix B.2 of the *White Paper: Quantitative Approach to the Human Health Assessment for the Risk Evaluation for Asbestos Part 2: Supplemental Evaluation Including Legacy Uses and Associated Disposals of Asbestos*, to be considered as being informative for dose-response analysis, metrics 4 and 5 would need metric ratings of Medium or High. This reference did not satisfy this requirement; therefore data quality evaluation is presented for only for metrics 4 and 5.

Study Citation:	Menegozzo, S., Comba, P., Ferrante, D., De Santis, M., Gorini, G., Izzo, F., Magnani, C., Pirastu, R., Simonetti, A., Tùnesi, S., Menegozzo, M. (2011). Mortality study in an asbestos cement factory in Naples, Italy. Annali dell'Istituto superiore di sanità 47(3):296-304.
Health Outcome:	Cardiovascular diseases, ischemic heart diseases
Target Organ(s):	Cardiovascular: Cardiovascular diseases (390-459) mortality, Ischemic heart diseases (410-414) mortality; Mortality: Cardiovascular diseases (390-459) mortality, Ischemic heart diseases (410-414) mortality
Asbestos Fiber Type(s):	Asbestos - Amosite (grunerite): 12172-73-5; Asbestos - Crocidolite (riebeckite): 12001-28-4; Asbestos - Chrysotile (serpentine): 12001-29-5
Linked HERO ID(s):	No linked references.
HERO ID:	3078781

Domain	Metric		Rating	Comments
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Low	This metric is rated Low because the study or any cited methods source does not explicitly mention the use of PCM or TEM. Authors provided a detailed history of asbestos work in the plant, but methodology of exposure measurement is limited. Generic dust measures were available from the 1960s and in 1979, 64 airborne asbestos fiber samplings were available (crocidolite specific). No information is provided regarding how measures were taken.
	Metric 5:	Exposure Levels	Medium	The study cohort includes workers hired from 1950-1986, and follow-up is from 1965-2005. Even though the environmental airborne generic asbestos fiber and crocidolite sampling in different areas in 1979, this study only presented "duration of exposure" that can be used as a surrogate of exposure assessment for several diseases and to determine exposure-response relationships.

Additional Comments:	NOTE: This study would not be fully evaluated under the current guidelines. This is due to the low rating for metric 4, as no PCM or TEM was mentioned in the study or a cited source.This study provides a comprehensive analysis of SMRs from workers in the Bagnoli factory cohort. Overall, the study describes metrics well, but lacks proper covariables and excluded smoking in their analyses. There is very little information regarding the measurements of asbestos dusts within the factory, with no mention of what tools were used or measures for non-crocidolite asbestos exposures.

* No biomarkers were identified for this evaluation.

** As described in Appendix B.2 of the *White Paper: Quantitative Approach to the Human Health Assessment for the Risk Evaluation for Asbestos Part 2: Supplemental Evaluation Including Legacy Uses and Associated Disposals of Asbestos*, to be considered as being informative for dose-response analysis, metrics 4 and 5 would need metric ratings of Medium or High. This reference did not satisfy this requirement; therefore data quality evaluation is presented for only for metrics 4 and 5.

Study Citation:	Menegozzo, S., Comba, P., Ferrante, D., De Santis, M., Gorini, G., Izzo, F., Magnani, C., Pirastu, R., Simonetti, A., Tùnesi, S., Menegozzo, M. (2011). Mortality study in an asbestos cement factory in Naples, Italy. Annali dell'Istituto superiore di sanità 47(3):296-304.
Health Outcome:	Diabetes
Target Organ(s):	Nutritional/Metabolic: Diabetes (250) mortality; Mortality: Diabetes (250) mortality
Asbestos Fiber Type(s):	Asbestos - Amosite (grunerite): 12172-73-5; Asbestos - Crocidolite (riebeckite): 12001-28-4; Asbestos - Chrysotile (serpentine): 12001-29-5
Linked HERO ID(s):	No linked references.
HERO ID:	3078781

Domain	Metric		Rating	Comments
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Low	This metric is rated Low because the study or any cited methods source does not explicitly mention the use of PCM or TEM. Authors provided a detailed history of asbestos work in the plant, but methodology of exposure measurement is limited. Generic dust measures were available from the 1960s and in 1979, 64 airborne asbestos fiber samplings were available (crocidolite specific). No information is provided regarding how measures were taken.
	Metric 5:	Exposure Levels	Medium	The study cohort includes workers hired from 1950-1986, and follow-up is from 1965-2005. Even though the environmental airborne generic asbestos fiber and crocidolite sampling in different areas in 1979, this study only presented "duration of exposure" that can be used as a surrogate of exposure assessment for several diseases and to determine exposure-response relationships.

Additional Comments:	NOTE: This study would not be fully evaluated under the current guidelines. This is due to the low rating for metric 4, as no PCM or TEM was mentioned in the study or a cited source.This study provides a comprehensive analysis of SMRs from workers in the Bagnoli factory cohort. Overall, the study describes metrics well, but lacks proper covariables and excluded smoking in their analyses. There is very little information regarding the measurements of asbestos dusts within the factory, with no mention of what tools were used or measures for non-crocidolite asbestos exposures.

* No biomarkers were identified for this evaluation.

** As described in Appendix B.2 of the *White Paper: Quantitative Approach to the Human Health Assessment for the Risk Evaluation for Asbestos Part 2: Supplemental Evaluation Including Legacy Uses and Associated Disposals of Asbestos*, to be considered as being informative for dose-response analysis, metrics 4 and 5 would need metric ratings of Medium or High. This reference did not satisfy this requirement; therefore data quality evaluation is presented for only for metrics 4 and 5.

Study Citation:	Metintas, M., Metintas, S., Hillerdal, G., Ucgun, I., Erginel, S., Alatas, F., Yildirim, H. (2005). Nonmalignant pleural lesions due to environmental exposure to asbestos: a field-based, cross-sectional study. European Respiratory Journal 26(5):875-880.
Health Outcome:	Pleural Plaques; mortality (circulation systems, COPD), Diffuse pleural fibrosis, asbestosis
Target Organ(s):	Lung/Respiratory: Diffuse pleural fibrosis (Metintas et al. 2005 709524), Pleural plaques (Metintas et al. 2005 709524), Asbestosis (Metintas et al. 2005 709524); Mortality: Circulation systems (Metintas et al. 2012 2325159), COPD (Metintas et al. 2012 2325159)
Asbestos Fiber Type(s):	Asbestos - Tremolite: 14567-73-8; Asbestos - Actinolite: 12172-67-7; Asbestos - Anthophyllite: 17068-78-9
Linked HERO ID(s):	No linked references.
HERO ID:	709524

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	High	The authors reported all key elements of the study, including location, and inclusion criteria. In total, 991 individuals aged 30 years and more were selected from 10 villages for the current study.
	Metric 2:	Attrition	High	Of the initial 991 individuals selected, 923 were included in the final analysis. Excluded individuals (n=68) where those who did not either had complete outcome data or lack of consensus among physician in ascertaining the outcome of interest.
	Metric 3:	Comparison Group	High	Key elements of the study design were reported, suggesting that the study subjects were recruited from the same eligible population i.e., individuals living in villages known to have asbestos-containing soil. The control population had similar demographic characteristics and the authors mention that the study participants were farmers in both the control and asbestos villages.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Medium	The air sampling methodology was not described in detail, missing the description sampling flowrate and sample processing for both publications (Metintas et al. 2005 709524 and Metintas et al. 2012 2325159). Nonetheless, both publications mentioned using phase-contrast microscope (PCM) to count the asbestos fibers.
	Metric 5:	Exposure Levels	Medium	The authors reported summary statistics representing multiple levels of exposure. Metintas et al. 2005 709524 reported indoor and outdoor concentrations and made assumptions to estimate the individual's exposure, reporting three different levels of exposure as shown in Table 4. Metintas et al. 2012 2325159 reported exposure summary statistics in the text, using a Cox model that considers exposure as a continuous variable. Both studies include analyses that only consider exposure as a binary variable (exposed vs. unexposed in Metintas et al. 2012 2325159, and greater or less than 5 f/y/mL for Metintas et al. 2005 709524).
	Metric 6:	Temporality	Medium	Temporality is established in both studies, but the consideration of latency may not be sufficiently long in both studies as they had young study participants (20 years old and above in Metintas et al. 2012 2325159, and 30 years old and above in Metintas 2005 709524).
Domain 3: Outcome Assessment				

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Study Citation:	Metintas, M., Metintas, S., Hillerdal, G., Ucgun, I., Erginel, S., Alatas, F., Yildirim, H. (2005). Nonmalignant pleural lesions due to environmental exposure to asbestos: a field-based, cross-sectional study. European Respiratory Journal 26(5):875-880.
Health Outcome:	Pleural Plaques; mortality (circulation systems, COPD), Diffuse pleural fibrosis, asbestosis
Target Organ(s):	Lung/Respiratory: Diffuse pleural fibrosis (Metintas et al. 2005 709524), Pleural plaques (Metintas et al. 2005 709524), Asbestosis (Metintas et al. 2005 709524); Mortality: Circulation systems (Metintas et al. 2012 2325159), COPD (Metintas et al. 2012 2325159)
Asbestos Fiber Type(s):	Asbestos - Tremolite: 14567-73-8; Asbestos - Actinolite: 12172-67-7; Asbestos - Anthophyllite: 17068-78-9
Linked HERO ID(s):	No linked references.
HERO ID:	709524

Domain	Metric		Rating	Comments
	Metric 7:	Outcome Measurement or Characterization	High	Pleural Plaques: The mortality outcomes (i.e., circulatory systems and COPD SMRs) were assessed using hospital records and household index cards (Metintas et al. 2012 2325159). In the study by Metintas et al. 2005 709524, all study participants completed a questionnaire and went through clinical and radiological examination with chest x-rays to evaluate if they had pleural plaques, diffuse pleural fibrosis or asbestosis. Study participants were also examined using CT scans if the x-rays suggested possible abnormal findings.; Other Non-Cancer Outcomes: The authors used hospital records to evaluate the mortality cause in Metintas et al. 2012 2325159 (circulatory systems and COPD SMRs). In Metintas et al. 2005 709524, the authors used x-rays followed by CT scans to see if the study participants had diffuse pleural fibrosis or asbestosis.
	Metric 8:	Reporting Bias	High	The authors reported results for all the outcomes mentioned in the methods section in both publications (Metintas et al. 2005 709524 and Metintas et al. 2012 2325159).
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Medium	Appropriate adjustments for age and sex were done in the analyses conducted in both publications but the authors did not describe the methods in detail (Metintas et al. 2005 709524 and Metintas et al. 2012 2325159). Metintas et al. 2012 2325159 mentioned data on smoker designation to study participants but it does not seem like the authors used it to estimate the effect estimates.
	Metric 10:	Covariate Characterization	High	The potential confounders (age, sex) data were collected through a questionnaire (Metintas et al. 2005 709524) or through medical records (Metintas et al. 2012 2325159).
	Metric 11:	Co-exposure Counfounding	Medium	Data on co-exposures were not reported in either Metintas et al., 2005 709524 or Metintas et al. 2012 2325159.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	Medium	The authors used appropriate statistical methods to evaluate the health outcomes in the studies' participants; OR, prevalence and logistic regression analysis in Metintas et al. 2005 709524, and standardized mortality ratios estimation in Metintas et al. 2012 2325159.
	Metric 13:	Statistical Power	Medium	The sample size in both studies was sufficiently large to detect an effect in the exposed population: n =943 individuals over 30 years old from 10 villages (Metintas et al. 2005 709524). n = 5318 individuals ages 20-70 and over from 15 villages (Metintas et al. 2012 2325159).
	Metric 14:	Reproducibility of Analyses	Medium	The description of the analysis in both studies (Metintas et al. 2005 709524 and Metintas et al. 2012 2325159) is sufficient to understand how the data were analyzed in order to reproduce the reported results.

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Study Citation:	Metintas, M., Metintas, S., Hillerdal, G., Ucgun, I., Erginel, S., Alatas, F., Yildirim, H. (2005). Nonmalignant pleural lesions due to environmental exposure to asbestos: a field-based, cross-sectional study. European Respiratory Journal 26(5):875-880.
Health Outcome:	Pleural Plaques; mortality (circulation systems, COPD), Diffuse pleural fibrosis, asbestosis
Target Organ(s):	Lung/Respiratory: Diffuse pleural fibrosis (Metintas et al. 2005 709524), Pleural plaques (Metintas et al. 2005 709524), Asbestosis (Metintas et al. 2005 709524); Mortality: Circulation systems (Metintas et al. 2012 2325159), COPD (Metintas et al. 2012 2325159)
Asbestos Fiber Type(s):	Asbestos - Tremolite: 14567-73-8; Asbestos - Actinolite: 12172-67-7; Asbestos - Anthophyllite: 17068-78-9
Linked HERO ID(s):	No linked references.
HERO ID:	709524

Domain	Metric		Rating	Comments
	Metric 15:	Statistical Analysis	Medium	The methods used to estimate ORs and SMRs are transparent in both studies (Metintas et al. 2005 709524 and Metintas et al. 2012 2325159)

Additional Comments:	The third study in this group (Akkurt et al. 2006, 2078953) does not belong to the cohort, as the location of the study cannot be identified as being the same, and the study population are workers, instead of the general population evaluated in the other two studies by Metintas et al. in 2005 and 2012.The measurement exposure (M4) and/or exposure levels (M5) metrics are rated as medium upon review by both set of reviewers. Also, the overall quality determination (OQD) is rated medium. Extraction has been completed and quality control reviewed.

Overall Quality Determination — Medium

* No biomarkers were identified for this evaluation.

Study Citation:	Metintas, S., Metintas, M., Ak, G., Kalyoncu, C. (2012). Environmental asbestos exposure in rural Turkey and risk of lung cancer. International Journal of Environmental Health Research 22(5):468-479.
Health Outcome:	COPD mortality, all-causes, circulation systems mortality
Target Organ(s):	Mortality: All causes of mortality, Chronic obstructive pulmonary disease (COPD) mortality, Circulation systems mortality; Lung/Respiratory: Chronic obstructive pulmonary disease (COPD) mortality; Cardiovascular: Circulation systems mortality
Asbestos Fiber Type(s):	Asbestos - Tremolite: 14567-73-8
Linked HERO ID(s):	No linked references.
HERO ID:	2325159

Domain	Metric		Rating	Comments
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Medium	White soil exposure was assessed both indoors and outdoors (two samples for each environment) in each village. Inclusion for indoor measurements included white-washed walls with white soil. Outdoor samples were taken from the center of the village on the main road. Samples were sent to specialists in the National Institute of Workers Health and Security (ISGUM), Ankara. A PCM was used to count fibres longer than 5 um. This has been marked medium as the authors don't clarify if multiple time periods were used for measures.
	Metric 5:	Exposure Levels	Low	Levels of exposure are by exposed and unexposed villages and by men and women. As there are only two levels of exposure, the metric is rated Low.

Additional Comments:	Overall, this study is robustly designed. There is not much information about the Household Detection Index Card, if the family self-reports cause of death to their village Family Health Center to record, or if a doctor/autopsy confirmed cause of death. This provides little validity in the health outcomes. The study also provides multiple analyses for cancer outcomes.Note: QC was not performed for any metrics except for Metric 4 and Metric 5 because Metric 5 was rated low.

* No biomarkers were identified for this evaluation.

** As described in Appendix B.2 of the *White Paper: Quantitative Approach to the Human Health Assessment for the Risk Evaluation for Asbestos Part 2: Supplemental Evaluation Including Legacy Uses and Associated Disposals of Asbestos*, to be considered as being informative for dose-response analysis, metrics 4 and 5 would need metric ratings of Medium or High. This reference did not satisfy this requirement; therefore data quality evaluation is presented for only for metrics 4 and 5.

Study Citation:	Metintas, S., Metintas, M., Ak, G., Kalyoncu, C. (2012). Environmental asbestos exposure in rural Turkey and risk of lung cancer. International Journal of Environmental Health Research 22(5):468-479.
Health Outcome:	Lung Cancer; GI system cancer, prostate cancer, larynx cancer, brain cancer, haemopeoitic system cancer, skin cancer and melanoma, bone cancer, neuroblastoma, thyroid cancer, breast cancer, and female genital tract cancer
Target Organ(s):	Lung/Respiratory: Lung cancer, Larynx cancer; Cancer/Carcinogenesis: Lung cancer, Gastrointestinal systems cancer, Prostate cancer, Larynx cancer, Brain cancer, Haemopoietic system cancer, Skin cancers and melanoma, Bone cancer, Neuroblastoma cancer, Thyroid cancer, Breast cancer, Female genital tract cancer; Gastrointestinal: Gastrointestinal systems cancer; Reproductive/Developmental: Prostate cancer, Breast cancer, Female genital tract cancer; Neurological/Behavioral: Brain cancer, Neuroblastoma cancer; Immune/Hematological: Haemopoietic system cancer; Skin/Connective Tissue: Skin cancers and melanoma; Musculoskeletal: Bone cancer; Thyroid: Thyroid cancer
Asbestos Fiber Type(s):	Asbestos - Tremolite: 14567-73-8
Linked HERO ID(s):	No linked references.
HERO ID:	2325159

Domain	Metric		Rating	Comments
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Medium	White soil exposure was assessed both indoors and outdoors (two samples for each environment) in each village. Inclusion for indoor measurements included white-washed walls with white soil. Outdoor samples were taken from the center of the village on the main road. Samples were sent to specialists in the National Institute of Workers Health and Security (ISGUM), Ankara. A PCM was used to count fibres longer than 5 um. This has been marked medium as the authors don't clarify if multiple time periods were used for measures.
	Metric 5:	Exposure Levels	Low	Levels of exposure are by exposed and unexposed villages and by men and women. As there are only two levels of exposure, the metric is rated Low.

Additional Comments:	HEROID 235159 was not evaluated for any metrics except Metric 4 and 5 and had no data extracted because it did not have sufficient exposure information to be useful for dose-response analysis. Metric 5 only provided 2 exposure levels, thus receiving a Low rating. Comments can still be found for all metric, but they are not rated.

* No biomarkers were identified for this evaluation.

** As described in Appendix B.2 of the *White Paper: Quantitative Approach to the Human Health Assessment for the Risk Evaluation for Asbestos Part 2: Supplemental Evaluation Including Legacy Uses and Associated Disposals of Asbestos*, to be considered as being informative for dose-response analysis, metrics 4 and 5 would need metric ratings of Medium or High. This reference did not satisfy this requirement; therefore data quality evaluation is presented for only for metrics 4 and 5.

Study Citation:	Mitchell, C. A., Charney, M., Schoenberg, J. B. (1978). Early lung disease in asbestos-product workers. Lung 154(4):261-272.
Health Outcome:	Pulmonary Function/Spirometry Results
Target Organ(s):	Lung/Respiratory: FVC, FEV1
Asbestos Fiber Type(s):	Asbestos - Chrysotile (serpentine): 12001-29-5; Asbestos - Anthophyllite: 17068-78-9
Linked HERO ID(s):	No linked references.
HERO ID:	3084463

Domain	Metric		Rating	Comments
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Low	Neither PCM nor TEM were used for measuring exposure. The study measures asbestos exposure using the membrane filter method. Measurements were made available after the authors conducted their study. Duration of asbestos exposure appears to be calculated from a modified British Medical Research Council questionnaire which collects information about occupational history.
	Metric 5:	Exposure Levels	Medium	Asbestos fibers were counted in different areas of the plant (corresponding with where each group was primarily located) with ranges of exposure reported.
Additional Comments:	The aim of the study was to assess the sensitivity of simple respiratory tests in detecting early stages of asbestos lung disease.			

* No biomarkers were identified for this evaluation.

** As described in Appendix B.2 of the *White Paper: Quantitative Approach to the Human Health Assessment for the Risk Evaluation for Asbestos Part 2: Supplemental Evaluation Including Legacy Uses and Associated Disposals of Asbestos*, to be considered as being informative for dose-response analysis, metrics 4 and 5 would need metric ratings of Medium or High. This reference did not satisfy this requirement; therefore data quality evaluation is presented for only for metrics 4 and 5.

Study Citation:	Mitchell, C. A., Charney, M., Schoenberg, J. B. (1978). Early lung disease in asbestos-product workers. Lung 154(4):261-272.
Health Outcome:	chest auscultation
Target Organ(s):	Lung/Respiratory: chest auscultation (Rales score)
Asbestos Fiber Type(s):	Asbestos - Chrysotile (serpentine): 12001-29-5; Asbestos - Anthophyllite: 17068-78-9
Linked HERO ID(s):	No linked references.
HERO ID:	3084463

Domain	Metric		Rating	Comments
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Low	Neither PCM nor TEM were used for measuring exposure. The study measures asbestos exposure using the membrane filter method. Measurements were made available after the authors conducted their study. Duration of asbestos exposure appears to be calculated from a modified British Medical Research Council questionnaire which collects information about occupational history.
	Metric 5:	Exposure Levels	Medium	Asbestos fibers were counted in different areas of the plant (corresponding with where each group was primarily located) with ranges of exposure reported.

Additional Comments: The aim of the study was to assess the sensitivity of simple respiratory tests in detecting early stages of asbestos lung disease.

* No biomarkers were identified for this evaluation.

** As described in Appendix B.2 of the *White Paper: Quantitative Approach to the Human Health Assessment for the Risk Evaluation for Asbestos Part 2: Supplemental Evaluation Including Legacy Uses and Associated Disposals of Asbestos*, to be considered as being informative for dose-response analysis, metrics 4 and 5 would need metric ratings of Medium or High. This reference did not satisfy this requirement; therefore data quality evaluation is presented for only for metrics 4 and 5.

Study Citation:	Mitchell, C. A., Charney, M., Schoenberg, J. B. (1978). Early lung disease in asbestos-product workers. Lung 154(4):261-272.
Health Outcome:	cough, sputum, wheeze, dyspnea
Target Organ(s):	Lung/Respiratory: Respiratory symptoms, loose cough test
Asbestos Fiber Type(s):	Asbestos - Chrysotile (serpentine): 12001-29-5; Asbestos - Anthophyllite: 17068-78-9
Linked HERO ID(s):	No linked references.
HERO ID:	3084463

Domain	Metric		Rating	Comments
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Low	Neither PCM nor TEM were used for measuring exposure. The study measures asbestos exposure using the membrane filter method. Measurements were made available after the authors conducted their study. Duration of asbestos exposure appears to be calculated from a modified British Medical Research Council questionnaire which collects information about occupational history.
	Metric 5:	Exposure Levels	Medium	Asbestos fibers were counted in different areas of the plant (corresponding with where each group was primarily located) with ranges of exposure reported.

Additional Comments: The aim of the study was to assess the sensitivity of simple respiratory tests in detecting early stages of asbestos lung disease.

* No biomarkers were identified for this evaluation.

** As described in Appendix B.2 of the *White Paper: Quantitative Approach to the Human Health Assessment for the Risk Evaluation for Asbestos Part 2: Supplemental Evaluation Including Legacy Uses and Associated Disposals of Asbestos*, to be considered as being informative for dose-response analysis, metrics 4 and 5 would need metric ratings of Medium or High. This reference did not satisfy this requirement; therefore data quality evaluation is presented for only for metrics 4 and 5.

Study Citation:	Mitchell, C. A., Charney, M., Schoenberg, J. B. (1978). Early lung disease in asbestos-product workers. Lung 154(4):261-272.
Health Outcome:	abnormal radiographs
Target Organ(s):	Lung/Respiratory: opacities from chest reading graphs
Asbestos Fiber Type(s):	Asbestos - Chrysotile (serpentine): 12001-29-5; Asbestos - Anthophyllite: 17068-78-9
Linked HERO ID(s):	No linked references.
HERO ID:	3084463

Domain	Metric		Rating	Comments
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Low	Neither PCM nor TEM were used for measuring exposure. The study measures asbestos exposure using the membrane filter method. Measurements were made available after the authors conducted their study. Duration of asbestos exposure appears to be calculated from a modified British Medical Research Council questionnaire which collects information about occupational history.
	Metric 5:	Exposure Levels	Medium	Asbestos fibers were counted in different areas of the plant (corresponding with where each group was primarily located) with ranges of exposure reported.

Additional Comments: The aim of the study was to assess the sensitivity of simple respiratory tests in detecting early stages of asbestos lung disease.

* No biomarkers were identified for this evaluation.

** As described in Appendix B.2 of the *White Paper: Quantitative Approach to the Human Health Assessment for the Risk Evaluation for Asbestos Part 2: Supplemental Evaluation Including Legacy Uses and Associated Disposals of Asbestos*, to be considered as being informative for dose-response analysis, metrics 4 and 5 would need metric ratings of Medium or High. This reference did not satisfy this requirement; therefore data quality evaluation is presented for only for metrics 4 and 5.

Study Citation:	Moshammer, H., Neuberger, M. (2009). Lung function predicts survival in a cohort of asbestos cement workers. International Archives of Occupational and Environmental Health 82(2):199-207.
Health Outcome:	Respiratory disease mortality, cardiovascular disease mortality, survival, total life expectancy
Target Organ(s):	Mortality: Respiratory disease mortality, Cardiovascular disease mortality, Survival; Lung/Respiratory: Respiratory disease mortality, FEV1, FVC, PEF, MEF75, MEF50, MEF25, Rounded small opacities, Irregular small opacities, Pleural thickening, Large opacities; Cardiovascular: Cardiovascular disease mortality; nan:
Asbestos Fiber Type(s):	Asbestos - Chrysotile (serpentine): 12001-29-5; Asbestos - Crocidolite (riebeckite): 12001-28-4
Linked HERO ID(s):	No linked references.
HERO ID:	2079066

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Medium	Key elements of study design were reported in this historical prospective study of n=309 asbestos cement factory workers who were in 1989/1990 aged 57.0 years (+/- 9.5 years) in Vocklabruck, Upper Austria and were followed from 1974-2006. Estimated cumulative exposure was based upon historical spot measurement data and exposure classifications assigned to each work area. Cohort formation began with workers in 1974 through 1981 when personal protective equipment became available to workers, and biannual medical evaluations were available beginning in 1989 and vital status was updated until the end of 2006. Workplace asbestos exposure spot measurement records were available from 1950 until 1981. The initial cohort of workers who agreed to participate in extended biannual medical evaluations beginning in 1989 consisted of n=322 active and retired workers. Of these, n=309 workers (n=270 males and n=39 females) with complete asbestos exposure history and whose vital status could be followed until the end of 2006 were included.
	Metric 2:	Attrition	High	There was minimal subject loss to follow-up and exclusions during the study, and outcome and exposure data were largely complete. Those workers (n=2) who had moved out of the country and were lost to follow-up were excluded. Those (n=2) with no asbestos exposure history were also excluded. Smoking history data was not provided by one worker. Radiological data was available for n=301 workers.
	Metric 3:	Comparison Group	Medium	Key elements of study design, such as inclusion and exclusion criteria and methods of participant selection, were reported and indicate that subjects were similar. Participant recruitment strategies were not detailed, but participating workers appear to have been from the same eligible population within the same time frame. It is unclear to what extent various aspects (healthy hire, healthy worker survivor, left truncation bias, exposure-dependent right censoring) of the healthy worker effect might have been a factor in the cohort for study.
Domain 2: Exposure Characterization				

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Study Citation:	Moshammer, H., Neuberger, M. (2009). Lung function predicts survival in a cohort of asbestos cement workers. International Archives of Occupational and Environmental Health 82(2):199-207.
Health Outcome:	Respiratory disease mortality, cardiovascular disease mortality, survival, total life expectancy
Target Organ(s):	Mortality: Respiratory disease mortality, Cardiovascular disease mortality, Survival; Lung/Respiratory: Respiratory disease mortality, FEV1, FVC, PEF, MEF75, MEF50, MEF25, Rounded small opacities, Irregular small opacities, Pleural thickening, Large opacities; Cardiovascular: Cardiovascular disease mortality; nan:
Asbestos Fiber Type(s):	Asbestos - Chrysotile (serpentine): 12001-29-5; Asbestos - Crocidolite (riebeckite): 12001-28-4
Linked HERO ID(s):	No linked references.
HERO ID:	2079066

Domain	Metric		Rating	Comments
	Metric 4:	Measurement of Exposure	Medium	Estimated cumulative exposure was described as based upon historical spot measurements analyzed by light microscopy and exposure classifications assigned to each work area. Workplace asbestos exposure spot measurement records were available from 1950 until 1981. Each worker was assigned a specific category of exposure for every year that worker worked at the asbestos cement factory. Details regarding consideration for changes in job area or task during that year were not provided. Authors did not discuss the potential for exposure misclassification within these methods, but the misclassification was likely non-differential. Mean (IQR) estimated cumulative exposure was reported in Table 2 as 72.62 fiber years (fibers x years/cm^3) (70.81).
	Metric 5:	Exposure Levels	Medium	In the Cox regression model asbestos exposure was modeled as a continuous variable, but amphibole exposure was model as binary. The range and distribution of estimated exposure across five workplace areas is presented in Table 1. Estimated cumulative exposures were utilized and 70 fibre years were chosen because it approximated the IQR
	Metric 6:	Temporality	Medium	The study establishes appropriate temporality. Depending upon the date of hire and outcome of interest, it is unclear if the interval between exposure and outcome was adequate for all participants for all outcomes by the end of follow up in 2006 .
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Medium	Other Non-Cancer Outcomes: Non-cancer outcomes of interest were mortality from respiratory disease, cardiovascular disease, as well as survival and total life expectancy,. Mortality data were obtained from official death certificates. Details regarding validity of death certificate data were lacking. ICD coding utilized for death certificates was not detailed.
	Metric 8:	Reporting Bias	High	There were no concerns for selective reporting as all outcomes which were outlined within methods were also reported within the results. Effect estimates were reported as hazard ratios with corresponding 95% confidence intervals (CI's) for results in Tables 4, 6 and 7 for mortality outcomes, as regression coefficients and 95% CI's within Table 8 for lung function outcomes and as odds ratios with 95% CI's for x-ray analysis outcomes.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Medium	Mortality analyses appear to have been adjusted for age and smoking. Lung function outcomes were adjusted for gender and age. Outcomes from x-ray analyses were adjusted for smoking history. The strategy for selection of potential confounders, as well as the distribution of potential confounders, was not detailed, however authors noted the use of stepwise regression with removal of model parameters with p>0.1 significance.

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Study Citation:	Moshammer, H., Neuberger, M. (2009). Lung function predicts survival in a cohort of asbestos cement workers. International Archives of Occupational and Environmental Health 82(2):199-207.
Health Outcome:	Respiratory disease mortality, cardiovascular disease mortality, survival, total life expectancy
Target Organ(s):	Mortality: Respiratory disease mortality, Cardiovascular disease mortality, Survival; Lung/Respiratory: Respiratory disease mortality, FEV1, FVC, PEF, MEF75, MEF50, MEF25, Rounded small opacities, Irregular small opacities, Pleural thickening, Large opacities; Cardiovascular: Cardiovascular disease mortality; nan:
Asbestos Fiber Type(s):	Asbestos - Chrysotile (serpentine): 12001-29-5; Asbestos - Crocidolite (riebeckite): 12001-28-4
Linked HERO ID(s):	No linked references.
HERO ID:	2079066

Domain	Metric		Rating	Comments
	Metric 10:	Covariate Characterization	Medium	Method of assessment of covariate data was not detailed, although can be assumed to have been from occupational personnel history and death certificate sources. Consideration for validation of covariates not detailed. Analyses of some outcomes (x-ray analyses outcomes) did not appear to have included all potential main confounders and distributions of potential covariates across exposure groups was not reported.
	Metric 11:	Co-exposure Counfounding	Low	The members of the cohort were workers at an asbestos cement factory in Austria. Potential co-exposures were not discussed, although there was no evidence that there was an unbalanced provision of potential co-exposures among exposure groups. Authors noted use of personal protective equipment after 1981. Considerations for workers who might have initially left and worked elsewhere with additional exposures but eventually returned to the asbestos plant and cohort for study were not detailed.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	Medium	The study utilized appropriate study design and statistical methods to address the research questions. Life expectancy and mortality outcomes were assessed using proportional hazards regression, lung function outcomes were assessed using linear regression, and presence of x-ray outcomes were assessed using logistic regression.
	Metric 13:	Statistical Power	Medium	The number of participants (n=309 for mortality and lung function, n=301 for x-ray outcomes) was adequate to address the research questions. The number of non-smokers within the cohort was not detailed.
	Metric 14:	Reproducibility of Analyses	Medium	In general, the statistical analyses were described within the text in a way that might facilitate reproducibility, although details regarding initial model covariates in each table of regression analyses were lacking, transformation of continuous variables was not detailed and there was no separate detailed section within the text for description of the statistical analyses.
	Metric 15:	Statistical Analysis	Medium	The method used for calculating risk estimates was adequately described.

Additional Comments: Asbestosis was mentioned as an outcome only in the sense that the study text mentions that no cases of asbestosis was found as a cause of death.

Overall Quality Determination — Medium

* No biomarkers were identified for this evaluation.

Study Citation: Moshammer, H., Neuberger, M. (2009). Lung function predicts survival in a cohort of asbestos cement workers. International Archives of Occupational and Environmental Health 82(2):199-207.
Health Outcome: Pulmonary Function/Spirometry Results; Pleural Plaques
Target Organ(s): Mortality: Respiratory disease mortality, Cardiovascular disease mortality, Survival; Lung/Respiratory: Respiratory disease mortality, FEV1, FVC, PEF, MEF75, MEF50, MEF25, Rounded small opacities, Irregular small opacities, Pleural thickening, Large opacities; Cardiovascular: Cardiovascular disease mortality; nan:
Asbestos Fiber Type(s): Asbestos - Chrysotile (serpentine): 12001-29-5; Asbestos - Crocidolite (riebeckite): 12001-28-4
Linked HERO ID(s): No linked references.
HERO ID: 2079066

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Medium	Key elements of study design were reported in this historical prospective study of n=309 asbestos cement factory workers who were in 1989/1990 aged 57.0 years (+/- 9.5 years) in Vocklabruck, Upper Austria and were followed from 1974-2006. Estimated cumulative exposure was based upon historical spot measurement data and exposure classifications assigned to each work area. Cohort formation began with workers in 1974 through 1981 when personal protective equipment became available to workers, and biannual medical evaluations were available beginning in 1989 and vital status was updated until the end of 2006. Workplace asbestos exposure spot measurement records were available from 1950 until 1981. The initial cohort of workers who agreed to participate in extended biannual medical evaluations beginning in 1989 consisted of n=322 active and retired workers. Of these, n=309 workers (n=270 males and n=39 females) with complete asbestos exposure history and whose vital status could be followed until the end of 2006 were included.
	Metric 2:	Attrition	High	There was minimal subject loss to follow-up and exclusions during the study, and outcome and exposure data were largely complete. Those workers (n=2) who had moved out of the country and were lost to follow-up were excluded. Those (n=2) with no asbestos exposure history were also excluded. Smoking history data was not provided by one worker. Radiological data was available for n=301 workers.
	Metric 3:	Comparison Group	Medium	Key elements of study design, such as inclusion and exclusion criteria and methods of participant selection, were reported and indicate that subjects were similar. Participant recruitment strategies were not detailed, but participating workers appear to have been from the same eligible population within the same time frame. It is unclear to what extent various aspects (healthy hire, healthy worker survivor, left truncation bias, exposure-dependent right censoring) of the healthy worker effect might have been a factor in the cohort for study.
Domain 2: Exposure Characterization				

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Study Citation: Moshammer, H., Neuberger, M. (2009). Lung function predicts survival in a cohort of asbestos cement workers. International Archives of Occupational and Environmental Health 82(2):199-207.
Health Outcome: Pulmonary Function/Spirometry Results; Pleural Plaques
Target Organ(s): Mortality: Respiratory disease mortality, Cardiovascular disease mortality, Survival; Lung/Respiratory: Respiratory disease mortality, FEV1, FVC, PEF, MEF75, MEF50, MEF25, Rounded small opacities, Irregular small opacities, Pleural thickening, Large opacities; Cardiovascular: Cardiovascular disease mortality; nan:
Asbestos Fiber Type(s): Asbestos - Chrysotile (serpentine): 12001-29-5; Asbestos - Crocidolite (riebeckite): 12001-28-4
Linked HERO ID(s): No linked references.
HERO ID: 2079066

Domain	Metric		Rating	Comments
	Metric 4:	Measurement of Exposure	Medium	Estimated cumulative exposure was described as based upon historical spot measurements analyzed by light microscopy and exposure classifications assigned to each work area. Workplace asbestos exposure spot measurement records were available from 1950 until 1981. Each worker was assigned a specific category of exposure for every year that worker worked at the asbestos cement factory. Details regarding consideration for changes in job area or task during that year were not provided. Authors did not discuss the potential for exposure misclassification within these methods, but the misclassification was likely non-differential. Mean (IQR) estimated cumulative exposure was reported in Table 2 as 72.62 fiber years (fibers x years/cm^3) (70.81).
	Metric 5:	Exposure Levels	Medium	In the Cox regression model asbestos exposure was modeled as a continuous variable, but amphibole exposure was model as binary. The range and distribution of estimated exposure across five workplace areas is presented in Table 1. Estimated cumulative exposures were utilized and 70 fibre years were chosen because it approximated the IQR
	Metric 6:	Temporality	Medium	The study establishes appropriate temporality. Depending upon the date of hire and outcome of interest, it is unclear if the interval between exposure and outcome was adequate for all participants for all outcomes by the end of follow up in 2006 .
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	High	Pulmonary Function/Spirometry Results: Pulmonary function outcomes of interest were lung function (FEV1, FVC, PEF, MEF75, MEF50, MEF25). Lung function testing was conducted by spirometry.; Pleural Plaques: Pleural plaque outcomes of interest were from x-ray findings (rounded small opacities, irregular small opacities, pleural thickening, large opacities). Opacities in x-ray results were described as classified according to ILO classification.
	Metric 8:	Reporting Bias	High	There were no concerns for selective reporting as all outcomes which were outlined within methods were also reported within the results. Effect estimates were reported as hazard ratios with corresponding 95% confidence intervals (CI's) for results in Tables 4, 6 and 7 for mortality outcomes, as regression coefficients and 95% CI's within Table 8 for lung function outcomes and as odds ratios with 95% CI's for x-ray analysis outcomes.
Domain 4: Potential Confounding / Variability Control				

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Study Citation:	Moshammer, H., Neuberger, M. (2009). Lung function predicts survival in a cohort of asbestos cement workers. International Archives of Occupational and Environmental Health 82(2):199-207.
Health Outcome:	Pulmonary Function/Spirometry Results; Pleural Plaques
Target Organ(s):	Mortality: Respiratory disease mortality, Cardiovascular disease mortality, Survival; Lung/Respiratory: Respiratory disease mortality, FEV1, FVC, PEF, MEF75, MEF50, MEF25, Rounded small opacities, Irregular small opacities, Pleural thickening, Large opacities; Cardiovascular: Cardiovascular disease mortality; nan:
Asbestos Fiber Type(s):	Asbestos - Chrysotile (serpentine): 12001-29-5; Asbestos - Crocidolite (riebeckite): 12001-28-4
Linked HERO ID(s):	No linked references.
HERO ID:	2079066

Domain	Metric		Rating	Comments
	Metric 9:	Covariate Adjustment	Medium	Mortality analyses appear to have been adjusted for age and smoking. Lung function outcomes were adjusted for gender and age. Outcomes from x-ray analyses were adjusted for smoking history. The strategy for selection of potential confounders, as well as the distribution of potential confounders, was not detailed, however authors noted the use of stepwise regression with removal of model parameters with p>0.1 significance.
	Metric 10:	Covariate Characterization	Medium	Method of assessment of covariate data was not detailed, although can be assumed to have been from occupational personnel history and death certificate sources. Consideration for validation of covariates not detailed. Analyses of some outcomes (x-ray analyses outcomes) did not appear to have included all potential main confounders and distributions of potential covariates across exposure groups was not reported.
	Metric 11:	Co-exposure Counfounding	Low	The members of the cohort were workers at an asbestos cement factory in Austria. Potential co-exposures were not discussed, although there was no evidence that there was an unbalanced provision of potential co-exposures among exposure groups. Authors noted use of personal protective equipment after 1981. Considerations for workers who might have initially left and worked elsewhere with additional exposures but eventually returned to the asbestos plant and cohort for study were not detailed.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	Medium	The study utilized appropriate study design and statistical methods to address the research questions. Life expectancy and mortality outcomes were assessed using proportional hazards regression, lung function outcomes were assessed using linear regression, and presence of x-ray outcomes were assessed using logistic regression.
	Metric 13:	Statistical Power	Medium	The number of participants (n=309 for mortality and lung function, n=301 for x-ray outcomes) was adequate to address the research questions. The number of non-smokers within the cohort was not detailed.
	Metric 14:	Reproducibility of Analyses	Medium	In general, the statistical analyses were described within the text in a way that might facilitate reproducibility, although details regarding initial model covariates in each table of regression analyses were lacking, transformation of continuous variables was not detailed and there was no separate detailed section within the text for description of the statistical analyses.
	Metric 15:	Statistical Analysis	Medium	The method used for calculating risk estimates was adequately described.

Additional Comments: Asbestosis was mentioned as an outcome only in the sense that the study text mentions that no cases of asbestosis was found as a cause of death.

Overall Quality Determination **Medium**

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Study Citation:	Moshammer, H., Neuberger, M. (2009). Lung function predicts survival in a cohort of asbestos cement workers. International Archives of Occupational and Environmental Health 82(2):199-207.
Health Outcome:	Pulmonary Function/Spirometry Results; Pleural Plaques
Target Organ(s):	Mortality: Respiratory disease mortality, Cardiovascular disease mortality, Survival; Lung/Respiratory: Respiratory disease mortality, FEV1, FVC, PEF, MEF75, MEF50, MEF25, Rounded small opacities, Irregular small opacities, Pleural thickening, Large opacities; Cardiovascular: Cardiovascular disease mortality; nan:
Asbestos Fiber Type(s):	Asbestos - Chrysotile (serpentine): 12001-29-5; Asbestos - Crocidolite (riebeckite): 12001-28-4
Linked HERO ID(s):	No linked references.
HERO ID:	2079066

Domain	Metric	Rating	Comments

* No biomarkers were identified for this evaluation.

Study Citation:	Murai, Y., Kitagawa, M., Hiraoka, T. (1997). Fiber analysis in lungs of residents of a Japanese town with endemic pleural plaques. Archives of Environmental Health 52(4):263-269.
Health Outcome:	Pleural Plaques
Target Organ(s):	Lung/Respiratory: Pleural plaque
Asbestos Fiber Type(s):	Asbestos - Chrysotile (serpentine): 12001-29-5; Asbestos - Actinolite: 12172-67-7; Asbestos - Crocidolite (riebeckite): 12001-28-4; Asbestos - Tremolite: 14567-73-8; Asbestos - Anthophyllite: 17068-78-9; Asbestos - Amosite (grunerite): 12172-73-5
Linked HERO ID(s):	No linked references.
HERO ID:	3081301

Domain	Metric		Rating	Comments
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	High	Asbestos fiber levels were assessed by TEM and method details were described in the study. The fiber quantification methods were applied for all samples. Comparison between asbestos bodies counted by optical microscope multiplied by the ratio of total asbestos fibers to coated asbestos fibers and the TEM results was performed as quality control step. There is minimal concern of exposure misclassification according to the description.
	Metric 5:	Exposure Levels	Uninformative	Mean fiber levels of each fiber type were reported and compared between patients with pleural plaque and those without. Description of exposure distribution is limited and not sufficient to determine an exposure-response relationship.

Additional Comments: None

* No biomarkers were identified for this evaluation.

** As described in Appendix B.2 of the *White Paper: Quantitative Approach to the Human Health Assessment for the Risk Evaluation for Asbestos Part 2: Supplemental Evaluation Including Legacy Uses and Associated Disposals of Asbestos*, to be considered as being informative for dose-response analysis, metrics 4 and 5 would need metric ratings of Medium or High. This reference did not satisfy this requirement; therefore data quality evaluation is presented for only for metrics 4 and 5.

Study Citation:	Murphy, R. L. H., Ferris, B. G., Jr, Burgess, W. A., Worcester, J., Gaensler, E. A. (1971). Effects of low concentrations of asbestos: clinical, environmental, radiologic and epidemiologic observations in shipyard pipe coverers and controls. New England Journal of Medicine 285(23):1271-1278.
Health Outcome:	Asbestosis
Target Organ(s):	Lung/Respiratory: Lung function (spirometry, respiratory questionnaires, physical exam, x-rays)., Asbestosis (3 or more of 5 symptoms: dyspnea, rales, spirometry, finger clubbing, x-rays).
Asbestos Fiber Type(s):	Asbestos - Amosite (grunerite): 12172-73-5; Asbestos - Chrysotile (serpentine): 12001-29-5
Linked HERO ID(s):	No linked references.
HERO ID:	144

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Medium	The authors included all 101 asbestos-exposed pipe coverers and 94 unexposed workers employed at a New England shipyard in November 1965. Pipe coverers were exposed to low levels of asbestos through work that involved preparing and applying insulating materials; materials and procedures had not varied appreciably since 1945. Ascertainment of prevalent workers was complete. The main issue of note is that no former workers were included, and no information on rates of or reasons for stopping pipe covering work provided. As notedin the literature, occupational epidemiology studies limited to prevalent workers are susceptible to healthy worker effect bias (Pearce et al 2007, HERO ID: 713676). HWE can result from “the phenomenon that sicker or more sensitive individuals may choose work environments in which exposures are low… or once hired, they may seek transfer to less exposed jobs or leave work” (Le Moual et al 2008 HERO ID: 1580313). Though there is no direct evidence of HWE, the authors mention the existence of company medical records that included information on cardiorespiratory health (e.g. indicating more frequent dyspnea in pipe coverers, less frequent non-obstructive lung disease).
	Metric 2:	Attrition	High	All currently employed pipe coverers participated in the study, along with 94 of the 101 initially selected controls (93%).
	Metric 3:	Comparison Group	High	The comparison group comprised shiplifters and pipefitters employed at the same shipyard in November 1965. This group was selected to be comparable to the exposed workers with the exception of asbestos-containing dust exposure. Controls were matched to the exposed subjects by age (+/- 1y), selecting the first eligible candidate on the list with “approximately the same time at the yard”. Mean age and years of employment in the exposed vs. the comparison group were similar (age 41.5 vs 40.9y, duration employed 17.4 vs 17.1y), as were height, weight, and smoking history. Details on work activities were not provided, but the authors stated that “cumulative years in dusty occupations other than pipe covering did not differ in the two groups” (results paragraph 1).
Domain 2: Exposure Characterization				

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Study Citation: Murphy, R. L. H., Ferris, B. G., Jr, Burgess, W. A., Worcester, J., Gaensler, E. A. (1971). Effects of low concentrations of asbestos: clinical, environmental, radiologic and epidemiologic observations in shipyard pipe coverers and controls. New England Journal of Medicine 285(23):1271-1278.
Health Outcome: Asbestosis
Target Organ(s): Lung/Respiratory: Lung function (spirometry, respiratory questionnaires, physical exam, x-rays)., Asbestosis (3 or more of 5 symptoms: dyspnea, rales, spirometry, finger clubbing, x-rays).
Asbestos Fiber Type(s): Asbestos - Amosite (grunerite): 12172-73-5; Asbestos - Chrysotile (serpentine): 12001-29-5
Linked HERO ID(s): No linked references.
HERO ID: 144

Domain	Metric		Rating	Comments
	Metric 4:	Measurement of Exposure	Medium	Quantitative exposure estimates were based on fiber concentrations from midget impinger measures obtained in a single year – 1965 – using the Public Health Service method, which involves PCM (see Edwards et al, 1968 HERO ID 783893). Details such as numbers and timing of samples were not provided. Historical measures using a konimeter from 1945, 1965 and 1966 counting ”particles with a length-to-diameter ratio greater than 3” were not used, as levels were considerably higher than simultaneous impinger data. For example, weighted averages for 1965 incorporating multiple work locations were 5.2 vs. 21.4 to 23.4 million particles per cubic foot (mppcf) (Table 1, text). Konimeter measures from the three periods indicated variation in exposure over time, with measures aboard ship decreasing (means = 49.2, 21.4 and 25.9 mppcf) and measures in sewing and fabrication areas increasing (11.4, 23.4 and 23.1 mppcf).
	Metric 5:	Exposure Levels	Medium	Exposure duration in years was categorized in 5 levels: 0-<5, 5-<11, 11-<15, 15-<20, and 20-35y. Quantification in millions of particles per cubic foot (mppcf) was estimated using midget impinger measures from 1965; historical midget impinger data were not available.
	Metric 6:	Temporality	Medium	The study design was cross-sectional, as outcomes were measured at the time the study was conducted. However, the use of historical exposure data and the long mean duration of employment (17y) ensures appropriate temporality, that exposure preceded outcome measures.

Domain 3: Outcome Assessment

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Study Citation: Murphy, R. L. H., Ferris, B. G., Jr, Burgess, W. A., Worcester, J., Gaensler, E. A. (1971). Effects of low concentrations of asbestos: clinical, environmental, radiologic and epidemiologic observations in shipyard pipe coverers and controls. New England Journal of Medicine 285(23):1271-1278.
Health Outcome: Asbestosis
Target Organ(s): Lung/Respiratory: Lung function (spirometry, respiratory questionnaires, physical exam, x-rays)., Asbestosis (3 or more of 5 symptoms: dyspnea, rales, spirometry, finger clubbing, x-rays).
Asbestos Fiber Type(s): Asbestos - Amosite (grunerite): 12172-73-5; Asbestos - Chrysotile (serpentine): 12001-29-5
Linked HERO ID(s): No linked references.
HERO ID: 144

Domain	Metric		Rating	Comments
	Metric 7:	Outcome Measurement or Characterization	High	Asbestosis: Diagnosis of asbestosis is based on a physical exam and known exposure to asbestos. Asbestosis was defined for this study as having 3 or more of the following 5 indications, all measured and evaluated by trained study staff: dyspnea, rales, finger clubbing, reduced FVC and x-ray shadows. Assessment of each indication was described briefly but adequately. (1) Habitual dyspnea, wheezing: self-reported using a respiratory symptom questionnaire adapted from one extensively used in the literature (one interviewer; reference cited. (2) Rales (breath sounds from 8 locations, recorded): physical exam (one physician, reference cited). (3) Finger clubbing: physical exam with frontal and lateral tracing outlines made used to measure hyponychial angle (fingernail) of the right index finger (one physician, reference cited). (4) Spirometry: FEV1, FVC and peak flow (PF) from tests administered in random order (calibration and analysis reference cited). (5) Chest x-rays (roentgenogram): posterior and lateral views examined and rated in random order by three radiologists blinded to exposure status, ratings based on combined readings. Negative TB tests were confirmed, none of the workers had diagnosed asthma. All 11 cases of asbestosis in pipe coverers met x-ray criteria; each of the other criteria was present in 8 or 9. Prevalence of each indication was correlated with measures of impaired lung diffusing capacity (Figure 2). Moreover, all 8 cases who consented to an independent medical exam were found to have symptoms consistent with asbestosis, and 3 cases who subsequently died had asbestosis.
	Metric 8:	Reporting Bias	Medium	Descriptive data comparing all outcomes exposed and unexposed workers were provided (Tables 2 and 3); p-values were shown when significant. The proportion of subjects with asbestosis and with each indication used to define asbestosis was shown stratified by increasing duration of exposure (Figures 3 and 4). However, numbers of participants by duration of exposure were not shown. For example, in Figure 3 there are data points shown for 5 exposure duration categories, based on only 11-12 individuals with asbestosis. Presenting only percentages masked the sparse sample available for these analyses. Because impinger data were available only for a snapshot in time, figures do not further quantify asbestos exposure in fiber-years. However, in the text they use the mean concentration measured by impinger to extrapolate cumulative exposure based on exposure duration.

Domain 4: Potential Confounding / Variability Control

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Study Citation:	Murphy, R. L. H., Ferris, B. G., Jr, Burgess, W. A., Worcester, J., Gaensler, E. A. (1971). Effects of low concentrations of asbestos: clinical, environmental, radiologic and epidemiologic observations in shipyard pipe coverers and controls. New England Journal of Medicine 285(23):1271-1278.
Health Outcome:	Asbestosis
Target Organ(s):	Lung/Respiratory: Lung function (spirometry, respiratory questionnaires, physical exam, x-rays)., Asbestosis (3 or more of 5 symptoms: dyspnea, rales, spirometry, finger clubbing, x-rays).
Asbestos Fiber Type(s):	Asbestos - Amosite (grunerite): 12172-73-5; Asbestos - Chrysotile (serpentine): 12001-29-5
Linked HERO ID(s):	No linked references.
HERO ID:	144

Domain	Metric		Rating	Comments
	Metric 9:	Covariate Adjustment	Medium	Analyses did not adjust for potential confounders. However, potential confounding by age and duration of employment was addressed by matching on these factors. The authors further assessed confounding by age by demonstrating that the prevalence of almost all asbestosis indications increased with age in exposed but not unexposed workers (Figure 5). The authors also showed that other potential confounders – smoking habits, weight, and height – were similar among exposed and unexposed subjects. Job selection for controls aimed to account for SES confounding: the authors state in the introduction that their aim was to identify a “control group comparable in all respects except for dust exposure”. Race was not discussed; all participants were male.
	Metric 10:	Covariate Characterization	Medium	Company records and an established questionnaire were used to characterize age, smoking history, and job function.
	Metric 11:	Co-exposure Counfounding	Medium	The authors stated that “cumulative years in dusty occupations other than pipe covering did not differ in the two groups (results paragraph 1). Other potential co-exposures were not discussed, but there is no evidence to suggest important co-exposure confounding.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	Medium	Appropriate comparisons of outcomes in exposed workers vs unexposed controls were presented as means with SDs and percentages in tables and figures. Methods used to derive p-values were not provided. Statistical testing was not reported for the main analyses shown in Figures 3 and 4. Note: there is an apparent labeling error in Figure 4. The 5 duration of exposure categories appear to have been mislabeled using the 5 age categories which are shown in relation to the same outcome measures in Figure 5.
	Metric 13:	Statistical Power	Medium	The sample of 195 participants (101 exposed) seems sufficient for analyses of numerous outcomes, including individual indications/symptoms of asbestosis. The prevalence of the majority of indications was on the order of 20% (13% for x-rays coded 5 or 6). For asbestosis, which is extremely rare, 12 cases were identified. The authors were able to illustrate and increasing prevalence of asbestosis with increasing duration of exposure. However, results were likely imprecise, and no confidence intervals or p-values were provided.
	Metric 14:	Reproducibility of Analyses	Medium	Information presented in tables and figures is sufficiently detailed to facilitate reconstructing the analyses. However, the specific statistical tests used were not described.
	Metric 15:	Statistical Analysis	Medium	Statistical modeling was not employed; confounding was addressed appropriately by matching on age and duration of employment, as well as by selecting workers from the same facility also employed doing skilled manual labor.

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Study Citation:	Murphy, R. L. H., Ferris, B. G., Jr, Burgess, W. A., Worcester, J., Gaensler, E. A. (1971). Effects of low concentrations of asbestos: clinical, environmental, radiologic and epidemiologic observations in shipyard pipe coverers and controls. New England Journal of Medicine 285(23):1271-1278.
Health Outcome:	Asbestosis
Target Organ(s):	Lung/Respiratory: Lung function (spirometry, respiratory questionnaires, physical exam, x-rays)., Asbestosis (3 or more of 5 symptoms: dyspnea, rales, spirometry, finger clubbing, x-rays).
Asbestos Fiber Type(s):	Asbestos - Amosite (grunerite): 12172-73-5; Asbestos - Chrysotile (serpentine): 12001-29-5
Linked HERO ID(s):	No linked references.
HERO ID:	144

Domain	Metric	Rating	Comments
Additional Comments:	This study analyzed health effects of low-level exposure to asbestos among all 101 pipe coverers working at a New England shipyard in 1965, employed for a mean of 17 years. Amosite and to a lesser extent chrysotile asbestos were used to insulate pipes. Exposed workers were compared with 94 unexposed shiplifters and pipefitters who were matched on age and duration of employment at the same shipyard. The study measured pulmonary function and physical exam indications used to diagnose asbestosis, defining asbestosis as 3 or more of the following 5 indications, measured by trained study staff: dyspnea, rales, finger clubbing, reduced FVC and x-ray shadows. The validity of diagnosis was supported by internal consistency of symptoms and independent medical exams. While duration of exposure was readily assessed, quantitative estimates based on fiber counts were crudely estimated based on midget impinger data from a 1965 because historical data measured by konimeter were not comparable, and not readily converted. The weighted mean concentration across locations was 5.2 million particles per cubic foot (mppcf), close to the threshold limit of 5 mppcf recommended at the time. Asbestosis was not identified among individuals with fewer than 10 years of exposure. The authors provide data illustrating increases in each of the indications of asbestosis, and of study-defined asbestosis, with increasing duration of this low level of exposure above that threshold. Issues of concern include the small numbers of cases, as well as limiting the sample to prevalent workers, which has the potential to induce a healthy worker effect bias due to selective attrition or transfer of individuals who are sicker or more susceptible to health effects of the occupational exposure.		

Overall Quality Determination **Medium**

* No biomarkers were identified for this evaluation.

Study Citation:	Mándi, A., Posgay, M., Vadász, P., Major, K., Rödelsperger, K., Tossavainen, A., Ungváry, G., Woitowitz, H. J., Galambos, E., Németh, L., Soltész, I., Egerváry, M., Böszörményi Nagy, G. (2000). Role of occupational asbestos exposure in Hungarian lung cancer patients. International Archives of Occupational and Environmental Health 73(8):555-560.
Health Outcome:	Lung Cancer
Target Organ(s):	Cancer/Carcinogenesis: Lung cancer, Mesothelioma; Lung/Respiratory: Diffuse pleural changes, Pleural plaques, Fibrosis, Mesothelioma, Lung cancer
Asbestos Fiber Type(s):	Asbestos - Not specified: 1332-21-4
Linked HERO ID(s):	No linked references.
HERO ID:	3080762

Domain	Metric		Rating	Comments
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Low	Exposure status was self-reported retrospectively at the time of recruitment (after outcome diagnosis). Exposure categories were never exposed, uncertain about exposure history, <25 fiber-years, and >25 fiber years. Substantial concern for recall bias and outcome misclassification due to reliance on retrospective self-reporting. Exposure estimates for the majority of subjects are not quantitative in nature.The presence of asbestos fibers in lung tissue was assessed by scanning transmission electron microscopy for 25/300 patients. Fiber counts were strongly correlated with self-reported cumulative fiber exposure values.
	Metric 5:	Exposure Levels	Low	No description is provided on levels or range of exposure other than fiber-years category (<25 or >25).The presence of asbestos fibers in lung tissue was assessed by scanning transmission electron microscopy for 25/300 patients. Fiber counts were strongly correlated with self-reported cumulative fiber exposure values.

Additional Comments: None

* No biomarkers were identified for this evaluation.

** As described in Appendix B.2 of the *White Paper: Quantitative Approach to the Human Health Assessment for the Risk Evaluation for Asbestos Part 2: Supplemental Evaluation Including Legacy Uses and Associated Disposals of Asbestos*, to be considered as being informative for dose-response analysis, metrics 4 and 5 would need metric ratings of Medium or High. This reference did not satisfy this requirement; therefore data quality evaluation is presented for only for metrics 4 and 5.

Study Citation:	Neuberger, M., Kundi, M. (1990). Individual asbestos exposure: Smoking and mortality—a cohort study in the asbestos cement industry. British Journal of Industrial Medicine 47(9):615-620.
Health Outcome:	Lung Cancer
Target Organ(s):	Lung/Respiratory: Lung cancer; Cancer/Carcinogenesis: Lung cancer
Asbestos Fiber Type(s):	Asbestos - Chrysotile (serpentine): 12001-29-5; Asbestos - Crocidolite (riebeckite): 12001-28-4; Asbestos - Not specified: 1332-21-4
Linked HERO ID(s):	No linked references.
HERO ID:	3082545

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Medium	Eligibility criteria not described in detail (e.g., ”of the 2816 persons eligible for the study”), but other key details of participants described. “A possible reason for underestimation of risk for lung cancer can be selection bias through a healthy worker effect, but the total SMR (overall mortality) and the mortality from lung cancer of the low exposure group (table 2) indicates that it did not play an important part in our study.” A brief description of the study setting and asbestos use was provided.
	Metric 2:	Attrition	Medium	A total of 121 persons lost to follow up. Authors note this was mostly due to emigration.
	Metric 3:	Comparison Group	High	SMRs were calculated using an ”age and sex matched reference population” (Table 2) from the same region–upper Austria.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Medium	”Individual exposures were estimated (from 1973) from personal records onduration of exposure at different workplaces, estimations of dust concentration until 1965, dust measurements mainly by a conimeter method until 1975, and by personal air samplers and membrane filter methods (Asbestos International Association, HERO 3648707) subsequently. ” The referenced study (HERO 3648707) cites the use of PCM methodology to count fibres. Details on implementation for this study were limited, but it appears they followed a standard protocol.
	Metric 5:	Exposure Levels	Medium	The study reports two exposure groups <=25 fibres/ml-year and >25 fibres/ml-year, in addition to the referent group.
	Metric 6:	Temporality	High	To investigate the latency of lung cancer induced by asbestos we removed from our cohort all persons who had not been observed for more than 15 years from start of exposure.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	High	Lung Cancer: Follow up on vital status for participants was undertaken using government registration offices, death registries, physicians, and pathologists. Lung cancer was identified using ICD-9 162.
	Metric 8:	Reporting Bias	High	Table 2 indicates mortality from lung cancer for Austrian asbestos cement workers from 1950-1986 for the 2 exposure groups. The number of observed, expected, and confidence intervals are provided.
Domain 4: Potential Confounding / Variability Control				

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Study Citation:	Neuberger, M., Kundi, M. (1990). Individual asbestos exposure: Smoking and mortality—a cohort study in the asbestos cement industry. British Journal of Industrial Medicine 47(9):615-620.
Health Outcome:	Lung Cancer
Target Organ(s):	Lung/Respiratory: Lung cancer; Cancer/Carcinogenesis: Lung cancer
Asbestos Fiber Type(s):	Asbestos - Chrysotile (serpentine): 12001-29-5; Asbestos - Crocidolite (riebeckite): 12001-28-4; Asbestos - Not specified: 1332-21-4
Linked HERO ID(s):	No linked references.
HERO ID:	3082545

Domain	Metric		Rating	Comments
	Metric 9:	Covariate Adjustment	High	Appropriate adjustments or explicit considerations were made for potential confounders including age, sex, and smoking.
	Metric 10:	Covariate Characterization	High	Smoking was recorded using a ”standardised questionnaire on occupational exposures and smoking.” Age and sex were presumably drawn from employment records.
	Metric 11:	Co-exposure Counfounding	Low	In an occupational setting, potential co-exposures are not discussed.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	Medium	SMRs were used to compare incidence of lung cancer mortality between the occupational group and the general population. Life-table analyses were used to compare rates of mortality among the two exposed groups.
	Metric 13:	Statistical Power	Medium	The overall population was 2,816, and authors observed 49 lung cancer cases, and 4 mesothelioma cases. No concerns.
	Metric 14:	Reproducibility of Analyses	Medium	SMR and Life-table analysis methodology described sufficiently for reproduction.
	Metric 15:	Statistical Analysis	Medium	Methods were standard. No concerns with SMRs or life-table analyses.

Additional Comments: Historical prospective cohort study analyzing 49 lung cancer and 4 mesothelioma cases from asbestos-exposed cement factory workers. Methods were generally standard, but some details were not present regarding selection and exposure measurement, however, this is not likely to appreciably impact the results. Study includes life table analysis, poison logistic regression, PCM, and SMR.

Overall Quality Determination **Medium**

* No biomarkers were identified for this evaluation.

Study Citation:	Newhouse, M. L., Sullivan, K. R. (1989). A mortality study of workers manufacturing friction materials: 1941-86. British Journal of Industrial Medicine 46(3):176-179.
Health Outcome:	Lung Cancer; other cancers mortality; gastrointestinal cancer mortality; respiratory disease mortality, mortality from other causes
Target Organ(s):	Lung/Respiratory: Respiratory disease mortality, Lung and pleural cancer mortality; Mortality: Mortality from other causes (other than lung and pleural cancer, gastrointestinal cancer, other cancers, and respiratory disease), Respiratory disease mortality, Lung and pleural cancer mortality, Gastrointestinal cancer mortality, Other cancers mortality; Cancer/Carcinogenesis: Lung and pleural cancer mortality, Gastrointestinal cancer mortality, Other cancers mortality; Gastrointestinal: Gastrointestinal cancer mortality
Asbestos Fiber Type(s):	Asbestos - Chrysotile (serpentine): 12001-29-5; Asbestos - Crocidolite (riebeckite): 12001-28-4
Linked HERO ID(s):	No linked references.
HERO ID:	3082792

Domain	Metric		Rating	Comments
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Low	This paper was evaluated for ovarian cancer mortality, lung cancer mortality, and laryngeal cancer mortality in Asbestos Part 1 and was rated Low for this metric. As described in the Final Risk Evaluation for Asbestos Part 1 Systematic Review Supplemental File, "Exposure assessed based solely on duration of employment at the plant. Job titles were not available. Exposure levels are reported at the plant level (over 20 fibers/ml before 1931, 5-20 f/mL from 1931-1950, less than 5 f/mL after 1970)."
	Metric 5:	Exposure Levels	Medium	This paper was evaluated for ovarian cancer mortality, lung cancer mortality, and laryngeal cancer mortality in Asbestos Part 1 but was not rated for this metric. Exposure levels at the plant ranged from less than 5 fibers/ml after 1970 to more than 20 fibers/ml before 1931. The paper presents SMRs for five categories of year of start of employment (pre-1940, 1941-1950, 1951-1960, 1961-1970, and 1971-). Year of start of employment is a proxy for exposure levels, with exposure levels being lower for later start years.

Additional Comments:	QC was not completed for metrics other than Metrics 4 and 5 because the study does not have sufficient exposure information to be useful for dose-response analysis. This paper was evaluated for lung cancer mortality and laryngeal cancer mortality in Asbestos Part 1 and was rated Low for Metric 4 and was not rated for Metric 5 for all three outcomes. The Overall Quality Determination for the study was Low for all three outcomes assessed in Asbestos Part 1. The methods for the other outcomes assessed in this paper were the same as the methods assessed in Asbestos Part 1, indicating that the Overall Quality Determination for this paper is likely to be Low.

* No biomarkers were identified for this evaluation.

** As described in Appendix B.2 of the *White Paper: Quantitative Approach to the Human Health Assessment for the Risk Evaluation for Asbestos Part 2: Supplemental Evaluation Including Legacy Uses and Associated Disposals of Asbestos*, to be considered as being informative for dose-response analysis, metrics 4 and 5 would need metric ratings of Medium or High. This reference did not satisfy this requirement; therefore data quality evaluation is presented for only for metrics 4 and 5.

Study Citation:	Nicholson, W. J., Selikoff, I. J., Seidman, H., Lilis, R., Formby, P. (1979). Long-term mortality experience of chrysotile miners and millers in Thetford Mines, Quebec. Annals of the New York Academy of Sciences, Vol. 330 330:21-Nov.
Health Outcome:	Lung Cancer; Asbestosis
Target Organ(s):	Lung/Respiratory: Asbestosis, Lung cancer; Mortality: All-cause mortality (excluding cancers), Lung cancer; Cancer/Carcinogenesis: Lung cancer
Asbestos Fiber Type(s):	Asbestos - Chrysotile (serpentine): 12001-29-5
Linked HERO ID(s):	No linked references.
HERO ID:	158

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Medium	This study revolved around a cohort of men employed for at least 20 years in one of four companies that mine and mill chrysotile, exclusively. This represented 544 individuals from four separate operations. These operations were examined in Thetford Mines, Quebec, Canada. The participants included represented a variety of potential job classifications. However, not many details beyond this were included pertaining to inclusion criteria, such as the total number of individuals that could have potentially been included.
	Metric 2:	Attrition	Medium	There was moderate exclusion of participants from analyses. The aim of this study was to determine mortality outcomes for participants enrolled from the asbestos mines. The authors were able to obtain 172 certificates of death, and there were an additional 130 cases for which the authors obtained clinical, surgical, and pathological data to supplement death certificate information.
	Metric 3:	Comparison Group	Medium	The expected number of deaths/illnesses included in this study were derived from the age-specific death rate data for white Canadian males. It is important to note that they did not use data specific to Quebec, but it is noted that "national rates are not importantly different from those of Quebec province but are likely to be significantly higher than those of the rural mining counties in which these workers lived" (Nicholson et al., 1979). The authors also explicitly discuss the potential for healthy worker effect, but they mention that "the effects of asbestos exposure appear to overcome the beneficial health status usually associated with employability" (Nicholson et al., 1979). As mentioned, the participants were compared to white Canadian males, but there was no discussion of the racial makeup of employees.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	High	The authors report that 97 air samples were collected from various work locations within five operating asbestos mines/mills. These samples were collected between 1973 and 1975, and a majority of them were personal samples. The concentrations varied greatly, but it is reported that "in virtually all work categories average dust concentrations exceeded the asbestos standard then current in the United States of 5 fibers longer than 5 micrometers/milliliter (5 f/ml)" (Nicholson et al., 1979). The authors detail that they followed the methods outlined by the National Institute of Occupational Safety and Health to determine asbestos concentrations, which utilizes a microscope with phase contrast optics (1972, 145).

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Study Citation:	Nicholson, W. J., Selikoff, I. J., Seidman, H., Lilis, R., Formby, P. (1979). Long-term mortality experience of chrysotile miners and millers in Thetford Mines, Quebec. Annals of the New York Academy of Sciences, Vol. 330 330:21-Nov.
Health Outcome:	Lung Cancer; Asbestosis
Target Organ(s):	Lung/Respiratory: Asbestosis, Lung cancer; Mortality: All-cause mortality (excluding cancers), Lung cancer; Cancer/Carcinogenesis: Lung cancer
Asbestos Fiber Type(s):	Asbestos - Chrysotile (serpentine): 12001-29-5
Linked HERO ID(s):	No linked references.
HERO ID:	158

Domain	Metric		Rating	Comments
	Metric 5:	Exposure Levels	Medium	Multiple levels of asbestos exposure were presented in the study. Table 3 includes a range, mean, and number of samples of asbestos in each of the mine/mill locations. It is also further divided into various work areas/activities, including general mill air, bagging asbestos, quality control laboratory, crusher, dryer, shops, and nonwork areas. This table highlights that a majority of the cohort was employed in facility two, and concentrations are reported in fibers longer than 5 micrometers/ml of air.
	Metric 6:	Temporality	High	One of the requirements to be included in this study was that the workers must have been employed for at least 20 years. This means that there is an appropriate temporality between exposure and outcome such that exposure occurred prior to the outcome.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Medium	Lung Cancer: To identify vital status of participants, the authors examined death certificates of those enrolled in the study. In instances where the authors were unable to obtain death certificates due to not receiving permission from next of kin, they instead looked at hospital records and autopsy protocols. In 130 cases (not necessarily lung cancer participants), clinical, surgical, or pathological data was available.; Asbestosis: Vital status for deceased participants were determined by examining death certificates. Some death certificates were unable to be examined because the next of kin refused or contact could not be made. There was no report of using imaging tests, but it is likely that a doctor performed the autopsies to identify asbestosis. The authors did report that there were some cases of misclassification of the health status. Due to asbestosis only developing from asbestos exposure in the lungs, it ”is an extremely rare cause of death in other than occupational circumstances, the general population rates are not subject to error from its misdiagnosis on certificated of death” (Nicholson et al., 1979).
	Metric 8:	Reporting Bias	Medium	The findings are reported at various points throughout the study. Expected and observed deaths are reported, along with the O/E calculations. However, information such as confidence intervals are not reported, contributing to the medium rating.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Low	No description is provided in this study that discusses considerations for potential confounders or their adjustment.
	Metric 10:	Covariate Characterization	N/A	Covariates were not assessed in this study.
	Metric 11:	Co-exposure Counfounding	Low	Potential co-exposures were not explicitly discussed in this study. It was mentioned in the discussion section that workers in some positions would work with materials other than asbestos, but no examples were provided.
Domain 5: Analysis				

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Study Citation:	Nicholson, W. J., Selikoff, I. J., Seidman, H., Lilis, R., Formby, P. (1979). Long-term mortality experience of chrysotile miners and millers in Thetford Mines, Quebec. Annals of the New York Academy of Sciences, Vol. 330 330:21-Nov.
Health Outcome:	Lung Cancer; Asbestosis
Target Organ(s):	Lung/Respiratory: Asbestosis, Lung cancer; Mortality: All-cause mortality (excluding cancers), Lung cancer; Cancer/Carcinogenesis: Lung cancer
Asbestos Fiber Type(s):	Asbestos - Chrysotile (serpentine): 12001-29-5
Linked HERO ID(s):	No linked references.
HERO ID:	158

Domain	Metric		Rating	Comments
	Metric 12:	Study Design and Methods	Medium	The study design and methods were appropriate for the research question being examined.
	Metric 13:	Statistical Power	Medium	The number of participants included in this study is appropriate to detect an effect in the exposed population.
	Metric 14:	Reproducibility of Analyses	Low	There was a very limited discussion of the analyses present in this study.
	Metric 15:	Statistical Analysis	Medium	SMRs were utilized, and it is clear why this analysis method was used.

Additional Comments: This study had some strengths and limitations. One benefit was the temporality component, since one of the inclusion criteria was that employees must have worked there for at least 20 years, providing a sufficient time from exposure to outcome. There was also an adequate number of participants included in the study to determine an effect. However, these results could be limited. It would have also been beneficial for the authors to provide more information about the causes of deaths, such as a discussion about diagnoses or specific indications of lung cancer and asbestosis, such as with cytological or histological means.

Overall Quality Determination — Medium

* No biomarkers were identified for this evaluation.

Study Citation:	Nicholson, W. J., Selikoff, I. J., Seidman, H., Lilis, R., Formby, P. (1979). Long-term mortality experience of chrysotile miners and millers in Thetford Mines, Quebec. Annals of the New York Academy of Sciences, Vol. 330 330:21-Nov.
Health Outcome:	MISSING
Target Organ(s):	Cancer/Carcinogenesis: All other cancers; Mortality: All other cancers, All cause mortality
Asbestos Fiber Type(s):	Asbestos - Chrysotile (serpentine): 12001-29-5
Linked HERO ID(s):	No linked references.
HERO ID:	158

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Medium	This study revolved around a cohort of men employed for at least 20 years in one of four companies that mine and mill chrysotile, exclusively. This represented 544 individuals from four separate operations. These operations were examined in Thetford Mines, Quebec, Canada. The participants included represented a variety of potential job classifications. However, not many details beyond this were included pertaining to inclusion criteria, such as the total number of individuals that could have potentially been included.
	Metric 2:	Attrition	Medium	There was moderate exclusion of participants from analyses. The aim of this study was to determine mortality outcomes for participants enrolled from the asbestos mines. The authors were able to obtain 172 certificates of death, and there were an additional 130 cases were the authors obtained clinical, surgical, and pathological data to supplement death certificate information.
	Metric 3:	Comparison Group	Medium	The expected number of deaths/illnesses included in this study were derived from the age-specific death rate data for white Canadian males. It is important to note that they did not use data specific to Quebec, but it is noted that ”national rates are not importantly different from those of Quebec province but are likely to be significantly higher than those of the rural mining counties in which these workers lived” (Nicholson et al., 1979). The authors also explicitly discuss the potential for healthy worker effect, but they mention that ”the effects of asbestos exposure appear to overcome the beneficial health status usually associated with employability” (Nicholson et al., 1979). As mentioned, the participants were compared to white Canadian males, but there was no discussion of the racial makeup of employees.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	High	The authors report that 97 air samples were collected from various work locations within five operating asbestos mines/mills. These samples were collected between 1973 and 1975, and a majority of them were personal samples. The concentrations varied greatly, but it is reported that ”in virtually all work categories average dust concentrations exceeded the asbestos standard then current in the United States of 5 fibers longer than 5 micrometers/milliliter (5 f/ml)” (Nicholson et al., 1979). The authors detail that they followed the methods outlined by the National Institute of Occupational Safety and Health to determine asbestos concentrations, which utilizes a microscope with phase contrast optics (1972, 145).

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Study Citation:	Nicholson, W. J., Selikoff, I. J., Seidman, H., Lilis, R., Formby, P. (1979). Long-term mortality experience of chrysotile miners and millers in Thetford Mines, Quebec. Annals of the New York Academy of Sciences, Vol. 330 330:21-Nov.
Health Outcome:	MISSING
Target Organ(s):	Cancer/Carcinogenesis: All other cancers; Mortality: All other cancers, All cause mortality
Asbestos Fiber Type(s):	Asbestos - Chrysotile (serpentine): 12001-29-5
Linked HERO ID(s):	No linked references.
HERO ID:	158

Domain	Metric		Rating	Comments
	Metric 5:	Exposure Levels	Medium	Multiple levels of asbestos exposure were presented in the study. Table 3 includes a range, mean, and number of samples of asbestos in each of the mine/mill locations. It is also further divided into various work areas/activities, including general mill air, bagging asbestos, quality control laboratory, crusher, dryer, shops, and nonwork areas. This table highlights that a majority of the cohort was employed in facility two, and concentrations are reported in fibers longer than 5 micrometers/ml of air.
	Metric 6:	Temporality	High	One of the requirements to be included in this study was that the workers must have been employed for at least 20 years. This means that there is an appropriate temporality between exposure and outcome such that exposure occurred prior to the outcome.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	High	Other Cancer(s): Death certificates and other vital records were used to ascertain the cause of death for participants.; Other Non-Cancer Outcomes: In Table 4, the authors include information pertaining to the ”all other causes” that were classified on death certificates.
	Metric 8:	Reporting Bias	Medium	The findings are reported at various points throughout the study. Expected and observed deaths are reported, along with the O/E calculations. However, information such as confidence intervals are not included, contributing to the medium rating.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Low	No description is provided in this study that discusses considerations for potential confounders or their adjustment.
	Metric 10:	Covariate Characterization	N/A	Covariates were not assessed in this study.
	Metric 11:	Co-exposure Counfounding	Low	Potential co-exposures were not explicitly discussed in this study. It was mentioned in the discussion section that workers in some positions would work with materials other than asbestos, but no examples were provided.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	Medium	The study design and methods were appropriate for the research question being examined.
	Metric 13:	Statistical Power	Medium	The number of participants included in this study is appropriate to detect an effect in the exposed population.
	Metric 14:	Reproducibility of Analyses	Low	There was a very limited discussion of the analyses present in this study.
	Metric 15:	Statistical Analysis	N/A	A statistical model was not used in this study.

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Study Citation:	Nicholson, W. J., Selikoff, I. J., Seidman, H., Lilis, R., Formby, P. (1979). Long-term mortality experience of chrysotile miners and millers in Thetford Mines, Quebec. Annals of the New York Academy of Sciences, Vol. 330 330:21-Nov.		
Health Outcome:	MISSING		
Target Organ(s):	Cancer/Carcinogenesis: All other cancers; Mortality: All other cancers, All cause mortality		
Asbestos Fiber Type(s):	Asbestos - Chrysotile (serpentine): 12001-29-5		
Linked HERO ID(s):	No linked references.		
HERO ID:	158		
Domain	Metric	Rating	Comments
Additional Comments:	This study had some strengths and limitations. One benefit was the temporality component, since one of the inclusion criteria was that employees must have worked there for at least 20 years, providing a sufficient time from exposure to outcome. There was also an adequate number of participants included in the study to determine an effect. However, these results could be limited. For one, there was little information provided about the methods used to ascertain asbestos concentrations. It would have also been beneficial for the authors to provide more information about the causes of deaths, such as a discussion about diagnoses or specific indications of other cancers in the patients, such as through cytological or histological means.		

Overall Quality Determination **Medium**

* No biomarkers were identified for this evaluation.

Study Citation:	Nokso-Koivisto, P., Pukkala, E. (1994). Past exposure to asbestos and combustion products and incidence of cancer among Finnish locomotive drivers. Occupational and Environmental Medicine 51(5):330-334.
Health Outcome:	Lung Cancer
Target Organ(s):	Gastrointestinal: Stomach cancer, Rectal cancer, Colon cancer, Oral cavity and pharynx cancer; Lung/Respiratory: Lung and trachea cancer, Mesothelioma; Renal/Kidney: Kidney cancer, Bladder, ureter, urethra cancer; Skin/Connective Tissue: Skin (non-melanoma) cancer, Skin melanoma; Immune/Hematological: Leukemia, Hodgkin's disease, Non-Hodgkin's lymphoma; Reproductive/Developmental: Prostate cancer; Cancer/Carcinogenesis: All site cancer, Oral cavity and pharynx cancer, Stomach cancer, Colon cancer, Rectal cancer, Lung and trachea cancer, Mesothelioma, Prostate cancer, Kidney cancer, Bladder, ureter, urethra cancer, Skin melanoma, Skin (non-melanoma), Non-Hodgkin's lymphoma, Hodgkin's disease, Leukemia
Asbestos Fiber Type(s):	Asbestos - Anthophyllite: 17068-78-9; Asbestos - Chrysotile (serpentine): 12001-29-5
Linked HERO ID(s):	No linked references.
HERO ID:	3081842

Domain		Metric	Rating	Comments
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Low	To estimate pre-1970s steam engine maintenance exposures in Finland, working conditions were reconstructed in two workshops with the assistance of workers who had been exposed. During reconstructed dismantling of the outer covers of the boilers of two engines, eight personal air samples were collected. The authors state that "asbestos exposure was measured with standardized techniques," but they don't specify what these techniques were. Therefore, it is unclear whether PCM, TEM, or another method was used. The authors also reported that asbestos concentrations in cabins of diesel locomotives with asbestos pipe insulation was measured.
	Metric 5:	Exposure Levels	Low	The range and distribution of exposure was limited. The authors reported that "the average number of fibres > 5 um was 5.0 (range 2.5-7.5)/cm^3, indicating medium exposure" (Nokso-Koivisto & Pukkala, 1994) for the reconstructed steam engine dismantling. The number of fibers was undetectable for diesel locomotive cabins. Furthermore, although different time periods were assessed, the study only assessed two exposure levels – standardized incidence ratios were used to compare locomotive drivers (exposed) to the Finnish population (presumed unexposed or lower exposed). Therefore, this study does not include sufficient information for dose-response assessment.

Additional Comments: None

** As described in Appendix B.2 of the *White Paper: Quantitative Approach to the Human Health Assessment for the Risk Evaluation for Asbestos Part 2: Supplemental Evaluation Including Legacy Uses and Associated Disposals of Asbestos*, to be considered as being informative for dose-response analysis, metrics 4 and 5 would need metric ratings of Medium or High. This reference did not satisfy this requirement; therefore data quality evaluation is presented for only for metrics 4 and 5.

Study Citation:	Nuyts, V., Vanhooren, H., Begyn, S., Nackaerts, K., Nemery, B. (2017). Asbestos bodies in bronchoalveolar lavage in the 21st century: a time-trend analysis in a clinical population. Occupational and Environmental Medicine 74(1):59-65.
Health Outcome:	Lung Cancer; Asbestosis; Pleural Plaques
Target Organ(s):	Lung/Respiratory: Pleural plaques, Asbestosis, lung cancer; Cancer/Carcinogenesis: lung cancer
Asbestos Fiber Type(s):	Asbestos - Not specified: 1332-21-4
Linked HERO ID(s):	No linked references.
HERO ID:	3531256

Domain	Metric		Rating	Comments
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Low	Asbestos bodies were quantified in BAL samples using light microscopy.
	Metric 5:	Exposure Levels	Medium	The range and distribution of exposure is sufficient to develop an exposure-response estimate, and an exposure-response model using a continuous measure of exposure was used for the analysis.Exposures ranged from 0 to 164.5 asbestos bodies (AB)/mL, with a median of 0.5 AB/mL and an arithmetic mean of 5 AB/mL.

Additional Comments: This retrospective study of clinical data quantified asbestos bodies in bronchoalveolar samples. The study found significant differences in concentrations of asbestos bodies among groups of participants with pulmonary diseases compared to those with no known diagnoses. The Matrix Adjustment metric was not rated for this study.

** As described in Appendix B.2 of the *White Paper: Quantitative Approach to the Human Health Assessment for the Risk Evaluation for Asbestos Part 2: Supplemental Evaluation Including Legacy Uses and Associated Disposals of Asbestos*, to be considered as being informative for dose-response analysis, metrics 4 and 5 would need metric ratings of Medium or High. This reference did not satisfy this requirement; therefore data quality evaluation is presented for only for metrics 4 and 5.

Study Citation: Nyberg, F., Gustavsson, P., Jarup, L., Bellander, T., Berglind, N., Jakobsson, R., Pershagen, G. (2000). Urban air pollution and lung cancer in Stockholm. Epidemiology 11(5):487-495.
Health Outcome: Lung Cancer
Target Organ(s): Lung/Respiratory: Lung cancer
Asbestos Fiber Type(s): Asbestos - Not specified: 1332-21-4
Linked HERO ID(s): No linked references.
HERO ID: 12511

Domain		Metric	Rating	Comments
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Uninformative	The authors detail that asbestos exposure estimates were determined through a job exposure matrix. An occupational hygienist was responsible for determining the cumulative exposure, which was the ”product of the intensity, the probability, and the duration of exposure, summed over all work periods in occupational history” (Nyberg et al., 2000). There was no information provided pertaining to actual quantitative measurements of asbestos.
	Metric 5:	Exposure Levels	Low	Only two levels of asbestos exposure are reported in this study. These are ”none or low,” and ”high (>/= 0.89 fiber-years/mL).

Additional Comments: None

** As described in Appendix B.2 of the *White Paper: Quantitative Approach to the Human Health Assessment for the Risk Evaluation for Asbestos Part 2: Supplemental Evaluation Including Legacy Uses and Associated Disposals of Asbestos*, to be considered as being informative for dose-response analysis, metrics 4 and 5 would need metric ratings of Medium or High. This reference did not satisfy this requirement; therefore data quality evaluation is presented for only for metrics 4 and 5.

Study Citation:	Offermans, N. S. M., Vermeulen, R., Burdorf, A., Goldbohm, R. A., Keszei, A. P., Peters, S., Kauppinen, T., Kromhout, H., van Den Brandt, P. A. (2014). Occupational asbestos exposure and risk of oral cavity and pharyngeal cancer in the prospective Netherlands Cohort Study. Scandinavian Journal of Work, Environment and Health 40(4):420-427.
Health Outcome:	oral cavity cancer, pharyngeal cancer, oral cavity cancer and pharyngeal cancer combined
Target Organ(s):	oral cavity: oral cavity cancer and pharyngeal cancer combined, oral cavity cancer; Cancer/Carcinogenesis: oral cavity cancer, oral cavity cancer and pharyngeal cancer combined, pharyngeal cancer; Lung/Respiratory: pharyngeal cancer, oral cavity cancer and pharyngeal cancer combined
Asbestos Fiber Type(s):	Asbestos - Not specified: 1332-21-4
Linked HERO ID(s):	No linked references.
HERO ID:	3091862

Domain	Metric		Rating	Comments
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Low	In this study of participants in the population-based Netherlands Cohort Study (NLCS), exposure was estimated using two different job-exposure matrices (JEMs) developed for the general population: DOMJEM (described in Offermans NS et al. 2012, HERO ID: 3091864) and FINJEM (Kauppinen T, Toikkanen J, Pukkala E. Am J Ind Med 1998, 33:409-417, not available in HERO). For both JEMs, asbestos exposures were assessed for different occupations using either professional judgement (DOMJEM) or measurement in a set of Finnish workplaces (FINJEM, exact methods not described). These occupation-specific estimates were then assigned to NLCS participants based on occupational history. A metric rating of "low" was assigned because exposures were not measured or otherwise assessed for the specific workplaces of NLCS participants.
	Metric 5:	Exposure Levels	Medium	Exposure levels estimated from each of the two JEMs were grouped into four categories (tertiles plus no exposure) for analysis. Exposures from each JEM were also evaluated continuously. Median exposure levels of all study participants within tertiles 1-3 were as follows – DOMJEM: 4, 20, 38 unit-years; FINJEM: 0.20, 1.59, 6.60 fiber-years/ml.

Additional Comments: None

** As described in Appendix B.2 of the *White Paper: Quantitative Approach to the Human Health Assessment for the Risk Evaluation for Asbestos Part 2: Supplemental Evaluation Including Legacy Uses and Associated Disposals of Asbestos*, to be considered as being informative for dose-response analysis, metrics 4 and 5 would need metric ratings of Medium or High. This reference did not satisfy this requirement; therefore data quality evaluation is presented for only for metrics 4 and 5.

Study Citation:	Offermans, N. S., Vermeulen, R., Burdorf, A., Goldbohm, R. A., Kauppinen, T., Kromhout, H., van den Brandt, P. A. (2014). Occupational asbestos exposure and risk of pleural mesothelioma, lung cancer, and laryngeal cancer in the prospective Netherlands cohort study. Journal of Occupational and Environmental Medicine 56(1):19-Jun.
Health Outcome:	Lung Cancer
Target Organ(s):	Cancer/Carcinogenesis: pleural mesothelioma, lung cancer, laryngeal cancer (glottis and supraglottis cancers); Lung/Respiratory: pleural mesothelioma, lung cancer, laryngeal cancer (glottis and supraglottis cancers)
Asbestos Fiber Type(s):	Asbestos - Not specified: 1332-21-4
Linked HERO ID(s):	No linked references.
HERO ID:	3078062

Domain	Metric		Rating	Comments
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Low	The study employed two job exposure matrices - the DOMJEM (the Netherlands) and the FINJEM (Finland) - however, only one matrix appears to leverage quantitative measures of exposure to asbestos, but it is unclear if TEM or PCM were used. It appears that the DOMJEM uses expert judgment only to assign semiquantitative exposure values with corresponding weighting. The FINJEM uses expert judgment and exposure measurement, though there is no discussion of the methodology used to make those measurements.
	Metric 5:	Exposure Levels	Medium	This study examines exposure by tertile of cumulative exposure, tertile of duration of exposure, and, among the exposed only, tertile of duration of high exposure. Many of the analyses use those who were not exposed to asbestos as the referent group. There is an appropriate range of exposure among the study population to assess the exposure-response relationship.

Additional Comments: This case-cohort study leverages the NLCS cohort to assess the association between occupational asbestos exposure and lung cancer cases. The study design and methodological approaches are robust, and the study employed the ICD-O-3 to identify lung cancer cases. There are no major concerns about residual bias in the observed results.

* No biomarkers were identified for this evaluation.

** As described in Appendix B.2 of the *White Paper: Quantitative Approach to the Human Health Assessment for the Risk Evaluation for Asbestos Part 2: Supplemental Evaluation Including Legacy Uses and Associated Disposals of Asbestos*, to be considered as being informative for dose-response analysis, metrics 4 and 5 would need metric ratings of Medium or High. This reference did not satisfy this requirement; therefore data quality evaluation is presented for only for metrics 4 and 5.

Study Citation:	Offermans, N. S., Vermeulen, R., Burdorf, A., Goldbohm, R. A., Kauppinen, T., Kromhout, H., van den Brandt, P. A. (2014). Occupational asbestos exposure and risk of pleural mesothelioma, lung cancer, and laryngeal cancer in the prospective Netherlands cohort study. Journal of Occupational and Environmental Medicine 56(1):19-Jun.
Health Outcome:	Laryngeal Cancer
Target Organ(s):	Cancer/Carcinogenesis: pleural mesothelioma, lung cancer, laryngeal cancer (glottis and supraglottis cancers); Lung/Respiratory: pleural mesothelioma, lung cancer, laryngeal cancer (glottis and supraglottis cancers)
Asbestos Fiber Type(s):	Asbestos - Not specified: 1332-21-4
Linked HERO ID(s):	No linked references.
HERO ID:	3078062

Domain	Metric		Rating	Comments
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Low	The study employed two job exposure matrices - the DOMJEM (the Netherlands) and the FINJEM (Finland) - however, only one matrix appears to leverage quantitative measures of exposure to asbestos, but it is unclear if TEM or PCM were used. It appears that the DOMJEM uses expert judgment only to assign semiquantitative exposure values with corresponding weighting. The FINJEM uses expert judgment and exposure measurement, though there is no discussion of the methodology used to make those measurements.
	Metric 5:	Exposure Levels	Medium	This study examines exposure by tertile of cumulative exposure, tertile of duration of exposure, and, among the exposed only, tertile of duration of high exposure. Many of the analyses use those who were not exposed to asbestos as the referent group. There is an appropriate range of exposure among the study population to assess the exposure-response relationship.

Additional Comments: This case-cohort study leverages the NLCS cohort to assess the association between occupational asbestos exposure and laryngeal cancer cases of the glottis and supraglottis. The study design and methodological approaches are robust, and the study employed the ICD-O-3 to identify laryngeal cancer cases. There are no major concerns about residual bias in the observed results.

* No biomarkers were identified for this evaluation.

** As described in Appendix B.2 of the *White Paper: Quantitative Approach to the Human Health Assessment for the Risk Evaluation for Asbestos Part 2: Supplemental Evaluation Including Legacy Uses and Associated Disposals of Asbestos*, to be considered as being informative for dose-response analysis, metrics 4 and 5 would need metric ratings of Medium or High. This reference did not satisfy this requirement; therefore data quality evaluation is presented for only for metrics 4 and 5.

Study Citation:	Ohlson, C. G., Bodin, L., Rydman, T., Hogstedt, C. (1985). Ventilatory decrements in former asbestos cement workers: a four year follow up. British Journal of Industrial Medicine 42(9):612-616.
Health Outcome:	Pulmonary Function/Spirometry Results
Target Organ(s):	Lung/Respiratory: Pleural plaques, Forced vital capacity (FVC), Forced expiratory volume in one second (FEV1)
Asbestos Fiber Type(s):	Asbestos - Chrysotile (serpentine): 12001-29-5; Asbestos - Crocidolite (riebeckite): 12001-28-4; Asbestos - Amosite (grunerite): 12172-73-5
Linked HERO ID(s):	2238789, 758934
HERO ID:	2238789

Domain	Metric		Rating	Comments
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Low	The authors did not specify the methods used to determine asbestos concentrations in the occupational settings. They did note that the information was limited, but the concentration was estimated to be 2 fibers/ml in the 1950s and 60s, and 1 fiber/ml during the 1970s. It was also indicated that "a general dust level of 10 mg/m3" was found in measurements before 1970 (Ohlson et al., 1985). Information on exposure measurements ascertainment was also limited in the secondary study, although some levels of exposure were reported (Jakobsson et al., 1995, RefID 758934).
	Metric 5:	Exposure Levels	Medium	In the methods section, it is mentioned that the workers at the asbestos plant were divided into three groups depending on their cumulative exposure, in fiber-years. The same groupings from the 1976 study were used. These fiber-year groupings include: </= 14 fiber-years, 15-22 fiber-years, and >/= 23 fiber-years (Ohlson et al., 1985, RefID 2238789). Three levels of cumulative asbestos dose were also reported in the secondary study: <10 f-y/ml, 10-30 f-y/ml, and >30 f-y/ml (Jakobsson et al., 1995, RefID 758934).

Additional Comments:	While there were some differences in the ratings for some metrics between these two studies, there were no major ones that stood out. Both studies utilized chest radiographs, although the (Jakobsson et al., 1995, 758934) study had more readers, which contributed to a high rating for that metric. Overall, both studies had some strengths and limitations contributing to their medium overall judgment.

* No biomarkers were identified for this evaluation.

** As described in Appendix B.2 of the *White Paper: Quantitative Approach to the Human Health Assessment for the Risk Evaluation for Asbestos Part 2: Supplemental Evaluation Including Legacy Uses and Associated Disposals of Asbestos*, to be considered as being informative for dose-response analysis, metrics 4 and 5 would need metric ratings of Medium or High. This reference did not satisfy this requirement; therefore data quality evaluation is presented for only for metrics 4 and 5.

Study Citation: Ohlson, C. G., Bodin, L., Rydman, T., Hogstedt, C. (1985). Ventilatory decrements in former asbestos cement workers: a four year follow up. British Journal of Industrial Medicine 42(9):612-616.
Health Outcome: Pleural Plaques
Target Organ(s): Lung/Respiratory: Pleural plaques, Forced vital capacity (FVC), Forced expiratory volume in one second (FEV1)
Asbestos Fiber Type(s): Asbestos - Chrysotile (serpentine): 12001-29-5; Asbestos - Crocidolite (riebeckite): 12001-28-4; Asbestos - Amosite (grunerite): 12172-73-5
Linked HERO ID(s): 2238789, 758934
HERO ID: 2238789

Domain	Metric		Rating	Comments
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Low	The authors did not specify the methods used to determine asbestos concentrations in the occupational settings. They did note that the information was limited, but the concentration was estimated to be 2 fibers/ml in the 1950s and 60s, and 1 fiber/ml during the 1970s. It was also indicated that "a general dust level of 10 mg/m3" was found in measurements before 1970 (Ohlson et al., 1985). Information on exposure measurements ascertainment was also limited in the secondary study, although some levels of exposure were reported (Jakobsson et al., 1995, RefID 758934).
	Metric 5:	Exposure Levels	Medium	In the methods section, it is mentioned that the workers at the asbestos plant were divided into three groups depending on their cumulative exposure, in fiber-years. The same groupings from the 1976 study were used. These fiber-year groupings include: </= 14 fiber-years, 15-22 fiber-years, and >/= 23 fiber-years (Ohlson et al., 1985, 2238789). Three levels of cumulative asbestos dose were also reported in the secondary study: <10 f-y/ml, 10-30 f-y/ml, and >30 f-y/ml (Jakobsson et al., 1995, RefID 758934).

Additional Comments: While there were some differences in the ratings for some metrics between these two studies, there were no major ones that stood out. Both studies utilized chest radiographs, although the (Jakobsson et al., 1995, RefID 758934) study had more readers, which contributed to a high rating for that metric. Overall, both studies had some strengths and limitations contributing to their medium overall judgment.

* No biomarkers were identified for this evaluation.
** As described in Appendix B.2 of the *White Paper: Quantitative Approach to the Human Health Assessment for the Risk Evaluation for Asbestos Part 2: Supplemental Evaluation Including Legacy Uses and Associated Disposals of Asbestos*, to be considered as being informative for dose-response analysis, metrics 4 and 5 would need metric ratings of Medium or High. This reference did not satisfy this requirement; therefore data quality evaluation is presented for only for metrics 4 and 5.

Study Citation:	Ohlson, C. G., Hogstedt, C. (1985). Lung cancer among asbestos cement workers. A Swedish cohort study and a review. British Journal of Industrial Medicine 42(6):397-402.		
Health Outcome:	Lung Cancer; gastrointestinal, pancreatic, intestinal, respiratory,; mortality by external causes, violent death, circulation, and respiratory tract		
Target Organ(s):	Lung/Respiratory: Lung cancer mortality, Respiratory cancer mortality, Non-malignant respiratory disease mortality, Diseases of the respiratory tract mortality; Cancer/Carcinogenesis: Lung cancer mortality, Respiratory cancer mortality, Malignant tumors mortality, Gastric cancer mortality, Intestinal cancer mortality, Pancreatic cancer mortality, Gastrointestinal cancer mortality; Mortality: Lung cancer mortality, Respiratory cancer mortality, Malignant tumors mortality, Gastric cancer mortality, Intestinal cancer mortality, Pancreatic cancer mortality, Gastrointestinal cancer mortality, Non-malignant respiratory disease mortality, Diseases of the respiratory tract mortality, Diseases of circulation mortality, All causes mortality, Violent death mortality, External causes mortality; Gastrointestinal: Gastric cancer mortality, Intestinal cancer mortality, Pancreatic cancer mortality, Gastrointestinal cancer mortality; Cardiovascular: Diseases of circulation mortality		
Asbestos Fiber Type(s):	Asbestos - Chrysotile (serpentine): 12001-29-5; Asbestos - Crocidolite (riebeckite): 12001-28-4; Asbestos - Amosite (grunerite): 12172-73-5		
Linked HERO ID(s):	3083459, 3082919		
HERO ID:	3083459		

Domain	Metric	Rating	Comments
Domain 2: Exposure Characterization			
	Metric 4: Measurement of Exposure	Low	Neither study in this cohort indicated the method of quantifying/counting fibres Ohlson and Hogstedt, 1985, HEROID: 3083459; Albin et al., 1988, HEROID: 3082919). Ohlson and Hogstedt state in the methods that a general dust level of 10 mg/m3 was applied for pre-1970s data, and that fibre concentrations ”averaged 1 fibre/ml based on several hundred samples from five investigations between 1970 and 1976” (Ohlson and Hogstedt, 1985, HEROID: 3083459). Albin et al. provides very little regarding measurements of exposure, only stating, ”Individual dose estimates were calculated for two thirds of the cohort, the median intensity was around 1 f/ml” (Albin et al., 1988, HEROID: 3082919). No methodology regarding how this was measured and calculated is provided.This metric is rated Low because the studies or any cited methods source do not explicitly mention the use of PCM or TEM.
	Metric 5: Exposure Levels	Medium	Ohlson and Hogstedt provide exposure levels by employment time (<2 years, 2-<5 years, and >= 5 years) and latency time (0 or 20 years) (Ohlson and Hogstedt, 1985, HEROID: 3083459). This study is a Medium. Albin et al. uses two levels of exposure levels (exposed asbestos cement workers and the general population as referents (Albin et al., 1988, HEROID: 3082919). This study would be rated Low in this regard.

Additional Comments: Overall, this cohort consists of two older studies (1980s) where there is lacking information and methods surrounding the measurement of exposure. HEROIDs 3083459 and 3082919 were not evaluated for any metrics except Metric 4 and 5 and had no data extracted because they did not have sufficient exposure information to be useful for dose-response analysis.QC was not completed for metrics other than Metrics 4 and 5 because the study does not have sufficient exposure information to be useful for dose-response analysis.

* No biomarkers were identified for this evaluation.

** As described in Appendix B.2 of the *White Paper: Quantitative Approach to the Human Health Assessment for the Risk Evaluation for Asbestos Part 2: Supplemental Evaluation Including Legacy Uses and Associated Disposals of Asbestos*, to be considered as being informative for dose-response analysis, metrics 4 and 5 would need metric ratings of Medium or High. This reference did not satisfy this requirement; therefore data quality evaluation is presented for only for metrics 4 and 5.

Study Citation:	Ohlson, C. G., Klaesson, B., Hogstedt, C. (1984). Mortality among asbestos-exposed workers in a railroad workshop. Scandinavian Journal of Work, Environment and Health 10(5):283-291.
Health Outcome:	Lung Cancer; Gastrointestinal; Chronic obstructive lung disease, other diseases of the respiratory tract
Target Organ(s):	Mortality: All cause mortality, Lung cancer mortality, Gastric cancer mortality, Chronic obstructive lung disease mortality, Diseases of the respiratory tract (excluding chronic obstructive lung disease) mortality; Lung/Respiratory: Lung cancer mortality, Chronic obstructive lung disease mortality, Diseases of the respiratory tract (excluding chronic obstructive lung disease) mortality; Gastrointestinal: Gastric cancer mortality; Cancer/Carcinogenesis: Lung cancer mortality, Gastric cancer mortality
Asbestos Fiber Type(s):	Asbestos - Chrysotile (serpentine): 12001-29-5; Asbestos - Crocidolite (riebeckite): 12001-28-4; Asbestos - Amosite (grunerite): 12172-73-5; Asbestos - Not specified: 1332-21-4
Linked HERO ID(s):	No linked references.
HERO ID:	3083565

Domain		Metric	Rating	Comments
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Low	This metric is rated Low because the study or any cited methods source does not explicitly mention the use of PCM or TEM. In addition, while conversion factors for measurements of dust are given in Table 1, these are based on professional judgement relying on conversion factors from American insulators (Nicholson et al., 1982, HEROID 160).
	Metric 5:	Exposure Levels	Medium	Five exposure levels (as dust scores ranging from 0-4) are presented in Table 1 with crude conversions to fiber counts (ranging between 0-20 fibers/ml).Pre-1970, 5 exposure levels are reported. Post-1970, fiber count measurements show adequate exposure distribution to detect present associations (0-20 fibers/mL). However, of the 64 total fiber count measurements available, only 8 were > 1 fibers/mL.SMR analyses incorporating relevant exposure concentrations are performed by 4 ordinal exposure intensity categories (Table 4).

Additional Comments: QC was not completed for metrics other than Metrics 4 and 5 because the study does not have sufficient exposure information to be useful for dose-response analysis. This study does contain dust exposure concentrations with a conversion factor, which allows it to technically meet PECO. However, the conversion factor is based solely on professional judgement. In addition, there is no mention of PCM or TEM to quantify fibers.

* No biomarkers were identified for this evaluation.

** As described in Appendix B.2 of the *White Paper: Quantitative Approach to the Human Health Assessment for the Risk Evaluation for Asbestos Part 2: Supplemental Evaluation Including Legacy Uses and Associated Disposals of Asbestos*, to be considered as being informative for dose-response analysis, metrics 4 and 5 would need metric ratings of Medium or High. This reference did not satisfy this requirement; therefore data quality evaluation is presented for only for metrics 4 and 5.

Study Citation:	Ohlson, C. G., Rydman, T., Sundell, L., Bodin, L., Hogstedt, C. (1984). Decreased lung function in long-term asbestos cement workers: a cross-sectional study. American Journal of Industrial Medicine 5(5):359-366.
Health Outcome:	Pulmonary Function/Spirometry Results
Target Organ(s):	Lung/Respiratory: Forced vital capacity (FVC), Forced expiratory volume in one second (FEV1), Forced expiratory flow at 25-75% FVC, Pleural abnormalities
Asbestos Fiber Type(s):	Asbestos - Chrysotile (serpentine): 12001-29-5; Asbestos - Crocidolite (riebeckite): 12001-28-4; Asbestos - Amosite (grunerite): 12172-73-5
Linked HERO ID(s):	No linked references.
HERO ID:	2238788

Domain	Metric		Rating	Comments
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Low	The authors highlight that the exposure data available for the plant is limited, especially for the 1950s and 60s. Some measurements ”indicated a general dust level of 10 mg/m3 and half the amount during the 1970s” (Ohlson et al., 1984). Five investigations were conducted between 1970 and 1976, and average fiber concentration was found to be 1 fiber/ml. Some assumptions were made by the authors due to less effective ventilation in earlier decades, so a value of 2 fibers/ml was given. They also note that the highest value recorded was 8 fibers/ml in 1970. However, the authors did not provide information pertaining to the methods utilized to determine these fiber concentrations.The study or any cited methods source does not explicitly mention the use of PCM or TEM.
	Metric 5:	Exposure Levels	Medium	Exposed individuals were grouped into one of three categories based on the number of fiber-years that they were exposed. These groupings included 0-14, 15-22, and 23+ fiber-years.

Additional Comments:	Overall, this study had a number of strengths pertaining to their analyses performed, and their consideration of potential covariates. However, there were also some limitations related to the exposure measurements taken, because there were no specifics given as to the methods used. The authors note that there was no statistically significant dose-effect relationship between fiber-year estimates and lung function values.NOTE: Based on the new guidance, this study would not have been evaluated fully. Metric 4 was rated as low because there was no mention within the study or a cited source about the use of PCM or TEM.

* No biomarkers were identified for this evaluation.

** As described in Appendix B.2 of the *White Paper: Quantitative Approach to the Human Health Assessment for the Risk Evaluation for Asbestos Part 2: Supplemental Evaluation Including Legacy Uses and Associated Disposals of Asbestos*, to be considered as being informative for dose-response analysis, metrics 4 and 5 would need metric ratings of Medium or High. This reference did not satisfy this requirement; therefore data quality evaluation is presented for only for metrics 4 and 5.

Study Citation:	Ohlson, C. G., Rydman, T., Sundell, L., Bodin, L., Hogstedt, C. (1984). Decreased lung function in long-term asbestos cement workers: a cross-sectional study. American Journal of Industrial Medicine 5(5):359-366.
Health Outcome:	Pleural Plaques
Target Organ(s):	Lung/Respiratory: Pleural abnormalities
Asbestos Fiber Type(s):	Asbestos - Chrysotile (serpentine): 12001-29-5; Asbestos - Crocidolite (riebeckite): 12001-28-4; Asbestos - Amosite (grunerite): 12172-73-5
Linked HERO ID(s):	No linked references.
HERO ID:	2238788

Domain	Metric		Rating	Comments
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Low	The authors highlight that the exposure data available for the plant is limited, especially for the 1950s and 60s. Some measurements ”indicated a general dust level of 10 mg/m3 and half the amount during the 1970s” (Ohlson et al., 1984). Five investigations were conducted between 1970 and 1976, and average fiber concentration was found to be 1 fiber/ml. Some assumptions were made by the authors due to less effective ventilation in earlier decades, so a value of 2 fibers/ml was given. They also note that the highest value recorded was 8 fibers/ml in 1970. However, the authors did not provide information pertaining to the methods utilized to determine these fiber concentrations.The study or any cited methods source does not explicitly mention the use of PCM or TEM.
	Metric 5:	Exposure Levels	Medium	Exposed individuals were grouped into one of three categories based on the number of fiber-years that they were exposed. These groupings included 0-14, 15-22, and 23+ fiber-years.

Additional Comments:	Overall, this study had a number of strengths pertaining to their analyses performed, and their consideration of potential covariates. However, there were also some limitations related to the exposure measurements taken, because there were no specifics given as to the methods used. The authors note that there was no statistically significant dose-effect relationship between fiber-year estimates and lung function values. There was no significant difference between those with and without pleural plaques when the exposure was comparable.NOTE: This study would not have been fully evaluated under the current guidance. This is due to metric 4 being rated as low because neither the study nor a cited methods source mentioned the use of PCM or TEM.

* No biomarkers were identified for this evaluation.

** As described in Appendix B.2 of the *White Paper: Quantitative Approach to the Human Health Assessment for the Risk Evaluation for Asbestos Part 2: Supplemental Evaluation Including Legacy Uses and Associated Disposals of Asbestos*, to be considered as being informative for dose-response analysis, metrics 4 and 5 would need metric ratings of Medium or High. This reference did not satisfy this requirement; therefore data quality evaluation is presented for only for metrics 4 and 5.

Study Citation:	Paris, C., Benichou, J., Raffaelli, C., Genevois, A., Fournier, L., Menard, G., Broessel, N., Ameille, J., Brochard, P., Gillon, J. C. (2004). Factors associated with early-stage pulmonary fibrosis as determined by high-resolution computed tomography among persons occupationally exposed to asbestos. Scandinavian Journal of Work, Environment and Health 30(3):206-214.
Health Outcome:	Pulmonary Function/Spirometry Results
Target Organ(s):	Lung/Respiratory: Pulmonary Fibrosis
Asbestos Fiber Type(s):	Asbestos - Not specified: 1332-21-4
Linked HERO ID(s):	No linked references.
HERO ID:	3080175

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Low	Tentative participants were pensioners or early retirees from companies in the Nomandy region with known occupational asbestos exposure, recruited via mail from their former employers or in local information meetings. Most had worked in a single asbestos textile and friction material factory. Some had worked in other environments such as shipyards, fossil fuel power stations, and industrial insulation contractors. Eligible individuals had to have no previous involvement in systematic HRCT screening campaigns in their former companies and have no known asbestos-related diseases prior to inclusion. 706 retired workers were recruited from 1991-1999. Participation rates are not directly reported, but authors note that participation varied widely among industries. Complete interpretable functional test results were available for 630 of these participants.Healthy worker selection bias is a concern because of the requirement for no known asbestos-related disease at inclusion. Differential participation by knowledge of exposure and outcome status is also a concern, as subjects with higher known occupational exposure and known health problems may have been more likely to participate. The large disparities in participation rate across industries exacerbates this concern.
	Metric 2:	Attrition	High	Cross-sectional study design with outcome information available for 630 of 706 recruited participants. No major concerns.
	Metric 3:	Comparison Group	Medium	Recruitment methods were consistent for subjects in all ecumulative asbestos xposure categories (<25, 25-99.9 and >= 100 fibers/mL*years).
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Medium	The study or any cited methods source does not explicitly mention the use of PCM or TEM to quantify fibres.For participants who had worked in the asbetsos textile and friction material plant, exposure was quantified using a job-exosure matrix determined from airborne measurements collected annually from 1959-1999 in various areas of the plant. For all other participants, exposure levels were assessed using published airborne measurements available in the French database Evalutil according to calendar period of exposure and typical reported tasks. Cumulative-exposure index (CEI) for asbestos was calculated based on asbestos air measurements, job category, date of hire, date of assignment end, and duration of exposure (fibers/mL*years). For analysis, CEI was categorized at 3 levels: <25, 25-99.9, and >= 100 fibers/mL*years, with the lowest level serving as the reference group.

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Study Citation: Paris, C., Benichou, J., Raffaelli, C., Genevois, A., Fournier, L., Menard, G., Broessel, N., Ameille, J., Brochard, P., Gillon, J. C. (2004). Factors associated with early-stage pulmonary fibrosis as determined by high-resolution computed tomography among persons occupationally exposed to asbestos. Scandinavian Journal of Work, Environment and Health 30(3):206-214.
Health Outcome: Pulmonary Function/Spirometry Results
Target Organ(s): Lung/Respiratory: Pulmonary Fibrosis
Asbestos Fiber Type(s): Asbestos - Not specified: 1332-21-4
Linked HERO ID(s): No linked references.
HERO ID: 3080175

Domain	Metric		Rating	Comments
	Metric 5:	Exposure Levels	Medium	3 levels of quantitative CEI are reported (<25, 25-99.9, and >= 100 fibers/mL*years, with the lowest level serving as the reference group).
	Metric 6:	Temporality	Low	Dates of exposure assessment and outcome ascertainment are sufficiently documented. However, length of latency period is not well established (exposure assessment lasted until 1999, and outcome ascertainment began in 1990). Authors report that all subjects were in retirement from their occupations at the time of inclusion, but an appropriate/consistent latency period is not established.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	High	Pulmonary Function/Spirometry Results: The outcome of interest was pulmonary fibrosis. CT exploration of the lungs with 6+ high-resolution millimetric sections were used to assess clinical features of pulmonary fibrosis, including lesions, subpleural curvilinear lines, and ground-glass opacity. A grading scale of 0-3 was used (0 = normal, 1 = mild interstitial abnormalities, 2 = bilateral interstitial abnormalities with limited extent, 3 = profuse interstitial abnormalities), with grades 2 and 3 diagnosed as pulmonary fibrosis.
	Metric 8:	Reporting Bias	High	All results are reported with sufficient detail for replication.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Medium	2 sets of adjustment factors were used for multivariate analyses. Model 1 included 5 dichotomous (yes/no or high/low) covariates: basilar crackles, observed-to-predicted ratio for TLC, observed-to-predicted ratio for TLCO, small irregular opacities, and pleural abnormalities in the X-ray. Model 2 employed a backward stepwise procedure to all variables that appeared to be separately associated (10% change in estimate) with pulmonary fibrosis in univariate analyses. BMI and smoking status were also included in models 1 and 2 based on previous literature. Age and gender were adjusted for a priori.
	Metric 10:	Covariate Characterization	High	Covariates were assessed by standard interview or clinical examination performed by a physician.
	Metric 11:	Co-exposure Counfounding	Low	Occupational study with no discussion of potential co-exposures.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	Medium	Study uses an appropriate statistical method (multiple logistic regression) for ordinal exposure levels and a dichotomized outcome variable.
	Metric 13:	Statistical Power	Medium	Study population (n=630) and observed exposure ranges ((<25 - >=100 fibers/mL*years) were adequate to detect present associations.
	Metric 14:	Reproducibility of Analyses	Medium	Description of analysis is sufficient for reproduction.

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Study Citation:	Paris, C., Benichou, J., Raffaelli, C., Genevois, A., Fournier, L., Menard, G., Broessel, N., Ameille, J., Brochard, P., Gillon, J. C. (2004). Factors associated with early-stage pulmonary fibrosis as determined by high-resolution computed tomography among persons occupationally exposed to asbestos. Scandinavian Journal of Work, Environment and Health 30(3):206-214.
Health Outcome:	Pulmonary Function/Spirometry Results
Target Organ(s):	Lung/Respiratory: Pulmonary Fibrosis
Asbestos Fiber Type(s):	Asbestos - Not specified: 1332-21-4
Linked HERO ID(s):	No linked references.
HERO ID:	3080175

Domain	Metric		Rating	Comments
	Metric 15:	Statistical Analysis	Medium	Model for generating effect estimates is well documented and basic model assumptions are met.

Additional Comments: None

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation:	Paris, C., Martin, A., Letourneux, M., Wild, P. (2008). Modelling prevalence and incidence of fibrosis and pleural plaques in asbestos-exposed populations for screening and follow-up: a cross-sectional study. Environmental Health: A Global Access Science Source 7:30.
Health Outcome:	Asbestosis; Pleural Plaques
Target Organ(s):	Lung/Respiratory: Asbestosis, Pleural plaques
Asbestos Fiber Type(s):	Asbestos - Not specified: 1332-21-4
Linked HERO ID(s):	No linked references.
HERO ID:	758967

Domain	Metric		Rating	Comments
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Low	This metric is rated Low because the study or any cited methods source does not explicitly mention the use of PCM or TEM. The cited method source entitled ”Use of a job-exposure matrix for the screening of occupational exposure to asbestos” by Fournier 2004 is not available on HERO nor accessible in public domains.Quantitative assessment of exposure obtained by occupational hygiene measurements and job-exposure matrix (JEM) elaborated from airborne measurements from 1959-1999 in various workshops of the plant. A cumulative exposure index (CEI) was then calculated and expressed in fibers/ml.years. Average exposure index calculated by dividing CEI by duration of exposure.
	Metric 5:	Exposure Levels	Medium	3 levels of exposure. Airborne measurements were collected annually 1959-1999 in various workshops of plants, other subjects estimation of exposure was used based on French Database Evalutil. Cumulative Exposure (y.f/ml) for healthy subjects was 88.9, $\pm$92.4; for pleural plaque subjects was 137.0, $\pm$140.8; and for asbestosis subjects was 143.3, $\pm$135.4. Other exposure metrics estimated in this study showed roughly similar patterns as observed with cumulative exposure.

Additional Comments:	This study was a cross-sectional occupational study and it examined which exposure parameters are most useful to the clinicians in the selection of asbestos-exposed subjectsto be submitted to a CT-Scan as part of a screening exercise. While it considered adjusting for confounders and variables, potential confounders such as age were not included in the multiple regression models. It employed tests fit of data while also highlighting assumptions and design flaws. Outcome/analysis of asbestosis vs. fibrosis terms used interchangeably throughout article. Overall, a well-conducted study with ample information provided.Overall, information on the measurement of exposure metric (M4) to assess exposure was limited. On the other hand, the exposure levels metric (M5) information reported was adequate to determine exposure-response relationships.

* No biomarkers were identified for this evaluation.

** As described in Appendix B.2 of the *White Paper: Quantitative Approach to the Human Health Assessment for the Risk Evaluation for Asbestos Part 2: Supplemental Evaluation Including Legacy Uses and Associated Disposals of Asbestos*, to be considered as being informative for dose-response analysis, metrics 4 and 5 would need metric ratings of Medium or High. This reference did not satisfy this requirement; therefore data quality evaluation is presented for only for metrics 4 and 5.

Study Citation:	Pearce, N. (1988). Multistage modelling of lung cancer mortality in asbestos textile workers. International Journal of Epidemiology 17(4):747-752.
Health Outcome:	Lung Cancer
Target Organ(s):	Cancer/Carcinogenesis: Lung cancer; Lung/Respiratory: Lung cancer
Asbestos Fiber Type(s):	Asbestos - Not specified: 1332-21-4
Linked HERO ID(s):	No linked references.
HERO ID:	3082886

Domain	Metric		Rating	Comments
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Low	Exposure data was expressed in fibers per cc of air (fibers/cc), and was available from 1930-1975. However, the authors do not provide details about the equipment or methods used to generate this data. All workers had an estimated cumulative exposure based on ”the summed products of air concentrations of asbestos and time (in days) spent in various jobs” (Pearce, 1988). A dichotomous classification of exposure was utilized because of the small numbers.
	Metric 5:	Exposure Levels	Low	During the statistical analysis, exposure to asbestos was categorized into low or high, with high being classified as 5000+ fibre/cc days and low as <5000 fibre/cc days. Table 2 also examined observed and expected number of lung cancer deaths among the workers based on their cumulative exposure between <1 and 100+ in thousand fibre/cc days. The authors indicated that this dichotomous classification of exposure was appropriate because it provided ”reasonable numbers in both exposure categories” (Pearce, 1988).

Additional Comments:	Overall, information on the measurement of exposure metric (M4) to assess exposure was limited. Additionally, the exposure levels metric (M5) information reported was limited to determine exposure-response relationships.

* No biomarkers were identified for this evaluation.

** As described in Appendix B.2 of the *White Paper: Quantitative Approach to the Human Health Assessment for the Risk Evaluation for Asbestos Part 2: Supplemental Evaluation Including Legacy Uses and Associated Disposals of Asbestos*, to be considered as being informative for dose-response analysis, metrics 4 and 5 would need metric ratings of Medium or High. This reference did not satisfy this requirement; therefore data quality evaluation is presented for only for metrics 4 and 5.

Study Citation:	Pesch, B., Taeger, D., Johnen, G., Gross, I. M., Weber, D. G., Gube, M., Müller-Lux, A., Heinze, E., Wiethege, T., Neumann, V., Tannapfel, A., Raithel, H. J., Brüning, T., Kraus, T. (2010). Cancer mortality in a surveillance cohort of German males formerly exposed to asbestos. International Journal of Hygiene and Environmental Health 213(1):44-51.
Health Outcome:	All cause mortality, Mortality from pneumoconioses and other lung diseases due to external agents
Target Organ(s):	Lung/Respiratory: Mortality from pneumoconioses and other lung diseases due to external agents (ICD9: 500-208); Mortality: Mortality from pneumoconioses and other lung diseases due to external agents (ICD9: 500-208), All causes (ICD9: 000-999)
Asbestos Fiber Type(s):	Asbestos - Not specified: 1332-21-4; Asbestos - Chrysotile (serpentine): 12001-29-5; Asbestos - Crocidolite (riebeckite): 12001-28-4
Linked HERO ID(s):	No linked references.
HERO ID:	3079156

Domain	Metric		Rating	Comments
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Low	Exposure was developed from expert input based on occupational history, job activity, and other characteristics, but no measures of asbestos concentration.
	Metric 5:	Exposure Levels	Low	Exposures are categorized into 3 ordinal groups of fiber years (< 25, 25-100, >100). It is unclear if distributions are wide enough, given they are broken into 3 categories.

Additional Comments: No additional comments. Overall, the measurement of exposure metric (M4) methods used to assess the exposure were not well defined, there were no quantitative measurements. Additionally, the exposure levels metric (M5) information reported was not adequate to determine an exposure-response relationship.

* No biomarkers were identified for this evaluation.

** As described in Appendix B.2 of the *White Paper: Quantitative Approach to the Human Health Assessment for the Risk Evaluation for Asbestos Part 2: Supplemental Evaluation Including Legacy Uses and Associated Disposals of Asbestos*, to be considered as being informative for dose-response analysis, metrics 4 and 5 would need metric ratings of Medium or High. This reference did not satisfy this requirement; therefore data quality evaluation is presented for only for metrics 4 and 5.

Study Citation:	Peto, J. (1980). Lung cancer mortality in relation to measured dust levels in an asbestos textile factory. IARC Scientific Publications (30):829-836.
Health Outcome:	Lung Cancer; other cancers mortality; asbestosis mortality, other respiratory disease mortality, other causes mortality
Target Organ(s):	Cancer/Carcinogenesis: lung cancer mortality, other cancers mortality; Mortality: lung cancer mortality, other cancers mortality, asbestosis mortality, other respiratory disease mortality, other causes mortality; Lung/Respiratory: lung cancer mortality, asbestosis mortality, other respiratory disease mortality; other causes: other causes mortality
Asbestos Fiber Type(s):	Asbestos - Chrysotile (serpentine): 12001-29-5; Asbestos - Crocidolite (riebeckite): 12001-28-4
Linked HERO ID(s):	No linked references.
HERO ID:	163

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Medium	This study is an extended follow up of the same North England asbestos textile factory worker cohort recruited from the work areas with highest expected asbestos exposure: fiberizing, carding, spinning, weaving, and plaiting. (Knox et al. 1968, HEROID: 115; Peto et al. 1977, HEROID: 3084525). Here, 679 men who had begun work after 1933 and who had accrued >10 total years of service by 1972 were included in the study. There is limited detail on recruitment or other inclusion criteria. There may be some selection bias, as only healthier workers would be able to complete >10 years of work in select high-exposure areas.
	Metric 2:	Attrition	High	Follow up for mortality continued through 1978 by the National Health Central Register and the factory personnel department. 41 of 679 (6%) men were unable to be traced. In this analysis, they were assumed to have been alive at the previous follow up date (12/31/1974), but their subsequent man-years were not included here. Deaths of workers over 85 are ignored. There is no other mention of drop-out or loss that was not included in follow-up.
	Metric 3:	Comparison Group	Low	The study only mentions ”unaffected controls” in the section on lung cancer mortality and dust levels. Another study using the same cohort (Knox et al. 1968, HEROID: 115) notes comparisons to ”national rates,” however it's not clear if this is the same comparison group for this study. The study does compare in text results workers first exposed before 1951 and those in 1951 and later (i.e., cohort 1 and 2).
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Low	Asbestos fiber exposure concentrations were reportedly measured using a thermal precipitator in years between 1951-1961. Additional support for understanding past area dust measures in particles/mL were taken in conversations with hygiene officers from the factory. Static membrane filters in years after 1961. Authors state that for each area of the factory, representative combinations of measures were used and averaged to be converted to modern counting methods. ”The revised estimates are based on preliminary data abstracted from a detailed analysis that is currently being conducted by T.B.A. Industrial Products Ltd and must be regarded as provisional. However, they indicate that average dust levels were in the region of 30 fibre/ml in 1951 and remained high until about 10 years ago.”
	Metric 5:	Exposure Levels	Low	Asbestos exposure appears to be continuous, however SMR analyses are stratified by years since first exposure and year of first exposure, not by a quantitative measure of asbestos exposure. This suggests the exposure for SMR analyses is dichotomous.

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Study Citation:	Peto, J. (1980). Lung cancer mortality in relation to measured dust levels in an asbestos textile factory. IARC Scientific Publications (30):829-836.
Health Outcome:	Lung Cancer; other cancers mortality; asbestosis mortality, other respiratory disease mortality, other causes mortality
Target Organ(s):	Cancer/Carcinogenesis: lung cancer mortality, other cancers mortality; Mortality: lung cancer mortality, other cancers mortality, asbestosis mortality, other respiratory disease mortality, other causes mortality; Lung/Respiratory: lung cancer mortality, asbestosis mortality, other respiratory disease mortality; other causes: other causes mortality
Asbestos Fiber Type(s):	Asbestos - Chrysotile (serpentine): 12001-29-5; Asbestos - Crocidolite (riebeckite): 12001-28-4
Linked HERO ID(s):	No linked references.
HERO ID:	163

Domain		Metric	Rating	Comments
	Metric 6:	Temporality	Medium	There is appropriate temporality reported (>10 years) to follow-up to establish exposure-outcome, however it is not clear what share of workers has longer follow up time, as only man-years are reported, not total workers by years of service. In the paper on the same cohort published prior to this one, which had more subjects (Peto et al. 1977, HEROID: 3084525), 406/1085 (37%) of workers had >20 years of service. It seems reasonable to assume a similar proportion in the current study.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Medium	Lung Cancer: No ICD codes were used to establish mortality, except for gastrointestinal cancer, however no version is explicitly listed. Authors report that follow-up was itself completed by National Health Central Register (NHCR) and by the factory personnel department.; Other Cancer(s): No ICD codes were used to establish mortality, except for gastrointestinal cancer (Codes 151-154), however no version is explicitly listed. Authors report that follow-up was itself completed by National Health Central Register (NHCR) and by the factory personnel department.; Other Non-Cancer Outcomes: No ICD codes were used to establish mortality, except for gastrointestinal cancer, however no version is explicitly listed. Authors report that follow-up was itself completed by National Health Central Register (NHCR) and by the factory personnel department.
	Metric 8:	Reporting Bias	High	Outcomes are reported in all parts of study along with p-values. Some data is available in text with confidence limits.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Low	Sex is adjusted for based on inclusion of only men. There is brief mention of adjustment for man-years in the analysis, but no other variables are discussed.
	Metric 10:	Covariate Characterization	Low	Covariate is assumed to have been collected from factory personnel records. No explicit detail is provided.
	Metric 11:	Co-exposure Counfounding	Low	Authors do not explicitly mention any co-exposures.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	Medium	The study design is appropriate for measuring relative risk and mortality rates of workers from the textile factory.
	Metric 13:	Statistical Power	Medium	The number of subjects (n=679) should be sufficient to find any true relationships between exposure and outcome.
	Metric 14:	Reproducibility of Analyses	Medium	The methods described in the paper are clear enough to be conceptually replicated.
	Metric 15:	Statistical Analysis	Medium	SMR analyses were appropriate, with no explicit assumptions to be met.

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Study Citation:	Peto, J. (1980). Lung cancer mortality in relation to measured dust levels in an asbestos textile factory. IARC Scientific Publications (30):829-836.
Health Outcome:	Lung Cancer; other cancers mortality; asbestosis mortality, other respiratory disease mortality, other causes mortality
Target Organ(s):	Cancer/Carcinogenesis: lung cancer mortality, other cancers mortality; Mortality: lung cancer mortality, other cancers mortality, asbestosis mortality, other respiratory disease mortality, other causes mortality; Lung/Respiratory: lung cancer mortality, asbestosis mortality, other respiratory disease mortality; other causes: other causes mortality
Asbestos Fiber Type(s):	Asbestos - Chrysotile (serpentine): 12001-29-5; Asbestos - Crocidolite (riebeckite): 12001-28-4
Linked HERO ID(s):	No linked references.
HERO ID:	163

Domain	Metric	Rating	Comments
Additional Comments:	Asbestos fiber types are detailed in an earlier iteration of the current study (Knox et al., 1968, HEROID: 115). There is limited detail on recruitment and participation methods and rates, as well as how outcomes were ascertained by the National Health Central Register and factory personnel departments.		

Overall Quality Determination **Low**

* No biomarkers were identified for this evaluation.

Study Citation:	Piolatto, G., Negri, E., La Vecchia, C., Pira, E., Decarli, A., Peto, J. (1990). An update of cancer mortality among chrysotile asbestos miners in Balangero, northern Italy. British Journal of Industrial Medicine 47(12):810-814.
Health Outcome:	Asbestosis
Target Organ(s):	Lung/Respiratory: chronic obstructive pulmonary diseases mortality, asbestosis mortality, mortality from COPD+asbestosis, chronic respiratory disease mortality; Cancer/Carcinogenesis: gastric cancer mortality or stomach cancer mortality, intestinal cancer mortality, prostate cancer mortality, bladder cancer mortality, lymphatic and haematopoietic cancer mortality, mortality from the following neoplastic causes: stomach, colorectal, pancreas, prostate, bladder, kidney, brain and CNS, lymphatic and hematopioetic; Mortality: gastric cancer mortality or stomach cancer mortality, intestinal cancer mortality, prostate cancer mortality, bladder cancer mortality, lymphatic and haematopoietic cancer mortality, mortality from the following neoplastic causes: stomach, colorectal, liver, pancreas, prostate, bladder, kidney, brain and CNS, lymphatic and hematopioeticcerebrovascular diseases mortality, stroke mortality, chronic obstructive pulmonary diseases mortality,mortality from COPD+asbestosis, asbestosis mortality, chronic respiratory disease mortality; Skin/Connective Tissue: pleural and peritoneal cancer mortality; Neurological/Behavioral: cerebrovascular diseases mortality, stroke mortality, mortality from the following neoplastic causes: brain and CNS; Cardiovascular: cerebrovascular diseases mortality, stroke mortality; Gastrointestinal: oro-pharyngeal cancer mortality or oral cavity/pharynx cancer mortality, gastric cancer mortality or stomach cancer mortality, intestinal cancer mortality,; Immune/Hematological: lymphatic and haematopoietic cancer mortality; Reproductive/Developmental: prostate cancer mortality; Renal/Kidney: mortality from the following neoplastic causes: kidney,
Asbestos Fiber Type(s):	Asbestos - Chrysotile (serpentine): 12001-29-5; Asbestos - Crocidolite (riebeckite): 12001-28-4
Linked HERO ID(s):	3082492, 2592425, 5060134
HERO ID:	3082492

Domain	Metric	Rating	Comments
Domain 1: Study Participation			

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Study Citation:	Piolatto, G., Negri, E., La Vecchia, C., Pira, E., Decarli, A., Peto, J. (1990). An update of cancer mortality among chrysotile asbestos miners in Balangero, northern Italy. British Journal of Industrial Medicine 47(12):810-814.
Health Outcome:	Asbestosis
Target Organ(s):	Lung/Respiratory: chronic obstructive pulmonary diseases mortality, asbestosis mortality, mortality from COPD+asbestosis, chronic respiratory disease mortality; Cancer/Carcinogenesis: gastric cancer mortality or stomach cancer mortality, intestinal cancer mortality, prostate cancer mortality, bladder cancer mortality, lymphatic and haematopoietic cancer mortality, mortality from the following neoplastic causes: stomach, colorectal, pancreas, prostate, bladder, kidney, brain and CNS, lymphatic and hematopioetic; Mortality: gastric cancer mortality or stomach cancer mortality, intestinal cancer mortality, prostate cancer mortality, bladder cancer mortality, lymphatic and haematopoietic cancer mortality, mortality from the following neoplastic causes: stomach, colorectal, liver, pancreas, prostate, bladder, kidney, brain and CNS, lymphatic and hematopioeticcerebrovascular diseases mortality, stroke mortality, chronic obstructive pulmonary diseases mortality,mortality from COPD+asbestosis, asbestosis mortality, chronic respiratory disease mortality; Skin/Connective Tissue: pleural and peritoneal cancer mortality; Neurological/Behavioral: cerebrovascular diseases mortality, stroke mortality, mortality from the following neoplastic causes: brain and CNS; Cardiovascular: cerebrovascular diseases mortality, stroke mortality; Gastrointestinal: oro-pharyngeal cancer mortality or oral cavity/pharynx cancer mortality, gastric cancer mortality or stomach cancer mortality, intestinal cancer mortality,; Immune/Hematological: lymphatic and haematopoietic cancer mortality; Reproductive/Developmental: prostate cancer mortality; Renal/Kidney: mortality from the following neoplastic causes: kidney,
Asbestos Fiber Type(s):	Asbestos - Chrysotile (serpentine): 12001-29-5; Asbestos - Crocidolite (riebeckite): 12001-28-4
Linked HERO ID(s):	3082492, 2592425, 5060134
HERO ID:	3082492

Domain	Metric		Rating	Comments
	Metric 1:	Participant Selection	Medium	These three studies, along with Rubino et al. 1979, HERO ID 000178, were evaluated for lung cancer as part of the Balangero, Italy cohort in the Draft Asbestos Part 1 Risk Evaluation (March 2020). Pira et al. 2017, HERO ID 5060134 was evaluated for lung cancer and laryngeal cancer in the Final Asbestos Part 1 Risk Evaluation (Dec. 2020). As described in the Draft Asbestos Part 1 Risk Evaluation Systematic Review Supplemental File, "Subjects included men from the Balangero mine worker cohort that were employed in an Italian asbestos mine. The initial cohort ((Rubino et al., 1979), pg 188) consisted of 952 men employed between 1/1/1930 and 12/31/1965, with at least 30 calendar days' employment during that period. Mortality data were collected from 1/1/1946 to 12/31/1975. Workers for which vital status could not be acertained and a small number of contract workers employed intermittently were excluded. In the first follow-up, 1058 workers were included that had worked at least one year between 1946 and 1987 and mortality follow-up was extended through 12/31/1987 ((Piolatto et al., 1990), pg 810). In subsequent follow-ups ((Pira et al., 2009) pg 805, and (Pira et al., 2017)), subjects included 1056 men from the Balangero mine worker cohort employed between 1930 and 1990, and mortality records were evaluated though 2003 and 2014, respectively. Records were not available between 1987 and 1990, when the mine closed, so workers employed in 1987 were assumed to be employed through 1990 unless they died during that period. Additional details in the most recent following indicated that the initial cohort included 1182 men; the 126 excluded subjects were contract workers, those employed <1 yr, those with inconsistencies in data, and those known to have died prior to 1946 (Pira et al., 2017) pg 558." As described in the final Asbestos Part 1 Risk Evaluation Supplemental File for Laryngeal Cancers, "Subjects were drawn from the employment records of an Italian asbestos mine (n=1056 men). Those eligible had worked for the mine for at least one year between 1930 and 1989. Description of the mine setting was described including some historical occupational measurements of dust and asbestos."This metric was rated High in the Draft and Medium in the Final Asbestos Part 1 Risk Evaluation.

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Study Citation:	Piolatto, G., Negri, E., La Vecchia, C., Pira, E., Decarli, A., Peto, J. (1990). An update of cancer mortality among chrysotile asbestos miners in Balangero, northern Italy. British Journal of Industrial Medicine 47(12):810-814.
Health Outcome:	Asbestosis
Target Organ(s):	Lung/Respiratory: chronic obstructive pulmonary diseases mortality, asbestosis mortality, mortality from COPD+asbestosis, chronic respiratory disease mortality; Cancer/Carcinogenesis: gastric cancer mortality or stomach cancer mortality, intestinal cancer mortality, prostate cancer mortality, bladder cancer mortality, lymphatic and haematopoietic cancer mortality, mortality from the following neoplastic causes: stomach, colorectal, pancreas, prostate, bladder, kidney, brain and CNS, lymphatic and hematopioetic; Mortality: gastric cancer mortality or stomach cancer mortality, intestinal cancer mortality, prostate cancer mortality, bladder cancer mortality, lymphatic and haematopoietic cancer mortality, mortality from the following neoplastic causes: stomach, colorectal, liver, pancreas, prostate, bladder, kidney, brain and CNS, lymphatic and hematopioeticcerebrovascular diseases mortality, stroke mortality, chronic obstructive pulmonary diseases mortality,mortality from COPD+asbestosis, asbestosis mortality, chronic respiratory disease mortality; Skin/Connective Tissue: pleural and peritoneal cancer mortality; Neurological/Behavioral: cerebrovascular diseases mortality, stroke mortality, mortality from the following neoplastic causes: brain and CNS; Cardiovascular: cerebrovascular diseases mortality, stroke mortality; Gastrointestinal: oro-pharyngeal cancer mortality or oral cavity/pharynx cancer mortality, gastric cancer mortality or stomach cancer mortality, intestinal cancer mortality,; Immune/Hematological: lymphatic and haematopoietic cancer mortality; Reproductive/Developmental: prostate cancer mortality; Renal/Kidney: mortality from the following neoplastic causes: kidney,
Asbestos Fiber Type(s):	Asbestos - Chrysotile (serpentine): 12001-29-5; Asbestos - Crocidolite (riebeckite): 12001-28-4
Linked HERO ID(s):	3082492, 2592425, 5060134
HERO ID:	3082492

Domain	Metric		Rating	Comments
	Metric 2:	Attrition	High	These three studies, along with Rubino et al. 1979, HERO ID 000178, were evaluated for lung cancer as part of the Balangero, Italy cohort in the Draft Asbestos Part 1 Risk Evaluation (March 2020). Pira et al. 2017, HERO ID 5060134 was evaluated for lung cancer and laryngeal cancer in the Final Asbestos Part 1 Risk Evaluation (Dec. 2020). As described in the Draft Asbestos Part 1 Risk Evaluation Systematic Review Supplemental File, ”In the most recent follow-up, study authors report that one of the strengths of the study is low proportion of subjects lost to follow-up (Pira et al., 2017) pg 562. Loss to follow-up was 2% in the initial cohort (Rubino et al., 1979), 3% in the first follow-up ((Piolatto et al., 1990), pg 810), and 4% in the most recent follow-ups (Pira et al., 2009) pg 805; (Pira et al., 2017) pg 559.”As described in the Final Asbestos Part 1 Risk Evaluation Systematic Review Supplemental File for Laryngeal Cancer ”The study authors note that the cause of death could not be determined for a small sample (n=6), and a small percentage (3.8%) of participants emigrated or were otherwise lost to follow-up. This level of attritionis not expected to appreciably bias the results.”This Metric was rated as High in both the Draft and Final Asbestos Part 1 Risk Evaluation.

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Study Citation:	Piolatto, G., Negri, E., La Vecchia, C., Pira, E., Decarli, A., Peto, J. (1990). An update of cancer mortality among chrysotile asbestos miners in Balangero, northern Italy. British Journal of Industrial Medicine 47(12):810-814.
Health Outcome:	Asbestosis
Target Organ(s):	Lung/Respiratory: chronic obstructive pulmonary diseases mortality, asbestosis mortality, mortality from COPD+asbestosis, chronic respiratory disease mortality; Cancer/Carcinogenesis: gastric cancer mortality or stomach cancer mortality, intestinal cancer mortality, prostate cancer mortality, bladder cancer mortality, lymphatic and haematopoietic cancer mortality, mortality from the following neoplastic causes: stomach, colorectal, pancreas, prostate, bladder, kidney, brain and CNS, lymphatic and hematopioetic; Mortality: gastric cancer mortality or stomach cancer mortality, intestinal cancer mortality, prostate cancer mortality, bladder cancer mortality, lymphatic and haematopoietic cancer mortality, mortality from the following neoplastic causes: stomach, colorectal, liver, pancreas, prostate, bladder, kidney, brain and CNS, lymphatic and hematopioeticcerebrovascular diseases mortality, stroke mortality, chronic obstructive pulmonary diseases mortality,mortality from COPD+asbestosis, asbestosis mortality, chronic respiratory disease mortality; Skin/Connective Tissue: pleural and peritoneal cancer mortality; Neurological/Behavioral: cerebrovascular diseases mortality, stroke mortality, mortality from the following neoplastic causes: brain and CNS; Cardiovascular: cerebrovascular diseases mortality, stroke mortality; Gastrointestinal: oro-pharyngeal cancer mortality or oral cavity/pharynx cancer mortality, gastric cancer mortality or stomach cancer mortality, intestinal cancer mortality,; Immune/Hematological: lymphatic and haematopoietic cancer mortality; Reproductive/Developmental: prostate cancer mortality; Renal/Kidney: mortality from the following neoplastic causes: kidney,
Asbestos Fiber Type(s):	Asbestos - Chrysotile (serpentine): 12001-29-5; Asbestos - Crocidolite (riebeckite): 12001-28-4
Linked HERO ID(s):	3082492, 2592425, 5060134
HERO ID:	3082492

Domain	Metric		Rating	Comments
	Metric 3:	Comparison Group	Medium	These three studies, along with Rubino et al. 1979, HERO ID 000178, were evaluated for lung cancer as part of the Balangero, Italy cohort in the Draft Asbestos Part 1 Risk Evaluation (March 2020). Pira et al. 2017, HERO ID 5060134 was evaluated for lung cancer and laryngeal cancer in the Final Asbestos Part 1 Risk Evaluation (Dec. 2020). As described in the Draft Asbestos Part 1 Risk Evaluation Systematic Review Supplemental File, "The most complete data on comparison groups is available from the most recent follow-up (Pira et al., 2017). General population mortality rates using the whole country from 1955 until 1980 and specifically the Piedmont Region (where the mine is located) from 1981 onwards (no regional rates available prior to 1981). The 1955-1959 rates were applied to 1946-1954 period (no available data); this may have led to an underestimate of expected deaths which may have showed and increased rate during this period. Expected numbers of deaths (overall and selected cancers) were computed using age-specific and calendar-year-specific (5-year categories) male death rates (Pira et al., 2017) pg 559. The only deviation from this was in the first follow-up, which used national mortality rates were for the entire follow-up period (through 1987) (Piolatto et al., 1990) pg. 811). In the initial study on this cohort ((Rubino et al., 1979), pg. 189), an additional case-control study was performed in which 5 age-matched controls were selected at random; they were confirmed alive at the time of death for the matched case. No details on what population provided controls. The evaluation is based on the cohort mortality study only, as this was the analysis carried through the 3 follow-up studies (Pira et al., 2017; Pira et al., 2009; Piolatto et al., 1990)."As described in the Final Asbestos Part 1 Risk Evaluation Systematic Review Supplemental File for Laryngeal Cancer, "Mortality rates for males from the Piedmont Region were used as a comparison group. This is a sufficiently similar group, however, the study authors note that mortality rates were not available for certain periods (e.g., 1946-1954) and rates from adjacent periods of time were used instead (1955-1959 rates applied to 1946-1954)."This metric was rated as High in the Draft and Medium in the Final Asbestos Part 1 Risk Evaluation.

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Study Citation:	Piolatto, G., Negri, E., La Vecchia, C., Pira, E., Decarli, A., Peto, J. (1990). An update of cancer mortality among chrysotile asbestos miners in Balangero, northern Italy. British Journal of Industrial Medicine 47(12):810-814.
Health Outcome:	Asbestosis
Target Organ(s):	Lung/Respiratory: chronic obstructive pulmonary diseases mortality, asbestosis mortality, mortality from COPD+asbestosis, chronic respiratory disease mortality; Cancer/Carcinogenesis: gastric cancer mortality or stomach cancer mortality, intestinal cancer mortality, prostate cancer mortality, bladder cancer mortality, lymphatic and haematopoietic cancer mortality, mortality from the following neoplastic causes: stomach, colorectal, pancreas, prostate, bladder, kidney, brain and CNS, lymphatic and hematopioetic; Mortality: gastric cancer mortality or stomach cancer mortality, intestinal cancer mortality, prostate cancer mortality, bladder cancer mortality, lymphatic and haematopoietic cancer mortality, mortality from the following neoplastic causes: stomach, colorectal, liver, pancreas, prostate, bladder, kidney, brain and CNS, lymphatic and hematopioeticcerebrovascular diseases mortality, stroke mortality, chronic obstructive pulmonary diseases mortality,mortality from COPD+asbestosis, asbestosis mortality, chronic respiratory disease mortality; Skin/Connective Tissue: pleural and peritoneal cancer mortality; Neurological/Behavioral: cerebrovascular diseases mortality, stroke mortality, mortality from the following neoplastic causes: brain and CNS; Cardiovascular: cerebrovascular diseases mortality, stroke mortality; Gastrointestinal: oro-pharyngeal cancer mortality or oral cavity/pharynx cancer mortality, gastric cancer mortality or stomach cancer mortality, intestinal cancer mortality,; Immune/Hematological: lymphatic and haematopoietic cancer mortality; Reproductive/Developmental: prostate cancer mortality; Renal/Kidney: mortality from the following neoplastic causes: kidney,
Asbestos Fiber Type(s):	Asbestos - Chrysotile (serpentine): 12001-29-5; Asbestos - Crocidolite (riebeckite): 12001-28-4
Linked HERO ID(s):	3082492, 2592425, 5060134
HERO ID:	3082492

Domain	Metric		Rating	Comments
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Medium	These three studies, along with Rubino et al. 1979, HERO ID 000178, were evaluated for lung cancer as part of the Balangero, Italy cohort in the Draft Asbestos Part 1 Risk Evaluation (March 2020). Pira et al. 2017, HERO ID 5060134 was evaluated for lung cancer and laryngeal cancer in the Final Asbestos Part 1 Risk Evaluation (Dec. 2020). As described in the Draft Asbestos Part 1 Risk Evaluation Systematic Review Supplemental File, "Most complete report of exposure assessment is in initial cohort study ((Rubino et al., 1979) pg 189). Chrysotile fiber counts were first measured in 1969 using membrane filter collection and phase contrast microscopy (frequency not reported). To estimate exposure from 1946-1969, factory records on daily production, equipment used, characteristics of the job and number of hours/day were used (this method has considerable limitations due to basis on mean values for large job categories and no allowance for changes in weather). Simulated and measured data were made comparable by using weighting factors (e.g., more dusty operation for 1-2 hr/d compared with longer working hours in the past). Less detailed information was included in follow-up reports ((Piolatto et al., 1990) pg. 810; (Pira et al., 2017), pg 558-559)."As described in the Final Asbestos Part 1 Risk Evaluation for Laryngeal Cancer, "Descriptions of the mine and occupational surveillance was described. Estimates of historical mean concentrations were 37 fibre/mL up to 1950 and 5 fibre/mL between 1971 and 1976. Exposure was determined by employment at the asbestos mine only."This metric was rated as Medium in the Draft and Low in the Final Risk Evaluation for Asbestos Part 1. However, the cohort meets the criteria for Medium as described above.

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Study Citation: Piolatto, G., Negri, E., La Vecchia, C., Pira, E., Decarli, A., Peto, J. (1990). An update of cancer mortality among chrysotile asbestos miners in Balangero, northern Italy. British Journal of Industrial Medicine 47(12):810-814.

Health Outcome: Asbestosis

Target Organ(s): Lung/Respiratory: chronic obstructive pulmonary diseases mortality, asbestosis mortality, mortality from COPD+asbestosis, chronic respiratory disease mortality; Cancer/Carcinogenesis: gastric cancer mortality or stomach cancer mortality, intestinal cancer mortality, prostate cancer mortality, bladder cancer mortality, lymphatic and haematopoietic cancer mortality, mortality from the following neoplastic causes: stomach, colorectal, pancreas, prostate, bladder, kidney, brain and CNS, lymphatic and hematopioetic; Mortality: gastric cancer mortality or stomach cancer mortality, intestinal cancer mortality, prostate cancer mortality, bladder cancer mortality, lymphatic and haematopoietic cancer mortality, mortality from the following neoplastic causes: stomach, colorectal, liver, pancreas, prostate, bladder, kidney, brain and CNS, lymphatic and hematopioeticcerebrovascular diseases mortality, stroke mortality, chronic obstructive pulmonary diseases mortality,mortality from COPD+asbestosis, asbestosis mortality, chronic respiratory disease mortality; Skin/Connective Tissue: pleural and peritoneal cancer mortality; Neurological/Behavioral: cerebrovascular diseases mortality, stroke mortality, mortality from the following neoplastic causes: brain and CNS; Cardiovascular: cerebrovascular diseases mortality, stroke mortality; Gastrointestinal: oro-pharyngeal cancer mortality or oral cavity/pharynx cancer mortality, gastric cancer mortality or stomach cancer mortality, intestinal cancer mortality,; Immune/Hematological: lymphatic and haematopoietic cancer mortality; Reproductive/Developmental: prostate cancer mortality; Renal/Kidney: mortality from the following neoplastic causes: kidney,

Asbestos Fiber Type(s): Asbestos - Chrysotile (serpentine): 12001-29-5; Asbestos - Crocidolite (riebeckite): 12001-28-4

Linked HERO ID(s): 3082492, 2592425, 5060134

HERO ID: 3082492

Domain	Metric		Rating	Comments
	Metric 5:	Exposure Levels	Medium	These three studies, along with Rubino et al. 1979, HERO ID 000178, were evaluated for lung cancer as part of the Balangero, Italy cohort in the Draft Asbestos Part 1 Risk Evaluation (March 2020). Pira et al. 2017, HERO ID 5060134 was evaluated for lung cancer and laryngeal cancer in the Final Asbestos Part 1 Risk Evaluation (Dec. 2020). As described in the Draft Asbestos Part 1 Risk Evaluation Systematic Review Supplemental File, "In the initial cohort ((Rubino et al., 1979), Table 8), exposure was reported as up to 100 fiber/yr or >100 fiber/year. In the follow-ups, exposure was reported as <100 fiber/mL-yr, 100-<400 fiber/mL-yr, and >=400 fiber/ml-yr ((Piolatto et al., 1990), Table 3; (Pira et al., 2009), Table 2; (Pira et al., 2017), Tables 3-4)." This metric was not rated in the Final Asbestos Part 1 Risk Evaluation.
	Metric 6:	Temporality	High	These three studies, along with Rubino et al. 1979, HERO ID 000178, were evaluated for lung cancer as part of the Balangero, Italy cohort in the Draft Asbestos Part 1 Risk Evaluation (March 2020). Pira et al. 2017, HERO ID 5060134 was evaluated for lung cancer and laryngeal cancer in the Final Asbestos Part 1 Risk Evaluation (Dec. 2020). The rating of High for other outcomes is based on the most recent publication, which has the longest follow-up duration for this cohort (follow up of the 1946-1990 cohort through 2014), as described in the Draft Risk Evaluation for Asbestos Part 1. The first two studies in the cohort (Rubino et al., 1979 and Piolatto et al., 1990) have inadequate follow-up durations (<15 years) considering the potential latency periods for some of the outcomes assessed. As described in the Asbestos Part 1 Final Risk Evaluation for Laryngeal Cancer, "Subjects were followed until loss to follow-up, their death, 85th birthday, or through 2014. This is a sufficiently long follow-up period." This metric was rated as High in both the Draft and Final Asbestos Part 1 Risk Evaluations.
Domain 3: Outcome Assessment				

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Health Outcome:	Asbestosis
Target Organ(s):	Lung/Respiratory: chronic obstructive pulmonary diseases mortality, asbestosis mortality, mortality from COPD+asbestosis, chronic respiratory disease mortality; Cancer/Carcinogenesis: gastric cancer mortality or stomach cancer mortality, intestinal cancer mortality, prostate cancer mortality, bladder cancer mortality, lymphatic and haematopoietic cancer mortality, mortality from the following neoplastic causes: stomach, colorectal, pancreas, prostate, bladder, kidney, brain and CNS, lymphatic and hematopioetic; Mortality: gastric cancer mortality or stomach cancer mortality, intestinal cancer mortality, prostate cancer mortality, bladder cancer mortality, lymphatic and haematopoietic cancer mortality, mortality from the following neoplastic causes: stomach, colorectal, liver, pancreas, prostate, bladder, kidney, brain and CNS, lymphatic and hematopioeticcerebrovascular diseases mortality, stroke mortality, chronic obstructive pulmonary diseases mortality,mortality from COPD+asbestosis, asbestosis mortality, chronic respiratory disease mortality; Skin/Connective Tissue: pleural and peritoneal cancer mortality; Neurological/Behavioral: cerebrovascular diseases mortality, stroke mortality, mortality from the following neoplastic causes: brain and CNS; Cardiovascular: cerebrovascular diseases mortality, stroke mortality; Gastrointestinal: oro-pharyngeal cancer mortality or oral cavity/pharynx cancer mortality, gastric cancer mortality or stomach cancer mortality, intestinal cancer mortality,; Immune/Hematological: lymphatic and haematopoietic cancer mortality; Reproductive/Developmental: prostate cancer mortality; Renal/Kidney: mortality from the following neoplastic causes: kidney,
Asbestos Fiber Type(s):	Asbestos - Chrysotile (serpentine): 12001-29-5; Asbestos - Crocidolite (riebeckite): 12001-28-4
Linked HERO ID(s):	3082492, 2592425, 5060134
HERO ID:	3082492

Domain	Metric		Rating	Comments
	Metric 7:	Outcome Measurement or Characterization	High	Other Cancer(s): These three studies, along with Rubino et al. 1979, HERO ID 000178, were evaluated for lung cancer as part of the Balangero, Italy cohort in the Draft Asbestos Part 1 Risk Evaluation (March 2020). Pira et al. 2017, HERO ID 5060134 was evaluated for lung cancer and laryngeal cancer in the Final Asbestos Part 1 Risk Evaluation (Dec. 2020). In the Draft Asbestos Part 1 Risk Evaluation, the cohort was rated as High for this Metric. In the Final Asbestos Part 1 Risk Evaluation this metric was rated as Medium for laryngeal cancer because ”Cause specific mortalities were obtained from death certificates collected from population registers, municipal registration offices, and local health authorities. Causes of death were coded using ICD-9, however, the study authors did not report whether cancer cases were histologically confirmed. It’s unclear if there may be any misclassification from obtaining vital status or cause of death from various sources.”Evaluation of all causes of death assessed in the cohort was based on death certificates and population registers and coded according to the International Classification of Diseases (ICD). Rubino et al., 1979, HERO ID 000178 coded causes of deaths according to ICD-7. Piolatto et al. 1990, HERO ID 3082492 did not specify which version of the ICD was used. Pira et al., 2009, HERO ID 2592425 and Pira et al., 2017, HERO ID 5060134 used ICD-9 codes. Numbers of certified deaths for each cause for the general population were obtained from the Italian National Institute of Statistics and the World Health Organization.; Asbestosis: These three studies, along with Rubino et al. 1979, HERO ID 000178, were evaluated for lung cancer as part of the Balangero, Italy cohort in the Draft Asbestos Part 1 Risk Evaluation (March 2020). Pira et al. 2017, HERO ID 5060134 was evaluated for lung cancer and laryngeal cancer in the Final Asbestos Part 1 Risk Evaluation (Dec. 2020). In the Draft Asbestos Part 1 Risk Evaluation, the cohort was rated as High for this Metric. In the Final Asbestos Part 1 Risk Evaluation this metric was rated as Medium for laryngeal cancer because ”Cause specific mortalities were obtained from death certificates collected from population registers, municipal registration offices, and local health authorities. Causes of death were coded using ICD-9, however, the study authors did not report whether cancer cases were histologically confirmed. It’s unclear if there may be any misclassification from obtaining vital status or cause of death from various sources.”Evaluation of all causes of death assessed in the cohort was based on death certificates and population registers and coded according to the International Classification of Diseases (ICD). Rubino

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Study Citation:	Piolatto, G., Negri, E., La Vecchia, C., Pira, E., Decarli, A., Peto, J. (1990). An update of cancer mortality among chrysotile asbestos miners in Balangero, northern Italy. British Journal of Industrial Medicine 47(12):810-814.
Health Outcome:	Asbestosis
Target Organ(s):	Lung/Respiratory: chronic obstructive pulmonary diseases mortality, asbestosis mortality, mortality from COPD+asbestosis, chronic respiratory disease mortality; Cancer/Carcinogenesis: gastric cancer mortality or stomach cancer mortality, intestinal cancer mortality, prostate cancer mortality, bladder cancer mortality, lymphatic and haematopoietic cancer mortality, mortality from the following neoplastic causes: stomach, colorectal, pancreas, prostate, bladder, kidney, brain and CNS, lymphatic and hematopioetic; Mortality: gastric cancer mortality or stomach cancer mortality, intestinal cancer mortality, prostate cancer mortality, bladder cancer mortality, lymphatic and haematopoietic cancer mortality, mortality from the following neoplastic causes: stomach, colorectal, liver, pancreas, prostate, bladder, kidney, brain and CNS, lymphatic and hematopioeticcerebrovascular diseases mortality, stroke mortality, chronic obstructive pulmonary diseases mortality,mortality from COPD+asbestosis, asbestosis mortality, chronic respiratory disease mortality; Skin/Connective Tissue: pleural and peritoneal cancer mortality; Neurological/Behavioral: cerebrovascular diseases mortality, stroke mortality, mortality from the following neoplastic causes: brain and CNS; Cardiovascular: cerebrovascular diseases mortality, stroke mortality; Gastrointestinal: oro-pharyngeal cancer mortality or oral cavity/pharynx cancer mortality, gastric cancer mortality or stomach cancer mortality, intestinal cancer mortality,; Immune/Hematological: lymphatic and haematopoietic cancer mortality; Reproductive/Developmental: prostate cancer mortality; Renal/Kidney: mortality from the following neoplastic causes: kidney,
Asbestos Fiber Type(s):	Asbestos - Chrysotile (serpentine): 12001-29-5; Asbestos - Crocidolite (riebeckite): 12001-28-4
Linked HERO ID(s):	3082492, 2592425, 5060134
HERO ID:	3082492

Domain	Metric		Rating	Comments
	Metric 8:	Reporting Bias	Medium	These three studies, along with Rubino et al. 1979, HERO ID 000178, were evaluated for lung cancer as part of the Balangero, Italy cohort in the Draft Asbestos Part 1 Risk Evaluation (March 2020). Pira et al. 2017, HERO ID 5060134 was evaluated for lung cancer and laryngeal cancer in the Final Asbestos Part 1 Risk Evaluation (Dec. 2020). This metric was rated as High in the Draft Asbestos Part 1 Risk Evaluation for lung cancer and High in the Draft Asbestos Part 1 Risk Evaluation for lung cancer and laryngeal cancer.However, results for some of the other outcomes assessed in the paper were reported in less detail than the results for lung cancer, resulting in a lower rating for this Metric for these other outcomes. For example, Table 4 in Pira et al., 2017, HERO ID 5060134 reports mortality rate ratios (MRR) for lung cancer for selected indicators of asbestos exposure, and does not include reporting of MRR for other outcomes. All three papers reported SMRs for several outcomes, though there were some differences between papers in terms of which specific outcomes were included. The most recent follow-up (Pira et al., 2017, HERO ID 5060134) had the most complete reporting with 95% confidence intervals. Some of the results reported in Piolatto et al., 1990, HERO ID 3082492 and Pira et al., 2009, HERO ID 2592425 did not include reporting of confidence intervals.
Domain 4: Potential Confounding / Variability Control				

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Health Outcome:	Asbestosis
Target Organ(s):	Lung/Respiratory: chronic obstructive pulmonary diseases mortality, asbestosis mortality, mortality from COPD+asbestosis, chronic respiratory disease mortality; Cancer/Carcinogenesis: gastric cancer mortality or stomach cancer mortality, intestinal cancer mortality, prostate cancer mortality, bladder cancer mortality, lymphatic and haematopoietic cancer mortality, mortality from the following neoplastic causes: stomach, colorectal, pancreas, prostate, bladder, kidney, brain and CNS, lymphatic and hematopioetic; Mortality: gastric cancer mortality or stomach cancer mortality, intestinal cancer mortality, prostate cancer mortality, bladder cancer mortality, lymphatic and haematopoietic cancer mortality, mortality from the following neoplastic causes: stomach, colorectal, liver, pancreas, prostate, bladder, kidney, brain and CNS, lymphatic and hematopioeticcerebrovascular diseases mortality, stroke mortality, chronic obstructive pulmonary diseases mortality,mortality from COPD+asbestosis, asbestosis mortality, chronic respiratory disease mortality; Skin/Connective Tissue: pleural and peritoneal cancer mortality; Neurological/Behavioral: cerebrovascular diseases mortality, stroke mortality, mortality from the following neoplastic causes: brain and CNS; Cardiovascular: cerebrovascular diseases mortality, stroke mortality; Gastrointestinal: oro-pharyngeal cancer mortality or oral cavity/pharynx cancer mortality, gastric cancer mortality or stomach cancer mortality, intestinal cancer mortality,; Immune/Hematological: lymphatic and haematopoietic cancer mortality; Reproductive/Developmental: prostate cancer mortality; Renal/Kidney: mortality from the following neoplastic causes: kidney,
Asbestos Fiber Type(s):	Asbestos - Chrysotile (serpentine): 12001-29-5; Asbestos - Crocidolite (riebeckite): 12001-28-4
Linked HERO ID(s):	3082492, 2592425, 5060134
HERO ID:	3082492

Domain	Metric		Rating	Comments
	Metric 9:	Covariate Adjustment	Medium	SMRs were stratified by age and five-year categories of calendar year. Only males were included. There is no mention of adjustment for race, but from 1981 onwards mortality ratios were standardized to male deaths from the Piedmont region where the mine was located, which likely reduced the potential for confounding by race or SES. Prior to 1981 mortality ratios were standardized to national mortality for Italy because regional data were not available. The authors noted that potential confounding by smoking and alcohol consumption were limitations for some of the outcomes assessed. However, as noted in the Draft Asbestos Part 1 Risk Evaluation, "In the most recent follow-up, data on smoking was limited to 14.5% of the cohort, but the prevalence of smoking in this subset of the cohort was comparable to that of the general male population." The outcomes that are known to be associated with alcohol consumption are assessed in a separate form. Alcohol is not likely to be a confounder for the outcomes assessed in this form.
	Metric 10:	Covariate Characterization	High	These three studies, along with Rubino et al. 1979, HERO ID 000178, were evaluated for lung cancer as part of the Balangero, Italy cohort in the Draft Asbestos Part 1 Risk Evaluation (March 2020). Pira et al. 2017, HERO ID 5060134 was evaluated for lung cancer and laryngeal cancer in the Final Asbestos Part 1 Risk Evaluation (Dec. 2020). This metric was rated High in the Draft and Medium in the Final Asbestos Part 1 Risk Evaluation.As described in the Draft Asbestos Part 1 Risk Evaluation Systematic Review Supplemental File, "Empirical data obtained from employment records. Smoking information was obtained from medical records (when available)."

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Health Outcome: Asbestosis

Target Organ(s): Lung/Respiratory: chronic obstructive pulmonary diseases mortality, asbestosis mortality, mortality from COPD+asbestosis, chronic respiratory disease mortality; Cancer/Carcinogenesis: gastric cancer mortality or stomach cancer mortality, intestinal cancer mortality, prostate cancer mortality, bladder cancer mortality, lymphatic and haematopoietic cancer mortality, mortality from the following neoplastic causes: stomach, colorectal, pancreas, prostate, bladder, kidney, brain and CNS, lymphatic and hematopioetic; Mortality: gastric cancer mortality or stomach cancer mortality, intestinal cancer mortality, prostate cancer mortality, bladder cancer mortality, lymphatic and haematopoietic cancer mortality, mortality from the following neoplastic causes: stomach, colorectal, liver, pancreas, prostate, bladder, kidney, brain and CNS, lymphatic and hematopioeticcerebrovascular diseases mortality, stroke mortality, chronic obstructive pulmonary diseases mortality,mortality from COPD+asbestosis, asbestosis mortality, chronic respiratory disease mortality; Skin/Connective Tissue: pleural and peritoneal cancer mortality; Neurological/Behavioral: cerebrovascular diseases mortality, stroke mortality, mortality from the following neoplastic causes: brain and CNS; Cardiovascular: cerebrovascular diseases mortality, stroke mortality; Gastrointestinal: oro-pharyngeal cancer mortality or oral cavity/pharynx cancer mortality, gastric cancer mortality or stomach cancer mortality, intestinal cancer mortality,; Immune/Hematological: lymphatic and haematopoietic cancer mortality; Reproductive/Developmental: prostate cancer mortality; Renal/Kidney: mortality from the following neoplastic causes: kidney,

Asbestos Fiber Type(s): Asbestos - Chrysotile (serpentine): 12001-29-5; Asbestos - Crocidolite (riebeckite): 12001-28-4

Linked HERO ID(s): 3082492, 2592425, 5060134

HERO ID: 3082492

Domain	Metric		Rating	Comments
	Metric 11:	Co-exposure Counfounding	Low	No adjustments for potential co-exposures were described. The authors mentioned the possibility of confounding by other occupational exposures. Samples of chrysotile from the mine were examined in detail for contamination from other materials (Piolatto et al., 1990 3082492) and fibrous amphiboles were not detected. Crocidolite was occasionally present at the mine. Balangeroite accounted for 0.2-0.5% of total mass chrysotile samples from the mine. Balangeroite is a fibrous silicate that is not considered a true asbestos fiber and has similar dimensions to amphiboles (Piolatto et al., 1990 3082492, Pira et al., 2009 2592425, Pira et al., 2017 5060134).
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	Medium	These three studies, along with Rubino et al. 1979, HERO ID 000178, were evaluated for lung cancer as part of the his Metric was rated as Medium in both the Draft and Final Risk Evaluations for Asbestos Part 1.Balangero, Italy cohort in the Draft Asbestos Part 1 Risk Evaluation (March 2020). Pira et al. 2017, HERO ID 5060134 was evaluated for lung cancer and laryngeal cancer in the Final Asbestos Part 1 Risk Evaluation (Dec. 2020). TAs described in the Asbestos Part 1 Final Risk Evaluation Systematic Review Supplemental File for laryngeal cancer, "SMRs were used to assess differences in cause specific mortality rates between employees of an asbestos mine compared to a reference population in the same region. This is an appropriate design for the study question."
	Metric 13:	Statistical Power	Medium	The cohort size was generally adequate, although some outcomes, particularly some of the cancer outcomes, had low numbers of observed causes of death.

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Health Outcome:	Asbestosis
Target Organ(s):	Lung/Respiratory: chronic obstructive pulmonary diseases mortality, asbestosis mortality, mortality from COPD+asbestosis, chronic respiratory disease mortality; Cancer/Carcinogenesis: gastric cancer mortality or stomach cancer mortality, intestinal cancer mortality, prostate cancer mortality, bladder cancer mortality, lymphatic and haematopoietic cancer mortality, mortality from the following neoplastic causes: stomach, colorectal, pancreas, prostate, bladder, kidney, brain and CNS, lymphatic and hematopioetic; Mortality: gastric cancer mortality or stomach cancer mortality, intestinal cancer mortality, prostate cancer mortality, bladder cancer mortality, lymphatic and haematopoietic cancer mortality, mortality from the following neoplastic causes: stomach, colorectal, liver, pancreas, prostate, bladder, kidney, brain and CNS, lymphatic and hematopioeticcerebrovascular diseases mortality, stroke mortality, chronic obstructive pulmonary diseases mortality,mortality from COPD+asbestosis, asbestosis mortality, chronic respiratory disease mortality; Skin/Connective Tissue: pleural and peritoneal cancer mortality; Neurological/Behavioral: cerebrovascular diseases mortality, stroke mortality, mortality from the following neoplastic causes: brain and CNS; Cardiovascular: cerebrovascular diseases mortality, stroke mortality; Gastrointestinal: oro-pharyngeal cancer mortality or oral cavity/pharynx cancer mortality, gastric cancer mortality or stomach cancer mortality, intestinal cancer mortality,; Immune/Hematological: lymphatic and haematopoietic cancer mortality; Reproductive/Developmental: prostate cancer mortality; Renal/Kidney: mortality from the following neoplastic causes: kidney,
Asbestos Fiber Type(s):	Asbestos - Chrysotile (serpentine): 12001-29-5; Asbestos - Crocidolite (riebeckite): 12001-28-4
Linked HERO ID(s):	3082492, 2592425, 5060134
HERO ID:	3082492

Domain	Metric		Rating	Comments
	Metric 14:	Reproducibility of Analyses	Medium	These three studies, along with Rubino et al. 1979, HERO ID 000178, were evaluated for lung cancer as part of the his Metric was rated as Medium in both the Draft and Final Risk Evaluations for Asbestos Part 1.Balangero, Italy cohort in the Draft Asbestos Part 1 Risk Evaluation (March 2020). Pira et al. 2017, HERO ID 5060134 was evaluated for lung cancer and laryngeal cancer in the Final Asbestos Part 1 Risk Evaluation (Dec. 2020). This metric was rated Medium in both the Draft and the Final Asbestos Part 1 Risk Evaluations.As described in the Final Asbestos Part 1 Risk Evaluation Systematic Review Supplemental File, "The analysis was well-described and could be reproduced with original data."
	Metric 15:	Statistical Analysis	Medium	The methods for calculating SMRs are transparent.

Additional Comments: These three studies, along with Rubino et al. 1979, HERO ID 000178, were evaluated for lung cancer as part of the Balangero, Italy cohort in the Draft Asbestos Part 1 Risk Evaluation (March 2020), with an overall quality determination of High for lung cancer. Pira et al. 2017, HERO ID 5060134 was evaluated for lung cancer and laryngeal cancer in the Final Risk Evaluation (Dec. 2020) with an overall quality determination of Medium for lung cancer and Medium for laryngeal cancer. Some of the analyses that were reported for lung cancer were not reported for other outcomes. There might not be sufficient information for dose-response assessment for the outcomes assessed on this form (in this row). Outcomes with sufficient dose-response information were evaluated in a separate form (row).The main fiber type was chrysotile. Crocidolite was occasionally present at the mine. Balangeroite, which is a fibrous silicate, accounted for 0.2-0.5% of total mass chrysotile samples from the mine.This study assessed a cohort who worked in an open-air mine, and thus these outdoor exposures might be different than exposures in other environments.

Overall Quality Determination — Medium

* No biomarkers were identified for this evaluation.

Study Citation:	Piolatto, G., Negri, E., La Vecchia, C., Pira, E., Decarli, A., Peto, J. (1990). An update of cancer mortality among chrysotile asbestos miners in Balangero, northern Italy. British Journal of Industrial Medicine 47(12):810-814.
Health Outcome:	MISSING
Target Organ(s):	Lung/Respiratory: pleural cancer mortality, mortality from cancer of the pleura only, mortality from cancer of the pleura and peritoneum,lung cancer mortality (assessed in Asbestos Part 1), laryngeal cancer mortality or larynx cancer mortality (assessed in Asbestos Part 1); Cancer/Carcinogenesis: pleural cancer mortality, peritoneal cancer mortality, mortality from cancer of the pleura only, mortality from cancer of the pleura and peritoneum, laryngeal cancer mortality or larynx cancer mortality (assessed in Asbestos Part 1), lung cancer mortality (assessed in Asbestos Part 1), all cancer mortality; Cardiovascular: ischemic heart disease; Mortality: pleural cancer mortality, peritoneal cancer mortality, mortality from cancer of the pleura only, mortality from cancer of the pleura and peritoneum,ischemic heart disease mortality,laryngeal cancer mortality or larynx cancer mortality (assessed in Asbestos Part 1), lung cancer mortality (assessed in Asbestos Part 1), all cancer mortality, all cause mortality
Asbestos Fiber Type(s):	Asbestos - Chrysotile (serpentine): 12001-29-5; Asbestos - Crocidolite (riebeckite): 12001-28-4
Linked HERO ID(s):	3082492, 2592425, 5060134
HERO ID:	3082492

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Medium	These three studies, along with Rubino et al. 1979, HERO ID 000178, were evaluated for lung cancer as part of the Balangero, Italy cohort in the Draft Asbestos Part 1 Risk Evaluation (March 2020). Pira et al. 2017, HERO ID 5060134 was evaluated for lung cancer and laryngeal cancer in the Final Asbestos Part 1 Risk Evaluation (Dec. 2020). As described in the Draft Asbestos Part 1 Risk Evaluation Systematic Review Supplemental File, "Subjects included men from the Balangero mine worker cohort that were employed in an Italian asbestos mine. The initial cohort ((Rubino et al., 1979), pg 188) consisted of 952 men employed between 1/1/1930 and 12/31/1965, with at least 30 calendar days' employment during that period. Mortality data were collected from 1/1/1946 to 12/31/1975. Workers for which vital status could not be acertained and a small number of contract workers employed intermittently were excluded. In the first follow-up, 1058 workers were included that had worked at least one year between 1946 and 1987 and mortality follow-up was extended through 12/31/1987 ((Piolatto et al., 1990), pg 810). In subsequent follow-ups ((Pira et al., 2009) pg 805, and (Pira et al., 2017)), subjects included 1056 men from the Balangero mine worker cohort employed between 1930 and 1990, and mortality records were evaluated though 2003 and 2014, respectively. Records were not available between 1987 and 1990, when the mine closed, so workers employed in 1987 were assumed to be employed through 1990 unless they died during that period. Additional details in the most recent following indicated that the initial cohort included 1182 men; the 126 excluded subjects were contract workers, those employed <1 yr, those with inconsistencies in data, and those known to have died prior to 1946 (Pira et al., 2017) pg 558." As described in the final Asbestos Part 1 Risk Evaluation Supplemental File for Laryngeal Cancers, "Subjects were drawn from the employment records of an Italian asbestos mine (n=1056 men). Those eligible had worked for the mine for at least one year between 1930 and 1989. Description of the mine setting was described including some historical occupational measurements of dust and asbestos."This metric was rated High in the Draft and Medium in the Final Asbestos Part 1 Risk Evaluation.

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Health Outcome:	MISSING
Target Organ(s):	Lung/Respiratory: pleural cancer mortality, mortality from cancer of the pleura only, mortality from cancer of the pleura and peritoneum,lung cancer mortality (assessed in Asbestos Part 1), laryngeal cancer mortality or larynx cancer mortality (assessed in Asbestos Part 1); Cancer/Carcinogenesis: pleural cancer mortality, peritoneal cancer mortality, mortality from cancer of the pleura only, mortality from cancer of the pleura and peritoneum, laryngeal cancer mortality or larynx cancer mortality (assessed in Asbestos Part 1), lung cancer mortality (assessed in Asbestos Part 1), all cancer mortality; Cardiovascular: ischemic heart disease; Mortality: pleural cancer mortality, peritoneal cancer mortality, mortality from cancer of the pleura only, mortality from cancer of the pleura and peritoneum,ischemic heart disease mortality,laryngeal cancer mortality or larynx cancer mortality (assessed in Asbestos Part 1), lung cancer mortality (assessed in Asbestos Part 1), all cancer mortality, all cause mortality
Asbestos Fiber Type(s):	Asbestos - Chrysotile (serpentine): 12001-29-5; Asbestos - Crocidolite (riebeckite): 12001-28-4
Linked HERO ID(s):	3082492, 2592425, 5060134
HERO ID:	3082492

Domain	Metric		Rating	Comments
	Metric 2:	Attrition	High	These three studies, along with Rubino et al. 1979, HERO ID 000178, were evaluated for lung cancer as part of the Balangero, Italy cohort in the Draft Asbestos Part 1 Risk Evaluation (March 2020). Pira et al. 2017, HERO ID 5060134 was evaluated for lung cancer and laryngeal cancer in the Final Asbestos Part 1 Risk Evaluation (Dec. 2020). As described in the Draft Asbestos Part 1 Risk Evaluation Systematic Review Supplemental File, ”In the most recent follow-up, study authors report that one of the strengths of the study is low proportion of subjects lost to follow-up (Pira et al., 2017) pg 562. Loss to follow-up was 2% in the initial cohort (Rubino et al., 1979), 3% in the first follow-up ((Piolatto et al., 1990), pg 810), and 4% in the most recent follow-ups (Pira et al., 2009) pg 805; (Pira et al., 2017) pg 559.”As described in the Final Asbestos Part 1 Risk Evaluation Systematic Review Supplemental File for Laryngeal Cancer ”The study authors note that the cause of death could not be determined for a small sample (n=6), and a small percentage (3.8%) of participants emigrated or were otherwise lost to follow-up. This level of attrition is not expected to appreciably bias the results.”This Metric was rated as High in both the Draft and Final Asbestos Part 1 Risk Evaluation.

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Health Outcome:	MISSING
Target Organ(s):	Lung/Respiratory: pleural cancer mortality, mortality from cancer of the pleura only, mortality from cancer of the pleura and peritoneum,lung cancer mortality (assessed in Asbestos Part 1), laryngeal cancer mortality or larynx cancer mortality (assessed in Asbestos Part 1); Cancer/Carcinogenesis: pleural cancer mortality, peritoneal cancer mortality, mortality from cancer of the pleura only, mortality from cancer of the pleura and peritoneum, laryngeal cancer mortality or larynx cancer mortality (assessed in Asbestos Part 1), lung cancer mortality (assessed in Asbestos Part 1), all cancer mortality; Cardiovascular: ischemic heart disease; Mortality: pleural cancer mortality, peritoneal cancer mortality, mortality from cancer of the pleura only, mortality from cancer of the pleura and peritoneum,ischemic heart disease mortality,laryngeal cancer mortality or larynx cancer mortality (assessed in Asbestos Part 1), lung cancer mortality (assessed in Asbestos Part 1), all cancer mortality, all cause mortality
Asbestos Fiber Type(s):	Asbestos - Chrysotile (serpentine): 12001-29-5; Asbestos - Crocidolite (riebeckite): 12001-28-4
Linked HERO ID(s):	3082492, 2592425, 5060134
HERO ID:	3082492

Domain	Metric	Rating	Comments
	Metric 3: Comparison Group	Medium	These three studies, along with Rubino et al. 1979, HERO ID 000178, were evaluated for lung cancer as part of the Balangero, Italy cohort in the Draft Asbestos Part 1 Risk Evaluation (March 2020). Pira et al. 2017, HERO ID 5060134 was evaluated for lung cancer and laryngeal cancer in the Final Asbestos Part 1 Risk Evaluation (Dec. 2020). As described in the Draft Asbestos Part 1 Risk Evaluation Systematic Review Supplemental File, "The most complete data on comparison groups is available from the most recent follow-up (Pira et al., 2017). General population mortality rates using the whole country from 1955 until 1980 and specifically the Piedmont Region (where the mine is located) from 1981 onwards (no regional rates available prior to 1981). The 1955-1959 rates were applied to 1946-1954 period (no available data); this may have led to an underestimate of expected deaths which may have showed and increased rate during this period. Expected numbers of deaths (overall and selected cancers) were computed using age-specific and calendar-year-specific (5-year categories) male death rates (Pira et al., 2017) pg 559. The only deviation from this was in the first follow-up, which used national mortality rates were for the entire follow-up period (through 1987) (Piolatto et al., 1990) pg. 811). In the initial study on this cohort ((Rubino et al., 1979), pg. 189), an additional case-control study was performed in which 5 age-matched controls were selected at random; they were confirmed alive at the time of death for the matched case. No details on what population provided controls. The evaluation is based on the cohort mortality study only, as this was the analysis carried through the 3 follow-up studies (Pira et al., 2017; Pira et al., 2009; Piolatto et al., 1990)."As described in the Final Asbestos Part 1 Risk Evaluation Systematic Review Supplemental File for Laryngeal Cancer, "Mortality rates for males from the Piedmont Region were used as a comparison group. This is a sufficiently similar group, however, the study authors note that mortality rates were not available for certain periods (e.g., 1946-1954) and rates from adjacent periods of time were used instead (1955-1959 rates applied to 1946-1954)."This metric was rated as High in the Draft and Medium in the Final Asbestos Part 1 Risk Evaluation.
Domain 2: Exposure Characterization			

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Health Outcome:	MISSING
Target Organ(s):	Lung/Respiratory: pleural cancer mortality, mortality from cancer of the pleura only, mortality from cancer of the pleura and peritoneum,lung cancer mortality (assessed in Asbestos Part 1), laryngeal cancer mortality or larynx cancer mortality (assessed in Asbestos Part 1); Cancer/Carcinogenesis: pleural cancer mortality, peritoneal cancer mortality, mortality from cancer of the pleura only, mortality from cancer of the pleura and peritoneum, laryngeal cancer mortality or larynx cancer mortality (assessed in Asbestos Part 1), lung cancer mortality (assessed in Asbestos Part 1), all cancer mortality; Cardiovascular: ischemic heart disease; Mortality: pleural cancer mortality, peritoneal cancer mortality, mortality from cancer of the pleura only, mortality from cancer of the pleura and peritoneum,ischemic heart disease mortality,laryngeal cancer mortality or larynx cancer mortality (assessed in Asbestos Part 1), lung cancer mortality (assessed in Asbestos Part 1), all cancer mortality, all cause mortality
Asbestos Fiber Type(s):	Asbestos - Chrysotile (serpentine): 12001-29-5; Asbestos - Crocidolite (riebeckite): 12001-28-4
Linked HERO ID(s):	3082492, 2592425, 5060134
HERO ID:	3082492

Domain	Metric		Rating	Comments
	Metric 4:	Measurement of Exposure	Medium	These three studies, along with Rubino et al. 1979, HERO ID 000178, were evaluated for lung cancer as part of the Balangero, Italy cohort in the Draft Asbestos Part 1 Risk Evaluation (March 2020). Pira et al. 2017, HERO ID 5060134 was evaluated for lung cancer and laryngeal cancer in the Final Asbestos Part 1 Risk Evaluation (Dec. 2020). As described in the Draft Asbestos Part 1 Risk Evaluation Systematic Review Supplemental File, "Most complete report of exposure assessment is in initial cohort study ((Rubino et al., 1979) pg 189). Chrysotile fiber counts were first measured in 1969 using membrane filter collection and phase contrast microscopy (frequency not reported). To estimate exposure from 1946-1969, factory records on daily production, equipment used, characteristics of the job and number of hours/day were used (this method has considerable limitations due to basis on mean values for large job categories and no allowance for changes in weather). Simulated and measured data were made comparable by using weighting factors (e.g., more dusty operation for 1-2 hr/d compared with longer working hours in the past). Less detailed information was included in follow-up reports ((Piolatto et al., 1990) pg. 810; (Pira et al., 2017), pg 558-559)."As described in the Final Asbestos Part 1 Risk Evaluation for Laryngeal Cancer, "Descriptions of the mine and occupational surveillance was described. Estimates of historical mean concentrations were 37 fibre/mL up to 1950 and 5 fibre/mL between 1971 and 1976. Exposure was determined by employment at the asbestos mine only."This metric was rated as Medium in the Draft and Low in the Final Risk Evaluation for Asbestos Part 1. However, the cohort meets the criteria for Medium as described above.
	Metric 5:	Exposure Levels	Medium	These three studies, along with Rubino et al. 1979, HERO ID 000178, were evaluated for lung cancer as part of the Balangero, Italy cohort in the Draft Asbestos Part 1 Risk Evaluation (March 2020). Pira et al. 2017, HERO ID 5060134 was evaluated for lung cancer and laryngeal cancer in the Final Asbestos Part 1 Risk Evaluation (Dec. 2020). As described in the Draft Asbestos Part 1 Risk Evaluation Systematic Review Supplemental File, "In the initial cohort ((Rubino et al., 1979), Table 8), exposure was reported as up to 100 fiber/yr or >100 fiber/year. In the follow-ups, exposure was reported as <100 fiber/mL-yr, 100-<400 fiber/mL-yr, and >=400 fiber/ml-yr ((Piolatto et al., 1990), Table 3; (Pira et al., 2009), Table 2; (Pira et al., 2017), Tables 3-4)." This metric was not rated in the Final Asbestos Part 1 Risk Evaluation.

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Health Outcome:	MISSING
Target Organ(s):	Lung/Respiratory: pleural cancer mortality, mortality from cancer of the pleura only, mortality from cancer of the pleura and peritoneum,lung cancer mortality (assessed in Asbestos Part 1), laryngeal cancer mortality or larynx cancer mortality (assessed in Asbestos Part 1); Cancer/Carcinogenesis: pleural cancer mortality, peritoneal cancer mortality, mortality from cancer of the pleura only, mortality from cancer of the pleura and peritoneum, laryngeal cancer mortality or larynx cancer mortality (assessed in Asbestos Part 1), lung cancer mortality (assessed in Asbestos Part 1), all cancer mortality; Cardiovascular: ischemic heart disease; Mortality: pleural cancer mortality, peritoneal cancer mortality, mortality from cancer of the pleura only, mortality from cancer of the pleura and peritoneum,ischemic heart disease mortality,laryngeal cancer mortality or larynx cancer mortality (assessed in Asbestos Part 1), lung cancer mortality (assessed in Asbestos Part 1), all cancer mortality, all cause mortality
Asbestos Fiber Type(s):	Asbestos - Chrysotile (serpentine): 12001-29-5; Asbestos - Crocidolite (riebeckite): 12001-28-4
Linked HERO ID(s):	3082492, 2592425, 5060134
HERO ID:	3082492

Domain	Metric		Rating	Comments
	Metric 6:	Temporality	High	These three studies, along with Rubino et al. 1979, HERO ID 000178, were evaluated for lung cancer as part of the Balangero, Italy cohort in the Draft Asbestos Part 1 Risk Evaluation (March 2020). Pira et al. 2017, HERO ID 5060134 was evaluated for lung cancer and laryngeal cancer in the Final Asbestos Part 1 Risk Evaluation (Dec. 2020). The rating of High for other outcomes is based on the most recent publication, which has the longest follow-up duration for this cohort (follow up of the 1946-1990 cohort through 2014), as described in the Draft Risk Evaluation for Asbestos Part 1. The first two studies in the cohort (Rubino et al., 1979 and Piolatto et al., 1990) have inadequate follow-up durations (<15 years) considering the potential latency periods for some of the outcomes assessed. As described in the Asbestos Part 1 Final Risk Evaluation for Laryngeal Cancer, "Subjects were followed until loss to follow-up, their death, 85th birthday, or through 2014. This is a sufficiently long follow-up period." This metric was rated as High in both the Draft and Final Asbestos Part 1 Risk Evaluations.
Domain 3: Outcome Assessment				

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Health Outcome:	MISSING
Target Organ(s):	Lung/Respiratory: pleural cancer mortality, mortality from cancer of the pleura only, mortality from cancer of the pleura and peritoneum,lung cancer mortality (assessed in Asbestos Part 1), laryngeal cancer mortality or larynx cancer mortality (assessed in Asbestos Part 1); Cancer/Carcinogenesis: pleural cancer mortality, peritoneal cancer mortality, mortality from cancer of the pleura only, mortality from cancer of the pleura and peritoneum, laryngeal cancer mortality or larynx cancer mortality (assessed in Asbestos Part 1), lung cancer mortality (assessed in Asbestos Part 1), all cancer mortality; Cardiovascular: ischemic heart disease; Mortality: pleural cancer mortality, peritoneal cancer mortality, mortality from cancer of the pleura only, mortality from cancer of the pleura and peritoneum,ischemic heart disease mortality,laryngeal cancer mortality or larynx cancer mortality (assessed in Asbestos Part 1), lung cancer mortality (assessed in Asbestos Part 1), all cancer mortality, all cause mortality
Asbestos Fiber Type(s):	Asbestos - Chrysotile (serpentine): 12001-29-5; Asbestos - Crocidolite (riebeckite): 12001-28-4
Linked HERO ID(s):	3082492, 2592425, 5060134
HERO ID:	3082492

Domain	Metric		Rating	Comments
	Metric 7:	Outcome Measurement or Characterization	High	Other Cancer(s): These three studies, along with Rubino et al. 1979, HERO ID 000178, were evaluated for lung cancer as part of the Balangero, Italy cohort in the Draft Asbestos Part 1 Risk Evaluation (March 2020). Pira et al. 2017, HERO ID 5060134 was evaluated for lung cancer and laryngeal cancer in the Final Asbestos Part 1 Risk Evaluation (Dec. 2020). In the Draft Asbestos Part 1 Risk Evaluation, the cohort was rated as High for this Metric. In the Final Asbestos Part 1 Risk Evaluation this metric was rated as Medium for laryngeal cancer because ”Cause specific mortalities were obtained from death certificates collected from population registers, municipal registration offices, and local health authorities. Causes of death were coded using ICD-9, however, the study authors did not report whether cancer cases were histologically confirmed. It's unclear if there may be any misclassification from obtaining vital status or cause of death from various sources.”Evaluation of all causes of death assessed in the cohort was based on death certificates and population registers and coded according to the International Classification of Diseases (ICD). Rubino et al., 1979, HERO ID 000178 coded causes of deaths according to ICD-7. Piolatto et al. 1990, HERO ID 3082492 did not specify which version of the ICD was used. Pira et al., 2009, HERO ID 2592425 and Pira et al., 2017, HERO ID 5060134 used ICD-9 codes. Numbers of certified deaths for each cause for the general population were obtained from the Italian National Institute of Statistics and the World Health Organization.; Other Non-Cancer Outcomes: These three studies, along with Rubino et al. 1979, HERO ID 000178, were evaluated for lung cancer as part of the Balangero, Italy cohort in the Draft Asbestos Part 1 Risk Evaluation (March 2020). Pira et al. 2017, HERO ID 5060134 was evaluated for lung cancer and laryngeal cancer in the Final Asbestos Part 1 Risk Evaluation (Dec. 2020). In the Draft Asbestos Part 1 Risk Evaluation, the cohort was rated as High for this Metric. In the Final Asbestos Part 1 Risk Evaluation this metric was rated as Medium for laryngeal cancer because ”Cause specific mortalities were obtained from death certificates collected from population registers, municipal registration offices, and local health authorities. Causes of death were coded using ICD-9, however, the study authors did not report whether cancer cases were histologically confirmed. It's unclear if there may be any misclassification from obtaining vital status or cause of death from various sources.”Evaluation of all causes of death assessed in the cohort was based on death certificates and population registers and coded according to the International Classification of Diseases (ICD). Rubino et al., 1979, HERO ID 000178 coded causes of deaths according to ICD-7. Piolatto et al. 1990, HERO ID 3082492 did not specify which version of the ICD was used. Pira et al., 2009, HERO ID 2592425 and Pira et al., 2017, HERO ID 5060134 used ICD-9 codes. Numbers of certified deaths for each cause for the general population were obtained from the Italian National Institute of Statistics and the World Health Organization.

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Health Outcome:	MISSING
Target Organ(s):	Lung/Respiratory: pleural cancer mortality, mortality from cancer of the pleura only, mortality from cancer of the pleura and peritoneum,lung cancer mortality (assessed in Asbestos Part 1), laryngeal cancer mortality or larynx cancer mortality (assessed in Asbestos Part 1); Cancer/Carcinogenesis: pleural cancer mortality, peritoneal cancer mortality, mortality from cancer of the pleura only, mortality from cancer of the pleura and peritoneum, laryngeal cancer mortality or larynx cancer mortality (assessed in Asbestos Part 1), lung cancer mortality (assessed in Asbestos Part 1), all cancer mortality; Cardiovascular: ischemic heart disease; Mortality: pleural cancer mortality, peritoneal cancer mortality, mortality from cancer of the pleura only, mortality from cancer of the pleura and peritoneum,ischemic heart disease mortality,laryngeal cancer mortality or larynx cancer mortality (assessed in Asbestos Part 1), lung cancer mortality (assessed in Asbestos Part 1), all cancer mortality, all cause mortality
Asbestos Fiber Type(s):	Asbestos - Chrysotile (serpentine): 12001-29-5; Asbestos - Crocidolite (riebeckite): 12001-28-4
Linked HERO ID(s):	3082492, 2592425, 5060134
HERO ID:	3082492

Domain	Metric		Rating	Comments
	Metric 8:	Reporting Bias	High	These three studies, along with Rubino et al. 1979, HERO ID 000178, were evaluated for lung cancer as part of the Balangero, Italy cohort in the Draft Asbestos Part 1 Risk Evaluation (March 2020). Pira et al. 2017, HERO ID 5060134 was evaluated for lung cancer and laryngeal cancer in the Final Asbestos Part 1 Risk Evaluation (Dec. 2020). This metric was rated as High in the Draft Asbestos Part 1 Risk Evaluation for lung cancer and High in the Draft Asbestos Part 1 Risk Evaluation for lung cancer and laryngeal cancer.All three papers reported SMRs for several outcomes, though there were some differences between papers in terms of which specific outcomes were included. The most recent follow-up (Pira et al., 2017, HERO ID 5060134) had the most complete reporting with 95% confidence intervals. Some of the results reported in Piolatto et al., 1990, HERO ID 3082492 and Pira et al., 2009, HERO ID 2592425 did not include reporting of confidence intervals.Dose-response information was reported for laryngeal cancer, lung cancer, pleural and peritoneal cancer, all cancer, and all causes in Table 2 of Pira et al., 2009, HERO ID 2592425 and for laryngeal cancer, lung cancer, pleural cancer, and ischemic heart disease in Table 3 of Pira et al., 2017, HERO ID 5060134.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Medium	SMRs were stratified by age and five-year categories of calendar year. Only males were included. There is no mention of adjustment for race, but from 1981 onwards mortality ratios were standardized to male deaths from the Piedmont region where the mine was located, which likely reduced the potential for confounding by race or SES. Prior to 1981 mortality ratios were standardized to national mortality for Italy because regional data were not available. The authors noted that potential confounding by smoking and alcohol consumption were limitations for some of the outcomes assessed. However, as noted in the Draft Asbestos Part 1 Risk Evaluation, "In the most recent follow-up, data on smoking was limited to 14.5% of the cohort, but the prevalence of smoking in this subset of the cohort was comparable to that of the general male population." The outcomes that are known to be associated with alcohol consumption are assessed in a separate form. Alcohol is not likely to be a confounder for the outcomes assessed in this form.

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Health Outcome:	MISSING
Target Organ(s):	Lung/Respiratory: pleural cancer mortality, mortality from cancer of the pleura only, mortality from cancer of the pleura and peritoneum,lung cancer mortality (assessed in Asbestos Part 1), laryngeal cancer mortality or larynx cancer mortality (assessed in Asbestos Part 1); Cancer/Carcinogenesis: pleural cancer mortality, peritoneal cancer mortality, mortality from cancer of the pleura only, mortality from cancer of the pleura and peritoneum, laryngeal cancer mortality or larynx cancer mortality (assessed in Asbestos Part 1), lung cancer mortality (assessed in Asbestos Part 1), all cancer mortality; Cardiovascular: ischemic heart disease; Mortality: pleural cancer mortality, peritoneal cancer mortality, mortality from cancer of the pleura only, mortality from cancer of the pleura and peritoneum,ischemic heart disease mortality,laryngeal cancer mortality or larynx cancer mortality (assessed in Asbestos Part 1), lung cancer mortality (assessed in Asbestos Part 1), all cancer mortality, all cause mortality
Asbestos Fiber Type(s):	Asbestos - Chrysotile (serpentine): 12001-29-5; Asbestos - Crocidolite (riebeckite): 12001-28-4
Linked HERO ID(s):	3082492, 2592425, 5060134
HERO ID:	3082492

Domain	Metric		Rating	Comments
	Metric 10:	Covariate Characterization	High	These three studies, along with Rubino et al. 1979, HERO ID 000178, were evaluated for lung cancer as part of the Balangero, Italy cohort in the Draft Asbestos Part 1 Risk Evaluation (March 2020). Pira et al. 2017, HERO ID 5060134 was evaluated for lung cancer and laryngeal cancer in the Final Asbestos Part 1 Risk Evaluation (Dec. 2020). This metric was rated High in the Draft and Medium in the Final Asbestos Part 1 Risk Evaluation.As described in the Draft Asbestos Part 1 Risk Evaluation Systematic Review Supplemental File, ”Empirical data obtained from employment records. Smoking information was obtained from medical records (when available).”
	Metric 11:	Co-exposure Counfounding	Low	No adjustments for potential co-exposures were described. The authors mentioned the possibility of confounding by other occupational exposures. Samples of chrysotile from the mine were examined in detail for contamination from other materials (Piolatto et al., 1990 3082492) and fibrous amphiboles were not detected. Crocidolite was occasionally present at the mine. Balangeroite accounted for 0.2-0.5% of total mass chrysotile samples from the mine. Balangeroite is a fibrous silicate that is not considered a true asbestos fiber and has similar dimensions to amphiboles (Piolatto et al., 1990 3082492, Pira et al., 2009 2592425, Pira et al., 2017 5060134).
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	Medium	These three studies, along with Rubino et al. 1979, HERO ID 000178, were evaluated for lung cancer as part of the Balangero, Italy cohort in the Draft Asbestos Part 1 Risk Evaluation (March 2020). Pira et al. 2017, HERO ID 5060134 was evaluated for lung cancer and laryngeal cancer in the Final Asbestos Part 1 Risk Evaluation (Dec. 2020). This Metric was rated as Medium in both the Draft and Final Risk Evaluations for Asbestos Part 1.As described in the Asbestos Part 1 Final Risk Evaluation Systematic Review Supplemental File for laryngeal cancer, ”SMRs were used to assess differences in cause specific mortality rates between employees of an asbestos mine compared to a reference population in the same region. This is an appropriate design for the study question.”
	Metric 13:	Statistical Power	Medium	The cohort size was generally adequate, although some outcomes, particularly some of the cancer outcomes, had low numbers of observed causes of death.

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Health Outcome:	MISSING
Target Organ(s):	Lung/Respiratory: pleural cancer mortality, mortality from cancer of the pleura only, mortality from cancer of the pleura and peritoneum,lung cancer mortality (assessed in Asbestos Part 1), laryngeal cancer mortality or larynx cancer mortality (assessed in Asbestos Part 1); Cancer/Carcinogenesis: pleural cancer mortality, peritoneal cancer mortality, mortality from cancer of the pleura only, mortality from cancer of the pleura and peritoneum, laryngeal cancer mortality or larynx cancer mortality (assessed in Asbestos Part 1), lung cancer mortality (assessed in Asbestos Part 1), all cancer mortality; Cardiovascular: ischemic heart disease; Mortality: pleural cancer mortality, peritoneal cancer mortality, mortality from cancer of the pleura only, mortality from cancer of the pleura and peritoneum,ischemic heart disease mortality,laryngeal cancer mortality or larynx cancer mortality (assessed in Asbestos Part 1), lung cancer mortality (assessed in Asbestos Part 1), all cancer mortality, all cause mortality
Asbestos Fiber Type(s):	Asbestos - Chrysotile (serpentine): 12001-29-5; Asbestos - Crocidolite (riebeckite): 12001-28-4
Linked HERO ID(s):	3082492, 2592425, 5060134
HERO ID:	3082492

Domain	Metric		Rating	Comments
	Metric 14:	Reproducibility of Analyses	Medium	These three studies, along with Rubino et al. 1979, HERO ID 000178, were evaluated for lung cancer as part of the his Metric was rated as Medium in both the Draft and Final Risk Evaluations for Asbestos Part 1.Balangero, Italy cohort in the Draft Asbestos Part 1 Risk Evaluation (March 2020). Pira et al. 2017, HERO ID 5060134 was evaluated for lung cancer and laryngeal cancer in the Final Asbestos Part 1 Risk Evaluation (Dec. 2020). This metric was rated Medium in both the Draft and the Final Asbestos Part 1 Risk Evaluations.As described in the Final Asbestos Part 1 Risk Evaluation Systematic Review Supplemental File, ”The analysis was well-described and could be reproduced with original data.”
	Metric 15:	Statistical Analysis	Medium	The methods for calculating SMRs are transparent.

Additional Comments: These three studies, along with Rubino et al. 1979, HERO ID 000178, were evaluated for lung cancer as part of the Balangero, Italy cohort in the Draft Asbestos Part 1 Risk Evaluation (March 2020), with an overall quality determination of High for lung cancer. Pira et al. 2017, HERO ID 5060134 was evaluated for lung cancer and laryngeal cancer in the Final Risk Evaluation (Dec. 2020) with an overall quality determination of Medium for lung cancer and Medium for laryngeal cancer. Dose-response information was reported for laryngeal cancer, lung cancer, pleural and peritoneal cancer, all cancer, and all causes in Table 2 of Pira et al., 2009, HERO ID 2592425 and for laryngeal cancer, lung cancer, pleural cancer, and ischemic heart disease in Table 3 of Pira et al., 2017, HERO ID 5060134.The main fiber type was chrysotile. Crocidolite was occasionally present at the mine. Balangeroite, which is a fibrous silicate, accounted for 0.2-0.5% of total mass chrysotile samples from the mine.This study assessed a cohort who worked in an open-air mine, and thus these outdoor exposures might be different than exposures in other environments.

Overall Quality Determination — Medium

* No biomarkers were identified for this evaluation.

Study Citation:	Piolatto, G., Negri, E., La Vecchia, C., Pira, E., Decarli, A., Peto, J. (1990). An update of cancer mortality among chrysotile asbestos miners in Balangero, northern Italy. British Journal of Industrial Medicine 47(12):810-814.
Health Outcome:	MISSING
Target Organ(s):	Hepatic/Liver: liver cancer mortality, liver cirrhosis mortality or hepatic cirrhosis mortality,; Cancer/Carcinogenesis: oro-pharyngeal cancer mortality or oral cavity/pharynx cancer mortality, esophageal cancer, liver cancer; Mortality: oro-pharyngeal cancer mortality or oral cavity/pharynx cancer mortality, esophageal cancer, liver cancer mortality, liver cirrhosis mortality or hepatic cirrhosis mortality, accidents and violence mortality
Asbestos Fiber Type(s):	Asbestos - Chrysotile (serpentine): 12001-29-5; Asbestos - Crocidolite (riebeckite): 12001-28-4
Linked HERO ID(s):	3082492, 2592425, 5060134
HERO ID:	3082492

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	High	These three studies were evaluated for lung cancer as part of the Balangero, Italy cohort in Asbestos Part 1. As described in the Asbestos Part 1 Risk Evaluation Systematic Review Supplemental File, "Subjects included men from the Balangero mine worker cohort that were employed in an Italian asbestos mine. The initial cohort ((Rubino et al., 1979), pg 188) consisted of 952 men employed between 1/1/1930 and 12/31/1965, with at least 30 calendar days' employment during that period. Mortality data were collected from 1/1/1946 to 12/31/1975. Workers for which vital status could not be acertained and a small number of contract workers employed intermittently were excluded. In the first follow-up, 1058 workers were included that had worked at least one year between 1946 and 1987 and mortality follow-up was extended through 12/31/1987 ((Piolatto et al., 1990), pg 810). In subsequent follow-ups ((Pira et al., 2009) pg 805, and (Pira et al., 2017)), subjects included 1056 men from the Balangero mine worker cohort employed between 1930 and 1990, and mortality records were evaluated though 2003 and 2014, respectively. Records were not available between 1987 and 1990, when the mine closed, so workers employed in 1987 were assumed to be employed through 1990 unless they died during that period. Additional details in the most recent following indicated that the initial cohort included 1182 men; the 126 excluded subjects were contract workers, those employed <1 yr, those with inconsistencies in data, and those known to have died prior to 1946 (Pira et al., 2017) pg 558."
	Metric 2:	Attrition	High	These three studies, along with Rubino et al. 1979, HERO ID 000178, were evaluated for lung cancer as part of the Balangero, Italy cohort in the Draft Asbestos Part 1 Risk Evaluation (March 2020). Pira et al. 2017, HERO ID 5060134 was evaluated for lung cancer and laryngeal cancer in the Final Asbestos Part 1 Risk Evaluation (Dec. 2020). As described in the Draft Asbestos Part 1 Risk Evaluation Systematic Review Supplemental File, "In the most recent follow-up, study authors report that one of the strengths of the study is low proportion of subjects lost to follow-up (Pira et al., 2017) pg 562. Loss to follow-up was 2% in the initial cohort (Rubino et al., 1979), 3% in the first follow-up ((Piolatto et al., 1990), pg 810), and 4% in the most recent follow-ups (Pira et al., 2009) pg 805; (Pira et al., 2017) pg 559."As described in the Final Asbestos Part 1 Risk Evaluation Systematic Review Supplemental File for Laryngeal Cancer "The study authors note that the cause of death could not be determined for a small sample (n=6), and a small percentage (3.8%) of participants emigrated or were otherwise lost to follow-up. This level of attrition is not expected to appreciably bias the results."This Metric was rated as High in both the Draft and Final Asbestos Part 1 Risk Evaluation.

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Study Citation: Piolatto, G., Negri, E., La Vecchia, C., Pira, E., Decarli, A., Peto, J. (1990). An update of cancer mortality among chrysotile asbestos miners in Balangero, northern Italy. British Journal of Industrial Medicine 47(12):810-814.

Health Outcome: MISSING

Target Organ(s): Hepatic/Liver: liver cancer mortality, liver cirrhosis mortality or hepatic cirrhosis mortality,; Cancer/Carcinogenesis: oro-pharyngeal cancer mortality or oral cavity/pharynx cancer mortality, esophageal cancer, liver cancer; Mortality: oro-pharyngeal cancer mortality or oral cavity/pharynx cancer mortality, esophageal cancer, liver cancer mortality, liver cirrhosis mortality or hepatic cirrhosis mortality, accidents and violence mortality

Asbestos Fiber Type(s): Asbestos - Chrysotile (serpentine): 12001-29-5; Asbestos - Crocidolite (riebeckite): 12001-28-4

Linked HERO ID(s): 3082492, 2592425, 5060134

HERO ID: 3082492

Domain	Metric		Rating	Comments
	Metric 3:	Comparison Group	High	These three studies were evaluated for lung cancer as part of the Balangero, Italy cohort in Asbestos Part 1. As described in the Asbestos Part 1 Risk Evaluation Systematic Review Supplemental File, ”The most complete data on comparison groups is available from the most recent follow-up (Pira et al., 2017). General population mortality rates using the whole country from 1955 until 1980 and specifically the Piedmont Region (where the mine is located) from 1981 onwards (no regional rates available prior to 1981). The 1955-1959 rates were applied to 1946-1954 period (no available data); this may have led to an underestimate of expected deaths which may have showed and increased rate during this period. Expected numbers of deaths (overall and selected cancers) were computed using age-specific and calendar-year-specific (5-year categories) male death rates (Pira et al., 2017) pg 559. The only deviation from this was in the first follow-up, which used national mortality rates were for the entire follow-up period (through 1987) (Piolatto et al., 1990) pg. 811). In the initial study on this cohort ((Rubino et al., 1979), pg. 189), an additional case-control study was performed in which 5 age-matched controls were selected at random; they were confirmed alive at the time of death for the matched case. No details on what population provided controls. The evaluation is based on the cohort mortality study only, as this was the analysis carried through the 3 follow-up studies (Pira et al., 2017; Pira et al., 2009; Piolatto et al., 1990).”
Domain 2: Exposure Characterization				

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Study Citation:	Piolatto, G., Negri, E., La Vecchia, C., Pira, E., Decarli, A., Peto, J. (1990). An update of cancer mortality among chrysotile asbestos miners in Balangero, northern Italy. British Journal of Industrial Medicine 47(12):810-814.
Health Outcome:	MISSING
Target Organ(s):	Hepatic/Liver: liver cancer mortality, liver cirrhosis mortality or hepatic cirrhosis mortality,; Cancer/Carcinogenesis: oro-pharyngeal cancer mortality or oral cavity/pharynx cancer mortality, esophageal cancer, liver cancer; Mortality: oro-pharyngeal cancer mortality or oral cavity/pharynx cancer mortality, esophageal cancer, liver cancer mortality, liver cirrhosis mortality or hepatic cirrhosis mortality, accidents and violence mortality
Asbestos Fiber Type(s):	Asbestos - Chrysotile (serpentine): 12001-29-5; Asbestos - Crocidolite (riebeckite): 12001-28-4
Linked HERO ID(s):	3082492, 2592425, 5060134
HERO ID:	3082492

Domain	Metric		Rating	Comments
	Metric 4:	Measurement of Exposure	Medium	These three studies, along with Rubino et al. 1979, HERO ID 000178, were evaluated for lung cancer as part of the Balangero, Italy cohort in the Draft Asbestos Part 1 Risk Evaluation (March 2020). Pira et al. 2017, HERO ID 5060134 was evaluated for lung cancer and laryngeal cancer in the Final Asbestos Part 1 Risk Evaluation (Dec. 2020). As described in the Draft Asbestos Part 1 Risk Evaluation Systematic Review Supplemental File, "Most complete report of exposure assessment is in initial cohort study ((Rubino et al., 1979) pg 189). Chrysotile fiber counts were first measured in 1969 using membrane filter collection and phase contrast microscopy (frequency not reported). To estimate exposure from 1946-1969, factory records on daily production, equipment used, characteristics of the job and number of hours/day were used (this method has considerable limitations due to basis on mean values for large job categories and no allowance for changes in weather). Simulated and measured data were made comparable by using weighting factors (e.g., more dusty operation for 1-2 hr/d compared with longer working hours in the past). Less detailed information was included in follow-up reports ((Piolatto et al., 1990) pg. 810; (Pira et al., 2017), pg 558-559)."As described in the Final Asbestos Part 1 Risk Evaluation for Laryngeal Cancer, "Descriptions of the mine and occupational surveillance was described. Estimates of historical mean concentrations were 37 fibre/mL up to 1950 and 5 fibre/mL between 1971 and 1976. Exposure was determined by employment at the asbestos mine only."This metric was rated as Medium in the Draft and Low in the Final Risk Evaluation for Asbestos Part 1. However, the cohort meets the criteria for Medium as described above.
	Metric 5:	Exposure Levels	Medium	These three studies, along with Rubino et al. 1979, HERO ID 000178, were evaluated for lung cancer as part of the Balangero, Italy cohort in the Draft Asbestos Part 1 Risk Evaluation (March 2020). Pira et al. 2017, HERO ID 5060134 was evaluated for lung cancer and laryngeal cancer in the Final Asbestos Part 1 Risk Evaluation (Dec. 2020). As described in the Draft Asbestos Part 1 Risk Evaluation Systematic Review Supplemental File, "In the initial cohort ((Rubino et al., 1979), Table 8), exposure was reported as up to 100 fiber/yr or >100 fiber/year. In the follow-ups, exposure was reported as <100 fiber/mL-yr, 100-<400 fiber/mL-yr, and >=400 fiber/ml-yr ((Piolatto et al., 1990), Table 3; (Pira et al., 2009), Table 2; (Pira et al., 2017), Tables 3-4)." This metric was not rated in the Final Asbestos Part 1 Risk Evaluation.

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Study Citation:	Piolatto, G., Negri, E., La Vecchia, C., Pira, E., Decarli, A., Peto, J. (1990). An update of cancer mortality among chrysotile asbestos miners in Balangero, northern Italy. British Journal of Industrial Medicine 47(12):810-814.
Health Outcome:	MISSING
Target Organ(s):	Hepatic/Liver: liver cancer mortality, liver cirrhosis mortality or hepatic cirrhosis mortality,; Cancer/Carcinogenesis: oro-pharyngeal cancer mortality or oral cavity/pharynx cancer mortality, esophageal cancer, liver cancer; Mortality: oro-pharyngeal cancer mortality or oral cavity/pharynx cancer mortality, esophageal cancer, liver cancer mortality, liver cirrhosis mortality or hepatic cirrhosis mortality, accidents and violence mortality
Asbestos Fiber Type(s):	Asbestos - Chrysotile (serpentine): 12001-29-5; Asbestos - Crocidolite (riebeckite): 12001-28-4
Linked HERO ID(s):	3082492, 2592425, 5060134
HERO ID:	3082492

Domain	Metric		Rating	Comments
	Metric 6:	Temporality	High	These three studies, along with Rubino et al. 1979, HERO ID 000178, were evaluated for lung cancer as part of the Balangero, Italy cohort in the Draft Asbestos Part 1 Risk Evaluation (March 2020). Pira et al. 2017, HERO ID 5060134 was evaluated for lung cancer and laryngeal cancer in the Final Asbestos Part 1 Risk Evaluation (Dec. 2020). The rating of High for other outcomes is based on the most recent publication, which has the longest follow-up duration for this cohort (follow up of the 1946-1990 cohort through 2014), as described in the Draft Risk Evaluation for Asbestos Part 1. The first two studies in the cohort (Rubino et al., 1979 and Piolatto et al., 1990) have inadequate follow-up durations (<15 years) considering the potential latency periods for some of the outcomes assessed. As described in the Asbestos Part 1 Final Risk Evaluation for Laryngeal Cancer, "Subjects were followed until loss to follow-up, their death, 85th birthday, or through 2014. This is a sufficiently long follow-up period." This metric was rated as High in both the Draft and Final Asbestos Part 1 Risk Evaluations.
Domain 3: Outcome Assessment				

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Study Citation:	Piolatto, G., Negri, E., La Vecchia, C., Pira, E., Decarli, A., Peto, J. (1990). An update of cancer mortality among chrysotile asbestos miners in Balangero, northern Italy. British Journal of Industrial Medicine 47(12):810-814.
Health Outcome:	MISSING
Target Organ(s):	Hepatic/Liver: liver cancer mortality, liver cirrhosis mortality or hepatic cirrhosis mortality,; Cancer/Carcinogenesis: oro-pharyngeal cancer mortality or oral cavity/pharynx cancer mortality, esophageal cancer, liver cancer; Mortality: oro-pharyngeal cancer mortality or oral cavity/pharynx cancer mortality, esophageal cancer, liver cancer mortality, liver cirrhosis mortality or hepatic cirrhosis mortality, accidents and violence mortality
Asbestos Fiber Type(s):	Asbestos - Chrysotile (serpentine): 12001-29-5; Asbestos - Crocidolite (riebeckite): 12001-28-4
Linked HERO ID(s):	3082492, 2592425, 5060134
HERO ID:	3082492

Domain	Metric		Rating	Comments
	Metric 7:	Outcome Measurement or Characterization	High	Other Cancer(s): These three studies, along with Rubino et al. 1979, HERO ID 000178, were evaluated for lung cancer as part of the Balangero, Italy cohort in the Draft Asbestos Part 1 Risk Evaluation (March 2020). Pira et al. 2017, HERO ID 5060134 was evaluated for lung cancer and laryngeal cancer in the Final Asbestos Part 1 Risk Evaluation (Dec. 2020). In the Draft Asbestos Part 1 Risk Evaluation, the cohort was rated as High for this Metric. In the Final Asbestos Part 1 Risk Evaluation this metric was rated as Medium for laryngeal cancer because ”Cause specific mortalities were obtained from death certificates collected from population registers, municipal registration offices, and local health authorities. Causes of death were coded using ICD-9, however, the study authors did not report whether cancer cases were histologically confirmed. It’s unclear if there may be any misclassification from obtaining vital status or cause of death from various sources.”Evaluation of all causes of death assessed in the cohort was based on death certificates and population registers and coded according to the International Classification of Diseases (ICD). Rubino et al., 1979, HERO ID 000178 coded causes of deaths according to ICD-7. Piolatto et al. 1990, HERO ID 3082492 did not specify which version of the ICD was used. Pira et al., 2009, HERO ID 2592425 and Pira et al., 2017, HERO ID 5060134 used ICD-9 codes. Numbers of certified deaths for each cause for the general population were obtained from the Italian National Institute of Statistics and the World Health Organization.; Other Non-Cancer Outcomes: These three studies, along with Rubino et al. 1979, HERO ID 000178, were evaluated for lung cancer as part of the Balangero, Italy cohort in the Draft Asbestos Part 1 Risk Evaluation (March 2020). Pira et al. 2017, HERO ID 5060134 was evaluated for lung cancer and laryngeal cancer in the Final Asbestos Part 1 Risk Evaluation (Dec. 2020). In the Draft Asbestos Part 1 Risk Evaluation, the cohort was rated as High for this Metric. In the Final Asbestos Part 1 Risk Evaluation this metric was rated as Medium for laryngeal cancer because ”Cause specific mortalities were obtained from death certificates collected from population registers, municipal registration offices, and local health authorities. Causes of death were coded using ICD-9, however, the study authors did not report whether cancer cases were histologically confirmed. It’s unclear if there may be any misclassification from obtaining vital status or cause of death from various sources.”Evaluation of all causes of death assessed in the cohort was based on death certificates and population registers and coded according to the International Classification of Diseases (ICD). Rubino et al., 1979, HERO ID 000178 coded causes of deaths according to ICD-7. Piolatto et al. 1990, HERO ID 3082492 did not specify which version of the ICD was used. Pira et al., 2009, HERO ID 2592425 and Pira et al., 2017, HERO ID 5060134 used ICD-9 codes. Numbers of certified deaths for each cause for the general population were obtained from the Italian National Institute of Statistics and the World Health Organization.

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Study Citation:	Piolatto, G., Negri, E., La Vecchia, C., Pira, E., Decarli, A., Peto, J. (1990). An update of cancer mortality among chrysotile asbestos miners in Balangero, northern Italy. British Journal of Industrial Medicine 47(12):810-814.
Health Outcome:	MISSING
Target Organ(s):	Hepatic/Liver: liver cancer mortality, liver cirrhosis mortality or hepatic cirrhosis mortality,; Cancer/Carcinogenesis: oro-pharyngeal cancer mortality or oral cavity/pharynx cancer mortality, esophageal cancer, liver cancer; Mortality: oro-pharyngeal cancer mortality or oral cavity/pharynx cancer mortality, esophageal cancer, liver cancer mortality, liver cirrhosis mortality or hepatic cirrhosis mortality, accidents and violence mortality
Asbestos Fiber Type(s):	Asbestos - Chrysotile (serpentine): 12001-29-5; Asbestos - Crocidolite (riebeckite): 12001-28-4
Linked HERO ID(s):	3082492, 2592425, 5060134
HERO ID:	3082492

Domain	Metric		Rating	Comments
	Metric 8:	Reporting Bias	Medium	These three studies, along with Rubino et al. 1979, HERO ID 000178, were evaluated for lung cancer as part of the Balangero, Italy cohort in the Draft Asbestos Part 1 Risk Evaluation (March 2020). Pira et al. 2017, HERO ID 5060134 was evaluated for lung cancer and laryngeal cancer in the Final Asbestos Part 1 Risk Evaluation (Dec. 2020). This metric was rated as High in the Draft Asbestos Part 1 Risk Evaluation for lung cancer and High in the Draft Asbestos Part 1 Risk Evaluation for lung cancer and laryngeal cancer.However, results for some of the other outcomes assessed in the paper were reported in less detail than the results for lung cancer, resulting in a lower rating for this Metric for these other outcomes. For example, Table 4 in Pira et al., 2017, HERO ID 5060134 reports mortality rate ratios (MRR) for lung cancer for selected indicators of asbestos exposure, and does not include reporting of MRR for other outcomes. All three papers reported SMRs for several outcomes, though there were some differences between papers in terms of which specific outcomes were included. The most recent follow-up (Pira et al., 2017, HERO ID 5060134) had the most complete reporting with 95% confidence intervals. Some of the results reported in Piolatto et al., 1990, HERO ID 3082492 and Pira et al., 2009, HERO ID 2592425 did not include reporting of confidence intervals.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Low	SMRs were stratified by age and five-year categories of calendar year. Only males were included. There is no mention of adjustment for race, but from 1981 onwards mortality ratios were standardized to male deaths from the Piedmont region where the mine was located, which likely reduced the potential for confounding by race or SES. Prior to 1981 mortality ratios were standardized to national mortality for Italy because regional data were not available. The authors noted that potential confounding by smoking and alcohol consumption were limitations. In particular, the authors note that potential confounding by alcohol consumption is a concern for oral cancer, esophageal cancer, liver cirrhosis, accidents and violence, which are known to be associated with alcohol consumption.
	Metric 10:	Covariate Characterization	High	These three studies, along with Rubino et al. 1979, HERO ID 000178, were evaluated for lung cancer as part of the Balangero, Italy cohort in the Draft Asbestos Part 1 Risk Evaluation (March 2020). Pira et al. 2017, HERO ID 5060134 was evaluated for lung cancer and laryngeal cancer in the Final Asbestos Part 1 Risk Evaluation (Dec. 2020). This metric was rated High in the Draft and Medium in the Final Asbestos Part 1 Risk Evaluation.As described in the Draft Asbestos Part 1 Risk Evaluation Systematic Review Supplemental File, ”Empirical data obtained from employment records. Smoking information was obtained from medical records (when available).”

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Study Citation:	Piolatto, G., Negri, E., La Vecchia, C., Pira, E., Decarli, A., Peto, J. (1990). An update of cancer mortality among chrysotile asbestos miners in Balangero, northern Italy. British Journal of Industrial Medicine 47(12):810-814.
Health Outcome:	MISSING
Target Organ(s):	Hepatic/Liver: liver cancer mortality, liver cirrhosis mortality or hepatic cirrhosis mortality,; Cancer/Carcinogenesis: oro-pharyngeal cancer mortality or oral cavity/pharynx cancer mortality, esophageal cancer, liver cancer; Mortality: oro-pharyngeal cancer mortality or oral cavity/pharynx cancer mortality, esophageal cancer, liver cancer mortality, liver cirrhosis mortality or hepatic cirrhosis mortality, accidents and violence mortality
Asbestos Fiber Type(s):	Asbestos - Chrysotile (serpentine): 12001-29-5; Asbestos - Crocidolite (riebeckite): 12001-28-4
Linked HERO ID(s):	3082492, 2592425, 5060134
HERO ID:	3082492

Domain	Metric		Rating	Comments
	Metric 11:	Co-exposure Counfounding	Low	No adjustments for potential co-exposures were described. The authors mentioned the possibility of confounding by other occupational exposures. Samples of chrysotile from the mine were examined in detail for contamination from other materials (Piolatto et al., 1990 3082492) and fibrous amphiboles were not detected. Crocidolite was occasionally present at the mine. Balangeroite accounted for 0.2-0.5% of total mass chrysotile samples from the mine. Balangeroite is a fibrous silicate that is not considered a true asbestos fiber and has similar dimensions to amphiboles (Piolatto et al., 1990 3082492, Pira et al., 2009 2592425, Pira et al., 2017 5060134).
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	Medium	These three studies, along with Rubino et al. 1979, HERO ID 000178, were evaluated for lung cancer as part of the Balangero, Italy cohort in the Draft Asbestos Part 1 Risk Evaluation (March 2020). Pira et al. 2017, HERO ID 5060134 was evaluated for lung cancer and laryngeal cancer in the Final Asbestos Part 1 Risk Evaluation (Dec. 2020). This Metric was rated as Medium in both the Draft and Final Risk Evaluations for Asbestos Part 1.As described in the Asbestos Part 1 Final Risk Evaluation Systematic Review Supplemental File for laryngeal cancer, ”SMRs were used to assess differences in cause specific mortality rates between employees of an asbestos mine compared to a reference population in the same region. This is an appropriate design for the study question.”
	Metric 13:	Statistical Power	Medium	The cohort size was generally adequate, although some outcomes, particularly some of the cancer outcomes, had low numbers of observed causes of death.
	Metric 14:	Reproducibility of Analyses	Medium	These three studies, along with Rubino et al. 1979, HERO ID 000178, were evaluated for lung cancer as part of the his Metric was rated as Medium in both the Draft and Final Risk Evaluations for Asbestos Part 1.Balangero, Italy cohort in the Draft Asbestos Part 1 Risk Evaluation (March 2020). Pira et al. 2017, HERO ID 5060134 was evaluated for lung cancer and laryngeal cancer in the Final Asbestos Part 1 Risk Evaluation (Dec. 2020). This metric was rated Medium in both the Draft and the Final Asbestos Part 1 Risk Evaluations.As described in the Final Asbestos Part 1 Risk Evaluation Systematic Review Supplemental File, ”The analysis was well-described and could be reproduced with original data.”
	Metric 15:	Statistical Analysis	Medium	The methods for calculating SMRs are transparent.

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Study Citation:	Piolatto, G., Negri, E., La Vecchia, C., Pira, E., Decarli, A., Peto, J. (1990). An update of cancer mortality among chrysotile asbestos miners in Balangero, northern Italy. British Journal of Industrial Medicine 47(12):810-814.
Health Outcome:	MISSING
Target Organ(s):	Hepatic/Liver: liver cancer mortality, liver cirrhosis mortality or hepatic cirrhosis mortality,; Cancer/Carcinogenesis: oro-pharyngeal cancer mortality or oral cavity/pharynx cancer mortality, esophageal cancer, liver cancer; Mortality: oro-pharyngeal cancer mortality or oral cavity/pharynx cancer mortality, esophageal cancer, liver cancer mortality, liver cirrhosis mortality or hepatic cirrhosis mortality, accidents and violence mortality
Asbestos Fiber Type(s):	Asbestos - Chrysotile (serpentine): 12001-29-5; Asbestos - Crocidolite (riebeckite): 12001-28-4
Linked HERO ID(s):	3082492, 2592425, 5060134
HERO ID:	3082492

Domain	Metric	Rating	Comments
Additional Comments:	These three studies, along with Rubino et al. 1979, HERO ID 000178, were evaluated for lung cancer as part of the Balangero, Italy cohort in the Draft Asbestos Part 1 Risk Evaluation (March 2020), with an overall quality determination of High for lung cancer. Pira et al. 2017, HERO ID 5060134 was evaluated for lung cancer and laryngeal cancer in the Final Risk Evaluation (Dec. 2020) with an overall quality determination of Medium for lung cancer and Medium for laryngeal cancer. Potential confounding by alcohol consumption is a concern for the specific outcomes evaluated on this form.The main fiber type was chrysotile. Crocidolite was occasionally present at the mine. Balangeroite, which is a fibrous silicate, accounted for 0.2-0.5% of total mass chrysotile samples from the mine.This study assessed a cohort who worked in an open-air mine, and thus these outdoor exposures might be different than exposures in other environments.		

Overall Quality Determination — Medium

* No biomarkers were identified for this evaluation.

Study Citation:	Pira, E., Turbiglio, M., Maroni, M., Carrer, P., La Vecchia, C., Negri, E., Iachetta, R. (1999). Mortality among workers in the geothermal power plants at Larderello, Italy. American Journal of Industrial Medicine 35(5):536-539.		
Health Outcome:	total mortality		
Target Organ(s):	Mortality: Total mortality, total cancer mortality		
Asbestos Fiber Type(s):	Asbestos - Not specified: 1332-21-4		
Linked HERO ID(s):	No linked references.		
HERO ID:	2964127		

Domain	Metric	Rating	Comments
Domain 2: Exposure Characterization			
	Metric 4: Measurement of Exposure	Low	This metric is rated Low because the study or any cited methods source does not explicitly mention the use of PCM or TEM. Authors relay the use of an extensive job exposure matrix that included quantitative exposure measures for asbestos, individual working histories, and information on specific job activities and was applied by professionals in toxicology, epidemiology, and occupational medicine. While the job exposure matrix is robust and allows for presentation of results based on cumulative asbestos fiber levels, there is no information provided on the analytical method used to measure asbestos fiber levels, meriting a medium rating.
	Metric 5: Exposure Levels	Medium	In analyses with asbestos exposure, authors apply three exposure groupings (unexposed, <= 5,000 fibers/L/year, >= 5,000 fibers/L/year) to the cohort. The range of exposure appears appropriate to assess the impact of asbestos on the health effects of interest.

Additional Comments: This large occupational cohort study (n=3,946) examined mortality among Italian male workers in a geothermal plant. The approaches for participant selection, exposure measurement, and outcome ascertainment were robust, but occupational co-exposures appear to have occurred. No adjustment for these co-exposures was included in the calculation of SMRs for the total mortality among the cohort. Additionally, the comparison group used to assess the SMR among this occupational population was the general population, which could have led to the healthy worker effect. Finally, recruitment and outcome assessment occurred simultaneously, which prevents the ability to establish temporality of exposure and outcome.

* No biomarkers were identified for this evaluation.

** As described in Appendix B.2 of the *White Paper: Quantitative Approach to the Human Health Assessment for the Risk Evaluation for Asbestos Part 2: Supplemental Evaluation Including Legacy Uses and Associated Disposals of Asbestos*, to be considered as being informative for dose-response analysis, metrics 4 and 5 would need metric ratings of Medium or High. This reference did not satisfy this requirement; therefore data quality evaluation is presented for only for metrics 4 and 5.

Study Citation:	Plato, N., Tornling, G., Hogstedt, C., Krantz, S. (1995). An index of past asbestos exposure as applied to car and bus mechanics. Annals of Occupational Hygiene 39(4):441-454.
Health Outcome:	Pulmonary Function/Spirometry Results
Target Organ(s):	Lung/Respiratory: Vital capacity (VC), Percent vital capacity (CV%), Transfer factor (TLco), total lung capacity (TLC), Forced volume in 1 second (FEV1)
Asbestos Fiber Type(s):	Asbestos - Chrysotile (serpentine): 12001-29-5
Linked HERO ID(s):	No linked references.
HERO ID:	3081596

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Medium	The relationship between estimated mean cumulative exposure, and exposure as represented by years of employment, with outcomes of spirometry lung function parameters of vital capacity (VC) forced volume in 1 second (FEV1), total lung capacity (TLC), percent vital capacity (CV%) and transfer factor (TLco) in Swedish car and bus mechanics (n=103) and a control group (n=83) of suburban bus drivers was investigated in what appears to be a retrospective cohort study (dates of health outcome assessments not detailed within text or main referenced study (Dahlqvist et al., 1992 (HERO ID 2248426)). The exposed study group was selected from local Swedish health records of the Stockholm Local Vehicle Health Service and the local bus transportation company. The criteria for selection included those workers of age greater than 40 years and with greater than 20 years of employment as car or bus mechanics. Those with job histories including spray painting, vehicle body repair activities, or asbestos exposure from other sources were excluded. Both car mechanics (n=95) and bus mechanics (n=8) were included for analyses. Dates of employment for selected sample of mechanics were not specified, however the text (page 446) indicates mean asbestos exposures were estimated for the period 1938-1986. The referenced study (Dahlqvist et al., 1992 (HERO ID 2248426), utilized a total of 89 control bus drivers selected from 315 blue collar workers and bus drivers within organizational and local Swedish traffic registries, with exclusions made for those with occupational exposure to asbestos or other lung irritants and other health disorders, and those dropping out. It is unclear if the number of car and bus mechanics (n= 103) selected for study adequately represented the totality of the exposure-outcome relationship for the reported approximately 25,000 Swedish car and bus mechanics employed in the mid-1980's.
	Metric 2:	Attrition	High	Characteristics, in terms of relevant variables of those possibly excluded due to missing outcome or exposure data, were not reported, however there was no indication that missing data or subject drop-out was an issue within this study.

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Study Citation: Plato, N., Tornling, G., Hogstedt, C., Krantz, S. (1995). An index of past asbestos exposure as applied to car and bus mechanics. Annals of Occupational Hygiene 39(4):441-454.
Health Outcome: Pulmonary Function/Spirometry Results
Target Organ(s): Lung/Respiratory: Vital capacity (VC), Percent vital capacity (CV%), Transfer factor (TLco), total lung capacity (TLC), Forced volume in 1 second (FEV1)
Asbestos Fiber Type(s): Asbestos - Chrysotile (serpentine): 12001-29-5
Linked HERO ID(s): No linked references.
HERO ID: 3081596

Domain	Metric		Rating	Comments
	Metric 3:	Comparison Group	Medium	A control group (n=83) of suburban bus drivers described as "without asbestos exposure" was utilized for analyses. Comparison of baseline characteristics between car and bus mechanics versus bus drivers was detailed, however text (page 445) lists smoking, age and height were studied as potential confounding variables, and text (page 442) indicates control bus drivers were investigated in the same way as mechanics. Text (page 442) noted a similar percentage of non-smokers in bus drivers and mechanics. It is unclear if consideration was given to the known potential for bus driver exposures to asbestos fibers released from brakes, gaskets and clutch pads during bus driving and spending time within bus garages. Uncertainty also exists regarding the potential Healthy Worker Effects due to selection criteria and lack of information of completeness of exposure and outcome data.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Medium	Estimated mean cumulative exposure and exposure classified by years of employment were the exposure variables utilized in analyses with lung function outcomes of interest (Table 2). Text (page 449) noted asbestos was defined as airborne fibers released from friction materials (brake shoes, pads, clutch linings) with length > 5 µm and aspect ratio >=3:1. Friction materials contained 30-70% chrysotile asbestos. Fiber counting was performed utilizing phase-contrast optical microscopy (PCOM). Available historical measured individual exposures for available work history years and those from a literature search were utilized within calculated asbestos index (AI; see Appendix of main text for detail) in constructing estimated mean cumulative exposure. Calculations for modeled AI utilized considerations for eight exposure variables representing job activity, technology level, workshop conditions and time. Models further utilized a job-exposure matrix which accounted for type of vehicle, room ventilation, working activity and working intensity. Job history and work activity data was obtained utilizing self-administered questionnaires and standardized personal interviews. Validation models utilized in confirming adequate precision of AI exposure estimates. There is uncertainty for exclusion of consideration of respiratory protection, however authors indicated face masks were not utilized by workers. There is uncertainty in the use of years of employment (Table 2) in terms of accurately representing the asbestos exposure in analyses with lung function outcomes within this effort, however text (page 448) notes employment time data from company records correlated closely to exposure time from interviews or questionnaires. Additional uncertainty was revealed within text (page 448) as some mechanics had worked in non-asbestos exposed tasks, such as supervisors, although their job title within company records was listed as "car mechanic".

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Study Citation:	Plato, N., Tornling, G., Hogstedt, C., Krantz, S. (1995). An index of past asbestos exposure as applied to car and bus mechanics. Annals of Occupational Hygiene 39(4):441-454.
Health Outcome:	Pulmonary Function/Spirometry Results
Target Organ(s):	Lung/Respiratory: Vital capacity (VC), Percent vital capacity (CV%), Transfer factor (TLco), total lung capacity (TLC), Forced volume in 1 second (FEV1)
Asbestos Fiber Type(s):	Asbestos - Chrysotile (serpentine): 12001-29-5
Linked HERO ID(s):	No linked references.
HERO ID:	3081596

Domain	Metric		Rating	Comments
	Metric 5:	Exposure Levels	Medium	The estimated mean cumulative asbestos exposure was 2.6 f mL * year (0.1 -11.6 f mL * year). The range and distribution of estimated exposure was adequate and exposure-response model utilized a continuous measure of exposure.
	Metric 6:	Temporality	Medium	The study group was restricted to mechanics with more than 20 years of employment as car and/or bus mechanics. Due to the uncertain timing of lung function tests as dates of testing were not detailed, there is uncertainty in terms of temporality between exposure and outcome.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	High	Pulmonary Function/Spirometry Results: Lung function testing was described as utilizing dynamic spirometry to measure parameters of vital capacity (VC) forced volume in 1 second (FEV1), total lung capacity (TLC), percent vital capacity (CV%) and transfer factor (TLco) utilizing standard methods according to guidelines within the American Thoracic Society which were outlined within main text and within the referenced study (Dahlqvist et al., 1992 (HERO ID 2248426)).
	Metric 8:	Reporting Bias	Medium	There were no concerns for selective reporting as all outcomes which were outlined within methods were also reported within the results. The effect estimates within Table 2 were reported only as slope, with detail on confidence intervals and standard errors lacking.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Medium	The final regression analyses results were reported as adjusted for smoking, age and height, however justification for use of these confounders was lacking. The analysis was restricted to males of age greater than 40 years and with more than 20 years of employment. A display table of the distribution of potential confounders between exposed and non-exposed groups was lacking.
	Metric 10:	Covariate Characterization	Medium	While the methods utilized to obtain and validate data regarding potential confounders were described only as obtained through interview within the referenced study (Dahlqvist et al., 1992 (HERO ID 2248426)), there is no indication that methods had poor validity.
	Metric 11:	Co-exposure Counfounding	Medium	Potential co-exposures, including brake dust, exhaust, welding fume, general dust and silica dust, which might be associated with lung function outcomes of interest, were discussed within this occupational study. There is some uncertainty regarding these exposures as exposure levels for these contaminants were not obtained within this study.
Domain 5: Analysis				

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Study Citation: Plato, N., Tornling, G., Hogstedt, C., Krantz, S. (1995). An index of past asbestos exposure as applied to car and bus mechanics. Annals of Occupational Hygiene 39(4):441-454.
Health Outcome: Pulmonary Function/Spirometry Results
Target Organ(s): Lung/Respiratory: Vital capacity (VC), Percent vital capacity (CV%), Transfer factor (TLco), total lung capacity (TLC), Forced volume in 1 second (FEV1)
Asbestos Fiber Type(s): Asbestos - Chrysotile (serpentine): 12001-29-5
Linked HERO ID(s): No linked references.
HERO ID: 3081596

Domain	Metric		Rating	Comments
	Metric 12:	Study Design and Methods	Medium	Multivariate regression was utilized for analysis of the relationship between estimated cumulative asbestos exposure and lung function outcomes of interest.
	Metric 13:	Statistical Power	Medium	The number of subjects (n=103 car and bus mechanics, n=83 control bus drivers) was adequate for this analysis.
	Metric 14:	Reproducibility of Analyses	Medium	General statistical analysis methods were briefly reported, however details such as rules for classification of smoking categories, consideration of outliers, transformation of continuous variables and methods for dealing with missing data were not detailed.
	Metric 15:	Statistical Analysis	Medium	The description of statistical analysis was very brief. However, details on some model assumptions regarding morphologic fiber changes during heating were described.

Additional Comments: This study estimated cumulative asbestos exposure within a sample (n=103) of Swedish car and bus mechanics utilizing a semi-quantitative Asbestos Index (AI) constructed from historical and literature -based measured exposures along with exposure scenarios derived from employee self-administered questionnaires and standardized personal work history interviews. The relationship between estimated mean cumulative asbestos exposure, and exposure as represented by years of employment, with spirometry lung function parameters of vital capacity (VC) forced volume in 1 second (FEV1), total lung capacity (TLC), percent vital capacity (CV%) and transfer factor (TLco) was investigated. The transfer factor (TLco) was lower than expected in car mechanics (Table 2), but no other lung function measures differed from those expected. Results (Table 1) also indicated a weak, non-significant relationship between cumulative asbestos exposure and CV%.

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation:	Polissar, L., Severson, R. K., Boatman, E. S. (1984). A case-control study of asbestos in drinking water and cancer risk. American Journal of Epidemiology 119(3):456-471.
Health Outcome:	Lung Cancer; Laryngeal Cancer; buccal cavity and pharnyx, mouth, pharynx, digestive system, stomach, colon, rectum, pancreas, gallbladder, respiratory system, bladder, kidney, all study sites cancer
Target Organ(s):	Mouth: Buccal cavity and pharynx cancer, Mouth cancer, Pharyngeal cancer; Cancer/Carcinogenesis: Buccal cavity and pharynx cancer, Mouth cancer, Pharyngeal cancer, Digestive system cancer, Stomach cancer, Colon cancer, Rectum cancer, Gallbladder cancer, Pancreatic cancer, Respiratory system cancer, Laryngeal cancer, Lung cancer, Bladder cancer, Kidney cancer, All study sites cancer (buccal cavity, pharynx, digestive system, stomach, colon, rectum gallbladder, pancreas, respiratory system, bladder, and kidney); Gastrointestinal: Digestive system cancer, Stomach cancer, Colon cancer, Rectum cancer, Gallbladder cancer, Pancreatic cancer; Lung/Respiratory: Respiratory system cancer, Laryngeal cancer, Lung cancer; Renal/Kidney: Bladder cancer, Kidney cancer
Asbestos Fiber Type(s):	Asbestos - Chrysotile (serpentine): 12001-29-5
Linked HERO ID(s):	3083628, 3083701
HERO ID:	3083628

Domain	Metric	Rating	Comments
Domain 1: Study Participation			

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Study Citation:	Polissar, L., Severson, R. K., Boatman, E. S. (1984). A case-control study of asbestos in drinking water and cancer risk. American Journal of Epidemiology 119(3):456-471.
Health Outcome:	Lung Cancer; Laryngeal Cancer; buccal cavity and pharnyx, mouth, pharynx, digestive system, stomach, colon, rectum, pancreas, gallbladder, respiratory system, bladder, kidney, all study sites cancer
Target Organ(s):	Mouth: Buccal cavity and pharynx cancer, Mouth cancer, Pharyngeal cancer; Cancer/Carcinogenesis: Buccal cavity and pharynx cancer, Mouth cancer, Pharyngeal cancer, Digestive system cancer, Stomach cancer, Colon cancer, Rectum cancer, Gallbladder cancer, Pancreatic cancer, Respiratory system cancer, Laryngeal cancer, Lung cancer, Bladder cancer, Kidney cancer, All study sites cancer (buccal cavity, pharynx, digestive system, stomach, colon, rectum gallbladder, pancreas, respiratory system, bladder, and kidney); Gastrointestinal: Digestive system cancer, Stomach cancer, Colon cancer, Rectum cancer, Gallbladder cancer, Pancreatic cancer; Lung/Respiratory: Respiratory system cancer, Laryngeal cancer, Lung cancer; Renal/Kidney: Bladder cancer, Kidney cancer
Asbestos Fiber Type(s):	Asbestos - Chrysotile (serpentine): 12001-29-5
Linked HERO ID(s):	3083628, 3083701
HERO ID:	3083628

Domain	Metric		Rating	Comments
	Metric 1:	Participant Selection	Medium	These cancer case-control studies were designed around the Everett, Washington area which uses the Sultan River as their primary source of drinking water. To address the concern that some census tracts with large rates of migration could produce a population with smaller than expected cumulative exposures, the study area was limited to 1970 census tracts that had lower than average migration rates. To determine migration rates, the authors used the percent of the heads of households in a census tract residing continuously at the 1970 residence for at least 10 years, with the caveat that this is biased towards including older persons as they are less likely to be migratory. The authors report a “stability indicator” of 12 percent or greater (median 24 percent) for the 25 census tracts included in this study. Census tracts included the numbers 401-415, 418, 420, 501-504, 510, 512, 515, and 519, which represented 70% of the total population who used the Sultan River as a drinking water source.Cases were identified through the Cancer Surveillance System, which is a population-based tumor registry that covers 13 counties and nearly 3 million people in western Washington state. Cases who had invasive or in situ cases of cancer of the buccal cavity (not the lip), pharynx, respiratory system, digestive system, bladder, or kidney newly diagnosed between November 1977 and December 1980 were included. These cancers were chosen a priori based on preceding studies. Only participants who were between the ages of 40 and 79 years of age who resided in the eligible census tracts at the time of diagnosis were included, and this analysis included both living and deceased participants. The authors explain that quality control studies have demonstrated that this registry misses less than 2% of the total cases eligible for inclusion, but this data is unpublished. In total, 445 cases were identified as eligible for this study, and after attrition the final analysis sample included 382 cases.Unmatched controls in the same age range and from the pooled group of tracts by selecting 4 households at random from 88 geographic strata (n=669 households), then contacted those that were not vacant for an interview (n=649). Authors obtained age-sex data on residents, then tried to schedule an interview with each person of eligible age. A control proxy (usually a spouse), were interviewed if the controls themselves was unavailable. The final number of controls included in analyses was 462. It is unclear what the ”88 geographic strata” are. However, it would suggest these are portions of the eligible census tracts from which cases were recruited, and would not be expected to substantively bias results.The choice to exclude census tracts with high migration rates may be considered an issue of external validity, as the authors aimed to examine a highly-exposed population and those with high migration rate may have lower levels of exposure. However, if understood as an issue of internal validity there is some limited concern for selection bias as this choice is unlikely to be related to outcome status.

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Study Citation:	Polissar, L., Severson, R. K., Boatman, E. S. (1984). A case-control study of asbestos in drinking water and cancer risk. American Journal of Epidemiology 119(3):456-471.
Health Outcome:	Lung Cancer; Laryngeal Cancer; buccal cavity and pharnyx, mouth, pharynx, digestive system, stomach, colon, rectum, pancreas, gallbladder, respiratory system, bladder, kidney, all study sites cancer
Target Organ(s):	Mouth: Buccal cavity and pharynx cancer, Mouth cancer, Pharyngeal cancer; Cancer/Carcinogenesis: Buccal cavity and pharynx cancer, Mouth cancer, Pharyngeal cancer, Digestive system cancer, Stomach cancer, Colon cancer, Rectum cancer, Gallbladder cancer, Pancreatic cancer, Respiratory system cancer, Laryngeal cancer, Lung cancer, Bladder cancer, Kidney cancer, All study sites cancer (buccal cavity, pharynx, digestive system, stomach, colon, rectum gallbladder, pancreas, respiratory system, bladder, and kidney); Gastrointestinal: Digestive system cancer, Stomach cancer, Colon cancer, Rectum cancer, Gallbladder cancer, Pancreatic cancer; Lung/Respiratory: Respiratory system cancer, Laryngeal cancer, Lung cancer; Renal/Kidney: Bladder cancer, Kidney cancer
Asbestos Fiber Type(s):	Asbestos - Chrysotile (serpentine): 12001-29-5
Linked HERO ID(s):	3083628, 3083701
HERO ID:	3083628

Domain	Metric		Rating	Comments
	Metric 2:	Attrition	Medium	Of 445 eligible cases, 13.5% refused participation. Of 549 eligible controls, 11.7% refused participation. Reasons for failure to interview cases were either refusal by the primary physician (3.1%), refusal by the patient (6.3%), or "other reasons" (4.0%). In controls, failure to interview was either due to refusal by the patient (10.4%) or "other reasons" (1.3%). Despite a lack of clarity as to what "other reasons" means, there is little reason to suspect that attrition was related to the true outcome due to the case identification happening prior to interview. The attrition rates are also relatively low and are not a cause for any specific concern. Due to there being only one non-white case, the study was limited to whites and thus that one case, and 23 corresponding controls, were excluded. Two cases were excluded as their interview data came from next-of-kin who answered "virtually" all questions as "unknown." There is no discussion of missing data.
	Metric 3:	Comparison Group	High	Controls were unmatched but were selected from the same age range (40-79) and from the same census tracts as the cases. Since the authors report a final eligible sample of 549 for their control population, it may be assumed that 100 of the 649 households available for interview did not fall within the inclusion age range of 40-79. However, this is not explicitly stated. After attrition, the final sample of controls was 462. Potential differences between cases and controls were controlled for in statistical analyses, such as age, alcohol consumption, sex, education, religion, race/ethnicity, family history, asbestos-related occupations, and smoking.
Domain 2: Exposure Characterization				

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Study Citation:	Polissar, L., Severson, R. K., Boatman, E. S. (1984). A case-control study of asbestos in drinking water and cancer risk. American Journal of Epidemiology 119(3):456-471.
Health Outcome:	Lung Cancer; Laryngeal Cancer; buccal cavity and pharnyx, mouth, pharynx, digestive system, stomach, colon, rectum, pancreas, gallbladder, respiratory system, bladder, kidney, all study sites cancer
Target Organ(s):	Mouth: Buccal cavity and pharynx cancer, Mouth cancer, Pharyngeal cancer; Cancer/Carcinogenesis: Buccal cavity and pharynx cancer, Mouth cancer, Pharyngeal cancer, Digestive system cancer, Stomach cancer, Colon cancer, Rectum cancer, Gallbladder cancer, Pancreatic cancer, Respiratory system cancer, Laryngeal cancer, Lung cancer, Bladder cancer, Kidney cancer, All study sites cancer (buccal cavity, pharynx, digestive system, stomach, colon, rectum gallbladder, pancreas, respiratory system, bladder, and kidney); Gastrointestinal: Digestive system cancer, Stomach cancer, Colon cancer, Rectum cancer, Gallbladder cancer, Pancreatic cancer; Lung/Respiratory: Respiratory system cancer, Laryngeal cancer, Lung cancer; Renal/Kidney: Bladder cancer, Kidney cancer
Asbestos Fiber Type(s):	Asbestos - Chrysotile (serpentine): 12001-29-5
Linked HERO ID(s):	3083628, 3083701
HERO ID:	3083628

Domain	Metric		Rating	Comments
	Metric 4:	Measurement of Exposure	Medium	Both papers (Polissar et al., 1983a, HEROID 3083628; Polissar et al., 1983b, HEROID 3083701) reported that the authors met with representatives of water companies to determine the source of tap water for given locations and dates. The authors provide a conversion factor to convert asbestos concentrations from each water district into units of Sultan River tap water asbestos concentration. The timing of water sampling for asbestos is unclear, so exposure might have been extrapolated for part of the study period. The methods for analyzing the asbestos fibers for part of the study are in cited references (Polissar et al. 1982, HERO ID 353) and (Millette et al. 1980, HERO ID 60455), which describe using EPA methods for the identification and quantification of asbestos fibers, including the use of transmission electron microscopy (TEM). Additional methods are in a cited EPA report ”Exposure to asbestos in drinking water in the United States,” which details the appropriate methods for analyzing asbestos in water samples. Tap water exposure may be oral (via drinking water) or dermal (via bathing). Information on individual water consumption levels was obtained via in-person interviews, which may be subject to recall bias, especially for 47% of cases for whom interviews were conducted with next-of-kin rather than the actual participant.
	Metric 5:	Exposure Levels	Medium	In both papers, exposure was assessed as a continuous variable in logistic regression models. Exposure levels are presented in ”equivalent years of exposure.” The authors report a range of 0-30+ ”equivalent years of exposure” and provide that 1 ”unit” is equivalent to 1 year x 207 million fibers/liter.
	Metric 6:	Temporality	Medium	Temporality is sufficiently established, as cases were required to reside in the relevant census tracts for exposure at the time of their diagnosis. However, it is unclear whether or not there is a sufficient consideration for latency. The authors do not report how far back they estimate exposure history to obtain year-by-year estimates of exposure. However, two of the asbestos exposure variables included in their models ignore all exposure history during a 10-year presumed latency period prior to diagnosis or interview, which would consider at least 10 years of latency for cancer outcomes.
Domain 3: Outcome Assessment				

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Study Citation:	Polissar, L., Severson, R. K., Boatman, E. S. (1984). A case-control study of asbestos in drinking water and cancer risk. American Journal of Epidemiology 119(3):456-471.
Health Outcome:	Lung Cancer; Laryngeal Cancer; buccal cavity and pharnyx, mouth, pharynx, digestive system, stomach, colon, rectum, pancreas, gallbladder, respiratory system, bladder, kidney, all study sites cancer
Target Organ(s):	Mouth: Buccal cavity and pharynx cancer, Mouth cancer, Pharyngeal cancer; Cancer/Carcinogenesis: Buccal cavity and pharynx cancer, Mouth cancer, Pharyngeal cancer, Digestive system cancer, Stomach cancer, Colon cancer, Rectum cancer, Gallbladder cancer, Pancreatic cancer, Respiratory system cancer, Laryngeal cancer, Lung cancer, Bladder cancer, Kidney cancer, All study sites cancer (buccal cavity, pharynx, digestive system, stomach, colon, rectum gallbladder, pancreas, respiratory system, bladder, and kidney); Gastrointestinal: Digestive system cancer, Stomach cancer, Colon cancer, Rectum cancer, Gallbladder cancer, Pancreatic cancer; Lung/Respiratory: Respiratory system cancer, Laryngeal cancer, Lung cancer; Renal/Kidney: Bladder cancer, Kidney cancer
Asbestos Fiber Type(s):	Asbestos - Chrysotile (serpentine): 12001-29-5
Linked HERO ID(s):	3083628, 3083701
HERO ID:	3083628

Domain	Metric		Rating	Comments
	Metric 7:	Outcome Measurement or Characterization	High	Lung Cancer: Cancer cases were selected from the Cancer Surveillance System, a population-based tumor registry with data on incident cancer cases. The registry is part of the Surveillance, Epidemiology, and End Results (SEER) program at the National Cancer Institute. The authors report ICD-O (ICD-Oncology) codes for each cancer outcome.ICD-O codes 1620-1629 were used to define lung cancer.; Laryngeal Cancer: Cancer cases were selected from the Cancer Surveillance System, a population-based tumor registry with data on incident cancer cases. The registry is part of the Surveillance, Epidemiology, and End Results (SEER) program at the National Cancer Institute. The authors report ICD-O (ICD-Oncology) codes for each cancer outcome.ICD-O codes 1610-1619 were used to define laryngeal cancer.; Other Cancer(s): Cancer cases were selected from the Cancer Surveillance System, a population-based tumor registry with data on incident cancer cases. The registry is part of the Surveillance, Epidemiology, and End Results (SEER) program at the National Cancer Institute. The authors report ICD-O (ICD-Oncology) codes for each cancer outcome.ICD-O codes 1410-1499 were used to define buccal cavaity and pharyngeal cancer.ICD-O codes 1410-1459 and 1490-1499 were used to define mouth cancer.ICD-O codes 1460-1489 were used to define pharyngeal cancer.ICD-O codes 1500-1599 were used to define digestive system cancer.ICD-O codes 1510-1519 were used to define stomach cancer.ICD-O coders 1530-1539 were used to define colon cancer.ICD-O codes 1540-1549 were used to define rectum cancer.ICD-O codes 1560-1569 were used to define gallblader cancer.ICD-O codes 1570-1579 were used to define pancreatic cancer.ICD-O codes 1610-639 and 1650-1659 were used to define respiratory system cancer.ICD-O codes 1880-1889 were used to define bladder cancer.ICD-O codes 1890-1899 were used to define kidney cancer.
	Metric 8:	Reporting Bias	Medium	All the study's findings are reported in the abstract, results, or discussion. Effect estimates are presented with standard errors. However, analyses of relative risk only present the lower bound of 95% confidence intervals and are missing the upper bound. Statistical significance is indicated.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Medium	Considered covariates included, age, smoking, alcohol consumption, sex, education, religion, ethnicity, family history, and asbestos-related occupations. Results were also sex-stratified. The authors state that these covariates were chosen as "well-established risk factors."

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Study Citation:	Polissar, L., Severson, R. K., Boatman, E. S. (1984). A case-control study of asbestos in drinking water and cancer risk. American Journal of Epidemiology 119(3):456-471.
Health Outcome:	Lung Cancer; Laryngeal Cancer; buccal cavity and pharnyx, mouth, pharynx, digestive system, stomach, colon, rectum, pancreas, gallbladder, respiratory system, bladder, kidney, all study sites cancer
Target Organ(s):	Mouth: Buccal cavity and pharynx cancer, Mouth cancer, Pharyngeal cancer; Cancer/Carcinogenesis: Buccal cavity and pharynx cancer, Mouth cancer, Pharyngeal cancer, Digestive system cancer, Stomach cancer, Colon cancer, Rectum cancer, Gallbladder cancer, Pancreatic cancer, Respiratory system cancer, Laryngeal cancer, Lung cancer, Bladder cancer, Kidney cancer, All study sites cancer (buccal cavity, pharynx, digestive system, stomach, colon, rectum gallbladder, pancreas, respiratory system, bladder, and kidney); Gastrointestinal: Digestive system cancer, Stomach cancer, Colon cancer, Rectum cancer, Gallbladder cancer, Pancreatic cancer; Lung/Respiratory: Respiratory system cancer, Laryngeal cancer, Lung cancer; Renal/Kidney: Bladder cancer, Kidney cancer
Asbestos Fiber Type(s):	Asbestos - Chrysotile (serpentine): 12001-29-5
Linked HERO ID(s):	3083628, 3083701
HERO ID:	3083628

Domain	Metric		Rating	Comments
	Metric 10:	Covariate Characterization	Medium	Covariate information was collected via interview with cases and controls, except in circumstances in which that was not possible. In those cases, interviews were conducted with next-of-kin. This impacted 7% of controls, and 47% of cases. It is uncertain how reliable next-of-kin interviews may be, and the impact of this is differential between cases and controls, leading to potential confounding bias. Quality control procedures on interviews (by checking 85 questionnaires via callback) found that four of the five questions included in the validation check had >=93% agreement between the interviewer and supervisor. A comparison of coding and independent recoding of answers found on average one disagreement per 69 general questions and 7-10 questions on an average of 14 different past residences/workplaces. The authors also compared the results of some subject interviews with the annual Everett City Directory address and occupational listings and found a low level of disagreements between the interviews and the directory, and indicate that this is not differential across different types of respondents. This may not be sufficient to rule out recall bias for consumption related questions, such as alcohol consumption, as it is unclear if next-of-kin interviews would know that information.
	Metric 11:	Co-exposure Counfounding	Medium	No relevant co-exposures are discussed or evaluated in this non-occupational population.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	Medium	The authors use a logistic regression model to assess the relationship between asbestos exposure and case/control status. Both regression coefficients and relative odds are calculated. The authors present regression coefficients for asbestos exposure when estimated using workplace and residence data only. Relative odds are presented for three other exposure variables, one of which was the same as the first exposure variable except that it also multiplied the first variable by the self-reported total amount of water intake. Two more were created that were similar to the first two, except that all residence and work locations during a presumed 10-year latent period prior to diagnosis or interview were ignored. This study design is appropriate for a case-control study and allows for the comparison of different exposure assessment methods.

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Study Citation: Polissar, L., Severson, R. K., Boatman, E. S. (1984). A case-control study of asbestos in drinking water and cancer risk. American Journal of Epidemiology 119(3):456-471.

Health Outcome: Lung Cancer; Laryngeal Cancer; buccal cavity and pharnyx, mouth, pharynx, digestive system, stomach, colon, rectum, pancreas, gallbladder, respiratory system, bladder, kidney, all study sites cancer

Target Organ(s): Mouth: Buccal cavity and pharynx cancer, Mouth cancer, Pharyngeal cancer; Cancer/Carcinogenesis: Buccal cavity and pharynx cancer, Mouth cancer, Pharyngeal cancer, Digestive system cancer, Stomach cancer, Colon cancer, Rectum cancer, Gallbladder cancer, Pancreatic cancer, Respiratory system cancer, Laryngeal cancer, Lung cancer, Bladder cancer, Kidney cancer, All study sites cancer (buccal cavity, pharynx, digestive system, stomach, colon, rectum gallbladder, pancreas, respiratory system, bladder, and kidney); Gastrointestinal: Digestive system cancer, Stomach cancer, Colon cancer, Rectum cancer, Gallbladder cancer, Pancreatic cancer; Lung/Respiratory: Respiratory system cancer, Laryngeal cancer, Lung cancer; Renal/Kidney: Bladder cancer, Kidney cancer

Asbestos Fiber Type(s): Asbestos - Chrysotile (serpentine): 12001-29-5

Linked HERO ID(s): 3083628, 3083701

HERO ID: 3083628

Domain	Metric		Rating	Comments
	Metric 13:	Statistical Power	Medium	The final sample of 382 cases and 462 controls was sufficient to detect an effect, although for some cancers the incidence is as low as 7 for both sexes and as low as 1 for males. Statistical power was calculated for specified number of cases that could be detected at the 5% one-sided level with 80% confidence. The authors report that for single-sex analyses, "the minimum risk that could be detected… was under 2.0 for each for the following sites or site groups: all study sites combined, digestive system, respiratory system, colon and lung."
	Metric 14:	Reproducibility of Analyses	Medium	Methods are sufficiently detailed so that, given access to the analytic data, the results could be reproduced.
	Metric 15:	Statistical Analysis	Medium	There are no significant assumptions in logistic regression models that would be expected to be violated in the present analysis.

Additional Comments: These case-control studies are different publications of the same data. The authors examined Everett, Washington residents exposed to asbestos-contaminated water from the Sultan River. They used a case-control design to assess asbestos exposure relative to cancer outcomes. There are some uncertainties in this study, as the data on water consumption used in statistical analyses may be subject to recall bias differential by case status.

Overall Quality Determination — Medium

* No biomarkers were identified for this evaluation.

Study Citation:	Polissar, L., Severson, R. K., Boatman, E. S., Thomas, D. B. (1982). Cancer incidence in relation to asbestos in drinking water in the Puget Sound region. American Journal of Epidemiology 116(2):314-328.
Health Outcome:	Ovarian Cancer; Laryngeal Cancer; buccal cavity and pharynx cancer, esophagus cancer, stomach cancer, small intestine cancer, colon cancer, rectum cancer, liver cancer, gallbladder cancer, pancreatic cancer, retroperitoneum cancer, respiratory system cancer, bones and joints cancer, soft tissue cancer, melanoma, breast cancer, cervix cancer, corpus uteri cancer, uterine cancer, residual female genital cancer, prostate cancer, testis cancer, residual male genital cancer, bladder cancer, kidney cancer, eye and orbit cancer, brain (CNS) cancer, thyroid cancer, Hodgkin's disease, Non-Hodgkin's lymphoma, multiple myeloma, leukemia, cancer of other sites
Target Organ(s):	Mortality: buccal cavity and pharynx cancer, esophagus cancer, stomach cancer, small intestine cancer, colon cancer, rectum cancer, liver cancer, gallbladder cancer, pancreatic cancer, retroperitoneum cancer, larynx cancer, respiratory system cancer, bones and joints cancer, soft tissue cancer, melanoma, breast cancer, cervix cancer, corpus uteri cancer, uterine cancer, ovarian cancer, residual female genital cancer, prostate cancer, testis cancer, residual male genital cancer, bladder cancer, kidney cancer, eye and orbit cancer, brain (CNS) cancer, thyroid cancer, Hodgkin's disease, Non-Hodgkin's lymphoma, multiple myeloma, leukemia, cancer of other sites; Other sites: cancer of other sites; Immune/Hematological: Hodgkin's disease, Non-Hodgkin's lymphoma, multiple myeloma, leukemia; Thyroid: thyroid cancer; Neurological/Behavioral: brain (CNS) cancer; Reproductive/Developmental: breast cancer, cervix cancer, corpus uteri cancer, uterine cancer, ovarian cancer, residual female genital cancer, prostate cancer, testis cancer, residual male genital cancer; Ocular/Sensory: eye and orbit cancer; Skin/Connective Tissue: melanoma; Musculoskeletal: bones and joints cancer, soft tissue cancer; Lung/Respiratory: larynx cancer, respiratory system cancer; Gastrointestinal: buccal cavity and pharynx cancer, esophagus cancer, stomach cancer, small intestine cancer, colon cancer, rectum cancer, liver cancer, gallbladder cancer, pancreatic cancer, retroperitoneum cancer; Cancer/Carcinogenesis: buccal cavity and pharynx cancer, esophagus cancer, stomach cancer, small intestine cancer, colon cancer, rectum cancer, liver cancer, gallbladder cancer, pancreatic cancer, retroperitoneum cancer, larynx cancer, respiratory system cancer, bones and joints cancer, soft tissue cancer, melanoma, breast cancer, cervix cancer, corpus uteri cancer, uterine cancer, ovarian cancer, residual female genital cancer, prostate cancer, testis cancer, residual male genital cancer, bladder cancer, kidney cancer, eye and orbit cancer, brain (CNS) cancer, thyroid cancer, Hodgkin's disease, Non-Hodgkin's lymphoma, multiple myeloma, leukemia, cancer of other sites; Renal/Kidney: bladder cancer, kidney cancer
Asbestos Fiber Type(s):	Asbestos - Chrysotile (serpentine): 12001-29-5
Linked HERO ID(s):	No linked references.
HERO ID:	353

Domain	Metric		Rating	Comments
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Uninformative	PRIMARY EVALUATION STOPPED AFTER REVIEW OF METRIC 4 AND UNINFORMATIVE RATING DETERMINATIONThere is substantial risk of exposure misclassification, as the study solely uses asbestos concentrations in drinking water with no consideration of individual factors or measure of exposure on the individual level. As such, exposure is anticipated to be subjected to substantial misclassification that would significantly bias the results.
	Metric 5:	Exposure Levels	Low	Exposure levels are reported as high vs. low exposure based on the drinking water source for the community, meriting a low rating for this domain. Different permutations of high and low exposure are used in analyses including Sultan River (high exposure) vs. all other areas (low exposure), Sultan River older districts (high exposure) vs. newer districts (low exposure), Sultan River long term use (high exposure) vs. short term use (low exposure).

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Study Citation:	Polissar, L., Severson, R. K., Boatman, E. S., Thomas, D. B. (1982). Cancer incidence in relation to asbestos in drinking water in the Puget Sound region. American Journal of Epidemiology 116(2):314-328.
Health Outcome:	Ovarian Cancer; Laryngeal Cancer; buccal cavity and pharynx cancer, esophagus cancer, stomach cancer, small intestine cancer, colon cancer, rectum cancer, liver cancer, gallbladder cancer, pancreatic cancer, retroperitoneum cancer, respiratory system cancer, bones and joints cancer, soft tissue cancer, melanoma, breast cancer, cervix cancer, corpus uteri cancer, uterine cancer, residual female genital cancer, prostate cancer, testis cancer, residual male genital cancer, bladder cancer, kidney cancer, eye and orbit cancer, brain (CNS) cancer, thyroid cancer, Hodgkin's disease, Non-Hodgkin's lymphoma, multiple myeloma, leukemia, cancer of other sites
Target Organ(s):	Mortality: buccal cavity and pharynx cancer, esophagus cancer, stomach cancer, small intestine cancer, colon cancer, rectum cancer, liver cancer, gallbladder cancer, pancreatic cancer, retroperitoneum cancer, larynx cancer, respiratory system cancer, bones and joints cancer, soft tissue cancer, melanoma, breast cancer, cervix cancer, corpus uteri cancer, uterine cancer, ovarian cancer, residual female genital cancer, prostate cancer, testis cancer, residual male genital cancer, bladder cancer, kidney cancer, eye and orbit cancer, brain (CNS) cancer, thyroid cancer, Hodgkin's disease, Non-Hodgkin's lymphoma, multiple myeloma, leukemia, cancer of other sites; Other sites: cancer of other sites; Immune/Hematological: Hodgkin's disease, Non-Hodgkin's lymphoma, multiple myeloma, leukemia; Thyroid: thyroid cancer; Neurological/Behavioral: brain (CNS) cancer; Reproductive/Developmental: breast cancer, cervix cancer, corpus uteri cancer, uterine cancer, ovarian cancer, residual female genital cancer, prostate cancer, testis cancer, residual male genital cancer; Ocular/Sensory: eye and orbit cancer; Skin/Connective Tissue: melanoma; Musculoskeletal: bones and joints cancer, soft tissue cancer; Lung/Respiratory: larynx cancer, respiratory system cancer; Gastrointestinal: buccal cavity and pharynx cancer, esophagus cancer, stomach cancer, small intestine cancer, colon cancer, rectum cancer, liver cancer, gallbladder cancer, pancreatic cancer, retroperitoneum cancer; Cancer/Carcinogenesis: buccal cavity and pharynx cancer, esophagus cancer, stomach cancer, small intestine cancer, colon cancer, rectum cancer, liver cancer, gallbladder cancer, pancreatic cancer, retroperitoneum cancer, larynx cancer, respiratory system cancer, bones and joints cancer, soft tissue cancer, melanoma, breast cancer, cervix cancer, corpus uteri cancer, uterine cancer, ovarian cancer, residual female genital cancer, prostate cancer, testis cancer, residual male genital cancer, bladder cancer, kidney cancer, eye and orbit cancer, brain (CNS) cancer, thyroid cancer, Hodgkin's disease, Non-Hodgkin's lymphoma, multiple myeloma, leukemia, cancer of other sites; Renal/Kidney: bladder cancer, kidney cancer
Asbestos Fiber Type(s):	Asbestos - Chrysotile (serpentine): 12001-29-5
Linked HERO ID(s):	No linked references.
HERO ID:	353

Domain	Metric	Rating	Comments
Additional Comments:	QC was not completed for metrics other than Metrics 4 and 5 because the study does not have sufficient exposure information to be useful for dose-response analysis. In addition (from metric 4): There is substantial risk of exposure misclassification, as the study solely uses asbestos concentrations in drinking water with no consideration of individual factors or measure of exposure on the individual level. As such, exposure is anticipated to be subjected to substantial misclassification that would significantly bias the results.		

* No biomarkers were identified for this evaluation.

** As described in Appendix B.2 of the *White Paper: Quantitative Approach to the Human Health Assessment for the Risk Evaluation for Asbestos Part 2: Supplemental Evaluation Including Legacy Uses and Associated Disposals of Asbestos*, to be considered as being informative for dose-response analysis, metrics 4 and 5 would need metric ratings of Medium or High. This reference did not satisfy this requirement; therefore data quality evaluation is presented for only for metrics 4 and 5.

Study Citation:	Raffn, E., Villadsen, E., Engholm, G., Lynge, E. (1996). Lung cancer in asbestos cement workers in Denmark. Occupational and Environmental Medicine 53(6):399-402.
Health Outcome:	Lung Cancer
Target Organ(s):	Cancer/Carcinogenesis: Lung cancer, including adenocarcinomas, squamous cell carcinomas, and anaplastic carcinomas
Asbestos Fiber Type(s):	Asbestos - Chrysotile (serpentine): 12001-29-5; Asbestos - Amosite (grunerite): 12172-73-5; Asbestos - Crocidolite (riebeckite): 12001-28-4
Linked HERO ID(s):	No linked references.
HERO ID:	3081452

Domain		Metric	Rating	Comments
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Low	Asbestos measurements were taken in 1948 and 1957, and were reported as 50-800 fibers/ml and 10-100 fibers/ml, respectively. 41% of measurements in 1973 were above 2 fibers/ml. However, not information is provided on the methods or type of equipment used to generate this data.
	Metric 5:	Exposure Levels	Low	Very limited information is provided pertaining to exposure levels for the individuals working in the factory. They highlighted that measurements were taken during feeding and unloading. In the discussion section, the authors mention that job titles were only reported for individuals employed between 1928 and 1941, and not all of the roles within the factory result in exposure to asbestos.

Additional Comments: As QC reviewer, I rate this study medium. This study investigated the relative and absolute risks of main types of lung cancer among asbestos cement workers in Denmark.It is important to note that while there were three types of asbestos mentioned by the authors, chrysolite comprised 90% of asbestos used in the factory examined. Only three cases of lung cancer were found for the women included, so only results for men were reported.

* No biomarkers were identified for this evaluation.

** As described in Appendix B.2 of the *White Paper: Quantitative Approach to the Human Health Assessment for the Risk Evaluation for Asbestos Part 2: Supplemental Evaluation Including Legacy Uses and Associated Disposals of Asbestos*, to be considered as being informative for dose-response analysis, metrics 4 and 5 would need metric ratings of Medium or High. This reference did not satisfy this requirement; therefore data quality evaluation is presented for only for metrics 4 and 5.

Study Citation:	Raffn, E., Villadsen, E., Lynge, E. (1996). Colorectal cancer in asbestos cement workers in Denmark. American Journal of Industrial Medicine 30(3):267-272.
Health Outcome:	Colorectal cancers
Target Organ(s):	Gastrointestinal: Colorectal cancer (all), Colorectal cancer (rectum), Colorectal cancer (NOS), Colon cancer (left side), Colon cancer (right side), Colon cancer (all); Cancer/Carcinogenesis: Colon cancer (all), Colorectal cancer (NOS), Colon cancer (left side), Colon cancer (right side), Colorectal cancer (all), Colorectal cancer (rectum)
Asbestos Fiber Type(s):	Asbestos - Chrysotile (serpentine): 12001-29-5; Asbestos - Amosite (grunerite): 12172-73-5; Asbestos - Crocidolite (riebeckite): 12001-28-4
Linked HERO ID(s):	No linked references.
HERO ID:	3583594

Domain	Metric		Rating	Comments
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Low	This metric is rated low because the study or any cited methods source does not explicitly mention the use of PCM or TEM. Atmospheric asbestos was measured in this asbestos factory. These measurements were taken during the feeding of the mill and the forming vessel, along with the unloading of containers. Measurements were taken in 1948 and 1957, and were recorded in particles per cubic centimeter. The Danish National Institute of Occupational Health used these results to estimate the exposure levels in 1948 and 1957.
	Metric 5:	Exposure Levels	Medium	There was a range of exposure levels included in this study, and they were sufficient to develop an exposure-response estimate. The range of exposures reported indicate that there was more than just exposed/unexposed in this cohort. For 1948, asbestos concentrations ranged from 50 and 800 f/ml. For 1957, concentrations were estimated between 10 and 100 f/ml. Some measurements were taken in 1973, and 41% of the measurements were >2.0 f/ml.

Additional Comments: QC was not completed for metrics other than Metrics 4 and 5 because the study does not have sufficient exposure information to be useful for dose-response analysis.

* No biomarkers were identified for this evaluation.

** As described in Appendix B.2 of the *White Paper: Quantitative Approach to the Human Health Assessment for the Risk Evaluation for Asbestos Part 2: Supplemental Evaluation Including Legacy Uses and Associated Disposals of Asbestos*, to be considered as being informative for dose-response analysis, metrics 4 and 5 would need metric ratings of Medium or High. This reference did not satisfy this requirement; therefore data quality evaluation is presented for only for metrics 4 and 5.

Study Citation:	Richardson, D. B. (2009). Lung cancer in chrysotile asbestos workers: Analyses based on the two-stage clonal expansion model. Cancer Causes and Control 20(6):917-923.
Health Outcome:	Lung Cancer
Target Organ(s):	Mortality: lung cancer mortality; Lung/Respiratory: lung cancer mortality
Asbestos Fiber Type(s):	Asbestos - Chrysotile (serpentine): 12001-29-5
Linked HERO ID(s):	3081832, 66, 2238696, 6860087
HERO ID:	2238696

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Medium	This occupational cohort study examines lung cancer mortality and its association with asbestos exposure among a sub-cohort of white men (n= 1,256) employed at a South Carolina asbestos textile plant. Men who had been employed for at least one month between 1940 and 1965. Follow-up to assess vital status continued through December 31, 2001. Authors note the cohort was restricted to male workers for simplicity of analyses, but there is no comparison of the full eligible and participating study population.
	Metric 2:	Attrition	High	There is no evidence of subject loss for reasons other than death (the outcome of interest), of subject exclusions from the analyses, or of substantial amounts of missing data among the study population.
	Metric 3:	Comparison Group	High	All members of the study cohort were white males from a South Carolina asbestos textile plant who worked for at least one month in production during the 1940-1965 time period. Sufficient information is provided to assert that individuals across exposure ranges were similar.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Medium	Study authors reference Dement et al., 1983, 66 for discussion of the exposure measurement approach including midget impinger and membrane filter sampling with data obtained ”from many sources including the company insurance carrier, the State Board of Health, the U.S. Public Health Service, and the Company sampling program.” The reference also discusses conversion factors, but it appears that these were used to convert midget impinger and membrane filter results to the comparable units. According to a methods paper on United States Public Health Service/NIOSH membrane filter sampling methods (Leidl et al., 1979, 237), PCM was used to analyze membrane filters and quantify fiber levels. While the original text does not explicitly communicate the use of PCM, the contextual information provided by these other citations and methods papers provides sufficient information to merit a medium rating.
	Metric 5:	Exposure Levels	Medium	The range and distribution of fiber levels based on cumulative exposure appears sufficient to assess the association between the exposure and outcome. Authors present continuous analyses with exposure increases per 10 fiber-years/mL and results from a two-stage clonal expansion model by quartile of exposure (Q1: 0-1.7 fiber-years/mL; Q2: 1.7-5.5 fiber-years/mL; Q3: 5.5-25.1 fiber-years/mL; Q4: 25.1-699.8 fiber-years/mL).

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Study Citation: Richardson, D. B. (2009). Lung cancer in chrysotile asbestos workers: Analyses based on the two-stage clonal expansion model. Cancer Causes and Control 20(6):917-923.
Health Outcome: Lung Cancer
Target Organ(s): Mortality: lung cancer mortality; Lung/Respiratory: lung cancer mortality
Asbestos Fiber Type(s): Asbestos - Chrysotile (serpentine): 12001-29-5
Linked HERO ID(s): 3081832, 66, 2238696, 6860087
HERO ID: 2238696

Domain	Metric		Rating	Comments
	Metric 6:	Temporality	High	The retrospective cohort study design enables establishment of temporality between exposure and outcome. Exposure can be demonstrated to have occurred prior to outcome ascertainment through the assessment of historical exposure records. Additionally, the study includes a follow up period ranging from 36-61 years, an appropriate length to assess lung cancer outcomes.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	High	Lung Cancer: Lung cancer data was collected from vital status records through December 31, 2001. Study authors identified cases using ICD codes at the time of death (from revisions 5, 6, 7, 8, 9, and 10) . The complete list of codes used for the study included ICD-5 codes 047B-047F, ICD-6 codes 162 and 163, ICD-7 code 162.0, 162.1, 162.8, 163, ICD-8/-9 code 162, ICD-10 codes C33, C34.
	Metric 8:	Reporting Bias	Medium	Results from two stage clonal expansion models and Cox proportional hazards regression models are reported as anticipated, including the effect estimates and confidence intervals for all anticipated analyses. However, the number of participants in different analytical groups is not reported, and many lower confidence limits are reported as not determined.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Low	Variations in race and sex were accounted for via the study design, as the population was restricted to white male workers from the plant. Additionally, authors report the development of age-specific two-stage clonal expansion models and report results from Cox proportional hazard models by different age groupings. However, there is no indication that smoking status was measured and considered in analyses, which serves as a key confounder for assessment of lung cancer. While authors note that confounding "by lifestyle factors...will be small in occupational analyses", the lack of consideration of this confounder merits a low rating.
	Metric 10:	Covariate Characterization	High	Due to the occupational nature of this study, it can be reasonably inferred that information on covariates (including age, sex, and race) was collected from plant personnel records.
	Metric 11:	Co-exposure Counfounding	Medium	There is no direct evidence of a suspected co-exposure that was not accounted for in the analyses. Authors report the cohort had "relatively pure exposures to chrysotile asbestos" in the textile plant. While this may indicate some minor potential for co-exposure, there is no direct evidence that would merit a low rating.
Domain 5: Analysis				

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Study Citation:	Richardson, D. B. (2009). Lung cancer in chrysotile asbestos workers: Analyses based on the two-stage clonal expansion model. Cancer Causes and Control 20(6):917-923.
Health Outcome:	Lung Cancer
Target Organ(s):	Mortality: lung cancer mortality; Lung/Respiratory: lung cancer mortality
Asbestos Fiber Type(s):	Asbestos - Chrysotile (serpentine): 12001-29-5
Linked HERO ID(s):	3081832, 66, 2238696, 6860087
HERO ID:	2238696

Domain	Metric		Rating	Comments
	Metric 12:	Study Design and Methods	Medium	The retrospective cohort study design was appropriate to assess the exposure-outcome relationship in the occupational setting, as was the use of the two-stage clonal expansion model and the Cox proportional hazard model.
	Metric 13:	Statistical Power	Medium	The sample size (n=1, 256) is sufficiently large to examine the outcome of interest, which is further demonstrated by the number of observed cases (n=116 lung cancer deaths).
	Metric 14:	Reproducibility of Analyses	Medium	Authors provide extensive information on development of statistical models used for analyses, including background information on the two-stage clonal expansion model approach.
	Metric 15:	Statistical Analysis	Medium	Authors appropriately employed the two-stage clonal expansion model to assess cancer outcomes and the Cox proportional hazards model with discussion of the proportional hazards assumption. The use of lags (assessed at 5, 10, and 15 years) in assessing the exposure-outcome relationship is transparently reported.

Additional Comments: This retrospective occupational cohort study examines lung cancer mortality and its association with cumulative asbestos exposure with an appropriate follow-up period. The cohort was of sufficient size to assess the relationship, and the methods for exposure measurement, outcome ascertainment, and statistical analyses were robust. A primary weakness in the study is the lack of consideration of smoking status as a potential confounder. While a clear deficiency, authors note that the influence of smoking may not substantially impact results among occupational cohorts.The measurement exposure (M4) and/or exposure levels (M5) metrics are rated as medium upon review by both set of reviewers. Note for M4: While the original text does not explicitly communicate the use of PCM, the context information provided by other cited articles. Also, the overall quality determination (OQD) is rated medium. Extraction has been completed and quality control reviewed.

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation:	Rodriguez-Roisin, R., Picado, C., Roca, J., Arrigo, S., Agusti-Vidal, A. (1986). Early lung function changes after short heavy exposure to chrysotile asbestos in non-smoking women. Bulletin Européen de Physiopathologie Respiratoire 22(3):225-229.
Health Outcome:	Pulmonary Function/Spirometry Results
Target Organ(s):	Lung/Respiratory: Forced vital capacity (FVC), Ratio of FEV1/FVC, Maximal expiratory flow at 75% of the forced vital capacity (MEF25%), Maximal expiratory flow at 50% of the forced vital capacity (MEF50%), Peak expiratory flow (PEF), Forced expiratory volume in 1 second (FEV1)
Asbestos Fiber Type(s):	Asbestos - Chrysotile (serpentine): 12001-29-5
Linked HERO ID(s):	No linked references.
HERO ID:	3083290

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Medium	35 non-smoker female workers at a textile factory in Barcelona were subjects in this occupational case-control study. The authors provide a reasonable amount of detail about inclusion/exclusion criteria but details about recruitment circumstances (e.g., timeline, method of recruitment) were not discussed.
	Metric 2:	Attrition	High	There was no subject withdrawal, and a complete dataset was used for the analyses of asbestos exposure with health outcomes.
	Metric 3:	Comparison Group	Medium	Controls were 35 non-smoking healthy females that were age- and height-matched and selected from a sample of 870 non-smoking individuals living in the same geographical area. They were randomly selected after stratification for sex, age, and height and ”had no known exposure to fibrogenic materials, no history of acute or chronic cardiorespiratory diseases, normal chest radiographs and absence of smoking habits.” Thus, controls were not recruited from the same population. The authors do not provide more information on how the sample of controls was recruited or whether they were employed, but concern for healthy worker effect is mitigated by the inclusion criteria.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	High	Quantitative measures of asbestos were ”sampled personally and randomly over a 13-week sampling period” and an exposure index that was dependent on time exposed and fiber concentration was calculated for each worker (according to recommendations of the British Occupational Hygiene Society). Exposure was measured using PCM.
	Metric 5:	Exposure Levels	Medium	The range and distribution of exposure is sufficient to develop an exposure-response estimate, and the authors report 3 levels of exposure.
	Metric 6:	Temporality	Low	Temporality is established, but the latency period is short (1-7 yr according to Table 1). It should be noted that the purpose of this study was to assess effects of high asbestos exposure within a short period of time, though, and workers who were employed at the factory for 10 years or more were excluded from the study.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	High	Pulmonary Function/Spirometry Results: Pulmonary function tests included standardized spirometric measures such as FEV1, FVC, PEF, and MEF.

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Study Citation:	Rodriguez-Roisin, R., Picado, C., Roca, J., Arrigo, S., Agusti-Vidal, A. (1986). Early lung function changes after short heavy exposure to chrysotile asbestos in non-smoking women. Bulletin Européen de Physiopathologie Respiratoire 22(3):225-229.
Health Outcome:	Pulmonary Function/Spirometry Results
Target Organ(s):	Lung/Respiratory: Forced vital capacity (FVC), Ratio of FEV1/FVC, Maximal expiratory flow at 75% of the forced vital capacity (MEF25%), Maximal expiratory flow at 50% of the forced vital capacity (MEF50%), Peak expiratory flow (PEF), Forced expiratory volume in 1 second (FEV1)
Asbestos Fiber Type(s):	Asbestos - Chrysotile (serpentine): 12001-29-5
Linked HERO ID(s):	No linked references.
HERO ID:	3083290

Domain	Metric		Rating	Comments
	Metric 8:	Reporting Bias	High	Results of the stepwise multiple regression, which analyzed associations of pulmonary function test results with a continuous measure of exposure, are shown. Effect estimates and standard errors are presented in the Results. Samples sizes are presumed (n=35 for both exposed and controls), as there is no mention of missing data.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	High	Appropriate adjustments were made in the stepwise multiple regression analysis for each lung function test. Age, height, weight, years of exposure, and cumulative exposure index were treated as covariates. For each maximal flow rate analysis, FVC was also included as a covariate. Smoking status was not included, because only non-smokers were included in the study.
	Metric 10:	Covariate Characterization	Medium	For this occupational study, it is presumed that personnel records were used to obtain covariate data, since the authors did not specify otherwise.
	Metric 11:	Co-exposure Counfounding	Low	The authors did not adjust for or measure potential co-exposures. Due to the lack of safety regulations and protective equipment available to asbestos workers in the study, it is quite possible that additional co-exposures in the factory were present. This could bias the results away from the null.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	Medium	This cross-sectional study uses an appropriate statistical method to address the research question; specifically, the authors used stepwise multiple regression analysis for each lung function test to analyze the correlation between lung function and duration and cumulative index of asbestos exposure.
	Metric 13:	Statistical Power	Medium	The number of cases and controls are adequate to detect an effect in the exposed population, and the authors report significantly lower FVC and FEV1 were found in the exposed compared to the matched control population.
	Metric 14:	Reproducibility of Analyses	Medium	The description of the analyses is clear and sufficient to understand how to conceptually reproduce the analysis with access to the analytic data.
	Metric 15:	Statistical Analysis	Low	Though it is explained why some covariates were included in the regression models, the authors do not explicitly state that the regression model assumptions were met.

Additional Comments: This occupational case-control study examined the association of severe asbestos exposure for a shorter duration with well-validated lung function tests. It reported that shortly after heavy exposure, non-smokers showed significant reductions in lung function parameters compared to the matched control population.

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Study Citation:	Rodriguez-Roisin, R., Picado, C., Roca, J., Arrigo, S., Agusti-Vidal, A. (1986). Early lung function changes after short heavy exposure to chrysotile asbestos in non-smoking women. Bulletin Européen de Physiopathologie Respiratoire 22(3):225-229.
Health Outcome:	Pulmonary Function/Spirometry Results
Target Organ(s):	Lung/Respiratory: Forced vital capacity (FVC), Ratio of FEV1/FVC, Maximal expiratory flow at 75% of the forced vital capacity (MEF25%), Maximal expiratory flow at 50% of the forced vital capacity (MEF50%), Peak expiratory flow (PEF), Forced expiratory volume in 1 second (FEV1)
Asbestos Fiber Type(s):	Asbestos - Chrysotile (serpentine): 12001-29-5
Linked HERO ID(s):	No linked references.
HERO ID:	3083290

Domain	Metric	Rating	Comments
Overall Quality Determination		**Medium**	

* No biomarkers were identified for this evaluation.

Study Citation:	Roggli, V. L., Pratt, P. C., Brody, A. R. (1986). Asbestos content of lung tissue in asbestos associated diseases: a study of 110 cases. British Journal of Industrial Medicine 43(1):18-28.
Health Outcome:	Lung Cancer; Asbestosis; Pleural Plaques
Target Organ(s):	Lung/Respiratory: Asbestosis, Parietal pleural plaques, lung cancer; Cancer/Carcinogenesis: lung cancer
Asbestos Fiber Type(s):	Asbestos - Amosite (grunerite): 12172-73-5; Asbestos - Crocidolite (riebeckite): 12001-28-4; Asbestos - Anthophyllite: 17068-78-9; Asbestos - Tremolite: 14567-73-8; Asbestos - Actinolite: 12172-67-7; Asbestos - Chrysotile (serpentine): 12001-29-5
Linked HERO ID(s):	No linked references.
HERO ID:	3083350

Domain	Metric		Rating	Comments
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Low	Asbestos bodies in lung tissue samples were quantified by LM and SEM, post-mortem.
	Metric 5:	Exposure Levels	Medium	The range and distribution of exposure is sufficient to develop an exposure-response estimate, which was done using a continuous measure of exposure.Median and range asbestos bodies (AB) exposures measured via LM were as follows:. Asbestosis: 106,000 (range: 2,400 – 684,000) AB/g. Mesothelioma: 550 (range: 0.2 – 13,3000) AB/g. Lung cancer: 102 (0.8 – 46,000) AB/g. Idiopathic pulmonary fibrosis: 9 (0.8 – 148) AB/g. Normal lungs: 3 (0.2 – 22) AB/g.

Additional Comments: The overall rating for this study is low. This study investigated the asbestos content of lung tissue in groups of cases of asbestosis, malignant mesothelioma, carcinoma of the lung, and parietal pleural plaques. Overall, this study was appropriately conducted, but not well powered (especially in terms of the number of controls used). Asbestos bodies, which are indicative of asbestos exposure, were used as exposure to examine associations with lung disease. When it came to findings, the authors reported statistically significant relationships between asbestos bodies asbestos fibers. While, this study had some strengths, there were several limitations. For example, exposure misclassification during exposure assessment may have occurred. Additionally, the number of controls used may be small to detect robust effect estimates.Overall, information on the measurement of exposure metric (M4) to assess exposure was limited or rated low (authors used Asbestos bodies in lung tissue samples were quantified by LM and SEM, post-mortem). The exposure levels metric (M5) information reported was adequate to determine exposure-response relationships.

** As described in Appendix B.2 of the *White Paper: Quantitative Approach to the Human Health Assessment for the Risk Evaluation for Asbestos Part 2: Supplemental Evaluation Including Legacy Uses and Associated Disposals of Asbestos*, to be considered as being informative for dose-response analysis, metrics 4 and 5 would need metric ratings of Medium or High. This reference did not satisfy this requirement; therefore data quality evaluation is presented for only for metrics 4 and 5.

Study Citation:	Rohs, A., Lockey, J., Dunning, K., Shukla, R., Fan, H., Hilbert, T., Borton, E., Wiot, J., Meyer, C., Shipley, R., Lemasters, G., Kapil, V. (2008). Low-level fiber-induced radiographic changes caused by Libby vermiculite: a 25-year follow-up study. American Journal of Respiratory and Critical Care Medicine 177(6):630-637.
Health Outcome:	Pleural Plaques
Target Organ(s):	Lung/Respiratory: Pleural changes (localized and/or diffuse pleural thickening), Parenchymal changes
Asbestos Fiber Type(s):	Asbestos - Tremolite: 14567-73-8; Asbestos - Winchite: 12425-92-2; Asbestos- Richterite: 17068-76-7; Asbestos- Libby amphibole: 1318-09-8
Linked HERO ID(s):	709486, 3014803
HERO ID:	709486

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	High	Rohs et al., 2008 (709486) and Lockey et al., 2012 3014803 analyze 25- and 3-year follow-up data, respectively, on a 1980 cohort of 512 workers at a facility that processed tremolite-contaminated Libby vermiculite (Lockey et al. 1984. 029685; 97% participation rate). At baseline, all employees exposed to vermiculite and a subset of unexposed workers from the same plant were enrolled. The 25-year follow-up analyzed chest radiographs for 280 workers taken in 2004-2005 (65% of 431 living; 55% of baseline). The 30-year follow-up analyzed chest CT scans for 191 workers (44% of 431 living) in their primary analyses (175 taken in 2010-11 for this study, 16 pre-existing). In addition, the longer follow-up used pre-existing x-rays taken from 2003-2011 to increase their chest imaging sample size to 306 (71% of those still living). Risk of HWE bias is limited given the lengthy follow-up and varied post-baseline duration of employment.
	Metric 2:	Attrition	High	In both Rohs et al., 2008 709486 and Lockey et al., 2012 3014803, potential attrition bias was evaluated in sensitivity analyses that used baseline data to incorporate all living subjects, assuming normal chest imaging in those who did not participate in follow-ups; results did not change meaningfully. Survivorship bias was not assessed, but additionally adding these 82 individuals to exposure categories would not eliminate associations of the magnitude reported. Given the higher mean exposure in deceased workers, the study may underestimate the prevalence of lung changes and the magnitude of associations.
	Metric 3:	Comparison Group	High	Rohs et al., 2008 RefID 709486 and Lockey et al., 2012 RefID 3014803 compared health outcomes among workers in the cohort with higher vs. lower past exposure past exposure. At baseline, the comparison group was selected to include workers whose exposure to other substances was similar to the vermiculite-exposed group, with the exception of limited or no vermiculite exposure.
Domain 2: Exposure Characterization				

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Study Citation:	Rohs, A., Lockey, J., Dunning, K., Shukla, R., Fan, H., Hilbert, T., Borton, E., Wiot, J., Meyer, C., Shipley, R., Lemasters, G., Kapil, V. (2008). Low-level fiber-induced radiographic changes caused by Libby vermiculite: a 25-year follow-up study. American Journal of Respiratory and Critical Care Medicine 177(6):630-637.
Health Outcome:	Pleural Plaques
Target Organ(s):	Lung/Respiratory: Pleural changes (localized and/or diffuse pleural thickening), Parenchymal changes
Asbestos Fiber Type(s):	Asbestos - Tremolite: 14567-73-8; Asbestos - Winchite: 12425-92-2; Asbestos- Richterite: 17068-76-7; Asbestos- Libby amphibole: 1318-09-8
Linked HERO ID(s):	709486, 3014803
HERO ID:	709486

Domain	Metric		Rating	Comments
	Metric 4:	Measurement of Exposure	Medium	MEDIUM. Rohs et al., 2008 RefID 709486 estimated retrospective cumulative fiber exposure (CFE) using detailed job histories and available fiber counts that used PCM and membrane filter samples (counting particles > 5μm in length, <9 μm in diameter, and aspect ratio of 3:1). Concerns: (i) Exposure monitoring was initiated in 1972; extrapolations to earlier years may be underestimates. The area level measures taken prior to 1976, when personal breathing zone sampling began, may also be less accurate than later estimates. (ii) Information on extensive overtime worked was not available, perhaps resulting in underestimates and/or misclassified exposure. (iii) Asbestos exposure was estimated for 1963 to 1980; exposure before and after was assumed to be zero, since Libby ore was not in use. However, ore used after 1980 was subsequently found to contain about 1% asbestiform minerals. HIGH. In Lockey et al., 2012 RefID 3014803, CFE estimates were refined using: (i) more detailed job information including improved information on overtime; (ii) three times the original number of fiber measures (n=899); and (iii) specific data on vermiculite sources both before and after Libby ore was used (Borton et al 2012, PMID 22544162). Exposure after 1980 was estimated using updated work histories collected in 2004 and/or 2010-11.
	Metric 5:	Exposure Levels	Medium	CFE quartiles were used by Rohs et al., 2008 RefID 709486, defined as: 0.005-0.24, 0.25-0.74, 0.75-1.91 and 1.92-19.03 fiber/cc-years. Mean CFE was estimated at 2.48 fiber/cc-years among study participants. In Lockey et al., 2012 RefID 3014803, 5 exposure categories were used (<0.15, 0.15-<0.45, 0.45-<1.35, 1.35-<10, and >=10 fiber-years/cc). Mean CFE using the refined methods was 6.98 fibers/cc-years through 1980, increasing to 7.5 fiber/cc-years through 2001 when vermiculite use was terminated.
	Metric 6:	Temporality	High	In Rohs et al., 2008 RefID 709486 exposure was assessed retrospectively. The mean time since initial exposure was 36.8 and 32.1 years, respectively, for participants with and without any pleural changes. Lockey et al., 2012 RefID 3014803 had 5 additional years of follow-up.
Domain 3: Outcome Assessment				

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Study Citation:	Rohs, A., Lockey, J., Dunning, K., Shukla, R., Fan, H., Hilbert, T., Borton, E., Wiot, J., Meyer, C., Shipley, R., Lemasters, G., Kapil, V. (2008). Low-level fiber-induced radiographic changes caused by Libby vermiculite: a 25-year follow-up study. American Journal of Respiratory and Critical Care Medicine 177(6):630-637.
Health Outcome:	Pleural Plaques
Target Organ(s):	Lung/Respiratory: Pleural changes (localized and/or diffuse pleural thickening), Parenchymal changes
Asbestos Fiber Type(s):	Asbestos - Tremolite: 14567-73-8; Asbestos - Winchite: 12425-92-2; Asbestos- Richterite: 17068-76-7; Asbestos- Libby amphibole: 1318-09-8
Linked HERO ID(s):	709486, 3014803
HERO ID:	709486

Domain	Metric		Rating	Comments
	Metric 7:	Outcome Measurement or Characterization	High	Pleural Plaques: Rohs et al., 2008 RefID 709486: Chest radiographs taken for the study in 2004-2005 were evaluated by 2 board certified radiologists using 2000 ILO criteria; a 3rd reader resolved disagreements. Radiographs had no identifiers;10% normal radiographs randomly interspersed were read correctly. Outcomes were defined as: localized pleural plaques, diffuse pleural thickening, and interstitial changes. The prevalence of pleural changes was 28.7%. Lockey et al., 2012 RefID 3014803 also used chest imaging without identifiers evaluated by 2 or 3 independent readers. Primary measures used high resolution CT (n=175) or CT (n=16 pre-existing) scans. Criteria used to evaluate HRCT/CT scans were described in detail. The prevalence of lung changes increased to >50%. HRCT/CT is generally more sensitive than X-rays; however, the authors noted that minor underestimation could occur. Outcomes were defined as: localized and/or diffuse pleural changes (52.9%) and parenchymal changes (13.7%). Pre-existing radiographs that had been taken from 2003-2011 among participants who did not complete HRCTs were also evaluated in a sensitivity analysis, increasing the imaging sample to 306.
	Metric 8:	Reporting Bias	High	Both studies presented results for all aims and showed details such as numbers of cases and non-cases by exposure category. Multivariable adjusted ORs were provided when there was potential or apparent confounding. In Rohs et al RefID 709486 a few minor aspects of multivariable models were not clear (treatment of missing BMI data in n=38 subjects with telephone interviews, inclusion or omission of non-participant baseline data).
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Medium	Most associations were unadjusted, but confounding was assessed. Rohs et al., RefID 709486 showed adjustments for age and hire date which attenuated ORs. Rohs et al., RefID 709486 also showed that smoking was not associated with radiographic lung change outcomes, so adjustment was not needed. In Lockey et al., RefID 3014803 models for parenchymal changes were adjusted for age and smoking a priori, and the authors stated that there was no confounding by age, BMI or smoking in pleural change models via results of backward elimination testing.
	Metric 10:	Covariate Characterization	Medium	Questionnaires and employment records were used in all studies. However, Rohs et al RefID 709486 noted that “20 persons reported never smoking in the 1980 questionnaire but subsequently reported a history of smoking in the 2004 questionnaire”.
	Metric 11:	Co-exposure Counfounding	Medium	Both Rohs et al RefID 709486 and Lockey et al RefID 3014803 evaluated co-exposure to commercial asbestos by excluding individuals with any such exposure in sensitivity analyses.

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Study Citation:	Rohs, A., Lockey, J., Dunning, K., Shukla, R., Fan, H., Hilbert, T., Borton, E., Wiot, J., Meyer, C., Shipley, R., Lemasters, G., Kapil, V. (2008). Low-level fiber-induced radiographic changes caused by Libby vermiculite: a 25-year follow-up study. American Journal of Respiratory and Critical Care Medicine 177(6):630-637.
Health Outcome:	Pleural Plaques
Target Organ(s):	Lung/Respiratory: Pleural changes (localized and/or diffuse pleural thickening), Parenchymal changes
Asbestos Fiber Type(s):	Asbestos - Tremolite: 14567-73-8; Asbestos - Winchite: 12425-92-2; Asbestos- Richterite: 17068-76-7; Asbestos- Libby amphibole: 1318-09-8
Linked HERO ID(s):	709486, 3014803
HERO ID:	709486

Domain	Metric		Rating	Comments
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	Medium	Appropriate analyses were used for all studies. Rohs et al RefID 709486 used logistic regression to calculate ORs, and Lockey et al RefID 3014803 used log-binomial GEE models to estimate RRs. Both follow-up studies evaluated the influence of including living non-participants assuming normal chest imaging, and of limited the analysis to workers hired after 1972 when exposure measures were based on monitoring data.
	Metric 13:	Statistical Power	Medium	Both studies had adequate numbers of cases with radiographic lung changes for analysis (n=80 in Rohs et al., RefID 709486, with additional cases in the subsequent follow-up).
	Metric 14:	Reproducibility of Analyses	Medium	The analyses presented are readily reproducible with sufficient detail provided.
	Metric 15:	Statistical Analysis	Medium	The authors explained the rationale for their statistical methods used and covariates examined (e.g. in Rohs et al., RefID 709486 BMI confounding was considered because subpleural fat can mimic pleural thickening). The follow-up studies also evaluated fit issues such as collinearity.

Additional Comments: Both of these studies had sufficient follow-up for asbestos-related lung changes to occur; the prevalence of radiographic pleural changes was 28.7% in Rohs et al 709486 and 52.9% in Lockey et al 3014803, who used HRCT/CT after a longer follow-up. In the later study, fiber measures were improved using updated information. Both authors conducted sensitivity analyses to evaluate bias due to attrition or non-participation; exposure measurement error; and occupational exposure to commercial asbestos. Both studies observed pleural changes even among individuals in the lowest occupational exposure categories, 0.005-0.24 fiber/cc-years in Rohs et al. 709486 and <0.15 fiber-years/cm3 in Lockey et al. 3014803. Lung changes were highly prevalent and associations of high magnitude in the 2nd exposure category: 24.6% and crude OR of 4.02 for individuals with 0.29 to 0.85 fiber/cc-years in Rohs et al, and 44.0% and crude RR of 5.0 for individuals with 0.15-<0.45 fiber-years/cm3 in Lockey et al. The Lockey et al 3014803 study also found associations between fiber exposure and parenchymal abnormalities. Lockey et al reported no meaningful confounding. Rohs et al presented multivariable-adjusted analyses which suggested some confounding by age and hire date but did not eliminate significance in the highest quartile. Lockey et al 3014803 also conducted spirometry measures and reported associations between lung change outcomes and impaired lung function. These authors did not list actinolite as a fiber.

Overall Quality Determination **High**

* No biomarkers were identified for this evaluation.

Study Citation:	Rubino, G. F., Piolatto, G., Newhouse, M. L., Scansetti, G., Aresini, G. A., Murray, R. (1979). Mortality of chrysotile asbestos workers at the Balangero Mine, northern Italy. Occupational and Environmental Medicine 36(3):187-194.
Health Outcome:	Laryngeal Cancer; gastrointestinal; lip, oral cavity and pharynx; stomach; colon and rectum, colon, rectum, peritoneum; respiratory organs; pleura; bladder; nervous system; unspecified; Asbestosis; cirrhosis, cardiovascular disease, tuberculosis, influenza, pneumonia, and other respiratory diseases, other pneumoconioses
Target Organ(s):	Laryngeal: Laryngeal neoplasm mortality; Cancer/Carcinogenesis: Laryngeal neoplasm mortality, Gastrointestinal neoplasm mortality, Other sites neoplasms mortality, Lip, oral cavity, and pharynx malignant neoplasm mortality, Stomach malignant neoplasm mortality, Digestive organs and peritoneum malignant neoplasm mortality, Respiratory organs neoplasm mortality, Pleura neoplasm mortality, Bladder neoplasm mortality, Nervous system neoplasm mortality, small intestine, colon, and rectum neoplasm mortality, All malignant neoplasms mortality, Malignant neoplasm mortality, Colon and rectum malignant neoplasm mortality, Colon malignant neoplasm mortality, Rectum malignant neoplasm mortality, Peritoneum malignant neoplasm mortality, Unspecified malignant neoplasm mortality; Mortality: Laryngeal neoplasm mortality, Gastrointestinal neoplasm mortality, Other sites neoplasms mortality, Influenza and pneumonia mortality, Asbestosis mortality, Tuberculosis of the lung mortality, Cardiovascular diseases mortality, Cirrhosis of the liver mortality, Accidents mortality, All causes of mortality, Lip, oral cavity, and pharynx malignant neoplasm mortality, Stomach malignant neoplasm mortality, Digestive organs and peritoneum malignant neoplasm mortality, Respiratory organs neoplasm mortality, Pleura neoplasm mortality, Bladder neoplasm mortality, Nervous system neoplasm mortality, Psychiatric disorder mortality, Ischemic cardiopathy mortality, Other respiratory diseases mortality, Other pneumoconioses mortality, Other digestive diseases mortality, small intestine, colon, and rectum neoplasm mortality, All malignant neoplasms mortality, Respiratory diseases (non-malignant) mortality, All other causes of mortality, Unknown cause of mortality, Malignant neoplasm mortality, Colon and rectum malignant neoplasm mortality, Colon malignant neoplasm mortality, Rectum malignant neoplasm mortality, Peritoneum malignant neoplasm mortality, Unspecified malignant neoplasm mortality, Digestive diseases mortality, Cirrhosis of the liver and other chronic liver dieseases mortality, External causes mortality, Poorly defined cause of mortality; Gastrointestinal: Gastrointestinal neoplasm mortality, Stomach malignant neoplasm mortality, Digestive organs and peritoneum malignant neoplasm mortality, Other digestive diseases mortality, small intestine, colon, and rectum neoplasm mortality, Colon malignant neoplasm mortality, Colon and rectum malignant neoplasm mortality, Rectum malignant neoplasm mortality, Digestive diseases mortality; Other sites: Other sites neoplasms mortality; Lung/Respiratory: Influenza and pneumonia mortality, Asbestosis mortality, Tuberculosis of the lung mortality, Respiratory organs neoplasm mortality, Pleura neoplasm mortality, Other respiratory diseases mortality, Other pneumoconioses mortality, Respiratory diseases (non-malignant) mortality; Cardiovascular: Cardiovascular diseases mortality, Ischemic cardiopathy mortality; Hepatic/Liver: Cirrhosis of the liver and other chronic liver dieseases mortality, Cirrhosis of the liver mortality; Head/mouth: Lip, oral cavity, and pharynx malignant neoplasm mortality; Renal/Kidney: Bladder neoplasm mortality; Neurological/Behavioral: Nervous system neoplasm mortality, Psychiatric disorder mortality; Abdomen: Peritoneum malignant neoplasm mortality
Asbestos Fiber Type(s):	Asbestos - Chrysotile (serpentine): 12001-29-5
Linked HERO ID(s):	178, 6861719
HERO ID:	178

Domain	Metric		Rating	Comments
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Medium	From asbestos part 1: ”Most complete report of exposure assessment is in initial cohort study ((Rubino et al., 1979) pg 189). Chrysotile fiber counts were first measured in 1969 using membrane filter collection and phase contrast microscopy (frequency not reported). To estimate exposure from 1946-1969, factory records on daily production, equipment used, characteristics of the job and number of hours/day were used (this method has considerable limitations due to basis on mean values for large job categories and no allowance for changes in weather). Simulated and measured data were made comparable by using weighting factors (e.g., more dusty operation for 1-2 hr/d compared with longer working hours in the past).”

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Study Citation:	Rubino, G. F., Piolatto, G., Newhouse, M. L., Scansetti, G., Aresini, G. A., Murray, R. (1979). Mortality of chrysotile asbestos workers at the Balangero Mine, northern Italy. Occupational and Environmental Medicine 36(3):187-194.
Health Outcome:	Laryngeal Cancer; gastrointestinal; lip, oral cavity and pharynx; stomach; colon and rectum, colon, rectum, peritoneum; respiratory organs; pleura; bladder; nervous system; unspecified; Asbestosis; cirrhosis, cardiovascular disease, tuberculosis, influenza, pneumonia, and other respiratory diseases, other pneumoconioses
Target Organ(s):	Laryngeal: Laryngeal neoplasm mortality; Cancer/Carcinogenesis: Laryngeal neoplasm mortality, Gastrointestinal neoplasm mortality, Other sites neoplasms mortality, Lip, oral cavity, and pharynx malignant neoplasm mortality, Stomach malignant neoplasm mortality, Digestive organs and peritoneum malignant neoplasm mortality, Respiratory organs neoplasm mortality, Pleura neoplasm mortality, Bladder neoplasm mortality, Nervous system neoplasm mortality, small intestine, colon, and rectum neoplasm mortality, All malignant neoplasms mortality, Malignant neoplasm mortality, Colon and rectum malignant neoplasm mortality, Colon malignant neoplasm mortality, Rectum malignant neoplasm mortality, Peritoneum malignant neoplasm mortality, Unspecified malignant neoplasm mortality; Mortality: Laryngeal neoplasm mortality, Gastrointestinal neoplasm mortality, Other sites neoplasms mortality, Influenza and pneumonia mortality, Asbestosis mortality, Tuberculosis of the lung mortality, Cardiovascular diseases mortality, Cirrhosis of the liver mortality, Accidents mortality, All causes of mortality, Lip, oral cavity, and pharynx malignant neoplasm mortality, Stomach malignant neoplasm mortality, Digestive organs and peritoneum malignant neoplasm mortality, Respiratory organs neoplasm mortality, Pleura neoplasm mortality, Bladder neoplasm mortality, Nervous system neoplasm mortality, Psychiatric disorder mortality, Ischemic cardiopathy mortality, Other respiratory diseases mortality, Other pneumoconioses mortality, Other digestive diseases mortality, small intestine, colon, and rectum neoplasm mortality, All malignant neoplasms mortality, Respiratory diseases (non-malignant) mortality, All other causes of mortality, Unknown cause of mortality, Malignant neoplasm mortality, Colon and rectum malignant neoplasm mortality, Colon malignant neoplasm mortality, Rectum malignant neoplasm mortality, Peritoneum malignant neoplasm mortality, Unspecified malignant neoplasm mortality, Digestive diseases mortality, Cirrhosis of the liver and other chronic liver dieseases mortality, External causes mortality, Poorly defined cause of mortality; Gastrointestinal: Gastrointestinal neoplasm mortality, Stomach malignant neoplasm mortality, Digestive organs and peritoneum malignant neoplasm mortality, Other digestive diseases mortality, small intestine, colon, and rectum neoplasm mortality, Colon malignant neoplasm mortality, Colon and rectum malignant neoplasm mortality, Rectum malignant neoplasm mortality, Digestive diseases mortality; Other sites: Other sites neoplasms mortality; Lung/Respiratory: Influenza and pneumonia mortality, Asbestosis mortality, Tuberculosis of the lung mortality, Respiratory organs neoplasm mortality, Pleura neoplasm mortality, Other respiratory diseases mortality, Other pneumoconioses mortality, Respiratory diseases (non-malignant) mortality; Cardiovascular: Cardiovascular diseases mortality, Ischemic cardiopathy mortality; Hepatic/Liver: Cirrhosis of the liver and other chronic liver dieseases mortality, Cirrhosis of the liver mortality; Head/mouth: Lip, oral cavity, and pharynx malignant neoplasm mortality; Renal/Kidney: Bladder neoplasm mortality; Neurological/Behavioral: Nervous system neoplasm mortality, Psychiatric disorder mortality; Abdomen: Peritoneum malignant neoplasm mortality
Asbestos Fiber Type(s):	Asbestos - Chrysotile (serpentine): 12001-29-5
Linked HERO ID(s):	178, 6861719
HERO ID:	178

Domain	Metric		Rating	Comments
	Metric 5:	Exposure Levels	Low	Rubino et al., 1979, HEROID: 178 and Ferrante et al., 2020, HEROID: 6861719 analyze these outcomes using dichotomous levels of exposure.

Additional Comments: QC was not completed for metrics other than Metrics 4 and 5 because the study does not have sufficient exposure information to be useful for dose-response analysis.

* No biomarkers were identified for this evaluation.

** As described in Appendix B.2 of the *White Paper: Quantitative Approach to the Human Health Assessment for the Risk Evaluation for Asbestos Part 2: Supplemental Evaluation Including Legacy Uses and Associated Disposals of Asbestos*, to be considered as being informative for dose-response analysis, metrics 4 and 5 would need metric ratings of Medium or High. This reference did not satisfy this requirement; therefore data quality evaluation is presented for only for metrics 4 and 5.

Study Citation: Rubino, G. F., Piolatto, G., Newhouse, M. L., Scansetti, G., Aresini, G. A., Murray, R. (1979). Mortality of chrysotile asbestos workers at the Balangero Mine, northern Italy. Occupational and Environmental Medicine 36(3):187-194.
Health Outcome: Lung Cancer
Target Organ(s): Cancer/Carcinogenesis: Lung malignant neoplasm mortality; Lung/Respiratory: Lung malignant neoplasm mortality; Mortality: Lung malignant neoplasm mortality
Asbestos Fiber Type(s): Asbestos - Chrysotile (serpentine): 12001-29-5
Linked HERO ID(s): 178, 6861719
HERO ID: 178

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	High	The rating is based on asbestos part 1 evaluation description: "Subjects included men from the Balangero mine worker cohort that were employed in an Italian asbestos mine. The initial cohort ((Rubino et al., 1979, HEROID: 178), pg 188) consisted of 952 men employed between 1/1/1930 and 12/31/1965, with at least 30 calendar days' employment during that period." and the description in the paper of interest (Ferrante et al., 2020, HEROID: 6861719: "The cohort included 974 male workers employed for at least 6 months and active at the Balangero mine on 1st January 1946 or hired subsequently until the cessation of activity." While these accounts differ, it is likely meant to suggest that only subjects with mortality, which began 1/1/46, are included in Ferrante et al., which extended mortality follow up to 5/31/2013.
	Metric 2:	Attrition	High	In Ferrante et al., 2020, HEROID: 6861719, only 21/974 (2%) workers were lost by follow up in 2013.
	Metric 3:	Comparison Group	High	As per asbestos part 1, this is rated high, however the paper in question Ferrante et al., 2020, HEROID 6861719 does not explicitly address this metric. As per asbestos part 1: "The most complete data on comparison groups is available from the most recent follow-up (Pira et al., 2017). General population mortality rates using the whole country from 1955 until 1980 and specifically the Piedmont Region (where the mine is located) from 1981 onwards (no regional rates available prior to 1981). The 1955-1959 rates were applied to 1946-1954 period (no available data); this may have led to an underestimate of expected deaths which may have showed and increased rate during this period. Expected numbers of deaths (overall and selected cancers) were computed using age-specific and calendar-year-specific (5-year categories) male death rates (Pira et al., 2017) pg 559."
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Medium	From asbestos part 1: "Most complete report of exposure assessment is in initial cohort study ((Rubino et al., 1979) pg 189). Chrysotile fiber counts were first measured in 1969 using membrane filter collection and phase contrast microscopy (frequency not reported). To estimate exposure from 1946-1969, factory records on daily production, equipment used, characteristics of the job and number of hours/day were used (this method has considerable limitations due to basis on mean values for large job categories and no allowance for changes in weather). Simulated and measured data were made comparable by using weighting factors (e.g., more dusty operation for 1-2 hr/d compared with longer working hours in the past)."

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Study Citation:	Rubino, G. F., Piolatto, G., Newhouse, M. L., Scansetti, G., Aresini, G. A., Murray, R. (1979). Mortality of chrysotile asbestos workers at the Balangero Mine, northern Italy. Occupational and Environmental Medicine 36(3):187-194.
Health Outcome:	Lung Cancer
Target Organ(s):	Cancer/Carcinogenesis: Lung malignant neoplasm mortality; Lung/Respiratory: Lung malignant neoplasm mortality; Mortality: Lung malignant neoplasm mortality
Asbestos Fiber Type(s):	Asbestos - Chrysotile (serpentine): 12001-29-5
Linked HERO ID(s):	178, 6861719
HERO ID:	178

Domain	Metric		Rating	Comments
	Metric 5:	Exposure Levels	Medium	The range and distribution of the cumulative exposure is sufficient to develop exposure-response relations and the study reports 3 levels of exposure for analyses completed in Ferrante et al., 2020, HEROID: 6861719, table 4.
	Metric 6:	Temporality	High	Ferrante et al., 2020, HEROID: 6861719 presents appropriate temporality between the exposure to asbestos and the outcome of disease mortality, with follow up spanning into 2013.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	High	Lung Cancer: Ferrante et al., 2020, HEROID: 6861719 notes that: ”Causes of death were provided by the Death and Births Registry Office of the municipality of death and were coded by us according to the International Classification of Diseases (ICD) classification (9th revision).” Authors do not explicitly state which code(s) were used in this paper nor do they reference a methods paper. However, the asbestos part 1 evaluation does state that certain ICD codes were referenced, and will use this rating as methods are presumably the same across updates of analyses.
	Metric 8:	Reporting Bias	High	Ferrante et al., 2020, HEROID: 6861719 reports Poisson regression outcomes with relative risks and 95% CIs.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Medium	Ferrante et al., 2020, HEROID: 6861719 adjusted for age explicitly and sex and race discretely based on the initial recruitment makeup of subjects, however there was no adjustment for smoking.
	Metric 10:	Covariate Characterization	High	Ferrante et al., 2020, HEROID: 6861719 used occupational data from employers: ”The list of cohort members and their working periods and job assignments were extracted from the factory rosters, stored after the mine bankruptcy in the Turin section of the Italian State Archives, where we had access to them.”
	Metric 11:	Co-exposure Counfounding	Low	Ferrante et al., 2020, HEROID: 6861719 did not adjust for coexposures.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	Medium	The study design (cohort with follow up and analyses of lung cancer mortality counts by Poisson regression) was appropriate (Ferrante et al., 2020, HEROID: 6861719). However it is unclear why authors did not complete a Cox survival model.
	Metric 13:	Statistical Power	Medium	The number of participants (n=953) are adequate to detect an effect in the exposed population (Ferrante et al., 2020, HEROID: 6861719).
	Metric 14:	Reproducibility of Analyses	Medium	The description of the analysis is sufficient to understand how to conceptually reproduce the analysis with access to the analytic data (Ferrante et al., 2020, HEROID: 6861719).

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Study Citation:	Rubino, G. F., Piolatto, G., Newhouse, M. L., Scansetti, G., Aresini, G. A., Murray, R. (1979). Mortality of chrysotile asbestos workers at the Balangero Mine, northern Italy. Occupational and Environmental Medicine 36(3):187-194.
Health Outcome:	Lung Cancer
Target Organ(s):	Cancer/Carcinogenesis: Lung malignant neoplasm mortality; Lung/Respiratory: Lung malignant neoplasm mortality; Mortality: Lung malignant neoplasm mortality
Asbestos Fiber Type(s):	Asbestos - Chrysotile (serpentine): 12001-29-5
Linked HERO ID(s):	178, 6861719
HERO ID:	178

Domain	Metric		Rating	Comments
	Metric 15:	Statistical Analysis	Low	Relative risks were calculated for lung cancer mortality using Poisson regression, however model assumptions were not explicitly addressed (i.e., does outcome data fit the Poisson distribution?). Authors state only: "95% CI were estimated assuming the Poisson distribution of observed cases." However, it is unclear if they mean all outcomes or a specific one (potentially only mesothelioma).

Additional Comments: This evaluation is solely for analyses done in Ferrante et al., 2020, HEROID: 6861719 for lung cancer mortality. All other analyses do not have a Medium or higher rating for Metric 5 or are not SMR or regression analyses. Rubino et al., 1979, HEROID: 178 has no outcomes not already evaluated which have a Medium or higher rating for Metric 5 or are not SMR or regression analyses and are thus not evaluated or extracted in any capacity here.

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation:	Ryan, P. H., Rice, C. H., Lockey, J. E., Black, B., Burkle, J., Hilbert, T. J., Levin, L., Cole, B., Mckay, R., Wolfe, C., Lemasters, G. K. (2017). Childhood exposure to Libby amphibole asbestos and respiratory health in young adults. Environmental Research 158:470-479.
Health Outcome:	Pleuritic chest pain, Regular cough, shortness of breath, wheezing or whistling in the chest
Target Organ(s):	Lung/Respiratory: Pleuritic chest pain, Regular cough, Shortness of breath, Wheezing or whistling in the chest
Asbestos Fiber Type(s):	Asbestos- Libby amphibole: 1318-09-8
Linked HERO ID(s):	No linked references.
HERO ID:	6866570

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Low	Most key elements of study design are described (setting, inclusion criteria, participant recruitment) but details regarding participation rate at all steps of the study are not provided. The is an analysis using subjects of the Childhood Health Investigation and Exposure Follow-Up Study (CHIEFS). To be eligible, children must have been part of 2000-2001 ATSDR screening and have been 10-17 years old at that time. Children the same age who did not participate but met ATSDR screening eligibility requirements were also eligible. "Recruitment efforts included contact with the parents of the previous ATSDR participants, posts to social media, public outreach events including health fairs, and advertisements in local and regional newspapers." A total of 312 subjects were enrolled and completed at least one portion of the study. Of these, 234 (75%) had previously participated in the ATSDR screening. 311 subjects had complete questionnaire data and 304 had spirometry data. There is no cited information on the ATSDR screening eligibility requirements or the subjects themselves who were recruited. Because of this, there is substantial potential for recruitment bias and no data to suggest differently.
	Metric 2:	Attrition	High	Of the 312 participants, 304 had total spirometry data and 311 had complete questionnaire data. Explanations for why some data are missing or the characteristics of individuals who did not provide some data were not discussed, but exposure and outcome data were largely complete.
	Metric 3:	Comparison Group	Medium	Based on what the authors present in the paper, there is some evidence that most participants are similar to each other (age, race/ethnicity). Statistical analyses adjusted for sex and smoking history. However, analyses were not adjusted for BMI which was approximately evenly distributed among the participants (normal - 39%; overweight - 32%; obese - 29%). It is possible that BMI could have an effect on some spirometry data/respiratory health outcomes.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Medium	Exposure was estimated for 12 different activities, and a cumulative 12-activity metric (fiber/cc - months) by combining previously completed exposure measurements using PCM or PCM equivalent methods from different but comparable time periods and activity frequency data from subject questionnaires. Exposure estimates and the rationale for each were based on "literature values, available activity-based sampling results, and the US EPA Contaminant Screening Survey results." While this method does use 'expert judgement', it is no different that the creation of JEM, except for a community setting.

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Study Citation:	Ryan, P. H., Rice, C. H., Lockey, J. E., Black, B., Burkle, J., Hilbert, T. J., Levin, L., Cole, B., Mckay, R., Wolfe, C., Lemasters, G. K. (2017). Childhood exposure to Libby amphibole asbestos and respiratory health in young adults. Environmental Research 158:470-479.
Health Outcome:	Pleuritic chest pain, Regular cough, shortness of breath, wheezing or whistling in the chest
Target Organ(s):	Lung/Respiratory: Pleuritic chest pain, Regular cough, Shortness of breath, Wheezing or whistling in the chest
Asbestos Fiber Type(s):	Asbestos- Libby amphibole: 1318-09-8
Linked HERO ID(s):	No linked references.
HERO ID:	6866570

Domain	Metric		Rating	Comments
	Metric 5:	Exposure Levels	Medium	Only analyses contributing to the creation of figure 2 present results using continuous (i.e., non-dichotomous) exposures. While distributions are highly skewed, it is feasible that these can be used in dose response analysis. The 12-activities cumulative exposure median was 4.99 f/cc - months, ranging from 0.01 - 114.3 f/cc - months.
	Metric 6:	Temporality	Low	Temporality is established, but it is not certain whether there was adequate follow-up in consideration of latency. However, the study's focus was to assess associations of estimated LAA exposure during childhood (<= 18 years of age) with adverse respiratory health effects and most participants were evaluated as young adults in their mid-20s, and 98% of subjects were born prior to the mine closing in 1990. The authors make the case that additional follow-up studies in this cohort should be done, and that the data presented in this paper should be thought of as ”baseline” data ”upon which future health outcomes can be compared.”
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Uninformative	Other Non-Cancer Outcomes: Only self-reported health outcomes were used without validation. There is little detail on how the survey was conducted (i.e., by a trained surveyor or nurse), that might increase confidence in the outcome measure.
	Metric 8:	Reporting Bias	High	The findings are clearly presented with adjusted odds ratios and 95% CI's as a log base 2 transformation (i.e., a 2-folder increase in exposure).
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Low	Final analyses were adjusted for sex and smoking history but not BMI or other potential important confounders, such as asthma. The authors do not provide reasoning or their methodology for selecting those particular covariates to be used in the analyses.
	Metric 10:	Covariate Characterization	High	Covariate data were assessed using valid and reliable methodology. A questionnaire adapted from the ATSDR medical screening survey was used to collect demographic information, residential and occupational history, and respiratory health history.
	Metric 11:	Co-exposure Counfounding	Low	There is no discussion of other exposures (i.e., other activities or jobs) might have impacted the subjects.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	Medium	The study design was appropriate for the research question, and the study used an appropriate statistical method to assess associations between estimated asbestos exposure during childhood with the health outcomes of interest in young adults (logistic regression analyses).

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Study Citation:	Ryan, P. H., Rice, C. H., Lockey, J. E., Black, B., Burkle, J., Hilbert, T. J., Levin, L., Cole, B., Mckay, R., Wolfe, C., Lemasters, G. K. (2017). Childhood exposure to Libby amphibole asbestos and respiratory health in young adults. Environmental Research 158:470-479.
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Target Organ(s):	Lung/Respiratory: Pleuritic chest pain, Regular cough, Shortness of breath, Wheezing or whistling in the chest
Asbestos Fiber Type(s):	Asbestos- Libby amphibole: 1318-09-8
Linked HERO ID(s):	No linked references.
HERO ID:	6866570

Domain	Metric		Rating	Comments
	Metric 13:	Statistical Power	Medium	The number of participants (n=311) was adequate to detect an effect in subgroups of the sample, specifically those subjects who reported being involved with certain activities related to increased asbestos exposure during childhood.
	Metric 14:	Reproducibility of Analyses	Medium	If given access to the analytic data, one would be able to reproduce the analyses based on the description of the statistical methodology.
	Metric 15:	Statistical Analysis	Low	Though the statistical model building process was appropriate, the authors do not explicitly state that model assumptions were met.

Additional Comments: Note that only analyses in figure 2 meet the ”medium or high” rating for metric 5, and thus are the focus of this evaluation. QC was not completed for extraction, as the overall quality determination was uninformative. This cohort study retrospectively estimated childhood exposure to Libby amphibole asbestos (LAA) in young adults who grew up in Libby, MT; of this sample 98% were born prior to the mine closure in 1990. Exposure estimates depended on participant report of the frequency of engaging certain activities related to LAA exposure during childhood, and they found that heating vermiculite, fishing on the Kootenai River, and engaging in activities along or near Rainy Creek Road were associated with respiratory symptoms (not spirometry outcomes) in young adulthood. One notable limitation not addressed in the metrics under consideration is that of possible recall bias among participants, which may impact exposure estimates. Another is that health outcomes are based solely on self-report without confirmation or validation.

Overall Quality Determination Uninformative

* No biomarkers were identified for this evaluation.

Study Citation:	Ryan, P. H., Rice, C. H., Lockey, J. E., Black, B., Burkle, J., Hilbert, T. J., Levin, L., Cole, B., Mckay, R., Wolfe, C., Lemasters, G. K. (2017). Childhood exposure to Libby amphibole asbestos and respiratory health in young adults. Environmental Research 158:470-479.
Health Outcome:	Pulmonary Function/Spirometry Results; Pleural and interstitial changes
Target Organ(s):	Lung/Respiratory: Forced expiratory volume in 1 second (FEV1) % predicted, Forced vital capacity (FVC) % predicted, FEV1/FVC % predicted, Pleural Changes, Interstitial Changes
Asbestos Fiber Type(s):	Asbestos- Libby amphibole: 1318-09-8
Linked HERO ID(s):	No linked references.
HERO ID:	6866570

Domain	Metric		Rating	Comments
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Medium	Exposure was estimated for 12 different activities, and a cumulative 12-activity metric (fiber/cc - months) by combining previously completed exposure measurements using PCM or PCM equivalent methods from different but comparable time periods and activity frequency data from subject questionnaires. Exposure estimates and the rationale for each were based on ”literature values, available activity-based sampling results, and the US EPA Contaminant Screening Survey results.” While this method does use ’expert judgement’, it is no different that the creation of JEM, except for a community setting.
	Metric 5:	Exposure Levels	Low	Analyses are only completed for these outcomes using dichotomous exposure variables.

Additional Comments:	QC was not completed for metrics other than Metrics 4 and 5 for these outcomes because the analysis does not have sufficient exposure information to be useful for dose-response analysis.

* No biomarkers were identified for this evaluation.

** As described in Appendix B.2 of the *White Paper: Quantitative Approach to the Human Health Assessment for the Risk Evaluation for Asbestos Part 2: Supplemental Evaluation Including Legacy Uses and Associated Disposals of Asbestos*, to be considered as being informative for dose-response analysis, metrics 4 and 5 would need metric ratings of Medium or High. This reference did not satisfy this requirement; therefore data quality evaluation is presented for only for metrics 4 and 5.

Study Citation:	Santibanez, M., Vioque, J., Alguacil, J., Barber, X., de la Hera, G., Kauppinen, T. (2008). Occupational exposures and risk of oesophageal cancer by histological type: a case-control study in eastern Spain. Occupational and Environmental Medicine 65(11):774-781.
Health Outcome:	Oesophageal cancer
Target Organ(s):	Gastrointestinal: Oesophageal cancer; Cancer/Carcinogenesis: Oesophageal cancer
Asbestos Fiber Type(s):	Asbestos - Not specified: 1332-21-4
Linked HERO ID(s):	No linked references.
HERO ID:	517889

Domain		Metric	Rating	Comments
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Low	There was an interview conducted to ascertain information about occupational history and resulting potential exposures . Asbestos exposure was classified as low (<0.26 fibres/cm^3) and high (>0.26 fibres/cm^3). These concentrations were “based on the product of the probability and the intensity of exposure to each agent for at least 1 year” (Santibanez et al., 2008).The study or any cited methods source does not explicitly mention the use of PCM or TEM.
	Metric 5:	Exposure Levels	Low	In Table 2, asbestos exposure levels were only reported as high or low, although the authors do note that there is an unexposed category. However, the range of exposure in the population is limited and is based on responses to interview questions.

Additional Comments: Based on the auto-calculated score, this paper was rated as a medium. However, there were some shortcomings in the paper that should be mentioned. The authors highlight that the case-control design of this study may not be the best option for occupational exposures. There also may have been a low number of individuals present in each job classification. They also noted that the FINJEM job exposure matrix may have resulted in overestimation of asbestos exposure, as there were no asbestos mines in Spain.NOTE: Based on the current guidelines, this study would not have undergone further evaluation after metric 4 and 5. Metric 4 was rated as low because there was no mention in the study or cited sources about the use of PCM or TEM.

* No biomarkers were identified for this evaluation.

** As described in Appendix B.2 of the *White Paper: Quantitative Approach to the Human Health Assessment for the Risk Evaluation for Asbestos Part 2: Supplemental Evaluation Including Legacy Uses and Associated Disposals of Asbestos*, to be considered as being informative for dose-response analysis, metrics 4 and 5 would need metric ratings of Medium or High. This reference did not satisfy this requirement; therefore data quality evaluation is presented for only for metrics 4 and 5.

Study Citation:	Santibañez, M., Alguacil, J., de La Hera, M. G., Navarrete-Muñoz, E. M., Llorca, J., Aragonés, N., Kauppinen, T., Vioque, J., PANESOES Study Group (2012). Occupational exposures and risk of stomach cancer by histological type. Occupational and Environmental Medicine 69(4):268-275.
Health Outcome:	stomach cancer–all histological subtypes, intestinal adenocarcinoma, diffuse adenocarcinoma, lymphoma
Target Organ(s):	Gastrointestinal: Stomach cancer–lymphoma, Stomach cancer–diffuse adenocarcinoma, Stomach cancer–intestinal adenocarcinoma, Stomach cancer–all histological subtypes
Asbestos Fiber Type(s):	Asbestos - Not specified: 1332-21-4
Linked HERO ID(s):	No linked references.
HERO ID:	2569533

Domain	Metric		Rating	Comments
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Low	The FINJEM job exposure matrix was utilized to explore occupational exposure to various chemical, physical, ergonomic and psychosocial factors, including asbestos. Further information on the FINJEM was noted within referenced details of Kauppinen et al., 1998 (full text found but HERO ID not available) which describes the JEM as utilizing detailed quantitative industrial hygiene sampling results over time ascribed to occupational job titles and overviewed by industry experts. Details regarding utilization of PCM or TEM for asbestos analysis are not provided. It is unclear if the time periods with quantitative measures within the JEM corresponded to the time periods of interest.
	Metric 5:	Exposure Levels	Low	Outcome odds ratios in Tables 3 and 4 were presented across only two asbestos exposure categories of Low (<=0.26 fibers/cm^3) and High (>0.26 fibers/cm^3), with the reference category for each odds ratio including all remaining exposed groups.

Additional Comments: HERO ID 2569533 Santibanez (2012) was not evaluated for any metrics except Metrics 4 and 5 and had no data extracted because it did not have sufficient exposure information to be useful for dose-response analysis.

** As described in Appendix B.2 of the *White Paper: Quantitative Approach to the Human Health Assessment for the Risk Evaluation for Asbestos Part 2: Supplemental Evaluation Including Legacy Uses and Associated Disposals of Asbestos*, to be considered as being informative for dose-response analysis, metrics 4 and 5 would need metric ratings of Medium or High. This reference did not satisfy this requirement; therefore data quality evaluation is presented for only for metrics 4 and 5.

Study Citation:	Satta, G., Serra, T., Meloni, F., Lazzarato, A., Argiolas, A., Bosu, E., Coratza, A., Frau, N., Lai, M., Lecca, L. I., Mascia, N., Pilia, I., Piras, V., Sferlazzo, G., Campagna, M., Cocco, P. (2019). Pulmonary Function and CT Scan Imaging at Low-Level Occupational Exposureto Asbestos. International Journal of Environmental Research and Public Health 17(1):50.
Health Outcome:	Pulmonary Function/Spirometry Results
Target Organ(s):	Lung/Respiratory: Vital capacity (VC), Forced expiratory volume in 1 second (FEV1), Residual volume (RV), Diffusion lung capacity test with carbon monoxide (DLCO)
Asbestos Fiber Type(s):	Asbestos - Not specified: 1332-21-4
Linked HERO ID(s):	No linked references.
HERO ID:	6868480

Domain	Metric		Rating	Comments
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Low	This study determined exposure estimates using a retrospective assessment approach that included referring to the Datamyant database and abstract the time-weighted average concentration of asbestos fibers for each job task. To estimate indirect exposure resulting from the contamination of the work environment, they based calculations on the Ev@lutil database. Overall they relied upon professional judgment and were not able to collect direct exposure samples. The methods of quantifying fiber was not specified.
	Metric 5:	Exposure Levels	Medium	Subjects were divided into exposure quartiles, indicating there were 4 exposure groups. The range of exposure is likely sufficient to detect a relationship, based on the exposure information in Table 1 and frequency distribution of exposures in Figure 1.

Additional Comments: This cross-sectional occupational study examined associations of retrospective estimates of low-level asbestos exposure with respiratory function tests and HRCT reports ((Gamsu grades for pleuro-parenchymal alterations). There were no associations of asbestos with pulmonary function, but the study reported increased odds of developing lung fibrosis: risk in the top quartile of cumulative exposure was increased 8-fold, and for cumulative exposures above 10 fibers/mL-years risk was increased 11-fold.

* No biomarkers were identified for this evaluation.

** As described in Appendix B.2 of the *White Paper: Quantitative Approach to the Human Health Assessment for the Risk Evaluation for Asbestos Part 2: Supplemental Evaluation Including Legacy Uses and Associated Disposals of Asbestos*, to be considered as being informative for dose-response analysis, metrics 4 and 5 would need metric ratings of Medium or High. This reference did not satisfy this requirement; therefore data quality evaluation is presented for only for metrics 4 and 5.

Study Citation:	Satta, G., Serra, T., Meloni, F., Lazzarato, A., Argiolas, A., Bosu, E., Coratza, A., Frau, N., Lai, M., Lecca, L. I., Mascia, N., Pilia, I., Piras, V., Sferlazzo, G., Campagna, M., Cocco, P. (2019). Pulmonary Function and CT Scan Imaging at Low-Level Occupational Exposureto Asbestos. International Journal of Environmental Research and Public Health 17(1):50.
Health Outcome:	Pleural Plaques
Target Organ(s):	Lung/Respiratory: Interstitial fibrosis of lung parenchyma based on result of high-resolution computerized tomography (HRCT) scan
Asbestos Fiber Type(s):	Asbestos - Not specified: 1332-21-4
Linked HERO ID(s):	No linked references.
HERO ID:	6868480

Domain	Metric		Rating	Comments
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Low	This study determined exposure estimates using a retrospective assessment approach that included referring to the Datamyant database and abstract the time-weighted average concentration of asbestos fibers for each job task. To estimate indirect exposure resulting from the contamination of the work environment, they based calculations on the Ev@lutil database. Overall they relied upon professional judgment and were not able to collect direct exposure samples. The methods of quantifying fiber was not specified.
	Metric 5:	Exposure Levels	Medium	Subjects were divided into exposure quartiles, indicating there were 4 exposure groups. The range of exposure is likely sufficient to detect a relationship, based on the exposure information in Table 1 and frequency distribution of exposures in Figure 1.

Additional Comments:	This cross-sectional occupational study examined associations of retrospective estimates of low-level asbestos exposure with respiratory function tests and HRCT reports ((Gamsu grades for pleuro-parenchymal alterations). There were no associations of asbestos with pulmonary function, but the study reported increased odds of developing lung fibrosis: risk in the top quartile of cumulative exposure was increased 8-fold, and for cumulative exposures above 10 fibers/mL-years risk was increased 11-fold.

* No biomarkers were identified for this evaluation.

** As described in Appendix B.2 of the *White Paper: Quantitative Approach to the Human Health Assessment for the Risk Evaluation for Asbestos Part 2: Supplemental Evaluation Including Legacy Uses and Associated Disposals of Asbestos*, to be considered as being informative for dose-response analysis, metrics 4 and 5 would need metric ratings of Medium or High. This reference did not satisfy this requirement; therefore data quality evaluation is presented for only for metrics 4 and 5.

Study Citation:	Schikowsky, C., Felten, M. K., Eisenhawer, C., Das, M., Kraus, T. (2017). Lung function not affected by asbestos exposure in workers with normal Computed Tomography scan. American Journal of Industrial Medicine 60(5):422-431.
Health Outcome:	Pulmonary Function/Spirometry Results
Target Organ(s):	Lung/Respiratory: Airway resistance, Carbon monoxide diffusing capacity adjusted for alveolar volume (DLCO/VA), Forced expiratory volume in 1 second, Forced vital capacity (FVC)
Asbestos Fiber Type(s):	Asbestos - Not specified: 1332-21-4
Linked HERO ID(s):	No linked references.
HERO ID:	3864418

Domain	Metric		Rating	Comments
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Low	For this study, the cumulative exposure to asbestos was estimated for each participant. These values were determined based on job titles, main occupational tasks, and self-reported periods of exposure. The authors indicated that a computer program was used to determine these concentrations based on ambient monitoring data at defined workplaces. Cumulative exposure ”was expressed as the product of the total exposure duration and the 8-h time weighted average fiber concentration” in fiber-years (Schikowsky et al., 2017). This metric is rated low because the study or any cited methods source does not mention the use of PCM or TEM.
	Metric 5:	Exposure Levels	Medium	The range of exposure present in this study is adequate for examining an exposure-response relationship. The average cumulative asbestos exposure for the participants was 49.0 fiber years, with a range of 0.1-844.9 fiber years.

Additional Comments: This study had a number of strengths and limitations. One of the biggest limitations is a lack of direct asbestos measurements. Cumulative asbestos exposure was estimated based on job titles, occupational tasks, and self-reported periods of exposure. This limits the potential for a dose-response relationship. The authors also reported that there was no statistically significant differences between lung function and asbestos exposure. Strengths of this study included using regression analyses to be able to perform intra-group comparisons, such as based on smoking status. It is important to note that metric 4 was rated as low because there was no mention of PCM or TEM in the methods or any cited source.

* No biomarkers were identified for this evaluation.

** As described in Appendix B.2 of the *White Paper: Quantitative Approach to the Human Health Assessment for the Risk Evaluation for Asbestos Part 2: Supplemental Evaluation Including Legacy Uses and Associated Disposals of Asbestos*, to be considered as being informative for dose-response analysis, metrics 4 and 5 would need metric ratings of Medium or High. This reference did not satisfy this requirement; therefore data quality evaluation is presented for only for metrics 4 and 5.

Study Citation:	Schnatter, A. R., Nicolich, M. J., Lewis, R. J., Thompson, F. L., Dineen, H. K., Drummond, I., Dahlman, D., Katz, A. M., Thériault, G. (2012). Lung cancer incidence in Canadian petroleum workers. Occupational and Environmental Medicine 69(12):877-882.
Health Outcome:	Lung Cancer
Target Organ(s):	Cancer/Carcinogenesis: Lung cancer; Lung/Respiratory: Lung cancer
Asbestos Fiber Type(s):	Asbestos - Not specified: 1332-21-4
Linked HERO ID(s):	No linked references.
HERO ID:	2558775

Domain	Metric		Rating	Comments
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Low	Quantitative asbestos exposure levels were reported and the source of exposure data was provided. Employment history for study subjects were obtained and largely complete. The study didn't mention exposure measurement methods, and the concentration were from industrial hygiene surveys and frequency scores. There is no direct evidence indicates exposure measurement were biased.
	Metric 5:	Exposure Levels	Low	Asbestos exposure in tertiles and continuous level were reported, but the range of exposure is not sufficient and lack of exposure contrast to develop an exposure-response estimate.

Additional Comments: The primary concern of this study is lack of sufficient exposure range to detect an effect. There are no other concerns of bias or study design deficiency.

* No biomarkers were identified for this evaluation.

** As described in Appendix B.2 of the *White Paper: Quantitative Approach to the Human Health Assessment for the Risk Evaluation for Asbestos Part 2: Supplemental Evaluation Including Legacy Uses and Associated Disposals of Asbestos*, to be considered as being informative for dose-response analysis, metrics 4 and 5 would need metric ratings of Medium or High. This reference did not satisfy this requirement; therefore data quality evaluation is presented for only for metrics 4 and 5.

Study Citation:	Seidler, A., Becker, N., Nieters, A., Arhelger, R., Mester, B., Rossnagel, K., Deeg, E., Elsner, G., Melis, M., Sesler, S., Avataneo, G., Meloni, M., Cocco, P. (2010). Asbestos exposure and malignant lymphoma: a multicenter case-control study in Germany and Italy. International Archives of Occupational and Environmental Health 83(5):563-570.
Health Outcome:	Lymphoma
Target Organ(s):	Cancer/Carcinogenesis: B-cell non-Hodgkin's lymphoma (B-NHL), Hodgkin's lymphoma (HL), T-cell non-Hodgkin's lymphoma (T-NHL)
Asbestos Fiber Type(s):	Asbestos - Not specified: 1332-21-4
Linked HERO ID(s):	No linked references.
HERO ID:	3531424

Domain	Metric		Rating	Comments
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Low	Exposure was estimates solely using professional judgement, no evidence of measurements was provided.
	Metric 5:	Exposure Levels	Medium	The authors reported four levels (in fiber-years) of exposure for regression analysis.
Additional Comments:	None			

* No biomarkers were identified for this evaluation.

** As described in Appendix B.2 of the *White Paper: Quantitative Approach to the Human Health Assessment for the Risk Evaluation for Asbestos Part 2: Supplemental Evaluation Including Legacy Uses and Associated Disposals of Asbestos*, to be considered as being informative for dose-response analysis, metrics 4 and 5 would need metric ratings of Medium or High. This reference did not satisfy this requirement; therefore data quality evaluation is presented for only for metrics 4 and 5.

Study Citation:	Seidman, H. (1984). Short-term asbestos work exposure and long-term observation.
Health Outcome:	Lung Cancer; Laryngeal Cancer; All cancer mortality; Non-respiratory infectious disease mortality
Target Organ(s):	Mortality: All cause mortality, Lung cancer mortality, Gastro-intestinal cancer (grouped together cancer of esophagus, stomach, and colon-rectum) mortality, Non-infectious respiratory diseases (including asbestosis) mortality, All "asbestos" diseases (lung cancer, gastrointestinal cancer, mesothelioma, cancers of buccal cavity, pharynx, larynx, and kidney and non-infectious respiratory diseases) mortality, All cancer mortality, Larynx, buccal, pharynx cancer mortality, Stomach cancer mortality, Colon-rectum cancer mortality, Pancreas cancer mortality, Other and unspecified cancer mortality, Cardiovascular diseases mortality; Lung/Respiratory: Lung cancer mortality, Non-infectious respiratory diseases (including asbestosis) mortality, Larynx, buccal, pharynx cancer mortality; Cancer/Carcinogenesis: Lung cancer mortality, Gastro-intestinal cancer (grouped together cancer of esophagus, stomach, and colon-rectum) mortality, All cancer mortality, Larynx, buccal, pharynx cancer mortality, Stomach cancer mortality, Colon-rectum cancer mortality, Pancreas cancer mortality, Other and unspecified cancer; Gastrointestinal: Gastro-intestinal cancer (grouped together cancer of esophagus, stomach, and colon-rectum) mortality, Stomach cancer mortality, Colon-rectum cancer mortality, Pancreas cancer mortality; Cardiovascular: Cardiovascular diseases mortality
Asbestos Fiber Type(s):	Asbestos - Amosite (grunerite): 12172-73-5
Linked HERO ID(s):	No linked references.
HERO ID:	257

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	High	In this retrospective cohort study, Seidel et al 1984 (HEROID 257) examined cause-specific mortality in a cohort of male workers at an amosite asbestos factory in Paterson, NJ that operated from June 1941 to November 1954. The cohort was described as almost entirely white (mentioned in Seidman et al., 1979 HEROID 94625). This study excluded deaths in the first five years, analyzing mortality occurring 5-40 years after employment. Of all 933 men recruited to work from June 1941 to December 1945, this study excluded 113: 35 who worked with asbestos elsewhere (21 before starting and 14 afterwards); 40 who died within 5 years; and 38 lost to follow-up shortly after leaving the plant. The remaining 820 participants had worked at the facility for as little as one month up to several years. The mean age at employment was 41.9 years (50.8% aged >40 years). Three aspects of participant selection helped to limit bias. First, the study avoided healthy worker selection bias because all workers were eligible for inclusion regardless of date of initial employment, and regardless of duration of employment. In addition, the study used an exposure lag to reduce potential bias by taking disease latency into account: asbestos exposure at this plant may not have been causally related to disease outcomes with latency periods of $\geq$5 years. Finally, participants exposed to asbestos in other work settings were excluded.
	Metric 2:	Attrition	High	Only a few eligible workers (n=38) had been lost to follow-up at the start of this study. There was little additional attrition of the 820 participants in this follow-up through 1982, which included: 4 additional men lost to follow-up, and 5 who contributed person-time until starting asbestos work elsewhere (i.e., became ineligible; see p. 3). Of the 811 remaining men, 593 had died and 218 were still alive, accounting for the complete cohort. A later publication (Seidman et al., 1986, HEROID 290) reported similar numbers (5 lost to follow-up, 6 who began asbestos work elsewhere, 216 alive). Table 1 shows, for each 5-year period of follow-up, the number of workers at risk, the mean age of those workers, and the number of deaths that occurred, along with the small number lost to follow-up.

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Study Citation:	Seidman, H. (1984). Short-term asbestos work exposure and long-term observation.
Health Outcome:	Lung Cancer; Laryngeal Cancer; All cancer mortality; Non-respiratory infectious disease mortality
Target Organ(s):	Mortality: All cause mortality, Lung cancer mortality, Gastro-intestinal cancer (grouped together cancer of esophagus, stomach, and colon-rectum) mortality, Non-infectious respiratory diseases (including asbestosis) mortality, All "asbestos" diseases (lung cancer, gastrointestinal cancer, mesothelioma, cancers of buccal cavity, pharynx, larynx, and kidney and non-infectious respiratory diseases) mortality, All cancer mortality, Larynx, buccal, pharynx cancer mortality, Stomach cancer mortality, Colon-rectum cancer mortality, Pancreas cancer mortality, Other and unspecified cancer mortality, Cardiovascular diseases mortality; Lung/Respiratory: Lung cancer mortality, Non-infectious respiratory diseases (including asbestosis) mortality, Larynx, buccal, pharynx cancer mortality; Cancer/Carcinogenesis: Lung cancer mortality, Gastro-intestinal cancer (grouped together cancer of esophagus, stomach, and colon-rectum) mortality, All cancer mortality, Larynx, buccal, pharynx cancer mortality, Stomach cancer mortality, Colon-rectum cancer mortality, Pancreas cancer mortality, Other and unspecified cancer; Gastrointestinal: Gastro-intestinal cancer (grouped together cancer of esophagus, stomach, and colon-rectum) mortality, Stomach cancer mortality, Colon-rectum cancer mortality, Pancreas cancer mortality; Cardiovascular: Cardiovascular diseases mortality
Asbestos Fiber Type(s):	Asbestos - Amosite (grunerite): 12172-73-5
Linked HERO ID(s):	No linked references.
HERO ID:	257

Domain	Metric		Rating	Comments
	Metric 3:	Comparison Group	High	Standardized mortality ratios were calculated comparing all eligible workers in the cohort to white male residents of New Jersey in the same 5-year age groups during the same calendar periods. The authors reported elsewhere (Seidman et al., 1979 HEROID 94625) that death rates from cancer in New Jersey were "among the highest in the United States". The choice of the state referent helped to account for the regional background rates of cancer mortality.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Low	No fiber or dust count measures were available for this facility. Estimates were based on measures taken in 1967, 1970 and 1971 at two other plants run by the same company (in Tyler, TX; Port Allegany, PA) making the same products with the same machinery. Details on sampling equipment and procedures, or references to obtain that information, were not provided. Dr. William Nicholson helped to "assign plausible estimates" to "particular jobs" (i.e., estimates were extrapolated from later measures at other facilities using professional judgment). There were no details on how data were used, no discussion of comparable ventilation/dust extraction, and no references cited. It is not possible to ascertain the likely validity of fiber count estimates. Fiber-years/cc for each worker was calculated by multiplying estimated fiber counts for each job duty by the duration of work in that post. The median count of fibers $> 5\mu$ per cc across jobs was 50; counts for a list of job titles were shown in Table 5 (e.g., 5 for office workers, 15 for inspectors and foremen, 50 for production supervisors, 100 for pulverizers). Potential sources of error noted by the authors included: (i) the tendency for industrial hygienists to oversample dustier areas (counts too high, underestimate dose-response); (ii) the possibility that short-term workers "may have experienced an apprenticeship period in which they did some of the dirtier work in their department" (counts too low, over-estimate effect of short-term exposure); and (iii) lack of information on use of respirators (measurement error, uncertain if a source of bias). The study reports that there was a "concerted effort to have the Paterson plant workers use respirator protectors" although no details on compliance are provided.

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Study Citation: Seidman, H. (1984). Short-term asbestos work exposure and long-term observation.

Health Outcome: Lung Cancer; Laryngeal Cancer; All cancer mortality; Non-respiratory infectious disease mortality

Target Organ(s): Mortality: All cause mortality, Lung cancer mortality, Gastro-intestinal cancer (grouped together cancer of esophagus, stomach, and colon-rectum) mortality, Non-infectious respiratory diseases (including asbestosis) mortality, All "asbestos" diseases (lung cancer, gastrointestinal cancer, mesothelioma, cancers of buccal cavity, pharynx, larynx, and kidney and non-infectious respiratory diseases) mortality, All cancer mortality, Larynx, buccal, pharynx cancer mortality, Stomach cancer mortality, Colon-rectum cancer mortality, Pancreas cancer mortality, Other and unspecified cancer mortality, Cardiovascular diseases mortality; Lung/Respiratory: Lung cancer mortality, Non-infectious respiratory diseases (including asbestosis) mortality, Larynx, buccal, pharynx cancer mortality; Cancer/Carcinogenesis: Lung cancer mortality, Gastro-intestinal cancer (grouped together cancer of esophagus, stomach, and colon-rectum) mortality, All cancer mortality, Larynx, buccal, pharynx cancer mortality, Stomach cancer mortality, Colon-rectum cancer mortality, Pancreas cancer mortality, Other and unspecified cancer; Gastrointestinal: Gastro-intestinal cancer (grouped together cancer of esophagus, stomach, and colon-rectum) mortality, Stomach cancer mortality, Colon-rectum cancer mortality, Pancreas cancer mortality; Cardiovascular: Cardiovascular diseases mortality

Asbestos Fiber Type(s): Asbestos - Amosite (grunerite): 12172-73-5

Linked HERO ID(s): No linked references.

HERO ID: 257

Domain	Metric		Rating	Comments
	Metric 5:	Exposure Levels	Medium	Exposure was analyzed using categories of fiber-years/cc and work duration. Data were presented using 8 categories of fiber-years/cc (<6, 6-11.9, 12-24.9, 25-49.9, 50-99.9, 100-149.9, 150-249.9, 250+ fiber-years/cc), as well as dichotomized (<25 vs 25+ fiber-years/cc). Exposure duration was classified in 7 categories (<1 month, 1 month, 2 months, 3-5 months, 6-11 months, 1 year, 2+ years); boundaries for these periods were not provided. In addition, some analyses calculated SMRs classified by department of work (e.g., Table 11 in HEROID 257; see also Table XIII in Seidman et al, 1986 HEROID 290).
	Metric 6:	Temporality	High	Temporality and duration of follow-up was appropriate for the outcomes evaluated (multiple cancers, mesothelioma, and asbestosis). Follow-up ranged from a minimum of 5 to a maximum of 40 years.
Domain 3: Outcome Assessment				

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Study Citation: Seidman, H. (1984). Short-term asbestos work exposure and long-term observation.

Health Outcome: Lung Cancer; Laryngeal Cancer; All cancer mortality; Non-respiratory infectious disease mortality

Target Organ(s): Mortality: All cause mortality, Lung cancer mortality, Gastro-intestinal cancer (grouped together cancer of esophagus, stomach, and colon-rectum) mortality, Non-infectious respiratory diseases (including asbestosis) mortality, All ”asbestos” diseases (lung cancer, gastrointestinal cancer, mesothelioma, cancers of buccal cavity, pharynx, larynx, and kidney and non-infectious respiratory diseases) mortality, All cancer mortality, Larynx, buccal, pharynx cancer mortality, Stomach cancer mortality, Colon-rectum cancer mortality, Pancreas cancer mortality, Other and unspecified cancer mortality, Cardiovascular diseases mortality; Lung/Respiratory: Lung cancer mortality, Non-infectious respiratory diseases (including asbestosis) mortality, Larynx, buccal, pharynx cancer mortality; Cancer/Carcinogenesis: Lung cancer mortality, Gastro-intestinal cancer (grouped together cancer of esophagus, stomach, and colon-rectum) mortality, All cancer mortality, Larynx, buccal, pharynx cancer mortality, Stomach cancer mortality, Colon-rectum cancer mortality, Pancreas cancer mortality, Other and unspecified cancer; Gastrointestinal: Gastro-intestinal cancer (grouped together cancer of esophagus, stomach, and colon-rectum) mortality, Stomach cancer mortality, Colon-rectum cancer mortality, Pancreas cancer mortality; Cardiovascular: Cardiovascular diseases mortality

Asbestos Fiber Type(s): Asbestos - Amosite (grunerite): 12172-73-5

Linked HERO ID(s): No linked references.

HERO ID: 257

Domain	Metric		Rating	Comments
	Metric 7:	Outcome Measurement or Characterization	Medium	Lung Cancer: The authors reported analyzing causes of death derived principally using the “best evidence” available to classify cause of death, as well as analyses using only death certificate (DC) information. Best evidence (BE) classification incorporated additional information from autopsy, surgical specimens, x-ray films and clinical findings (Seidman et al., 1979 HEROID 94625). Tables indicate when BE or DC coding was used, and comparisons of counts based on each method are shown (e.g., Table 6A). The authors did not describe best evidence sources or methods used to link participants to these sources or death certificates, did not provide ICD codes, and did not discuss involving a nosologist. Insights on BE sources can be inferred from acknowledgements (e.g., see Seidman et al, 1986 HEROID 290), which mention receiving generous help from medical facilities including hospitals, pathologists, and state health departments, with several facilities and clinicians listed by name.; Laryngeal Cancer: The authors reported analyzing causes of death derived principally using the “best evidence” available to classify cause of death, as well as analyses using only death certificate (DC) information. Best evidence (BE) classification incorporated additional information from autopsy, surgical specimens, x-ray films and clinical findings (Seidman et al., 1979 HEROID 94625). Tables indicate when BE or DC coding was used, and comparisons of counts based on each method are shown (e.g., Table 6A). The authors did not describe best evidence sources or methods used to link participants to these sources or death certificates, did not provide ICD codes, and did not discuss involving a nosologist. Insights on BE sources can be inferred from acknowledgements (e.g., see Seidman et al, 1986 HEROID 290), which mention receiving generous help from medical facilities including hospitals, pathologists, and state health departments, with several facilities and clinicians listed by name. There were limited details on how outcomes were defined. In this study, cancers of the larynx, buccal and pharynx were combined.; Other Cancer(s): The authors reported analyzing causes of death derived principally using the “best evidence” available to classify cause of death, as well as analyses using only death certificate (DC) information. Best evidence (BE) classification incorporated additional information from autopsy, surgical specimens, x-ray films and clinical findings (Seidman et al., 1979 HEROID 94625). Tables indicate when BE or DC coding was used, and comparisons of counts based on each method are shown (e.g., Table 6A). The authors did not describe best evidence sources or methods used to link participants to these sources or death certificates, did not provide ICD codes, and did not discuss involving a nosologist. Insights on BE sources can be inferred from acknowledgements (e.g., see Seidman et al, 1986 HEROID 290), which mention receiving generous help from medical facilities including

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Study Citation: Seidman, H. (1984). Short-term asbestos work exposure and long-term observation.
Health Outcome: Lung Cancer; Laryngeal Cancer; All cancer mortality; Non-respiratory infectious disease mortality
Target Organ(s): Mortality: All cause mortality, Lung cancer mortality, Gastro-intestinal cancer (grouped together cancer of esophagus, stomach, and colon-rectum) mortality, Non-infectious respiratory diseases (including asbestosis) mortality, All "asbestos" diseases (lung cancer, gastrointestinal cancer, mesothelioma, cancers of buccal cavity, pharynx, larynx, and kidney and non-infectious respiratory diseases) mortality, All cancer mortality, Larynx, buccal, pharynx cancer mortality, Stomach cancer mortality, Colon-rectum cancer mortality, Pancreas cancer mortality, Other and unspecified cancer mortality, Cardiovascular diseases mortality; Lung/Respiratory: Lung cancer mortality, Non-infectious respiratory diseases (including asbestosis) mortality, Larynx, buccal, pharynx cancer mortality; Cancer/Carcinogenesis: Lung cancer mortality, Gastro-intestinal cancer (grouped together cancer of esophagus, stomach, and colon-rectum) mortality, All cancer mortality, Larynx, buccal, pharynx cancer mortality, Stomach cancer mortality, Colon-rectum cancer mortality, Pancreas cancer mortality, Other and unspecified cancer; Gastrointestinal: Gastro-intestinal cancer (grouped together cancer of esophagus, stomach, and colon-rectum) mortality, Stomach cancer mortality, Colon-rectum cancer mortality, Pancreas cancer mortality; Cardiovascular: Cardiovascular diseases mortality
Asbestos Fiber Type(s): Asbestos - Amosite (grunerite): 12172-73-5
Linked HERO ID(s): No linked references.
HERO ID: 257

Domain	Metric		Rating	Comments
	Metric 8:	Reporting Bias	High	Information is presented for all outcomes described. The authors present details on the observed and expected numbers of deaths stratified by categories of exposure or time period, along with the resulting SMRs; statistical significance is indicated. There is no evidence of selective reporting.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	High	SMR calculations accounted for expected cases based on 5-year age groups and calendar period of death. The participants were male and described as almost exclusively white, so sex and race adjustments were not needed. No other covariates were considered (e.g., smoking, alcohol), as is habitual in SMR studies.
	Metric 10:	Covariate Characterization	Medium	Information on age and calendar period of death were likely obtained from plant records, death certificates and other medical record sources.
	Metric 11:	Co-exposure Counfounding	Low	In this occupational setting, potential co-exposures are not discussed. There is no information to suggest the presence of other important co-exposures in this setting. The factory supplied the US. Navy with asbestos insulation for the pipes, boilers, and turbines of its ships. The procedures in the factory were described on p. 5 (Seidman et al., 1984, HEROID 257).
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	Medium	The retrospective cohort design was appropriate. The study used appropriate methods to calculate SMRs. Poisson distribution assumptions were used to calculate two-sided tests of significance. This study calculated SMRs for increasing cumulative follow-up, adding 5-year increments of elapsed time since first employment (e.g., 5-10y, 5-15y).
	Metric 13:	Statistical Power	Medium	Sample size was adequate (n=820) and mortality was high (>50%). Cancer types were pooled when data were sparse (e.g., gastrointestinal). The authors noted, however, that the number of man-years included in the analyses was short due to the high death rates.
	Metric 14:	Reproducibility of Analyses	Medium	The descriptions of analyses are brief but adequate. Tables included detailed counts of observed and expected deaths.

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Study Citation:	Seidman, H. (1984). Short-term asbestos work exposure and long-term observation.
Health Outcome:	Lung Cancer; Laryngeal Cancer; All cancer mortality; Non-respiratory infectious disease mortality
Target Organ(s):	Mortality: All cause mortality, Lung cancer mortality, Gastro-intestinal cancer (grouped together cancer of esophagus, stomach, and colon-rectum) mortality, Non-infectious respiratory diseases (including asbestosis) mortality, All "asbestos" diseases (lung cancer, gastrointestinal cancer, mesothelioma, cancers of buccal cavity, pharynx, larynx, and kidney and non-infectious respiratory diseases) mortality, All cancer mortality, Larynx, buccal, pharynx cancer mortality, Stomach cancer mortality, Colon-rectum cancer mortality, Pancreas cancer mortality, Other and unspecified cancer mortality, Cardiovascular diseases mortality; Lung/Respiratory: Lung cancer mortality, Non-infectious respiratory diseases (including asbestosis) mortality, Larynx, buccal, pharynx cancer mortality; Cancer/Carcinogenesis: Lung cancer mortality, Gastro-intestinal cancer (grouped together cancer of esophagus, stomach, and colon-rectum) mortality, All cancer mortality, Larynx, buccal, pharynx cancer mortality, Stomach cancer mortality, Colon-rectum cancer mortality, Pancreas cancer mortality, Other and unspecified cancer; Gastrointestinal: Gastro-intestinal cancer (grouped together cancer of esophagus, stomach, and colon-rectum) mortality, Stomach cancer mortality, Colon-rectum cancer mortality, Pancreas cancer mortality; Cardiovascular: Cardiovascular diseases mortality
Asbestos Fiber Type(s):	Asbestos - Amosite (grunerite): 12172-73-5
Linked HERO ID(s):	No linked references.
HERO ID:	257

Domain	Metric		Rating	Comments
	Metric 15:	Statistical Analysis	Medium	The SMR methods used were appropriate.

Additional Comments: This retrospective cohort study evaluated mortality in 820 workers at an amosite factory in New Jersey that operated between 1941 and 1954. Workers were almost exclusively white males. Results are presented as SMRs using the New Jersey population as the referent. The cohort had important strengths. First, analyses included deaths that occurred from 5 to 40 years after employment, incorporating a lag to accommodate disease latency and reducing potential attribution bias. Second, the study reduced the likelihood of healthy worker selection bias by including all workers who were not exposed to asbestos elsewhere regardless of date of initial employment, and regardless of duration of employment. Third, employment patterns facilitated the analysis of mortality in workers with as little as one month of employment, and included multiple time windows of less than one year duration of employment. The authors noted that this cohort offered a unique opportunity to study "men with a very limited duration of intense work exposure to amosite asbestos, followed by long observation". Fourth, with a mean age at employment of more than 40 years (due to the ongoing war "siphoning off" younger men), mortality was high, with deaths accumulating after a relatively short period. 52 deaths occurred within 5-10 years of employment, and cumulative mortality through 40 years of follow-up was high (n=593). Finally, the authors were able to access medical records that appear to have improved the characterization of outcomes such as mesotheliomas. Details on the methods used were not included in this manuscript, but are discussed elsewhere (e.g., Selikoff et al., 1992 HEROID 709720). The study's major limitation is that fiber count data were not available for this facility. Estimates were extrapolated based on measures taken at later dates at other locations operated by the same company, based on professional judgment. Validity of these estimates cannot be ascertained.

Overall Quality Determination — Medium

⋆ No biomarkers were identified for this evaluation.

Study Citation:	Seidman, H., Selikoff, I. J., Gelb, S. K. (1986). Mortality experience of amosite asbestos factory workers: Dose-response relationships 5 to 40 years after onset of short-term work exposure. American Journal of Industrial Medicine 10(5-6):479-514.
Health Outcome:	Lung Cancer; Laryngeal Cancer; GI cancers, Renal/kidney cancers,; Asbestosis; non-infectious pulmonary diseases
Target Organ(s):	Cancer/Carcinogenesis: All cancer, lung cancer, pleural mesothelioma, peritoneal mesothelioma, mesothelioma non-specified, larynx buccal and pharynx cancer, esophagus cancer, stomach cancer, colon-rectum cancer, kidney cancer, bladder cancer, pancreas cancer, other and unspecified cancer mortality; Lung/Respiratory: Lung cancer mortality, Non-infectious pulmonary diseases mortality, Asbestosis mortality; Gastrointestinal: Esophagus cancer mortality, Stomach cancer mortality, Colon-rectum cancer mortality, Pancreas cancer mortality; Renal/Kidney: Kidney cancer mortality, bladder cancer mortality; Cardiovascular: Cardiovascular diseases mortality; Mortality: Lung cancer mortality, Non-infectious pulmonary diseases mortality, Asbestosis mortality, Esophagus cancer mortality, Stomach cancer mortality, Colon-rectum cancer mortality, Pancreas cancer mortality, Kidney cancer mortality, Bladder cancer mortality, Cardiovascular diseases mortality
Asbestos Fiber Type(s):	Asbestos - Amosite (grunerite): 12172-73-5
Linked HERO ID(s):	No linked references.
HERO ID:	290

Domain		Metric	Rating	Comments
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Low	This metric is rated Low because the study or any cited methods source does not explicitly mention the use of PCM or TEM.Authors state that there was ”no direct observations of fiber counts in this factory”. Instead, fiber counts from other Paterson factories were used in this study. There is more information of the earlier version of this study, which reports that that Paterson factory used the same fibers and followed the same production process. Samples were made in October 1971 and followed ”5u + fibers averaged as high as 23 fibers/ml (Seidman et al., 1979). There is no defining of what tools were used to measure fibers in either study.
	Metric 5:	Exposure Levels	Medium	Range of exposure is appropriate, as it ranges in elapsed number of years since onset of work as 5-9 years, 5-14 years, 5-19 years, 5-24 years, 5-29 years, 5-34 years, and 5-39 years. However, the exposure dose is not based on fiber concentration but on exposure time.

Additional Comments:	Please note that this study would not be fully evaluated under the current guidelines. This is due to the low rating for metric 4, as no PCM or TEM was mentioned in the study or a cited sourceThis study is a follow-up to RefID 94625 by the same authors. Comments referencing this study will be cited as (Seidman et al., 1979).Overall, this study provides an analysis of workers from the Paterson factory to that of the general New Jersey population. There is some discrepancy when it comes to the race of the cohort and the comparison groups, and age is not provided in the study. Confidence intervals are also not provided in the study results of SMRs and SIRs, but significant is noted when appropriate. Smoking is not a part of the analysis as a confounder, which may have introduced bias to both the workers and comparison group.

* No biomarkers were identified for this evaluation.

** As described in Appendix B.2 of the *White Paper: Quantitative Approach to the Human Health Assessment for the Risk Evaluation for Asbestos Part 2: Supplemental Evaluation Including Legacy Uses and Associated Disposals of Asbestos*, to be considered as being informative for dose-response analysis, metrics 4 and 5 would need metric ratings of Medium or High. This reference did not satisfy this requirement; therefore data quality evaluation is presented for only for metrics 4 and 5.

Study Citation:	Seidman, H., Selikoff, I. J., Hammond, E. C. (1979). Short-term asbestos work exposure and long-term observation. Annals of the New York Academy of Sciences 330:61-89.
Health Outcome:	Lung Cancer
Target Organ(s):	Mortality: Lung cancer mortality; Cancer/Carcinogenesis: Lung cancer mortality; Lung/Respiratory: Lung cancer mortality
Asbestos Fiber Type(s):	Asbestos - Amosite (grunerite): 12172-73-5
Linked HERO ID(s):	No linked references.
HERO ID:	94625

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Medium	Key elements of the study design were reported within this retrospective cohort study of an initial group of n=933 males recruited to work at an amosite asbestos factory in Paterson, New Jersey from June, 1941 through December, 1945 who were followed up for mortality outcomes from five through 35 years after onset of work. The authors aimed to study a population of men with a limited duration of intense work exposure to amosite asbestos with a long observation period. Authors described the population in the initial years as almost entirely white. Authors noted that n=113 men were excluded from analysis including n=20 with prior asbestos work. Additional men with less than five years of employment were excluded due to leaving work to take up asbestos work elsewhere (n=14), death in the first five years of employment (n=41), and loss to follow-up after leaving work in the first five years of employment (n=38). A total of n=820 male workers were left for the current analysis. The distributions of these exclusions with respect to exposure and outcomes were not reported.
	Metric 2:	Attrition	Medium	Cause of death information was available for all n=528 deaths occurring after 5 years from onset of asbestos work among the n=820 workers in the cohort for study. The authors described a number of workers withdrawn alive at some time between 5 and 35 years of work to include n=5 men lost to follow-up, n=5 men who left the study site work to work elsewhere, and n=155 men who had begun work 1943-1945 but who had not yet attained their 35th year of observation by December 31, 1977. Exposure data for participants and those lost follow-up were not obtained as the study authors noted use of length of time worked in the amosite asbestos factory as the measure of asbestos dose with no measured exposure estimates given for categories of years worked.
	Metric 3:	Comparison Group	Medium	The choice of a reference population is reported as the age- and year-specific white male general New Jersey population for the SMR analyses results. There is potential for healthy worker effect in terms of possible left truncation bias, as the cohort for the current study was restricted to workers with at least five years of employment, such that all workers had to survive for at least five years to be included.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Low	Method of quantifying/counting fibers was not specified.
	Metric 5:	Exposure Levels	Medium	Medium based on use of US PHS NIOSH data (collected via PCM) for asbestos estimates extrapolated from PA and TX plant. Some professional judgement exercised in deriving estimates based on job function but estimates not solely based on judgement.

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Study Citation:	Seidman, H., Selikoff, I. J., Hammond, E. C. (1979). Short-term asbestos work exposure and long-term observation. Annals of the New York Academy of Sciences 330:61-89.
Health Outcome:	Lung Cancer
Target Organ(s):	Mortality: Lung cancer mortality; Cancer/Carcinogenesis: Lung cancer mortality; Lung/Respiratory: Lung cancer mortality
Asbestos Fiber Type(s):	Asbestos - Amosite (grunerite): 12172-73-5
Linked HERO ID(s):	No linked references.
HERO ID:	94625

Domain	Metric		Rating	Comments
	Metric 6:	Temporality	Medium	The study presents an appropriate temporality and the interval between exposure and outcome is appropriate considering the latency of disease. The range of elapsed years since onset of work ranged from 5-10 to 30-35 years.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Medium	Lung Cancer: Lung cancer mortality data for the worker population was described as obtained through death certificate information only for some analyses, as well as according to "best evidence" established from additional information obtained from autopsy, surgical specimens, x-ray films and clinical findings for other analyses. ICD codes were not detailed, however authors noted that coding for the cause of death was that of the VI through VIII revisions of the International List in use in the U.S. from 1949 onward. Data for the number of deaths by cause of death in the New Jersey general white male population through 1975 was described as available through the annual vital statistics publications, with additional data for 1976 obtained from the National Center for Health Statistics. As mortality data for 1977 was not yet available, the study authors extrapolated for 1977 the data from 1970-1976. Authors described additional extrapolations necessary to account for the V to VI revision of the International List, as well as assumptions made in calculations of the comparison population rates for lung cancer, as the numbers of deaths by age were described as available for total cancer of the respiratory system but not for lung cancer specifically for New Jersey white males.
	Metric 8:	Reporting Bias	Medium	There were no concerns for selective reporting. SMRs in Table 2 and mortality rates across age and time since first exposure groups per man years in production workers in Table 3 were reported as single values, with no measures of variation or confidence intervals.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Medium	Other than stratification for years since first exposure and age in SMR results, no additional adjustments or consideration for differences between exposed and comparison groups regarding distributions of relevant covariates (such as smoking status) were detailed. The cohort for study and the comparison population for SMR analyses was restricted to males. The study also notes that the initial group was "almost entirely white."
	Metric 10:	Covariate Characterization	Medium	Although not specified within this occupational study, it is assumed that personnel files were utilized to obtain age and time since first employed/exposed data.

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Study Citation:	Seidman, H., Selikoff, I. J., Hammond, E. C. (1979). Short-term asbestos work exposure and long-term observation. Annals of the New York Academy of Sciences 330:61-89.
Health Outcome:	Lung Cancer
Target Organ(s):	Mortality: Lung cancer mortality; Cancer/Carcinogenesis: Lung cancer mortality; Lung/Respiratory: Lung cancer mortality
Asbestos Fiber Type(s):	Asbestos - Amosite (grunerite): 12172-73-5
Linked HERO ID(s):	No linked references.
HERO ID:	94625

Domain	Metric		Rating	Comments
	Metric 11:	Co-exposure Counfounding	Low	Potential co-exposures were not detailed. The members of the cohort were described only as males recruited to work at an amosite asbestos factory in Paterson, New Jersey from June, 1941 through December, 1945 and followed up for mortality outcomes from five through 35 years after onset of work. Considerations for workers who might have initially left and worked elsewhere with additional exposures but eventually returned to asbestos work were not detailed. However, there was no evidence that there was an unbalanced provision of co-exposures among exposure groups. There is no mention of co-exposure , so Low is appropriate based on that.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	Medium	The study design was appropriate as an early study to address the research aims, however no quantitative measures of exposure were described for the groups utilized within the SMR analyses presented.
	Metric 13:	Statistical Power	Medium	The number of participants (n=820) was adequate, however formal statistical comparisons between exposed and non-exposed workers, or across elapsed years since onset of work groups were not detailed.
	Metric 14:	Reproducibility of Analyses	Medium	The description of SMR analyses and formation of rates for the comparison population was presented in detail and generally sufficient to understand.
	Metric 15:	Statistical Analysis	N/A	Model building was not presented, but the study's approach of calculating SMRs is appropriate.

Additional Comments: This study extended the follow-up of a previous report on the mortality experience of a group of Paterson, New Jersey amosite asbestos factory workers followed from the onset of work, 1941-1945, through 30 years of observation. The current study extended the observation period to 35 years after onset of work and noted that several men previously lost to follow up were located and included in this study reporting mortality experience for workers 5 through 35 years after onset of work. There were no direct asbestos or asbestos dust counts available for this facility. Although authors noted a single average fiber count from 1971 within a similar factory, no other quantitative estimates of exposures were included within the analysis of this population, which reported SMR's across elapsed years since onset of work. Authors noted use of length of time worked in the amosite asbestos factory as a measure of asbestos dosage.

Overall Quality Determination — Medium

* No biomarkers were identified for this evaluation.

Study Citation:	Seidman, H., Selikoff, I. J., Hammond, E. C. (1979). Short-term asbestos work exposure and long-term observation. Annals of the New York Academy of Sciences 330:61-89.
Health Outcome:	all cancers mortality; all cause mortality, all asbestos diseases mortality
Target Organ(s):	Mortality: All cause mortality, All asbestos diseases mortality (asbestosis, other noninfectious pulmonary diseases, lung cancer, mesotheliomas, esophagus cancer, stomach cancer, colon-rectum cancel, laryngeal cancer), All cancers mortality; Cancer/Carcinogenesis: All cancers mortality
Asbestos Fiber Type(s):	Asbestos - Amosite (grunerite): 12172-73-5
Linked HERO ID(s):	No linked references.
HERO ID:	94625

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Medium	Key elements of the study design were reported within this retrospective cohort study of an initial group of n=933 males recruited to work at an amosite asbestos factory in Paterson, New Jersey from June, 1941 through December, 1945 who were followed up for mortality outcomes from five through 35 years after onset of work. Authors described the population in the initial years as almost entirely white. Authors noted that n=113 men were excluded from analysis including n=20 with prior asbestos work. Additional men with less than five years of employment were excluded due to leaving work to take up asbestos work elsewhere (n=14), death in the first five years of employment (n=41), and loss to follow-up after leaving work in the first five years of employment (n=38). A total of n=820 male workers were left for the current analysis. The distributions of these exclusions with respect to exposure and outcomes were not reported.
	Metric 2:	Attrition	Medium	Cause of death information was available for all n=528 deaths occurring after 5 years from onset of asbestos work among the n=820 workers in the cohort for study. The authors described a number of workers withdrawn alive at some time between 5 and 35 years of work to include n=5 men lost to follow-up, n=5 men who left the study site work to work elsewhere, and n=155 men who had begun work 1943-1945 but who had not yet attained their 35th year of observation by December 31, 1977. Exposure data for participants was not obtained as the study authors noted use of length of time worked in the amosite asbestos factory as the measure of asbestos dose with no measured exposure estimates given for categories of years worked.
	Metric 3:	Comparison Group	Medium	The choice of a reference population is reported as the age- and year-specific white male general New Jersey population for the SMR analyses results. There is potential for healthy worker effect in terms of possible left truncation bias, as the cohort for the current study was restricted to workers with at least five years of employment, such that all workers had to survive for at least five years to be included.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Low	Method of quantifying/counting fibers was not specified.
	Metric 5:	Exposure Levels	Medium	Medium based on use of US PHS NIOSH data (collected via PCM) for asbestos estimates extrapolated from PA and TX plant. Some professional judgement exercised in deriving estimates based on job function but estimates not solely based on judgement.
	Metric 6:	Temporality	Medium	The study presents an appropriate temporality and the interval between exposure and outcome is appropriate considering the latency of disease.
Domain 3: Outcome Assessment				

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Study Citation:	Seidman, H., Selikoff, I. J., Hammond, E. C. (1979). Short-term asbestos work exposure and long-term observation. Annals of the New York Academy of Sciences 330:61-89.
Health Outcome:	all cancers mortality; all cause mortality, all asbestos diseases mortality
Target Organ(s):	Mortality: All cause mortality, All asbestos diseases mortality (asbestosis, other noninfectious pulmonary diseases, lung cancer, mesotheliomas, esophagus cancer, stomach cancer, colon-rectum cancel, laryngeal cancer), All cancers mortality; Cancer/Carcinogenesis: All cancers mortality
Asbestos Fiber Type(s):	Asbestos - Amosite (grunerite): 12172-73-5
Linked HERO ID(s):	No linked references.
HERO ID:	94625

Domain	Metric		Rating	Comments
	Metric 7:	Outcome Measurement or Characterization	Medium	Other Cancer(s): SMR results were reported for cumulative probabilities of death from all causes, all asbestos diseases, all cancers, and lung cancer. Additional mortality count data was reported for detailed cancer sites within Tables 3A and 3B, however SMR analyses were not conducted for such detail. Authors noted the “all asbestos diseases” category included asbestosis and other noninfectious pulmonary diseases, lung cancer, mesotheliomas, cancers of the esophagus, stomach and colon-rectum, cancers of the larynx, buccal cavity, pharynx and kidney. Mortality data for the worker population was described as obtained through death certificate information only for some analyses, as well as according to “best evidence” established from additional information obtained from autopsy, surgical specimens, x-ray films and clinical findings for other analyses. ICD codes were not detailed, however authors noted that coding for the cause of death was that of the VI through VIII revisions of the International List in use in the U.S. from 1949 onward. Data for the number of deaths by cause of death in the New Jersey general white male population through 1975 was described as available through the annual vital statistics publications, with additional data for 1976 obtained from the National Center for Health Statistics. As mortality data for 1977 was not yet available, the study authors extrapolated for 1977 the data from 1970-1976. Authors described additional extrapolations necessary to account for the V to VI revision of the International List, as well as assumptions made in calculations of the comparison population rates for lung cancer, as the numbers of deaths by age were described as available for total cancer of the respiratory system but not for lung cancer specifically for New Jersey white males.; Other Non-Cancer Outcomes: SMR results were reported for cumulative probabilities of death from all causes, all asbestos diseases, and all cancers. Additional mortality count data was reported for detailed cancer sites within Tables 3A and 3B, however SMR analyses were not conducted for such detail. Authors noted the “all asbestos diseases” category included asbestosis and other noninfectious pulmonary diseases, lung cancer, mesotheliomas, cancers of the esophagus, stomach and colon-rectum, cancers of the larynx, buccal cavity, pharynx and kidney. Mortality data for the worker population was described as obtained through death certificate information only for some analyses, as well as according to “best evidence” established from additional information obtained from autopsy, surgical specimens, x-ray films and clinical findings for other analyses. ICD codes were not detailed, however authors noted that coding for the cause of death was that of the VI through VIII revisions of the International List in use in the U.S. from 1949 onward. Data for the number of deaths by cause of death in the New Jersey general white male population through 1975 was described as available through the annual vital statistics publications, with additional data for 1976 obtained from the National Center for Health Statistics. As mortality data for 1977 was not yet available, the study authors extrapolated for 1977 the data from 1970-1976. Authors described additional extrapolations necessary to account for the V to VI revision of the International List.

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Study Citation: Seidman, H., Selikoff, I. J., Hammond, E. C. (1979). Short-term asbestos work exposure and long-term observation. Annals of the New York Academy of Sciences 330:61-89.

Health Outcome: all cancers mortality; all cause mortality, all asbestos diseases mortality

Target Organ(s): Mortality: All cause mortality, All asbestos diseases mortality (asbestosis, other noninfectious pulmonary diseases, lung cancer, mesotheliomas, esophagus cancer, stomach cancer, colon-rectum cancel, laryngeal cancer), All cancers mortality; Cancer/Carcinogenesis: All cancers mortality

Asbestos Fiber Type(s): Asbestos - Amosite (grunerite): 12172-73-5

Linked HERO ID(s): No linked references.

HERO ID: 94625

Domain	Metric		Rating	Comments
	Metric 8:	Reporting Bias	Medium	There were no concerns for selective reporting. SMR's in Table 2 and mortality rates across age and time since first exposure groups per man years in production workers in Table 3 were reported as single values, with no measures of variation or confidence intervals.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Medium	Other than stratification for years since first exposure and age in SMR results, no additional adjustments or consideration for differences between exposed and comparison groups regarding distributions of relevant covariates (such as smoking status) were detailed. The cohort for study and the comparison population for SMR analyses was restricted to males.
	Metric 10:	Covariate Characterization	Medium	Although not specified within this occupational study, it is assumed that personnel files were utilized to obtain age and time since first employed/exposed data.
	Metric 11:	Co-exposure Counfounding	Low	Potential co-exposures were not detailed. The members of the cohort were described only as males recruited to work at an amosite asbestos factory in Paterson, New Jersey from June, 1941 through December, 1945 and followed up for mortality outcomes from five through 35 years after onset of work. Considerations for workers who might have initially left and worked elsewhere with additional exposures but eventually returned to asbestos work were not detailed. However, there was no evidence that there was an unbalanced provision of co-exposures among exposure groups. There is no mention of co-exposure, so Low is appropriate based on that.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	Medium	The study design was appropriate as an early study to address the research aims, however no quantitative measures of exposure were described for the groups utilized within the SMR analyses presented.
	Metric 13:	Statistical Power	Medium	The number of participants (n=820) was adequate, however formal statistical comparisons between exposed and non-exposed workers, or across elapsed years since onset of work groups were not detailed.
	Metric 14:	Reproducibility of Analyses	Medium	There was no presentation of analyses presenting results associated with exposures or estimated exposures and no formal statistical analysis was conducted to examine differences between exposure groups as represented by length of time worked. The description of SMR analyses and formation of rates for the comparison population was presented in detail and generally sufficient to understand.
	Metric 15:	Statistical Analysis	Medium	Model building was not presented.

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Study Citation:	Seidman, H., Selikoff, I. J., Hammond, E. C. (1979). Short-term asbestos work exposure and long-term observation. Annals of the New York Academy of Sciences 330:61-89.
Health Outcome:	all cancers mortality; all cause mortality, all asbestos diseases mortality
Target Organ(s):	Mortality: All cause mortality, All asbestos diseases mortality (asbestosis, other noninfectious pulmonary diseases, lung cancer, mesotheliomas, esophagus cancer, stomach cancer, colon-rectum cancel, laryngeal cancer), All cancers mortality; Cancer/Carcinogenesis: All cancers mortality
Asbestos Fiber Type(s):	Asbestos - Amosite (grunerite): 12172-73-5
Linked HERO ID(s):	No linked references.
HERO ID:	94625

Domain	Metric	Rating	Comments
Additional Comments:	This study extended the follow-up of a previous report on the mortality experience of a group of Paterson, New Jersey amosite asbestos factory workers followed from the onset of work, 1941-1945, through 30 years of observation. The current study extended the observation period to 35 years after onset of work and noted that several men previously lost to follow up were located and included in this study reporting mortality experience for workers 5 through 35 years after onset of work. There were no direct asbestos or asbestos dust counts available for this facility. Although authors noted a single average fiber count from 1971 within a similar factory, no other quantitative estimates of exposures were included within the analysis of this population, which reported SMR's across elapsed years since onset of work. Authors noted use of length of time worked in the amosite asbestos factory as a measure of asbestos dosage.		

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation:	Seldén, A. I., Berg, N. P., Lundgren, E. A., Hillerdal, G., Wik, N. G., Ohlson, C. G., Bodin, L. S. (2001). Exposure to tremolite asbestos and respiratory health in Swedish dolomite workers. Occupational and Environmental Medicine 58(10):670-677.
Health Outcome:	Pulmonary Function/Spirometry Results
Target Organ(s):	Lung/Respiratory: Vital capacity (VC), Forced expiratory volume in 1 second (FEV1)
Asbestos Fiber Type(s):	Asbestos - Tremolite: 14567-73-8
Linked HERO ID(s):	No linked references.
HERO ID:	2079021

Domain		Metric	Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Medium	All participants were invited to participate, and ~95% participated. Available information indicates a low risk of selection bias.
	Metric 2:	Attrition	High	Most data was available, however several participants declined to participate in the radiographical portion of the study (n=3), and one participants film could not be retrieved. These participants were excluded from the analysis of pleural plaques.
	Metric 3:	Comparison Group	High	The study population consisted of workers from two different facilities. Based on demographic data from table 3, it appears that these two populations are similar enough to be comparable.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Medium	Fiber counting was conducted using microscopy, and the methodology is well described. Personal air monitoring of total dust and tremolite asbestos was also conducted, but there is no mention of midget impingers; however, the study did specify that "The dust sampling method conformed to the corresponding United States standard and had been used since the 1960s". Overall mean exposure to dust was based on a JEM, but information on how the JEM was derived is not provided.
	Metric 5:	Exposure Levels	Medium	Exposure was adequately measured, able to develop an exposure response estimate.
	Metric 6:	Temporality	Low	Temporality cannot be established in cross-sectional studies.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	High	Pulmonary Function/Spirometry Results: FEV1 and FVC measured using a dry wedge spirometer according to the standards of the American Thoracic Society.
	Metric 8:	Reporting Bias	High	All results are reported, no concerns for reporting bias.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	High	Appropriate adjustments were made. Models were adjusted for age, sex, smoking habits, BMI, and duration of employment.
	Metric 10:	Covariate Characterization	Medium	Covariate data was self-reported on questionnaires.
	Metric 11:	Co-exposure Counfounding	Low	potential co-exposures were not assessed or discussed.
Domain 5: Analysis				

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Study Citation:	Seldén, A. I., Berg, N. P., Lundgren, E. A., Hillerdal, G., Wik, N. G., Ohlson, C. G., Bodin, L. S. (2001). Exposure to tremolite asbestos and respiratory health in Swedish dolomite workers. Occupational and Environmental Medicine 58(10):670-677.
Health Outcome:	Pulmonary Function/Spirometry Results
Target Organ(s):	Lung/Respiratory: Vital capacity (VC), Forced expiratory volume in 1 second (FEV1)
Asbestos Fiber Type(s):	Asbestos - Tremolite: 14567-73-8
Linked HERO ID(s):	No linked references.
HERO ID:	2079021

Domain	Metric		Rating	Comments
	Metric 12:	Study Design and Methods	Medium	Multiple logistic regression was used to determine the association between dust exposure and respiratory symptoms. Lung function was assessed with linear regression models.
	Metric 13:	Statistical Power	Medium	The final sample size was 137, which may be adequate to detect an overall robust effect.
	Metric 14:	Reproducibility of Analyses	Medium	The description of the analysis is adequate to be reproducible.
	Metric 15:	Statistical Analysis	Low	Statistical model building is not discussed. Evaluation of covariates is not discussed, handling of missing data is not discussed, regression model assumptions and linearity are not discussed.

Additional Comments: As QC reviewer, I rate this study medium. The authors investigated exposure to tremolite asbestos and respiratory health among Swedish dolomite workers. While they did not find strong relationships between exposure to tremolite asbestos and respiratory outcomes, they had developed a robust exposure assessment associated the workers. The authors were also able account for potential confounders in their statistical models when assessing the potential impact of exposures on respiratory health outcomes.The measurement exposure (M4) and/or exposure levels (M5) metrics are rated as medium upon review by both set of reviewers. Also, the overall quality determination (OQD) is rated medium. Extraction has been completed and quality control reviewed.

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation:	Sichletidis, L., Chloros, D., Spyratos, D., Haidich, A. B., Fourkiotou, I., Kakoura, M., Patakas, D. (2009). Mortality from occupational exposure to relatively pure chrysotile: A 39-year study. Respiration 78(1):63-68.
Health Outcome:	Lung Cancer; Cardiovascular mortality
Target Organ(s):	Mortality: All-cause mortality; Lung/Respiratory: Lung neoplasms mortality; Cancer/Carcinogenesis: Malignant neoplasms mortality
Asbestos Fiber Type(s):	Asbestos - Chrysotile (serpentine): 12001-29-5
Linked HERO ID(s):	No linked references.
HERO ID:	3079343

Domain		Metric	Rating	Comments
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Low	The paper reported that the plant used chrysotile asbestos with low amphibole contamination, and that exposure was assessed in 32 areas 4 times/year over a mean of 8h (Casella air pump, Millipore AA filters). Fibers were “counted in 100 different optical fields of filter surface” by “contrast phase microscope (x450)”, limited to “fibers with length >5 µm, diameter <3µm and length/diameter ratio $\geq 3/1$” per EEC directive. These data were used to calculate cumulative years and fiber-years of exposure for each participant. The manuscript does not describe the use of detailed employment records to estimate individual exposure.
	Metric 5:	Exposure Levels	Medium	Airborne asbestos fiber concentration was measured at 32 different points 4 times annually. Exposure was highly variable. Median (IQR) fibers/cm3 x years were 44.5 (15.6–66.6) and 54.7 (37.4–71.9) among living and deceased participants, respectively. Exposure was treated continuously.

Additional Comments:	This study analyzed mortality among 317 cement workers at a factory in Greece with low-level exposure to chrysotile asbestos. 52 deaths (16 lung cancer) occurred between 1968 and 2006. SMRs vs the general population indicated decreased overall mortality, suggesting risk of a healthy worker effect (HWE) bias. HRs showed no increase in mortality associated with fiber-years of exposure, and reduced mortality associated with greater years of exposure, while smoking was associated with mortality. These findings led the researchers to postulate that the SMR of 1.7 for lung cancer was largely attributable to smoking. However, failure to account for differential duration of employment - the tendency for earlier “selection of unhealthy people out of the workforce” – recommended to reduce HWE bias, might also contribute to the absence of an association.

* No biomarkers were identified for this evaluation.

** As described in Appendix B.2 of the *White Paper: Quantitative Approach to the Human Health Assessment for the Risk Evaluation for Asbestos Part 2: Supplemental Evaluation Including Legacy Uses and Associated Disposals of Asbestos*, to be considered as being informative for dose-response analysis, metrics 4 and 5 would need metric ratings of Medium or High. This reference did not satisfy this requirement; therefore data quality evaluation is presented for only for metrics 4 and 5.

Study Citation:	Sluis-Cremer, G. K., Hnizdo, E. (1989). Progression of irregular opacities in asbestos miners. British Journal of Industrial Medicine 46(12):846-852.
Health Outcome:	Irregular lung opacities (suggestive of asbestosis)
Target Organ(s):	Lung/Respiratory: Progression of irregular lung opacities suggestive of asbestosis
Asbestos Fiber Type(s):	Asbestos - Crocidolite (riebeckite): 12001-28-4; Asbestos - Amosite (grunerite): 12172-73-5
Linked HERO ID(s):	No linked references.
HERO ID:	3082687

Domain	Metric		Rating	Comments
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Low	The study or any cited methods source does not explicitly mention the use of PCM or TEM.Sluis-Cremer et al. 1989 RefID 3082687: The study used available and ongoing fiber concentration measures (since 1945) at asbestos mines (p. 847). Duration of exposure was estimated based on numbers of shifts worked (280 shifts = 1 year), with fiber-years calculated as duration X concentration. No details on methods used were provided, but the precision and validity of pre-1975 measures are uncertain. (Sluis-Cremer et al. 1990 RefID 3082523 indicates that konimeters and thermal precipitators were used through 1975 when membrane filter methods were initiated). Fiber years before 1970 were estimated based on self-reported work histories; subsequent exposure was continuously computed and updated every 6 months. One concern is the statement that "In the earlier period if the total exposure of the man who left the mine amounted to less than 500 fibre-shifts the exposure was recorded as zero." It is not known if this assumption was applied to any study participants, and if so to how many.
	Metric 5:	Exposure Levels	Medium	Sluis-Cremer et al. 1989 RefID 3082687: The exposure-outcome gradient was assessed using continuous exposure measures that included: years of exposure prior to baseline, years of exposure and fiber-years of exposure among those exposed after baseline (see Table 4). Analyses were also stratified by any vs no exposure after baseline.

Additional Comments:	This large prospective study examined whether asbestos exposure was associated with progression of irregular lung opacities in 1454 asbestos mine workers (67% of participants in an earlier cross-sectional study). Participants had an x-ray taken as part of the baseline study and were identified as having a subsequent x-ray a mean of 8-9 years later. Asbestos exposure before the baseline x-ray was associated with progression among workers regardless of whether exposure was discontinued after that time. Exposure after the 1st x-ray was also associated with progression in the group with such exposure. Indications for the 2nd x-ray, which was not conducted as part of this study, were not discussed. Given the long latency for asbestosis, is a potential concern that in the follow-up time available, the analysis sample of men who had an indication for a follow-up x-ray may not be equally representative of lung changes progressing relatively slowly vs relatively quickly.

* No biomarkers were identified for this evaluation.

** As described in Appendix B.2 of the *White Paper: Quantitative Approach to the Human Health Assessment for the Risk Evaluation for Asbestos Part 2: Supplemental Evaluation Including Legacy Uses and Associated Disposals of Asbestos*, to be considered as being informative for dose-response analysis, metrics 4 and 5 would need metric ratings of Medium or High. This reference did not satisfy this requirement; therefore data quality evaluation is presented for only for metrics 4 and 5.

Study Citation:	Sluis-Cremer, G. K., Hnizdo, E., u Toit, R. S. J. (1990). Evidence for an amphibole asbestos threshold exposure for asbestosis assessed by autopsy in South African asbestos miners. Annals of Occupational Hygiene 34(5):443-451.
Health Outcome:	Asbestosis
Target Organ(s):	Lung/Respiratory: Asbestosis (lung autopsy, histological)
Asbestos Fiber Type(s):	Asbestos - Crocidolite (riebeckite): 12001-28-4; Asbestos - Amosite (grunerite): 12172-73-5; Asbestos - Tremolite: 14567-73-8; Asbestos - Anthophyllite: 17068-78-9
Linked HERO ID(s):	No linked references.
HERO ID:	3082523

Domain	Metric		Rating	Comments
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Low	The study or any cited methods source does not explicitly mention the use of PCM or TEM.Exposure was quantified using available fiber measures and the duration of work at each mine (primarily from annual worker interviews). Chronological exposures were summed; average fiber-years were obtained dividing this sum by years of exposure. Several sources of error are of concern. First, as measurement methods at the mines changed over time, comparability and validity are uncertain, particularly before 1975 when membrane filter measures were initiated. Also, measurement intervals were generally 5-10 years prior to 1965, and subsequently 1-2 years. Second, for workers who stopped mining prior to the start of annual interviewing in 1954, family members provided less reliable work histories. Finally, for smaller mines with limited data, industry mean exposures were used. Details on temporal changes in fiber measurement methods included: (i) 1940-1965 konimeter measures of particles $< 5\mu m$ and aspect ratio ≥ 2; (ii) thermal precipitator (reported to undercount) measures from 1965-1970 of particles $> 5\ \mu m$ and aspect ratio ≥ 3, then 1970-1975 of particles $> 3\mu m$ and maximum length $100\mu m$; and (iii) the International Membrane Filter method from 1975 on (i.e. $> 5\ \mu m$). Unspecified conversion factors were used to improve comparability.
	Metric 5:	Exposure Levels	Medium	The exposure-outcome gradient was assessed using continuous exposure measures that included: age at first exposure, years of exposure, residence time in mining areas, average fiber concentration, and cumulative fiber-years of exposure. Fiber-years, average fiber concentrations, and mining area residence time were also categorized for descriptive analyses (Tables 4-6).

Additional Comments:	This study analyzed associations between multiple measures of asbestos exposure and the probability of asbestosis identified post-mortem in lung tissue among 807 S. African asbestos miners. The aim was to evaluate whether there appears to be a threshold dose below which asbestosis may not occur. The authors found cases of asbestosis among miners exposed to concentrations as low as <=2 fibers/mL (Table 5), and among subjects with >2-5 fiber-years of cumulative exposure (Table 4). Dose-response estimates used continuous exposure variables; however, use of a stepwise algorithm to fit those models is a limitation.2/7/2023 UPDATE: DUE TO CHANGES IN THE GUIDANCE FOR SQE, ALL METRICS RATINGS EXCEPT FOR 4 AND 5 SHOULD BE IGNORED BECAUSE METRIC 4 WAS RATED "LOW".

** As described in Appendix B.2 of the *White Paper: Quantitative Approach to the Human Health Assessment for the Risk Evaluation for Asbestos Part 2: Supplemental Evaluation Including Legacy Uses and Associated Disposals of Asbestos*, to be considered as being informative for dose-response analysis, metrics 4 and 5 would need metric ratings of Medium or High. This reference did not satisfy this requirement; therefore data quality evaluation is presented for only for metrics 4 and 5.

Study Citation:	Smailyte, G., Kurtinaitis, J., Andersen, A. (2004). Cancer mortality and morbidity among Lithuanian asbestos-cement producing workers. Scandinavian Journal of Work, Environment and Health 30(1):64-70.
Health Outcome:	Lung Cancer; Laryngeal Cancer; Stomach, colon, rectal, laryngeal
Target Organ(s):	Mortality: All cause, Infectious disease, Malignant neoplasms, Circulatory diseases, Respiratory diseases, Diseases of the digestive system, Cirrhosis of the liver, Diseases of the genitourinary system; Cancer/Carcinogenesis: Malignant neoplasms, Stomach cancer, Colon and rectum cancer, Lung cancer, Pleura cancer (mesothelioma), Breast cancer, Female genital organs mortality, Alcohol-related cancers, Other types of cancer, Laryngeal cancer; Cardiovascular: Circulatory diseases; Gastrointestinal: Diseases of the digestive system, Stomach cancer, Colon and rectum cancer; Lung/Respiratory: Respiratory disease mortality, Lung cancer, Pleura cancer (mesothelioma), Laryngeal cancer; Reproductive/Developmental: Breast cancer, Female genital organs cancer
Asbestos Fiber Type(s):	Asbestos - Chrysotile (serpentine): 12001-29-5
Linked HERO ID(s):	No linked references.
HERO ID:	3080235

Domain	Metric		Rating	Comments
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Low	The authors highlight that the exposure data for both facilities is limited. No measurements were taken at factory A, so no data is available. Factory B had annual dust mass measurements from 1975-1993, and fibers per milliliter were available for 1996-1998. There was no discussion of the tools used to ascertain these measurements. There is a discussion that preparation and handling of the asbestos products remained largely the same over time, but there were improvements in ventilation.This metric is rated low because the study or any cited methods source does not explicitly mention the use of PCM or TEM.
	Metric 5:	Exposure Levels	Low	There was no information available for exposure levels in factory A. The authors report the dust concentrations of asbestos in factory B varied from 1.9-4.0 mg/m^3 for 1975-89, and was 1.2-2.2 mg/m^3 from 1990-1993. In 1996-1998, the fiber concentration showed the highest levels for workers who fed the mill with asbestos from sacks and for those involved in sawing the end products. The exposure level for these two groups was 0.5-1.0 f/ml.

Additional Comments: There were several concerns with this paper. One that stood out was a lack of exposure measurements for one of the factories included in the study. Another shortcoming was a lack of in-depth description of the analyses that they conducted. There was also a lack of discussion about potential co-exposures participants may have faced. All of these issues contributed to a low confidence rating.NOTE: Under the new guidance, this study would not have undergone further evaluation because metric 4 was rated as low due to no explicit mention of PCM or TEM in this study or cited methods sources.

* No biomarkers were identified for this evaluation.

** As described in Appendix B.2 of the *White Paper: Quantitative Approach to the Human Health Assessment for the Risk Evaluation for Asbestos Part 2: Supplemental Evaluation Including Legacy Uses and Associated Disposals of Asbestos*, to be considered as being informative for dose-response analysis, metrics 4 and 5 would need metric ratings of Medium or High. This reference did not satisfy this requirement; therefore data quality evaluation is presented for only for metrics 4 and 5.

Study Citation:	Soldan, K., Pooley, F. D., Hansen, J., Andersen, A., Chang-Claude, J., Ferro, G., Ohgaki, H., Skov, B. G., Cherrie, J. W., Saracci, R., Boffetta, P. (2006). Lung fibre burden in lung cancer cases employed in the rock and slag wool industry. Annals of Occupational Hygiene 50(3):241-248.
Health Outcome:	Lung Cancer
Target Organ(s):	Cancer/Carcinogenesis: Lung cancer; Mortality: Lung cancer
Asbestos Fiber Type(s):	Asbestos - Amosite (grunerite): 12172-73-5; Asbestos - Crocidolite (riebeckite): 12001-28-4; Asbestos - Chrysotile (serpentine): 12001-29-5; Asbestos - Tremolite: 14567-73-8
Linked HERO ID(s):	No linked references.
HERO ID:	3079871

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	High	This is a retrospective case-control study of male rock and slag workers from seven different factories who died of primary lung cancer between 1971 and 1994 (up to 1996 in Denmark). This study population makes up the European cohort of rock and slag workers from Denmark, Germany, Norway and Sweden. Lung samples were taken from 30 lung cancer cases from the cohort. More details are reported in a previous paper (Kjærheim et al., 2002, HEROID: 6874042), where the original cohort size consisted of 9,174 men.
	Metric 2:	Attrition	High	Of the original 9,174 eligible workers in the cohort, this study only utilized 30 lung samples from cases. Of those 30, 13 cases were deemed to be abnormal lung tissue and were not sent for further pathology/fibre analysis, adequately describing the reason why those cases were excluded.
	Metric 3:	Comparison Group	Medium	This study did not describe the controls, but referenced a previous study (Kjærheim et al., 2002, HEROID: 6874042) where two control series were created and then combined into one control group. Control series 1 consisted of male workers from the same factories who were alive and eligible in the cohort but had died before interviews. Control series 2 consisted of incidence density-sampled controls matched to cases on plant and date of birth.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Medium	Authors report that dust was extracted from lung tissue samples of cases using a F.E.I. Technai 12 analytical transmission electron microscope (TEM). This was completed only once/for one time period.
	Metric 5:	Exposure Levels	Medium	Authors used tertiles for duration of exposure (T1, T2, T3) and for cumulative exposure (T1, T2, T3) for combined amosite and crocidolite concentration (per gram lung tissue * 10^6).
	Metric 6:	Temporality	High	Study consisted of male workers employed from start of production (between 1937 and 1950) until the end of 1976. Follow up occurred from 1971-1996 (1995 for Denmark), presenting appropriate temporality between exposure and outcome.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Medium	Lung Cancer: Lung cancer cases were confirmed by International Classification of Diseases, 9th revision [ICD-9], codes (Kjærheim et al., 2002, HEROID: 6874042). The exact codes were not provided.

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Study Citation:	Soldan, K., Pooley, F. D., Hansen, J., Andersen, A., Chang-Claude, J., Ferro, G., Ohgaki, H., Skov, B. G., Cherrie, J. W., Saracci, R., Boffetta, P. (2006). Lung fibre burden in lung cancer cases employed in the rock and slag wool industry. Annals of Occupational Hygiene 50(3):241-248.
Health Outcome:	Lung Cancer
Target Organ(s):	Cancer/Carcinogenesis: Lung cancer; Mortality: Lung cancer
Asbestos Fiber Type(s):	Asbestos - Amosite (grunerite): 12172-73-5; Asbestos - Crocidolite (riebeckite): 12001-28-4; Asbestos - Chrysotile (serpentine): 12001-29-5; Asbestos - Tremolite: 14567-73-8
Linked HERO ID(s):	No linked references.
HERO ID:	3079871

Domain	Metric		Rating	Comments
	Metric 8:	Reporting Bias	Medium	Findings are reported consistently throughout the paper and are extractable, but they were not complete; Chrysotile and Tremolite concentrations per gram dry lung tissue X 10^6 were reported per sample but were not part of the odds ratios' analyses.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	High	Age, cigarette consumption, and time between end of exposure and lung sampling (clearance time) were adjusted for in all models.
	Metric 10:	Covariate Characterization	High	Authors collected questionnaire responses from relatives of cases and controls with questions regarding demographic variables, residential history, general occupational history, occupational history within the rock, slag and wool (RSW) companies, tobacco smoking and alcohol drinking.
	Metric 11:	Co-exposure Counfounding	Medium	Man-made vitreous fibres (MMVF) are observed and analyzed in this paper alongside asbestos. Authors address these fibres separately and are adjusted for in their respective models.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	Medium	This study uses an appropriate statistical method to address the relationship between the lung asbestos fibres and the variables of estimated exposure, with and without additional variables that may affect fibre retention in lung cancer cases (odds ratio).
	Metric 13:	Statistical Power	Uninformative	This case control study consisted of only 13 cases and controls. Authors mention in the discussion section that this weakness resulted in low statistical power and highlighted that a large pathology department had incinerated many of the eligible samples.
	Metric 14:	Reproducibility of Analyses	Medium	The description of the analysis is sufficient to understand how to conceptually reproduce the analysis with access to the analytic data.
	Metric 15:	Statistical Analysis	Medium	The models for calculating the odds ratios are transparent and authors described which variables were included (except for the exclusion of Chrysotile and Tremolite).
Domain 6: Other (if applicable) Considerations for Biomarker Selection and Measurement (Lakind et al. 2014)				
	Metric 16:	Use of Biomarker of Exposure	Medium	The biomarker is derived from multiple parent chemicals (MMVF, amosite, crocidolite, chrysotile and tremolite)
	Metric 17:	Effect Biomarker	Medium	Thirteen lung tissue samples were used for fibre analysis and fibre burden with validated methods, but an AOP is not clear.
	Metric 18:	Method Sensitivity	Medium	Authors report that "examination of the extracted dust preparationsdetermined fibre type, fibre dimension and numbers of fibres per gram of dry lung tissue. All fibres detected were included, irrespective of size. The limit of detection in all cases was ~0.03 million fibres g^-1 of dried tissue"

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Study Citation:	Soldan, K., Pooley, F. D., Hansen, J., Andersen, A., Chang-Claude, J., Ferro, G., Ohgaki, H., Skov, B. G., Cherrie, J. W., Saracci, R., Boffetta, P. (2006). Lung fibre burden in lung cancer cases employed in the rock and slag wool industry. Annals of Occupational Hygiene 50(3):241-248.
Health Outcome:	Lung Cancer
Target Organ(s):	Cancer/Carcinogenesis: Lung cancer; Mortality: Lung cancer
Asbestos Fiber Type(s):	Asbestos - Amosite (grunerite): 12172-73-5; Asbestos - Crocidolite (riebeckite): 12001-28-4; Asbestos - Chrysotile (serpentine): 12001-29-5; Asbestos - Tremolite: 14567-73-8
Linked HERO ID(s):	No linked references.
HERO ID:	3079871

Domain	Metric		Rating	Comments
	Metric 19:	Biomarker Stability	High	Storage history was known and investigated via death certificates and medical files. When confirmed, a pathologist was contacted to arrange and prepare the samples.
	Metric 20:	Sample Contamination	Medium	There is no information included about contamination.
	Metric 21:	Method Requirements	Low	Authors only discuss using ”a F.E.I. Technai 12 analytical transmission electron microscope (TEM), giving a magnification of 20 000–30 000” for the dust extracted from tissue samples.
	Metric 22:	Matrix Adjustment	Low	No established matrix adjustment was conducted.

Additional Comments: Overall, this study was well done but had a major issue in its sampling. This study has a low sample size which weakens the statistical power and potentially skews the results (deeming the study uninformative). As a result, data were not extracted.

Overall Quality Determination Uninformative

Study Citation:	Sullivan, P. A. (2007). Vermiculite, respiratory disease, and asbestos exposure in Libby, Montana: update of a cohort mortality study. Environmental Health Perspectives 115(4):579-585.
Health Outcome:	Lung Cancer; Asbestosis
Target Organ(s):	Mortality: All causes mortality, Lung cancer mortality, Nonmalignant respiratory disease mortality, Asbestosis mortality; Lung/Respiratory: Lung cancer mortality, Nonmalignant respiratory disease mortality, Asbestosis mortality; Cancer/Carcinogenesis: Lung cancer mortality
Asbestos Fiber Type(s):	Asbestos- Libby amphibole: 1318-09-8; Asbestos- Richterite: 17068-76-7; Asbestos - Winchite: 12425-92-2; Asbestos - Tremolite: 14567-73-8
Linked HERO ID(s):	709497, 709457, 711560, 2238712
HERO ID:	709497

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Medium	Subjects were vermiculite miners, millers, and processors from a mine operating in Libby, Montana. The authors specify that some subjects may have been “assigned jobs in the screening plant, railroad loading dock, expansion plants, or an office located in the town of Libby (several miles from the mine).” The cohort was designed to include all white males hired at Libby from September 1935 to December 1981, and the total cohort was identified in May 1982 and subjects were followed through December 2001. It is not clear exactly how subjects were recruited or identified, though it is implied that the authors used data from an existing NIOSH database. Demographic data was collected from a NIOSH database and then validated against microfilm company records. One person originally identified (presumably from the NIOSH database) was removed due to company records stating that the employee never actually worked. After excluding 9 participants for missing demographic data, there were 1,871 study subjects. However, after additional exclusions based on missing outcome data and to limit the analysis sample to only white men, the final analytic sample consisted of 1,672 workers (Sullivan et al. 2007 HERO ID: 709497).Moolgavkar et al. 2010 (HERO ID: 709457) used the same cohort as Sullivan et al. 2007 (HERO ID: 709497) but they also excluded 10 individuals who were missing vital status and thus resulted in a final analytic sample of 1,662. Bateson et al. 2010 (HERO ID: 2238712) used the same cohort data as Sullivan et al. 2007 (HERO ID: 709497), but do not appear to have made any exclusions for missing data and do not appear to have limited their sample to only white men, resulting in a final sample of 1,871 subjects. However, they also analyzed a sub-cohort of workers only hired after 12/31/1959 (n=880) to control for missing employment data in workers hired earlier. The authors also followed up their participants through 12/31/2006, five years longer than the other studies in this cohort.There is no evidence that the exposure-outcome distribution of those included in these studies is different from those excluded.
	Metric 2:	Attrition	High	In Sullivan et al. 2007 (HERO ID: 709497), after 1,871 subjects were identified for inclusion, 104 were excluded due to not being white males, and 95 were excluded due to dying or being lost to follow-up before 1960. Prior to 1960 comparison rates for asbestosis in NIOSH Life Table Analysis system were not available, requiring exclusion from the analysis sample. In Moolgavkar et al. 2010 (HERO ID: 709457) an additional 10 participants were excluded due to missing vital status, although it is not clear how these cases were handled in the original study. Bateson et al. 2014 (HERO ID: 2238712) does not appear to have made any exclusions. There is overall a low rate of attrition and it is unlikely to be influenced by both exposure and outcome.

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Study Citation:	Sullivan, P. A. (2007). Vermiculite, respiratory disease, and asbestos exposure in Libby, Montana: update of a cohort mortality study. Environmental Health Perspectives 115(4):579-585.
Health Outcome:	Lung Cancer; Asbestosis
Target Organ(s):	Mortality: All causes mortality, Lung cancer mortality, Nonmalignant respiratory disease mortality, Asbestosis mortality; Lung/Respiratory: Lung cancer mortality, Nonmalignant respiratory disease mortality, Asbestosis mortality; Cancer/Carcinogenesis: Lung cancer mortality
Asbestos Fiber Type(s):	Asbestos- Libby amphibole: 1318-09-8; Asbestos- Richterite: 17068-76-7; Asbestos - Winchite: 12425-92-2; Asbestos - Tremolite: 14567-73-8
Linked HERO ID(s):	709497, 709457, 711560, 2238712
HERO ID:	709497

Domain	Metric		Rating	Comments
	Metric 3:	Comparison Group	Medium	In Sullivan et al. 2007 (HERO ID: 709497) and Moolgavkar et al. 2010 (HERO ID: 709457) SMRs were calculated as the primary statistical analysis. Reference mortality rates were pulled from the NIOSH Life Table Analysis system. It is not specified whether this reference population was the general US population or an occupational-only population. Since the analysis samples only contained white males, there was no need to adjust by race or sex. However, SMRs were adjusted for age at risk and calendar-year of follow-up in Sullivan et al. 2007 (HERO ID: 709497). There is no discussion of other SMR adjustments in Moolgavkar et al. 2010 (HERO ID: 709457), but it is possible that they used the same adjustment factors as Sullivan et al. 2007 (HERO ID: 709497), since the authors pulled the majority of their data from that study.Moolgavkar et al. 2010 (HERO ID: 709457) also performed two regression analyses, one of which was only reported to control for year of birth, and another for mesothelioma that did not report any adjustments.Bateson et al. 2014 (HERO ID: 2238712) also conducted a regression analysis and thus participants were compared to each other in statistical analyses. Statistical analysis controlled for age, gender, race, and date of birth to ensure comparisons were appropriate.

Domain 2: Exposure Characterization

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Health Outcome:	Lung Cancer; Asbestosis
Target Organ(s):	Mortality: All causes mortality, Lung cancer mortality, Nonmalignant respiratory disease mortality, Asbestosis mortality; Lung/Respiratory: Lung cancer mortality, Nonmalignant respiratory disease mortality, Asbestosis mortality; Cancer/Carcinogenesis: Lung cancer mortality
Asbestos Fiber Type(s):	Asbestos- Libby amphibole: 1318-09-8; Asbestos- Richterite: 17068-76-7; Asbestos - Winchite: 12425-92-2; Asbestos - Tremolite: 14567-73-8
Linked HERO ID(s):	709497, 709457, 711560, 2238712
HERO ID:	709497

Domain	Metric		Rating	Comments
	Metric 4:	Measurement of Exposure	Medium	In this cohort, all studies used the exact same method of assessing exposure through quantification using PCM and assignment to participants via a job-exposure matrix, based on one used in an earlier NIOSH study (Amandus and Wheeler, 1987 HERO ID: 29839). In Sullivan et al. 2007 (HERO ID: 709497) and Moolgavkar et al. 2010 (HERO ID: 709457) adjustments to the JEM were made, most notably to assign workers with the "common laborer" job assignments or unknown job assignments the average estimated exposure intensity for all unskilled jobs, as opposed to using the relatively low exposure estimate for the mill yard in Libby. Thus, estimates of cumulative exposure were higher in this cohort study than other studies using the same JEM. Obtaining work histories for these studies resulted in additional jobs that were not detailed in the original NIOSH JEM. Exposure estimates for these jobs and corresponding calendar periods were extrapolated based on review of exposure records from other studies of Libby workers and professional judgment. Work history to assign exposure was gathered from a NIOSH database created in the 1980's and was validated against microfilm company records. The authors do not specify how many samples were analyzed for use in the JEM. In statistical analysis results were presented in terms of cumulative exposure (fiber/cc-years).The authors in Bateson et al. 2014 (HERO ID: 2238712) used the same exposure data as the other studies in this cohort, but they were concerned about potential exposure misclassification due to the missing job data indicated in the Sullivan et al. 2007 (HERO ID: 709497) study, which was originally compensated for by assigning them the average level of exposure. The authors in Bateson et al. 2014 (HERO ID: 2238712) noted that most workers missing job data were hired before 1960, and thus analyzed both the full cohort and only those hired after 12/31/1959 to address this issue. The authors also reported residence-time-weighted exposure, which is a metric that provides additional weight to earlier exposure. In statistical analysis results were presented in terms of cumulative exposure (fiber/cc-years).
	Metric 5:	Exposure Levels	Medium	All studies in the cohort have an adequate distribution of exposure to detect an effect. All studies report at least three levels of exposure or use a continuous model of exposure in their SMR analyses.
	Metric 6:	Temporality	High	In all studies there was a minimum of 20 years of follow-up since a participant's first exposure, and the workers hired earliest had >65 years of prior exposure data since the study was designed to capture those employed between 1935 and 1981.
Domain 3: Outcome Assessment				

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Study Citation:	Sullivan, P. A. (2007). Vermiculite, respiratory disease, and asbestos exposure in Libby, Montana: update of a cohort mortality study. Environmental Health Perspectives 115(4):579-585.
Health Outcome:	Lung Cancer; Asbestosis
Target Organ(s):	Mortality: All causes mortality, Lung cancer mortality, Nonmalignant respiratory disease mortality, Asbestosis mortality; Lung/Respiratory: Lung cancer mortality, Nonmalignant respiratory disease mortality, Asbestosis mortality; Cancer/Carcinogenesis: Lung cancer mortality
Asbestos Fiber Type(s):	Asbestos- Libby amphibole: 1318-09-8; Asbestos- Richterite: 17068-76-7; Asbestos - Winchite: 12425-92-2; Asbestos - Tremolite: 14567-73-8
Linked HERO ID(s):	709497, 709457, 711560, 2238712
HERO ID:	709497

Domain	Metric		Rating	Comments
	Metric 7:	Outcome Measurement or Characterization	Medium	Lung Cancer: Vital status was determined through 2001 by the National Death Index resources, the Social Security Administration resources, the internet (Ancestry.com; RootsWeb.com, and electronic links to state death records). And a tracking service. Workers found to be alive on or after 1/1/1979, when the National Death Index tracking began, but not found in the Index, were assumed to be alive as of 12/31/2001. Vital status follow-up was successful for 97.8% of the cohort. While some of the resources have a high degree of certainty, others such as the internet-based resources are of questionable quality. There is no explanation of what percentage each resource was used to ascertain vital status, but the more reliable method such as National Death Index are likely to be more informative and thus used more often. Thus, while there is some uncertainty that the vital status ascertainment was fully accurate, it is unlikely that a significant number of participants would have their vital status changed or that this would be related to their exposure status. Additionally, Bateson et al. 2014 (HERO ID: 2238712) report that all outcome data was retrieved from the National Death Index.For 97% of the participants known to be deceased, exact cause of death was pulled from death certificates and coded using the ICD codes relevant at the time of death, ranging from ICD-8 to ICD-10. Deaths prior to 1979 were coded by a single National Center for Health Statistics-trained nosologist; after 1979 ICD codes were obtained from the National Death Index. Final results present ICD-9 codes, so it can be assumed that all codes were converted to that system, although their methodology is not explained.ICD-9 code 162 was reported for lung cancer.; Asbestosis: Vital status was determined through 2001 by the National Death Index resources, the Social Security Administration resources, the internet (Ancestry.com; RootsWeb.com, and electronic links to state death records). And a tracking service. Workers found to be alive on or after 1/1/1979, when the National Death Index tracking began, but not found in the Index, were assumed to be alive as of 12/31/2001. Vital status follow-up was successful for 97.8% of the cohort. While some of the resources have a high degree of certainty, others such as the internet-based resources are of questionable quality. There is no explanation of what percentage each resource was used to ascertain vital status, but the more reliable method such as National Death Index are likely to be more informative and thus used more often. Thus, while there is some uncertainty that the vital status ascertainment was fully accurate, it is unlikely that a significant number of participants would have their vital status changed or that this would be related to their exposure status. Additionally, Bateson et al. 2014 (HERO ID: 2238712) report that all outcome data was retrieved from the National Death Index.For 97% of the participants known to be deceased, exact cause of death was pulled from death certificates and coded using the ICD codes relevant at the time of death, ranging from ICD-8 to ICD-10. Deaths prior to 1979 were coded by a single National Center for Health Statistics-trained nosologist; after 1979 ICD codes were obtained from the National Death Index. Final results present ICD-9 codes, so it can be assumed that all codes were converted to that system, although their methodology is not explained.ICD-9 code 151 was reported for asbestosis.; Other Non-Cancer Outcomes: Vital status was determined through 2001 by the National Death Index resources, the Social Security Administration resources, the internet (Ancestry.com; RootsWeb.com, and electronic links to state death records). And a tracking service. Workers found to be alive on or af

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Study Citation:	Sullivan, P. A. (2007). Vermiculite, respiratory disease, and asbestos exposure in Libby, Montana: update of a cohort mortality study. Environmental Health Perspectives 115(4):579-585.
Health Outcome:	Lung Cancer; Asbestosis
Target Organ(s):	Mortality: All causes mortality, Lung cancer mortality, Nonmalignant respiratory disease mortality, Asbestosis mortality; Lung/Respiratory: Lung cancer mortality, Nonmalignant respiratory disease mortality, Asbestosis mortality; Cancer/Carcinogenesis: Lung cancer mortality
Asbestos Fiber Type(s):	Asbestos- Libby amphibole: 1318-09-8; Asbestos- Richterite: 17068-76-7; Asbestos - Winchite: 12425-92-2; Asbestos - Tremolite: 14567-73-8
Linked HERO ID(s):	709497, 709457, 711560, 2238712
HERO ID:	709497

Domain	Metric		Rating	Comments
	Metric 8:	Reporting Bias	High	All stated outcomes are reported in the results.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Medium	In both Sullivan et al. 2007 (HERO ID: 709497) and Moolgavkar et al. 2010 (HERO ID: 709457) SMRs were calculated and the sample only included white males, so there was no need to adjust for race and gender. While Sullivan et al. 2007 (HERO ID: 709497) state that they also adjusted for age at risk and calendar year of follow-up, there is no discussion of other SMR adjustments in Moolgavkar et al. 2010 (HERO ID: 709457). It is unlikely that they did not adjust for age, but this cannot be assumed. Moolgavkar et al. 2010 (HERO ID: 709457) also performed a Cox proportional hazards model analysis in which they adjusted for year of birth. They state that they used year of birth as a “rough surrogate” for smoking habits as well, which is not a sufficient consideration for smoking. Bateson et al. 2014 (HERO ID: 2238712) also performed a Cox proportional hazards model, and adjustments were made for gender, race, date of birth, and age. This metric would be rated as “Low” for lung cancer-related outcomes if the only analyses were regression analyses due to the lack of formal adjustment for smoking habits.
	Metric 10:	Covariate Characterization	Medium	All covariate information was obtained from the NIOSH database and cross-checked against microfilmed company records.
	Metric 11:	Co-exposure Counfounding	Low	In this occupational setting, no co-exposures are adjusted for. Sullivan et al. 2007 (HERO ID: 709497) notes that there was insufficient data to estimate exposure to other contaminants such as diesel particulate generated by mine machinery, or exposure to silica.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	Medium	The use of SMRs and regression analyses to understand the long-term impact of asbestos exposure on mortality is appropriate. The use of a cohort design is also appropriate to assess outcomes with a long latency such as lung cancer.
	Metric 13:	Statistical Power	Medium	The number of participants used in the analysis sample varies by study, but is always sufficiently large to detect an effect. Sullivan et al. 2007 (HERO ID: 709497) had a final analysis sample of 1,672; Moolgavkar et al. 2010 (HERO ID: 709457) had a final analysis sample of 1,662; and Bateson et al. 2014 (HERO ID: 2238712) had a final analysis sample of 1,871 and sub-cohort samples of 991 and 890. There is not a significant discussion of power, but Sullivan et al. 2007 (HERO ID: 709497) states that the study has low power for lung cancer outcomes at lower exposure levels.

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Health Outcome:	Lung Cancer; Asbestosis
Target Organ(s):	Mortality: All causes mortality, Lung cancer mortality, Nonmalignant respiratory disease mortality, Asbestosis mortality; Lung/Respiratory: Lung cancer mortality, Nonmalignant respiratory disease mortality, Asbestosis mortality; Cancer/Carcinogenesis: Lung cancer mortality
Asbestos Fiber Type(s):	Asbestos- Libby amphibole: 1318-09-8; Asbestos- Richterite: 17068-76-7; Asbestos - Winchite: 12425-92-2; Asbestos - Tremolite: 14567-73-8
Linked HERO ID(s):	709497, 709457, 711560, 2238712
HERO ID:	709497

Domain	Metric		Rating	Comments
	Metric 14:	Reproducibility of Analyses	Medium	While several details are not explained in detail, such as how the ICD-8 through ICD-10 codes were converted to ICD-9 codes, overall the descriptions of methods across the cohort are detailed enough that it would be possible to reproduce the results given access to the analytic data.
	Metric 15:	Statistical Analysis	Medium	While there is no formal discussion of assumptions in statistical models in both Sullivan et al. 2007 (HERO ID: 709497) and Bateson et al. 2014 (HERO ID: 2238712, there are no assumptions in SMR or Cox proportional hazards model that would reasonably expect to be unmet. Moolgavkar et al. 2010 (HERO ID: 709457) contains those same analyses without a formal discussion of assumptions, but also analyses mesothelioma using a maximum likelihood equation in which they assume a Poisson distribution.

Additional Comments: In these cohort studies of Libby, Montana employees exposure was measured via PCM and assigned using a JEM. Participants were followed up for a minimum of 20 years from first exposure, and mortality outcomes were examined in relation to asbestos exposure through SMR and regression analysis. While there is some potential for outcome and exposure misclassification, the impact of potential misclassification is unlikely to significantly bias the results of the cohort. Significant effects were found for most outcomes, in particular asbestosis and lung cancer.The measurement exposure (M4) and/or exposure levels (M5) metrics are rated as medium upon review by both set of reviewers. Also, the overall quality determination (OQD) is rated medium. Extraction has been completed and quality control reviewed.

Overall Quality Determination **Medium**

* No biomarkers were identified for this evaluation.

Study Citation:	Sullivan, P. A. (2007). Vermiculite, respiratory disease, and asbestos exposure in Libby, Montana: update of a cohort mortality study. Environmental Health Perspectives 115(4):579-585.
Health Outcome:	Asbestosis
Target Organ(s):	Mortality: All cancer mortality, Cancer of the pleura mortality, Cancer of unspecified sites mortality, Connective tissue cancer mortality, Chronic obstructive pulmonary disease mortality, Other nonmalignant respiratory disease mortality (non-asbestosis, non-COPD); Cancer/Carcinogenesis: All cancer mortality, Cancer of the pleura mortality, Cancer of unspecified sites mortality, Connective tissue cancer mortality; Lung/Respiratory: Cancer of the pleura mortality, Chronic obstructive pulmonary disease mortality, Other nonmalignant respiratory disease mortality (non-asbestosis, non-COPD); Skin/Connective Tissue: Connective tissue cancer mortality
Asbestos Fiber Type(s):	Asbestos- Libby amphibole: 1318-09-8; Asbestos- Richterite: 17068-76-7; Asbestos - Winchite: 12425-92-2; Asbestos - Tremolite: 14567-73-8
Linked HERO ID(s):	709497, 709457, 711560, 2238712
HERO ID:	709497

Domain	Metric		Rating	Comments
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Medium	In this cohort, all studies used the exact same method of assessing exposure through quantification using PCM and assignment to participants via a job-exposure matrix, based on one used in an earlier NIOSH study (Amandus and Wheeler, 1987 HERO ID: 29839). In Sullivan et al. 2007 (HERO ID: 709497) and Moolgavkar et al. 2010 (HERO ID: 709457) adjustments to the JEM were made, most notably to assign workers with the “common laborer” job assignments or unknown job assignments the average estimated exposure intensity for all unskilled jobs, as opposed to using the relatively low exposure estimate for the mill yard in Libby. Thus, estimates of cumulative exposure were higher in this cohort study than other studies using the same JEM. Additionally, obtaining work histories for these studies resulted in additional jobs that were not detailed in the original NIOSH JEM. Exposure estimates for these jobs and corresponding calendar periods were extrapolated based on review of exposure records from other studies of Libby workers and professional judgment. Work history to assign exposure was gathered from a NIOSH database created in the 1980’s and was validated against microfilm company records. The authors do not specify how many samples were analyzed for use in the JEM. In statistical analysis results were presented in terms of cumulative exposure (fiber/cc-years).The authors in Bateson et al. 2014 (HERO ID: 2238712) were concerned about potential exposure misclassification due to the missing job data indicated in the Sullivan et al. 2007 study, which was originally compensated for by assigning them the average level of exposure. The authors in Bateson et al. 2014 (HERO ID: 2238712) noted that most workers missing job data were hired before 1960, and thus analyzed both the full cohort and only those hired after 12/31/1959 to address this issue. The authors also reported residence-time-weighted exposure, which is a metric that provides additional weight to earlier exposure. In statistical analysis results were presented in terms of cumulative exposure (fiber/cc-years).
	Metric 5:	Exposure Levels	Low	All outcome evaluated in this form were only analyzed as ”unexposed vs, exposed”, thus limting their usefulness in dose-response analysis.

Additional Comments: The outcomes in this evaluation did not meet the criteria for dose-response analysis due to a ”Low” rating for Metric 5.

** As described in Appendix B.2 of the *White Paper: Quantitative Approach to the Human Health Assessment for the Risk Evaluation for Asbestos Part 2: Supplemental Evaluation Including Legacy Uses and Associated Disposals of Asbestos*, to be considered as being informative for dose-response analysis, metrics 4 and 5 would need metric ratings of Medium or High. This reference did not satisfy this requirement; therefore data quality evaluation is presented for only for metrics 4 and 5.

Study Citation:	Suraya, A., Nowak, D., Sulistomo, A. W., Ghanie Icksan, A., Syahruddin, E., Berger, U., Bose-O'Reilly, S. (2020). Asbestos-Related Lung Cancer: A Hospital-Based Case-Control Study in Indonesia. International Journal of Environmental Research and Public Health 17(2):591-591.
Health Outcome:	Lung Cancer
Target Organ(s):	Lung/Respiratory: Lung cancer; Cancer/Carcinogenesis: Lung cancer
Asbestos Fiber Type(s):	Asbestos - Not specified: 1332-21-4
Linked HERO ID(s):	No linked references.
HERO ID:	6868329

Domain	Metric		Rating	Comments
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Low	The cumulative occupational asbestos exposure was expressed in fiber-years, which was fiber concentration in weighted arithmetic mean (WAM), expressed in fiber/milliliter (f/mL) of air multiplied by the total duration of exposure in years. It was not mentioned that TEM and PCM were used.
	Metric 5:	Exposure Levels	Medium	Range of exposure sufficient to develop exposure-response estimate (Table 5). Exposed >=10 fiber-years, exposed <10 fiber-years, not exposed referent groups.

Additional Comments: "Five subjects were suspected mesothelioma cases, three subjects were suspected asbestosis, and two subjects were suspected of interstitial lung diseases," however not analyzed for or confirmed so did not include as outcomes. Metric 4 low, so stopped evaluation.

** As described in Appendix B.2 of the *White Paper: Quantitative Approach to the Human Health Assessment for the Risk Evaluation for Asbestos Part 2: Supplemental Evaluation Including Legacy Uses and Associated Disposals of Asbestos*, to be considered as being informative for dose-response analysis, metrics 4 and 5 would need metric ratings of Medium or High. This reference did not satisfy this requirement; therefore data quality evaluation is presented for only for metrics 4 and 5.

Study Citation:	Szeszenia-Dąbrowska, N., Wilczyńska, U., Szymczak, W., Strzelecka, A. (2002). Mortality study of workers compensated for asbestosis in Poland, 1970-1997. International Journal of Occupational Medicine and Environmental Health 15(3):267-278.
Health Outcome:	Lung Cancer; Ovarian Cancer; Laryngeal Cancer; Rectum and anus, liver, stomach, gallbladder, pancreas, prostate, bladder, kidney, brain, thyroid, bone, skin, breast; Asbestosis; Circulatory system diseases, respiratory system diseases, digestive system diseases, genitourinary system diseases, musculoskeletal system diseases, ill-defined conditions
Target Organ(s):	Lung/Respiratory: Respiratory diseasesMalignant neoplasms; Mortality: Malignant neoplasmsPancreas cancer
Asbestos Fiber Type(s):	Asbestos - Not specified: 1332-21-4
Linked HERO ID(s):	No linked references.
HERO ID:	3080436

Domain	Metric		Rating	Comments
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Low	The authors do not describe the process used to determine asbestos exposure concentrations. It is mentioned that ”weighted asbestos concentrations, expressed in mg/m^3 of air were usually the basis for assessing the exposure” (Szeszenia-Dąbrowska et al., 2002).
	Metric 5:	Exposure Levels	Medium	The authors provide information on the estimated exposure that workers in various settings experienced during their tenure.

Additional Comments:	This study assessed the risk of asbestos-related malignancies among individuals with diagnosed asbestosis. This study provided a lot of information on SMR for individuals diagnosed with asbestosis in Poland, using the general population as the comparison group. When it comes exposure of interest, the authors used weighted asbestos concentrations to assessing exposures; they did not provide details about the methods and equipment used to generate these values. On the other hand, they used ICD-9 codes to ascertain health and mortality outcomes.While information on the measurement of exposure metric (M4) to assess exposure was limited or rated low. The exposure levels metric (M5) information reported was adequate or rated medium to determine exposure-response relationships. The overall rating for this outcome/study is medium.

* No biomarkers were identified for this evaluation.

** As described in Appendix B.2 of the *White Paper: Quantitative Approach to the Human Health Assessment for the Risk Evaluation for Asbestos Part 2: Supplemental Evaluation Including Legacy Uses and Associated Disposals of Asbestos*, to be considered as being informative for dose-response analysis, metrics 4 and 5 would need metric ratings of Medium or High. This reference did not satisfy this requirement; therefore data quality evaluation is presented for only for metrics 4 and 5.

Study Citation:	Tamura, M., Okamoto, Y., Tokuyama, T., Yoneda, T., Kasuga, H., Miyazaki, R., Narita, N. (1998). Correlation of total amount of exposure and dust concentration at first exposure to chest X-P course findings in asbestos plant employees. International Congress Series, vol. 1153 :653-657.
Health Outcome:	Asbestosis
Target Organ(s):	Lung/Respiratory: Asbestosis
Asbestos Fiber Type(s):	Asbestos - Chrysotile (serpentine): 12001-29-5
Linked HERO ID(s):	No linked references.
HERO ID:	6861363

Domain	Metric		Rating	Comments
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Low	The method of quantifying/counting fibers was not specified by the authors.
	Metric 5:	Exposure Levels	Low	The authors only reported yearly fiber concentrations from 1945-1966.

Additional Comments: None

* No biomarkers were identified for this evaluation.

** As described in Appendix B.2 of the *White Paper: Quantitative Approach to the Human Health Assessment for the Risk Evaluation for Asbestos Part 2: Supplemental Evaluation Including Legacy Uses and Associated Disposals of Asbestos*, to be considered as being informative for dose-response analysis, metrics 4 and 5 would need metric ratings of Medium or High. This reference did not satisfy this requirement; therefore data quality evaluation is presented for only for metrics 4 and 5.

Study Citation:	Terra-Filho, M., Bagatin, E., Nery, L. E., Nápolis, L. M., Neder, J. A., de Souza Portes Meirelles, G., Silva, C. I., Muller, N. L. (2015). Screening of miners and millers at decreasing levels of asbestos exposure: comparison of chest radiography and thin-section computed tomography. PLoS ONE 10(3):e0118585.
Health Outcome:	Asbestosis; Pulmonary Function/Spirometry Results; Pleural Plaques; interstitial abnormalities
Target Organ(s):	Lung/Respiratory: lung function (FVC, FEV1, FVC/FEV1, FEF25-75%), Asbestosis, pleural abnormalities, interstitial abnormalities
Asbestos Fiber Type(s):	Asbestos - Chrysotile (serpentine): 12001-29-5; Asbestos - Tremolite: 14567-73-8
Linked HERO ID(s):	No linked references.
HERO ID:	3077807

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Medium	Some key elements of the study design were not present but available information indicates a low risk of selection bias. All workers were employed at an asbestos mining and milling company based in Brazil. Participants had worked at the company for at least a year (Bagatin et al., 2005 RefID 2078960). To capture the development of asbestos mining and milling in the country, four groups were created from different time periods: Group 1 taking place in 1940-1966, Group 2 in 1967-1976, Group 3 in 1977-1980, and Group 4 taking place after 1981. All groups were exposed to chrysotile and Group 1 was also exposed to tremolite. Characteristics such as gender, age, time of exposure, smoking, and mean spirometry measures are provided in Table 1. Exclusion criteria are not known. While recruitment methods aren't clear, Bagatin et al., 2005 RefID 2078960 stated a four-year "multi-institutional effort, which included local municipalities and union workers, was responsible for recruiting the subjects who participated in the study."
	Metric 2:	Attrition	High	This study reports cross-sectional retrospective data and thus subject withdrawal from the study is not of concern. Outcome and exposure data appear to be complete.
	Metric 3:	Comparison Group	Medium	Differences in SES or race/ethnicity are plausible given that the groups represent two different regions of Brazil (Bahia and Goias) but not provided in the study. Nonetheless, all subjects appear to be recruited from the same eligible population and appear to be similar. Healthy worker effect may be of concern due to spirometric values being compared to predicted values of the adult Brazilian population.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	High	For Groups 3 and 4 (after 1976), airborne samples from occupational settings were routinely collected via a constant-flow sampler, followed by a membrane filter to collect fibers and PCM to count fibers.
	Metric 5:	Exposure Levels	Medium	The range and distribution of exposure was sufficient to develop and exposure-response estimate. Mean cumulative exposure for groups were: "Group I: 110.9 $\pm$ 140.3 fibres-cc-years; Group II: 44.1 $\pm$ 49.4 fibres-cc-years; Group III: 7.6 $\pm$ 5.4 fibres-cc-years; Group IV: 3.6 $\pm$ 4.4 fibres-cc-years"

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Health Outcome:	Asbestosis; Pulmonary Function/Spirometry Results; Pleural Plaques; interstitial abnormalities
Target Organ(s):	Lung/Respiratory: lung function (FVC, FEV1, FVC/FEV1, FEF25-75%), Asbestosis, pleural abnormalities, interstitial abnormalities
Asbestos Fiber Type(s):	Asbestos - Chrysotile (serpentine): 12001-29-5; Asbestos - Tremolite: 14567-73-8
Linked HERO ID(s):	No linked references.
HERO ID:	3077807

Domain	Metric		Rating	Comments
	Metric 6:	Temporality	Medium	The longitudinal analysis conducted in the study established temporality but adequate follow-up is unclear. 301 subjects who were free of any asbestos-related abnormalities were first evaluated in 1997-2000 and then reevaluated in 2007-2010 which seems to imply a 10-year latency period, though it's not clear if a subject evaluated in 2000 and would've been reevaluated in 2007 (i.e. 7-year latency which is grounds for "Low"). For the cross-sectional data, temporality is unclear. Although exposure measurements are retrospective, it is unclear, if signs of adverse health outcomes preceded exposure as the health history of these workers at the beginning of employment is not available.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	High	Asbestosis: Determined by two independent thoracic radiologists who knew about subjects' exposure to asbestos but were blinded to other demographic and lung function characteristics. Readers assessed different kinds of pulmonary abnormalities via Thin-section computed tomography (CT) images to determine if they were or not "definitely-indicative" of lung fibrosis compatible with asbestosis.; Pulmonary Function/Spirometry Results: FVC, FEV1, FEV1/FVC ratio, and forced expiratory flow between 25% and 75% of FVC (FEF25-75%) were measured using a calibrated pneumotachograph in Multispiro System.; Pleural Plaques: Through chest radiography (CXR), pleural plaques were determined by three blinded radiologists who followed ILO standards for classification. Through Thin-section CT scans (via X-vision scanner), pleural plaques were assessed by two independent thoracic radiologists who knew about subjects' exposure to asbestos but were blinded to other demographic and lung function characteristics. Presence of pleural plaques was determined if the follow pleural abnormality was found: "circumscribedquadrangular pleural elevation with sharp borders and soft tissue density, possibly calcified, in typical posterolateral and anterolateral location."; Other Non-Cancer Outcomes: Through chest radiography (CXR), interstitial abnormalities were determined by three blinded radiologists who followed ILO standards for classification. Through Thin-section CT scans (via X-vision scanner), interstitial abnormalities were assessed by two independent thoracic radiologists who knew about subjects' exposure to asbestos but were blinded to other demographic and lung function characteristics.
	Metric 8:	Reporting Bias	High	All results seem to be reported in all aspects of the report, including p-values sample sizes, confidence intervals, and standard deviations. Footnotes are provided for additional clarification on analyses.
Domain 4: Potential Confounding / Variability Control				

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Study Citation:	Terra-Filho, M., Bagatin, E., Nery, L. E., Nápolis, L. M., Neder, J. A., de Souza Portes Meirelles, G., Silva, C. I., Muller, N. L. (2015). Screening of miners and millers at decreasing levels of asbestos exposure: comparison of chest radiography and thin-section computed tomography. PLoS ONE 10(3):e0118585.
Health Outcome:	Asbestosis; Pulmonary Function/Spirometry Results; Pleural Plaques; interstitial abnormalities
Target Organ(s):	Lung/Respiratory: lung function (FVC, FEV1, FVC/FEV1, FEF25-75%), Asbestosis, pleural abnormalities, interstitial abnormalities
Asbestos Fiber Type(s):	Asbestos - Chrysotile (serpentine): 12001-29-5; Asbestos - Tremolite: 14567-73-8
Linked HERO ID(s):	No linked references.
HERO ID:	3077807

Domain	Metric		Rating	Comments
	Metric 9:	Covariate Adjustment	Medium	Authors mentioned that confounders were controlled for in logistic regression analyses, but the exact variables considered as confounding are not specified. Knowing the exact confounding variables is critical given that the groups represent different regions of Brazil, which is known to be a culturally-diverse country. Table 4 presents smoking adjusted estimates for lung function are provided.
	Metric 10:	Covariate Characterization	Medium	As an occupational study, it can be assumed that covariate data were collected from personnel records. Information on gender, age, time of exposure, smoking history, and mean spirometric test values are provided in Table 1.
	Metric 11:	Co-exposure Counfounding	Low	Co-exposures were not explicitly assessed. Although subjects came from an asbestos mining and milling company, co-exposures may be likely for workers present prior to 1976 where no formal fiber counting method was established yet. In the cases of asbestosis, the etiology of asbestosis rules out other potential co-exposures.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	Medium	The study design was appropriate to address the research question. Kolmogorov-Smirnov test was used to test for normality. “Categorical variables were tested using the chi-squared or Fisher exact tests. Continuous variables were compared with analysis of variance (ANOVA) or Kruskal-Wallis test, with Bonferroni correction for multiple comparisons.” Additionally, Poisson regression models were used for the longitudinal analyses.
	Metric 13:	Statistical Power	Medium	The number of participants (n = 1418) seemed adequate to detect an effect in all groups (n= 123, 600, 479, 216). The case-control study had small sample sizes (cases = 73; controls = 21).
	Metric 14:	Reproducibility of Analyses	Medium	The description of the analyses is sufficient to understand how to conceptually reproduce the analysis with access to the analytic data.
	Metric 15:	Statistical Analysis	Low	Description of assumptions made in the models are not provided.

Additional Comments: Prior to 1976, no formal fiber measurement was used. As a result, a subjective, logarithmic scale was used to estimate levels in groups 1 and 2. Exposure estimates in Groups 1 and 2 may not be reliable due to the lack of a formal fiber counting method during the time frames of each group.

Overall Quality Determination — Medium

* No biomarkers were identified for this evaluation.

Study Citation:	van Cleemput, J., de Raeve, H., Verschakelen, J. A., Rombouts, J., Lacquet, L. M., Nemery, B. (2001). Surface of localized pleural plaques quantitated by computed tomography scanning: No relation with cumulative asbestos exposure and no effect on lung function. American Journal of Respiratory and Critical Care Medicine 163(3 Pt 1):705-710.
Health Outcome:	Pulmonary Function/Spirometry Results; Pleural Plaques
Target Organ(s):	Lung/Respiratory: Size of pleural plaques, Pulmonary function: FEV1, FVC, and transfer factor for carbon monoxide
Asbestos Fiber Type(s):	Asbestos - Amosite (grunerite): 12172-73-5; Asbestos - Chrysotile (serpentine): 12001-29-5
Linked HERO ID(s):	No linked references.
HERO ID:	783706

Domain	Metric		Rating	Comments
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Low	The authors did not specify the method for quantifying fibers so it is unknown whether PCM, TEM, or another microscopy method was used, but exposure was quantified in fiber-years/ml. Fiber measurements from 1970-1985 were obtained by static sampling during peak installation activities, which the authors noted may have contributed to overestimations. Measurements after 1985 were obtained by personal monitoring that measured 8-h time-weighted personal exposures, which likely better captured true exposures.
	Metric 5:	Exposure Levels	Medium	There was a sufficiently wide range and distribution of exposure. The study used a continuous measurement of cumulative asbestos exposure with estimates ranging from 16.4 to 98.7 fiber-years/ml with a mean of 26.3 +/- 12.6 fiber-years/ml. However, there was no statistically significant association between cumulative asbestos exposure and pleural plaque surface area.

Additional Comments: QC was not completed for metrics other than Metrics 4 and 5 because the study does not have sufficient exposure information to be useful for dose-response analysis. Metric 4 was rated Low because the method for quantifying fibers was not specified. The authors did not specify the method for quantifying fibers so it is unknown whether PCM, TEM, or another microscopy method was used, but exposure was quantified in fiber-years/ml, which could potentially be useful. However, the study assessed the association between past asbestos exposure and the size (rather than the prevalence) of pleural plaques, and found no statistically significant association. The study also assessed the association between pleural plaque size (rather than asbestos exposure) and pulmonary function. Thus, the study does not have sufficient information for dose-response quantification for the association between asbestos exposure and the prevalence of pleural plaques or pulmonary function levels.

* No biomarkers were identified for this evaluation.

** As described in Appendix B.2 of the *White Paper: Quantitative Approach to the Human Health Assessment for the Risk Evaluation for Asbestos Part 2: Supplemental Evaluation Including Legacy Uses and Associated Disposals of Asbestos*, to be considered as being informative for dose-response analysis, metrics 4 and 5 would need metric ratings of Medium or High. This reference did not satisfy this requirement; therefore data quality evaluation is presented for only for metrics 4 and 5.

Study Citation:	Vathesatogkit, P., Harkin, T. J., Addrizzo-Harris, D. J., Bodkin, M., Crane, M., Rom, W. N. (2004). Clinical correlation of asbestos bodies in BAL fluid. Chest 126(3):966-971.
Health Outcome:	Pleural Plaques; Chronic cough, sputum production, dyspnea, wheeze, total macrophages, total lymphocytes, total neutrophils, total eosinophils, diffuse pleural thickening, sublpleural reticular changes, subpleural lines, fibrosis, bronchiectesis, emphysema, rounded atelectesis
Target Organ(s):	Lung/Respiratory: Asbestos bodies
Asbestos Fiber Type(s):	Asbestos - Not specified: 1332-21-4
Linked HERO ID(s):	No linked references.
HERO ID:	1093622

Domain	Metric		Rating	Comments
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Uninformative	Subjects were categorized as exposed or unexposed. Subjects who worked at the electric utility company. For exposed subjects, no information about timing, length, frequency, or nature of exposure is reported.BAL fluid was inspected for asbestos bodies as a form of biomonitoring in asbestos-exposed subjects only.
	Metric 5:	Exposure Levels	Uninformative	Exposure was dichotomized: exposed or unexposed. For exposed subjects, no information about timing, length, frequency, or nature of exposure is reported.BAL fluid was inspected for asbestos bodies as a form of biomonitoring in asbestos-exposed subjects only.

Additional Comments: None

** As described in Appendix B.2 of the *White Paper: Quantitative Approach to the Human Health Assessment for the Risk Evaluation for Asbestos Part 2: Supplemental Evaluation Including Legacy Uses and Associated Disposals of Asbestos*, to be considered as being informative for dose-response analysis, metrics 4 and 5 would need metric ratings of Medium or High. This reference did not satisfy this requirement; therefore data quality evaluation is presented for only for metrics 4 and 5.

Study Citation:	W. R. Grace & Co., (1988). Health of vermiculite miners exposed to trace amounts of fibrous tremolite with cover letter dated 022988.
Health Outcome:	Lung Cancer; Abdominal, Other Malignant Neoplasms; All cause mortality, respiratory, circulatory disease, all other causes
Target Organ(s):	Mortality: Other cause of mortality, Respiratory, Circulatory disease; Cancer/Carcinogenesis: Respiratory, Abdominal, Other malignant neoplasms; Lung/Respiratory: Respiratory malignant neoplasms; Gastrointestinal: Abdominal malignant neoplasms; Other malignant neoplasms: Other malignant neoplasms
Asbestos Fiber Type(s):	Asbestos - Tremolite: 14567-73-8; Asbestos- Exposure reported as PCM or TEM (including conversion factors for dust)
Linked HERO ID(s):	No linked references.
HERO ID:	3656846

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	High	The cohort included 194 men in the mining and milling of vermiculite in South Carolina
	Metric 2:	Attrition	High	There was no subject loss to follow up during the study (or exclusion from the analysis sample) and outcome and exposure data were largely complete.
	Metric 3:	Comparison Group	Medium	Mortality of cohort was compared with white and black men in USA. “The age distribution of the non-exposed group was unknown.” The authors did not provide detailed information about the control group.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	High	Air samples were collected using membrane filters, and fibers were measured through PCM and ’analytical electron microscopy’.
	Metric 5:	Exposure Levels	Medium	The authors reported cumulative exposure of 3 groups (units: f/ml.y): <1, n=103; 1 - <10, n=83; $>= 10$, n=8.
	Metric 6:	Temporality	Medium	Temporality is established between exposure and outcome - 15 years or more from 1st employment that lasted 6 months or more (minimum latency of 15 years).
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Medium	Lung Cancer: Death certificates were obtained, registered causes of death were coded by a qualified nosologist, including ICD codes but without being specific (reported ranges of ICD codes).; Other Cancer(s): The authors state that they identified a specific health outcome, but less-established methods were used and they did not conduct method validation (Histology/pathology not specified).; Other Non-Cancer Outcomes: The authors state that they identified a specific health outcome including ranges of ICD codes per mortality cause category, but validation methods were not reported (Histology/pathology not specified).
	Metric 8:	Reporting Bias	High	All the study findings were reported throughout the manuscript, including the number of cases/controls by race, and cumulative exposure for the combined study population.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Low	The authors reported mortality data by race but SMRs were estimated for the totals, only. Smoking was not considered as a potential confounder.
	Metric 10:	Covariate Characterization	Medium	Age, latency period, exposure level, race, and biomarkers were assessed but detailed methods were not reported.

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Study Citation: W. R. Grace & Co., (1988). Health of vermiculite miners exposed to trace amounts of fibrous tremolite with cover letter dated 022988.
Health Outcome: Lung Cancer; Abdominal, Other Malignant Neoplasms; All cause mortality, respiratory, circulatory disease, all other causes
Target Organ(s): Mortality: Other cause of mortality, Respiratory, Circulatory disease; Cancer/Carcinogenesis: Respiratory, Abdominal, Other malignant neoplasms; Lung/Respiratory: Respiratory malignant neoplasms; Gastrointestinal: Abdominal malignant neoplasms; Other malignant neoplasms: Other malignant neoplasms
Asbestos Fiber Type(s): Asbestos - Tremolite: 14567-73-8; Asbestos- Exposure reported as PCM or TEM (including conversion factors for dust)
Linked HERO ID(s): No linked references.
HERO ID: 3656846

Domain	Metric		Rating	Comments
	Metric 11:	Co-exposure Counfounding	Low	Co-exposures were not discussed; however, sputum specimen biomarkers were detected through light microscopy.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	Medium	The cohort study design was appropriate to evaluate the impact of exposure to tremolite and mortality outcomes.
	Metric 13:	Statistical Power	Medium	Mortality of cohort was compared with white and black men in USA using "person-years at risk method" to compute expected number of deaths and SMRs using monson's computer program.
	Metric 14:	Reproducibility of Analyses	Medium	The description of the analysis is sufficient to understand how to conceptually reproduce the analysis with access to the analytic data.
	Metric 15:	Statistical Analysis	Medium	The calculation of SMRs was transparent.
Domain 6: Other (if applicable) Considerations for Biomarker Selection and Measurement (Lakind et al. 2014)				
	Metric 16:	Use of Biomarker of Exposure	Low	7 of 76 saliva specimens were not analyzed because of technical difficulties, therefore 69 samples were analyzed. 9 of 69 had atypical ferruginous bodies not exceeding 4 per pellet. 2 of 69 had typical ferruginous bodies (1 and 5 per pellet). No details of accuracy and precision were included.
	Metric 17:	Effect Biomarker	N/A	Effect biomarkers were not sampled. only exposure biomarkers.
	Metric 18:	Method Sensitivity	Low	LOD/LOQ were not reported.
	Metric 19:	Biomarker Stability	Low	The authors did not report a specified storage history of the sputum samples.
	Metric 20:	Sample Contamination	Low	Contamination or lack thereof of samples was not reported. There is no use or documentation of the steps taken to provide the necessary assurance that the study data is reliable.
	Metric 21:	Method Requirements	Medium	Samples were "digested and then filtered to count the typical and atypical ferruglnous bodies by light microscopy EH 300 x magnification." It is unclear if the method has known interferants.
	Metric 22:	Matrix Adjustment	Low	No established method for matrix adjustment was conducted for sputum samples.

Additional Comments: Did not extract data related to malignant neoplasm deaths as we aren't extracting data on cancer. Analyzed outcomes of radiology and mortality in separate forms, as the methodology was different for the radiology vs. mortality outcomes. Study analyzes deaths by race (black and white). Radiology groups involved 68 employees who were filmed (total of 83 films across participants), 25 films taken from employees in another division of the company who were "not believed to have been exposed to dust", and 25 films from Montana mine selected at random from men with and without parenchymal small opacities. Did not select libby amphibole since South Carolina would likely not be considered close to Libby MT. Did not extract any data on cancer (including for mortality results) but did mark them since they were addressed in the paper in the extraction form.

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Study Citation:	W. R. Grace & Co., (1988). Health of vermiculite miners exposed to trace amounts of fibrous tremolite with cover letter dated 022988.
Health Outcome:	Lung Cancer; Abdominal, Other Malignant Neoplasms; All cause mortality, respiratory, circulatory disease, all other causes
Target Organ(s):	Mortality: Other cause of mortality, Respiratory, Circulatory disease; Cancer/Carcinogenesis: Respiratory, Abdominal, Other malignant neoplasms; Lung/Respiratory: Respiratory malignant neoplasms; Gastrointestinal: Abdominal malignant neoplasms; Other malignant neoplasms: Other malignant neoplasms
Asbestos Fiber Type(s):	Asbestos - Tremolite: 14567-73-8; Asbestos- Exposure reported as PCM or TEM (including conversion factors for dust)
Linked HERO ID(s):	No linked references.
HERO ID:	3656846

Domain	Metric	Rating	Comments
Overall Quality Determination		**Medium**	

Study Citation:	Wang, X. R., Yu, I. T. S., Qiu, H., Wang, M. Z., Lan, Y. J., Tse, L. Y., Yano, E., Christiani, D. C. (2012). Cancer mortality among Chinese chrysotile asbestos textile workers. Lung Cancer 75(2):151-155.
Health Outcome:	Lung Cancer; Asbestosis
Target Organ(s):	Cancer/Carcinogenesis: All cancer mortality, lung cancer mortality, gastrointestinal cancer mortality.; Lung/Respiratory: lung cancer mortality, nonmalignant respiratory disease mortality, asbestosis mortality, mesothelioma mortality; Mortality: all cause mortality, all cancer mortality, lung cancer mortality, gastrointestinal cancer mortality, nonmalignant respiratory disease mortality, asbestosis mortality
Asbestos Fiber Type(s):	Asbestos - Chrysotile (serpentine): 12001-29-5
Linked HERO ID(s):	No linked references.
HERO ID:	2638749

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Medium	This prospective occupational study examined the health effects of asbestos exposure among a group of workers from an asbestos textile factory in China. Male workers were included in the study if they were registered workers in the factory on January 1972 and did not have signs of malignant tumors. Follow up continued through 2008. 586 workers were recruited for the original cohort, and 577 workers remained through the follow up period (98.5% participation rate at final follow up). While the study authors boast a high participation rate, it is unclear what percentage of the total eligible workers were initially recruited in 1972..
	Metric 2:	Attrition	High	This study had a participation rate of 98.5% at the final follow up, a high rate that minimizes concerns about bias introduced via subject attrition. Analyses were limited to the 577 subjects that had complete follow up information. Outcome and exposure data were complete for study subjects.
	Metric 3:	Comparison Group	High	Authors provide a description of comparisons between the three exposure groups and noted differences in age, exposure duration, and smoking in the three groups. These variables were included as cofounders in Cox proportional hazard models, thus effectively controlling for the differences between the groups.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Medium	Asbestos levels in the factory were quantitatively measured via TEM in 1982 and 2006, with an assertion that levels remained over 2 mg/m^3 during the study period. Personal sampling was conducted to assess the levels in different areas of the factory, which was ultimately used to construct three exposure groups (high, medium, low). Authors note that 70% of the workers had stable positions in the factory for the duration of the study. These positions were used to place workers into exposure categories. While these exposure estimates were based on quantitative measures and the role in the factory, there is still potential for nondifferential misclassification of exposure due to the limited quantitative measuring and the lack of specificity about those who did have varying roles during their employment.
	Metric 5:	Exposure Levels	Medium	Exposure categories were high, medium, and low, based on the job description of workers and sampling results from the factory. The low category was used as a reference group for comparison purposes.

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Study Citation:	Wang, X. R., Yu, I. T. S., Qiu, H., Wang, M. Z., Lan, Y. J., Tse, L. Y., Yano, E., Christiani, D. C. (2012). Cancer mortality among Chinese chrysotile asbestos textile workers. Lung Cancer 75(2):151-155.
Health Outcome:	Lung Cancer; Asbestosis
Target Organ(s):	Cancer/Carcinogenesis: All cancer mortality, lung cancer mortality, gastrointestinal cancer mortality.; Lung/Respiratory: lung cancer mortality, nonmalignant respiratory disease mortality, asbestosis mortality, mesothelioma mortality; Mortality: all cause mortality, all cancer mortality, lung cancer mortality, gastrointestinal cancer mortality, nonmalignant respiratory disease mortality, asbestosis mortality
Asbestos Fiber Type(s):	Asbestos - Chrysotile (serpentine): 12001-29-5
Linked HERO ID(s):	No linked references.
HERO ID:	2638749

Domain		Metric	Rating	Comments
	Metric 6:	Temporality	High	This study has over 30 years of follow-up, and subjects did not have signs of malignancies during recruitment. This is an appropriate timeframe to assess lung cancer or other outcomes of interest.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Medium	Lung Cancer: Lung cancer deaths were identified through personnel records from the factory. There is no indication that ICD codes were used to identify cases. Authors note that half of the cases were confirmed pathologically, though because half of the cases were not confirmed, this domain was rated medium.; Asbestosis: Asbestosis deaths were also ascertained through personnel records from the factory. There is no indication that ICD codes or lung tissue scarring were used to identify cases.
	Metric 8:	Reporting Bias	High	Hazard ratios and 95% confidence intervals (CI) were reported for lung cancer and asbestosis mortality. Cases for each exposure category were reported in a separate table. While these numbers were not reported directly in the results table, there is enough information to merit a high rating.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	High	The study authors appropriately adjusted for variables that vary among the three exposure groups. Age, duration of exposure, and smoking were included as covariates in Cox proportional hazard models.
	Metric 10:	Covariate Characterization	Medium	Data on covariates was collected from factory records. Additionally, smoking information was collected from individuals via interview or from family members via interview. There was no indication of validation of factory records, though the records can be assumed to be fairly accurate.
	Metric 11:	Co-exposure Counfounding	Medium	This study took place in an asbestos textile factory. There is no indication that co-exposures were present in the occupational setting.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	Medium	This study used a prospective cohort design to assess lung cancer mortality, which has a long latency period. This is an appropriate design for this health outcome. Additionally, Cox proportional hazard models were used to compare the medium and high exposure groups to the low exposure group (referent).
	Metric 13:	Statistical Power	Medium	While the overall cohort numbers are appropriate, there are concerns about the statistical power of the model to assess lung cancer and asbestosis. While some the low exposure group had less than 10 subjects, the effect estimates presented appear to be robust for these two outcomes.

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Study Citation:	Wang, X. R., Yu, I. T. S., Qiu, H., Wang, M. Z., Lan, Y. J., Tse, L. Y., Yano, E., Christiani, D. C. (2012). Cancer mortality among Chinese chrysotile asbestos textile workers. Lung Cancer 75(2):151-155.
Health Outcome:	Lung Cancer; Asbestosis
Target Organ(s):	Cancer/Carcinogenesis: All cancer mortality, lung cancer mortality, gastrointestinal cancer mortality.; Lung/Respiratory: lung cancer mortality, nonmalignant respiratory disease mortality, asbestosis mortality, mesothelioma mortality; Mortality: all cause mortality, all cancer mortality, lung cancer mortality, gastrointestinal cancer mortality, nonmalignant respiratory disease mortality, asbestosis mortality
Asbestos Fiber Type(s):	Asbestos - Chrysotile (serpentine): 12001-29-5
Linked HERO ID(s):	No linked references.
HERO ID:	2638749

Domain	Metric		Rating	Comments
	Metric 14:	Reproducibility of Analyses	Medium	Adequate information is provided to conceptually reproduce the analyses reported in the study.
	Metric 15:	Statistical Analysis	Low	While the model to assess the hazard of lung cancer and asbestosis mortality is clear, it is unclear if Cox proportional hazard model assumptions were met. Authors do not discuss any tests to assess the appropriateness of the statistical model.

Additional Comments: For the lung cancer and asbestosis assessments, there are a limited number of cases across the exposure categories. For the low exposure category, <10 cases were present, which limits the statistical power of the analysis and brings into question the ability of the study to detect an effect. Otherwise, the study presents appropriate approaches to participant selection, exposure assessment, and control for potential confounders.The measurement exposure (M4) and/or exposure levels (M5) metrics are rated medium upon review by both set of reviewers. However, the overall quality determination (OQD) is rated uninformative, upgraded to medium.

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation:	Wang, X. R., Yu, I. T. S., Qiu, H., Wang, M. Z., Lan, Y. J., Tse, L. Y., Yano, E., Christiani, D. C. (2012). Cancer mortality among Chinese chrysotile asbestos textile workers. Lung Cancer 75(2):151-155.
Health Outcome:	gastrointestinal cancer
Target Organ(s):	Cancer/Carcinogenesis: All cancer mortality, lung cancer mortality, gastrointestinal cancer mortality.; Gastrointestinal: gastrointestinal cancer mortality; Mortality: all cause mortality, all cancer mortality, lung cancer mortality, gastrointestinal cancer mortality, nonmalignant respiratory disease mortality, asbestosis mortality
Asbestos Fiber Type(s):	Asbestos - Chrysotile (serpentine): 12001-29-5
Linked HERO ID(s):	No linked references.
HERO ID:	2638749

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Medium	This prospective occupational study examined the health effects of asbestos exposure among a group of workers from an asbestos textile factory in China. Male workers were included in the study if they were registered workers in the factory on January 1972 and did not have signs of malignant tumors. Follow up continued through 2008. 586 workers were recruited for the original cohort, and 577 workers remained through the follow up period (98.5% participation rate at final follow up). While the study boasts a high participation rate, it is unclear what percentage of the total eligible workers were initially recruited in 1972, preventing a high rating in this domain.
	Metric 2:	Attrition	High	This study had a participation rate of 98.5% at the final follow up, a high rate that minimizes concerns about bias introduced via subject attrition. Analyses were limited to the 577 subjects that had complete follow up information. Outcome and exposure data are complete for study subjects.
	Metric 3:	Comparison Group	High	Authors provide a description of comparisons between the three exposure groups and noted differences in age, exposure duration, and smoking in the three groups. These variables were included as cofounders in Cox proportional hazard models, thus effectively controlling for the differences between the groups.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Medium	Asbestos levels in the factory were quantitatively measured via TEM in 1982 and 2006, with an assertion that levels remained over 2 mg/m^3 during the study period. Personal sampling was conducted to assess the levels in different areas of the factory, which was ultimately used to construct three exposure groups (high, medium, low). Authors note that 70% of the workers had stable positions in the factory for the duration of the study. These positions were used to place workers into exposure categories. While these exposure estimates were based on quantitative measures and the role in the factory, there is still potential for nondifferential misclassification of exposure due to the limited quantitative measuring and the lack of specificity about those who did have varying roles during their employment.
	Metric 5:	Exposure Levels	Medium	Exposure categories were high, medium, and low, based on the job description of workers and sampling results from the factory.
	Metric 6:	Temporality	High	This study has over 30 years of follow-up, and subjects did not have signs of malignancies during recruitment. This is an appropriate timeframe to assess malignancies.
Domain 3: Outcome Assessment				

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Study Citation:	Wang, X. R., Yu, I. T. S., Qiu, H., Wang, M. Z., Lan, Y. J., Tse, L. Y., Yano, E., Christiani, D. C. (2012). Cancer mortality among Chinese chrysotile asbestos textile workers. Lung Cancer 75(2):151-155.
Health Outcome:	gastrointestinal cancer
Target Organ(s):	Cancer/Carcinogenesis: All cancer mortality, lung cancer mortality, gastrointestinal cancer mortality.; Gastrointestinal: gastrointestinal cancer mortality; Mortality: all cause mortality, all cancer mortality, lung cancer mortality, gastrointestinal cancer mortality, nonmalignant respiratory disease mortality, asbestosis mortality
Asbestos Fiber Type(s):	Asbestos - Chrysotile (serpentine): 12001-29-5
Linked HERO ID(s):	No linked references.
HERO ID:	2638749

Domain	Metric		Rating	Comments
	Metric 7:	Outcome Measurement or Characterization	Medium	Other Cancer(s): Gastrointestinal cancer deaths were identified through personnel records from the factory. There is no indication that ICD codes were used to identify cases. Authors note that half of the cases were confirmed pathologically, though because half of the cases were not confirmed, this domain was rated medium.
	Metric 8:	Reporting Bias	High	Hazard ratios and 95% CI are reported for gastrointestinal cancer mortality. Cases for each exposure category are reported in a separate table. While these numbers are not reported directly in the results table, there is enough information to merit a high rating.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	High	The authors appropriately adjust for variables that vary among the three exposure groups. Age, duration of exposure, and smoking were included as covariates in Cox proportional hazard models.
	Metric 10:	Covariate Characterization	Medium	Data on covariates was collected from factory records. Additionally, smoking information was collected from individuals via interview or from family members via interview. There was no indication of validation of factory records, though the records can be assumed to be fairly accurate, thus meriting a medium rating.
	Metric 11:	Co-exposure Counfounding	Medium	This study took place in an asbestos textile factory. There is no indication that co-exposures were present in the occupational setting.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	Medium	This study used a prospective cohort design to assess gastrointestinal cancer mortality, which has a long latency period. This is an appropriate design for this health outcome. Additionally a Cox proportional hazard model was used to compare the medium and high exposure groups to the low exposure group (referent).
	Metric 13:	Statistical Power	Medium	While the overall cohort numbers are appropriate, there are concerns about the statistical power of the model to assess gastrointestinal cancer. Two exposure categories (low and high) have less than 10 subjects, which could limit the ability to detect robust effect estimates.
	Metric 14:	Reproducibility of Analyses	Medium	Overall, adequate information was provided to conceptually reproduce the analyses reported in the study.
	Metric 15:	Statistical Analysis	Low	While the model to assess the hazard of gastrointestinal cancer mortality is clear, it is unclear if Cox proportional hazard model assumptions were met. Authors did not discuss any tests to assess the appropriateness of the statistical model.

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Study Citation:	Wang, X. R., Yu, I. T. S., Qiu, H., Wang, M. Z., Lan, Y. J., Tse, L. Y., Yano, E., Christiani, D. C. (2012). Cancer mortality among Chinese chrysotile asbestos textile workers. Lung Cancer 75(2):151-155.
Health Outcome:	gastrointestinal cancer
Target Organ(s):	Cancer/Carcinogenesis: All cancer mortality, lung cancer mortality, gastrointestinal cancer mortality.; Gastrointestinal: gastrointestinal cancer mortality; Mortality: all cause mortality, all cancer mortality, lung cancer mortality, gastrointestinal cancer mortality, nonmalignant respiratory disease mortality, asbestosis mortality
Asbestos Fiber Type(s):	Asbestos - Chrysotile (serpentine): 12001-29-5
Linked HERO ID(s):	No linked references.
HERO ID:	2638749

Domain	Metric	Rating	Comments
Additional Comments:	For the gastrointestinal cancer assessment, there were a limited number of cases across the exposure categories. Two exposure categories (low and high) have less than 10 subjects, which could limit the ability to detect robust effect estimates. Otherwise, the study presents appropriate approaches to participant selection, exposure assessment, and control for potential confounders (including smoking).The measurement exposure (M4) and/or exposure levels (M5) metrics are rated medium upon review by both set of reviewers. However, the overall quality determination (OQD) was initially rated uninformative, but upgraded to medium.		

Overall Quality Determination	**Medium**

* No biomarkers were identified for this evaluation.

Study Citation:	Wang, X. R., Yu, I. T. S., Qiu, H., Wang, M. Z., Lan, Y. J., Tse, L. Y., Yano, E., Christiani, D. C. (2012). Cancer mortality among Chinese chrysotile asbestos textile workers. Lung Cancer 75(2):151-155.
Health Outcome:	non malignant respiratory disease mortality
Target Organ(s):	Lung/Respiratory: lung cancer mortality, nonmalignant respiratory disease mortality, asbestosis mortality, mesothelioma mortality; Mortality: all cause mortality, all cancer mortality, lung cancer mortality, gastrointestinal cancer mortality, nonmalignant respiratory disease mortality, asbestosis mortality
Asbestos Fiber Type(s):	Asbestos - Chrysotile (serpentine): 12001-29-5
Linked HERO ID(s):	No linked references.
HERO ID:	2638749

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Medium	This prospective occupational study examined the health effects of asbestos exposure among a group of workers from an asbestos textile factory in China. Male workers were included in the study if they were registered workers in the factory on January 1972 and did not have signs of malignant tumors. Follow up continued through 2008. 586 workers were recruited for the original cohort, and 577 workers remained through the follow up period (98.5% participation rate at final follow up). While the study boasts a high participation rate, it is unclear what percentage of the total eligible workers were initially recruited in 1972, preventing a high rating in this domain.
	Metric 2:	Attrition	High	This study had a participation rate of 98.5% at the final follow up, a high rate that minimizes concerns about bias introduced via subject attrition. Analyses were limited to the 577 subjects that had complete follow up information. Outcome and exposure data are complete for study subjects.
	Metric 3:	Comparison Group	High	Authors provide a description of comparisons between the three exposure groups and noted differences in age, exposure duration, and smoking in the three groups. These variables were included as cofounders in Cox proportional hazard models, thus effectively controlling for the differences between the groups.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Medium	Asbestos levels in the factory were quantitatively measured via TEM in 1982 and 2006, with an assertion that levels remained over 2 mg/m^3 during the study period. Personal sampling was conducted to assess the levels in different areas of the factory, which was ultimately used to construct three exposure groups (high, medium, low). Authors note that 70% of the workers had stable positions in the factory for the duration of the study. These positions were used to place workers into exposure categories. While these exposure estimates were based on quantitative measures and the role in the factory, there is still potential for nondifferential misclassification of exposure due to the limited quantitative measuring and the lack of specificity about those who did have varying roles during their employment.
	Metric 5:	Exposure Levels	Medium	Exposure categories were high, medium, and low, based on the job description of workers and sampling results from the factory.
	Metric 6:	Temporality	High	This study has over 30 years of follow-up, and subjects did not have signs of malignancies during recruitment. This is an appropriate timeframe to assess nonmalignant respiratory disease and sufficiently accounts for temporality.
Domain 3: Outcome Assessment				

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Study Citation:	Wang, X. R., Yu, I. T. S., Qiu, H., Wang, M. Z., Lan, Y. J., Tse, L. Y., Yano, E., Christiani, D. C. (2012). Cancer mortality among Chinese chrysotile asbestos textile workers. Lung Cancer 75(2):151-155.
Health Outcome:	non malignant respiratory disease mortality
Target Organ(s):	Lung/Respiratory: lung cancer mortality, nonmalignant respiratory disease mortality, asbestosis mortality, mesothelioma mortality; Mortality: all cause mortality, all cancer mortality, lung cancer mortality, gastrointestinal cancer mortality, nonmalignant respiratory disease mortality, asbestosis mortality
Asbestos Fiber Type(s):	Asbestos - Chrysotile (serpentine): 12001-29-5
Linked HERO ID(s):	No linked references.
HERO ID:	2638749

Domain	Metric		Rating	Comments
	Metric 7:	Outcome Measurement or Characterization	Medium	Other Non-Cancer Outcomes: Non-malignant respiratory disease deaths were ascertained through personnel records from the factory. There is no indication that ICD codes were used to identify cases or that all death certificate fields were searched to identify cases.
	Metric 8:	Reporting Bias	High	Hazard ratios and 95% CI are reported for nonmalignant respiratory mortality. Cases for each exposure category are reported in a separate table. While these numbers are not reported directly in the results table, there is enough information to merit a high rating.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	High	The authors appropriately adjust for variables that vary among the three exposure groups. Age, duration of exposure, and smoking were included as covariates in Cox proportional hazard models.
	Metric 10:	Covariate Characterization	Medium	Data on covariates was collected from factory records. Additionally, smoking information was collected from individuals via interview or from family members via interview. There was no indication of validation of factory records, though the records can be assumed to be fairly accurate, thus meriting a medium rating.
	Metric 11:	Co-exposure Counfounding	Medium	This study took place in an asbestos textile factory. There is no indication that co-exposures were present in the occupational setting.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	Medium	This study used a prospective cohort design to assess nonmalignant respiratory mortality. This is an appropriate design for this health outcome. Additionally a Cox proportional hazard models were used to compare the medium and high exposure groups to the low exposure group (referent).
	Metric 13:	Statistical Power	Medium	The number of participants in each exposure group appears adequate to detect robust effect estimates when assessing exposures and nonmalignant respiratory disease.
	Metric 14:	Reproducibility of Analyses	Medium	Adequate information is provided to conceptually reproduce the analyses reported in the study.
	Metric 15:	Statistical Analysis	Low	While the model to assess the hazard of non-malignant respiratory mortality is clear, it is unclear if Cox proportional hazard model assumptions were met. Authors do not discuss any tests to assess the appropriateness of the statistical model.

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Study Citation:	Wang, X. R., Yu, I. T. S., Qiu, H., Wang, M. Z., Lan, Y. J., Tse, L. Y., Yano, E., Christiani, D. C. (2012). Cancer mortality among Chinese chrysotile asbestos textile workers. Lung Cancer 75(2):151-155.
Health Outcome:	non malignant respiratory disease mortality
Target Organ(s):	Lung/Respiratory: lung cancer mortality, nonmalignant respiratory disease mortality, asbestosis mortality, mesothelioma mortality; Mortality: all cause mortality, all cancer mortality, lung cancer mortality, gastrointestinal cancer mortality, nonmalignant respiratory disease mortality, asbestosis mortality
Asbestos Fiber Type(s):	Asbestos - Chrysotile (serpentine): 12001-29-5
Linked HERO ID(s):	No linked references.
HERO ID:	2638749

Domain	Metric	Rating	Comments
Additional Comments:	For the nonmalignant respiratory disease assessment, there are a limited number of cases across the exposure categories. For some exposure categories, <50 cases were present, which limits the statistical power of the analysis and brings into question the ability of the study to detect an effect. Otherwise, the study presents appropriate approaches to participant selection, exposure assessment, and control for potential confounders.The measurement exposure (M4) and/or exposure levels (M5) metrics are rated medium upon review by both set of reviewers. However, the overall quality determination (OQD) was rated uninformative, but then upgraded to medium.		

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation: Wang, X. R., Yu, I. T. S., Qiu, H., Wang, M. Z., Lan, Y. J., Tse, L. Y., Yano, E., Christiani, D. C. (2012). Cancer mortality among Chinese chrysotile asbestos textile workers. Lung Cancer 75(2):151-155.
Health Outcome: all cause mortality
Target Organ(s): Mortality: all cause mortality, all cancer mortality, lung cancer mortality, gastrointestinal cancer mortality, nonmalignant respiratory disease mortality, asbestosis mortality
Asbestos Fiber Type(s): Asbestos - Chrysotile (serpentine): 12001-29-5
Linked HERO ID(s): No linked references.
HERO ID: 2638749

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Medium	This prospective occupational study examined the health effects of asbestos exposure among a group of workers from an asbestos textile factory in China. Male workers were included in the study if they were registered workers in the factory on January 1972 and did not have signs of malignant tumors. Follow up continued through 2008. 586 workers were recruited for the original cohort, and 577 workers remained through the follow up period (98.5% participation rate at final follow up). While the study boasts a high participation rate, it is unclear what percentage of the total eligible workers were initially recruited in 1972, preventing a high rating in this domain.
	Metric 2:	Attrition	High	This study had a participation rate of 98.5% at the final follow up, a high rate that minimizes concerns about bias introduced via subject attrition. Analyses were limited to the 577 subjects that had complete follow up information. Outcome and exposure data are complete for study subjects.
	Metric 3:	Comparison Group	High	Authors provide a description of comparisons between the three exposure groups and noted differences in age, exposure duration, and smoking in the three groups. These variables were included as cofounders in Cox proportional hazard models, thus effectively controlling for the differences between the groups.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Medium	Asbestos levels in the factory were quantitatively measured via TEM in 1982 and 2006, with an assertion that levels remained over 2 mg/m^3 during the study period. Personal sampling was conducted to assess the levels in different areas of the factory, which was ultimately used to construct three exposure groups (high, medium, low). Authors note that 70% of the workers had stable positions in the factory for the duration of the study. These positions were used to place workers into exposure categories. While these exposure estimates were based on quantitative measures and the role in the factory, there is still potential for nondifferential misclassification of exposure due to the limited quantitative measuring and the lack of specificity about those who did have varying roles during their employment.
	Metric 5:	Exposure Levels	Medium	Exposure categories were high, medium, and low, based on the job description of workers and sampling results from the factory.
	Metric 6:	Temporality	High	This study has over 30 years of follow-up, and subjects did not have signs of malignancies during recruitment. This is an appropriate timeframe to assess all cause mortality and sufficiently accounts for temporality.
Domain 3: Outcome Assessment				

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Study Citation:	Wang, X. R., Yu, I. T. S., Qiu, H., Wang, M. Z., Lan, Y. J., Tse, L. Y., Yano, E., Christiani, D. C. (2012). Cancer mortality among Chinese chrysotile asbestos textile workers. Lung Cancer 75(2):151-155.
Health Outcome:	all cause mortality
Target Organ(s):	Mortality: all cause mortality, all cancer mortality, lung cancer mortality, gastrointestinal cancer mortality, nonmalignant respiratory disease mortality, asbestosis mortality
Asbestos Fiber Type(s):	Asbestos - Chrysotile (serpentine): 12001-29-5
Linked HERO ID(s):	No linked references.
HERO ID:	2638749

Domain	Metric		Rating	Comments
	Metric 7:	Outcome Measurement or Characterization	High	Other Non-Cancer Outcomes: Deaths were identified through personnel records from the factory and from death registries, which is a valid approach to capture mortality data.
	Metric 8:	Reporting Bias	High	Hazard ratios and 95% CI are reported for nonmalignant respiratory mortality. Cases for each exposure category are reported in a separate table. While these numbers are not reported directly in the results table, there is enough information to merit a high rating.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	High	The authors appropriately adjust for variables that vary among the three exposure groups. Age, duration of exposure, and smoking were included as covariates in Cox proportional hazard models.
	Metric 10:	Covariate Characterization	Medium	Data on covariates was collected from factory records. Additionally, smoking information was collected from individuals via interview or from family members via interview. There was no indication of validation of factory records, though the records can be assumed to be fairly accurate, thus meriting a medium rating.
	Metric 11:	Co-exposure Counfounding	Medium	This study took place in an asbestos textile factory. There is no indication that co-exposures were present in the occupational setting.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	Medium	This study used a prospective cohort design to assess all cause mortality. This is an appropriate design for this health outcome. Additionally a Cox proportional hazard model was used to compare the medium and high exposure groups to the low exposure group (referent).
	Metric 13:	Statistical Power	Medium	The sample size was appropriate to generate adequate statistical power to assess the hazard of all cause mortality in the study cohort.
	Metric 14:	Reproducibility of Analyses	Medium	Adequate information is provided to conceptually reproduce the analyses reported in the study.
	Metric 15:	Statistical Analysis	Low	While the model to assess the hazard of all cause mortality is clear, it is unclear if Cox proportional hazard model assumptions were met. Authors do not discuss any tests to assess the appropriateness of the statistical model.

Additional Comments:	Medium. This prospective cohort study examined the hazard of all cause mortality among an occupational population of male asbestos textile workers in China. The paper presents appropriate approaches to participant selection, exposure assessment, and control for potential confounders. Additionally, the sample sizes of the cohort and subgroups were adequate to detect robust effect estimates.The measurement exposure (M4) and/or exposure levels (M5) metrics are rated as medium upon review by both set of reviewers. Also, the overall quality determination (OQD) for this outcome is rated medium. Extraction has been completed and quality control reviewed.

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Study Citation:	Wang, X. R., Yu, I. T. S., Qiu, H., Wang, M. Z., Lan, Y. J., Tse, L. Y., Yano, E., Christiani, D. C. (2012). Cancer mortality among Chinese chrysotile asbestos textile workers. Lung Cancer 75(2):151-155.
Health Outcome:	all cause mortality
Target Organ(s):	Mortality: all cause mortality, all cancer mortality, lung cancer mortality, gastrointestinal cancer mortality, nonmalignant respiratory disease mortality, asbestosis mortality
Asbestos Fiber Type(s):	Asbestos - Chrysotile (serpentine): 12001-29-5
Linked HERO ID(s):	No linked references.
HERO ID:	2638749

Domain	Metric	Rating	Comments
Overall Quality Determination		**Medium**	

* No biomarkers were identified for this evaluation.

Study Citation:	Wang, X. R., Yu, I. T. S., Qiu, H., Wang, M. Z., Lan, Y. J., Tse, L. Y., Yano, E., Christiani, D. C. (2012). Cancer mortality among Chinese chrysotile asbestos textile workers. Lung Cancer 75(2):151-155.
Health Outcome:	all cancer mortality
Target Organ(s):	Cancer/Carcinogenesis: All cancer mortality, lung cancer mortality, gastrointestinal cancer mortality.; Mortality: all cause mortality, all cancer mortality, lung cancer mortality, gastrointestinal cancer mortality, nonmalignant respiratory disease mortality, asbestosis mortality
Asbestos Fiber Type(s):	Asbestos - Chrysotile (serpentine): 12001-29-5
Linked HERO ID(s):	No linked references.
HERO ID:	2638749

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Medium	This prospective occupational study examined the health effects of asbestos exposure among a group of workers from an asbestos textile factory in China. Male workers were included in the study if they were registered workers in the factory on January 1972 and did not have signs of malignant tumors. Follow up continued through 2008. 586 workers were recruited for the original cohort, and 577 workers remained through the follow up period (98.5% participation rate at final follow up). While the study boasts a high participation rate, it is unclear what percentage of the total eligible workers were initially recruited in 1972, preventing a high rating in this domain.
	Metric 2:	Attrition	High	This study had a participation rate of 98.5% at the final follow up, a high rate that minimizes concerns about bias introduced via subject attrition. Analyses were limited to the 577 subjects that had complete follow up information. Outcome and exposure data are complete for study subjects.
	Metric 3:	Comparison Group	High	Authors provide a description of comparisons between the three exposure groups and noted differences in age, exposure duration, and smoking in the three groups. These variables were included as cofounders in Cox proportional hazard models, thus effectively controlling for the differences between the groups.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Medium	Asbestos levels in the factory were quantitatively measured via TEM in 1982 and 2006, with an assertion that levels remained over 2 mg/m^3 during the study period. Personal sampling was conducted to assess the levels in different areas of the factory, which was ultimately used to construct three exposure groups (high, medium, low). Authors note that 70% of the workers had stable positions in the factory for the duration of the study. These positions were used to place workers into exposure categories. While these exposure estimates were based on quantitative measures and the role in the factory, there is still potential for nondifferential misclassification of exposure due to the limited quantitative measuring and the lack of specificity about those who did have varying roles during their employment.
	Metric 5:	Exposure Levels	Medium	Exposure categories were high, medium, and low, based on the job description of workers and sampling results from the factory.
	Metric 6:	Temporality	High	This study has over 30 years of follow-up, and subjects did not have signs of malignancies during recruitment. This is an appropriate timeframe to assess cancer mortality, which has a long latency period, and sufficiently accounts for temporality.
Domain 3: Outcome Assessment				

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Study Citation: Wang, X. R., Yu, I. T. S., Qiu, H., Wang, M. Z., Lan, Y. J., Tse, L. Y., Yano, E., Christiani, D. C. (2012). Cancer mortality among Chinese chrysotile asbestos textile workers. Lung Cancer 75(2):151-155.
Health Outcome: all cancer mortality
Target Organ(s): Cancer/Carcinogenesis: All cancer mortality, lung cancer mortality, gastrointestinal cancer mortality.; Mortality: all cause mortality, all cancer mortality, lung cancer mortality, gastrointestinal cancer mortality, nonmalignant respiratory disease mortality, asbestosis mortality
Asbestos Fiber Type(s): Asbestos - Chrysotile (serpentine): 12001-29-5
Linked HERO ID(s): No linked references.
HERO ID: 2638749

Domain	Metric		Rating	Comments
	Metric 7:	Outcome Measurement or Characterization	Medium	Other Cancer(s): Cancer deaths were identified through personnel records from the factory. There is no indication that ICD codes were used to identify cases. Authors note that half of the cases were confirmed pathologically, though because half of the cases were not confirmed, this domain was rated medium.
	Metric 8:	Reporting Bias	High	Hazard ratios and 95% CI are reported for all cancer mortality. Cases for each exposure category are reported in a separate table. While these numbers are not reported directly in the results table, there is enough information to merit a high rating.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	High	The authors appropriately adjust for variables that vary among the three exposure groups. Age, duration of exposure, and smoking were included as covariates in Cox proportional hazard models.
	Metric 10:	Covariate Characterization	Medium	Data on covariates was collected from factory records. Additionally, smoking information was collected from individuals via interview or from family members via interview. There was no indication of validation of factory records, though the records can be assumed to be fairly accurate, thus meriting a medium rating.
	Metric 11:	Co-exposure Counfounding	Medium	This study took place in an asbestos textile factory. There is no indication that co-exposures were present in the occupational setting.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	Medium	This study used a prospective cohort design to assess all cancer mortality. This is an appropriate design for this health outcome. Additionally a Cox proportional hazard model was used to compare the medium and high exposure groups to the low exposure group (referent).
	Metric 13:	Statistical Power	Medium	While the overall cohort numbers are appropriate, there are concerns about the statistical power of the model to assess nonmalignant respiratory disease. The lowest exposure group had 15 cases while the other exposure groups had fewer than 50, which may limit the ability to detect an effect.
	Metric 14:	Reproducibility of Analyses	Medium	Adequate information is provided to conceptually reproduce the analyses reported in the study.
	Metric 15:	Statistical Analysis	Low	While the model to assess the hazard of all cancer mortality is clear, it is unclear if Cox proportional hazard model assumptions were met. Authors do not discuss any tests to assess the appropriateness of the statistical model.

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Study Citation:	Wang, X. R., Yu, I. T. S., Qiu, H., Wang, M. Z., Lan, Y. J., Tse, L. Y., Yano, E., Christiani, D. C. (2012). Cancer mortality among Chinese chrysotile asbestos textile workers. Lung Cancer 75(2):151-155.
Health Outcome:	all cancer mortality
Target Organ(s):	Cancer/Carcinogenesis: All cancer mortality, lung cancer mortality, gastrointestinal cancer mortality.; Mortality: all cause mortality, all cancer mortality, lung cancer mortality, gastrointestinal cancer mortality, nonmalignant respiratory disease mortality, asbestosis mortality
Asbestos Fiber Type(s):	Asbestos - Chrysotile (serpentine): 12001-29-5
Linked HERO ID(s):	No linked references.
HERO ID:	2638749

Domain	Metric	Rating	Comments
Additional Comments:	For the all cancer mortality assessment, there are a limited number of cases across the exposure categories. For the low exposure category, fewer than 20 cases were reported, and for the other exposure categories, <50 cases were present, which limits the statistical power of the analysis and brings into question the ability of the study to detect an effect. Otherwise, this prospective cohort study examined all cancer mortality among a group of male asbestos textile workers and presents appropriate approaches to participant selection, exposure assessment, and control for potential confounders.The measurement exposure (M4) and/or exposure levels (M5) metrics are rated as medium upon review by both set of reviewers. However, the overall quality determination (OQD) for this outcome was initially rated uninformative, but upgraded to medium.		

Overall Quality Determination **Medium**

* No biomarkers were identified for this evaluation.

Study Citation:	Wang, X., Lin, S., Yano, E., Qiu, H., Yu, I. T., Tse, L., Lan, Y., Wang, M. (2012). Mortality in a Chinese chrysotile miner cohort. International Archives of Occupational and Environmental Health 85(4):405-412.
Health Outcome:	GI cancer, all cancer; All cause mortality, non-malignant respiratory disease mortality
Target Organ(s):	Mortality: All cause mortality, All cancer mortality, GI cancer mortality, Non-malignant respiratory disease mortality; Gastrointestinal: GI cancer mortality; Lung/Respiratory: Non-malignant respiratory disease mortality
Asbestos Fiber Type(s):	Asbestos - Chrysotile (serpentine): 12001-29-5
Linked HERO ID(s):	No linked references.
HERO ID:	2572504

Domain	Metric		Rating	Comments
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Medium	Asbestos dust concentrations in the mine were described as measured periodically for total dust with available data up to 1995 briefly summarized in the text. Additional fixing point sampling in various workshops in 2006 with 28 breathing-zone samples in eight workshops collected and analyzed in accordance with HSE Methods (HSE 2000) was also briefly summarized. Conversion factors were applied to the dust measurements in 2006 with resulting average 2006 fiber concentration in the mine reported as 29.0 f/mL (range: 2.9 to 63.8 f/mL). However, side-by-side sampling and analysis were not noted.
	Metric 5:	Exposure Levels	Low	The data to develop adquate exposure-response relationships is limited.

Additional Comments:	This retrospective cohort study examined the association between asbestos exposure and cause-specific mortality in a cohort of chrysotile asbestos miners in China 1981-2006. A total of n=1,539 male mine workers, with n=1,080 mining (“miner and miller group” composed of those directly engaged in asbestos mining and milling, mechanical maintenance and transportation) workers and n=459 controls (administrative management, office work, cooks) were included for study. Authors noted workers were followed up 1981 through 2006 “irrespective of retirement status”, however it was unclear if workers were followed who might have left the mine prior to the retirement. Average dust and fiber/mL exposure was briefly detailed within text for the overall population, but not specific populations within results or utilized within SMR or Cox regression results. However Cox regression utilized length of follow-up as the time dimension, while taking into account employment years. Authors noted that control workers were exposed to asbestos, and control worker SMR of nonmalignant respiratory disease was 85% greater than expected, although had mortality rates similar to national rates for other causes. All mortality rates of selected causes were substantially higher in the miner group than in the controls. The authors reported SMR’s of nonmalignant respiratory diseases in the miners as 3.53 (2.78, 4.48), and noted that asbestos exposure was related to over a threefold risk for respiratory diseases and all cancers, while adjusting for smoking and age.

* No biomarkers were identified for this evaluation.

** As described in Appendix B.2 of the *White Paper: Quantitative Approach to the Human Health Assessment for the Risk Evaluation for Asbestos Part 2: Supplemental Evaluation Including Legacy Uses and Associated Disposals of Asbestos*, to be considered as being informative for dose-response analysis, metrics 4 and 5 would need metric ratings of Medium or High. This reference did not satisfy this requirement; therefore data quality evaluation is presented for only for metrics 4 and 5.

Study Citation:	Weiderpass, E., Pukkala, E., Kauppinen, T., Mutanen, P., Paakkulainen, H., Vasama-Neuvonen, K., Boffetta, P., Partanen, T. (1999). Breast cancer and occupational exposures in women in Finland. American Journal of Industrial Medicine 36(1):48-53.			
Health Outcome:	breast cancer			
Target Organ(s):	Cancer/Carcinogenesis: Breast cancer; Reproductive/Developmental: Breast cancer			
Asbestos Fiber Type(s):	Asbestos - Not specified: 1332-21-4			
Linked HERO ID(s):	No linked references.			
HERO ID:	730085			

Domain	Metric		Rating	Comments
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Low	Asbestos analytic method for data within the FINJEM was not specified. Methods used to quantify the exposure were not well defined, and sources of data and detailed methods of exposure assessment were not reported. Asbestos exposure was defined in models as the product of probability and exposure level obtained from data from the Finnish national job exposure matrix (FINJEM) developed at the Finnish Institute of Occupational Health, which included data described as estimates based on professional judgment and derived from industrial hygiene measurements when available 1960-1984. Details of analytical method (PCM/TEM) for asbestos samples were not provided within the main text or the referenced article by Kauppinen et al., 1998 (HERO ID not available). Additional searches regarding FINJEM data analytical methods located Kauppinen et al., 2013 (HERO ID 2634525), which noted levels of chemical exposures in FINJEM were determined by experienced IH's using "...data from the Database of Occupational Exposure Measurements (DOEM) (Kauppinen, 2001; Heikkilä et al., 2005; Saalo et al., 2010), the Register of Employees Exposed to Carcinogens (ASA) (Kauppinen et al., 2007; Saalo et al., 2011), and the Finnish Work and Health Surveys (Perkiö-Mäkelä et al., 2010)". Checking for information on the DOEM, Kauppinen et al., 2014 (HERO ID 6735112) "Use of the Finnish Information System on Occupational Exposure (FINJEM) in epidemiologic, surveillance, and other applications" was found which also did not detail asbestos sampling and analytic methods.
	Metric 5:	Exposure Levels	Low	The range and distribution of exposure was described only as subdivided into three factored categories for each agent: zero; low (roughly below median among job titles with exposure probability .0); and medium/high. Measured levels were not summarized.

Additional Comments: Weiderpass et al., 1999 (HERO ID 730085) was not evaluated for any metrics except Metric 4 and 5 as it did not have sufficient exposure information to be useful for dose-response analysis.

** As described in Appendix B.2 of the *White Paper: Quantitative Approach to the Human Health Assessment for the Risk Evaluation for Asbestos Part 2: Supplemental Evaluation Including Legacy Uses and Associated Disposals of Asbestos*, to be considered as being informative for dose-response analysis, metrics 4 and 5 would need metric ratings of Medium or High. This reference did not satisfy this requirement; therefore data quality evaluation is presented for only for metrics 4 and 5.

Study Citation: Weill, H., Hughes, J., Waggenspack, C. (1979). Influence of dose and fiber type on respiratory malignancy risk in asbestos cement manufacturing. American Review of Respiratory Disease 120(2):345-354.

Health Outcome: Lung Cancer; Digestive system, other (residual) cancers; Cardiovascular diseases, all other causes mortality

Target Organ(s): Gastrointestinal: Digestive system neoplasm mortality; Mortality: Digestive system neoplasm mortality, Respiratory system neoplasm mortality, Other neoplasm mortality, Major cardiovascular diseases mortality, Total neoplasm mortality, All other causes mortality; Cancer/Carcinogenesis: Digestive system neoplasm mortality, Respiratory system neoplasm mortality, Other neoplasm mortality, Total neoplasm mortality; Lung/Respiratory: Respiratory system neoplasm mortality; other neoplasms, unspecified: Other neoplasm mortality; Cardiovascular: Major cardiovascular diseases mortality; Total neoplasm mortality: Total neoplasm mortality; other, unspecified: All other causes mortality

Asbestos Fiber Type(s): Asbestos - Chrysotile (serpentine): 12001-29-5; Asbestos - Crocidolite (riebeckite): 12001-28-4; Asbestos - Amosite (grunerite): 12172-73-5

Linked HERO ID(s): No linked references.

HERO ID: 263

Domain		Metric	Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Medium	This study focuses on a cohort of 5645 men across two asbestos cement building materials plants New Orleans, LA who had at least 20 years of follow-up available. 35% worked at the first plant (roofing products), 64% worked at the second plant (roofing, piping, and flooring products), and 1% worked at both plants with a similar distribution of lengths of employment in both plants however a greater proportion of workers in the second plant were employed for more than 20 years. No recruitment methods were or other inclusion or exclusion criteria were described.
	Metric 2:	Attrition	Medium	The study authors were able to confirm that 11% of the cohort were known to have died and that approximately 64% were known to be alive in 1974 however for the remaining 25% were unable to be traced and the authors stated analysis adjustments were not possible for this group. These primarily would have been subjects between 45 an 64 years of age in 1974. Based on subsequent discussion and review of additional information, the rating was adjusted based on adequately addressed is from either imputation or if there aren't differences between groups in terms of reasons for loss.
	Metric 3:	Comparison Group	Medium	The subjects were categorized into 5 exposure categories and mean follow-up and mean age at initial exposure were similar across the groups however no statement was provided about the distribution of age across the exposure groups. SMR analysis was conducted on the basis of race-age-cause specific rates for both the U.S. and for Louisiana male populations for 1950, 1960, and 1970.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	High	Hammad et al. 1979 details the sampling data collected and the determination of asbestos fiber measurements in the samples. Impinger filter pairs were collected from personal samples. Asbestos fibers were counted on filter samples using PCM. Paired samples were collected for various job functions or "zones".
	Metric 5:	Exposure Levels	Medium	Table 1 and 2 in the publication present 5 different exposure levels, including SMRs in Table 2. Table 3-25 in the 1986 assessment presents SMRs and RRs for the 5 exposure groups.
	Metric 6:	Temporality	High	The study presents appropriate temporality between exposure and outcome, with all workers having >=20 years of follow up.

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Study Citation: Weill, H., Hughes, J., Waggenspack, C. (1979). Influence of dose and fiber type on respiratory malignancy risk in asbestos cement manufacturing. American Review of Respiratory Disease 120(2):345-354.

Health Outcome: Lung Cancer; Digestive system, other (residual) cancers; Cardiovascular diseases, all other causes mortality

Target Organ(s): Gastrointestinal: Digestive system neoplasm mortality; Mortality: Digestive system neoplasm mortality, Respiratory system neoplasm mortality, Other neoplasm mortality, Major cardiovascular diseases mortality, Total neoplasm mortality, All other causes mortality; Cancer/Carcinogenesis: Digestive system neoplasm mortality, Respiratory system neoplasm mortality, Other neoplasm mortality, Total neoplasm mortality; Lung/Respiratory: Respiratory system neoplasm mortality; other neoplasms, unspecified: Other neoplasm mortality; Cardiovascular: Major cardiovascular diseases mortality; Total neoplasm mortality: Total neoplasm mortality; other, unspecified: All other causes mortality

Asbestos Fiber Type(s): Asbestos - Chrysotile (serpentine): 12001-29-5; Asbestos - Crocidolite (riebeckite): 12001-28-4; Asbestos - Amosite (grunerite): 12172-73-5

Linked HERO ID(s): No linked references.

HERO ID: 263

Domain		Metric	Rating	Comments
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	High	Lung Cancer: High - Death certificates were coded by a nosologist with the U.S. Public Heatlh Service according to ICD-8 codes (160-163).; Other Cancer(s): High - Death certificates were coded by a nosologist with the U.S. Public Heatlh Service according to ICD-8 codes (all malignant neoplasms: 140-209; digestive system neoplasms: 150-159).; Other Non-Cancer Outcomes: High - Death certificates were coded by a nosologist with the U.S. Public Heatlh Service according to ICD-8 codes (cardiovascular diseases: 390-448).
	Metric 8:	Reporting Bias	High	Findings of SMR and OR analyses are reported with case numbers.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	High	SMR analysis was conducted on the basis of race-age-cause specific rates for both the U.S. and for Louisiana male populations for 1950, 1960, and 1970.
	Metric 10:	Covariate Characterization	High	The study assessed age and sex and these are assumed to have been obtained from personnel records. Assessment of SES was not described however this is unlikely to introduce bias as the exposure was based on job history and it is assumed that the workers in the asbestos cement building materials plants have similar SES.
	Metric 11:	Co-exposure Counfounding	Medium	Co-exposures are not discussed in detail, but authors note the use of silica in plants and there is no direct evidence for an unbalanced provision of additional co-exposure across study groups.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	Medium	The cohort study design is appropriate for the analysis of SMR by asbestos dust exposure categories. Further analysis utilized a matched case-control design for lung cancer cases that were assigned 4 controls matched on same birth year, race, survived into the same year as the case, and did not subsequently die to a malignancy.
	Metric 13:	Statistical Power	Medium	There is adequate power to detect an association in this study, which utilized 5645 male subjects with at least 20 years of follow-up. Of these subjects, 11% were known to have died.
	Metric 14:	Reproducibility of Analyses	Medium	The description of the analysis is sufficient to understand how to conceptually reproduce the analysis with access to the data and the U.S. and Louisiana race-age-cause-specific mortality rates.

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Study Citation:	Weill, H., Hughes, J., Waggenspack, C. (1979). Influence of dose and fiber type on respiratory malignancy risk in asbestos cement manufacturing. American Review of Respiratory Disease 120(2):345-354.
Health Outcome:	Lung Cancer; Digestive system, other (residual) cancers; Cardiovascular diseases, all other causes mortality
Target Organ(s):	Gastrointestinal: Digestive system neoplasm mortality; Mortality: Digestive system neoplasm mortality, Respiratory system neoplasm mortality, Other neoplasm mortality, Major cardiovascular diseases mortality, Total neoplasm mortality, All other causes mortality; Cancer/Carcinogenesis: Digestive system neoplasm mortality, Respiratory system neoplasm mortality, Other neoplasm mortality, Total neoplasm mortality; Lung/Respiratory: Respiratory system neoplasm mortality; other neoplasms, unspecified: Other neoplasm mortality; Cardiovascular: Major cardiovascular diseases mortality; Total neoplasm mortality: Total neoplasm mortality; other, unspecified: All other causes mortality
Asbestos Fiber Type(s):	Asbestos - Chrysotile (serpentine): 12001-29-5; Asbestos - Crocidolite (riebeckite): 12001-28-4; Asbestos - Amosite (grunerite): 12172-73-5
Linked HERO ID(s):	No linked references.
HERO ID:	263

Domain	Metric	Rating	Comments
	Metric 15: Statistical Analysis	Medium	The method for calculating the SMR is transparently reported as in the study. Further analysis utilized a matched case-control design for lung cancer cases that were assigned 4 controls matched on same birth year, race, survived into the same year as the case, and did not subsequently die to a malignancy. There are no explicit modeling assumptions to meet.

Additional Comments: Occupational cohort study of 5645 workers in two asbestos cement building materials plants in New Orleans, LA. Subjects were exposed primarily to chrysotile dust however crocidolite was mentioned as another form of asbestos used in the plants and the study referenced workers exposed to amosite in one factory. Exposures were only in particle units, with no fiber conversion factors.

Overall Quality Determination **High**

* No biomarkers were identified for this evaluation.

Study Citation:	Wigle, D. T., Mao, Y., Semenciw, R., Smith, M. H., Toft, P. (1986). Contaminants in drinking water and cancer risks in canadian cities. Canadian Journal of Public Health 77(5):335-342.
Health Outcome:	Tongue, pharynx, esophagus, stomach, large intestine including rectum, pancreas, gastrointestinal, breast, ovary, prostate, kidney, bladder; coronary heart disease
Target Organ(s):	Cancer/Carcinogenesis: breast, bladder, kidney, prostate, ovary, large intestine including rectum, stomach, esophagus, Tongue, mouth and pharynx, Gastrointestinal (ICDA 150-159), pancreas; Cardiovascular: coronary heart disease
Asbestos Fiber Type(s):	Asbestos - Chrysotile (serpentine): 12001-29-5
Linked HERO ID(s):	No linked references.
HERO ID:	677716

Domain	Metric		Rating	Comments
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Low	The method of quantifying/counting asbestos fibers was not specified. The authors only cited the sources of the monitoring data. There was no clear description of how exposure was measured.
	Metric 5:	Exposure Levels	Low	The range of fibers/L for the different localities was wide. Table III presents two level of asbestos concentration of localities associated with age-standardized mortality rates of multiple cancer sites. Even though Table VII presented beta coefficients in the multiple regression analysis, the asbestos exposure levels were not presented.

Additional Comments: None

* No biomarkers were identified for this evaluation.

** As described in Appendix B.2 of the *White Paper: Quantitative Approach to the Human Health Assessment for the Risk Evaluation for Asbestos Part 2: Supplemental Evaluation Including Legacy Uses and Associated Disposals of Asbestos*, to be considered as being informative for dose-response analysis, metrics 4 and 5 would need metric ratings of Medium or High. This reference did not satisfy this requirement; therefore data quality evaluation is presented for only for metrics 4 and 5.

Study Citation:	Wortley, P., Vaughan, T. L., Davis, S., Morgan, M. S., Thomas, D. B. (1992). A case-control study of occupational risk factors for laryngeal cancer. British Journal of Industrial Medicine 49(12):837-844.
Health Outcome:	Laryngeal Cancer
Target Organ(s):	Cancer/Carcinogenesis: Laryngeal cancer; Lung/Respiratory: Laryngeal cancer
Asbestos Fiber Type(s):	Asbestos - Not specified: 1332-21-4
Linked HERO ID(s):	No linked references.
HERO ID:	626626

Domain	Metric		Rating	Comments
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Uninformative	Exposure in this study was estimated solely by professional judgment. Job titles and industry were coded according to the 1980 United States census codes. 505 individual occupation codes were consolidated into 62 broader categories. A panel of four industrial hygienists from the University of Washington developed the job exposure matrix for participants. They had created JEMs previously. They classified the exposures examined into four levels based on likelihood and degree of exposure. There were no quantitative measures of exposure mentioned in this study.
	Metric 5:	Exposure Levels	Medium	Four levels of exposure were generated for each individual participating in the study. These were classified as no, low, medium, and high levels of exposure. These levels were determined for participants based on the number of years employed in their jobs.

Additional Comments: While the authors were extremely thorough in their description of the steps taken for this study, there were some limitations in terms of being useful for asbestos studies. There was a lack of power to detect an increase in risk. There were some positives for this study, such as adjusting for smoking and drinking in their models, which has not been often in some other studies.Overall, information on the measurement of exposure metric (M4) to assess exposure was limited. Therefore, the overall quality determination (OQD) is rated uninformative.

* No biomarkers were identified for this evaluation.

** As described in Appendix B.2 of the *White Paper: Quantitative Approach to the Human Health Assessment for the Risk Evaluation for Asbestos Part 2: Supplemental Evaluation Including Legacy Uses and Associated Disposals of Asbestos*, to be considered as being informative for dose-response analysis, metrics 4 and 5 would need metric ratings of Medium or High. This reference did not satisfy this requirement; therefore data quality evaluation is presented for only for metrics 4 and 5.

Study Citation:	Yano, E., Wang, Z. M., Wang, X. R., Wang, M. Z., Lan, Y. J. (2001). Cancer mortality among workers exposed to amphibole-free chrysotile asbestos. American Journal of Epidemiology 154(6):538-543.			
Health Outcome:	Lung Cancer; All cancers mortality; All cause mortality			
Target Organ(s):	Mortality: Lung cancer mortality, All cancers mortality, All cause mortality; Lung/Respiratory: Lung cancer mortality; Cancer/Carcinogenesis: All cancers mortality, Lung cancer mortality			
Asbestos Fiber Type(s):	Asbestos - Chrysotile (serpentine): 12001-29-5			
Linked HERO ID(s):	2538846, 3080569			
HERO ID:	3080569			
Domain		Metric	Rating	Comments
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Low	This metric is rated Low because authors in this paper do not explicitly cite use of PCM or TEM for use with the samples used in this analysis. While they mention use of TEM, they appear to reference chrysotile in general: "The amphibole contamination in commercial chrysotile has been assessed by N. Kohyama (National Institute for Industrial Health, Kawasaki, Japan, personal communication, 2000). He used the x-ray diffraction analysis and analytical transmission electron microscopy method, which can detect amphibole contamination of 0.001 percent or more." The actual measurements used in analysis are reported to be from "personal samplers that workers wore for 3 days in June 1999." The quantification method is not specified. The authors also mention collecting dust measurements, but no conversion factors are reported.
	Metric 5:	Exposure Levels	Medium	The authors reported summary statistics for multiple levels of exposure.
Additional Comments:	QC was not completed for metrics other than Metrics 4 and 5 because the study does not have sufficient exposure information to be useful for dose-response analysis.			

* No biomarkers were identified for this evaluation.

** As described in Appendix B.2 of the *White Paper: Quantitative Approach to the Human Health Assessment for the Risk Evaluation for Asbestos Part 2: Supplemental Evaluation Including Legacy Uses and Associated Disposals of Asbestos*, to be considered as being informative for dose-response analysis, metrics 4 and 5 would need metric ratings of Medium or High. This reference did not satisfy this requirement; therefore data quality evaluation is presented for only for metrics 4 and 5.