United States
Environmental Protection Agency

Office of Chemical Safety and
Pollution Prevention

Final Risk Evaluation for Asbestos Part 1: Chrysotile Asbestos

Systematic Review Supplemental File:

Data Quality Evaluation for Epidemiological Studies of Ovarian and Laryngeal Cancers

December 2020

Table Listing

Table 1: **Acheson et al. 1982: Evaluation of Cancer for Ovarian Cancer Mortality Outcomes**

Study Citation:	Acheson, E. D., Gardner, M. J., Pippard, E. C., Grime, L. P. (1982). Mortality of two groups of women who manufactured gas masks from chrysotile and crocidolite asbestos: a 40-year follow-up Occupational and Environmental Medicine, 39(4,4), 344-348
Data Type:	gasmask_manufacturing_women_ovarian-Cancer
HERO ID:	32

Domain	Metric		Rating[†]	MWF[⋆]	Score	Comments[††]
Domain 1: Study Participation						
	Metric 1:	Participant selection	Medium	× 0.4	0.8	The study setting was described and details on the mask manufacturing process and products were provided. Subjects were included based on residence in Blackburn in 1939 and indication of mask manufacturing on their employment records from the Office of Population Censuses and Surveys. There is some uncertainty whether employment records from this resource would be complete for all women in the area.
	Metric 2:	Attrition	High	× 0.4	0.4	A small number of women (4) died before the follow-up period began (1951), but this is not expected to appreciably bias the results. No other indication of loss-to-follow-up was provided.
	Metric 3:	Comparison Group	Medium	× 0.2	0.4	Rates of mortality for England and Wales (1951-1980) were used to compare with women from Blackburn. Local mortality rates 1968-1978 were used to adjust for location. The study authors note that rates of cause-specific mortality for the relevant area (Blackburn, Leyland, and Preston) were only available for this time period. Applying mortality rates from this specific time period to the full follow-up period may insert some uncertainty into the results.
Domain 2: Exposure Characterization						
	Metric 4:	Measurement of Exposure	Low	× 0.5	1.5	Exposure was assessed by employment at each of the asbestos gas mask manufacturing facilities only.
	Metric 5:	Exposure levels	Not Rated	NA	NA	
	Metric 6:	Temporality	High	× 0.5	0.5	Temporality was established. Women residing in Blackburn in 1939 with employment records showing gas mask manufacturing were followed until 1980. This is a sufficiently long follow-up period for determining rates of cause-specific mortality.
Domain 3: Outcome Assessment						

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Study Citation: Acheson, E. D., Gardner, M. J., Pippard, E. C., Grime, L. P. (1982). Mortality of two groups of women who manufactured gas masks from chrysotile and crocidolite asbestos: a 40-year follow-up Occupational and Environmental Medicine, 39(4,4), 344-348
Data Type: gasmask_manufacturing_women_ovarian-Cancer
HERO ID: 32

Domain	Metric		Rating†	MWF*	Score	Comments††
	Metric 7:	Outcome measurement or characterization	Medium	× 0.667	1.33	Vital status was determined form 1951 to 1980 for all subjects. It was not expressly stated, however, vital status was presumably obtained from the National Health Service Central Register. Mortality from cancer was detailed using ICD-8 codes. Histological confirmation of cancer deaths was not described.
	Metric 8:	Reporting Bias	Medium	× 0.333	0.67	Outcomes prespecified in the abstract, introduction, and methods were provided either qualitatively or quantitatively in the results. SMR estimates were provided with observed cases, expected cases, and confidence intervals.
Domain 4: Potential Confounding/Variable Control						
	Metric 9:	Covariate Adjustment	Medium	× 0.5	1	Only women were included in the analysis. Age- and calendar period-specific (in 5-year bins) mortality rates were calculated, accounting for age and time period. Individual smoking information was not available and not accounted for in the analysis.
	Metric 10:	Covariate Characterization	Medium	× 0.25	0.5	Covariate information was presumably obtained from the same source as vital status and employment--the National Health Service Central Register, Office of Population Censuses and Surveys.
	Metric 11:	Co-exposure Confounding	Medium	× 0.25	0.5	Masks manufactured at the Blackburn facility were noted to contain only chrysotile, charcoal, and merino wool. Crocidolite was not reported to be used at the relevant manufacturing facility.
Domain 5: Analysis						
	Metric 12:	Study Design and Methods	Medium	× 0.4	0.8	Cause-specific mortality for women employed in the mask manufacturing industry in Blackburn were determined by calculating SMRs using the person-years method. This is an appropriate design for the study question.
	Metric 13:	Statistical power	Medium	× 0.2	0.4	A total of 570 women were included in the analysis and followed for a total of 14,324 person-years. This is a sufficiently large population to detect an effect. The number of women observed with ovarian cancer was relatively low (n=5) and may need to be interpreted with caution.
	Metric 14:	Reproducibility of analyses	Medium	× 0.2	0.4	Analyses were adequately described and could be reproduced given original data.

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Study Citation:	Acheson, E. D., Gardner, M. J., Pippard, E. C., Grime, L. P. (1982). Mortality of two groups of women who manufactured gas masks from chrysotile and crocidolite asbestos: a 40-year follow-up Occupational and Environmental Medicine, 39(4,4), 344-348
Data Type:	gasmask_manufacturing_women_ovarian-Cancer
HERO ID:	32

Domain	Metric	Rating†	MWF⋆	Score	Comments††
	Metric 15: Statistical models	Medium	× 0.2	0.4	The statistical methods used were transparent. Details on the area adjustment were limited, however, this was not the primary outcome of the study.
Domain 6: Other Considerations for Biomarker Selection and Measurement					
	Metric 16: Use of Biomarker of Exposure		NA	NA	
	Metric 17: Effect biomarker		NA	NA	
	Metric 18: Method Sensitivity		NA	NA	
	Metric 19: Biomarker stability		NA	NA	
	Metric 20: Sample contamination		NA	NA	
	Metric 21: Method requirements		NA	NA	
	Metric 22: Matrix adjustment		NA	NA	
Overall Quality Determination‡		Medium		1.9	
Extracted		Yes			

⋆ MWF = Metric Weighting Factor

† High = 1; Medium = 2; Low = 3; Unacceptable = 4; N/A has no value.

‡ The overall rating is calculated as necessary. EPA may not always provide a comment for a metric that has been categorized as High.

$$\text{Overall rating} = \begin{cases} 4 & \text{if any metric is Unacceptable} \\ \left\lfloor \sum_i (\text{Metric Score}_i \times \text{MWF}_i) \,/\, \sum_j \text{MWF}_j \right\rceil_{0.1} & \text{(round to the nearest tenth) otherwise} \end{cases},$$

where High $=\geq 1$ to < 1.7; Medium $=\geq 1.7$ to < 2.3; Low $=\geq 2.3$ to ≤ 3.0. If the reviewer determines that the overall rating needs adjustment, the original rating is crossed out and an arrow points to the new rating.

†† This metric met the criteria for high confidence as expected for this type of study

Table 2: **Acheson et al. 1982: Evaluation of Cancer for Lung Cancer Mortality Outcomes**

Study Citation:	Acheson, E. D., Gardner, M. J., Pippard, E. C., Grime, L. P. (1982). Mortality of two groups of women who manufactured gas masks from chrysotile and crocidolite asbestos: a 40-year follow-up Occupational and Environmental Medicine, 39(4,4), 344-348
Data Type:	gasmask_manufacturing_women_lung-Cancer
HERO ID:	32

Domain	Metric		Rating[†]	MWF[⋆]	Score	Comments[††]
Domain 1: Study Participation						
	Metric 1:	Participant selection	Medium	× 0.4	0.8	The study setting was described and details on the mask manufacturing process and products were provided. Subjects were included based on residence in Blackburn in 1939 and indication of mask manufacturing on their employment records from the Office of Population Censuses and Surveys. There is some uncertainty whether employment records from this resource would be complete for all women in the area.
	Metric 2:	Attrition	High	× 0.4	0.4	A small number of women (4) died before the follow-up period began (1951), but this is not expected to appreciably bias the results. No other indication of loss-to-follow-up was provided.
	Metric 3:	Comparison Group	Medium	× 0.2	0.4	Rates of mortality for England and Wales (1951-1980) were used to compare with women from Blackburn. Local mortality rates 1968-1978) were used to adjust for location. The study authors note that rates of cause-specific mortality for the relevant area (Blackburn, Leyland, and Preston) were only available for this time period. Applying mortality rates from this specific time period to the full follow-up period may insert some uncertainty into the results.
Domain 2: Exposure Characterization						
	Metric 4:	Measurement of Exposure	Low	× 0.5	1.5	Exposure was assessed by employment at each of the asbestos gas mask manufacturing facilities only.
	Metric 5:	Exposure levels	Not Rated	NA	NA	
	Metric 6:	Temporality	High	× 0.5	0.5	Temporality was established. Women residing in Blackburn in 1939 with employment records showing gas mask manufacturing were followed until 1980. This is a sufficiently long follow-up period for determining rates of cause-specific mortality.
Domain 3: Outcome Assessment						

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Study Citation: Acheson, E. D., Gardner, M. J., Pippard, E. C., Grime, L. P. (1982). Mortality of two groups of women who manufactured gas masks from chrysotile and crocidolite asbestos: a 40-year follow-up Occupational and Environmental Medicine, 39(4,4), 344-348
Data Type: gasmask_manufacturing_women_lung-Cancer
HERO ID: 32

Domain	Metric		Rating†	MWF*	Score	Comments††
	Metric 7:	Outcome measurement or characterization	Medium	× 0.667	1.33	Vital status was determined form 1951 to 1980 for all subjects. It was not expressly stated, however, vital status was presumably obtained from the National Health Service Central Register. Mortality from cancer was detailed using ICD-8 codes. Histological confirmation of cancer deaths was not described.
	Metric 8:	Reporting Bias	Low	× 0.333	1.0	Outcomes prespecified in the abstract, introduction, and methods were provided either qualitatively or quantitatively in the results. SMR estimates were provided with observed cases, expected cases, and confidence intervals. Reported cases included one mesothelioma case
Domain 4: Potential Confounding/Variable Control						
	Metric 9:	Covariate Adjustment	Medium	× 0.5	1	Only women were included in the analysis. Age- and calendar period-specific (in 5-year bins) mortality rates were calculated, accounting for age and time period. Individual smoking information was not available and not accounted for in the analysis.
	Metric 10:	Covariate Characterization	Medium	× 0.25	0.5	Covariate information was presumably obtained from the same source as vital status and employment--the National Health Service Central Register, Office of Population Censuses and Surveys.
	Metric 11:	Co-exposure Confounding	Medium	× 0.25	0.5	Masks manufactured at the Blackburn facility were noted to contain only chrysotile, charcoal, and merino wool. Crocidolite was not reported to be used at the relevant manufacturing facility.
Domain 5: Analysis						
	Metric 12:	Study Design and Methods	Medium	× 0.4	0.8	Cause-specific mortality for women employed in the mask manufacturing industry in Blackburn were determined by calculating SMRs using the person-years method. This is an appropriate design for the study question.
	Metric 13:	Statistical power	Medium	× 0.2	0.4	A total of 570 women were included in the analysis and followed for a total of 14,324 person-years. This is a sufficiently large population to detect an effect.
	Metric 14:	Reproducibility of analyses	Medium	× 0.2	0.4	Analyses were adequately described and could be reproduced given original data.
	Metric 15:	Statistical models	Medium	× 0.2	0.4	The statistical methods used were transparent. Details on the area adjustment were limited, however, this was not the primary outcome of the study.

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Study Citation:	Acheson, E. D., Gardner, M. J., Pippard, E. C., Grime, L. P. (1982). Mortality of two groups of women who manufactured gas masks from chrysotile and crocidolite asbestos: a 40-year follow-up Occupational and Environmental Medicine, 39(4,4), 344-348
Data Type:	gasmask_manufacturing_women_lung-Cancer
HERO ID:	32

Domain	Metric	Rating†	MWF⋆	Score	Comments††
Domain 6: Other Considerations for Biomarker Selection and Measurement					
	Metric 16: Use of Biomarker of Exposure		NA	NA	
	Metric 17: Effect biomarker		NA	NA	
	Metric 18: Method Sensitivity		NA	NA	
	Metric 19: Biomarker stability		NA	NA	
	Metric 20: Sample contamination		NA	NA	
	Metric 21: Method requirements		NA	NA	
	Metric 22: Matrix adjustment		NA	NA	
Overall Quality Determination‡		Medium		2.0	
Extracted		Yes			

⋆ MWF = Metric Weighting Factor

† High = 1; Medium = 2; Low = 3; Unacceptable = 4; N/A has no value.

‡ The overall rating is calculated as necessary. EPA may not always provide a comment for a metric that has been categorized as High.

$$\text{Overall rating} = \begin{cases} 4 & \text{if any metric is Unacceptable} \\ \left\lfloor \sum_i (\text{Metric Score}_i \times \text{MWF}_i) \,/\, \sum_j \text{MWF}_j \right\rceil_{0.1} & \text{(round to the nearest tenth) otherwise} \end{cases},$$

where High $=\geq 1$ to < 1.7; Medium $=\geq 1.7$ to < 2.3; Low $=\geq 2.3$ to ≤ 3.0. If the reviewer determines that the overall rating needs adjustment, the original rating is crossed out and an arrow points to the new rating.

†† This metric met the criteria for high confidence as expected for this type of study

Table 3: **Newhouse and Sullivan 1989: Evaluation of Cancer for Ovarian Cancer Mortality Outcomes**

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(3,3), 176-179
Data Type:	Asbestos_workers_SMR_women_ovary-Cancer
HERO ID:	3082792

Domain	Metric		Rating[†]	MWF[⋆]	Score	Comments[††]
Domain 1: Study Participation						
	Metric 1:	Participant selection	Medium	× 0.4	0.8	Retrospective occupational mortality cohort including 13 450 subjects (men and women) first employed between 1941 and 1979 in one factory located in the UK. Follow-up is until 1986. Nine men and one woman with unknown dates of birth have been excluded from the original cohort. At the end of 1979, 2.6% of workers had emigrated. Setting of the plant is well described. No other details are provided on participants.
	Metric 2:	Attrition	High	× 0.4	0.4	Little loss to follow-up due to emigration (2.6%).
	Metric 3:	Comparison Group	Medium	× 0.2	0.4	Although not clearly spelled out in this reference, Berry and Newhouse 1983 (HERO ID 43) mentions use of national death rates as comparison group.
Domain 2: Exposure Characterization						
	Metric 4:	Measurement of Exposure	Low	× 0.5	1.5	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	Not Rated	NA	NA	
	Metric 6:	Temporality	Medium	× 0.5	1	Adequate follow-up (43 years) for cancer mortality to be observed.
Domain 3: Outcome Assessment						
	Metric 7:	Outcome measurement or characterization	Low	× 0.667	2	Death certificates from the National Health Service Central Registrar, were coded to the 8th revision of the International Classification of Disease (ICD). There are no other details provided on outcome assessment, and ICD codes are only reported for chronic respiratory diseases.
	Metric 8:	Reporting Bias	Medium	× 0.333	0.67	Some cancer mortality results are reported for "other causes", some are spelled out in the text, but it is unclear if all are reported. 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).
Domain 4: Potential Confounding/Variable Control						

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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(3,3), 176-179
Data Type: Asbestos_workers_SMR_women_ovary-Cancer
HERO ID: 3082792

Domain	Metric		Rating†	MWF*	Score	Comments††
	Metric 9:	Covariate Adjustment	Medium	× 0.5	1	Sex, age and period were accounted for. Smoking was not accounted for.
	Metric 10:	Covariate Characterization	Low	× 0.25	0.75	There is no discussion of covariate characterization, but likely it came from employment records and death certificates.
	Metric 11:	Co-exposure Confounding	Low	× 0.25	0.75	There is no specific discussion of potential co-exposures, however the occupational setting suggests potential for other exposures, which could be differential depending on the job titles of the workers.
Domain 5: Analysis						
	Metric 12:	Study Design and Methods	Medium	× 0.4	0.8	SMRs were calculated using the subject year method, with 90% confidence intervals (90% CI). Poisson or normal approximation were used depending on the number of observed deaths.
	Metric 13:	Statistical power	Medium	× 0.2	0.4	The number of participants, number of observed deaths and length of follow-up are adequate.
	Metric 14:	Reproducibility of analyses	Medium	× 0.2	0.4	Basic details are provided in the report.
	Metric 15:	Statistical models	Medium	× 0.2	0.4	Adequate models. SMRs based on 30 or fewer deaths confidence intervals were computed with the exact method based on the Poisson distribution. The normal approximation was used for others.
Domain 6: Other Considerations for Biomarker Selection and Measurement						
	Metric 16:	Use of Biomarker of Exposure		NA	NA	
	Metric 17:	Effect biomarker		NA	NA	
	Metric 18:	Method Sensitivity		NA	NA	
	Metric 19:	Biomarker stability		NA	NA	
	Metric 20:	Sample contamination		NA	NA	
	Metric 21:	Method requirements		NA	NA	
	Metric 22:	Matrix adjustment		NA	NA	
Overall Quality Determination‡			Low		2.3	
Extracted			Yes			

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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(3,3), 176-179
Data Type:	Asbestos_workers_SMR_women_ovary-Cancer
HERO ID:	3082792

Domain	Metric	Rating†	MWF⋆	Score	Comments††

⋆ MWF = Metric Weighting Factor
† High = 1; Medium = 2; Low = 3; Unacceptable = 4; N/A has no value.
‡ The overall rating is calculated as necessary. EPA may not always provide a comment for a metric that has been categorized as High.

$$\text{Overall rating} = \begin{cases} 4 & \text{if any metric is Unacceptable} \\ \left\lfloor \sum_i (\text{Metric Score}_i \times \text{MWF}_i) \,/\, \sum_j \text{MWF}_j \right\rceil_{0.1} & \text{(round to the nearest tenth) otherwise} \end{cases},$$

where High $=\geq 1$ to < 1.7; Medium $=\geq 1.7$ to < 2.3; Low $=\geq 2.3$ to ≤ 3.0. If the reviewer determines that the overall rating needs adjustment, the original rating is crossed out and an arrow points to the new rating.
†† This metric met the criteria for high confidence as expected for this type of study

Table 4: **Newhouse and Sullivan 1989: Evaluation of Cancer for Female Lung Cancer Mortality Outcomes**

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(3,3), 176-179
Data Type:	Asbestos_workers_SMR_women_lung-Cancer
HERO ID:	3082792

Domain	Metric		Rating[†]	MWF[⋆]	Score	Comments[††]
Domain 1: Study Participation						
	Metric 1:	Participant selection	Medium	× 0.4	0.8	Retrospective occupational mortality cohort including 13 450 subjects (men and women) first employed between 1941 and 1979 in one factory located in the UK. Follow-up is until 1986. Nine men and one woman with unknown dates of birth have been excluded from the original cohort. At the end of 1979, 2.6% of workers had emigrated. Setting of the plant is well described. No other details are provided on participants.
	Metric 2:	Attrition	High	× 0.4	0.4	Little loss to follow-up due to emigration (2.6%).
	Metric 3:	Comparison Group	Medium	× 0.2	0.4	Although not clearly spelled out in this reference, Berry and Newhouse 1983 (HERO ID 43) mentions use of national death rates as comparison group.
Domain 2: Exposure Characterization						
	Metric 4:	Measurement of Exposure	Low	× 0.5	1.5	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	Not Rated	NA	NA	
	Metric 6:	Temporality	Medium	× 0.5	1	Adequate follow-up (43 years) for cancer mortality to be observed.
Domain 3: Outcome Assessment						
	Metric 7:	Outcome measurement or characterization	Low	× 0.667	2	Death certificates from the National Health Service Central Registrar, were coded to the 8th revision of the International Classification of Disease (ICD). There are no other details provided on outcome assessment, and ICD codes are only reported for chronic respiratory diseases.
	Metric 8:	Reporting Bias	Medium	× 0.333	0.67	Some cancer mortality results are reported for "other causes", some are spelled out in the text, but it is unclear if all are reported. 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).
Domain 4: Potential Confounding/Variable Control						

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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(3,3), 176-179
Data Type: Asbestos_workers_SMR_women_lung-Cancer
HERO ID: 3082792

Domain	Metric		Rating†	MWF*	Score	Comments††
	Metric 9:	Covariate Adjustment	Medium	× 0.5	1	Sex, age and period were accounted for. Smoking was not accounted for.
	Metric 10:	Covariate Characterization	Low	× 0.25	0.75	There is no discussion of covariate characterization, but likely it came from employment records and death certificates.
	Metric 11:	Co-exposure Confounding	Low	× 0.25	0.75	There is no specific discussion of potential co-exposures, however the occupational setting suggests potential for other exposures, which could be differential depending on the job titles of the workers.
Domain 5: Analysis						
	Metric 12:	Study Design and Methods	Medium	× 0.4	0.8	SMRs were calculated using the subject year method, with 90% confidence intervals (90% CI). Poisson or normal approximation were used depending on the number of observed deaths.
	Metric 13:	Statistical power	Medium	× 0.2	0.4	The number of participants, number of observed deaths and length of follow-up are adequate.
	Metric 14:	Reproducibility of analyses	Medium	× 0.2	0.4	Basic details are provided in the report.
	Metric 15:	Statistical models	Medium	× 0.2	0.4	Adequate models. SMRs based on 30 or fewer deaths confidence intervals were computed with the exact method based on the Poisson distribution. The normal approximation was used for others.
Domain 6: Other Considerations for Biomarker Selection and Measurement						
	Metric 16:	Use of Biomarker of Exposure		NA	NA	
	Metric 17:	Effect biomarker		NA	NA	
	Metric 18:	Method Sensitivity		NA	NA	
	Metric 19:	Biomarker stability		NA	NA	
	Metric 20:	Sample contamination		NA	NA	
	Metric 21:	Method requirements		NA	NA	
	Metric 22:	Matrix adjustment		NA	NA	
Overall Quality Determination‡			Low		2.3	
Extracted			Yes			

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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(3,3), 176-179
Data Type:	Asbestos_workers_SMR_women_lung-Cancer
HERO ID:	3082792

Domain	Metric	Rating†	MWF⋆	Score	Comments††

⋆ MWF = Metric Weighting Factor
† High = 1; Medium = 2; Low = 3; Unacceptable = 4; N/A has no value.
‡ The overall rating is calculated as necessary. EPA may not always provide a comment for a metric that has been categorized as High.

$$\text{Overall rating} = \begin{cases} 4 & \text{if any metric is Unacceptable} \\ \left\lfloor \sum_i (\text{Metric Score}_i \times \text{MWF}_i) \,/\, \sum_j \text{MWF}_j \right\rceil_{0.1} & \text{(round to the nearest tenth) otherwise} \end{cases},$$

where High $=\geq 1$ to < 1.7; Medium $=\geq 1.7$ to < 2.3; Low $=\geq 2.3$ to ≤ 3.0. If the reviewer determines that the overall rating needs adjustment, the original rating is crossed out and an arrow points to the new rating.

†† This metric met the criteria for high confidence as expected for this type of study

Table 5: **Newhouse and Sullivan 1989: Evaluation of Cancer for Male and Female Lung Cancer Mortality Outcomes**

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(3,3), 176-179
Data Type:	Asbestos_workers_SMR_combined_lung-Cancer
HERO ID:	3082792

Domain	Metric		Rating†	MWF⋆	Score	Comments††
Domain 1: Study Participation						
	Metric 1:	Participant selection	Medium	× 0.4	0.8	Retrospective occupational mortality cohort including 13 450 subjects (men and women) first employed between 1941 and 1979 in one factory located in the UK. Follow-up is until 1986. Nine men and one woman with unknown dates of birth have been excluded from the original cohort. At the end of 1979, 2.6% of workers had emigrated. Setting of the plant is well described. No other details are provided on participants.
	Metric 2:	Attrition	High	× 0.4	0.4	Little loss to follow-up due to emigration (2.6%).
	Metric 3:	Comparison Group	Medium	× 0.2	0.4	Although not clearly spelled out in this reference, Berry and Newhouse 1983 (HERO ID 43) mentions use of national death rates as comparison group.
Domain 2: Exposure Characterization						
	Metric 4:	Measurement of Exposure	Low	× 0.5	1.5	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	Not Rated	NA	NA	
	Metric 6:	Temporality	Medium	× 0.5	1	Adequate follow-up (43 years) for cancer mortality to be observed.
Domain 3: Outcome Assessment						
	Metric 7:	Outcome measurement or characterization	Low	× 0.667	2	Death certificates from the National Health Service Central Registrar, were coded to the 8th revision of the International Classification of Disease (ICD). There are no other details provided on outcome assessment, and ICD codes are only reported for chronic respiratory diseases.
	Metric 8:	Reporting Bias	Medium	× 0.333	0.67	Some cancer mortality results are reported for "other causes", some are spelled out in the text, but it is unclear if all are reported. 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).
Domain 4: Potential Confounding/Variable Control						

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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(3,3), 176-179
Data Type: Asbestos_workers_SMR_combined_lung-Cancer
HERO ID: 3082792

Domain		Metric	Rating†	MWF*	Score	Comments††
	Metric 9:	Covariate Adjustment	Medium	× 0.5	1	Sex, age and period were accounted for. Smoking was not accounted for.
	Metric 10:	Covariate Characterization	Low	× 0.25	0.75	There is no discussion of covariate characterization, but likely it came from employment records and death certificates.
	Metric 11:	Co-exposure Confounding	Low	× 0.25	0.75	There is no specific discussion of potential co-exposures, however the occupational setting suggests potential for other exposures, which could be differential depending on the job titles of the workers.
Domain 5: Analysis						
	Metric 12:	Study Design and Methods	Medium	× 0.4	0.8	SMRs were calculated using the subject year method, with 90% confidence intervals (90% CI). Poisson or normal approximation were used depending on the number of observed deaths.
	Metric 13:	Statistical power	Medium	× 0.2	0.4	The number of participants, number of observed deaths and length of follow-up are adequate.
	Metric 14:	Reproducibility of analyses	Medium	× 0.2	0.4	Basic details are provided in the report.
	Metric 15:	Statistical models	Medium	× 0.2	0.4	Adequate models. SMRs based on 30 or fewer deaths confidence intervals were computed with the exact method based on the Poisson distribution. The normal approximation was used for others.
Domain 6: Other Considerations for Biomarker Selection and Measurement						
	Metric 16:	Use of Biomarker of Exposure		NA	NA	
	Metric 17:	Effect biomarker		NA	NA	
	Metric 18:	Method Sensitivity		NA	NA	
	Metric 19:	Biomarker stability		NA	NA	
	Metric 20:	Sample contamination		NA	NA	
	Metric 21:	Method requirements		NA	NA	
	Metric 22:	Matrix adjustment		NA	NA	
Overall Quality Determination‡			Low		2.3	
Extracted			Yes			

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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(3,3), 176-179
Data Type:	Asbestos_workers_SMR_combined_lung-Cancer
HERO ID:	3082792

Domain	Metric	Rating†	MWF⋆	Score	Comments††

⋆ MWF = Metric Weighting Factor
† High = 1; Medium = 2; Low = 3; Unacceptable = 4; N/A has no value.
‡ The overall rating is calculated as necessary. EPA may not always provide a comment for a metric that has been categorized as High.

$$\text{Overall rating} = \begin{cases} 4 & \text{if any metric is Unacceptable} \\ \left\lfloor \sum_i (\text{Metric Score}_i \times \text{MWF}_i) \,/\, \sum_j \text{MWF}_j \right\rceil_{0.1} & \text{(round to the nearest tenth) otherwise} \end{cases},$$

where High $=\geq 1$ to < 1.7; Medium $=\geq 1.7$ to < 2.3; Low $=\geq 2.3$ to ≤ 3.0. If the reviewer determines that the overall rating needs adjustment, the original rating is crossed out and an arrow points to the new rating.

†† This metric met the criteria for high confidence as expected for this type of study

Table 6: **Newhouse and Sullivan 1989: Evaluation of Cancer for Laryngeal Cancer Mortality Outcomes**

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(3,3), 176-179
Data Type:	Asbestos_workers_SMR_men_larynx-Cancer
HERO ID:	3082792

Domain	Metric		Rating[†]	MWF[⋆]	Score	Comments[††]
Domain 1: Study Participation						
	Metric 1:	Participant selection	Medium	× 0.4	0.8	Retrospective occupational mortality cohort including 13 450 subjects (men and women) first employed between 1941 and 1979 in one factory located in the UK. Follow-up is until 1986. Nine men and one woman with unknown dates of birth have been excluded from the original cohort. At the end of 1979, 2.6% of workers had emigrated. Setting of the plant is well described. No other details are provided on participants.
	Metric 2:	Attrition	High	× 0.4	0.4	Little loss to follow-up due to emigration (2.6%).
	Metric 3:	Comparison Group	Medium	× 0.2	0.4	Although not clearly spelled out in this reference, Berry and Newhouse 1983 (HERO ID 43) mentions use of national death rates as comparison group.
Domain 2: Exposure Characterization						
	Metric 4:	Measurement of Exposure	Low	× 0.5	1.5	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	Not Rated	NA	NA	
	Metric 6:	Temporality	Medium	× 0.5	1	Adequate follow-up (43 years) for cancer mortality to be observed.
Domain 3: Outcome Assessment						
	Metric 7:	Outcome measurement or characterization	Low	× 0.667	2	Death certificates from the National Health Service Central Registrar, were coded to the 8th revision of the International Classification of Disease (ICD). There are no other details provided on outcome assessment, and ICD codes are only reported for chronic respiratory diseases.
	Metric 8:	Reporting Bias	Medium	× 0.333	0.67	Some cancer mortality results are reported for "other causes", some are spelled out in the text, but it is unclear if all are reported. 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).
Domain 4: Potential Confounding/Variable Control						

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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(3,3), 176-179
Data Type: Asbestos_workers_SMR_men_larynx-Cancer
HERO ID: 3082792

Domain	Metric		Rating†	MWF⋆	Score	Comments††
	Metric 9:	Covariate Adjustment	Medium	× 0.5	1	Sex, age and period were accounted for. Smoking was not accounted for.
	Metric 10:	Covariate Characterization	Low	× 0.25	0.75	There is no discussion of covariate characterization, but likely it came from employment records and death certificates.
	Metric 11:	Co-exposure Confounding	Low	× 0.25	0.75	There is no specific discussion of potential co-exposures, however the occupational setting suggests potential for other exposures, which could be differential depending on the job titles of the workers.
Domain 5: Analysis						
	Metric 12:	Study Design and Methods	Medium	× 0.4	0.8	SMRs were calculated using the subject year method, with 90% confidence intervals (90% CI). Poisson or normal approximation were used depending on the number of observed deaths.
	Metric 13:	Statistical power	Medium	× 0.2	0.4	The number of participants, number of observed deaths and length of follow-up are adequate.
	Metric 14:	Reproducibility of analyses	Medium	× 0.2	0.4	Basic details are provided in the report.
	Metric 15:	Statistical models	Medium	× 0.2	0.4	Adequate models. SMRs based on 30 or fewer deaths confidence intervals were computed with the exact method based on the Poisson distribution. The normal approximation was used for others.
Domain 6: Other Considerations for Biomarker Selection and Measurement						
	Metric 16:	Use of Biomarker of Exposure		NA	NA	
	Metric 17:	Effect biomarker		NA	NA	
	Metric 18:	Method Sensitivity		NA	NA	
	Metric 19:	Biomarker stability		NA	NA	
	Metric 20:	Sample contamination		NA	NA	
	Metric 21:	Method requirements		NA	NA	
	Metric 22:	Matrix adjustment		NA	NA	
Overall Quality Determination‡			Low		2.3	
Extracted			Yes			

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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(3,3), 176-179
Data Type:	Asbestos_workers_SMR_men_larynx-Cancer
HERO ID:	3082792

Domain	Metric	Rating†	MWF⋆	Score	Comments††

⋆ MWF = Metric Weighting Factor
† High = 1; Medium = 2; Low = 3; Unacceptable = 4; N/A has no value.
‡ The overall rating is calculated as necessary. EPA may not always provide a comment for a metric that has been categorized as High.

$$\text{Overall rating} = \begin{cases} 4 & \text{if any metric is Unacceptable} \\ \left\lfloor \sum_i (\text{Metric Score}_i \times \text{MWF}_i) \,/\, \sum_j \text{MWF}_j \right\rceil_{0.1} & \text{(round to the nearest tenth) otherwise} \end{cases},$$

where High $=\geq 1$ to < 1.7; Medium $=\geq 1.7$ to < 2.3; Low $=\geq 2.3$ to ≤ 3.0. If the reviewer determines that the overall rating needs adjustment, the original rating is crossed out and an arrow points to the new rating.

†† This metric met the criteria for high confidence as expected for this type of study

Table 7: **Gardner and Powell 1986: Evaluation of Cancer for Ovarian Cancer Mortality Outcomes**

Study Citation:	Gardner, M. J., Powell, C. A. (1986). Mortality of asbestos cement workers using almost exclusively chrysotile fibre Journal of the Society of Occupational Medicine, 36(4,4), 124-126					
Data Type:	Asbestos_workers_SMR_ovary-Cancer					
HERO ID:	3083384					
Domain		Metric	Rating†	MWF⋆	Score	Comments††
Domain 1: Study Participation						
	Metric 1:	Participant selection	Low	× 0.4	1.2	Retrospective occupational cohort study of 2167 workers (1510 men and 657 women) employed between 1941 and 1983 in chrysotile asbestos cement products factories in England, South Wales and Sweden . This study combines three occupational cohorts. Only the results for men are described. The periods of employment varied between plants/studies. Eligibility criteria vary between plants (employment for at least 6 months (plant 1), Thomas et al 1982 HERO ID 207), 3 months (plant 2/Swedish cohort, Ohlson and Hogstedt 1985 HERO D: 3083459), none for plant 3 (Garner et al 1986 HERO ID 3083223) Follow-up for ascertainment of vital status was until December 1977 (plant 1), 1982 (plant 2) and December 1984 for plant 3. Comparability of cohorts is not discussed.
	Metric 2:	Attrition	High	× 0.4	0.4	Loss to follow-up was minimal: 5% in Plant 1, 2% in Plant 2/Swedish cohort (1%), 30% for men in Plant 3 cohort.
	Metric 3:	Comparison Group	Low	× 0.2	0.6	SMRs were estimated using England and Wales for comparison population (plants 1 and 3), and Swedish national death rates (Plant 2 cohort). is is unclear what the comparison population for total mortality rates were calculated.
Domain 2: Exposure Characterization						
	Metric 4:	Measurement of Exposure	Low	× 0.5	1.5	Exposures were based on employment at the respective plants, Industrial hygiene measures are described confirming exposure. For the combined analyses type of job was not considered.
	Metric 5:	Exposure levels	Not Rated	NA	NA	
	Metric 6:	Temporality	Low	× 0.5	1.5	Follow-up sometimes ended the year after employment, making it an inadequate length of time for cancer mortality to be observed.
Domain 3: Outcome Assessment						

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Study Citation: Gardner, M. J., Powell, C. A. (1986). Mortality of asbestos cement workers using almost exclusively chrysotile fibre Journal of the Society of Occupational Medicine, 36(4,4), 124-126
Data Type: Asbestos_workers_SMR_ovary-Cancer
HERO ID: 3083384

Domain	Metric		Rating†	MWF⋆	Score	Comments††
	Metric 7:	Outcome measurement or characterization	Low	× 0.667	2	Sources were different by cohort. Plant 1 and 3 cohorts used death certificates from the National Health Service Central Register and the Department of Health and Social Security. ICD codes are listed for Plant 1 cohort. In the Plant 2 cohort, vital status was traced through the death and burial books of the parishes. Death certificates were checked with the Swedish National Central Bureau of Statistics and the officially determined underlying cause of death has been used. ICD codes are not listed for cohort 3. There is potential for outcome misclassification from death certificates. In addition, for the analysis combining the three cohorts, there is high potential misclassification due to various sources, national practices, etc .
	Metric 8:	Reporting Bias	Medium	× 0.333	0.67	Measured outcomes were reported, out unclear how the reference population was used for the combined cancers across cohorts.
Domain 4: Potential Confounding/Variable Control						
	Metric 9:	Covariate Adjustment	Low	× 0.5	1.5	Although not specifically stated, age and calendar year were accounted for in the Plant-specific analyses, making it likely that the total SMR would be adjusted similarly.
	Metric 10:	Covariate Characterization	Low	× 0.25	0.75	No discussion of covariate characterization, likely from plant records and death certificates.
	Metric 11:	Co-exposure Confounding	Medium	× 0.25	0.5	For plant 2: "The vast majority of asbestos used was chrysotile but 630 tons of amosite were used between 1949 and 1951 and 400 tons of crocidolite in 1962. The use of these amphiboles was estimated to be less than 1% of all asbestos used." Plant 3 only used chrysotile asbestos except for a “small” amount of amosite during 4 months in 1976. This is not expected to appreciably bias the results.
Domain 5: Analysis						
	Metric 12:	Study Design and Methods	Medium	× 0.4	0.8	Adequate design and methods. SMRs were estimated using Poisson distribution assumptions (plant 2), or by the person years method using a computer program (Plants 1 and 3).
	Metric 13:	Statistical power	Medium	× 0.2	0.4	2167 workers (1510 men and 657 women) were included in the analysis, however the short follow-up may limit the power to detect an effect.

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Study Citation:	Gardner, M. J., Powell, C. A. (1986). Mortality of asbestos cement workers using almost exclusively chrysotile fibre Journal of the Society of Occupational Medicine, 36(4,4), 124-126
Data Type:	Asbestos_workers_SMR_ovary-Cancer
HERO ID:	3083384

Domain	Metric		Rating†	MWF⋆	Score	Comments††
	Metric 14:	Reproducibility of analyses	Medium	× 0.2	0.4	Unclear how/what the referent group was used for the combined cohorts analysis.
	Metric 15:	Statistical models	Low	× 0.2	0.6	There is no description of how the combined SMRs were calculated.
Domain 6: Other Considerations for Biomarker Selection and Measurement						
	Metric 16:	Use of Biomarker of Exposure		NA	NA	
	Metric 17:	Effect biomarker		NA	NA	
	Metric 18:	Method Sensitivity		NA	NA	
	Metric 19:	Biomarker stability		NA	NA	
	Metric 20:	Sample contamination		NA	NA	
	Metric 21:	Method requirements		NA	NA	
	Metric 22:	Matrix adjustment		NA	NA	
Overall Quality Determination‡			Low		2.6	
Extracted			Yes			

⋆ MWF = Metric Weighting Factor

† High = 1; Medium = 2; Low = 3; Unacceptable = 4; N/A has no value.

‡ The overall rating is calculated as necessary. EPA may not always provide a comment for a metric that has been categorized as High.

$$\text{Overall rating} = \begin{cases} 4 & \text{if any metric is Unacceptable} \\ \left\lfloor \sum_i (\text{Metric Score}_i \times \text{MWF}_i) \,/\, \sum_j \text{MWF}_j \right\rceil_{0.1} & \text{(round to the nearest tenth) otherwise} \end{cases},$$

where High $=\geq 1$ to < 1.7; Medium $=\geq 1.7$ to < 2.3; Low $=\geq 2.3$ to ≤ 3.0. If the reviewer determines that the overall rating needs adjustment, the original rating is crossed out and an arrow points to the new rating.

†† This metric met the criteria for high confidence as expected for this type of study

Table 8: **Gardner and Powell 1986: Evaluation of Cancer for Female Lung Cancer Mortality Outcomes**

Study Citation:	Gardner, M. J., Powell, C. A. (1986). Mortality of asbestos cement workers using almost exclusively chrysotile fibre Journal of the Society of Occupational Medicine, 36(4,4), 124-126
Data Type:	Asbestos_workers_SMR_lung-Cancer
HERO ID:	3083384

Domain	Metric		Rating[†]	MWF[⋆]	Score	Comments[††]
Domain 1: Study Participation						
	Metric 1:	Participant selection	Low	× 0.4	1.2	Retrospective occupational cohort study of 2167 workers (1510 men and 657 women) employed between 1941 and 1983 in chrysotile asbestos cement products factories in England, South Wales and Sweden . This study combines three occupational cohorts. Only the results for men are described. The periods of employment varied between plants/studies. Eligibility criteria vary between plants (employment for at least 6 months (plant 1), Thomas et al 1982 HERO ID 207), 3 months (plant 2/Swedish cohort, Ohlson and Hogstedt 1985 HERO D: 3083459), none for plant 3 (Garner et al 1986 HERO ID 3083223) Follow-up for ascertainment of vital status was until December 1977 (plant 1), 1982 (plant 2) and December 1984 for plant 3. Comparability of cohorts is not discussed.
	Metric 2:	Attrition	High	× 0.4	0.4	Loss to follow-up was minimal: 5% in Plant 1, 2% in Plant 2/Swedish cohort (1%), 30% for men in Plant 3 cohort.
	Metric 3:	Comparison Group	Low	× 0.2	0.6	SMRs were estimated using England and Wales for comparison population (plants 1 and 3), and Swedish national death rates (Plant 2 cohort). is is unclear what the comparison population for total mortality rates were calculated.
Domain 2: Exposure Characterization						
	Metric 4:	Measurement of Exposure	Low	× 0.5	1.5	Exposures were based on employment at the respective plants, Industrial hygiene measures are described confirming exposure. For the combined analyses type of job was not considered.
	Metric 5:	Exposure levels	Not Rated	NA	NA	
	Metric 6:	Temporality	Low	× 0.5	1.5	Follow-up sometimes ended the year after employment, making it an inadequate length of time for cancer mortality to be observed.
Domain 3: Outcome Assessment						

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Study Citation: Gardner, M. J., Powell, C. A. (1986). Mortality of asbestos cement workers using almost exclusively chrysotile fibre Journal of the Society of Occupational Medicine, 36(4,4), 124-126
Data Type: Asbestos_workers_SMR_lung-Cancer
HERO ID: 3083384

Domain	Metric		Rating†	MWF*	Score	Comments††
	Metric 7:	Outcome measurement or characterization	Low	× 0.667	2	Sources were different by cohort. Plant 1 and 3 cohorts used death certificates from the National Health Service Central Register and the Department of Health and Social Security. ICD codes are listed for Plant 1 cohort. In the Plant 2 cohort, vital status was traced through the death and burial books of the parishes. Death certificates were checked with the Swedish National Central Bureau of Statistics and the officially determined underlying cause of death has been used. ICD codes are not listed for cohort 3. There is potential for outcome misclassification from death certificates. In addition, for the analysis combining the three cohorts, there is high potential misclassification due to various sources, national practices, etc .
	Metric 8:	Reporting Bias	Medium	× 0.333	0.67	Measured outcomes were reported, out unclear how the reference population was used for the combined cancers across cohorts.
Domain 4: Potential Confounding/Variable Control						
	Metric 9:	Covariate Adjustment	Low	× 0.5	1.5	Although not specifically stated, age and calendar year were accounted for in the Plant-specific analyses, making it likely that the total SMR would be adjusted similarly.
	Metric 10:	Covariate Characterization	Low	× 0.25	0.75	No discussion of covariate characterization, likely from plant records and death certificates.
	Metric 11:	Co-exposure Confounding	Medium	× 0.25	0.5	For plant 2: "The vast majority of asbestos used was chrysotile but 630 tons of amosite were used between 1949 and 1951 and 400 tons of crocidolite in 1962. The use of these amphiboles was estimated to be less than 1% of all asbestos used." Plant 3 only used chrysotile asbestos except for a “small” amount of amosite during 4 months in 1976. This is not expected to appreciably bias the results.
Domain 5: Analysis						
	Metric 12:	Study Design and Methods	Medium	× 0.4	0.8	Adequate design and methods. SMRs were estimated using Poisson distribution assumptions (plant 2), or by the person years method using a computer program (Plants 1 and 3).
	Metric 13:	Statistical power	Medium	× 0.2	0.4	2167 workers (1510 men and 657 women) were included in the analysis, however the short follow-up may limit the power to detect an effect.

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Study Citation:	Gardner, M. J., Powell, C. A. (1986). Mortality of asbestos cement workers using almost exclusively chrysotile fibre Journal of the Society of Occupational Medicine, 36(4,4), 124-126
Data Type:	Asbestos_workers_SMR_lung-Cancer
HERO ID:	3083384

Domain	Metric		Rating†	MWF⋆	Score	Comments††
	Metric 14:	Reproducibility of analyses	Medium	× 0.2	0.4	Unclear how/what the referent group was used for the combined cohorts analysis.
	Metric 15:	Statistical models	Low	× 0.2	0.6	There is no description of how the combined SMRs were calculated.
Domain 6: Other Considerations for Biomarker Selection and Measurement						
	Metric 16:	Use of Biomarker of Exposure		NA	NA	
	Metric 17:	Effect biomarker		NA	NA	
	Metric 18:	Method Sensitivity		NA	NA	
	Metric 19:	Biomarker stability		NA	NA	
	Metric 20:	Sample contamination		NA	NA	
	Metric 21:	Method requirements		NA	NA	
	Metric 22:	Matrix adjustment		NA	NA	
Overall Quality Determination‡			Low		2.6	
Extracted			Yes			

⋆ MWF = Metric Weighting Factor

† High = 1; Medium = 2; Low = 3; Unacceptable = 4; N/A has no value.

‡ The overall rating is calculated as necessary. EPA may not always provide a comment for a metric that has been categorized as High.

$$\text{Overall rating} = \begin{cases} 4 & \text{if any metric is Unacceptable} \\ \left\lfloor \sum_i (\text{Metric Score}_i \times \text{MWF}_i) \,/\, \sum_j \text{MWF}_j \right\rceil_{0.1} & \text{(round to the nearest tenth) otherwise} \end{cases},$$

where High $=\geq 1$ to < 1.7; Medium $=\geq 1.7$ to < 2.3; Low $=\geq 2.3$ to ≤ 3.0. If the reviewer determines that the overall rating needs adjustment, the original rating is crossed out and an arrow points to the new rating.

†† This metric met the criteria for high confidence as expected for this type of study

Table 9: **Gardner and Powell 1986: Evaluation of Cancer for Male and Female Lung Cancer Mortality Outcomes**

Study Citation:	Gardner, M. J., Powell, C. A. (1986). Mortality of asbestos cement workers using almost exclusively chrysotile fibre Journal of the Society of Occupational Medicine, 36(4,4), 124-126
Data Type:	Asbestos_workers_SMR_lung_combined-Cancer
HERO ID:	3083384

Domain	Metric		Rating†	MWF⋆	Score	Comments††
Domain 1: Study Participation						
	Metric 1:	Participant selection	Low	× 0.4	1.2	Retrospective occupational cohort study of 2167 workers (1510 men and 657 women) employed between 1941 and 1983 in chrysotile asbestos cement products factories in England, South Wales and Sweden . This study combines three occupational cohorts. Only the results for men are described. The periods of employment varied between plants/studies. Eligibility criteria vary between plants (employment for at least 6 months (plant 1), Thomas et al 1982 HERO ID 207), 3 months (plant 2/Swedish cohort, Ohlson and Hogstedt 1985 HERO D: 3083459), none for plant 3 (Garner et al 1986 HERO ID 3083223) Follow-up for ascertainment of vital status was until December 1977 (plant 1), 1982 (plant 2) and December 1984 for plant 3. Comparability of cohorts is not discussed.
	Metric 2:	Attrition	High	× 0.4	0.4	Loss to follow-up was minimal: 5% in Plant 1, 2% in Plant 2/Swedish cohort (1%), 30% for men in Plant 3 cohort.
	Metric 3:	Comparison Group	Low	× 0.2	0.6	SMRs were estimated using England and Wales for comparison population (plants 1 and 3), and Swedish national death rates (Plant 2 cohort). is is unclear what the comparison population for total mortality rates were calculated.
Domain 2: Exposure Characterization						
	Metric 4:	Measurement of Exposure	Low	× 0.5	1.5	Exposures were based on employment at the respective plants, Industrial hygiene measures are described confirming exposure. For the combined analyses type of job was not considered.
	Metric 5:	Exposure levels	Not Rated	NA	NA	
	Metric 6:	Temporality	Low	× 0.5	1.5	Follow-up sometimes ended the year after employment, making it an inadequate length of time for cancer mortality to be observed.
Domain 3: Outcome Assessment						

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Study Citation: Gardner, M. J., Powell, C. A. (1986). Mortality of asbestos cement workers using almost exclusively chrysotile fibre Journal of the Society of Occupational Medicine, 36(4,4), 124-126
Data Type: Asbestos_workers_SMR_lung_combined-Cancer
HERO ID: 3083384

Domain	Metric		Rating†	MWF*	Score	Comments††
	Metric 7:	Outcome measurement or characterization	Low	× 0.667	2	Sources were different by cohort. Plant 1 and 3 cohorts used death certificates from the National Health Service Central Register and the Department of Health and Social Security. ICD codes are listed for Plant 1 cohort. In the Plant 2 cohort, vital status was traced through the death and burial books of the parishes. Death certificates were checked with the Swedish National Central Bureau of Statistics and the officially determined underlying cause of death has been used. ICD codes are not listed for cohort 3. There is potential for outcome misclassification from death certificates. In addition, for the analysis combining the three cohorts, there is high potential misclassification due to various sources, national practices, etc .
	Metric 8:	Reporting Bias	Medium	× 0.333	0.67	Measured outcomes were reported, out unclear how the reference population was used for the combined cancers across cohorts.
Domain 4: Potential Confounding/Variable Control						
	Metric 9:	Covariate Adjustment	Low	× 0.5	1.5	Although not specifically stated, age and calendar year were accounted for in the Plant-specific analyses, making it likely that the total SMR would be adjusted similarly.
	Metric 10:	Covariate Characterization	Low	× 0.25	0.75	No discussion of covariate characterization, likely from plant records and death certificates.
	Metric 11:	Co-exposure Confounding	Medium	× 0.25	0.5	For plant 2: "The vast majority of asbestos used was chrysotile but 630 tons of amosite were used between 1949 and 1951 and 400 tons of crocidolite in 1962. The use of these amphiboles was estimated to be less than 1% of all asbestos used." Plant 3 only used chrysotile asbestos except for a “small” amount of amosite during 4 months in 1976. This is not expected to appreciably bias the results.
Domain 5: Analysis						
	Metric 12:	Study Design and Methods	Medium	× 0.4	0.8	Adequate design and methods. SMRs were estimated using Poisson distribution assumptions (plant 2), or by the person years method using a computer program (Plants 1 and 3).
	Metric 13:	Statistical power	Medium	× 0.2	0.4	2167 workers (1510 men and 657 women) were included in the analysis, however the short follow-up may limit the power to detect an effect.

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Study Citation:	Gardner, M. J., Powell, C. A. (1986). Mortality of asbestos cement workers using almost exclusively chrysotile fibre Journal of the Society of Occupational Medicine, 36(4,4), 124-126
Data Type:	Asbestos_workers_SMR_lung_combined-Cancer
HERO ID:	3083384

Domain	Metric		Rating†	MWF⋆	Score	Comments††
	Metric 14:	Reproducibility of analyses	Medium	× 0.2	0.4	Unclear how/what the referent group was used for the combined cohorts analysis.
	Metric 15:	Statistical models	Low	× 0.2	0.6	There is no description of how the combined SMRs were calculated.
Domain 6: Other Considerations for Biomarker Selection and Measurement						
	Metric 16:	Use of Biomarker of Exposure		NA	NA	
	Metric 17:	Effect biomarker		NA	NA	
	Metric 18:	Method Sensitivity		NA	NA	
	Metric 19:	Biomarker stability		NA	NA	
	Metric 20:	Sample contamination		NA	NA	
	Metric 21:	Method requirements		NA	NA	
	Metric 22:	Matrix adjustment		NA	NA	
Overall Quality Determination‡			Low		2.6	
Extracted			Yes			

⋆ MWF = Metric Weighting Factor

† High = 1; Medium = 2; Low = 3; Unacceptable = 4; N/A has no value.

‡ The overall rating is calculated as necessary. EPA may not always provide a comment for a metric that has been categorized as High.

$$\text{Overall rating} = \begin{cases} 4 & \text{if any metric is Unacceptable} \\ \left\lfloor \sum_i (\text{Metric Score}_i \times \text{MWF}_i) \,/\, \sum_j \text{MWF}_j \right\rceil_{0.1} & \text{(round to the nearest tenth) otherwise} \end{cases},$$

where High $=\geq 1$ to < 1.7; Medium $=\geq 1.7$ to < 2.3; Low $=\geq 2.3$ to ≤ 3.0. If the reviewer determines that the overall rating needs adjustment, the original rating is crossed out and an arrow points to the new rating.

†† This metric met the criteria for high confidence as expected for this type of study

Table 10: **Gardner and Powell 1986: Evaluation of Cancer for Laryngeal Cancer Mortality Outcomes**

Study Citation:	Gardner, M. J., Powell, C. A. (1986). Mortality of asbestos cement workers using almost exclusively chrysotile fibre Journal of the Society of Occupational Medicine, 36(4,4), 124-126					
Data Type:	Asbestos_workers_SMR_larynx-Cancer					
HERO ID:	3083384					
Domain		Metric	Rating†	MWF⋆	Score	Comments††
Domain 1: Study Participation						
	Metric 1:	Participant selection	Low	× 0.4	1.2	Retrospective occupational cohort study of 2167 workers (1510 men and 657 women) employed between 1941 and 1983 in chrysotile asbestos cement products factories in England, South Wales and Sweden . This study combines three occupational cohorts. Only the results for men are described. The periods of employment varied between plants/studies. Eligibility criteria vary between plants (employment for at least 6 months (plant 1), Thomas et al 1982 HERO ID 207), 3 months (plant 2/Swedish cohort, Ohlson and Hogstedt 1985 HERO D: 3083459), none for plant 3 (Garner et al 1986 HERO ID 3083223) Follow-up for ascertainment of vital status was until December 1977 (plant 1), 1982 (plant 2) and December 1984 for plant 3. Comparability of cohorts is not discussed.
	Metric 2:	Attrition	High	× 0.4	0.4	Loss to follow-up was minimal: 5% in Plant 1, 2% in Plant 2/Swedish cohort (1%), 30% for men in Plant 3 cohort.
	Metric 3:	Comparison Group	Low	× 0.2	0.6	SMRs were estimated using England and Wales for comparison population (plants 1 and 3), and Swedish national death rates (Plant 2 cohort). is is unclear what the comparison population for total mortality rates were calculated.
Domain 2: Exposure Characterization						
	Metric 4:	Measurement of Exposure	Low	× 0.5	1.5	Exposures were based on employment at the respective plants, Industrial hygiene measures are described confirming exposure. For the combined analyses type of job was not considered.
	Metric 5:	Exposure levels	Not Rated	NA	NA	
	Metric 6:	Temporality	Low	× 0.5	1.5	Follow-up sometimes ended the year after employment, making it an inadequate length of time for cancer mortality to be observed.
Domain 3: Outcome Assessment						

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Study Citation: Gardner, M. J., Powell, C. A. (1986). Mortality of asbestos cement workers using almost exclusively chrysotile fibre Journal of the Society of Occupational Medicine, 36(4,4), 124-126
Data Type: Asbestos_workers_SMR_larynx-Cancer
HERO ID: 3083384

Domain	Metric		Rating†	MWF*	Score	Comments††
	Metric 7:	Outcome measurement or characterization	Low	× 0.667	2	Sources were different by cohort. Plant 1 and 3 cohorts used death certificates from the National Health Service Central Register and the Department of Health and Social Security. ICD codes are listed for Plant 1 cohort. In the Plant 2 cohort, vital status was traced through the death and burial books of the parishes. Death certificates were checked with the Swedish National Central Bureau of Statistics and the officially determined underlying cause of death has been used. ICD codes are not listed for cohort 3. There is potential for outcome misclassification from death certificates. In addition, for the analysis combining the three cohorts, there is high potential misclassification due to various sources, national practices, etc .
	Metric 8:	Reporting Bias	Medium	× 0.333	0.67	Measured outcomes were reported, out unclear how the reference population was used for the combined cancers across cohorts.
Domain 4: Potential Confounding/Variable Control						
	Metric 9:	Covariate Adjustment	Low	× 0.5	1.5	Although not specifically stated, age and calendar year were accounted for in the Plant-specific analyses, making it likely that the total SMR would be adjusted similarly.
	Metric 10:	Covariate Characterization	Low	× 0.25	0.75	No discussion of covariate characterization, likely from plant records and death certificates.
	Metric 11:	Co-exposure Confounding	Medium	× 0.25	0.5	For plant 2: "The vast majority of asbestos used was chrysotile but 630 tons of amosite were used between 1949 and 1951 and 400 tons of crocidolite in 1962. The use of these amphiboles was estimated to be less than 1% of all asbestos used." Plant 3 only used chrysotile asbestos except for a “small” amount of amosite during 4 months in 1976. This is not expected to appreciably bias the results.
Domain 5: Analysis						
	Metric 12:	Study Design and Methods	Medium	× 0.4	0.8	Adequate design and methods. SMRs were estimated using Poisson distribution assumptions (plant 2), or by the person years method using a computer program (Plants 1 and 3).
	Metric 13:	Statistical power	Medium	× 0.2	0.4	2167 workers (1510 men and 657 women) were included in the analysis, however the short follow-up may limit the power to detect an effect.

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Study Citation:	Gardner, M. J., Powell, C. A. (1986). Mortality of asbestos cement workers using almost exclusively chrysotile fibre Journal of the Society of Occupational Medicine, 36(4,4), 124-126
Data Type:	Asbestos_workers_SMR_larynx-Cancer
HERO ID:	3083384

Domain	Metric		Rating†	MWF⋆	Score	Comments††
	Metric 14:	Reproducibility of analyses	Medium	× 0.2	0.4	Unclear how/what the referent group was used for the combined cohorts analysis.
	Metric 15:	Statistical models	Low	× 0.2	0.6	There is no description of how the combined SMRs were calculated.
Domain 6: Other Considerations for Biomarker Selection and Measurement						
	Metric 16:	Use of Biomarker of Exposure		NA	NA	
	Metric 17:	Effect biomarker		NA	NA	
	Metric 18:	Method Sensitivity		NA	NA	
	Metric 19:	Biomarker stability		NA	NA	
	Metric 20:	Sample contamination		NA	NA	
	Metric 21:	Method requirements		NA	NA	
	Metric 22:	Matrix adjustment		NA	NA	
Overall Quality Determination‡			Low		2.6	
Extracted			Yes			

⋆ MWF = Metric Weighting Factor

† High = 1; Medium = 2; Low = 3; Unacceptable = 4; N/A has no value.

‡ The overall rating is calculated as necessary. EPA may not always provide a comment for a metric that has been categorized as High.

$$\text{Overall rating} = \begin{cases} 4 & \text{if any metric is Unacceptable} \\ \left\lfloor \sum_i (\text{Metric Score}_i \times \text{MWF}_i) \,/\, \sum_j \text{MWF}_j \right\rceil_{0.1} & \text{(round to the nearest tenth) otherwise} \end{cases},$$

where High $=\geq 1$ to < 1.7; Medium $=\geq 1.7$ to < 2.3; Low $=\geq 2.3$ to ≤ 3.0. If the reviewer determines that the overall rating needs adjustment, the original rating is crossed out and an arrow points to the new rating.

†† This metric met the criteria for high confidence as expected for this type of study

Table 11: **Pira et al. 2017: Evaluation of Cancer for Lung Cancer Mortality Outcomes**

Study Citation:	Pira, E., Romano, C., Donat , F., Pelucchi, C., La Vecchia, C., Boffetta, P. (2017). Mortality from cancer and other causes among Italian chrysotile asbestos miners Occupational and Environmental Medicine, 74(8,8), 558-563
Data Type:	Italian_chrysotile_miners_lung_cancer-Cancer
HERO ID:	5060134

Domain	Metric		Rating[†]	MWF[⋆]	Score	Comments[††]
Domain 1: Study Participation						
	Metric 1:	Participant selection	Medium	× 0.4	0.8	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. There is potential for some healthy worker effect in this population.
	Metric 2:	Attrition	High	× 0.4	0.4	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.
	Metric 3:	Comparison Group	Medium	× 0.2	0.4	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).
Domain 2: Exposure Characterization						
	Metric 4:	Measurement of Exposure	Medium	× 0.5	1	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.
	Metric 5:	Exposure levels	Not Rated	NA	NA	
	Metric 6:	Temporality	High	× 0.5	0.5	Subjects were followed until loss to follow-up, their death, 85th birthday, or through 2014. This is a sufficiently long follow-up period.
Domain 3: Outcome Assessment						

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Study Citation:	Pira, E., Romano, C., Donat , F., Pelucchi, C., La Vecchia, C., Boffetta, P. (2017). Mortality from cancer and other causes among Italian chrysotile asbestos miners Occupational and Environmental Medicine, 74(8,8), 558-563
Data Type:	Italian_chrysotile_miners_lung_cancer-Cancer
HERO ID:	5060134

Domain	Metric		Rating†	MWF⋆	Score	Comments††
	Metric 7:	Outcome measurement or characterization	Medium	× 0.667	1.33	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.
	Metric 8:	Reporting Bias	High	× 0.333	0.33	Outcomes specified in the abstract, introduction, and methods were provided in the results. SMRs were presented with observed cases, expected cases, and a confidence interval.
Domain 4: Potential Confounding/Variable Control						
	Metric 9:	Covariate Adjustment	Medium	× 0.5	1	SMRs for male miners were calculated, stratified for age- and calendar-year-specific mortality rates. Information on individual smoking behavior was described, but was not accounted for in the analysis.
	Metric 10:	Covariate Characterization	Medium	× 0.25	0.5	Covariates were presumably drawn from employment records
	Metric 11:	Co-exposure Confounding	Low	× 0.25	0.75	Co-exposures are not expressly discussed. There may be additional occupational exposures in this group, which may depend on job title or position.
Domain 5: Analysis						
	Metric 12:	Study Design and Methods	Medium	× 0.4	0.8	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	× 0.2	0.4	There were a sufficient number of employees included in the analysis. No concerns with low case numbers.
	Metric 14:	Reproducibility of analyses	Medium	× 0.2	0.4	The analysis was well-described and could be reproduced with original data.
	Metric 15:	Statistical models	Medium	× 0.2	0.4	The method for calculating SMRs was transparent and appropriate.
Domain 6: Other Considerations for Biomarker Selection and Measurement						
	Metric 16:	Use of Biomarker of Exposure		NA	NA	
	Metric 17:	Effect biomarker		NA	NA	
	Metric 18:	Method Sensitivity		NA	NA	
	Metric 19:	Biomarker stability		NA	NA	

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Study Citation:	Pira, E., Romano, C., Donat , F., Pelucchi, C., La Vecchia, C., Boffetta, P. (2017). Mortality from cancer and other causes among Italian chrysotile asbestos miners Occupational and Environmental Medicine, 74(8,8), 558-563
Data Type:	Italian_chrysotile_miners_lung_cancer-Cancer
HERO ID:	5060134

Domain	Metric	Rating†	MWF⋆	Score	Comments††
	Metric 20: Sample contamination		NA	NA	
	Metric 21: Method requirements		NA	NA	
	Metric 22: Matrix adjustment		NA	NA	
Overall Quality Determination‡		Medium		1.8	
Extracted		Yes			

⋆ MWF = Metric Weighting Factor

† High = 1; Medium = 2; Low = 3; Unacceptable = 4; N/A has no value.

‡ The overall rating is calculated as necessary. EPA may not always provide a comment for a metric that has been categorized as High.

$$\text{Overall rating} = \begin{cases} 4 & \text{if any metric is Unacceptable} \\ \left\lfloor \sum_i (\text{Metric Score}_i \times \text{MWF}_i) \,/\, \sum_j \text{MWF}_j \right\rceil_{0.1} & \text{(round to the nearest tenth) otherwise} \end{cases},$$

where High $=\geq 1$ to < 1.7; Medium $=\geq 1.7$ to < 2.3; Low $=\geq 2.3$ to ≤ 3.0. If the reviewer determines that the overall rating needs adjustment, the original rating is crossed out and an arrow points to the new rating.

†† This metric met the criteria for high confidence as expected for this type of study

Table 12: **Pira et al. 2017: Evaluation of Cancer for Laryngeal Cancer Mortality Outcomes**

Study Citation:	Pira, E., Romano, C., Donat , F., Pelucchi, C., La Vecchia, C., Boffetta, P. (2017). Mortality from cancer and other causes among Italian chrysotile asbestos miners Occupational and Environmental Medicine, 74(8,8), 558-563
Data Type:	Italian_chrysotile_miners_laryngeal_cancer-Cancer
HERO ID:	5060134

Domain	Metric		Rating†	MWF⋆	Score	Comments††
Domain 1: Study Participation						
	Metric 1:	Participant selection	Medium	× 0.4	0.8	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.
	Metric 2:	Attrition	High	× 0.4	0.4	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.
	Metric 3:	Comparison Group	Medium	× 0.2	0.4	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).
Domain 2: Exposure Characterization						
	Metric 4:	Measurement of Exposure	Low	× 0.5	1.5	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.
	Metric 5:	Exposure levels	Not Rated	NA	NA	
	Metric 6:	Temporality	High	× 0.5	0.5	Subjects were followed until loss to follow-up, their death, 85th birthday, or through 2014. This is a sufficiently long follow-up period.
Domain 3: Outcome Assessment						
	Metric 7:	Outcome measurement or characterization	Medium	× 0.667	1.33	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.

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Study Citation:	Pira, E., Romano, C., Donat , F., Pelucchi, C., La Vecchia, C., Boffetta, P. (2017). Mortality from cancer and other causes among Italian chrysotile asbestos miners Occupational and Environmental Medicine, 74(8,8), 558-563
Data Type:	Italian_chrysotile_miners_laryngeal_cancer-Cancer
HERO ID:	5060134

Domain	Metric		Rating†	MWF⋆	Score	Comments††
	Metric 8:	Reporting Bias	High	× 0.333	0.33	Outcomes specified in the abstract, introduction, and methods were provided in the results. SMRs were presented with observed cases, expected cases, and a confidence interval.
Domain 4: Potential Confounding/Variable Control						
	Metric 9:	Covariate Adjustment	Medium	× 0.5	1	SMRs for male miners were calculated, stratified for age- and calendar-year-specific mortality rates. Information on individual smoking behavior was described, but was not accounted for in the analysis.
	Metric 10:	Covariate Characterization	Medium	× 0.25	0.5	Covariates were presumably drawn from employment records
	Metric 11:	Co-exposure Confounding	Low	× 0.25	0.75	Co-exposures are not expressly discussed. There may be additional occupational exposures in this group, which may depend on job title or position.
Domain 5: Analysis						
	Metric 12:	Study Design and Methods	Medium	× 0.4	0.8	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	× 0.2	0.4	There were a sufficient number of employees included in the analysis. No concerns with low case numbers.
	Metric 14:	Reproducibility of analyses	Medium	× 0.2	0.4	The analysis was well-described and could be reproduced with original data.
	Metric 15:	Statistical models	Medium	× 0.2	0.4	The method for calculating SMRs was transparent and appropriate.
Domain 6: Other Considerations for Biomarker Selection and Measurement						
	Metric 16:	Use of Biomarker of Exposure		NA	NA	
	Metric 17:	Effect biomarker		NA	NA	
	Metric 18:	Method Sensitivity		NA	NA	
	Metric 19:	Biomarker stability		NA	NA	
	Metric 20:	Sample contamination		NA	NA	
	Metric 21:	Method requirements		NA	NA	
	Metric 22:	Matrix adjustment		NA	NA	
Overall Quality Determination‡			Medium		1.9	
Extracted			Yes			

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Study Citation:	Pira, E., Romano, C., Donat , F., Pelucchi, C., La Vecchia, C., Boffetta, P. (2017). Mortality from cancer and other causes among Italian chrysotile asbestos miners Occupational and Environmental Medicine, 74(8,8), 558-563
Data Type:	Italian_chrysotile_miners_laryngeal_cancer-Cancer
HERO ID:	5060134

Domain	Metric	Rating†	MWF⋆	Score	Comments††

⋆ MWF = Metric Weighting Factor

† High = 1; Medium = 2; Low = 3; Unacceptable = 4; N/A has no value.

‡ The overall rating is calculated as necessary. EPA may not always provide a comment for a metric that has been categorized as High.

$$\text{Overall rating} = \begin{cases} 4 & \text{if any metric is Unacceptable} \\ \left\lfloor \sum_i (\text{Metric Score}_i \times \text{MWF}_i) \,/\, \sum_j \text{MWF}_j \right\rceil_{0.1} & \text{(round to the nearest tenth) otherwise} \end{cases},$$

where High =≥ 1 to < 1.7; Medium =≥ 1.7 to < 2.3; Low =≥ 2.3 to ≤ 3.0. If the reviewer determines that the overall rating needs adjustment, the original rating is crossed out and an arrow points to the new rating.

†† This metric met the criteria for high confidence as expected for this type of study

Table 13: **Mamo and Costa 2004: Evaluation of Cancer for Ovarian Cancer Mortality Outcomes**

Study Citation:	Mamo, C., Costa, G. (2004). Mortality experience in an historical cohort of chrysotile asbestos textile workers Global asbestos congress 2004 in Tokyo,
Data Type:	Italian_asbestos_product_workers_ovarian_cancer-Cancer
HERO ID:	6912534

Domain	Metric		Rating[†]	MWF[⋆]	Score	Comments[††]
Domain 1: Study Participation						
	Metric 1:	Participant selection	High	× 0.4	0.4	Subjects consisted of former employees of an asbestos-based products manufacturing plant in Grugliasco, Italy, hired before 1971. Subjects were followed from 1981 through 1995.
	Metric 2:	Attrition	Medium	× 0.4	0.8	The initial study sample consisted of 1653 employees. The study authors note that the analysis sample consisted of 967 individuals, selected as 18-74 y of age, with concern about dropping older individuals.
	Metric 3:	Comparison Group	Medium	× 0.2	0.4	The study authors attempted to find a similar population to the asbestos-products employees by using a reference population consisting of residents from the same area (Turin) whom were manual workers--this was an attempt to mitigate healthy worker effect.
Domain 2: Exposure Characterization						
	Metric 4:	Measurement of Exposure	Low	× 0.5	1.5	Exposure was determined by occupation only. Basic descriptions of the asbestos product facility were provided.
	Metric 5:	Exposure levels	Not Rated	NA	NA	
	Metric 6:	Temporality	Medium	× 0.5	1	Subjects employed in 1971 were followed-up from 1981 to 1995 which is a sufficiently long follow-up period to detect an effect.
Domain 3: Outcome Assessment						
	Metric 7:	Outcome measurement or characterization	Medium	× 0.667	1.33	Causes of death were obtained from the Italian National Registry of Deaths (ISTAT) and consulting death certificates at the Piedmont Cancer Registry. It was not reported whether cancer cases were histologically confirmed, and it appears that causes of death were coded using ICD-9 .
	Metric 8:	Reporting Bias	High	× 0.333	0.33	Outcomes specified in the abstract, introduction, and methods were provided in results. SMRs were provided with the number of cases and 95% confidence intervals.
Domain 4: Potential Confounding/Variable Control						
	Metric 9:	Covariate Adjustment	Medium	× 0.5	1	Individual smoking behaviors were not able to be controlled for.

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Study Citation:	Mamo, C., Costa, G. (2004). Mortality experience in an historical cohort of chrysotile asbestos textile workers Global asbestos congress 2004 in Tokyo,
Data Type:	Italian_asbestos_product_workers_ovarian_cancer-Cancer
HERO ID:	6912534

Domain	Metric		Rating†	MWF⋆	Score	Comments††
	Metric 10:	Covariate Characterization	Medium	× 0.25	0.5	Covariates were largely not collected except sex, which was presumably taken from employment records.
	Metric 11:	Co-exposure Confounding	Medium	× 0.25	0.5	This is an occupational cohort and co-exposures were not addressed. Co-exposures may be present depending on specific job titles and positions.
Domain 5: Analysis						
	Metric 12:	Study Design and Methods	Medium	× 0.4	0.8	SMRs were calculated to estimate the effect of occupational asbestos exposure on cancer mortality rates. This is an appropriate study design for the study question.
	Metric 13:	Statistical power	Medium	× 0.2	0.4	A total of 967 individuals were included in the analysis sample, which is sufficiently large to detect an effect. There is some concern for the limited number of cases of laryngeal and ovarian cancer mortality (3 and 1, respectively) which may make estimates unstable.
	Metric 14:	Reproducibility of analyses	Medium	× 0.2	0.4	The analysis was sufficiently described and could be reproduced given original data.
	Metric 15:	Statistical models	Medium	× 0.2	0.4	The calculation of sex-specific SMRs was detailed and transparent. No concerns.
Domain 6: Other Considerations for Biomarker Selection and Measurement						
	Metric 16:	Use of Biomarker of Exposure		NA	NA	
	Metric 17:	Effect biomarker		NA	NA	
	Metric 18:	Method Sensitivity		NA	NA	
	Metric 19:	Biomarker stability		NA	NA	
	Metric 20:	Sample contamination		NA	NA	
	Metric 21:	Method requirements		NA	NA	
	Metric 22:	Matrix adjustment		NA	NA	
Overall Quality Determination‡			Medium		2.0	
Extracted			Yes			

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Study Citation:	Mamo, C., Costa, G. (2004). Mortality experience in an historical cohort of chrysotile asbestos textile workers Global asbestos congress 2004 in Tokyo,
Data Type:	Italian_asbestos_product_workers_ovarian_cancer-Cancer
HERO ID:	6912534

Domain	Metric	Rating†	MWF⋆	Score	Comments††

⋆ MWF = Metric Weighting Factor
† High = 1; Medium = 2; Low = 3; Unacceptable = 4; N/A has no value.
‡ The overall rating is calculated as necessary. EPA may not always provide a comment for a metric that has been categorized as High.

$$\text{Overall rating} = \begin{cases} 4 & \text{if any metric is Unacceptable} \\ \left\lfloor \sum_i (\text{Metric Score}_i \times \text{MWF}_i) \,/\, \sum_j \text{MWF}_j \right\rceil_{0.1} & \text{(round to the nearest tenth) otherwise} \end{cases},$$

where High $=\geq 1$ to < 1.7; Medium $=\geq 1.7$ to < 2.3; Low $=\geq 2.3$ to ≤ 3.0. If the reviewer determines that the overall rating needs adjustment, the original rating is crossed out and an arrow points to the new rating.
†† This metric met the criteria for high confidence as expected for this type of study

Table 14: **Mamo and Costa 2004: Evaluation of Cancer for Female Lung Cancer Mortality Outcomes**

Study Citation:	Mamo, C., Costa, G. (2004). Mortality experience in an historical cohort of chrysotile asbestos textile workers Global asbestos congress 2004 in Tokyo,
Data Type:	Italian_asbestos_product_workers_lung_cancer_female-Cancer
HERO ID:	6912534

Domain	Metric		Rating[†]	MWF[⋆]	Score	Comments[††]
Domain 1: Study Participation						
	Metric 1:	Participant selection	High	× 0.4	0.4	Subjects consisted of former employees of an asbestos-based products manufacturing plant in Grugliasco, Italy, hired before 1971. Subjects were followed from 1981 through 1995.
	Metric 2:	Attrition	Medium	× 0.4	0.8	The initial study sample consisted of 1653 employees. The study authors note that the analysis sample consisted of 967 individuals, selected as 18-74 y of age, with concern about dropping older individuals.
	Metric 3:	Comparison Group	Medium	× 0.2	0.4	The study authors attempted to find a similar population to the asbestos-products employees by using a reference population consisting of residents from the same area (Turin) whom were manual workers--this was an attempt to mitigate healthy worker effect.
Domain 2: Exposure Characterization						
	Metric 4:	Measurement of Exposure	Low	× 0.5	1.5	Exposure was determined by occupation only. Basic descriptions of the asbestos product facility were provided.
	Metric 5:	Exposure levels	Not Rated	NA	NA	
	Metric 6:	Temporality	Medium	× 0.5	1	Subjects employed in 1971 were followed-up from 1981 to 1995 which is a sufficiently long follow-up period to detect an effect. It's not clear whether individuals were followed between 1971 and 1981.
Domain 3: Outcome Assessment						
	Metric 7:	Outcome measurement or characterization	Medium	× 0.667	1.33	Causes of death were obtained from the Italian National Registry of Deaths (ISTAT) and consulting death certificates at the Piedmont Cancer Registry. It was not reported whether cancer cases were histologically confirmed, and it appears that causes of death were coded using ICD-9 .
	Metric 8:	Reporting Bias	High	× 0.333	0.33	Outcomes specified in the abstract, introduction, and methods were provided in results. SMRs were provided with the number of cases and 95% confidence intervals.
Domain 4: Potential Confounding/Variable Control						
	Metric 9:	Covariate Adjustment	Medium	× 0.5	1	Individual smoking behaviors were not able to be controlled for.

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Study Citation:	Mamo, C., Costa, G. (2004). Mortality experience in an historical cohort of chrysotile asbestos textile workers Global asbestos congress 2004 in Tokyo,
Data Type:	Italian_asbestos_product_workers_lung_cancer_female-Cancer
HERO ID:	6912534

Domain	Metric		Rating†	MWF⋆	Score	Comments††
	Metric 10:	Covariate Characterization	Medium	× 0.25	0.5	Covariates were largely not collected except sex, which was presumably taken from employment records.
	Metric 11:	Co-exposure Confounding	Medium	× 0.25	0.5	This is an occupational cohort and co-exposures were not addressed. Co-exposures may be present depending on specific job titles and positions.
Domain 5: Analysis						
	Metric 12:	Study Design and Methods	Medium	× 0.4	0.8	SMRs were calculated to estimate the effect of occupational asbestos exposure on cancer mortality rates. This is an appropriate study design for the study question.
	Metric 13:	Statistical power	Medium	× 0.2	0.4	A total of 967 individuals were included in the analysis sample, which is sufficiently large to detect an effect.
	Metric 14:	Reproducibility of analyses	Medium	× 0.2	0.4	The analysis was sufficiently described and could be reproduced given original data.
	Metric 15:	Statistical models	Medium	× 0.2	0.4	The calculation of sex-specific SMRs was detailed and transparent. No concerns.
Domain 6: Other Considerations for Biomarker Selection and Measurement						
	Metric 16:	Use of Biomarker of Exposure		NA	NA	
	Metric 17:	Effect biomarker		NA	NA	
	Metric 18:	Method Sensitivity		NA	NA	
	Metric 19:	Biomarker stability		NA	NA	
	Metric 20:	Sample contamination		NA	NA	
	Metric 21:	Method requirements		NA	NA	
	Metric 22:	Matrix adjustment		NA	NA	
Overall Quality Determination‡			Medium		2.0	
Extracted			Yes			

⋆ MWF = Metric Weighting Factor

† High = 1; Medium = 2; Low = 3; Unacceptable = 4; N/A has no value.

‡ The overall rating is calculated as necessary. EPA may not always provide a comment for a metric that has been categorized as High.

$$\text{Overall rating} = \begin{cases} 4 & \text{if any metric is Unacceptable} \\ \left\lfloor \sum_i (\text{Metric Score}_i \times \text{MWF}_i) \,/\, \sum_j \text{MWF}_j \right\rceil_{0.1} & \text{(round to the nearest tenth) otherwise} \end{cases},$$

where High $=\geq 1$ to < 1.7; Medium $=\geq 1.7$ to < 2.3; Low $=\geq 2.3$ to ≤ 3.0. If the reviewer determines that the overall rating needs adjustment, the original rating is crossed out and an arrow points to the new rating.

†† This metric met the criteria for high confidence as expected for this type of study

Table 15: **Mamo and Costa 2004: Evaluation of Cancer for Male and Female Lung Cancer Mortality Outcomes**

Study Citation:	Mamo, C., Costa, G. (2004). Mortality experience in an historical cohort of chrysotile asbestos textile workers Global asbestos congress 2004 in Tokyo,
Data Type:	Italian_asbestos_product_workers_lung_cancer_combined-Cancer
HERO ID:	6912534

Domain	Metric		Rating[†]	MWF[⋆]	Score	Comments[††]
Domain 1: Study Participation						
	Metric 1:	Participant selection	High	× 0.4	0.4	Subjects consisted of former employees of an asbestos-based products manufacturing plant in Grugliasco, Italy, hired before 1971. Subjects were followed from 1981 through 1995.
	Metric 2:	Attrition	Medium	× 0.4	0.8	The initial study sample consisted of 1653 employees. The study authors note that the analysis sample consisted of 967 individuals, selected as 18-74 y of age, with concern about dropping older individuals.
	Metric 3:	Comparison Group	Medium	× 0.2	0.4	The study authors attempted to find a similar population to the asbestos-products employees by using a reference population consisting of residents from the same area (Turin) whom were manual workers--this was an attempt to mitigate healthy worker effect.
Domain 2: Exposure Characterization						
	Metric 4:	Measurement of Exposure	Low	× 0.5	1.5	Exposure was determined by occupation only. Basic descriptions of the asbestos product facility were provided.
	Metric 5:	Exposure levels	Not Rated	NA	NA	
	Metric 6:	Temporality	Medium	× 0.5	1	Subjects employed in 1971 were followed-up from 1981 to 1995 which is a sufficiently long follow-up period to detect an effect.
Domain 3: Outcome Assessment						
	Metric 7:	Outcome measurement or characterization	Medium	× 0.667	1.33	Causes of death were obtained from the Italian National Registry of Deaths (ISTAT) and consulting death certificates at the Piedmont Cancer Registry. It was not reported whether cancer cases were histologically confirmed, and it appears that causes of death were coded using ICD-9 .
	Metric 8:	Reporting Bias	High	× 0.333	0.33	Outcomes specified in the abstract, introduction, and methods were provided in results. SMRs were provided with the number of cases and 95% confidence intervals.
Domain 4: Potential Confounding/Variable Control						
	Metric 9:	Covariate Adjustment	Medium	× 0.5	1	Individual smoking behaviors were not able to be controlled for.

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Study Citation:	Mamo, C., Costa, G. (2004). Mortality experience in an historical cohort of chrysotile asbestos textile workers Global asbestos congress 2004 in Tokyo,
Data Type:	Italian_asbestos_product_workers_lung_cancer_combined-Cancer
HERO ID:	6912534

Domain	Metric		Rating†	MWF⋆	Score	Comments††
	Metric 10:	Covariate Characterization	Medium	× 0.25	0.5	Covariates were largely not collected except sex, which was presumably taken from employment records.
	Metric 11:	Co-exposure Confounding	Medium	× 0.25	0.5	This is an occupational cohort and co-exposures were not addressed. Co-exposures may be present depending on specific job titles and positions.
Domain 5: Analysis						
	Metric 12:	Study Design and Methods	Medium	× 0.4	0.8	SMRs were calculated to estimate the effect of occupational asbestos exposure on cancer mortality rates. This is an appropriate study design for the study question.
	Metric 13:	Statistical power	Medium	× 0.2	0.4	A total of 967 individuals were included in the analysis sample, which is sufficiently large to detect an effect.
	Metric 14:	Reproducibility of analyses	Medium	× 0.2	0.4	The analysis was sufficiently described and could be reproduced given original data.
	Metric 15:	Statistical models	Medium	× 0.2	0.4	The calculation of sex-specific SMRs was detailed and transparent. No concerns.
Domain 6: Other Considerations for Biomarker Selection and Measurement						
	Metric 16:	Use of Biomarker of Exposure		NA	NA	
	Metric 17:	Effect biomarker		NA	NA	
	Metric 18:	Method Sensitivity		NA	NA	
	Metric 19:	Biomarker stability		NA	NA	
	Metric 20:	Sample contamination		NA	NA	
	Metric 21:	Method requirements		NA	NA	
	Metric 22:	Matrix adjustment		NA	NA	
Overall Quality Determination‡			Medium		2.0	
Extracted			Yes			

⋆ MWF = Metric Weighting Factor

† High = 1; Medium = 2; Low = 3; Unacceptable = 4; N/A has no value.

‡ The overall rating is calculated as necessary. EPA may not always provide a comment for a metric that has been categorized as High.

$$\text{Overall rating} = \begin{cases} 4 & \text{if any metric is Unacceptable} \\ \left\lfloor \sum_i (\text{Metric Score}_i \times \text{MWF}_i) \,/\, \sum_j \text{MWF}_j \right\rceil_{0.1} & \text{(round to the nearest tenth) otherwise} \end{cases},$$

where High $=\geq 1$ to < 1.7; Medium $=\geq 1.7$ to < 2.3; Low $=\geq 2.3$ to ≤ 3.0. If the reviewer determines that the overall rating needs adjustment, the original rating is crossed out and an arrow points to the new rating.

†† This metric met the criteria for high confidence as expected for this type of study

Table 16: **Mamo and Costa 2004: Evaluation of Cancer for Laryngeal Cancer Mortality Outcomes**

Study Citation:	Mamo, C., Costa, G. (2004). Mortality experience in an historical cohort of chrysotile asbestos textile workers Global asbestos congress 2004 in Tokyo,
Data Type:	Italian_asbestos_product_workers_laryngeal_cancer-Cancer
HERO ID:	6912534

Domain	Metric		Rating[†]	MWF[⋆]	Score	Comments[††]
Domain 1: Study Participation						
	Metric 1:	Participant selection	High	× 0.4	0.4	Subjects consisted of former employees of an asbestos-based products manufacturing plant in Grugliasco, Italy, hired before 1971. Subjects were followed from 1981 through 1995.
	Metric 2:	Attrition	Medium	× 0.4	0.8	The initial study sample consisted of 1653 employees. The study authors note that the analysis sample consisted of 967 individuals, selected as 18-74 y of age, with concern about dropping older individuals.
	Metric 3:	Comparison Group	Medium	× 0.2	0.4	The study authors attempted to find a similar population to the asbestos-products employees by using a reference population consisting of residents from the same area (Turin) whom were manual workers--this was an attempt to mitigate healthy worker effect.
Domain 2: Exposure Characterization						
	Metric 4:	Measurement of Exposure	Low	× 0.5	1.5	Exposure was determined by occupation only. Basic descriptions of the asbestos product facility were provided.
	Metric 5:	Exposure levels	Not Rated	NA	NA	
	Metric 6:	Temporality	Medium	× 0.5	1	Subjects employed in 1971 were followed-up from 1981 to 1995 which is a sufficiently long follow-up period to detect an effect.
Domain 3: Outcome Assessment						
	Metric 7:	Outcome measurement or characterization	Medium	× 0.667	1.33	Causes of death were obtained from the Italian National Registry of Deaths (ISTAT) and consulting death certificates at the Piedmont Cancer Registry. It was not reported whether cancer cases were histologically confirmed, and it appears that causes of death were coded using ICD-9 .
	Metric 8:	Reporting Bias	High	× 0.333	0.33	Outcomes specified in the abstract, introduction, and methods were provided in results. SMRs were provided with the number of cases and 95% confidence intervals.
Domain 4: Potential Confounding/Variable Control						
	Metric 9:	Covariate Adjustment	Medium	× 0.5	1	Individual smoking behaviors were not able to be controlled for.

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Study Citation:	Mamo, C., Costa, G. (2004). Mortality experience in an historical cohort of chrysotile asbestos textile workers Global asbestos congress 2004 in Tokyo,
Data Type:	Italian_asbestos_product_workers_laryngeal_cancer-Cancer
HERO ID:	6912534

Domain	Metric		Rating†	MWF⋆	Score	Comments††
	Metric 10:	Covariate Characterization	Medium	× 0.25	0.5	Covariates were largely not collected except sex, which was presumably taken from employment records.
	Metric 11:	Co-exposure Confounding	Medium	× 0.25	0.5	This is an occupational cohort and co-exposures were not addressed. Co-exposures may be present depending on specific job titles and positions.
Domain 5: Analysis						
	Metric 12:	Study Design and Methods	Medium	× 0.4	0.8	SMRs were calculated to estimate the effect of occupational asbestos exposure on cancer mortality rates. This is an appropriate study design for the study question.
	Metric 13:	Statistical power	Medium	× 0.2	0.4	A total of 967 individuals were included in the analysis sample, which is sufficiently large to detect an effect. There is some concern for the limited number of cases of laryngeal and ovarian cancer mortality (3 and 1, respectively) which may make estimates unstable.
	Metric 14:	Reproducibility of analyses	Medium	× 0.2	0.4	The analysis was sufficiently described and could be reproduced given original data.
	Metric 15:	Statistical models	Medium	× 0.2	0.4	The calculation of sex-specific SMRs was detailed and transparent. No concerns.
Domain 6: Other Considerations for Biomarker Selection and Measurement						
	Metric 16:	Use of Biomarker of Exposure		NA	NA	
	Metric 17:	Effect biomarker		NA	NA	
	Metric 18:	Method Sensitivity		NA	NA	
	Metric 19:	Biomarker stability		NA	NA	
	Metric 20:	Sample contamination		NA	NA	
	Metric 21:	Method requirements		NA	NA	
	Metric 22:	Matrix adjustment		NA	NA	
Overall Quality Determination‡			Medium		2.0	
Extracted			Yes			

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Study Citation:	Mamo, C., Costa, G. (2004). Mortality experience in an historical cohort of chrysotile asbestos textile workers Global asbestos congress 2004 in Tokyo,
Data Type:	Italian_asbestos_product_workers_laryngeal_cancer-Cancer
HERO ID:	6912534

Domain	Metric	Rating†	MWF⋆	Score	Comments††

⋆ MWF = Metric Weighting Factor
† High = 1; Medium = 2; Low = 3; Unacceptable = 4; N/A has no value.
‡ The overall rating is calculated as necessary. EPA may not always provide a comment for a metric that has been categorized as High.

$$\text{Overall rating} = \begin{cases} 4 & \text{if any metric is Unacceptable} \\ \left\lfloor \sum_i (\text{Metric Score}_i \times \text{MWF}_i) \,/\, \sum_j \text{MWF}_j \right\rceil_{0.1} & \text{(round to the nearest tenth) otherwise} \end{cases},$$

where High $=\geq 1$ to < 1.7; Medium $=\geq 1.7$ to < 2.3; Low $=\geq 2.3$ to ≤ 3.0. If the reviewer determines that the overall rating needs adjustment, the original rating is crossed out and an arrow points to the new rating.
†† This metric met the criteria for high confidence as expected for this type of study

Table 17: **Germani et al. 1999: Evaluation of Cancer for Ovarian Cancer Mortality Outcomes**

Study Citation:	Germani, D., Belli, S., Bruno, C., Grignoli, M., Nesti, M., Pirastu, R., Comba, P. (1999). Cohort mortality study of women compensated for asbestosis in Italy American Journal of Industrial Medicine, 36(1,1), 129-134
Data Type:	Italian_women_asbestosis_ovarian_cancer-Cancer
HERO ID:	709605

Domain	Metric		Rating[†]	MWF[⋆]	Score	Comments[††]
Domain 1: Study Participation						
	Metric 1:	Participant selection	Medium	× 0.4	0.8	Study participants were drawn from the Italian National Institute for Insurance of Occupational Accidents (INAIL). Eligibility criteria were not expressly stated beyond membership in the asbestosis compensation cohort and being alive at the study's onset (1979). Most women entered the asbestosis compensation cohort around 50 years of age; some healthy worker effect may be present.
	Metric 2:	Attrition	High	× 0.4	0.4	The number of individuals lost to follow-up was provided and appeared minimal for all groups (total cohort = 0.6 percent). The study authors do not suggest any other missing data.
	Metric 3:	Comparison Group	Low	× 0.2	0.6	Rates of mortality in the asbestosis compensation cohort were compared with Italian national mortality rates, stratifying for gender-, age-, and calendar period-specific rates. This represents consideration of potential covariates. The study group of those compensated for asbestosis may have been different from national comparison group.
Domain 2: Exposure Characterization						
	Metric 4:	Measurement of Exposure	Low	× 0.5	1.5	Exposure was assigned only by the women's occupation. No further characterization of the occupational exposure was provided.
	Metric 5:	Exposure levels	Not Rated	NA	NA	
	Metric 6:	Temporality	High	× 0.5	0.5	Asbestosis compensation cohort members were eligible if they were alive and enrolled at the end of 1979. Women were followed until October 1997, allowing for a sufficient follow-up period.
Domain 3: Outcome Assessment						
	Metric 7:	Outcome measurement or characterization	Medium	× 0.667	1.33	The cause of death was obtained for deceased subjects from the Registry Office of the municipality of residence or death. Causes of death were coded according to ICD-9 codes, but no details were provided about histological confirmation.

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Study Citation: Germani, D., Belli, S., Bruno, C., Grignoli, M., Nesti, M., Pirastu, R., Comba, P. (1999). Cohort mortality study of women compensated for asbestosis in Italy American Journal of Industrial Medicine, 36(1,1), 129-134
Data Type: Italian_women_asbestosis_ovarian_cancer-Cancer
HERO ID: 709605

Domain	Metric		Rating†	MWF⋆	Score	Comments††
	Metric 8:	Reporting Bias	High	× 0.333	0.33	Outcomes specified in the abstract, introduction, and methods were provided in the results. The results provide the number of observations, the SMR, and a confidence interval.
Domain 4: Potential Confounding/Variable Control						
	Metric 9:	Covariate Adjustment	Medium	× 0.5	1	SMRs were stratified for gender, age, and calendar period. Individual smoking data was not available and may be of concern for outcomes including lung cancer.
	Metric 10:	Covariate Characterization	Medium	× 0.25	0.5	Covariates were drawn from information collected by INAIL for asbestosis compensation. It is not entirely clear how INAIL may have collected the covariates.
	Metric 11:	Co-exposure Confounding	Low	× 0.25	0.75	This is an occupational cohort and co-exposures were not addressed. Co-exposures may be present depending on specific job titles and positions.
Domain 5: Analysis						
	Metric 12:	Study Design and Methods	Medium	× 0.4	0.8	SMRs were used to achieve the study objective of comparing cause-specific mortality rates of an occupational cohort to the Italian national population (stratifying for relevant characteristics).
	Metric 13:	Statistical power	Medium	× 0.2	0.4	A total of 631 women compensated for asbestosis were included in the overall cohort, with 276 and 278 women in the textile and asbestos cement industry, respectively.
	Metric 14:	Reproducibility of analyses	Medium	× 0.2	0.4	The analysis is well described and transparent. Given the same data, the analysis could be easily reproduced.
	Metric 15:	Statistical models	Medium	× 0.2	0.4	SMRs and 95% confidence intervals were provided, and the method to calculate the SMRs was sufficiently explained.
Domain 6: Other Considerations for Biomarker Selection and Measurement						
	Metric 16:	Use of Biomarker of Exposure		NA	NA	
	Metric 17:	Effect biomarker		NA	NA	
	Metric 18:	Method Sensitivity		NA	NA	
	Metric 19:	Biomarker stability		NA	NA	
	Metric 20:	Sample contamination		NA	NA	
	Metric 21:	Method requirements		NA	NA	
	Metric 22:	Matrix adjustment		NA	NA	

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Study Citation:	Germani, D., Belli, S., Bruno, C., Grignoli, M., Nesti, M., Pirastu, R., Comba, P. (1999). Cohort mortality study of women compensated for asbestosis in Italy American Journal of Industrial Medicine, 36(1,1), 129-134
Data Type:	Italian_women_asbestosis_ovarian_cancer-Cancer
HERO ID:	709605

Domain	Metric	Rating†	MWF⋆	Score	Comments††
Overall Quality Determination‡		Medium		1.9	
Extracted		Yes			

⋆ MWF = Metric Weighting Factor

† High = 1; Medium = 2; Low = 3; Unacceptable = 4; N/A has no value.

‡ The overall rating is calculated as necessary. EPA may not always provide a comment for a metric that has been categorized as High.

$$\text{Overall rating} = \begin{cases} 4 & \text{if any metric is Unacceptable} \\ \left\lfloor \sum_i (\text{Metric Score}_i \times \text{MWF}_i) \,/\, \sum_j \text{MWF}_j \right\rceil_{0.1} & \text{(round to the nearest tenth) otherwise} \end{cases},$$

where High $=\geq 1$ to < 1.7; Medium $=\geq 1.7$ to < 2.3; Low $=\geq 2.3$ to ≤ 3.0. If the reviewer determines that the overall rating needs adjustment, the original rating is crossed out and an arrow points to the new rating.

†† This metric met the criteria for high confidence as expected for this type of study

Table 18: **Germani et al. 1999: Evaluation of Cancer for Lung Cancer Mortality Outcomes**

Study Citation:	Germani, D., Belli, S., Bruno, C., Grignoli, M., Nesti, M., Pirastu, R., Comba, P. (1999). Cohort mortality study of women compensated for asbestosis in Italy American Journal of Industrial Medicine, 36(1,1), 129-134
Data Type:	Italian_women_asbestosis_lung_cancer-Cancer
HERO ID:	709605

Domain	Metric		Rating[†]	MWF[⋆]	Score	Comments[††]
Domain 1: Study Participation						
	Metric 1:	Participant selection	Medium	× 0.4	0.8	Study participants were drawn from the Italian National Institute for Insurance of Occupational Accidents (INAIL). Eligibility criteria were not expressly stated beyond membership in the asbestosis compensation cohort and being alive at the study's onset (1979). Most women entered the asbestosis compensation cohort around 50 years of age; some healthy worker effect may be present.
	Metric 2:	Attrition	High	× 0.4	0.4	The number of individuals lost to follow-up was provided and appeared minimal for all groups (total cohort = 0.6 percent). The study authors do not suggest any other missing data.
	Metric 3:	Comparison Group	Low	× 0.2	0.6	Rates of mortality in the asbestosis compensation cohort were compared with Italian national mortality rates, stratifying for gender-, age-, and calendar period-specific rates. This represents consideration of potential covariates. The study group of those compensated for asbestosis may have been different from national comparison group.
Domain 2: Exposure Characterization						
	Metric 4:	Measurement of Exposure	Low	× 0.5	1.5	Exposure was assigned only by the women's occupation. No further characterization of the occupational exposure was provided.
	Metric 5:	Exposure levels	Not Rated	NA	NA	
	Metric 6:	Temporality	High	× 0.5	0.5	Asbestosis compensation cohort members were eligible if they were alive and enrolled at the end of 1979. Women were followed until October 1997, allowing for a sufficient follow-up period.
Domain 3: Outcome Assessment						
	Metric 7:	Outcome measurement or characterization	Medium	× 0.667	1.33	The cause of death was obtained for deceased subjects from the Registry Office of the municipality of residence or death. Causes of death were coded according to ICD-9 codes, but no details were provided about histological confirmation.

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Study Citation: Germani, D., Belli, S., Bruno, C., Grignoli, M., Nesti, M., Pirastu, R., Comba, P. (1999). Cohort mortality study of women compensated for asbestosis in Italy American Journal of Industrial Medicine, 36(1,1), 129-134
Data Type: Italian_women_asbestosis_lung_cancer-Cancer
HERO ID: 709605

Domain	Metric		Rating†	MWF⋆	Score	Comments††
	Metric 8:	Reporting Bias	High	× 0.333	0.33	Outcomes specified in the abstract, introduction, and methods were provided in the results. The results provide the number of observations, the SMR, and a confidence interval.
Domain 4: Potential Confounding/Variable Control						
	Metric 9:	Covariate Adjustment	Medium	× 0.5	1	SMRs were stratified for gender, age, and calendar period. Individual smoking data was not available and may be of concern for outcomes including lung cancer.
	Metric 10:	Covariate Characterization	Medium	× 0.25	0.5	Covariates were drawn from information collected by INAIL for asbestosis compensation. It is not entirely clear how INAIL may have collected the covariates.
	Metric 11:	Co-exposure Confounding	Low	× 0.25	0.75	This is an occupational cohort and co-exposures were not addressed. Co-exposures may be present depending on specific job titles and positions.
Domain 5: Analysis						
	Metric 12:	Study Design and Methods	Medium	× 0.4	0.8	SMRs were used to achieve the study objective of comparing cause-specific mortality rates of an occupational cohort to the Italian national population (stratifying for relevant characteristics).
	Metric 13:	Statistical power	Medium	× 0.2	0.4	A total of 631 women compensated for asbestosis were included in the overall cohort, with 276 and 278 women in the textile and asbestos cement industry, respectively.
	Metric 14:	Reproducibility of analyses	Medium	× 0.2	0.4	The analysis is well described and transparent. Given the same data, the analysis could be easily reproduced.
	Metric 15:	Statistical models	Medium	× 0.2	0.4	SMRs and 95% confidence intervals were provided, and the method to calculate the SMRs was sufficiently explained.
Domain 6: Other Considerations for Biomarker Selection and Measurement						
	Metric 16:	Use of Biomarker of Exposure		NA	NA	
	Metric 17:	Effect biomarker		NA	NA	
	Metric 18:	Method Sensitivity		NA	NA	
	Metric 19:	Biomarker stability		NA	NA	
	Metric 20:	Sample contamination		NA	NA	
	Metric 21:	Method requirements		NA	NA	
	Metric 22:	Matrix adjustment		NA	NA	

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Study Citation:	Germani, D., Belli, S., Bruno, C., Grignoli, M., Nesti, M., Pirastu, R., Comba, P. (1999). Cohort mortality study of women compensated for asbestosis in Italy American Journal of Industrial Medicine, 36(1,1), 129-134
Data Type:	Italian_women_asbestosis_lung_cancer-Cancer
HERO ID:	709605

Domain	Metric	Rating†	MWF⋆	Score	Comments††
Overall Quality Determination‡		Medium		1.9	
Extracted		Yes			

⋆ MWF = Metric Weighting Factor

† High = 1; Medium = 2; Low = 3; Unacceptable = 4; N/A has no value.

‡ The overall rating is calculated as necessary. EPA may not always provide a comment for a metric that has been categorized as High.

$$\text{Overall rating} = \begin{cases} 4 & \text{if any metric is Unacceptable} \\ \left\lfloor \sum_i (\text{Metric Score}_i \times \text{MWF}_i) \,/\, \sum_j \text{MWF}_j \right\rceil_{0.1} & \text{(round to the nearest tenth) otherwise} \end{cases},$$

where High $=\geq 1$ to < 1.7; Medium $=\geq 1.7$ to < 2.3; Low $=\geq 2.3$ to ≤ 3.0. If the reviewer determines that the overall rating needs adjustment, the original rating is crossed out and an arrow points to the new rating.

†† This metric met the criteria for high confidence as expected for this type of study

Table 19: **Germani et al. 1999: Evaluation of Cancer for Laryngeal Cancer Mortality Outcomes**

Study Citation:	Germani, D., Belli, S., Bruno, C., Grignoli, M., Nesti, M., Pirastu, R., Comba, P. (1999). Cohort mortality study of women compensated for asbestosis in Italy American Journal of Industrial Medicine, 36(1,1), 129-134
Data Type:	Italian_women_asbestosis_larynx_cancer-Cancer
HERO ID:	709605

Domain	Metric		Rating[†]	MWF[⋆]	Score	Comments[††]
Domain 1: Study Participation						
	Metric 1:	Participant selection	Medium	× 0.4	0.8	Study participants were drawn from the Italian National Institute for Insurance of Occupational Accidents (INAIL). Eligibility criteria were not expressly stated beyond membership in the asbestosis compensation cohort and being alive at the study's onset (1979). Most women entered the asbestosis compensation cohort around 50 years of age; some healthy worker effect may be present.
	Metric 2:	Attrition	High	× 0.4	0.4	The number of individuals lost to follow-up was provided and appeared minimal for all groups (total cohort = 0.6 percent). The study authors do not suggest any other missing data.
	Metric 3:	Comparison Group	Low	× 0.2	0.6	Rates of mortality in the asbestosis compensation cohort were compared with Italian national mortality rates, stratifying for gender-, age-, and calendar period-specific rates. This represents consideration of potential covariates. The study group of those compensated for asbestosis may have been different from national comparison group.
Domain 2: Exposure Characterization						
	Metric 4:	Measurement of Exposure	Low	× 0.5	1.5	Exposure was assigned only by the women's occupation. No further characterization of the occupational exposure was provided.
	Metric 5:	Exposure levels	Not Rated	NA	NA	
	Metric 6:	Temporality	High	× 0.5	0.5	Asbestosis compensation cohort members were eligible if they were alive and enrolled at the end of 1979. Women were followed until October 1997, allowing for a sufficient follow-up period.
Domain 3: Outcome Assessment						
	Metric 7:	Outcome measurement or characterization	Medium	× 0.667	1.33	The cause of death was obtained for deceased subjects from the Registry Office of the municipality of residence or death. Causes of death were coded according to ICD-9 codes, but no details were provided about histological confirmation.

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Study Citation: Germani, D., Belli, S., Bruno, C., Grignoli, M., Nesti, M., Pirastu, R., Comba, P. (1999). Cohort mortality study of women compensated for asbestosis in Italy American Journal of Industrial Medicine, 36(1,1), 129-134
Data Type: Italian_women_asbestosis_larynx_cancer-Cancer
HERO ID: 709605

Domain	Metric		Rating†	MWF⋆	Score	Comments††
	Metric 8:	Reporting Bias	High	× 0.333	0.33	Outcomes specified in the abstract, introduction, and methods were provided in the results. The results provide the number of observations, the SMR, and a confidence interval.
Domain 4: Potential Confounding/Variable Control						
	Metric 9:	Covariate Adjustment	Medium	× 0.5	1	SMRs were stratified for gender, age, and calendar period. Individual smoking data was not available and may be of concern for outcomes including lung cancer.
	Metric 10:	Covariate Characterization	Medium	× 0.25	0.5	Covariates were drawn from information collected by INAIL for asbestosis compensation. It is not entirely clear how INAIL may have collected the covariates.
	Metric 11:	Co-exposure Confounding	Low	× 0.25	0.75	This is an occupational cohort and co-exposures were not addressed. Co-exposures may be present depending on specific job titles and positions.
Domain 5: Analysis						
	Metric 12:	Study Design and Methods	Medium	× 0.4	0.8	SMRs were used to achieve the study objective of comparing cause-specific mortality rates of an occupational cohort to the Italian national population (stratifying for relevant characteristics).
	Metric 13:	Statistical power	Medium	× 0.2	0.4	A total of 631 women compensated for asbestosis were included in the overall cohort, with 276 and 278 women in the textile and asbestos cement industry, respectively.
	Metric 14:	Reproducibility of analyses	Medium	× 0.2	0.4	The analysis is well described and transparent. Given the same data, the analysis could be easily reproduced.
	Metric 15:	Statistical models	Medium	× 0.2	0.4	SMRs and 95% confidence intervals were provided, and the method to calculate the SMRs was sufficiently explained.
Domain 6: Other Considerations for Biomarker Selection and Measurement						
	Metric 16:	Use of Biomarker of Exposure		NA	NA	
	Metric 17:	Effect biomarker		NA	NA	
	Metric 18:	Method Sensitivity		NA	NA	
	Metric 19:	Biomarker stability		NA	NA	
	Metric 20:	Sample contamination		NA	NA	
	Metric 21:	Method requirements		NA	NA	
	Metric 22:	Matrix adjustment		NA	NA	

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Study Citation:	Germani, D., Belli, S., Bruno, C., Grignoli, M., Nesti, M., Pirastu, R., Comba, P. (1999). Cohort mortality study of women compensated for asbestosis in Italy American Journal of Industrial Medicine, 36(1,1), 129-134
Data Type:	Italian_women_asbestosis_larynx_cancer-Cancer
HERO ID:	709605

Domain	Metric	Rating†	MWF⋆	Score	Comments††
Overall Quality Determination‡		Medium		1.9	
Extracted		Yes			

⋆ MWF = Metric Weighting Factor

† High = 1; Medium = 2; Low = 3; Unacceptable = 4; N/A has no value.

‡ The overall rating is calculated as necessary. EPA may not always provide a comment for a metric that has been categorized as High.

$$\text{Overall rating} = \begin{cases} 4 & \text{if any metric is Unacceptable} \\ \left\lfloor \sum_i (\text{Metric Score}_i \times \text{MWF}_i) \,/\, \sum_j \text{MWF}_j \right\rceil_{0.1} & \text{(round to the nearest tenth) otherwise} \end{cases},$$

where High $=\geq 1$ to < 1.7; Medium $=\geq 1.7$ to < 2.3; Low $=\geq 2.3$ to ≤ 3.0. If the reviewer determines that the overall rating needs adjustment, the original rating is crossed out and an arrow points to the new rating.

†† This metric met the criteria for high confidence as expected for this type of study

Table 20: **Tarchi et al. 1994: Evaluation of Cancer for Ovarian Cancer Mortality Outcomes**

Study Citation:	Tarchi, M., Orsi, D., Comba, P., De Santis, M., Pirastu, R., Battista, G., Valiani, M. (1994). Cohort mortality study of rock salt workers in Italy American Journal of Industrial Medicine, 25(2,2), 251-256
Data Type:	rock_salt_workers_ovarian_cancer_mortality-Cancer
HERO ID:	2739094

Domain	Metric		Rating[†]	MWF[⋆]	Score	Comments[††]
Domain 1: Study Participation						
	Metric 1:	Participant selection	High	× 0.4	0.4	The setting and activities conducted in the rock salt mine were described. All employees of the rock salt mine for any duration of length between 1965 and the end of 1989 were eligible (n=487).
	Metric 2:	Attrition	High	× 0.4	0.4	Vital status was determined for all cohort members, indicating no loss to follow-up. The cause of death could not be determined for two individuals, which is not expected to appreciably bias the results.
	Metric 3:	Comparison Group	Medium	× 0.2	0.4	Rates of mortality were compared for employees in a rock salt mine compared to those of the Tuscany region (where the mine is located). It was not clear whether age was considered for stratification when calculating SMRs.
Domain 2: Exposure Characterization						
	Metric 4:	Measurement of Exposure	Low	× 0.5	1.5	Exposure was based on employment at the rock salt mine only.
	Metric 5:	Exposure levels	Not Rated	NA	NA	
	Metric 6:	Temporality	Low	× 0.5	1.5	Participants were included if they were employed between 1965 and 1989, and followed only until 1989. Those becoming eligible later during the eligibility period may have had less time for onset of disease.
Domain 3: Outcome Assessment						
	Metric 7:	Outcome measurement or characterization	High	× 0.667	0.67	Vital status and cause of death were determined at the registrar's office of the individual subject's place of residence or death using ICD-9 codes. The study authors note that classification was carried out independently by two physicians.
	Metric 8:	Reporting Bias	High	× 0.333	0.33	Outcomes specified in the abstract, introduction, and methods were provided in the results. Effect estimates were provided as SMRs, observed cases, expected cases, and a 90% confidence interval.
Domain 4: Potential Confounding/Variable Control						
	Metric 9:	Covariate Adjustment	Medium	× 0.5	1	Sex-specific SMRs were provided, however, individual smoking rates did not appear to be considered.
	Metric 10:	Covariate Characterization	Medium	× 0.25	0.5	Covariates were presumably taken from employment records.

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Study Citation:	Tarchi, M., Orsi, D., Comba, P., De Santis, M., Pirastu, R., Battista, G., Valiani, M. (1994). Cohort mortality study of rock salt workers in Italy American Journal of Industrial Medicine, 25(2,2), 251-256
Data Type:	rock_salt_workers_ovarian_cancer_mortality-Cancer
HERO ID:	2739094

Domain	Metric		Rating†	MWF⋆	Score	Comments††
	Metric 11:	Co-exposure Confounding	Low	× 0.25	0.75	This is an occupational cohort and co-exposures were not addressed. Co-exposures may be present depending on specific job titles and positions.
Domain 5: Analysis						
	Metric 12:	Study Design and Methods	Medium	× 0.4	0.8	Standardized mortality ratios were used to determine excess risk of various cause-specific mortalities related to cancer. This is an appropriate study design for the study question.
	Metric 13:	Statistical power	Medium	× 0.2	0.4	A total of 487 individuals (367 men, 120 women) were in the analysis sample. There is some concern due to the low number of cases of ovarian and laryngeal cancers, making the estimates unstable.
	Metric 14:	Reproducibility of analyses	Medium	× 0.2	0.4	The description of the analysis was sufficient that, given original data, the analysis could be reproduced.
	Metric 15:	Statistical models	Medium	× 0.2	0.4	The calculation of SMRs was transparent and model assumptions appear to be met.
Domain 6: Other Considerations for Biomarker Selection and Measurement						
	Metric 16:	Use of Biomarker of Exposure		NA	NA	
	Metric 17:	Effect biomarker		NA	NA	
	Metric 18:	Method Sensitivity		NA	NA	
	Metric 19:	Biomarker stability		NA	NA	
	Metric 20:	Sample contamination		NA	NA	
	Metric 21:	Method requirements		NA	NA	
	Metric 22:	Matrix adjustment		NA	NA	
Overall Quality Determination‡			~~Medium~~ ⟶ Low§		~~1.9~~	
Extracted			Yes			

⋆ MWF = Metric Weighting Factor

† High = 1; Medium = 2; Low = 3; Unacceptable = 4; N/A has no value.

‡ The overall rating is calculated as necessary. EPA may not always provide a comment for a metric that has been categorized as High.

$$\text{Overall rating} = \begin{cases} 4 & \text{if any metric is Unacceptable} \\ \left\lfloor \sum_i (\text{Metric Score}_i \times \text{MWF}_i) \,/\, \sum_j \text{MWF}_j \right\rceil_{0.1} & \text{(round to the nearest tenth) otherwise} \end{cases},$$

where High $=\geq 1$ to < 1.7; Medium $=\geq 1.7$ to < 2.3; Low $=\geq 2.3$ to ≤ 3.0. If the reviewer determines that the overall rating needs adjustment, the original rating is crossed out and an arrow points to the new rating.

†† This metric met the criteria for high confidence as expected for this type of study

§ Evaluator's explanation for rating change: "Low number of mortality cases for ovarian cancer."

Table 21: **Tarchi et al. 1994: Evaluation of Cancer for Male and Female Lung Cancer Mortality Outcomes**

Study Citation:	Tarchi, M., Orsi, D., Comba, P., De Santis, M., Pirastu, R., Battista, G., Valiani, M. (1994). Cohort mortality study of rock salt workers in Italy American Journal of Industrial Medicine, 25(2,2), 251-256
Data Type:	rock_salt_workers_lung_cancer_mortality-Cancer
HERO ID:	2739094

Domain	Metric		Rating[†]	MWF[⋆]	Score	Comments[††]
Domain 1: Study Participation						
	Metric 1:	Participant selection	High	× 0.4	0.4	The setting and activities conducted in the rock salt mine were described. All employees of the rock salt mine for any duration of length between 1965 and the end of 1989 were eligible (n=487).
	Metric 2:	Attrition	High	× 0.4	0.4	Vital status was determined for all cohort members, indicating no loss to follow-up. The cause of death could not be determined for two individuals, which is not expected to appreciably bias the results.
	Metric 3:	Comparison Group	Medium	× 0.2	0.4	Rates of mortality were compared for employees in a rock salt mine compared to those of the Tuscany region (where the mine is located). It was not clear whether age was considered for stratification when calculating SMRs.
Domain 2: Exposure Characterization						
	Metric 4:	Measurement of Exposure	Low	× 0.5	1.5	Exposure was based on employment at the rock salt mine only.
	Metric 5:	Exposure levels	Not Rated	NA	NA	
	Metric 6:	Temporality	Low	× 0.5	1.5	Participants were included if they were employed between 1965 and 1989, and followed only until 1989. Those becoming eligible later during the eligibility period may have had less time for onset of disease.
Domain 3: Outcome Assessment						
	Metric 7:	Outcome measurement or characterization	High	× 0.667	0.67	Vital status and cause of death were determined at the registrar's office of the individual subject's place of residence or death using ICD-9 codes. The study authors note that classification was carried out independently by two physicians.
	Metric 8:	Reporting Bias	High	× 0.333	0.33	Outcomes specified in the abstract, introduction, and methods were provided in the results. Effect estimates were provided as SMRs, observed cases, expected cases, and a 90% confidence interval.
Domain 4: Potential Confounding/Variable Control						
	Metric 9:	Covariate Adjustment	Medium	× 0.5	1	Sex-specific SMRs were provided, however, individual smoking rates did not appear to be considered.
	Metric 10:	Covariate Characterization	Medium	× 0.25	0.5	Covariates were presumably taken from employment records.

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Study Citation:	Tarchi, M., Orsi, D., Comba, P., De Santis, M., Pirastu, R., Battista, G., Valiani, M. (1994). Cohort mortality study of rock salt workers in Italy American Journal of Industrial Medicine, 25(2,2), 251-256
Data Type:	rock_salt_workers_lung_cancer_mortality-Cancer
HERO ID:	2739094

Domain	Metric		Rating†	MWF⋆	Score	Comments††
	Metric 11:	Co-exposure Confounding	Low	× 0.25	0.75	This is an occupational cohort and co-exposures were not addressed. Co-exposures may be present depending on specific job titles and positions.
Domain 5: Analysis						
	Metric 12:	Study Design and Methods	Medium	× 0.4	0.8	Standardized mortality ratios were used to determine excess risk of various cause-specific mortalities related to cancer. This is an appropriate study design for the study question.
	Metric 13:	Statistical power	Medium	× 0.2	0.4	A total of 487 individuals (367 men, 120 women) were in the analysis sample.
	Metric 14:	Reproducibility of analyses	Medium	× 0.2	0.4	The description of the analysis was sufficient that, given original data, the analysis could be reproduced.
	Metric 15:	Statistical models	Medium	× 0.2	0.4	The calculation of SMRs was transparent and model assumptions appear to be met.
Domain 6: Other Considerations for Biomarker Selection and Measurement						
	Metric 16:	Use of Biomarker of Exposure		NA	NA	
	Metric 17:	Effect biomarker		NA	NA	
	Metric 18:	Method Sensitivity		NA	NA	
	Metric 19:	Biomarker stability		NA	NA	
	Metric 20:	Sample contamination		NA	NA	
	Metric 21:	Method requirements		NA	NA	
	Metric 22:	Matrix adjustment		NA	NA	
Overall Quality Determination‡			Medium		1.9	
Extracted			Yes			

⋆ MWF = Metric Weighting Factor

† High = 1; Medium = 2; Low = 3; Unacceptable = 4; N/A has no value.

‡ The overall rating is calculated as necessary. EPA may not always provide a comment for a metric that has been categorized as High.

$$\text{Overall rating} = \begin{cases} 4 & \text{if any metric is Unacceptable} \\ \left\lfloor \sum_i (\text{Metric Score}_i \times \text{MWF}_i) \,/\, \sum_j \text{MWF}_j \right\rceil_{0.1} & \text{(round to the nearest tenth) otherwise} \end{cases},$$

where High =≥ 1 to < 1.7; Medium =≥ 1.7 to < 2.3; Low =≥ 2.3 to ≤ 3.0. If the reviewer determines that the overall rating needs adjustment, the original rating is crossed out and an arrow points to the new rating.

†† This metric met the criteria for high confidence as expected for this type of study

Table 22: **Tarchi et al. 1994: Evaluation of Cancer for Female Lung Cancer Mortality Outcomes**

Study Citation:	Tarchi, M., Orsi, D., Comba, P., De Santis, M., Pirastu, R., Battista, G., Valiani, M. (1994). Cohort mortality study of rock salt workers in Italy American Journal of Industrial Medicine, 25(2,2), 251-256
Data Type:	rock_salt_workers_female_lung_cancer_mortality-Cancer
HERO ID:	2739094

Domain	Metric		Rating[†]	MWF[⋆]	Score	Comments[††]
Domain 1: Study Participation						
	Metric 1:	Participant selection	High	× 0.4	0.4	The setting and activities conducted in the rock salt mine were described. All employees of the rock salt mine for any duration of length between 1965 and the end of 1989 were eligible (n=487).
	Metric 2:	Attrition	High	× 0.4	0.4	Vital status was determined for all cohort members, indicating no loss to follow-up. The cause of death could not be determined for two individuals, which is not expected to appreciably bias the results.
	Metric 3:	Comparison Group	Medium	× 0.2	0.4	Rates of mortality were compared for employees in a rock salt mine compared to those of the Tuscany region (where the mine is located). It was not clear whether age was considered for stratification when calculating SMRs.
Domain 2: Exposure Characterization						
	Metric 4:	Measurement of Exposure	Low	× 0.5	1.5	Exposure was based on employment at the rock salt mine only.
	Metric 5:	Exposure levels	Not Rated	NA	NA	
	Metric 6:	Temporality	Low	× 0.5	1.5	Participants were included if they were employed between 1965 and 1989, and followed only until 1989. Those becoming eligible later during the eligibility period may have had less time for onset of disease.
Domain 3: Outcome Assessment						
	Metric 7:	Outcome measurement or characterization	High	× 0.667	0.67	Vital status and cause of death were determined at the registrar's office of the individual subject's place of residence or death using ICD-9 codes. The study authors note that classification was carried out independently by two physicians.
	Metric 8:	Reporting Bias	High	× 0.333	0.33	Outcomes specified in the abstract, introduction, and methods were provided in the results. Effect estimates were provided as SMRs, observed cases, expected cases, and a 90% confidence interval.
Domain 4: Potential Confounding/Variable Control						
	Metric 9:	Covariate Adjustment	Medium	× 0.5	1	Sex-specific SMRs were provided, however, individual smoking rates did not appear to be considered.
	Metric 10:	Covariate Characterization	Medium	× 0.25	0.5	Covariates were presumably taken from employment records.

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Study Citation: Tarchi, M., Orsi, D., Comba, P., De Santis, M., Pirastu, R., Battista, G., Valiani, M. (1994). Cohort mortality study of rock salt workers in Italy American Journal of Industrial Medicine, 25(2,2), 251-256
Data Type: rock_salt_workers_female_lung_cancer_mortality-Cancer
HERO ID: 2739094

Domain	Metric		Rating†	MWF⋆	Score	Comments††
	Metric 11:	Co-exposure Confounding	Low	× 0.25	0.75	This is an occupational cohort and co-exposures were not addressed. Co-exposures may be present depending on specific job titles and positions.
Domain 5: Analysis						
	Metric 12:	Study Design and Methods	Medium	× 0.4	0.8	Standardized mortality ratios were used to determine excess risk of various cause-specific mortalities related to cancer. This is an appropriate study design for the study question.
	Metric 13:	Statistical power	Medium	× 0.2	0.4	A total of 487 individuals (367 men, 120 women) were in the analysis sample.
	Metric 14:	Reproducibility of analyses	Medium	× 0.2	0.4	The description of the analysis was sufficient that, given original data, the analysis could be reproduced.
	Metric 15:	Statistical models	Medium	× 0.2	0.4	The calculation of SMRs was transparent and model assumptions appear to be met.
Domain 6: Other Considerations for Biomarker Selection and Measurement						
	Metric 16:	Use of Biomarker of Exposure		NA	NA	
	Metric 17:	Effect biomarker		NA	NA	
	Metric 18:	Method Sensitivity		NA	NA	
	Metric 19:	Biomarker stability		NA	NA	
	Metric 20:	Sample contamination		NA	NA	
	Metric 21:	Method requirements		NA	NA	
	Metric 22:	Matrix adjustment		NA	NA	
Overall Quality Determination‡			Medium		1.9	
Extracted			Yes			

⋆ MWF = Metric Weighting Factor
† High = 1; Medium = 2; Low = 3; Unacceptable = 4; N/A has no value.
‡ The overall rating is calculated as necessary. EPA may not always provide a comment for a metric that has been categorized as High.

$$\text{Overall rating} = \begin{cases} 4 & \text{if any metric is Unacceptable} \\ \left\lfloor \sum_i (\text{Metric Score}_i \times \text{MWF}_i) \,/\, \sum_j \text{MWF}_j \right\rceil_{0.1} & \text{(round to the nearest tenth) otherwise} \end{cases},$$

where High =≥ 1 to < 1.7; Medium =≥ 1.7 to < 2.3; Low =≥ 2.3 to ≤ 3.0. If the reviewer determines that the overall rating needs adjustment, the original rating is crossed out and an arrow points to the new rating.

†† This metric met the criteria for high confidence as expected for this type of study

Table 23: **Tarchi et al. 1994: Evaluation of Cancer for Laryngeal Cancer Mortality Outcomes**

Study Citation:	Tarchi, M., Orsi, D., Comba, P., De Santis, M., Pirastu, R., Battista, G., Valiani, M. (1994). Cohort mortality study of rock salt workers in Italy American Journal of Industrial Medicine, 25(2,2), 251-256
Data Type:	rock_salt_workers_larynx_cancer_mortality-Cancer
HERO ID:	2739094

Domain	Metric		Rating[†]	MWF[⋆]	Score	Comments[††]
Domain 1: Study Participation						
	Metric 1:	Participant selection	High	× 0.4	0.4	The setting and activities conducted in the rock salt mine were described. All employees of the rock salt mine for any duration of length between 1965 and the end of 1989 were eligible (n=487).
	Metric 2:	Attrition	High	× 0.4	0.4	Vital status was determined for all cohort members, indicating no loss to follow-up. The cause of death could not be determined for two individuals, which is not expected to appreciably bias the results.
	Metric 3:	Comparison Group	Medium	× 0.2	0.4	Rates of mortality were compared for employees in a rock salt mine compared to those of the Tuscany region (where the mine is located). It was not clear whether age was considered for stratification when calculating SMRs.
Domain 2: Exposure Characterization						
	Metric 4:	Measurement of Exposure	Low	× 0.5	1.5	Exposure was based on employment at the rock salt mine only.
	Metric 5:	Exposure levels	Not Rated	NA	NA	
	Metric 6:	Temporality	Low	× 0.5	1.5	Participants were included if they were employed between 1965 and 1989, and followed only until 1989. Those becoming eligible later during the eligibility period may have had less time for onset of disease.
Domain 3: Outcome Assessment						
	Metric 7:	Outcome measurement or characterization	High	× 0.667	0.67	Vital status and cause of death were determined at the registrar's office of the individual subject's place of residence or death using ICD-9 codes. The study authors note that classification was carried out independently by two physicians.
	Metric 8:	Reporting Bias	High	× 0.333	0.33	Outcomes specified in the abstract, introduction, and methods were provided in the results. Effect estimates were provided as SMRs, observed cases, expected cases, and a 90% confidence interval.
Domain 4: Potential Confounding/Variable Control						
	Metric 9:	Covariate Adjustment	Medium	× 0.5	1	Sex-specific SMRs were provided, however, individual smoking rates did not appear to be considered.
	Metric 10:	Covariate Characterization	Medium	× 0.25	0.5	Covariates were presumably taken from employment records.

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Study Citation:	Tarchi, M., Orsi, D., Comba, P., De Santis, M., Pirastu, R., Battista, G., Valiani, M. (1994). Cohort mortality study of rock salt workers in Italy American Journal of Industrial Medicine, 25(2,2), 251-256
Data Type:	rock_salt_workers_larynx_cancer_mortality-Cancer
HERO ID:	2739094

Domain	Metric		Rating†	MWF⋆	Score	Comments††
	Metric 11:	Co-exposure Confounding	Low	× 0.25	0.75	This is an occupational cohort and co-exposures were not addressed. Co-exposures may be present depending on specific job titles and positions.
Domain 5: Analysis						
	Metric 12:	Study Design and Methods	Medium	× 0.4	0.8	Standardized mortality ratios were used to determine excess risk of various cause-specific mortalities related to cancer. This is an appropriate study design for the study question.
	Metric 13:	Statistical power	Medium	× 0.2	0.4	A total of 487 individuals (367 men, 120 women) were in the analysis sample. There is some concern due to the low number of cases of ovarian and laryngeal cancers, making the estimates unstable.
	Metric 14:	Reproducibility of analyses	Medium	× 0.2	0.4	The description of the analysis was sufficient that, given original data, the analysis could be reproduced.
	Metric 15:	Statistical models	Medium	× 0.2	0.4	The calculation of SMRs was transparent and model assumptions appear to be met.
Domain 6: Other Considerations for Biomarker Selection and Measurement						
	Metric 16:	Use of Biomarker of Exposure		NA	NA	
	Metric 17:	Effect biomarker		NA	NA	
	Metric 18:	Method Sensitivity		NA	NA	
	Metric 19:	Biomarker stability		NA	NA	
	Metric 20:	Sample contamination		NA	NA	
	Metric 21:	Method requirements		NA	NA	
	Metric 22:	Matrix adjustment		NA	NA	
Overall Quality Determination‡			~~Medium~~ ⟶ Low§		~~1.9~~	
Extracted			Yes			

⋆ MWF = Metric Weighting Factor

† High = 1; Medium = 2; Low = 3; Unacceptable = 4; N/A has no value.

‡ The overall rating is calculated as necessary. EPA may not always provide a comment for a metric that has been categorized as High.

$$\text{Overall rating} = \begin{cases} 4 & \text{if any metric is Unacceptable} \\ \left\lfloor \sum_i (\text{Metric Score}_i \times \text{MWF}_i) \,/\, \sum_j \text{MWF}_j \right\rceil_{0.1} & \text{(round to the nearest tenth) otherwise} \end{cases},$$

where High $=\geq 1$ to < 1.7; Medium $=\geq 1.7$ to < 2.3; Low $=\geq 2.3$ to ≤ 3.0. If the reviewer determines that the overall rating needs adjustment, the original rating is crossed out and an arrow points to the new rating.

†† This metric met the criteria for high confidence as expected for this type of study

§ Evaluator's explanation for rating change: "Low number of mortality cases for laryngeal cancer."