Background and Methods

Background/Aim

The analysis of studies across a set of studies is a powerful tool that can help with decisions about whether a potential bias is an important concern for an individual study, and to illuminate a pattern within apparent inconsistent effects. The heterogeneity may stem from differing study designs examining varying outcome and exposure definitions and be influenced to varying degrees by sources of bias and other factors that affect the magnitude, direction, and precision of effect estimates. Influential aspects include potential bias (e.g., selection, information, confounding) and other quality aspects (e.g., sensitivity, precision). This type of analysis also can include factors, such as exposure levels, that are important for the interpretation of results. Studies of the association between indoor formaldehyde exposure and current asthma and pulmonary function were used as a case study to illustrate the impact of bias and other study attributes on the analysis of consistency across studies.

Methods:

- Studies included a range spanning at least 0.01 mg/m³ across a range spanning at least 0.01 mg/m³.
- Differences in means of spirometry measurements taken before shift comparing exposed to unexposed. Means adjusted for age, height, and sex.

Current Asthma in Children and Adults

Current asthma is defined as a report of asthma symptoms during the last 12 months. Studies limited to “ever had asthma” were not included because the formaldehyde measures available did not reflect cumulative exposure that could be related to cumulative risk. The population relevant in the PECS for this analysis included children and adults in 22 studies of workers with occupational exposures, and 5 occupational studies involving manufacturer of pressed wood products, chemical production and embalming. These studies evaluated the variation in risk of prevalence of current asthma. Incidence of asthma was used to indicate control for other study attributes on the analysis of consistency across studies.

Conclusion

When studies are ordered alphabetically, results appear heterogeneous, but when exposure levels and study confidence are considered, a pattern of increasing risk with increasing exposure levels is apparent among the high and medium confidence studies. No single-domain limitation was a primary reason for the low confidence determinations, but collectively results of these studies are more variable.

Current Asthma: Sorting by Rating for Confounding

For studies in residential or school settings with lower exposure levels, a deficient rating for confounding with a predicted direction away from the null provides a potential explanation for some of the heterogeneity in odds ratios.

Occupational Studies of Pulmonary Function: Confounding

Forced expiratory volume in 1 second (FEV₁) and forced vital capacity (FVC) were the most common measures analyzed by the studies of formaldehyde exposure. The population relevant to the PECS for this analysis included workers with occupational exposure to formaldehyde in studies where exposure was confirmed by air measurements, VOCs, or involved professional categories of embalmers and anatomist/pathologists. A total of 21 studies included manufacturing of wood products, chemical production, embalming or offices in mobile trailers were identified, which analyzed variation in pulmonary function outcomes in relation to variation in formaldehyde at exposures above 0.010 mg/m³ across a range spanning at least 0.01 mg/m³. Of the 21 studies, 5 were not large, but is consistently observed in one or more critical differences, one reported additional analyses in the same cohort, and group presented longitudinal analyses or cross-shift changes, which are not shown in this example.

Notes on forest plots

- Different methods of spirometry measurements taken before shift comparing exposed to unexposed. Means adjusted for age, height and sex.
- Study regression analyses also adjusted for smoking, and coefficients were in the same direction as those in forest plots.
- Two studies were not plotted because the studies reported only means of the unadjusted absolute values. Holmstrom et al. (1999) found a statistically significant decrease in FEV₁/FVC in analyses adjusted for age, height, sex and smoking, and Khamgaonkar et al. (1991) found a statistically significant decrease in FEV₁ and FVC in analyses adjusted for age, height, weight and sex.

Conclusion

Overall, mean values of pulmonary function among exposed workers were lower than those of unexposed comparison groups. The difference in FEV₁/FVC was observed in most of the studies, which were limited by a healthy worker survivor bias, which may have attenuated the size of the observed difference. Concern for residual confounding is lessened because findings were consistent between the wood products and chemical manufacturing industries, which involve different coexposures.

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