

Authors' response: A systematic review of the association between pleural plaques and changes in lung function

We welcome the opportunity to respond to Goodman *et al.*,¹ and to correct their misperceptions about our paper.² As noted in their letter, Kerper *et al.*³ also recently analysed lung function decrements associated with pleural plaques. While the methodological details of our publications differed somewhat, the identified literature and the conclusions regarding magnitude of effect on lung function were well aligned. We found statistically significant 2–4% decrements in lung function in people exposed to asbestos with pleural plaques relative to asbestos-exposed people without abnormalities. Kerper *et al.*³ reported 3–5% decrements. It is not clear why Kerper *et al.*³ chose to ignore differences in study size: all studies were considered equally in their analysis, despite sample sizes ranging from tens to thousands, and a summary estimate was not calculated.

With respect to the specific points raised,¹ although we did not use the term 'risk of bias' (a term ie, also sometimes used for 'internal validity'), our approach certainly meets standards of systematic review.⁴ We systematically evaluated studies using predefined criteria related to study methodology and potential biases (eg, consideration of potential confounding by smoking), and incorporated this information through a series of sensitivity analyses. The decrements in lung function associated with the presence of pleural plaques were similar or larger in the meta-analysis of studies without identified limitations, as outlined in the predefined criteria, compared to the meta-analysis of all studies. In addition, all of the studies used an internal comparison group of asbestos-exposed people without abnormalities, and some included additional adjustment for asbestos

exposure. We conducted analyses limited to HRCT studies that excluded early signs of parenchymal changes, demonstrating that the decrements in lung function cannot be attributed² to undetected asbestos-related disease, and we examined and addressed BMI in our analysis and discussion. We noted that the pattern of results among the five excluded studies was consistent with the pattern seen in the included studies; these were not 'null' studies, as was characterised by Goodman *et al.*² In addition, we see no basis for a concern that imputation of variances for the four studies that did not provide these data biased our results.

Despite concerns¹ that one of the longitudinal studies⁵ had no comparison population, the comparison of measured lung function to predicted lung function accounts for potential longitudinal declines due solely to increasing age and allows subjects to serve as their own comparison over time. The study⁵ showed that plaques and measured lung function relative to predicted lung function both worsen over time even without additional asbestos exposure.

Our and Kerper *et al.*'s³ search results differed by one foreign-language paper and one study published after our cut-off date. The other differences in the set of studies arose from our more restrictive inclusion criteria (eg, excluding studies that included people with asbestosis). We see this as an example of methodological rigour, not an 'insufficiency' of the search strategy as characterised in reference 1.

In summary, our systematic review and meta-analysis found statistically significant decrements in lung function in asbestos-exposed people with pleural plaques relative to exposed people without abnormalities. Our analysis does not support the suggestion¹ that the results are due to methodological limitations of the studies, undetected asbestos-related disease, a biased analysis, or the exclusion of studies. Small but significant permanent changes in group mean lung function can be indicative of functional impairment at the population level;⁶ the focus on population-level versus clinical-level effects is at the heart of our and Kerper *et al.*'s³ differing interpretations of the observed decrement in lung function.

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