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The critical requirement for asbestos is to be able to identify occupational and environmental exposure limits, which, if adequately enforced, would reduce excess deaths to "acceptable" levels. Such limits would also permit objective prioritisation of remediation work with asbestos-containing materials. The excellent paper by Hodgson and Darnton (2000) partly answers the above needs. However, from an occupational hygienist's viewpoint there are some aspects of the paper which require comment or further information.

The risk estimates are based on observed disease in the study cohorts. However, cohort mortality in the majority of the cohorts is low, particularly for those exposed to amphiboles, e.g. 13% in SA crocidolite mines and 21% in SA amosite mines (Sluis-Cremer *et al.*, 1992), 20% at Wittenoom (de Klerk *et al.*, 1994) and 26% in Ontario asbestos-cement workers (Finkelstein, 1984). Given that the median ages for deaths from lung cancer and mesothelioma are both 70–74 and 75th percentile ages at death are both 75–79, from RGS (1996–2000), it is evident that until almost all cohort members have either died or reached about age 80 only a small proportion of both lung cancers and mesotheliomas will be observed. All else being equal, cohorts with low mortality are relatively young and have not had the chance to develop the eventual numbers of lung cancers or mesotheliomas. This can be seen, for example, from Selikof and Seidman (1973) where deaths due to mesothelioma, expressed as a proportion of the cohort, increased with mortality from 0.32% at 12% mortality, to 1.1% at 38% mortality to 5.1% at 68% mortality. That is, the proportion of the cohort dying from mesothelioma increased about 16-fold as mortality increased from 12% to 68%. Risk estimates based on data from cohorts with low mortality are therefore likely to underestimate the eventual risk, the degree of underestimation increasing as cohort mortality decreases. Standards based on such underestimates are likely to put those intended to be protected at unnecessary and avoidable risk.

To ensure that unduly low Standards are not adopted, estimates should be made for each cohort of the eventual consequences of exposure, e.g. see de Klerk *et al.* (1989) and Berry (1991), and Standards should be based on such final consequence estimates.

It is appreciated that the risk estimates in the paper were based on first exposure at age 30 to aid analysis. However, to be useful in the context of setting Standards it is necessary for occupational exposures that the estimates cover the age range 16 to 60 and for environmental exposures cover the age range 0 upwards. From the information provided in the paper it is not unambiguously possible to derive such estimates.

The inclusion of data for mining severely skews the risk estimates, particularly for chrysotile where the mining data reduce the lung cancer risk estimate by about a factor of 37. Given that asbestos mining is of no relevance outside asbestos producing areas, the inclusion of mining data for chrysotile must be questioned.

Given the limited data for crocidolite and amosite and the much higher potency of these forms of asbestos for mesothelioma and lung cancer, it seems unsafe to base any assumption on the nature of the dose-response relationships for these types on a summation of their data with those for chrysotile, particularly for lung cancer where it is assumed that risk falls faster than exposure levels.

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We thank Drs Liddell and Browne and Mr Howie for their interest in our paper (Hodgson and Darnton, 2000), and their generally supportive comments. Between them they make a number of points which we would like to respond to. We will first deal with the comments from Drs Liddell and Browne.

CAROLINA COHORT

Both correspondents challenge in one way or another our treatment of the Carolina cohort. It is clear that there are difficulties in interpreting the observations from this cohort and a number of approaches are possible. As far as the assessment of mesothelioma risk is concerned, whether one counts the Carolina cohort along with the other chrysotile cohorts or not makes very little difference to the overall risk estimate. With only two mesothelioma cases, the Carolina cohort's statistical weight here is small. Our suggested risk is 0.001% per f/ml.yr, implying that the Carolina observations (0.013) do indeed overstate the true risk (whether by chance or otherwise).

Dr Browne thinks we should have made more of the possible role of amphibole in the Carolina cohort. It is true that this is a possible explanation for this cohort's "exceptional" status, though as we point out, the fact that significant levels of amphibole were found post mortem in the lungs of only one of ten lung cancer cases examined (Green *et al.*, 1997) limits the confidence one might otherwise have in this explanation.

COHORT AVERAGES

Another general criticism focuses on our use of what we have called "cohort average" data, rather than using (where available) more detailed exposure specific breakdowns within cohorts. Our reasons for this are discussed in the paper, and amount to a judgement that more is gained by improving the stability of observations and avoiding the probable errors of individual exposure estimation than is lost by pooling observations on individuals with very different exposures. Where both cohort average and internal analyses are available, we compare the two measures (figures 10 and 11 of our paper) and show a good degree of concordance between them. It is not true that "regression between cohorts is irrelevant to [the form of the individual dose response]". For a linear relationship the two approaches will give identical estimates. It is of course true that non-linearity will distort the correspondence between individual and cohort level measures but the extent of this distortion for the degree of non-linearity we suggest will be small.

SMOKING

Dr Liddell also challenges our treatment of smoking effects. Clearly the reality of the joint effect of asbestos and smoking is more complicated than implied by a simple multiplicative adjustment for "smokers" and "non-smokers". However in the context of other substantial uncertainties such refinements are arguably inappropriate and in any case our paper was challenging the limits of reasonable length already.

TREMOLITE

Dr Browne refers to evidence that the tremolite contamination in Quebec chrysotile is a major factor in the observed mortality there, coupled with the claim that levels of asbestos related disease are very low or non-existent in cohorts exposed to chrysotile uncontaminated by tremolite, in South Africa, the former USSR and Brazil. The evidence from Quebec that tremolite plays an important role in the observed mortality there is reasonably convincing. Unfortunately there is no good epidemiology on the low tremolite cohorts elsewhere. The reference cited in this connection by Dr Browne (Rees *et al.*, 1999) does show that in a sixteen month case-ascertainment period covering most of South Africa no cases of mesothelioma associated with chrysotile mining were

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