the same range of possible slopes for the chrysotile lung cancer relationship as for the amphiboles, and determine the scaling constant by fixing the predicted excess mortality at the median exposure for chrysotile cohorts (70 f/ml.yr) to 0.1% for the best estimate and 0.5% for the cautious estimate. The resulting values are shown in Table 10.

The pattern of excess lung cancer—broadly constant relative excess from 10 to 40 (perhaps more) years from exposure (see Appendix A) implies that for exposure starts between 20 and 40 yr of age there is very little difference in the predicted risk. There may be some decline for very long follow up, but the rate of decline is unknown. As for mesothelioma we address this possibility approximately by truncating the predicted excess at age 80.

IS THERE A THRESHOLD?

Another question with important implications for risk at low levels of exposure is whether there is a threshold for cancer initiation by asbestos. The HSE's recent *Review of fibre toxicology* (Meldrum, 1996), presents arguments mainly on a toxicological basis for believing that there may be a threshold for asbestos induced lung cancer. The argument is essentially based on a view of the carcinogenic process induced by asbestos as being an extension of the chronic inflammatory processes producing fibrosis. It is widely agreed that heavy doses of chrysotile are required to produce lung fibrosis. And some evidence has been derived from the New Orleans cohort suggesting a threshold dose of about 30 f/ml.yr for radiological fibrosis (Weill, 1994). Analysis of necropsy material from the Carolina cohort also shows a distinct step increase in fibrosis score for cumulative exposures around 20–30 f/ml.yr (Green *et al.*, 1997). This does not apply to amphibole exposure: radiological fibrosis which progressed after the cessation of exposure has been documented (Sluis-Cremer, 1991), in South African amphibole miners under medical surveillance and with cumulative doses less than 5 f/ml.yr. This suggests that if a threshold applies to the lung cancer effect of amphibole asbestos, it is very low. The adoption of a slightly concave exposure response slope entails a moderately threshold-like behaviour.

Several lines of argument also suggest that any threshold for mesothelioma is at a very low level. Some cohorts (Neuberger and Kundi, 1990; Newhouse and Sullivan, 1989; McDonald and McDonald, 1978; Thomas *et al.*, 1982; Rossiter and Coles, 1980), have produced mesotheliomas in conditions where no excess lung cancer was seen. Occupational PMRs for British men suggest that the range of jobs for which mesothelioma rates are above background levels is very wide (Hutchings *et al.*, 1995; Hodgson *et al.*, 1997). Also the proportion of mesothelioma cases in population studies for whom no likely source of asbestos exposure can be identified is often quite high. All these observations suggest that relatively brief exposures may carry a low, but non-zero, risk of causing mesothelioma.

Some authors (Ilgren and Browne, 1991; Liddell, 1993) have argued for a mesothelioma threshold, or threshold-like behaviour of the dose–response. Such arguments are fraught with statistical and logical difficulties. The attempt (Ilgren and Browne, 1991) to deduce a 'threshold' by identifying the lowest estimated dose received by any observed case is a logical nonsense. Furthermore, the existence of zero cases in a dose category (human or animal) should not be automatically interpeted as zero risk. Direct statistical confirmation of a threshold from human data is virtually impossible. One would need accurate assessment of very low doses across a large population with long term follow up. Case-control studies with lung content measures of exposure (McDonald *et al.*, 1989; Rödelsperger *et al.*, 1999; Rogers *et al.*, 1991) do not suggest any threshold, or downward inflexion of the dose response at the lower end of their exposure scales. Some of the animal data cited by Ilgren and Browne are suggestive of a threshold—particularly that from intra-pleural and intra-peritoneal injection—but it is not clear how this would translate into a estimated human effect threshold for exposure by inhalation. Taking this evidence together we do not believe there is a good case for assuming any threshold for mesothelioma risk.

QUANTIFIED RISK ASSESSMENT

Under current conditions, the main interest in the health risks of asbestos relates to exposure circumstances well outside the range for which we have direct observations. The statements we can make about risk therefore incorporate two kinds of uncertainty. First there is the usual statistical uncertainty of inferring underlying risk from observations in particular groups. This kind of uncertainty depends essentially on the number of events (in this case cancer deaths) observed. The uncertainty can therefore—given some assumptions—be quantified: the more observed events, the less the statistical uncertainty. Statistical uncertainty is expressed as a confidence interval (a range of values with—conventionally—a 95% probability of covering the true value).

The second kind of uncertainty relates to the question whether the relationship between exposure and outcome seen in the observed range continues to hold outside that range. This kind of uncertainty cannot be quantified statistically. Qualitatively one can reasonably argue that the agreement will be better for exposures close to the observed range, but with increasing distance from the observed range our confidence that we know what to expect decreases. For example, previous assessments of cancer risk from asbestos have all assumed that the effect is linear.