## APPENDIX

## AGE AND CALENDAR YEAR MODEL

Following Hodgson *et al*,[6] we assumed: (1) that the mesothelioma rate for a cohort aged $a$ at time $t$ exposed to asbestos at time $u$ in the past was proportional to the earlier asbestos dose (that is, rate$(a,t|u)$ was proportional to dose$(a\text{-}u,t\text{-}u)$); (2) that dose was multiplicative by age and time, that is, dose$(a,t)$ was proportional to $W(a)D(t)$, for dose potentials by age ($=W$) and by time ($=D$); (3) that the rate was proportional to time from exposure to malignant conversion raised to some power $k$ together with an effect due to clearance of asbestos fibres from the lung, where the half-life is represented by $H$ and $\tau$ is the average latency time from malignant conversion of the cancer to clinical detection; and (4) that the observed number of cases followed a Poisson distribution with mean $\mu_{at}$.[12] To model the mesothelioma rate, we averaged the rates across all of the times since exposure from $\tau$ to $a$. The predicted number of cases $\mu_{at}$ was calculated by weighting the mesothelioma rate by the person-years at risk estimated by the population ($=P_{at}$) and scaled by the fraction of correctly diagnosed cases at year $t$ ($=D_x(t)$). Taking $\beta$ as a constant, the Poisson regression model was:

$$\mu_{at} = \left[\beta\int_{\tau}^{a} D(t-u)\,W(a-u)(u-\tau)^{k}\,0.5^{[u-\tau)/H}\,du\right]P_{at}D_x(t)$$

We modelled the rates for the mid-point of the five-year age intervals (for example, for ages 40–44 years, $a=42.5$). The mean rate $\mu_{at}$ was numerical integrated using Simpson's rule, with functional evaluations at single-year increments for $u=\tau+0.5$ to $u=a$.[20] The dose potential functions $W(a)$ and $D(t)$ were specified as exponentials of natural splines with one internal knot and two parameters to be estimated.[21] For $W(a)$, the spline functions were defined for boundary knots at ages 20 and 65 years and $W(a)$ was defined to be 1 at age 50 years; for $D(t)$, the spline functions were defined with boundary knots at 1945 and 1980 and $D(t)$ was defined to be 1 in 1970; internal knots were assumed to be at the mid-point between the boundary knots.

The five parameters to be estimated included the log of the constant $\beta$ and four parameters for the spline functions $\log(W)$ and $\log(D)$. We assumed that $k$ was fixed at 3.5. The asbestos half-life $H$ was given a value of 15 years. For incidence data, the latency period $\tau$ was assumed to be 5 years. As in Model 1 of Hodgson *et al*,[6] the diagnosis fraction $D_x(t)$ was assumed to be almost complete (98%) in 1997, with a 5% annual percentage trend in the missing cases, such that $D_x(t) = 1\text{–}0.02\times1.05^{1997-t}$.

The models were fitted using the mle() function in the R statistical package,[22] which uses a quasi-Newton approach to maximise the Poisson log-likelihood. The design matrices for the spline functions were calculated using the ns( ) function in R. We assessed goodness of fit by performing a likelihood ratio test using the residual deviance with the residual degrees of freedom. For interval estimation for predictions, we used the bootstrap, re-sampling from Pearson's residuals.[23] Following Friedl, we standardised the residuals by dividing by the square root of (1–model degrees of freedom/number of observations) and scaled the residuals to have zero mean.[24]