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AN EXPOSURE–RESPONSE ANALYSIS OF RESPIRATORY DISEASE RISK ASSOCIATED WITH OCCUPATIONAL EXPOSURE TO CHRYSOTILE ASBESTOS

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INTRODUCTION

There has been considerable debate in the scientific literature concerning the significance of the risks associated with exposure to chrysotile asbestos (Mossman *et al.*, 1990; Stayner *et al.*, 1996). This paper presents the findings from exposure–response and risk analyses of lung cancer and asbestosis mortality based on a cohort mortality study of U.S. textile workers exposed to chrysotile asbestos.

MATERIAL AND METHODS

Data were used from a recent update of a cohort mortality study of workers exposed to chrysotile asbestos in a South Carolina textile factory (Dement *et al.*, 1994). The analysis was restricted to include workers employed in the textile production operations for at least 1 month between 1 January, 1940 and 31 December, 1975. Follow-up of this cohort for vital status was until 31 December, 1990. Chrysotile exposure levels by areas of the plant, specific jobs and calendar years have been previously estimated and were used with work history information to estimate individual cumulative exposures for this analysis.

Exposure–response analyses were conducted for cancers of the trachea, bronchus and lung ("lung cancer") and for asbestosis and pneumoconiosis ("asbestosis"). The underlying cause of death was used for lung cancer (ICD9 = 162) and a multiple cause of death approach (Steenland *et al.*, 1992) was used for "asbestosis" (ICD9 = 501 and 505). Based on these definitions, there was a total of 126 lung cancer and 45 cases of asbestosis available for analysis.

Poisson regression methods were used to analyze the exposure–response relationship between chrysotile asbestos exposure and respiratory disease mortality. For lung cancer, the person–years and observed deaths were restricted to include only those with at least 15 years of time since the date of first exposure.

A wide variety of parametric models were evaluated including additive, log–linear, log–quadratic, additive relative rate and power function models (Stayner *et al.*, 1995). The fit of these models was contrasted by comparing their deviances and by graphically comparing them with a categorical model, and a restricted cubic

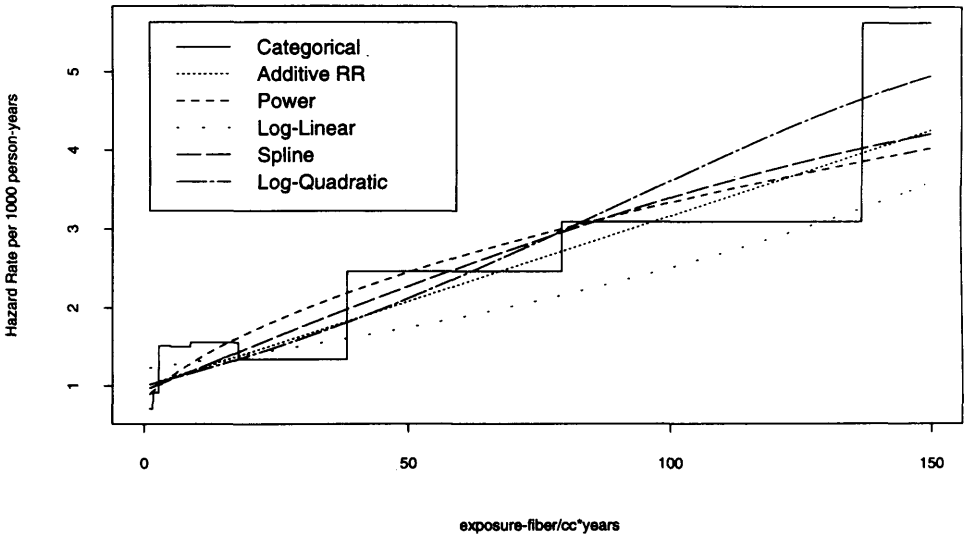

Fig. 1. Lung cancer mortality rates as a function of cumulative asbestos exposure predicted by alternative models for white males, age 50 in 1940–1969.

spline model (Herndon and Harrell, 1995). Finally, a "threshold" model (Ulm, 1990) was evaluated to test whether the fit of the model was improved by including a threshold parameter.

Estimates of excess lifetime risk of dying from lung cancer and asbestosis were developed for varying levels of chrysotile asbestos exposure based upon an actuarial method, which accounts for the influence of competing risks (BEIR IV, 1988).

RESULTS

The results from fitting alternative Poisson regression models to the lung cancer rates are illustrated in Fig. 1. Exposure was a highly significant predictor ($P < 0.001$) of lung cancer mortality in all of the models evaluated. The additive relative rate (ARR) model gave the best fit to the data and provided similar estimates of the rate as the spline model and the categorical model.

A significant interaction was found between cumulative exposure and time since first exposure ($P = 0.04$), and an additive relative rate model with separate slopes for cumulative exposures with 15 to < 30, 30 to < 40 and ≥ 40 years of latency was chosen as the final model for estimating lifetime risks.

The results from fitting alternative Poisson regression models for asbestosis are illustrated graphically in Fig. 2. The exposure–response relationship was found to be highly statistically significant ($P < 0.001$) in all of the models evaluated. The power model was found to provide the best fit to the data of all of the parametric models, and produced similar estimates of the hazard rate as the categorical mode and somewhat lower estimates than the spline model. The fit of the models for lung cancer and asbestosis were not improved by the inclusion of a threshold parameter, and thus there was no evidence for a "threshold" type response for these outcomes.

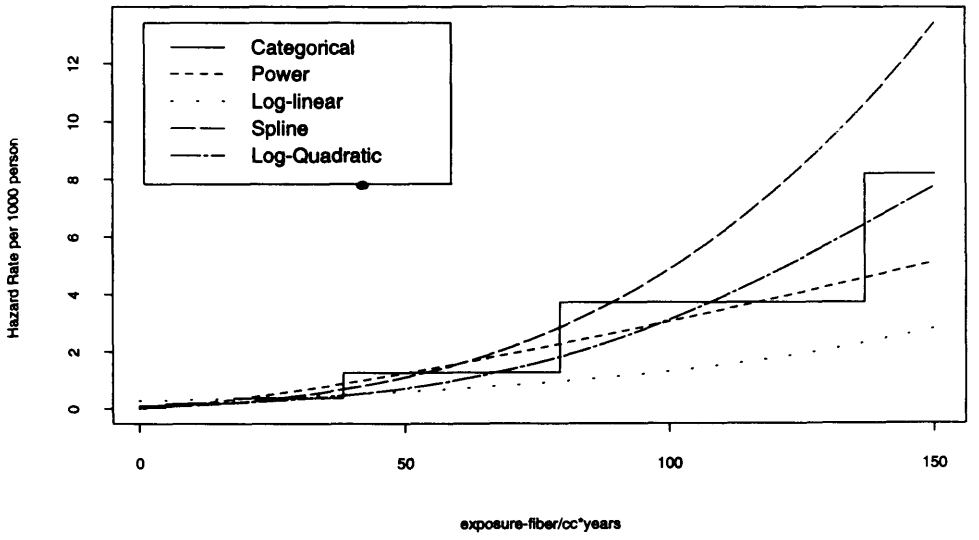

Fig. 2. Asbestosis mortality rates as a function of cumulative asbestos exposure predicted by alternative models for white males, age 50 in 1940–1969.

Predicted lifetime excess risks of lung cancer and asbestosis assuming 45 years of exposure to varying chrysotile asbestos exposure levels are presented in Fig. 3 for lung cancer and in Fig. 4 for asbestosis. The risks vary by gender and race because of differences in the background rates used in the models. The predicted risks for asbestosis are less than those for lung cancer at low exposure levels (e.g. < 0.5). At

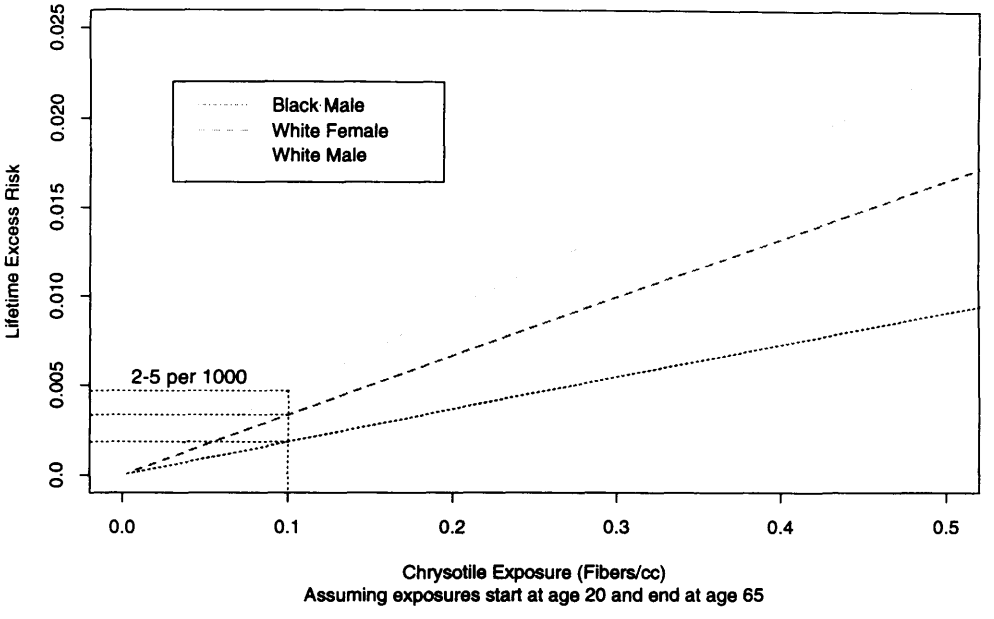

Fig. 3. Lifetime excess risk for lung cancer assuming 45 years of exposure to varying concentrations of chrysotile asbestos.

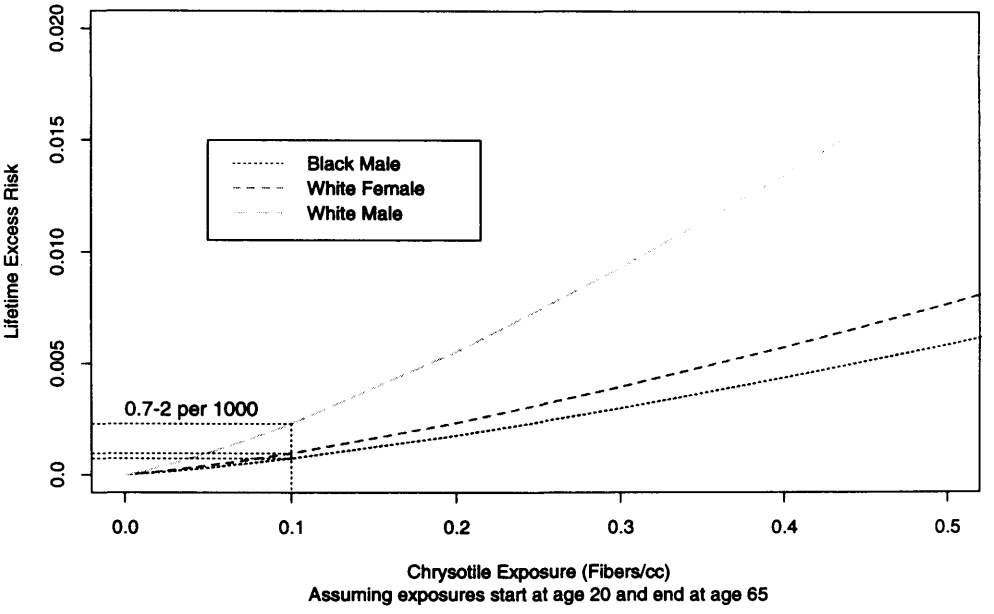

Fig. 4. Lifetime excess risk for asbestosis assuming 45 years of exposure to varying concentrations of chrysotile asbestos.

higher exposure levels this pattern is reversed with the predicted risks for asbestosis being higher than those for lung cancer.

DISCUSSION

The results from these analyses clearly demonstrate a strong exposure–response relationship between chrysotile exposure and mortality from asbestosis and lung cancer, which is not surprising given the results from previous studies. The exposure–response relationship for lung cancer appeared to be linear on a multiplicative scale, whereas the exposure–response relationship for asbestosis appeared to be sub-linear.

There was no statistical evidence for a threshold in either the lung cancer or asbestosis model. Thus the results from this analysis fail to provide any support for arguments that have been made for a threshold for the effects of chrysotile asbestos on lung cancer and asbestosis risks (Browne, 1986). Based on this analysis, the predictions of excess lifetime risk for white males exposed for 45 years at the recently revised OSHA standard of 0.1 fibers cc^{-1} was predicted to be approximately 5 per 1000 for lung cancer and 2 per 1000 for asbestosis. The lung cancer risks estimated in this analysis were substantially higher than what was observed in previous analyses of Quebec chrysotile miners and millers (McDonald *et al.*, 1980, 1994). The reasons for these widely varying results are not known.

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