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Objectives: Workers in the asbestos industry tend to have high smoking rates compared to the general population. Both asbestos exposure and cigarette smoking are recognized risk factors for lung cancer mortality, but the exact nature of the interaction between the two remains uncertain. The aim of this study was to examine the effect of smoking and smoking cessation among asbestos workers in Great Britain (GB) and investigate the interaction between asbestos exposure and smoking. Methods: The study population consisted of 98 912 asbestos workers recruited into the GB Asbestos Survey from 1971, followed-up to December 2005. Poisson regression was used to estimate relative risks of lung cancer mortality associated with smoking habits of the asbestos workers and to assess whether these effects differed within various categories of asbestos exposure. The interaction between asbestos exposure and smoking was examined using the Synergy (S) and Multiplicativity (V) indices, which test the hypotheses of additive and multiplicative interaction, respectively. The proportion of lung cancers among smokers attributable to the interaction of asbestos and smoking was also estimated. Results: During 1 780 233 person-years of follow-up, there were 1878 deaths from lung cancer (12% of all deaths). Risk of lung cancer mortality increased with packs smoked per day, smoking duration, and total smoke exposure (pack-years). Asbestos workers who stopped smoking remained at increased risk of lung cancer mortality up to 40 years after smoking cessation compared to asbestos workers who never smoked. The effects of smoking and stopping smoking did not differ by duration of asbestos exposure, main occupation, age at first asbestos exposure, year of first exposure, or latency period. The interaction between asbestos exposure and smoking for asbestos workers was greater than additive [S 1.4, 95% confidence interval (CI) 1.2–1.6], and the multiplicative hypothesis could not be rejected (V 0.9, 95% CI 0.3–2.4). For those asbestos workers who smoked, an estimated 26% (95% CI 14–38%) of lung cancer deaths were attributable to the interaction of asbestos and smoking. Conclusions: This study emphasizes the importance of smoking prevention and cessation among those who work in the asbestos industry.

Keywords: Great Britain; lung cancer mortality; occupational asbestos exposure; smoking; smoking cessation

INTRODUCTION

Smoking tobacco is the major determinant of lung cancer and accounts for ~90% of all cases (Quinn et al., 2001). The relationship between smoking and lung cancer is well documented (Doll and Peto, 1978; Doll et al., 2004; IARC, 2004), along with the benefits of smoking cessation (US DHHS, 1990; Peto et al., 2000). Asbestos is also an important lung carcinogen, accounting for an estimated 2–3% of lung cancer deaths in Britain during 1980–2000 (Darnton et al., 2006). However, the combined effect of asbestos exposure and smoking on lung cancer...
risk remains uncertain despite many studies of asbestos exposed groups. Most studies have focused on two hypotheses: whether the combined effect of asbestos and smoking is additive (each factor acts independently) or multiplicative (the effect of asbestos exposure on lung cancer risk is proportional to the effect of smoking) (Doll and Peto, 1985; Hammond et al., 1979; Lee, 2001). However, some recent reviews have suggested that while there is some interaction between the factors (their combined effect is more than additive), its extent is less than multiplicative (Liddell, 2001; Berry and Liddell, 2004). Furthermore, of the many studies of asbestos-exposed cohorts that have now been reported, few have examined the association between lung cancer risk and more specific smoking habits such as intensity and duration (Liddell and Armstrong, 2002) and smoking cessation in combination with asbestos exposure (de Klerk et al., 1991; Reid et al., 2006).

The Great Britain (GB) Asbestos Survey was established in 1971 by the Health and Safety Executive to monitor the long-term health of asbestos workers. The survey comprises a large cohort of asbestos-exposed workers from the former asbestos product manufacturing industry and, more recently, workers in the asbestos removal industry. The objective of this study was to examine lung cancer mortality risk associated with smoking and smoking cessation among asbestos workers and also to examine the interaction between exposure to asbestos and smoking on lung cancer mortality risk.

**METHODS**

The cohort includes all asbestos workers in GB who have had medical examinations because of regular work with asbestos. The British Medical Association Research Ethics Committee gave approval for the survey. Participants were initially recruited on a voluntary basis into the GB Asbestos Survey, which was established in 1971 to monitor mortality among workers in the asbestos products manufacturing industry. The cohort was expanded to include those working with insulation (application or removal) who were required to undergo statutory medicals under the Asbestos Licensing Regulations 1983 and later to all those exposed to asbestos above the specified ‘action limit’ as required by the Control of Asbestos at Work Regulations 1987. Medical examinations were carried out at 2-yearly intervals during the period over which they were working with asbestos (Harding et al., 2009).

At each medical examination, workers completed the survey questionnaire, which recorded personal details, date of first occupational exposure to asbestos, current employment details, and smoking history. Details collected about smoking habits included current smoking habit (whether a current, former, or non-smoker), the number of cigarettes smoked per day, and the age started smoking if a current or former smoker, and the age stopped smoking if a former smoker. Data collected at follow-up medical examinations were used to update smoking status and job details.

Survey participants were flagged for death registrations at the National Health Service Central Register (NHSCR) for England and Wales or the General Register Office for Scotland (GROS). Deaths were also identified through the GB mesothelioma register (McElvenny et al., 2005).

**Statistical methods**

Poisson regression was used to estimate relative risks (RRs) of lung cancer mortality among the asbestos workers. Deaths occurring until December 2005 were included in the analyses. The dependent variable was the number of deaths, with the person-years at risk as offset variable. Person-years were calculated from the date of first medical examination (entry into the study) as the starting date and the date of death, loss to follow-up (for example, emigration from GB), or the end of the study period, whichever occurred first, as the ending date.

RRs were estimated for smoking-related variables with adjustment for age (5-year classes, 40–75+ years), calendar period (5-year periods, 1980–2000+), sex, and proxy measures of asbestos exposure. Main occupation (manufacturing, insulation work, removal work, or ‘other’ exposed work) and length of occupational exposure to asbestos (three categories: <10, 10–29, 30+ years) were used as proxies for type of asbestos exposure and cumulative exposure, respectively. The covariates of interest were smoking status, age started smoking, smoking intensity (packs smoked per day), smoking duration, total smoke exposure (pack-years), age stopped smoking, and time since smoking cessation. Length of occupational exposure to asbestos, smoking duration, pack-years of exposure, and time since smoking cessation were considered time-dependent covariates.

The number of cigarettes smoked per day was taken as the average recorded over all of the participants’ examinations for former smokers. For current smokers, the number of cigarettes smoked per day could vary from one examination to the next, and the number recorded at their final examination was assumed to apply to the end of follow-up. For the purpose of the analyses packs per day were used,
where one pack was equivalent to 20 cigarettes. For current smokers, smoking duration was calculated from the age started smoking to current age, age at death, loss to follow-up, or end of follow-up and for former smokers, age started smoking to current age or age stopped smoking. Total smoke exposure (pack-years) was computed as the product of the number of packs smoked per day and smoking duration. For former smokers, the time since smoking cessation was calculated from the age stopped smoking to current age, age at death, loss to follow-up, or end of follow-up. All variables were entered as a series of indicator variables and used never-smokers as the reference category.

Harding et al. (2009) demonstrated that, among the GB asbestos workers, length of asbestos exposure, main occupation, age at first exposure, year of first exposure, and latency (time since first exposure) were statistically significantly associated with lung cancer mortality. These variables were therefore used to assess whether the effects of smoking varied with asbestos exposure. Both duration of exposure and main occupation were categorized as above. Age at first exposure (<20, 20–39, 40+ years), year of first exposure (pre-1950, 1950–1969, post-1969), and latency (<20, 20–39, 40+ years) were also considered categorical variables with latency as a time-dependent covariate. The basic model for the interaction analysis included age, calendar period, sex, main occupation, and duration of exposure as before but also included total smoke exposure (pack-years) in order to adjust for potential differences in smoking exposure. The interaction between each smoking variable and each asbestos exposure variable was entered into the model (including the main effects) one at a time, and the $P$-value of the interaction was assessed using the Wald test. Hommel’s procedure (Wright, 1992) was used to adjust $P$-values for the large number of tests performed ($n = 35$). Only interactions that were statistically significant (adjusted $P \leq 0.05$) would be investigated further.

The nature of the joint effect of smoking and asbestos exposure on lung cancer mortality was investigated using two indices for interaction effects: the Synergy ($S$) and Multiplicativity ($V$) indices (Rothman, 1976; Lee, 2001). The index $S$ is given by $(R_{AS} - R_0) / (R_A + R_S - 2R_0)$ (Rothman, 1976) and $V$ by $R_0 R_{AS} / R_A R_S$ (Lee, 2001), where $R_A$ is the risk of lung cancer mortality for never-smokers exposed to asbestos, $R_S$ is the risk for current smokers not exposed to asbestos, and $R_{AS}$ is the risk for current smokers exposed to asbestos, each relative to the risk for never-smokers not exposed to asbestos ($R_0 = 1$).

A value of $S$ greater than one indicates some degree of interaction between smoking and asbestos exposure on lung cancer mortality (which could include a multiplicative effect), with a value of $S$ equal to one indicating no interaction (i.e. the effect of the two factors on risk is additive). The second index $V$ is the reciprocal of the relative asbestos effect (RAE), a term first used by Berry et al. (1985) to describe the ratio of the RR due to asbestos exposure in non-smokers to that in smokers. The index $V$ was used in this study due to its more intuitive interpretation than the RAE: a value of $V$ greater than one corresponds to an interaction that is more than multiplicative, $V$ less than one corresponding to less than multiplicative (including no interaction at all), and equal to one indicates a multiplicative interaction.

A reference group of workers unexposed to asbestos could not be identified within the cohort and so indices were calculated based on comparisons of risks for those classified as having ‘low’ asbestos exposure versus those with ‘high’ asbestos exposure for never and current smokers. Workers were assigned to the low or high asbestos exposure categories based on the length of occupational asbestos exposure. Low exposure was classed as <10 years of occupational exposure and high exposure as 30+ years of exposure.

Poisson regression was used to estimate the lung cancer risks $R_0$, $R_A$, $R_S$, and $R_{AS}$ with adjustment made for age, calendar period, sex, and main occupation. The 95% confidence intervals (CIs) for $S$ were obtained using the delta method to form CIs for $\ln(S)$ and exponentiating the limits (Hosmer and Lemeshow, 1992; Rongling and Chambless, 2007). CIs for $V$ were calculated assuming the RR estimate is log-normally distributed (Lee, 2001).

Sensitivity analysis was carried out to investigate whether the results were affected by choice of categories for low and high asbestos exposure. Other categories considered included <3 years for low and 40+ years for high asbestos exposure, <5 years and 35+ years, and <7 years and 30+ years. In order to increase the number of cases in the never-smoker categories, the possibility of including former smokers with never-smokers was also investigated. Also assessed was the use of an alternative definition of low and high asbestos exposure that was not based on the duration of exposure. Harding et al. (2009) found that those employed in insulation work had the greatest risk of mesothelioma mortality and those in manufacturing had the lowest. Using this as a marker for asbestos exposure, the synergy and multiplicity indices were again estimated but using employment in the manufacturing industry
as low asbestos exposure and employment in the insulation industry as high.

The RRs estimated from the above model ($R_0$, $R_A$, $R_S$, and $R_{AS}$) were also used to estimate the proportion of deaths attributable to asbestos exposure, smoking, and the interaction of the two among asbestos workers who were current or never-smokers, using the methods of Lee (2001). CIs were calculated from the variance of the attributable fraction estimated using the delta method (Hosmer and Lemeshow, 1992; Rongling and Chambless, 2007). All analyses were carried out in Stata 10 (StataCorp, 2007).

RESULTS

Altogether 98,912 asbestos workers were followed-up for a total of 1,780,233 person-years between 1971 and 2005. This differs from what was previously reported (Harding et al., 2009) because the database has since been updated with further survey questionnaires and death notifications relevant to the study period. Ninety-eight per cent of workers were traced for follow-up with the NHSCR and GROS. By the end of 2005, there had been 15,553 deaths in the study population, with lung cancer accounting for 12% ($n = 1,878$) of all deaths. Ninety-five per cent of participants were males and >50% were smokers at the time of the last medical examination. A majority of workers (56%) reported asbestos removal work as their main occupation during the study, and experienced, on average, 11 years of occupational exposure to asbestos (Table 1). On average, both current and former smokers started to smoke while in their teens and smoked around one packet of cigarettes a day. Participants who were current smokers at the time of their last examination had been smoking for an average of 35 years and former smokers reported smoking for ~17 years. On average, former smokers stopped smoking at 35 years of age and, by the end of follow-up, had ceased smoking for ~25 years (Table 2).

After adjustment for age, calendar period, sex, main occupation, and length of occupational exposure to asbestos, both current and former smokers had statistically significantly elevated risks of lung cancer mortality compared to never-smokers (RR 14.7, 95% CI 10.5–20.6 and RR 4.6, 95% CI 3.3–6.6, respectively; Fig. 1). Starting to smoke at any age statistically significantly increased the risk of lung cancer mortality compared to never-smokers (Fig. 1), with starting to smoke before 16 years of age associated with the greatest risk (RR 13.7, 95% CI 9.7–19.4). The risk of lung cancer mortality initially increased with the number of cigarette packs smoked per day but levelled out at two or more packs a day (Fig. 1). There was a strong dose–response relationship, with the risk of lung cancer mortality increasing with both smoking duration and total smoke exposure (Fig. 1). Among former smokers, the risk of lung cancer mortality was lowest for those who had stopped smoking before 30 years of age (Fig. 1) but remained statistically significantly higher than never-smokers (RR 1.8, 95% CI 1.01–3.2). There was an inverse relationship between time since smoking cessation and lung cancer mortality risk (Fig. 1). The risk for former smokers who had stopped smoking for 40+ years was not statistically significantly different to that of never-smokers (RR 1.5, 95% CI 0.8–2.8). The interaction analysis did not reveal any interactions that were statistically significant at the 5% level (all adjusted $P > 0.70$; results not shown).

Table 3 shows the results of the Poisson regression subdividing the asbestos workers by smoking status

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Smoking status</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Current</td>
</tr>
<tr>
<td>Age started smoking, years</td>
<td>17 (4)</td>
</tr>
<tr>
<td>Average packs smoked per day</td>
<td>0.9 (0.4)</td>
</tr>
<tr>
<td>Smoking duration, years</td>
<td>35 (15)</td>
</tr>
<tr>
<td>Total smoke exposure, pack-years</td>
<td>30 (22)</td>
</tr>
<tr>
<td>Age stopped smoking, years</td>
<td>—</td>
</tr>
<tr>
<td>Years since smoking cessation</td>
<td>—</td>
</tr>
</tbody>
</table>

Data are means, with standard deviations in parentheses.
and duration of asbestos exposure and the corresponding synergy ($S$) and multiplicativity ($V$) indices. Although the risk of mortality from lung cancer for never-smokers with high exposure was greater than never-smokers with low exposure, this was not statistically significant (RR 1.6, 95% CI 0.6–4.2). Index $S$ was statistically significantly greater than 1, providing evidence against the additive hypothesis of no interaction between smoking and asbestos exposure ($S$ 1.4, 95% CI 1.2–1.6). Index $V$ was less than 1, but this was not a statistically significant difference and so the multiplicative hypothesis could not be rejected ($V$ 0.9, 95% CI 0.3–2.4).

Table 3. Synergy and multiplicativity indices for GB asbestos workers (1971–2005)

<table>
<thead>
<tr>
<th>Smoking status</th>
<th>Asbestos exposure</th>
<th>Label</th>
<th>Deaths</th>
<th>Person-years</th>
<th>RR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Never</td>
<td>Low</td>
<td>$R_0$</td>
<td>8</td>
<td>280 812</td>
<td>1.0</td>
</tr>
<tr>
<td></td>
<td>Medium</td>
<td>—</td>
<td>19</td>
<td>127 484</td>
<td>1.9 (0.8–4.3)</td>
</tr>
<tr>
<td></td>
<td>High</td>
<td>$R_A$</td>
<td>8</td>
<td>23 686</td>
<td>1.6 (0.6–4.2)</td>
</tr>
<tr>
<td>Former</td>
<td>Low</td>
<td>—</td>
<td>61</td>
<td>156 892</td>
<td>5.6 (2.7–11.7)***</td>
</tr>
<tr>
<td></td>
<td>Medium</td>
<td>—</td>
<td>125</td>
<td>143 494</td>
<td>6.5 (3.2–13.3)***</td>
</tr>
<tr>
<td></td>
<td>High</td>
<td>—</td>
<td>116</td>
<td>48 028</td>
<td>9.7 (4.7–20.0)***</td>
</tr>
<tr>
<td>Current</td>
<td>Low</td>
<td>$R_S$</td>
<td>473</td>
<td>581 497</td>
<td>18.8 (9.4–37.9)***</td>
</tr>
<tr>
<td></td>
<td>Medium</td>
<td>—</td>
<td>636</td>
<td>257 181</td>
<td>22.7 (11.3–45.6)***</td>
</tr>
<tr>
<td></td>
<td>High</td>
<td>$R_{AS}$</td>
<td>322</td>
<td>50 590</td>
<td>26.2 (13.0–53.1)***</td>
</tr>
</tbody>
</table>

Synergy index ($S$) 1.4 (1.2–1.6)***

Multiplicativity index ($V$) 0.9 (0.3–2.4)

RRs adjusted for age, calendar period, sex, main occupation using Poisson regression; low, <10 years occupational exposure to asbestos; medium, 10–29 years occupational exposure to asbestos; high, ≥30 years occupational exposure to asbestos.

***Significant at $P \leq 0.001$.

The use of different low and high asbestos exposure categories did not greatly affect results (data not shown). For all categorizations, never-smokers with high asbestos exposure had greater risk of lung cancer mortality compared to never-smokers with low asbestos exposure, but this was never a statistically significant result. For the synergy index, the results led to the same conclusion in all cases, except when using the most extreme categorization of low and high asbestos exposure (<3 years versus 40+ years duration), where $S$ was not statistically significantly different to unity. In all cases, the multiplicativity index was not statistically significantly different to unity. As discussed above, this study found that the risk of lung cancer mortality was not statistically significantly different to never-smokers for those who had stopped smoking for

Fig. 1. RR of lung cancer mortality for GB asbestos workers adjusted for age, calendar period, sex, main occupation, and length of occupational exposure to asbestos (1971–2005).
Therefore, in order to increase the number of cases in the never-smoker categories, these former smokers were included with the never-smokers and the analysis repeated. The estimates of the two indices were again similar to those presented here (results not shown). When using occupation to define low and high asbestos exposure (manufacturing and insulation industries, respectively), never-smokers with high asbestos exposure had greater risk of lung cancer mortality compared to never-smokers with low asbestos exposure, but again this was not a statistically significant result (RR 2.0, 95% CI 0.8–5.0). Both the synergy and multiplicativity indices were similar to those obtained when duration was used to classify asbestos exposure (S 1.7, 95% CI 1.4–2.1; V 0.9, 95% CI 0.4–2.3).

Table 4 shows the percentage of lung cancer deaths attributable to asbestos and smoking among asbestos workers who were never and current smokers, which were calculated using the RRs from Table 3. For those exposed to both smoking and asbestos, an estimated 26% (95% CI 14–38%) of lung cancer deaths were attributable to the interaction between asbestos and smoking. Among this group, there were more deaths attributable to smoking only than asbestos exposure only (68% versus 2%). Consequently, the estimated fraction of lung cancer deaths prevented if workers had not smoked (risk attributable to smoking in the presence of asbestos) was 94% (=26% + 68%); the estimated fraction of lung cancer deaths prevented if workers had not been exposed to asbestos (risk attributable to asbestos in the presence of smoking) was 28% (=26% + 2%); and the fraction of lung cancer deaths prevented if neither exposure had occurred (risk attributable to the combined effect of asbestos and smoking) was 96% (=26% + 68% + 2%) among asbestos workers who smoked.

**DISCUSSION**

The GB Asbestos Survey is an important study set up to monitor the long-term health and mortality of workers occupationally exposed to asbestos. Since 1971, it has been successful in recruiting and following a large number of these workers and continues to do so today. The survey not only collects personal details and information regarding occupational exposure to asbestos but also asks questions about current smoking habits. Few asbestos studies have detailed information on the smoking habits of asbestos workers, but this study enabled a detailed examination into the effect of smoking and smoking cessation on lung cancer mortality risk among asbestos workers in GB and also an investigation into the interaction between exposure to asbestos and smoking on lung cancer mortality risk.

One limitation of the survey is the lack of detailed exposure measurements and information about the type of asbestos fibres. There is evidence that different forms of asbestos pose different health risks. A review published in 2000 (Hodgson and Darnton, 2000) suggested that the risk differential between the carcinogenic potency of chrysotile and amphibole fibres for lung cancer was between 1:10 and 1:50. A recent meta-analysis by Berman and Crump (2008a) investigated differences in carcinogenic potency of chrysotile and amphibole asbestos, incorporating the effect
of fibre size. They estimated that chrysotile was less potent than amphibole asbestos for lung cancer by factors ranging between 6 and 60. There was also an indication that the relative potency of chrysotile to amphibole asbestos varied with fibre size; hypotheses that the two fibre types are equally potent were rejected for the two metrics based on thin fibres (widths <0.4 or <0.2 μm), but not rejected for the metrics based on larger fibres (widths >0.2 μm) (Berman and Crump, 2008a). Workers employed in different sectors of the asbestos industry were likely to come into contact with different forms of asbestos. Variations in risk by occupation are therefore likely to reflect, to some extent, differences in the type of asbestos workers were exposed to. Therefore, this study used main occupation as a proxy for the type of asbestos exposure.

Cumulative exposure is also related to lung cancer risk, displaying an increase in risk with increasing exposure (Boffetta, 1998; Henderson et al., 2004). Although length of occupational exposure was used as a proxy for cumulative exposure in this study, this would not necessarily account for variations in intensity of asbestos exposure.

Lung cancer is the most common cancer (Quinn et al., 2001) and also the most common cause of death from cancer (WHO, 2009), in the world. In England and Wales in 2005, lung cancer was the second and third most common cancer for males and females, respectively (ONS, 2008) and accounted for ~5% of all deaths (ONS, 2006). However, lung cancer accounted for 12% of all deaths among the GB asbestos workers. This difference is, in part, due to the smoking habits of the asbestos workers, with a large proportion (53%) of the participants being current smokers at the time of their final examination. Throughout the study period, the proportion of current smokers among the asbestos workers was greater than that in the national population, where just 45% of persons aged ≥16 were current smokers in 1974, dropping to a minimum of ~28% in the 1990s (Walker et al., 2002) and 24% in England in 2005 (Goddard, 2008).

The analysis of the smoking habits of the asbestos workers showed that lung cancer risk was greatest among those who smoked the most cigarettes over the longest period of time and also for those with greatest total smoking exposure. These results mirror those from investigations into smoking without asbestos exposure (Doll and Peto, 1978; Zang and Wynder, 1992; Lubin and Caporaso, 2006). Starting to smoke at an early age also increased the risk of lung cancer mortality for asbestos workers. It has been suggested that young smokers may be more susceptible to smoking-related DNA damage (Wiencke et al., 1999).

Smoking cessation has major and immediate health benefits. Stopping smoking at any age reduces the risk of lung cancer mortality compared with continued smoking (Doll et al., 1994), and the greater the length of time since smoking cessation, the greater the benefit (Rogot and Murray, 1980; Peto et al., 2000). A reduced risk of lung cancer is usually evident within 5 years of cessation, but convergence towards the lung cancer rates of those who have never smoked for former smokers has not been consistently observed (US DHHS, 1990). For workers of the crocidolite mine and mill at Wittenoom, de Klerk et al. (1991) and Reid et al. (2006) reported a convergence to near never smoking rates of lung cancer incidence among those who had stopped smoking for ≥10 years (OR 1.30, 95% CI 0.25–6.90) and ≥20 years (OR 1.9, 95% CI 0.5–7.2), respectively. These values are much less than found in this study, where convergence was not seen until ≥40 years after smoking cessation (RR 1.6, 95% CI 0.9–2.9), and this rate of decline did not vary by duration of asbestos exposure or occupation type.

From an asbestos workers’ perspective, smoking cessation represents the most practical and effective means of promoting good health. Changing occupation may not be a viable option for many workers, but also there is conflicting evidence as to the effect of removal from asbestos exposure. Many studies have reported a decline in the risk of lung cancer after removal from asbestos exposure (Walker, 1984), but some studies continue to find that the risk of lung cancer does not decrease after removal of exposure (Jarvholm and Sanden, 1998) or even that it initially increases after removal (Pira et al., 2005). A recent review of the mathematical models used in the US Environmental Protection Agency health assessment document for asbestos found no convincing evidence against the assumption that the RR of lung cancer remains constant after 10 years from last exposure (Berman and Crump, 2008b). However, it is important to note that even if the risk of lung cancer does not decrease following cessation of asbestos exposure, removal from exposure would prevent an increase in cumulative dosage.

Synergy and multiplicativity indices were used to test for additive and multiplicative interaction (respectively) between asbestos exposure and smoking. There was no control group of workers unexposed to asbestos in this study, and so current and never-smokers were subdivided into low and high exposure according to the length of occupational exposure to asbestos. Using these categories, the synergy index was statistically significantly >1 (9.4, 95% CI 1.2–1.6), providing evidence against the additive hypothesis of no interaction. The multiplicativity index
was not statistically significantly different to 1 (V 0.9, 95% CI 0.3–2.4), and so the multiplicative hypothesis could not be rejected. These results were consistent when the durations used in defining low and high asbestos exposure were altered and also when the division was made based on occupation.

The results of this study indicated that there was some level of interaction between asbestos exposure and smoking and that the multiplicative hypothesis could not be rejected. This is consistent with a recent meta-analysis by Wraith and Mengersen (2007), which combined separate indices to obtain an overall estimate of 1.70 (95% credible interval 1.09–2.67) for the synergy index and 0.86 (95% credible interval 0.52–1.41) for the multiplicativity index. However, another review using similar literature found evidence that, on average, the interaction between smoking and asbestos exposure was less than multiplicative with a ‘best estimate’ of the average RAE of 2.04 (95% CI 1.28–3.25), which corresponds to a multiplicativity index of 0.49 (95% CI 0.31–0.78) (Liddell, 2001).

The attributable proportion due to the interaction between smoking and asbestos is very closely related to the value of the synergy index. This study estimated that among asbestos workers who smoked, ~26% (95% CI 14–38%) of lung cancer deaths were attributable to the interaction between asbestos and smoking. This was generally slightly lower than the estimates found in the literature, although it appears to be statistically consistent. The estimate of the attributable proportion corresponding to the synergy index obtained by Wraith and Mengersen (2007) was 41% (95% credible interval 8–63%). Erren et al. (1999) calculated a weighted average synergy index across 12 studies of 1.64 (95% CI 1.33–2.03), which corresponded to an estimated attributable proportion of 33% (95% CI 22–45%). Also, Lee (2001) found a mean attributable proportion of 36% (no CI given) for seven cohort studies that did not use external comparisons. The differences between the attributable proportion due to interaction found in this study to those in the literature could be due to the use of low versus high asbestos exposure rather than unexposed versus exposed. This could lead to the estimated attributable proportion of lung cancer due to ‘background’ risk being greater than perhaps it should be, and therefore reducing the attributable proportion due to asbestos only, smoking only, and the interaction of the two. That is, if a comparison group was used that was truly unexposed, then the attributable proportion due to asbestos among never-smokers would probably have been >37%.

CONCLUSIONS

The GB asbestos workers have a greater proportion of smokers than the national population. This study investigated the effect of smoking and smoking cessation among asbestos workers. Starting to smoke at an early age and high intensity smoking for long periods of time increased the risk of lung cancer mortality. However, the earlier asbestos workers stopped smoking the greater the benefit. Asbestos workers who stopped smoking remained at an increased risk of lung cancer mortality up to 40 years after smoking cessation compared to asbestos workers who had never smoked. The effects of smoking and stopping smoking did not differ by asbestos exposure.

There was evidence of an interaction between asbestos exposure and smoking, and the hypothesis of a multiplicative interaction could not be rejected. For those asbestos workers who smoked, an estimated 2% of lung cancer deaths were attributable to asbestos only, 68% to smoking only, and 26% to the interaction of asbestos and smoking.

Those who both smoke and have been exposed to asbestos have the greatest risk of lung cancer mortality. This study emphasizes the importance of smoking prevention and cessation within this high-risk cohort.

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