

# Trends in Incidence of Mesothelioma and Evaluation of Exposure to Asbestos

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## ABSTRACT

We describe, analyze, and contrast historical trends in mesothelioma cases in the US and the UK and discuss these trends in relation to trends in asbestos exposure over the past 60 years. In the US, the number of mesothelioma cases for men is projected to peak at approximately 2,300 cases per year before the year 2000. Based on the historical trend and assumptions concerning current and projected exposure to asbestos, the annual number of male cases in the US is projected to decline to the background rate of approximately 500 cases per year around the year 2055. The time pattern for the number of female cases in the US has been constant at approximately 500 cases per year and is projected to remain at that level. In the UK, the number of male cases is projected to peak in the year 2020 somewhere between 2700 and 3300 cases per year depending on assumptions concerning asbestos exposure for men born after 1958. The time pattern of female cases in the UK mirrors the pattern for males, but at a lower level. The 20-year difference in the timing of the peak occurrence of cases between the US and the UK may be explained by a 20-year difference in the timing of peak exposures. We briefly address the interpretation of these trends for differentiating the mesothelioma potency of amphibole fibers from chrysotile fibers. We conclude, based on trend and exposure projections for the US, that the amphibole-chrysotile debate has little practical significance for risk management if exposures to asbestos continue to be maintained at the low levels of today.

*Keywords:* mesothelioma, asbestos, exposure, lifetime risk, asbestiform minerals

## INTRODUCTION

Because exposure to asbestos is considered the principal cause of mesothelioma, the incidence of this disease is commonly interpreted as an index of past exposure to asbestos. To that extent, therefore, patterns in time trends in incidence of mesothelioma or related deaths reflect historical patterns of exposure after accounting for latency. We describe mesothelioma trends in the US and the UK and discuss these trends in relation to trends in asbestos exposure over the past 60 years. Also, we briefly discuss the significance of exposure to specific types of asbestiform minerals, specifically, amphibole fibers, particularly the sodic amphibole riebeckite ("crocidolite"), which have greater potency than chrysotile for mesothelioma. We note, however, that the amphibole-chrysotile debate has little practical significance for risk management if exposures to asbestos continue to be maintained at the low levels of today.

## US TRENDS IN INCIDENCE OF MESOTHELIOMA

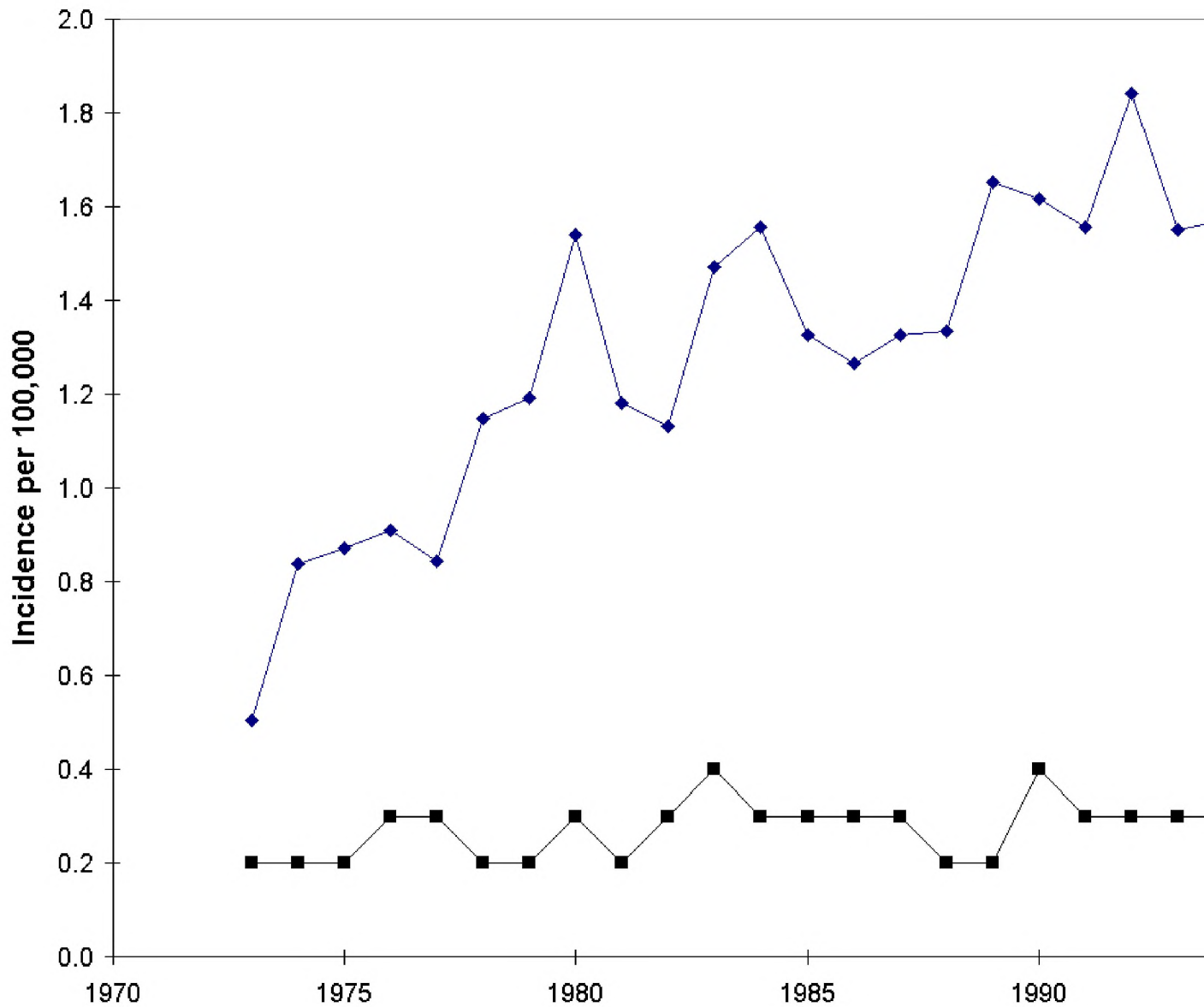
Trends in mesothelioma over time have been studied in the US (Price, 1997; Spirtas et al., 1986; Nicholson, 1982; McDonald 1985; Peto et al., 1981) and in the UK (Peto et al., 1995; Hutchings et al., 1995; Peto et al., 1999). For the US, Spirtas et al. (1986) used data on incidence from New York State, Los Angeles County, and the Surveillance, Epidemiology, and End Results (SEER) Program, to demonstrate a statistically significant increase of mesothelioma for males over time by comparing data for 1977-1980 with data for 1973-1976. The trend has been attributed to occupational exposure to asbestos, which, for some workers, was substantial from the 1930s through the 1960s (Nicholson 1982; Dupre et al., 1984). Occupational exposure during this time period in the US occurred in the shipbuilding industry during World War II, in manufacturing, and during building construction (Nicholson 1982; McDonald 1985). Price (1997) used mesothelioma data (pleural plus peritoneal) from the SEER Program database (National Cancer Institute 1995) for 1973-1992 to analyze current trends in age-adjusted and age-specific US mesothelioma rates, and to project lifetime probabilities of contracting mesothelioma for birth-cohorts beginning with the 1885-1889 cohort and continuing through the 1955-1959 cohort.

### Age-Adjusted Rates

Price (1997) analyzed trends in age-adjusted incidence of mesothelioma for males and females for the period 1973 to 1992. We have added data for 1993 and 1994, the most current data available from the SEER database, and plotted the age-adjusted rates in Figure 1.

These plots show: (i) a consistently higher rate for males versus females across all years (ii) a positive time trend for males and (iii) a virtually constant rate for females over the observed period. Figure 1 also indicates a declining annual growth-rate for males that, on average, is approximately zero after 1989. The average growth-rate for females is zero with the exception of 1982-1983 when a one-time increase in the level by approximately 20% occurred. The incidence of mesothelioma rate among females for 1973 through 1982 is constant, 0.25 per 100,000, and for 1983 through 1994, a different constant, 0.30 per 100,000. Price (1997) argued that the shift at 1982-1983 is an effect of change in diagnostic information.

**Figure 1. Age-Adjusted Mesothelioma Incidence (per 1**

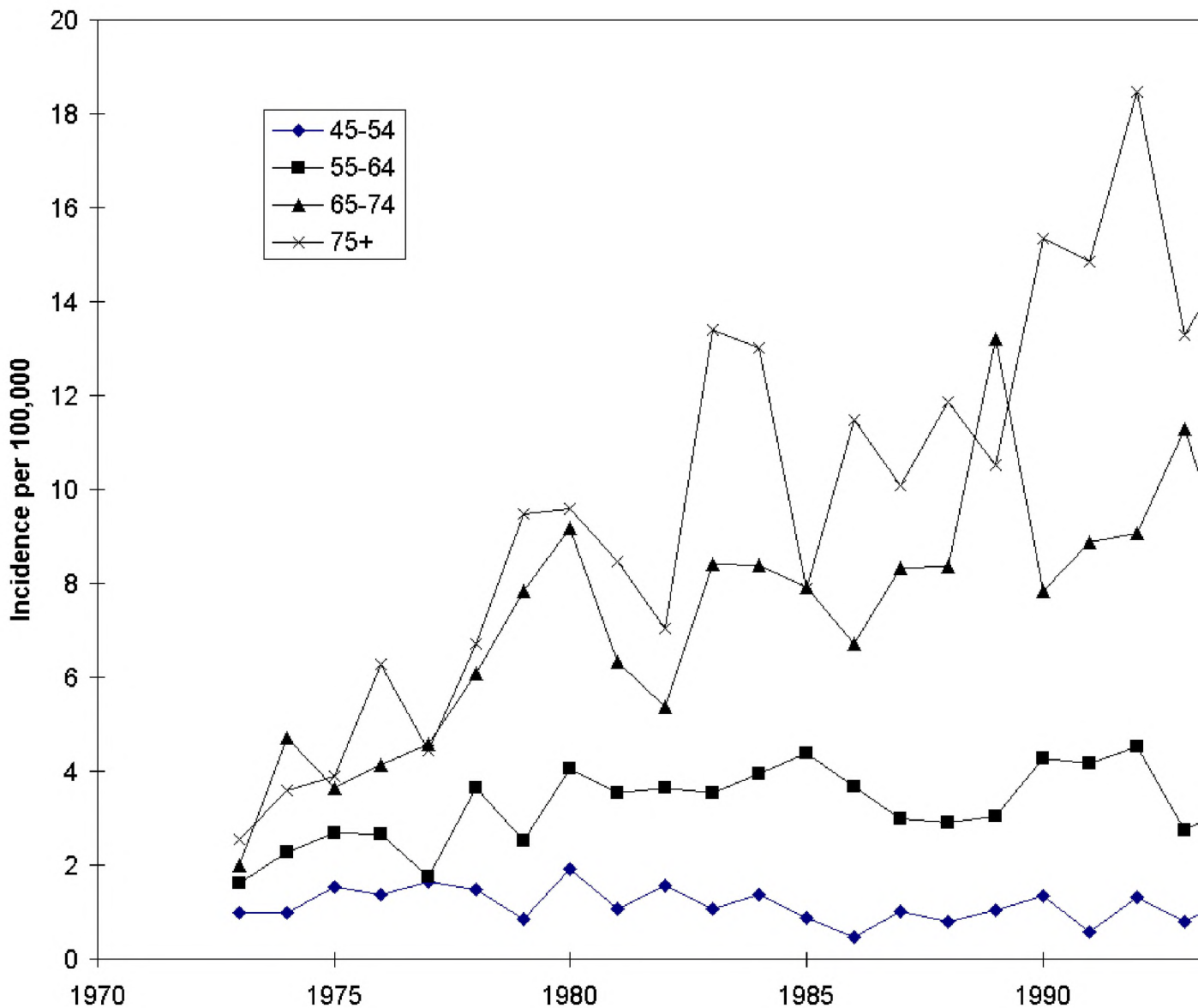


#### Male Age-Specific Rates

Trends in male age-specific rates of incidence for age groups 45-54, 55-64, 65-74, and 75+ are shown in Figure 2. For age groups 55-64 and 65-74, the trend is flat after 1983. For

the 75+ age group, the trend is flat or starting to decline after 1989. The 45-54 age group is characterized by a slight downward slope in the rate over time. (See Price, 1997 for quantification of these trends.)

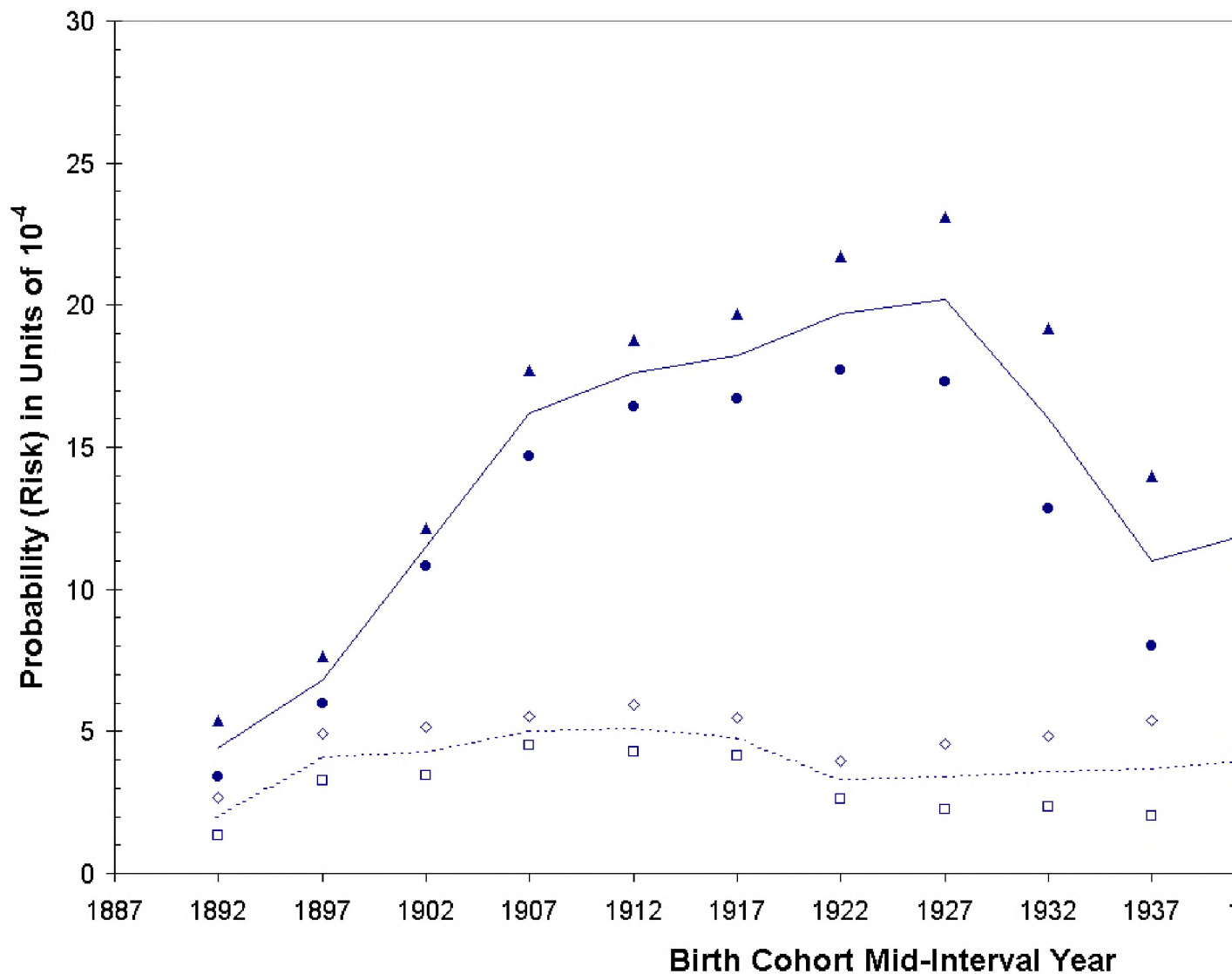
**Figure 2. Male Age-Specific Mesothelioma Incidence (per**



Predicted Counts and Lifetime Risk of Mesothelioma

Price (1997) used a Poisson regression model applied to the SEER data to analyze and predict mesothelioma counts, and used life-table methods to compute the lifetime probability (risk) of mesothelioma for males and females by birth cohort. In the Poisson regression model, mesothelioma counts are assumed to follow a Poisson probability distribution. The expected mesothelioma rate for each age and birth cohort combination is expressed as the product of two parameters, the incidence rate for the age category and the relative risk for the birth cohort. (Details of the model are described in Price, 1997.) The Poisson regression modeling results are shown in Figure 3. (The bars in Figure 3 correspond approximately to 95% confidence limits.) The lifetime risk of mesothelioma for males increases, reaching a maximum of approximately  $2 \times 10^{-3}$  for the 1925-1929 birth cohort, and then decreases. The risk for females is essentially flat, at an average level approximately equal to  $2.5 \times 10^{-4}$ .

**Figure 3. Lifetime Probability (Risk) of Mesothelioma (Pleural + Peritoneal) and 95% Confidence Limits**



#### Projected Number of Mesothelioma Cases

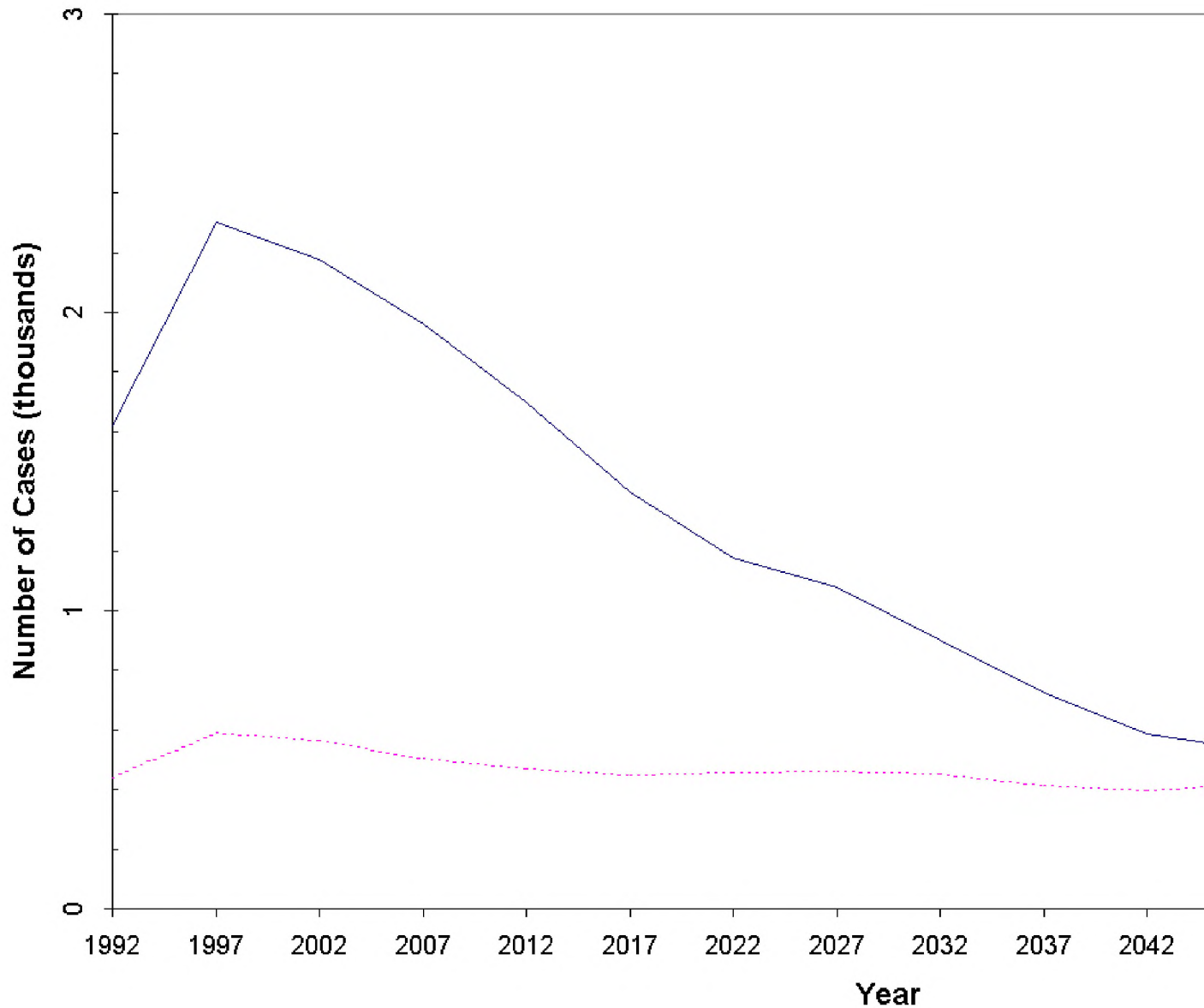
Price (1997) applied life-table methods with the modeling results and assumptions consistent with the patterns of mesothelioma incidence described above to project the numbers of mesothelioma cases expected in the future. These results are displayed in Figure 4. The number of mesothelioma cases among females is expected to remain constant at approximately 500 per year. The number of mesothelioma cases among males is likely to peak before the year 2000 at

approximately 2,300 cases per year, and then decline to approximately 500 cases per year by 2055. (The peak shown in Figure 4 occurs in 1997.)

To project the numbers of mesothelioma cases shown in Figure 4 for males, we assumed that the mesothelioma rate for males born after 1959 would continue its downward trend and then level-off. In further support of the validity of these assumptions, we note the reductions in occupational exposure to airborne asbestos that has occurred as a consequence of regulatory action. We assume exposure will remain at low levels in the future. (Refer to the discussion under Exposure Trends, that follows.) Specifically, we applied the rate for the 1890-1894 birth cohort to the 1960-1964 birth cohort and continued forward using the background level characterized by the rate for females, which, historically, has been constant. We projected the number of cases for females by applying the historical rate for females.

Our assumptions are reasonable and consistent with the historical data. Any variation of these assumptions, however, would lead to a different projection of cases in the future. A partial check on the validity of the model for making projections, in addition to the statistical evaluation of the model fit to historical data (Price, 1997), is a comparison of predicted values from the model with the SEER data reported for 1993 and 1994. (Recall that the model was derived from data through 1992, which was the most current data available when the modeling was conducted. Two additional years of SEER data have since been reported.) For males, the raw SEER data show 182 and 188 cases of mesothelioma in 1993 and 1994, respectively. These values are shown in Figure 5, which is a plot of the raw SEER mesothelioma counts versus year. The SEER data represent approximately 10% of the US population; therefore, projections of the total number of cases among males for 1993 and 1994 based on the raw data are 1,820 and 1,880, respectively. These values, and the pattern shown in Figure 5, are consistent with the projected number of cases, the pattern based on historical data, and Poisson modeling summarized in Figure 4. For females, the raw SEER data show 46 and 48 cases in 1993 and 1994, respectively. Using the 10% projection factor described above, the total number of cases among females in 1993 and 1994 would be 460 and 480, respectively. These projections based on raw SEER data are consistent with the projections based on the Poisson regression model for females obtained using the 1973 to 1992 data, which indicate approximately 500 cases annually (Fig. 4).

**Figure 4. Projected Number of Mesothelioma Cases**



#### Exposure Trends

Because mesothelioma is interpreted as an index of exposure to asbestos, the downward trends observed and projected in the number of mesothelioma cases in the US imply that downward trends in exposure to asbestos occurred 20-30 years before. Individuals who are potentially exposed to other than ambient levels of airborne asbestos include: asbestos workers (e.g., mining, milling, manufacturing, and insulation); removal workers (i.e., workers who rip out

asbestos-containing material (ACM) such as sprayed-on fireproofing and pipe and boiler insulation from buildings); maintenance and repair (M/R) workers, including custodians; and the general public, including office workers, school teachers, school children, and others who, at times, occupy buildings with ACM. The downward trends in exposure in the US suggested by declining incidence of mesothelioma was, to a great extent, stimulated by government regulations aimed at controlling exposure to asbestos. Federal agencies have established asbestos exposure limits for workers, promulgated work-practice regulations, and required inspections of school buildings for ACM and assessments of exposure potential in buildings with ACM.

In the mid 1960s, the Department of Labor (DoL) initiated respiratory protection guidance for construction work involving ACM. Coinciding with its formation in 1971, the Occupational Safety and Health Administration (OSHA) established an exposure limit or PEL of 12 f/cm<sup>3</sup> in 1972, which was rapidly reduced to 2 f/cm<sup>3</sup> in 1976. In 1986, the PEL was further reduced to 0.20 f/cm<sup>3</sup> and in 1994 to 0.10 f/cm<sup>3</sup>. Engineering controls in industry workplaces typically would limit airborne concentrations to a fraction of the PEL to allow for variation in

levels of airborne asbestos. If airborne concentrations approach the PEL, respirators would be employed to reduce personal exposure to a virtual zero level.

In construction work, the principal activities leading to exposure involved the installation of asbestos-containing insulation, including spray-on insulation. Spray-on asbestos insulation was banned by the US Environmental Protection Agency (USEPA) for most uses in 1973 (38 Federal Register (FR) 8829), eliminating that potentially significant source of exposure. USEPA's asbestos program also established asbestos management practices through guidance documents (USEPA, 1985; USEPA, 1990) and regulations addressing asbestos in schools in 1982 and 1987 (47 FR 23360; 52 FR 41826).

OSHA regulations for construction work, including maintenance and repair (M/R) activities in buildings with ACM, were made explicit in 1986, and further refined in 1994 (29 CFR 1926.1101). Studies by Price (1992), Corn et al. (1994), and Mlynarek et al. (1996), which analyze exposure data for M/R workers, show that M/R exposures are very low relative to OSHA exposure limits. Combining air-sampling measurements (1,227 samples) and data on the frequency and duration of M/R activities, Price et al. (1992) projected annual average levels of exposure ranging from a median of 0.002 f/cm<sup>3</sup> to 0.02 f/cm<sup>3</sup> (90<sup>th</sup> percentile). Corn et al. (1994) published similar results to the Price et al. (1992) results, and Mlynarek et al. (1996) reported 8-hr time-weighted averages for M/R work no greater than 0.03 f/cm<sup>3</sup> for 302 personal air samples covering nine M/R work categories.

Exposure to airborne asbestos experienced by office workers, school teachers, school children, and others who work or live in buildings with ACM was perceived by some in the late 1970s and early 1980s as a significant health risk. This perception, which may be characterized as a hysterical but misguided response to the experience of asbestos workers exposed to extremely high levels during the 1930s through the 1960s, subsequently was shown to be false (Wilson et al., 1994; Mossman et al., 1990; USEPA, 1992; 56 FR 13472). The exposure levels for this group of building occupants have been quantified at much less than 0.005 f/cm<sup>3</sup>, and typically

0.0005 f/cm<sup>3</sup> and below (USEPA, 1988; HEI, 1991). The corresponding risk has been characterized as a "very slight risk, if any." (USEPA, 1990).

One partial gap exists in the US data, namely exposure data for workers who remove ACM from buildings. USEPA, through its NESHAP regulations in 1978 (43 FR 26372), specified various work-practices for the removal of ACM. By the mid-1980s, USEPA and OSHA had designed approaches for conducting asbestos removal that included wet methods, containment, negative air pressure, and respirators (USEPA, 1985; 49 FR 14116). Air-monitoring data collected during ACM removal activities show that when these work practices are employed, little if any asbestos escapes the contained work-area, and exposure inside the contained area is controlled by using wet removal methods and respirators (HEI, 1991). It is possible that there are some asbestos removals where none of the exposure control methods are used, although the full magnitude and extent of these removals and their associated exposures are unknown. Owing to long latency-periods for asbestos-related diseases, the consequences of these uncontrolled removal-induced exposures, if any, have not yet appeared in epidemiological data. We expect that by the 1980s, uncontrolled removals were infrequent. Recalling that the risk of asbestos-related disease is proportional to cumulative exposure to asbestos over a lifetime and accounting for likely frequency and duration of exposure associated with uncontrolled removals, it is unlikely that the exposures of asbestos-removal workers who would participate in but a limited number of uncontrolled removals would have significant consequences with respect to risk.

#### UK TRENDS IN THE INCIDENCE OF MESOTHELIOMA

Peto et al. (1995) analyzed death rates from mesothelioma registries in England, Wales, and Scotland for 1968 through 1991. Hutchings et al. (1995) analyzed the same mesothelioma registry data as Peto and in addition reported on data collected in the Health and Safety Executive (HSE) mortality survey of British asbestos workers. The UK data were recently updated through 1995, but no analyses of trends incorporating these data have been reported.

For the 1968-1991 data, Peto reported a trend of increasing incidence of mesothelioma in the 1970s and 1980s, and a continuation of the trend for men now under the age of fifty, most of whom began work in the mid-1960s or later. The results of Peto et al. indicate that lifetime probability of dying from mesothelioma for males achieved its maximum of  $1.3 \times 10^{-3}$  for the 1943-1948 birth-cohort. Peto concluded that exposure in the UK was greater around 1970 than in any previous period, and that mesothelioma incidence rates will continue to increase as that

generation ages. Peto et al. stated that up to the year 2020, over "70% of all mesothelioma deaths will still be occurring in men born before 1948. After 2020, however, the prediction will be rapidly dominated by men born after 1958 for whom no data are yet available. If their risk is negligible, the epidemic will peak at about 2700 deaths per year and will disappear rapidly after 2020. If their lifetime risk is 50% of the 1943-1948 maximum, the annual total will peak at 3300 deaths around 2020 and then fall to about 2300 deaths per year. The risk is likely to lie somewhere between these limits."

Hutchings et al. (1995) summarized the same data as used by Peto et al. for his analysis in a variety of ways. The results are similar and consistent with Peto's findings. One notable result in

the analysis by Hutchings is the similarity of the female mesothelioma-incidence trend to the trend among males. The rates among females increase steadily until the 1940 and 1945 cohorts, and then fall. The decrease for females in the 1950 and 1955 cohorts from the 1940-45 maximum is similar to that for males (30% and 40%, respectively). Hutchings et al. noted that interpretations of the data for females are based on smaller numbers (than for males) and, therefore, are subject to greater statistical uncertainty.

A partial check on the model of Peto et al. for making projections, in addition to the statistical evaluation of the model fit to historical data (Peto et al., 1995), is to compare predicted values for future years with actual values for those years. Peto et al. based their analysis and predictions on data covering 1968 through 1991. These data now have been extended through 1995. Although data for making year-by-year comparisons for 1992 through 1995 are not available, it appears generally that the actual number of mesothelioma-induced deaths are running about 10% more than the projections of Peto et al. It also appears that the data Peto et al. relied on may have been revised. For 1990, Peto et al. reported approximately 700 mesothelioma deaths among males (Peto et al., 1995; Figure 2). The updated HSE data indicates 768 deaths. For 1995, the projection of Peto et al. is approximately 1000 deaths. The HSE data indicate 1140 deaths. The implications of this 10% increase in the ratio of actual versus projected mesothelioma-induced deaths are unclear. One possibility, however, is that the peak in mesothelioma deaths will be reached earlier than the date projected by Peto et al., 2020, and, therefore, the corresponding maximum exposures occurred earlier than 1970.

## COMPARISONS BETWEEN US AND UK RATES

**Background Incidence:** In the US, it is generally accepted that women were not commonly involved in occupations where they would experience exposure to asbestos. Therefore, the rate of mesothelioma incidence among females may be interpreted as a background rate. The SEER data show the lifetime probability of mesothelioma for women to be constant across birth cohorts and also indicate a constant annual incidence of about 500 cases. In the UK, Hutchings et al. (1995) reported that the mesothelioma pattern for females is very similar to that for males. The

female rates increase steadily until the 1940 and 1945 cohorts, and then fall. The results for females are based on smaller numbers than for males and, therefore, are subject to greater statistical uncertainty than the statistical uncertainty in the results for males. Nevertheless, this suggested trend for UK females is decidedly different than the trend for females in the US. An explanation for part of this difference in trend is that many women in the UK worked in factories where asbestos was used during the Second World War (Browne, pers. commun., 1997). This explanation does not fully account for the difference, which needs to be investigated further.

**Peaks in Incidence for Males:** In the US, on the basis of reasonable assumptions reflected in the SEER data and exposure measurements from studies conducted in the 1990s, mesothelioma cases will peak before the year 2000 at approximately 2,300 cases. The number of cases then will decline over the next 50 years to the background level (i.e., the female rate) of approximately 500 cases per year. Equating cases with deaths (mesothelioma is judged to be fatal within 1-2 years following diagnosis), at the peak, the rate of mesothelioma-induced deaths among males

would be approximately 19 per million or 0.22% of all male deaths. At the background level, mesothelioma would account for approximately 0.05% of all male deaths.

The timing of 50 years to return to the background level is based on the projection by Price (1997), which may be conservative. The 1960 birth cohort began work in the late 1970s, after many of the federal regulatory programs to limit exposure to asbestos were in place. It is likely that males in the 1960 and subsequent birth cohorts will not have experienced high

exposure to asbestos, and, therefore the male incidence should return to the background level more rapidly, in less than 50 years.

In the UK, Peto et al. projected a peak of 2,700 deaths in 2020 or, if the underlying data include a 20% diagnostic effect, the peak will be 1,300 deaths in 2010. It is notable that the peak number of mesothelioma deaths in the UK approximates the peak number in the US although the US population is approximately four times larger than the UK population. This comparison suggests that exposure to high levels of airborne asbestos was experienced by a larger segment of the population in the UK than in the US.

The difference between the peak year in the UK versus the US (2020 versus 2000) is a reflection of the difference in inferred patterns of exposure. The maximum exposure in the US occurred in manufacturing and construction in the 1930s-1960s. Peto et al. interpreted their results to mean that exposure was greatest in the 1970s than any previous period and suggested that these exposures were common among construction and building-maintenance workers. The 10- to 20-year shift in maximum exposure in the UK versus the US explains the 10- to 20-year shift in the expected peak of mesothelioma-related deaths.

## MESOTHELIOMA AND EXPOSURE TO AMPHIBOLE ASBESTOS

The epidemiology literature on asbestos-related disease historical assessments of exposure generally support the hypothesis that mesothelioma risk is much higher where exposure included amphiboles, specifically fibrous riebeckite ("crocidolite") and grunerite ("amosite"), than when exposure was to chrysotile alone (McDonald & McDonald 1996). Does the mesothelioma trend for males in the US add any further support for this hypothesis of greater potency of amphibole-group minerals? In principle it could, but in practice the answer is no. The increase in male mesothelioma is a consequence of exposure during the 1930 to 1960 time-period, which is heavily influenced by insulator exposures. It is generally acknowledged that these workers principally were exposed to amphibole-group minerals and mixtures of amphiboles and chrysotile (McDonald & McDonald 1996; Selikoff, et al., 1979). The number of mesothelioma cases in the US is projected to peak before the year 2000 (Price, 1997). The exposures responsible for the peak occurred during the 1930s through the 1960s, the period of significant exposure to amphibole and mixed fibers. Following the peak, mesothelioma incidence is projected to decline to background levels over the subsequent 50 years. Exposures that coincide with the decline were experienced beginning in the 1960's. By the early 1970s, there had been two changes in the characteristics of asbestos exposure. First, building construction became an important activity for asbestos exposure, and the predominant type of asbestos used in building construction in this period was chrysotile. Second, OSHA established exposure limits for

asbestos workers and required workers to use respirators where the limits could not otherwise be achieved. The mesothelioma trend, therefore, does not provide clear evidence to support the hypothesis of greater potency of amphibole-group minerals for mesothelioma because the change to predominantly chrysotile exposure coincided with reductions in overall exposure to asbestos.

The reductions in exposure were and continue to be significant. Cumulative lifetime exposure, the measure of exposure used to assess the risk of asbestos-related disease, typically was hundreds of fiber-years per cubic centimeter of air (f-yrs/cm<sup>3</sup>) for workers during the 1930s to the 1960s. For example, an estimate for exposures by insulation worker is 4-12 f/cm<sup>3</sup> (as a time-weighted average) for 25 years (Selikoff et al., 1979; USEPA, 1986). These estimates translate into cumulative exposure ranging from 100 to 300 f-yrs/cm<sup>3</sup>. Beginning in the late 1970s, annual average daily exposure for workers conducting activities involving asbestos would have been a fraction of one f/cm<sup>3</sup>. To compare levels of exposure for the 1930s to 1960s versus the 1970s and forward, note that 100 to 1000 working years would be required in the latter time-period to accumulate the levels of exposures experienced during the former period.

## SUMMARY AND CONCLUSIONS

The annual number of mesothelioma cases among males in the US is near its peak and has been projected to decline to a background level of approximately 500 cases per year. The historical increase in mesothelioma cases was a consequence of exposures to high levels of airborne amphiboles and mixed-fiber asbestos during the 1930s through the 1960s among insulators and building trades working near insulation activities. The subsequent decline may be due, in part, to a change in exposure, predominantly to chrysotile asbestos, but another very important factor is the significant reduction in exposure levels among workers over the past 25 years. In the UK, the mesothelioma pattern is similar to the pattern in the US, but is shifted 20 years into the future. The peak is projected for the year 2020, and is attributed to maximum exposure of construction workers to asbestiform amphibole in the 1970s, 20 years later than maximum exposures in the US.

Although the trends are similar and can be explained, in part, by increases and reductions in levels of exposure, the types of exposures that are responsible for the mesothelioma peaks are different. It is surprising, considering the US experience, that maximum exposures in the UK occurred in the construction industry as late as the 1970s. Projections based on modeling of UK

data from 1968 through 1991 are falling short of the actual number of cases. The historical data were revised in 1997 and, beginning in 1986, reflect more cases than were used to develop the models and projections. These revised data, if reanalyzed, could indicate an earlier peak in the number of cases, which may be closer to the pattern in the US.

In the US, general awareness of the numbers of workers with asbestos-related diseases as a consequence of high-level historical exposures, government regulations, and government guidance programs have led to dramatic reductions in exposure. US regulations and guidance aimed at limiting exposure to asbestos do not account for differences in the potencies of amphibole-group minerals and chrysotile asbestos. Nevertheless, typical levels of exposure currently appear to be low enough to render the risk of mesothelioma and other asbestos-related

diseases negligible. On the basis of an analysis of US trends of incidence of asbestos-related disease and exposure data collected in the US, exposure levels in the US are projected to remain low in the future. Under these circumstances, differentiating amphibole-group minerals exposures from exposures to chrysotile would have no practical significance in terms of risk management.

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