

Analysis of Current Trends in United States Mesothelioma Incidence

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Mesothelioma incidence often is interpreted as an index of past exposure to airborne asbestos. The mesothelioma rate for US males exhibits an increasing trend throughout the 1970s and early 1980s. The trend has been attributed to occupational exposure in the shipbuilding industry during World War II, in manufacturing, and in building construction. Incidence data (1973-1992) from the Surveillance, Epidemiology, and End Results Program were used to investigate current trends in age-adjusted and age-specific mesothelioma rates. An age and birth-cohort model was used to project both lifetime probabilities of mesothelioma by cohort and the annual number of cases expected over the next 70 years. The current trend in female rates is flat (age-adjusted rate = 0.30 per 100,000). The estimated lifetime risk for females is 2.5×10^{-4} , independent of birth cohort. The projected average annual number of female cases is 500. For males, the age-adjusted mesothelioma rate is increasing solely due to the age group 75 years and over, albeit at a declining growth rate. Lifetime risk for males peaks at 2×10^{-3} for the 1925-1929 birth cohort, then decreases to 5×10^{-4} for the 1955-1959 birth cohort. The pattern of rates reflected in the age and birth-cohort model suggests a peak in the annual number of mesothelioma cases for males at 2,300 before the year 2000. The number of male cases then will drop during the next 50-60 years toward 500. These trends mirror the US trend in raw asbestos consumption and a reduction in workplace airborne asbestos levels. *Am J Epidemiol* 1997;145:111-18.

asbestos; incidence; mesothelioma

Mesothelioma incidence often is interpreted as all index of past exposure to airborne asbestos. The incidence of mesothelioma for United States males exhibits a generally increasing trend throughout the 1970s and early 1980s (1-3). The trend has been attributed to occupational exposure to asbestos, which, for some workers, was substantial from the 1930s through the 1960s (1, 4). Occupational exposure in the United States during this time period occurred in the shipbuilding industry during World War II, in manufacturing, and during building construction (1, 2). Currently, exposure potential exists for asbestos removal workers; workers conducting renovations in buildings with asbestos-containing material; and maintenance, repair, and custodial workers in buildings with asbestos-containing materials. These exposures, however, are orders of magnitude lower than historical occupational exposures (5).

Trends in mesothelioma incidence rates have been studied using various databases and methods both in

the United States (3, 6-8) and in the United Kingdom (9). Spirtas et al. (3), using incidence data from New York State; Los Angeles County, California; and the Surveillance, Epidemiology, and End Results (SEER) Program demonstrated a statistically significant increase for males over time by comparing data for 1977-1980 with data for 1973-1976. Peto et al. (9) analyzed death rates from mesothelioma registries in England, Wales, and Scotland. They reported an increasing trend in the 1970s and 1980s and a continuation of the trend for men now under age 50 years, most of whom began work in the mid-1960s or later. They concluded that exposure in the United Kingdom was greater around 1970 than in any previous period and that mesothelioma rates will continue to increase as that generation ages.

Mesothelioma data from the SEER Program database (10) for 1973-1992 were used 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. The results of the analysis show the downward direction of mesothelioma incidence in the United States. The pattern of mesothelioma incidence mirrors the US trend in raw asbestos consumption, which approached peak levels during World War

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Abbreviations: SEER, Surveillance, Epidemiology, and End Results; SMSA, Standard Metropolitan Statistical Area.

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II, as well as the timing and impact of government regulations that address asbestos exposure.

MATERIALS AND METHODS

Mesothelioma (pleural plus *peritoneal*) incidence rates were developed from the SEER database, which represents 9.5 percent of the US population (11). The database is organized by case. Each case is identified by age, sex, race, date of diagnosis, and other information characterizing the cancer type. Data on malignant mesothelioma of the pleura and peritoneum were compiled by selecting cases with *Intentional Classification of Diseases*, Ninth Revision, morphology code 905 and topography code 163.9 for pleural mesothelioma and codes 158.8/158.9 for peritoneal mesothelioma. These data were used to develop rates for 5-year age groups in each diagnosis year. Three sets of rates were analyzed: 1) age-adjusted rates; 2) age-specific rates for 10-year age groups; and 3) 5-year age-specific rates for 5-year birth cohorts beginning with the 1885-1889 cohort and continuing through the 1955-1959 cohort.

Trends in age-adjusted and age-specific rates were investigated by fitting a three-parameter logistic growth curve (12) to the data. The logistic curve smooths fluctuations in the *observed* incidence rates and highlights trends. The logistic growth curve equation is:

$$Y = 01/(1 + R_f \times \exp[-R_3 \times X])$$

where Y = age-adjusted or age-specific mesothelioma rate; X = diagnosis year and J3 = growth curve parameters.

The distribution of male and female mesothelioma incidence rates by age and birth cohort were analyzed by Poisson regression (13, 14) to obtain models that could be used to project future mesothelioma incidence and lifetime mesothelioma risk. Mesothelioma counts extracted from the SEER database by age and year of diagnosis were translated into 5-year age group counts for each 5-year birth cohort. Person-years for each age and birth-cohort group were developed in a similar manner using population counts recorded in the SEER database. These data were used to fit a standard age and birth-cohort model: $u_{ij} = a_i \times c_j$ where u_{ij} is the incidence rate for the i th age category and j th birth cohort; a_i is the age-specific incidence rate for the i th age category; and c_j is a measure of the cohort effect for the j th birth cohort.

The model was fit by the maximum likelihood method using GAUSS (Aptech Systems, Inc., Maple Valley, Washington). The cohort effects (i.e., $\{c_j\}$) were normalized by forcing c_9 , the effect for the

1925-1929 birth cohort, to take the value 1.0. The other cohort parameter values, therefore, may be interpreted as estimates of relative risk (i.e., relative to the 1925-1929 cohort). For this parameterization of the age and birth-cohort model, $\{a_i\}$ represent age-specific mesothelioma incidence rates for the 1925-1929 birth cohort. Predicted mesothelioma counts were obtained for the i th age group and j th birth cohort group by multiplying the incidence rate ($uv = a_i \times c_j$) by the person-years for that group.

DEVCAN (15), the National Cancer Institute life table analysis procedure for estimating lifetime cancer probabilities, was used to project the lifetime probability (also referred to as lifetime risk) of contracting mesothelioma for each birth cohort. DEVCAN requires age-specific mesothelioma incidence rates, age-specific mesothelioma death rates, and age-specific death rates for all causes. For each cohort, the mesothelioma incidence rates used with DEVCAN were the observed rates calculated directly from SEER data, where available, or the predicted rates from the Poisson regression otherwise (i.e., $a_i \times c_j$ for the (i,j) th age and birth-cohort group). Because mesothelioma is considered to be fatal within 1 or 2 years after diagnosis, the mesothelioma death rate was set equal to the incidence rate. Male and female death rates for all causes were based on US mortality statistics for 1990.

Approximate 95 percent confidence intervals for lifetime risk were determined by Monte Carlo simulation. Monte Carlo replicates of lifetime risk were developed by using the observed mesothelioma counts for each age and birth cohort group as expected values for the Poisson distribution. Based on these expected values, a new set of Poisson distributed mesothelioma counts were generated (16), the parameters of the age and birth-cohort model were estimated from these counts, and DEVCAN was applied to compute lifetime risk for each cohort. This procedure was replicated 100 times. A confidence interval was calculated for each cohort from the mean and standard deviation of the 100 replicates.

The Poisson regression models and DEVCAN also were used to project the number of mesothelioma cases for males and females in the future. Historical counts of male and female births were used as starting populations through the 1990-1994 birth cohort. Future birth cohort populations were assumed to be the same size as the 1990-1994 cohort. To project beyond the 1955-1959 cohort, the downward male trend was continued by using the 1885-1889 birth cohort incidence rates for the 1960-1964 birth cohort and the average female rates for all subsequent cohorts. To project mesothelioma cases for females, the average

female rate was applied to all cohorts after the 1955-1959 cohort. Other parameters required for the analysis were the same as those used to project mesothelioma risk. Mesothelioma death rates were set equal to incidence rates, and mortality from all causes was based on US 1990 mortality data.

RESULTS

Trends in age-adjusted rates

Trends in age-adjusted mesothelioma incidence were analyzed for males and females by fitting a three-parameter logistic growth curve (figure 1). The logistic growth curve does not provide a completely satisfactory fit for the female rate ($p = 0.13$), which is small and virtually constant over the 1973-1992 interval. An alternative model, with a constant mesothelioma rate for 1973 through 1982 and a different constant rate for 1983 through 1992, provides a better fit to the data ($p = 0.03$). The rate estimated for 1973-1982 is 0.25 per 100,000; the rate for 1983-1992 is 0.30 per 100,000.

Plots of the observed and fitted rates (figure 1) show: 1) a consistently higher rate for males versus females across all years; 2) a positive trend versus year for males; and 3) a virtually constant rate for females versus year. Figure 1 also indicates a declining annual growth rate for males and a zero growth rate for females. Based on the fitted curves, the growth rate for males fell from 14.0 percent for 1973-1974 to 0.4 percent for 1991-1992. The growth rate for females is

zero, with the exception of 1982-1983, when a one-time increase in the level by 20 percent occurred.

Trends in age-specific rates

Trends in age-specific incidence rates for age groups 45-54, 55-64, 65-74, and 75 years or more are shown in figure 2. For age groups 55-64 and 65-74 years, the trend is flat after 1983. For the age group 75 or more, incidence still is increasing in 1992, however, at a lower growth rate than in previous years. For each age group, the growth rate is declining. With the exception of the age group 45-54 years, which shows a decline in the rate over time, the logistic growth curve was fit to each set of data (fitted curves not shown). Table 1 contains a summary and comparison of growth rates for 1982 and 1992 estimated from the fitted curves. The age group 75 years or more has the highest growth rate in 1992, 3.0 percent, down from 7.7 percent in 1982. Growth rates in 1992 for the other age groups are virtually zero, and for the age group 45-54 years, the growth rate is negative.

Predicted counts and lifetime probability (risk) of mesothelioma

Predicted and observed mesothelioma counts for males on the basis of Poisson regression analysis of the SEER data are shown in table 2. The relatively small differences between observed and predicted

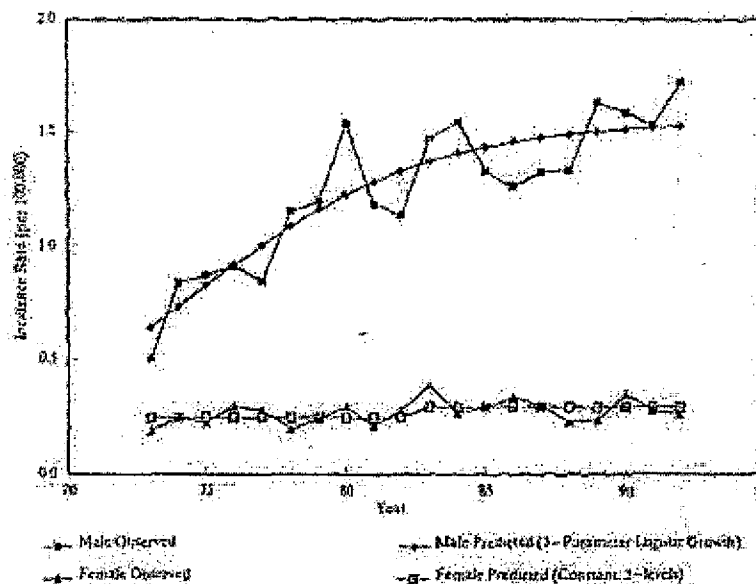


FIGURE 1. Age-adjusted mesothelioma incidence (pleural + peritoneal) - observed and predicted. Based on SEER data, November 1995.

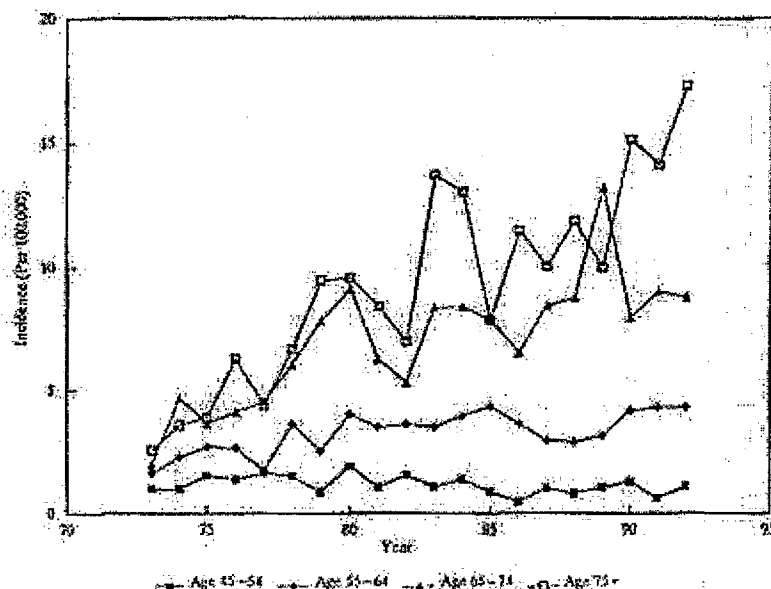


FIGURE 2. Male age-specific mesothelioma incidence (pleural + peritoneal) - 1973-1992. Based on SEER data, November 1995.

TABLE 1. Male age-specific mesothelioma incidence (pleural + peritoneal) growth rates in 1982 and 1992 based on the three-parameter logistic growth curve.

Age group (year)	Year	
	1982 (%)	1992 (%)
45-54*	-2.2	-2.8
55-64	2.5	0.1
65-74†	3.2	0.1
≥75	7.7	3.0

* The logistic growth curve was not fit to these data because the incidence rate declines over time. The growth rates in the table were derived from a straight line fit ($y = 1.413 - 0.026 \times t$, $t = 1, 2, \dots, 20$; $R^2 = 0.172$, p value = 0.009).

† The data observation for 1989 was treated as an outlier and was not used to obtain the logistic fit (see figure 2).

counts indicate that the model adequately captures the mesothelioma incidence trends.

DEVCAN life table analysis results are shown in figure 3. The two curves in figure 3 display lifetime mesothelioma risk versus birth cohort for males and females. (The bars are approximate 95 percent confidence limits obtained from Monte Carlo simulation.) The curve for males increases, reaching a maximum risk of approximately 2×10^{-3} for the 1925-1929 birth cohort, and then decreases. Statistical tests (not shown) comparing the risk for the 1925-1929 cohort with risks for subsequent cohorts substantiate the downward trend for males. The risk curve for females is essentially flat, at an average level approximately equal to 2.5×10^{-4} .

Projected number of mesothelioma cases

The projected numbers of mesothelioma cases are displayed in figure 4. On the basis of characteristics of mesothelioma incidence described above, the number of female cases will remain constant at approximately 500 per year. The number of male mesothelioma cases is likely to peak before the year 2000 at approximately 2,300 cases and then decline to approximately 500 cases per year by 2055.

DISCUSSION

The analysis of mesothelioma incidence trends reported here is based on data collected in the SEER program, which may be interpreted as a sample representing the US population. The SEER Program covers five states: Connecticut, Iowa, New Mexico, Utah, and Hawaii, and four metropolitan areas: Detroit Standard Metropolitan Statistical Area (SMSA), Atlanta SMSA, San Francisco-Oakland SMSA, and Seattle-Puget Sound. These regions include 9.5 percent of the US population (11). Walker et al. (17) suggested that SEER data overestimate mesothelioma incidence because of a disproportionate number of shipbuilding areas in the SEER regions. Nicholson (1) argued that the SEER data underestimate mesothelioma incidence because large urban areas where asbestos was used in manufacturing and construction are underrepresented. Spirtas et al. (3) compared the white male pleural cancer mortality rate for the SEER regions with the

TABLE 2. Male total mesotheliomas: observed and predicted by age and birth-cohort model

Cohort/ year	20-24 0.098	25-29 0.108	30-34 0.328	35-39 0.346	40-44 0.625	45-49 1.336	50-54 1.737	55-59 2.088	60-64 4.506	65-69 7.641	70-74 11.634	75-79 15.178	80-84 16.932	85-89 30.393
1885-1889† 0.0565													1 0.2	4 4.8
1890-1894 0.232												1 0.9	10 12.6	29 20.6
1895-1899 0.396											1 1.8	35 32.5	37 33.7	27 32.0
1900-1904 0.591										1 2.7	47 53.2	70 69.7	51 65.8	31 27.5
1905-1909 0.782								3 2.7	43 02.4	102 100.4	103 103.7	79 85.2	18 7.5	
1910-1914 0.787								4 2.2	43 54.1	106 100.6	117 117.7	116 118.8	27 22.8	
1915-1919 0.873							3 1.7	37 47.9	91 84.7	120 124.1	155 139.1	27 35.5		
1920-1924 0.938						3 1.4	32 34.8	67 71.2	103 96.8	140 137.6	30 39.6			
1925-1929 1.090					0 0.7	27 29.2	53 46.9	81 74.2	90 98.1	28 37.0				
1930-1934 0.789				0 -0.3	12 9.7	23 27.5	29 34.6	63 52.8	17 19.1					
1935-1939 0.527			0 0.2	5 3.9	7 8.7	22 10.9	24 22.6	5 8.6						
1940-1944 0.573		0 0.1	5 5.0	4 0.6	13 11.3	25 23.4	8 6.5							
1945-1949 0.402	0 0.1	3 1.4	4 5.6	6 5.9	10 9.6	4 4.6								
1950-1954 0.238	1 1.0	1 1.5	0 4.6	7 4.6	0 1.9									
1955-1959 0.101	1 0.9	0 1.1	5 0.2	0 0.8										

* Poisson regression estimates of birth cohort parameters are displayed between birth years in the first column.

† Poisson regression estimates of age-specific mesothelioma parameters (incidence per 100,000) are displayed in the second row between the age interval.

‡ First row for each birth cohort: observed number of mesotheliomas.

§ Second row for each birth cohort: (birth cohort parameter) × (age-specific rate) × (person-years); predicted number of mesotheliomas (Poisson regression).

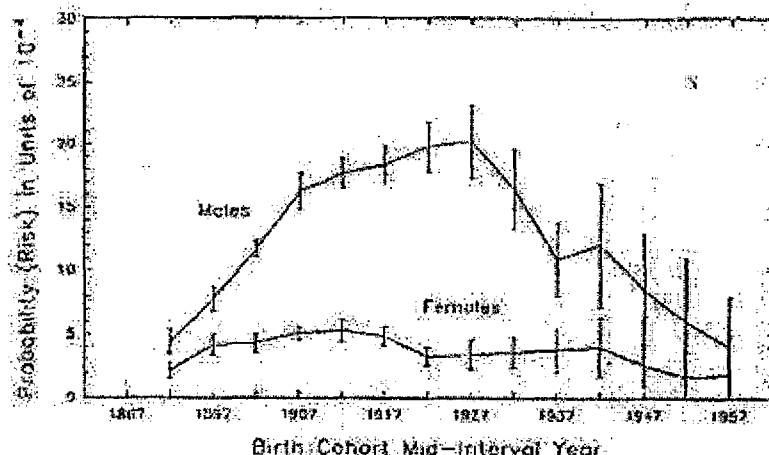


FIGURE 3. Lifetime probability (risk) of mesothelioma (pleural + peritoneal) and 95% confidence intervals. DEVCAN life table analysis based on mesothelioma incidence rates recorded in the SEER database, November 1995.

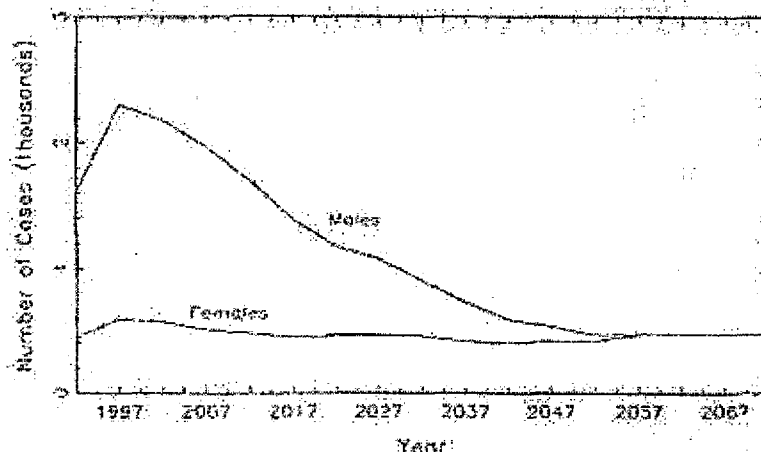


FIGURE 4. Projected number of mesothelioma cases. Poisson regression and DEVCAN life table analysis used to project the number of mesothelioma cases into the future based on SEER data, November 1995.

total US rate and concluded that the SEER data may overestimate the national incidence, but that analyses of trends based on these data would not be affected. With respect to selected demographic and epidemiologic factors, the SEER regions are reasonably representative of the US population (11).

The trend in female rates is a baseline or background for evaluating mesothelioma incidence trends in general (2). The trend in age-adjusted incidence for females is essentially flat, exhibiting a constant rate of 0.25 per 100,000 until 1982 and then a slight increase to 0.30 per 100,000 from 1983 through 1992 (figure 1). The shift that occurs in the 1982-1983 time interval is most likely a diagnostic effect, a consequence of

Environmental Protection Agency regulatory activities during the 1980s (18-27). Connolly et al. (8) conclude that the diagnostic effect in US data is real, but note that any large impact due to diagnostic changes is unlikely. An alternative explanation of the small shift in the female rate, namely that environmental exposure to airborne asbestos is increasing, is not supported by the data. The absence of a steadily increasing age-adjusted rate for females makes "increasing environmental asbestos exposure" unlikely as an explanation for the shift.

The increasing trend in age-adjusted rates for males is due to the continuing upward trend in the age group 75 years or more. Growth rates for the age group 75 or

more, although positive, are falling (table 1). Growth rates for all other age groups are near zero or are negative.

These general trends in age-adjusted and age-specific rates (figures 1 and 2) are represented by the three-parameter logistic growth curve. The curve is a model for quantities with growth rates that decline linearly as the quantity increases (12). The logistic curve has been used in this analysis to smooth fluctuations in incidence rates over the range of the observed data and thereby highlight trends. It cannot, however, capture downward trends in incidence. Therefore, it has not been used in this analysis to make quantitative projections of incidence beyond the range of observed data.

The overall dynamics of long-term growth and decline in male mesothelioma incidence are reflected in the pattern of lifetime risk (figure 3). The maximum lifetime risk appears for the 1925-1929 birth cohort. Male members of this cohort would have been at work in shipyards, manufacturing, and construction during the years 1930-1960, a period of increasing and maximum asbestos consumption in the United States. Significant growth in the use of asbestos began in the 1930s, was halfway to peak consumption in 1940, peaked in 1950, where it remained until 1970, and then declined precipitously (2, 28). Workers born after 1929 have experienced fewer years of exposure at peak asbestos consumption levels.

Workers born after 1929 also benefit from the Occupational Safety and Health Administration and the Environmental Protection Agency asbestos programs. The Occupational Safety and Health Administration has reduced its permissible exposure limit four times since 1971 (29-31), and the Environmental Protection Agency restricted the use of asbestos in building construction and imposed work practices for building demolitions (32). Currently, the potential for asbestos exposure, albeit at very low levels relative to historical worker exposures, remains only for asbestos removal workers; workers conducting renovations in buildings with asbestos-containing material; and workers conducting maintenance, repair, or custodial activities in buildings with asbestos-containing material.

The overall dynamics of long-term growth and decline in mesothelioma incidence have been analyzed using the standard age and birth-cohort model. From a modeling perspective, the age and birth-cohort model provides a more detailed and accurate basis for projecting mesothelioma trends than do trends derived from age-adjusted and age-specific aggregates. Nevertheless, the model is an approximation, and the amount of data available for the earliest and most recent cohorts is sparse. However, the relatively small

differences between observed and predicted mesothelioma counts (table 2) indicate that the model adequately captures the general trend in mesothelioma risk. The estimates of lifetime risk reflect a relatively large degree of statistical uncertainty for the most recent birth cohorts (refer to the 95 percent confidence intervals in figure 3), but not large enough to obscure the overall downward trend.

The projected number of mesothelioma cases for future years is sensitive to assumptions concerning the incidence rates for birth cohorts after 1959. For females, the average historical mesothelioma rate was applied to all cohorts after the 1955-1959 cohort. This assumption is not controversial because the trend for females has been virtually constant for the past 20 years. The projected numbers of male cases are based on stronger assumptions. To project beyond the 1955-1959 cohort, the downward male trend was continued by substituting the 1885-1889 birth cohort incidence rates for the 1960-1964 birth cohort and the average female rates for all subsequent cohorts. Different assumptions about future rates could either increase or decrease the number of cases projected for the future or extend the time it will take to reach background levels. However, independent of the particular assumptions selected, the characteristics of the trend would not change, with a peak around the year 2000 at approximately 2,300 cases, followed by a decline to a constant background level.

The analysis by Peto et al. (9) of mesothelioma in the United Kingdom indicates a peak around the year 2020. The difference between the United States and United Kingdom results is a consequence of the timing of maximum exposure. Peto et al. report that maximum exposure in the United Kingdom occurred around 1970, whereas maximum exposure in the United States occurred from the 1930s to the 1960s.

Considering the time period of maximum exposure, the subsequent downward trend in exposure, and the currently low exposure levels experienced by workers (5), the assumptions used to project the number of future US cases are reasonable. The US peak in cases occurring approximately in the year 2000, and the decline during the next 50-60 years toward 500 reflects both the US trend in raw asbestos consumption and reductions in workplace asbestos exposure levels over time.

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