Explaining Alberta's rising mesothelioma rates

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Abstract

Although mesothelioma rates have been rising worldwide, little is known about mesothelioma trends in Alberta. This population-based descriptive study used Alberta Cancer Board Registry data from 1980 to 2004 to develop an age-period–cohort model of male pleural mesothelioma incidence rates over time. Both age and cohort effects are associated with incidence rates. The highest-risk cohort comprised men born between 1930 and 1939, reflecting widespread asbestos use and exposure beginning in the 1940s in Canada. We predict that 1393 Albertan men 40 years and older will die of pleural mesothelioma between 1980 and 2024; 783 (56.2%) of these deaths will occur between 2010 and 2024. The total number of mesothelioma deaths in Alberta will be higher when all age groups, both sexes, and all disease sites are included, with numbers likely peaking sometime between 2015 and 2019. In addition to the ongoing efforts that focus on eliminating asbestos-related disease in Alberta, the challenge is to implement surveillance systems to prevent future epidemics of preventable occupational cancers in Alberta.

***Key words**: mesothelioma, pleural neoplasms, incidence, asbestos*

Introduction

Mesothelioma is a tumour of the mesothelium, the "thin lining on the surface of the body cavities and of the organs that are contained within them."[1] It most often occurs in the pleural cavity from inhaling asbestos fibres but can develop in the peritoneal cavity when asbestos fibres are swallowed. It is thought that up to 90% of male pleural mesotheliomas[2] and 60% of male peritoneal mesotheliomas[2] are caused by asbestos exposure, and that some 70-80% of mesotheliomas are related to occupational asbestos exposure.[3]

Asbestos comprises a heterogeneous group of magnesium silicate fibres, at least some of which increase mesothelioma risk.[4,5] The durability of these asbestos fibre types allows them to remain in lung tissue for years and may explain the elevated mesothelioma risk 20 to 50 years after first exposure.[6,7] Mesothelioma incidence rates, which have been rising over the past 30 years,[8-16] are expected to peak somewhere between 2010 and 2020 in Western Europe.[10] During this time of increased rates, the economic cost of asbestos-related mesothelioma litigation and compensation may approach US$200 billion in the United States[17] and US$80 billion in Europe.[18]

In 2003, 343 mesothelioma deaths were recorded in Canada, a 17% increase over 2000.[19] Occupational asbestos exposure in Canada is most often associated with asbestos mining, which occurs primarily in Quebec,[20] thus drawing away attention from the potential for exposure in other provinces, including Alberta. However, between 1920 and 1970, asbestos was commonly used in home and school construction as well as in manufacturing and the automotive industry, exposing groups such as construction workers and car mechanics to high levels of asbestos[21] and potentially exposing most Albertans to some degree. The amount of illness created by asbestos use and removal in Alberta is currently unknown but could be substantial if large numbers of Albertans were exposed over a long time.

This study describes temporal trends in Alberta's mesothelioma rates from 1980 to 2004 and identifies the age, period and cohort effects underlying these trends. We then predict future mesothelioma incidence up to 2024.

Methods

Data sources

Mesothelioma incidence data from 1980 to 2004 were extracted from the Alberta Cancer Registry maintained by the Alberta Cancer Board. The Alberta Cancer Registry is a population-based, continuously updated database of all cancers diagnosed in Alberta; it is certified by the North American Association for Central Cancer Registries for its high-quality data and completeness in capturing at least 95% of Alberta's new cancer cases annually. Mortality data were obtained through Alberta Vital Statistics on place, cause and date of death. These are routinely linked to cancer registry data to identify patients' vital status (dead or alive). All subjects included in this study had malignant

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mesothelioma at diagnosis and were identified by the morphology code (M-905) following the International Classification of Diseases for Oncology (ICD-O-3).[22] In addition to cancer morphology and type of mesothelioma (pleural, peritoneal or other), the following cancer registry information was extracted for each patient: date and place of birth; date, age and residence (Regional Health Authority) at diagnosis; date of death; gender; and vital status. All actual (or observed) and projected population figures were provided by Alberta Health and Wellness.[23]

Statistical analysis

To facilitate temporal comparisons, rates were directly age-sex-standardized to the 1991 Canadian census population,[24] which is the standard used by most Canadian cancer agencies. We report average percentage changes in male incidence rates over the entire study period; average percentage changes in female rates were limited to 1987–2004 because the zero counts in 1980 and 1986 precluded the inclusion of the earlier years. To accommodate the possibility of changing mesothelioma incidence throughout the study period (i.e. incidence may be low initially, then increase before leveling off near the end of the study period), we chose to describe any changes in trends using joinpoint regression models which have been successfully applied in other cancer analyses.[25] The Joinpoint Regression Program version 3.3 developed by the National Cancer Institute was used to compute average annual percent changes (APC) with 95% confidence intervals (CI).

As much of the increase in mesothelioma occurred in men aged 40 to 94 years with pleural mesothelioma, we focused our statistical analysis on this age group. To describe rates over time, we used an age-period–cohort model with nine five-year age groupings (40 to 44, 45 to 49, through to 80+); five five-year periods (year of diagnosis) encompassing 1980 to 1984 up to 2000 to 2004; and 13 overlapping ten-year birth cohorts represented by respective means of 1900, 1905, up to 1960 (for example, the cohort 1905 comprised those born between 1900 and 1909). Because we expected a curvilinear shape to the graph, with rates peaking and then decreasing, we chose to model the study data using regression splines.[26] Specifically, we opted to use natural splines because they are more stable in the tails than other commonly used splines.

The general form of the natural spline age-period–cohort model we used for the rate was log

$$(\lambda_{apc}) = \mu + f(a) + g(p) + h(c),$$

where a and p were the mean age and period for the five-year grouping, and c was the mean birth cohort for the ten-year grouping. For example, the mean age for the group 40 to 44 was 42.5; the mean date for the period 1980 to 1984 was 1982.5; the corresponding mean birth cohort (1940) was the difference between period and age, $c = p - a$. The term μ was an intercept, and the functions $f(a)$, $g(p)$ and $h(c)$ were the natural spline functions for age, period and cohort, respectively (after adjusting for the intercept term).

We tested a hierarchy of log-linear spline models[27-29] to discern the effects of age, period and cohort on the prediction of mesothelioma incidence rates. The criteria for selecting the best of the hierarchy of tested models was a deviance score (i.e. the ratio of deviance to the degrees of freedom) close to one.

Since there was a positive association between age and pleural mesothelioma rate in men, we began with a model containing age and assessed improvements in this model upon the addition of drift, nonlinear period and nonlinear cohort effects. The drift effect combined the linear components of period; the cohort and nonlinear effects (also called curvature effects) were deviations from the linear trends.[26-28,30] We used the same number of knots in each of the tested models: four knots for age (at 47.5, 57.5, 67.7, 77.5); two knots for period (at 1987.5, 1997.5); and six knots for cohort (at 1915, 1920, 1925, 1935, 1940, 1945). Although the choice of the number of knots has little effect on model fit,[31] we attempted to choose the number of knots that maximized the fit of the model based on exploratory data analysis.

Using the best model to predict future incidence of mesothelioma up to the year 2025, we investigated when the number of cases is expected to peak in Alberta in two steps. In the first step, we estimated the future rate for each cohort through continuous extrapolation of our estimated cohort effects (i.e. estimated natural spline functions for each cohort) up to the year 2025. In the second step, we calculated the predicted number of cases for each cohort by multiplying the estimated rates from step one by the corresponding population estimates and summing all predicted cases over the cohorts to obtain the total number of predicted cases. All modeling used the R statistical package (Version 2.5.1)[32] and the statistical testing was done at the 0.05 level of significance.

Results

Between 1980 and 2004, a total of 570 cases of mesothelioma were diagnosed in Alberta (Table 1), of which 487 (85%) were pleural mesotheliomas. Of the total 570 mesotheliomas, 470 (82%) occurred in men. Among the 487 pleural cases, 412 (85%) were in men. The majority of men (217 or 53%) with pleural mesothelioma were between the ages of 50 and 70. By the end of the study period, 445 (95%) men and 88 (88%) women had died.

Age-standardized incidence rates increased steadily throughout the study period, reflecting the increases in male pleural mesothelioma. The number of cases in women remained low (Figure 1) and constant (APC between 1987 and 2004 was 1.49; 95% CI of -5.40 to 8.89).

In men 60 years and older, the age-standardized rates of pleural mesothelioma increased 9.42% (95% CI of 6.91 to 12.00) per year over the study period. Age-specific rates more than doubled in those aged 60 to 69 years, but men 70 years and older showed the highest rate and largest increase between 1980 and 2004 (Figure 2).

Age-period–cohort analysis of male pleural mesothelioma

The incidence of male pleural mesothelioma generally increased with age group at each diagnosis period (Figure 3).

TABLE 1
Mesothelioma cases and age-specific incidence rate* (per 100 000) in Alberta, 1980 to 2004†

Number of cases and incidence rate by five-year grouping (men with pleural mesothelioma)												
Age group	1980-1984		1985-1989		1990-1994		1995-1999		2000-2004		1980-2004	
	Count	Rate	Count	Rate	Count	Rate	Count	Rate	Count	Rate	Count	Rate
20-24	1 (1)	0.07 (0.14)	0 (0)	0.00 (0.00)	1 (0)	0.10 (0.00)	0 (0)	0.00 (0.00)	0 (0)	0.00 (0.00)	2 (1)	0.04 (0.04)
25-29	0 (0)	0.00 (0.00)	0 (0)	0.00 (0.00)	0 (0)	0.00 (0.00)	0 (0)	0.00 (0.00)	0 (0)	0.00 (0.00)	0 (0)	0.00 (0.00)
30-34	0 (0)	0.00 (0.00)	2 (0)	0.17 (0.00)	0 (0)	0.00 (0.00)	1 (0)	0.09 (0.00)	0 (0)	0.00 (0.00)	3 (0)	0.05 (0.00)
35-39	3 (1)	0.38 (0.24)	1 (1)	0.10 (0.20)	0 (0)	0.00 (0.00)	1 (0)	0.08 (0.00)	1 (0)	0.08 (0.00)	6 (2)	0.11 (0.07)
40-44	2 (1)	0.33 (0.31)	3 (2)	0.39 (0.51)	2 (0)	0.20 (0.00)	6 (4)	0.50 (0.66)	3 (1)	0.22 (0.15)	16 (8)	0.33 (0.32)
45-49	4 (4)	0.74 (1.43)	4 (3)	0.67 (0.98)	5 (5)	0.66 (1.29)	4 (1)	0.41 (0.20)	13 (6)	1.07 (0.97)	30 (19)	0.73 (0.91)
50-54	8 (6)	1.59 (2.29)	11 (9)	2.10 (3.34)	4 (4)	0.68 (1.35)	15 (13)	2.00 (3.42)	12 (11)	1.23 (2.22)	50 (43)	1.50 (2.52)
55-59	5 (5)	1.13 (2.27)	14 (12)	2.88 (4.81)	17 (13)	3.34 (5.02)	14 (9)	2.45 (3.12)	20 (12)	2.71 (3.22)	70 (51)	2.55 (3.67)
60-64	6 (2)	1.63 (1.13)	10 (8)	2.39 (3.90)	17 (14)	3.64 (5.96)	31 (23)	6.31 (9.35)	14 (11)	2.52 (3.97)	78 (58)	3.39 (5.09)
65-69	8 (6)	2.70 (4.31)	12 (7)	3.44 (4.29)	15 (11)	3.73 (5.76)	27 (20)	6.07 (9.13)	28 (21)	5.95 (9.05)	90 (65)	4.59 (6.88)
70-74	4 (0)	1.76 (0.00)	8 (6)	2.94 (4.90)	21 (14)	6.48 (9.65)	23 (18)	6.31 (10.74)	36 (30)	8.82 (15.38)	92 (68)	5.77 (9.25)
75-79	3 (2)	1.83 (2.68)	8 (7)	4.11 (8.31)	14 (11)	5.97 (11.10)	14 (7)	5.13 (6.08)	33 (27)	10.53 (19.73)	72 (54)	6.10 (10.59)
80-84	4 (0)	4.09 (0.00)	1 (1)	0.80 (1.92)	5 (4)	3.33 (6.78)	13 (10)	7.41 (14.81)	24 (22)	11.34 (26.78)	47 (37)	6.18 (12.26)
85-89	4 (1)	7.96 (5.16)	0 (0)	0.00 (0.00)	0 (0)	0.00 (0.00)	1 (0)	1.08 (0.00)	5 (3)	4.39 (7.84)	10 (4)	2.49 (2.81)
90-94	0 (0)	0.00 (0.00)	1 (0)	2.97 (0.00)	0 (0)	0.00 (0.00)	1 (1)	1.97 (6.05)	2 (1)	3.60 (6.66)	4 (2)	1.89 (2.95)
Total	**52 (29)**	**0.61 (0.66)**	**75 (56)**	**0.75 (1.17)**	**101 (76)**	**0.91 (1.46)**	**151 (106)**	**1.20 (1.79)**	**191 (145)**	**1.29 (2.17)**	**570 (412)**	**1.00 (1.55)**

* age-standardized rate using total population in the denominator

† Numbers in parentheses represent males with pleural mesothelioma.

Both the age-cohort and age-period–cohort models had goodness-of-fit scores (or deviance scores) close to one, satisfying our criteria for a good fit between the data and the model. The curvature effect for period was found to be insignificant (p = 0.62). Overall, the age-cohort model fit the data well (deviance score close to one) and prompted us to fit spline functions for age and cohort.

Table 2 presents the observed and predicted numbers of pleural mesothelioma cases in 40 to 94 year-old men diagnosed in Alberta between 1984 and 2004. Each cohort-age combination in Table 2 consists of two numbers: the predicted count (top un-bolded number) resulting from the age-cohort model and the actual or observed count (bottom bolded number). For example, when people born between 1940 and 1949 (cohort: 1940 to 1949) reached age 40 to 44 years (age group: 40-44), there were two observed cases of mesothelioma compared to the 1.4 predicted cases. The observed counts corresponding to each cohort-age combination are similar to the predicted counts, indicating that, despite the sparse data, the model adequately predicts mesothelioma cases. The age and cohort spline functions were reparametrized to improve interpretability.[29,30] Specifically, we presented the age function as age-specific log rates of a reference cohort (Figure 4) and the cohort function as the log rate ratio compared to a reference cohort (Figure 5). The reparametrized age function shows the increase in mesothelioma rate as a cohort is followed over time (Figure 4). For example, in following the 1925 to 1934 cohort over time, we see that the rate per 100 000 increases from 9.1 (when aged 65 to 69 years) to 16.8 (when aged 70 to 74 years). Age-specific rates for other cohorts exhibit similar changes over time, with the highest rates pertaining to the 1930 to 1939 cohort. Figure 5 presents the rate ratio of mesothelioma compared to the reference (1925 to 1934) cohort. Specifically, compared to the 1925 to 1934 cohort, the 1930 to 1939 cohort has 1.13 times the risk of mesothelioma; all other cohorts have lower risk than the 1925 to 1934 cohort. We chose to use the 1925 to 1934 cohort as the reference because it is the middle cohort and therefore more reliably estimated.[30] Although the birth cohort years overlap, the people in each cohort differ and therefore the increased risk is not attenuated by the overlap. Figures 4 and 5 also present 95% confidence bars which are fairly wide around some of the estimates due to exponentiation (the estimate and its standard error were originally on the log scale).

Predicted mesothelioma incidence

Based on our developed age-cohort model and assuming current trends and conditions continue in men 40 years and older, the number of pleural mesotheliomas is expected to increase to 247 cases between 2010 and 2014 and peak at 269 cases between 2015 and 2019. The number of cases will drop slightly to 267 between 2020 and 2024.

Discussion

The purpose of this study was to describe temporal variations in Alberta's mesothelioma rates and to explore how age, period and cohort effects explain these trends. Mesothelioma rates in Alberta appear to

FIGURE 1
Age-standardized incidence rates (/100 000) of mesothelioma by year of diagnosis and gender in Alberta, 1980 to 2004

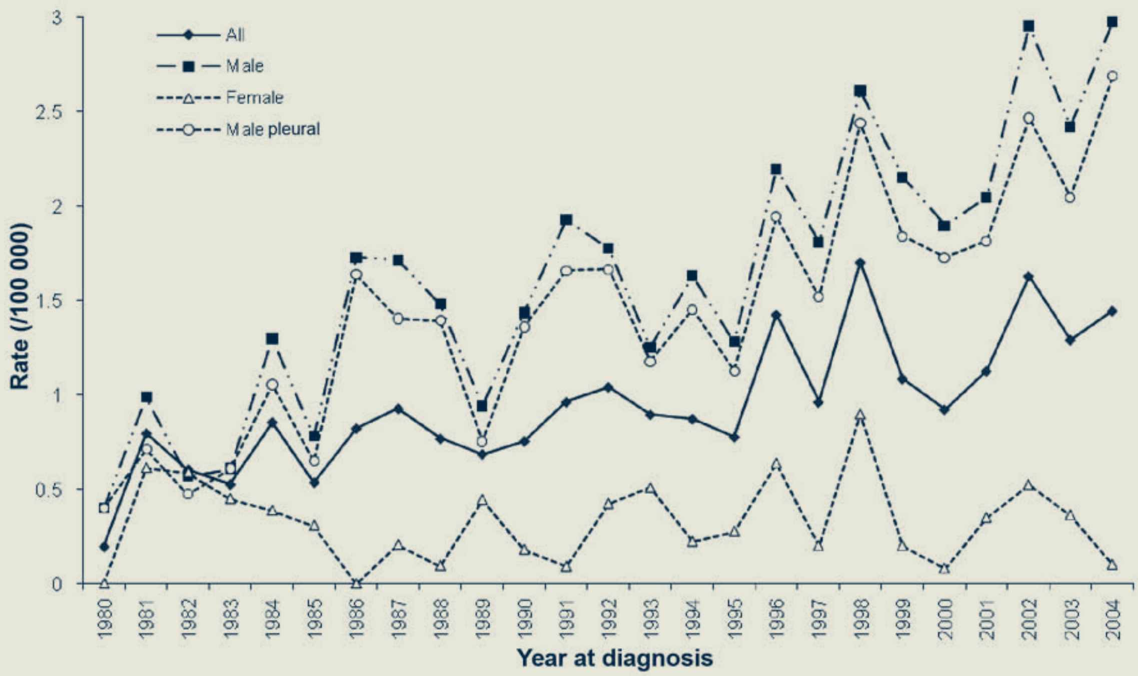


FIGURE 2
Age-specific incidence rates of male pleural mesothelioma in Alberta, 1980 to 2004

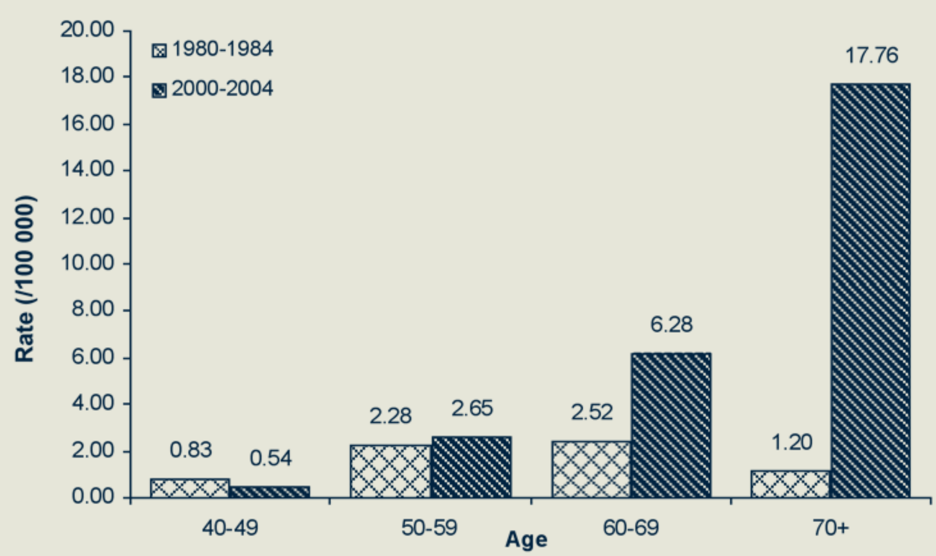


FIGURE 3
Age-specific incidence of male pleural mesothelioma by age group and year of diagnosis in Alberta, 1980 to 2004

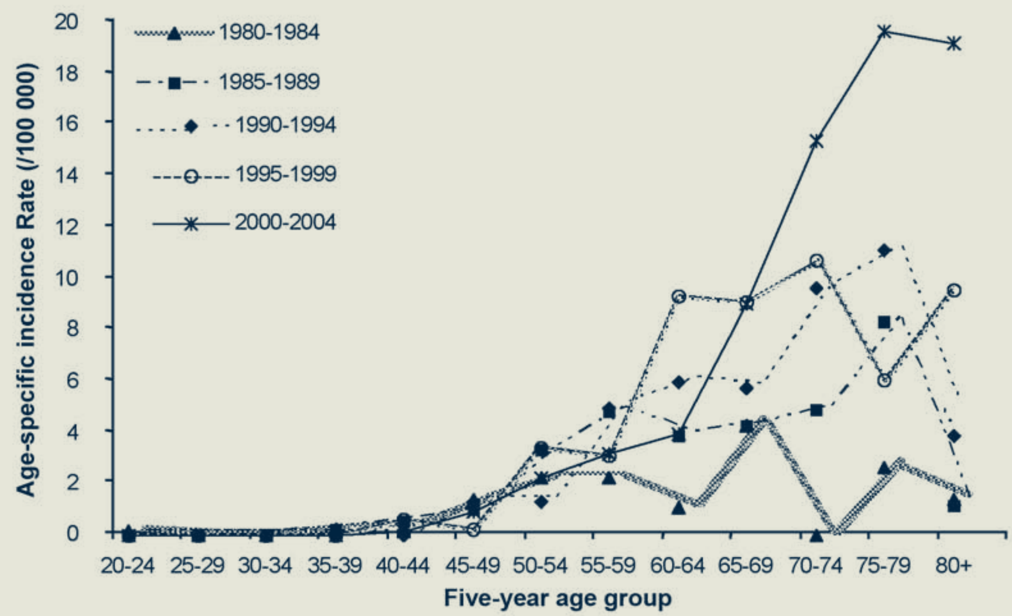


FIGURE 4
Age-specific incidence for birth cohort 1925 to 1934 based on age-cohort model

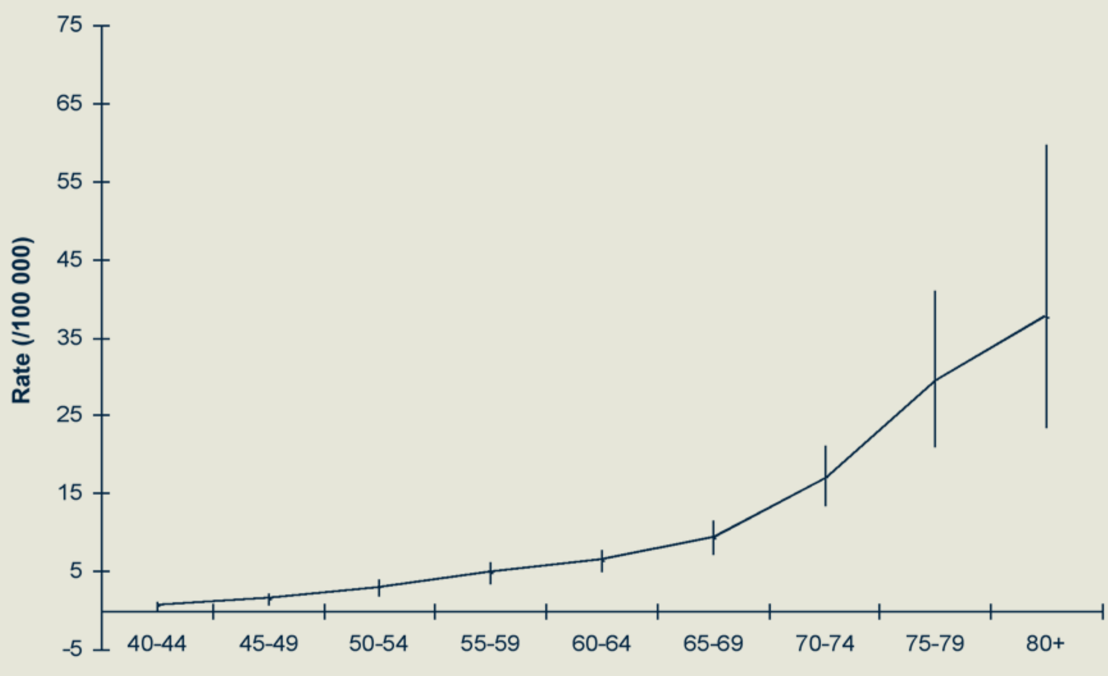
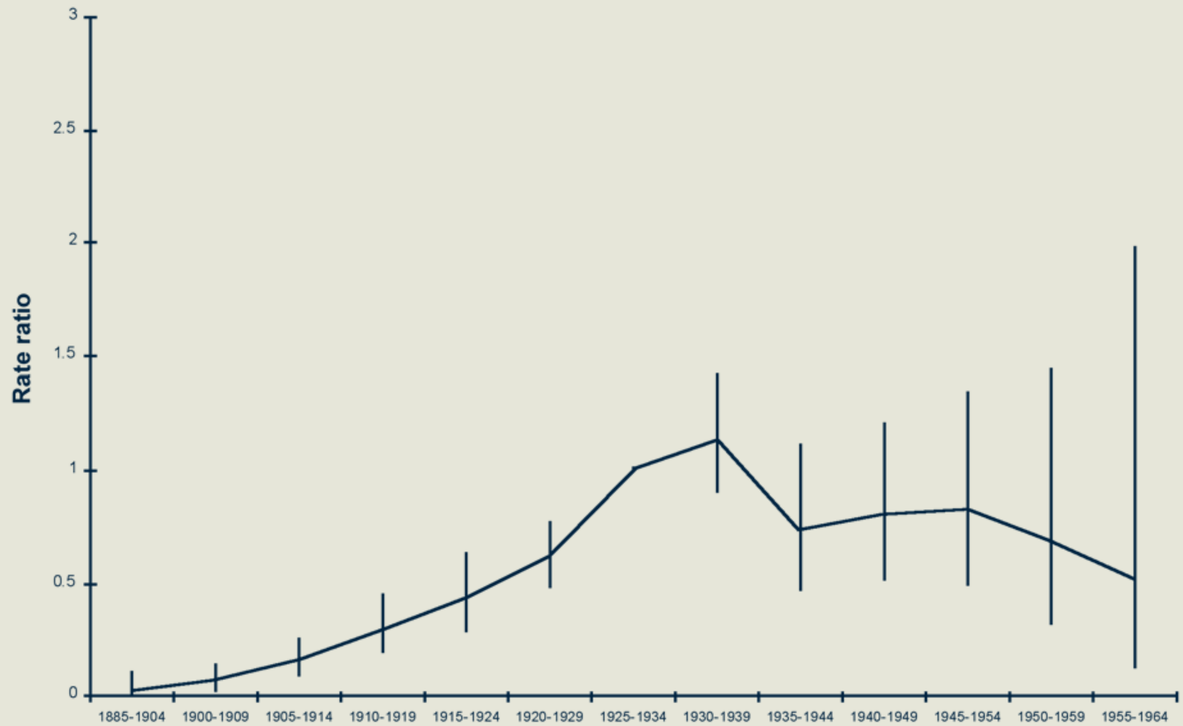


FIGURE 5
Incidence ratios relative to cohort 1925 to 1934 based on age-cohort model



be increasing in tandem with prevalent asbestos use in the 1970s and are expected to peak sometime between 2015 and 2019. The increase is driven primarily by pleural mesothelioma in older men. Between 1980 and 2025, male pleural mesothelioma will be the cause of death of an estimated 1393 Albertans over the age of 39 years; this is likely a conservative estimate considering asbestos-related illnesses are typically underreported.[33]

We found both age and cohort effects predict mesothelioma rates. Consistent with other research,[34] we found a dramatic increase in cancer rates among men born between 1920 and 1935 (70 years and older) that is suggestive of asbestos exposure beginning in the 1940s and extending through to the mid-1970s when asbestos was commonly used in Canada. Our highest-risk cohort was the 1930-to-1939 one, differing somewhat from the highest-risk cohorts of other countries such as Britain (1920 to 1924),[13] United States (1925 to 1929)[15] and Europe (1945 to 1950).[10] The significance of this difference is unclear and may be due to differences in latency period related to exposure intensity and industry.[35] For example, the median latency for workers in the shipbuilding industry has been estimated at 52 years compared to 29 years for those in the insulation industry.[35]

Although many countries worldwide have banned the import or sale of asbestos or asbestos products, Canada has opted to limit its use. Given the long latency period, banning asbestos now would not reduce the high number of cases expected in the next 15 to 20 years as incidence peaks sometime after 2010 to 2020.[19] Our data predict cases will peak between 2015 and 2019, ten to 15 years after the United States (peak years of 2000 to 2004)[15] and five to ten years after Great Britain (peak years of 2011 to 2015).[13]

The low and constant mesothelioma rates among women agree with trends observed in women in the United States;[15,36] the age-standardized incidence rate in female Albertans averaged 0.3 per 100 000 between 1987 and 2004. The primary source of asbestos exposure for women has traditionally been environmental rather than occupational. Prior to 1961, mesothelioma rates among men and women were similar in Canada.[37] Rates among men began to rise after 1961 which, given the long latency period, would be expected if the cause was occupational asbestos exposure beginning in the 1940s. Rates among women, on the other hand, remained low and constant suggesting a baseline mesothelioma level exists and excess male rates are occupationally related. The origin of mesothelioma in women is somewhat controversial[38] and merits further study, particularly in terms of the potential for misdiagnosis of peritoneal mesothelioma as ovarian cancer.[39,40]

This study has a number of limitations. Firstly, despite the well-established link between asbestos exposure and mesothelioma,[35] information on the source of exposure was not available for the majority of our study participants. Alberta's buoyant oil-based economy has attracted migrants who may have been exposed to asbestos while working in asbestos mining, shipbuilding or other high-risk industries in other Canadian provinces; immigrants may have also been occupationally exposed in countries with lower safety standards prior to moving to Alberta. We have no estimate on how many high-risk adults have moved to Alberta during the study period, but the second component of our study investigating Workers' Compensation Board of Alberta (WCB) filing and compensation rates among the same cohort of subjects may provide some clarity in this regard.[41] Secondly, our patient numbers may have been underestimated by as much as 30%[37] for the early years of our study period; however, diagnostic accuracy has likely improved over time, and we expect any underreporting will have had relatively little impact on our trends or the reliability of our results for health services planning. Conversely, a tendency to misdiagnose a lesion as mesothelioma when it is actually a different cancer (overdiagnosis) has been noted in some exposed patient populations such as asbestos miners in Quebec.[42,43] However, similar high-risk occupations have not been identified in Alberta, and therefore we believe overdiagnosis is likely not a major problem in our results.

Our future research will focus on pinpointing sources of asbestos exposure in Alberta and on describing WCB compensation rates. Under Alberta's Occupational Health and Safety Act, mesothelioma is a reportable disease and therefore monitored by the Director of Medical Services. We know that so far less than half of our study subjects filed for WCB compensation. Those who did were commonly employed in the construction and automotive industries, typical sources of asbestos exposure between 1940 and 1970. Albertans' low filing rates are on par with findings from other provinces,[39,44] and we have yet to examine who is uncompensated.

If present trends continue, we expect to see at least 783 new cases of pleural mesothelioma diagnosed in men 40 years and older in Alberta between 2010 and 2024. The total number of mesothelioma cases will be higher when combining all age groups, both sexes and all types of mesothelioma. Most of these cases will have been exposed to asbestos sometime after 1970, about 10 years after the causal link between mesothelioma and asbestos was generally accepted.[45] Although asbestos is not mined in Alberta, we still record a substantial number of mesothelioma diagnoses. The future challenge is to identify the sources of asbestos exposure in Alberta, because we now know that "prevention is the only cure for asbestos diseases."[46] With the frequent introduction of new chemicals and man-made or organic asbestos-like substitutes into the workplace, the broader challenge is to avoid future epidemics of preventable

TABLE 2
Total male pleural mesothelioma cases: observed* and predicted† by natural spline age-cohort model

Cohort/age	40-44	45-49	50-54	55-59	60-64	65-69	70-74	75-79	80+
1885-1904									0.6
									1
1900-1909								1.3	2
								2	**1**
1905-1914							2.7	3.8	5.9
							0	**7**	**4**
1910-1919						3.8	6.2	8.7	12.9
						6	**6**	**11**	**11**
1915-1924					4.8	6.4	10.5	14.6	21.9
					2	**7**	**14**	**7**	**26**
1920-1929				6.1	6.4	10.6	17.1	24.5	
				5	**8**	**11**	**18**	**27**	
1925-1934			7.1	11.3	14.6	19.9	32.8		
			6	**12**	**14**	**20**	**30**		
1930-1939		3.9	8.3	13.3	17.3	23.9			
		4	**9**	**13**	**23**	**21**			
1935-1944	1	2.7	5.8	9.4	12.4				
	1	**3**	**4**	**9**	**11**				
1940-1949	1.4	3.8	8.1	13.3					
	2	**5**	**13**	**12**					
1945-1954	1.8	5	11						
	0	**1**	**11**						
1950-1959	1.8	5.2							
	4	**6**							
1955-1964	1.5								
	1								

* bolded numbers – observed (bottom)

† unbolded numbers – predicted (top)

occupational cancers through instituting carcinogen-exposure surveillance systems and evidence-based policies.

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