

MESOTHELIOMA MORTALITY IN MEN: TRENDS DURING 1977-2001 AND PROJECTIONS FOR 2002-2016 IN SPAIN.

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ABSTRACT

Objectives: To evaluate mesothelioma death trends in Spain and to predict future cases of mesothelioma.

Methods: After descriptive analysis of mesothelioma mortality data, an age-period-cohort model was applied to make projections of mesothelioma deaths.

Results: From 1977 to 2001, 1,928 men older than 35 died of mesothelioma in Spain. Projections indicate that 1,321 men are expected to die from mesothelioma between 2007 and 2016.

Conclusion: It is expected that mesothelioma deaths will increase at least until 2016. Available data do not allow a prediction of the year mortality will start decreasing.

INTRODUCTION

Exposure to asbestos is the main cause of mesothelioma [1]. The number of mesothelioma deaths reflects past exposure to asbestos and can be used to make future projections. Increases in mesothelioma deaths in recent years have been reported in several countries and future projections indicate a continuation of this increase in mortality for the next years even though use of asbestos has been banned in most industrialised countries [2-6].

Spain was not an asbestos producing country, but around 800 companies used 2,6 million tonnes of asbestos between 1900 and 2000 (chrysotile was 90% of the total) [7]. Use was especially high between 1960 and the mid eighties, reaching its peak in 1973 (113,000 tonnes) [7]. Asbestos regulations started being introduced in 1984, and asbestos was banned in 2001; residual activities involving asbestos exposure were regulated in 2006 [8].

An estimate of occupational exposure to asbestos in Spain indicate that 56,600 workers were exposed to asbestos in the late 90s, mainly in construction industry [9].

The main aim of this study was to analyze trends in mesothelioma mortality and to predict the number of deaths due to mesothelioma in men for the coming years in Spain. This estimation may be useful for planning and supporting active medical surveillance programs that aim to increase awareness of asbestos exposure in Spain and favor the discovery of unregistered formerly exposed workers, and to identify and compensate for occupational diseases when necessary.

MATERIAL AND METHODS

The pleural cancer mortality is an acknowledged indicator of exposure to asbestos and mesothelioma mortality. Tables with number of pleural neoplasms deaths for men and women between 1977 and 2001 (ICD-9:163) were provided by Centro Nacional de Epidemiología [10] arranged in five 5-year periods (1977-1981, 1982-1986, 1987-1991, 1992-1996 and 1997-2001) and nine 5-year age groups (35-39 to 75-79). To avoid strata without deaths, considering that mesothelioma with less than 20 years latency [11] is only rarely observed and assuming earliest entry to industrial work at age 15, the lowest age-group we used was 35-39. Mesothelioma deaths in people of age 80 or older were excluded from the analysis due to the lack of accuracy in determining the cause of death [12].

These calendar periods and the age groups examined involved 13 overlapping birth cohorts, defined by their central year of birth beginning in 1902 and ending in 1962. Data were analyzed by log-linear Poisson regression, assuming that the number of deaths follows a Poisson distribution; we fitted the complete age-period-cohort model to the age-specific death rates, investigating model fitting through the Akaike Information Criterion (AIC) and the deviance (DEV). The assessment and graphical representation of age, period and cohort effects was performed through a sequential fitting of an Age-Cohort model and an Age-Period model with the fitted rates of the AC model as an offset, taking the 1932 birth cohort as the reference cohort.

These effects have been assessed by means of their 95% confidence intervals. The annual percent change of rates has been estimated through the Age-Drift model. The Age-Drift model is a submodel of both Age-Period model and of Age-Cohort model. It should be noted that when we have a constant annual change in rates it makes no sense to attribute this to either period or cohort. Whatever the “true” mechanism behind such a regular temporal variation of rates were, the observed rates would be the same [13].

A Bayesian age-period-cohort model with an autoregressive structure for each of the parameters [14] has been used to project mesothelioma mortality in Spain for the periods 2002-2006, 2007-2011 and 2012-2016. Mesothelioma projections in Spain were estimated based on mesothelioma mortality data in men from 1977 to 2001. Mortality projections in women are not shown in this article because we have not observed changes in rates for the analysed period, and mesothelioma in women is more commonly related to household and neighbourhood exposures. For that reason, it can not be legally recognized as occupational disease (data available by request)..

RESULTS

From 1977 to 2001, 2,929 people older than 35 died of mesothelioma in Spain: 1,928 were men (65.8%) and 1,001 women (34.2%), with the male to female ratio of 2 approximately. The crude rate rose from 0.73 per 100,000 (270 cases) in 1977-1981 to 1.13 per 100,000 (520 cases) in 1997-2001, while in women, rates remained stable or even decreased, from 0.50 (207 cases) in 1977-1981 to 0.34 (169 cases) in 1997-2001. Deceased cases and mortality rates per 100,000 men-years by birth cohort and age at death are shown in Table 1.

Birth cohort	Age group								
	35-39	40-44	45-49	50-54	55-59	60-64	65-69	70-74	75-79
1902									35
									2.23
1907								59	66
								2.43	3.56
1912							48	48	48
							1.57	1.82	2.37
1917						41	54	66	70
						1.17	1.71	2.44	3.32
1922					38	48	73	92	97
					0.82	1.11	1.85	2.71	3.97
1927				26	42	70	78	114	
				0.49	0.82	1.44	1.75	3.04	
1932			15	26	50	85	102		
			0.26	0.46	0.92	1.85	2.17		
1937		3	10	32	51	66			
		0.06	0.19	0.83	1.04	1.32			
1942	5	9	13	41	66				
	0.09	0.17	0.25	0.81	1.40				
1947	3	11	34	33					
	0.05	0.18	0.58	0.59					
1952	5	6	24						
	0.08	0.09	0.39						
1957	7	14							
	0.11	0.21							
1962	4								
	0.05								

Table 1. Age-specific mesothelioma death numbers and rates (in italicised numbers) by birth cohort and age at death. Spain, 1977-2001.

Older age groups show the highest mortality rates by birth cohort (Figure 1A, left side), and by period of death (Figure 1A, right side). Mortality rose dramatically in cohorts after 1930. A statistically significant increase of death rates by 1,96% per year was detected by means of the Age-Drift model. The age-cohort model (AIC=301.2 and DEV=23.9) did not differ statistically from the age-period-cohort (AIC=305.8 and DEV=22.5) model in terms of model fitting;. For that reason, cohort effect was considered more important than period effect. Graphical representation of APC effects (graphic not shown) depicted an exponential rising of mortality rates since the age of 50 (age effect), an increase for cohorts between 1937 and 1947 (cohort effect), and a flat period effect.

Projections indicate that numbers of deaths due to mesothelioma among men will increase until 2016 (Figure 1B). Specifically it can be expected that 636 deaths will occur between 2007 and 2011 (95%CRI: 499-656), and 685 deaths between 2012 and 2016 (95%CRI: 497-960).

DISCUSSION

Mesothelioma deaths for men increased from 1977 until 2001, and projections indicate a continuous increase until 2016. We estimated that 1,321 deaths from

mesothelioma will occur until the year 2016. This is the first prediction of mesothelioma deaths in Spain.

Analyses of mortality data in men by birth cohort showed a clear age effect with exponential rising. Moreover, the youngest birth cohorts of each age group presented an increasing trend that suggested a birth cohort effect. We did not observe such a pattern when we analyzed the same data by period of death. Results support the idea of a non-existing period effect since deviation from linearity has not been detected for this effect.

This predicted death increase in Spain is low compared to other countries. For example, a peak of 3,300 annual deaths has been predicted around the year 2020 in the UK [2], and in Italy, which was an asbestos producer country, 800 annual deaths have been predicted between 2012 and 2024 [4]. The highest number of deaths have been predicted in Japan, with 101,400 deaths for the period 1000-2039 [6]. Large amounts of asbestos were used in Japan during the seventies (350,000 tonnes per year) and that was the last country to introduce preventive measures in 2003. The low prediction numbers for Spain are due to considerably smaller amount of asbestos used compared to other countries [7]. Spain, however, was one of the last countries to introduce regulations in 1984, and ban asbestos in 2001, and this would prolong the increase in mortality over time.

In making the predictions for Spain, we did not take into account the possible change in asbestos exposure during the period. For instance, in the UK [2] it was assumed that people born after 1953 had a 50% lower risk of mesothelioma death than people born before that date. The prediction in France established a similar cut-off at 1964 because asbestos consumption started later in France than in the UK [5]. In the Spanish projection, no reduced risk assumptions were adopted because the asbestos regulations in Spain began in 1984, and it was not until 2001 that chrysotile was banned. Therefore, given a latency period of 30-40 years [11], these regulations might start taking effect on mortality approximately around 2014-2024. However, projections based on these assumptions have to be interpreted carefully because there are many factors that might influence exposure such as the fulfillment of legal measures, the amount and type of asbestos used, etc..., and that could modify mortality trends. In the Netherlands, where over 950 annual mesothelioma deaths among men were initially predicted around the year 2025, a recent updated study has reduced this number to 490 in 2017, and 338 in 2028 [15].

Changes in death classification criteria may influence the evaluation of mortality trends. Some projections multiplied the number of deaths coded as ICD-9:163 (pleural cancer) by a factor to provide a comparable classification with the more specific code used in ICD-10 (C45.0 pleural mesothelioma). For example, a factor of 0.797 was used in France to estimate pleural mesothelioma cases from the total number of pleural cancer deaths [5], and a factor of 0.73 was used in Italy [4]. The ICD-10 classification was introduced in 1999 in Spain, but for reasons of consistency we used deaths coded by ICD-9 for the entire study period. In Spain, there are no studies that would let us estimate the number of pleural mesothelioma from the total number of pleural cancer.

We focused this analysis on mesothelioma in men, because asbestos exposure has been mainly occupational [16]. Nevertheless, a high but uncertain number of cases mainly in women are caused by environmental exposure to asbestos (asbestos cement industry neighbours, asbestos workers' relatives, etc.). Agudo et al estimated that 38% of mesotheliomas can be attributed to environmental exposure [17].

These projections show a constant increase in the number of deaths due to mesothelioma in men during the next decade. This is an expected consequence of past occupational exposure to asbestos. These figures differ widely from the number of cases of lung cancer related to asbestos exposure recognized as occupational diseases in Spain that were 6 cases in 2003 and 5 in 2004 [18]. These results support the necessity to initiate an active medical surveillance program based on all workers with asbestos exposure history in order to recognize and compensate their occupational diseases. A condition for the success of the program is to guarantee accessibility of the most sophisticated diagnostic tests for that population.

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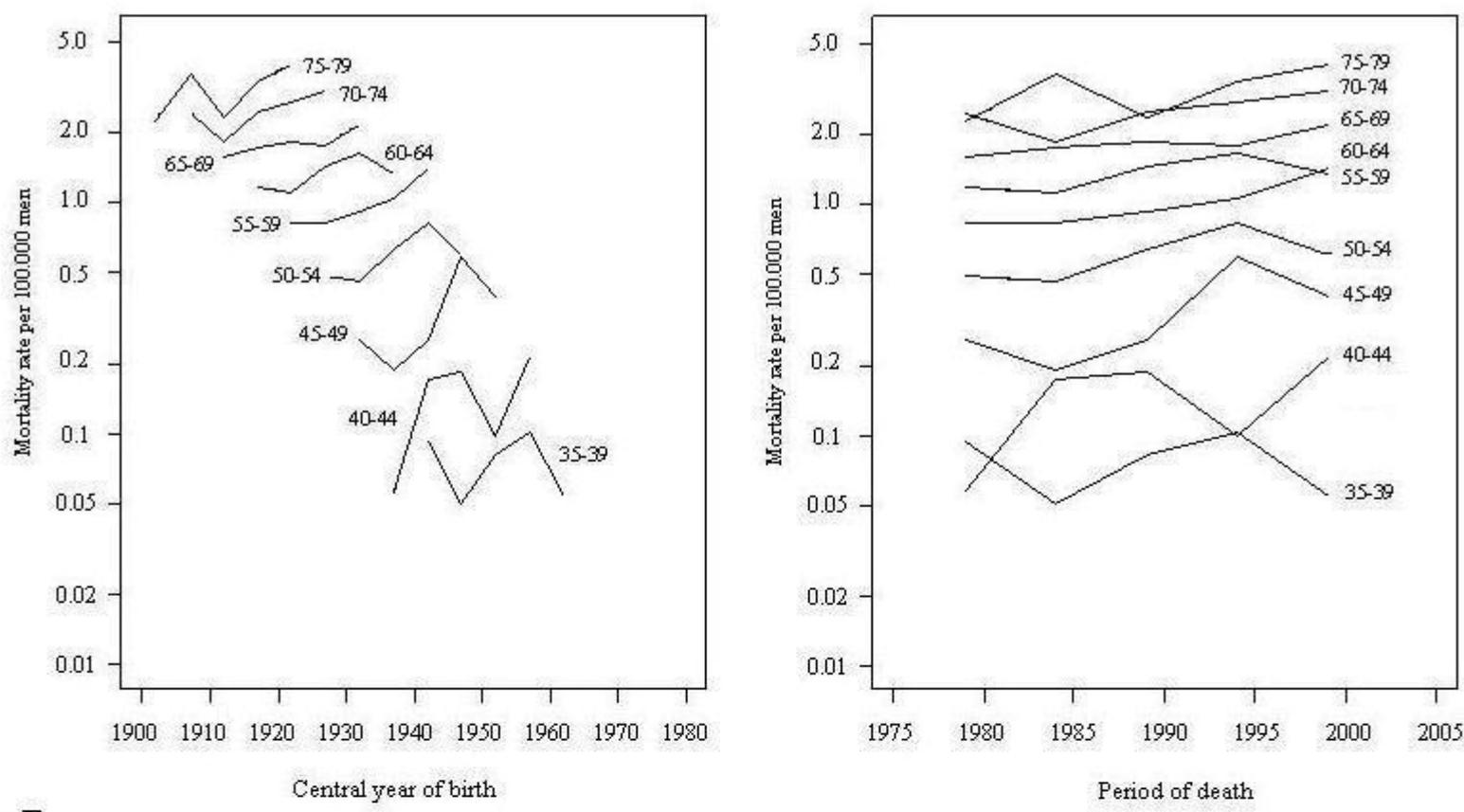
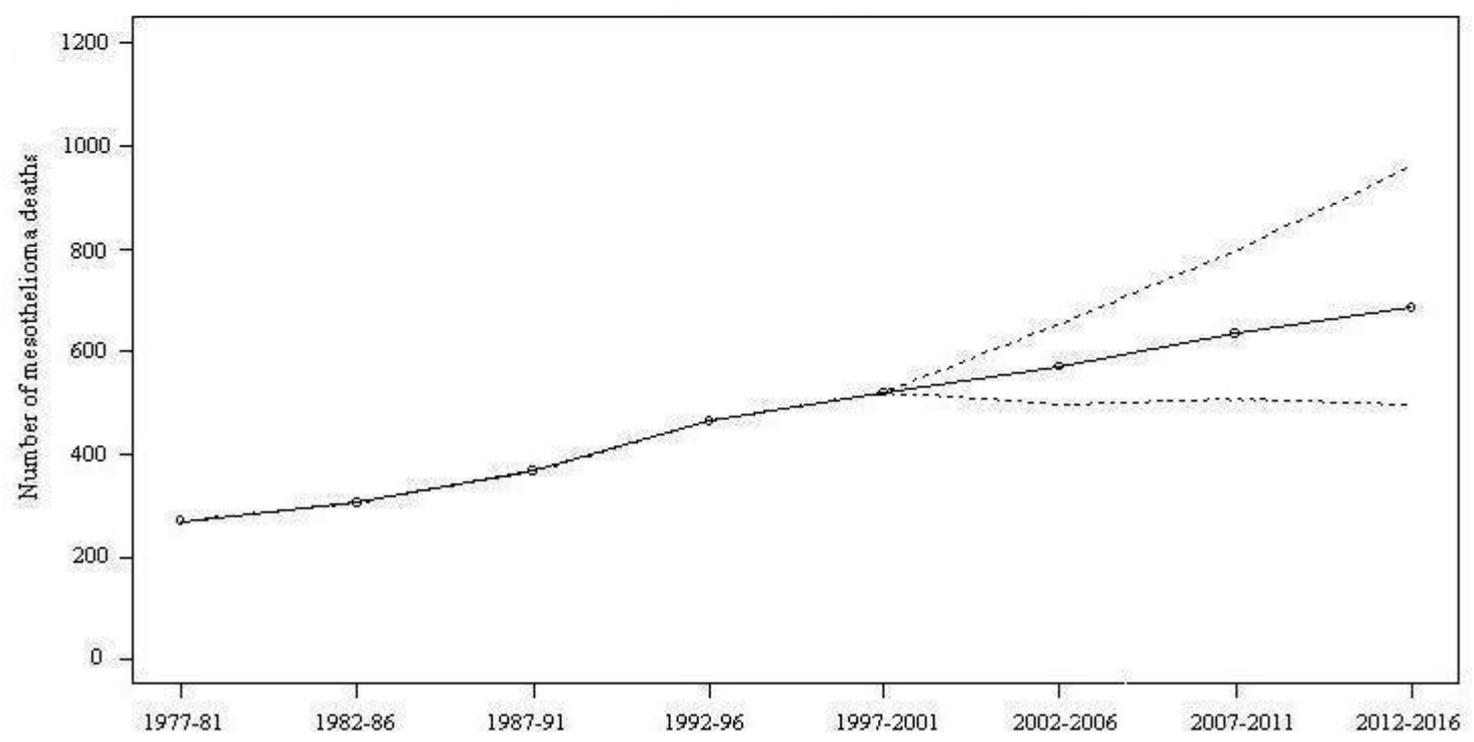
A**B**

Figure 1. Mesothelioma men mortality rates by birth cohort and period of death (A), and mesothelioma death projections for men based on 1977-2001 mortality data (B): solid line represents numbers of cases observed for 1977-2001, broken lines show the 95% credibility intervals for projected deaths during 2002-2016.