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Pleural mesothelioma incidence in Europe: evidence of some deceleration in the increasing trends☆

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Abstract

Objective: To summarize the geographical and temporal variations in incidence of pleural mesothelioma in Europe, using the extensive data available from European general cancer registries, and consider these in light of recent trends in asbestos extraction, use and import in European countries.
Material and methods: The data were extracted from the European Cancer Incidence and Mortality database (EUROCIM). The inclusion criteria was acceptance in Volume VII of Cancer Incidence in Five Continents. Truncated age-standardized rates per 100,000 for the ages 40–74 were used to summarise recent geographical variations. Standardized rate ratios and 95% confidence intervals for the periods 1986–1990 and 1991–1995 were compared to assess geographical variations in risk. To investigate changes in the magnitude of most recent trends, regression models fitted to the latest available 10-year period (1988–1997) were compared with trends in the previous decade. Fitted rates in younger (40–64) and older adults (65–74) in the most recent period were also compared.
Results: There was a great deal of geographical variation in the risk of mesothelioma, annual rates ranging from around 8 per 100,000 in Scotland, England and The Netherlands, to lower than 1 per 100,000 in Spain (0.96), Estonia (0.85), Poland (0.85) and Yugoslavia, Vojvodina (0.56) among men. The rank of the rates for women was similar to that observed for men, although rates were considerably lower. Between 1978 and 1987, rates in men significantly increased in all countries (excepting Denmark). In the following 10 years, there was a deceleration in trend, and a significant increase was detectable only in England and France. In addition, the magnitude of recent trends in younger men was generally lower than those estimated for older men, in both national and regional cancer registry settings.
Conclusions: While mesothelioma incidence rates are still rising in Europe, a deceleration has started in some countries. A decrease may begin in the next few years in certain European populations considering the deceleration of observed trends in mesothelioma and asbestos exposure, as well as the recent ban on its use.

Introduction

The association between asbestos exposure and pleural mesothelioma (PM) is well established. The background incidence of PM (without asbestos exposure) is estimated to be about 1–2 cases per million per year [1]. Among asbestos-exposed populations, the observed number of cases is much higher than expected. In the industrialized world, about 80% of malignant PM develop in

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individuals with higher than background levels of exposure to asbestos [2, 3].

Workers involved in the extraction and manufacturing of asbestos fibres – *i.e.* miners, asbestos-cement workers, shipyards workers, insulators – have the highest risk of PM [1, 4]. Recently, mesothelioma cases and deaths have been found in other workplaces, where asbestos exposure was at a low level (bakeries) [5] or confined to specific subgroup of workers (maintenance workers in oil refineries) [3, 6]. The role of co-factors in the development of the disease (chiefly, SV40 and family history) have been also indicated [7, 8].

The mean latency time for PM has been repeatedly found to be between 30 and 40 years [2, 9]. As a consequence of the strong cause–effect relationship, the incidence and mortality trends observed recently follow the asbestos exposure trends with a mean lag time of about 30–40 years. The number of mesothelioma cases reported began to increase around 1950 in some countries, with a steep increase noted during 1960s and 1970s.

Although preventive measures have been taken at different time points in Europe, European cancer registries have described constant increases in the incidence rates of PM in the last few decades [10–14]. In addition, recent projections have suggested that PM mortality rates, estimated using mortality from primary pleural tumours (PPT), will continue to increase in the next 20 years in most European countries [15–20].

This paper aims to summarize the incidence of PM in terms of the geographical and temporal variations, using the good-quality data available from cancer registries in Europe. This was made possible by the availability of recent incidence data in the European Cancer Incidence and Mortality (EUROCIM) database and software package [21], an initiative of the European Network of Cancer Registries (ENCR). Member registries regularly submit information on cancer incidence in their catchment area for inclusion in the EUROCIM package, thus providing all members with a resource to compare their own incidence with data from other European cancer registries. This study is one of several ENCR-sponsored studies examining time trends in cancer-specific incidence and mortality in Europe.

Material and methods

EUROCIM Database

The EUROCIM database comprises of cancer incidence and mortality data from 118 European Cancer Registries in 25 Countries [21]. Cancer registries accepted for the Volume VII of Cancer Incidence in Five Continents [22] were initially included in the analysis (Table 1), with the exception of Malta and Iceland, for which very few cases occurred. While for several European countries, cancer registration coverage is nationwide, in others there exist good-quality regional cancer registries. In order to compare PM incidence in different countries, data from regional registries were combined, minimising the loss of coverage in terms of both the number of registries involved and the length of the time period under study. In addition, data from several regional registries where incidence rates were particularly high were also analysed separately.

Statistical methods

Incidence rates

Truncated age-standardized rates per 100,000 for the age range 40–74 ($ASR_{(40-74)}$) were calculated using the European Standard population. Cases aged 75 or more were excluded as the accuracy of cancer diagnosis has been shown to decline in the very oldest age groups, leading to an underestimation of mesothelioma rates [23]. The very few cases aged under 40 were also removed from the analyses. Male/Female Ratios (M:F Ratios) were calculated by dividing the $ASR_{(40-74)}$ for males by the corresponding rate in women.

To compare the absolute change in the rates between 1986–1990 and 1991–1995, the standardized rate ratio (SRR) and 95% confidence intervals (95% CI) were calculated [24]. Geographical comparisons were performed using the same consecutive 5-year periods, analysed for all countries.

Linear trend analysis

To investigate changes in the magnitude of very recent trends in mesothelioma, regression models were fitted to the annual rates in the latest 10-year period by country and sex to obtain the estimated annual percent change in the rates over time (EAPC). To assess the differences in the last two decades, the models were also fitted to the previous 10 years of data, and the EAPC compared. Changes in rates among younger (40–64) and older adults (65–74) were also estimated and compared. The models were fitted using STATA [25].

The joinpoint regression model [26] describes continuous changes in rates and uses the grid-search method to fit the regression function with unknown joinpoints (points in time where significant changes in the trend occurred) assuming constant variance and uncorrelated errors. The analysis, performed by way of the statistical software Joinpoint [26], is a useful way to characterize the trends in cancer rates succinctly and, connecting linear line segments on a log scale, allows one to estimate recent changes in trend.

Table 1. Mean annual number of cases of PM, truncated age (40–74) standardized rates per 100,000 ($\mathrm{ASR}_{(40-74)}$ – European Standard), mean annual person years (PY) by sex and ratios between $\mathrm{ASR}_{(40-74)}$ for men and the corresponding rate in women (M:F ratio) in European cancer registries in most recent 5-year period

Registry	Period	Males			Females			M:F ratio
		Cases	$\mathrm{ASR}_{(40-74)}$	PY	Cases	$\mathrm{ASR}_{(40-74)}$	PY	
National cancer registries								
Scotland	1993–1997	88	8.81	932,577	15	1.28	1,022,477	6.9
England	1991–1995	763	8.01	9,031,280	115	1.11	945,844	7.2
The Netherlands	1993–1997	219	7.40	3,080,261	28	0.82	3,154,205	9.0
Italy[a]	1991–1995	59	4.24	1,405,127	21	1.27	1,569,770	3.3
Switzerland[a]	1992–1996	26	4.16	625,703	4	0.54	677,542	7.7
Denmark	1992–1996	39	3.87	1,013,574	8	0.67	1,049,215	5.8
Norway	1993–1997	31	3.82	797,954	4	0.47	815,031	8.2
Croatia	1993–1997	29	3.43	846,220	8	0.73	981,960	4.7
Sweden	1993–1997	61	3.37	1,725,898	11	0.52	1,768,269	6.5
Finland	1993–1997	31	3.22	1,013,637	8	0.72	1,085,264	4.5
France[a]	1992–1996	30	2.94	998,568	8	0.67	1,067,507	4.4
Slovenia	1993–1997	7	1.95	372,089	2	0.35	416,871	5.6
Republic of Ireland	1994–1997	11	1.88	580,675	1	0.23	593,302	8.2
Germany[a]	1993–1997	4	1.53	225,865	1	0.19	244,058	8.1
Slovakia	1993–1997	9	1.06	872,381	5	0.42	1,010,438	2.5
Czech Republic	1993–1997	19	1.01	1,956,163	9	0.41	2,197,439	2.5
Spain[a]	1990–1994	13	0.96	1,213,357	7	0.49	1,295,769	2.0
Estonia	1993–1997	2	0.85	251,562	2	0.48	329,687	1.8
Poland[a]	1992–1996	7	0.85	828,725	4	0.37	976,749	2.3
Yugoslavia[a]	1993–1997	2	0.56	430,411	1	0.29	462,045	1.9
Regional cancer registries								
Trieste (I)	1989–1992	11	17.17	56,659	1	1.79	67,243	9.6
Genoa (I)	1991–1995	24	14.42	148,514	6	3.06	173,700	4.7
Rotterdam (NL)	1993–1997	56	13.10	436,962	4	0.92	449,053	14.2
Amsterdam (NL)	1993–1997	48	10.35	491,774	6	1.12	506,659	9.2
Maastricht (NL)	1993–1997	17	9.60	179,252	2	0.92	181,928	10.4
Twente (NL)	1993–1997	16	7.19	219,251	4	1.58	225,444	4.6
Isere (F)	1993–1997	9	4.56	188,770	2	0.72	197,858	6.3
Varese (I)	1993–1997	5	2.88	164,446	5	2.31	181,073	1.2

[a] Selected areas only. Italy: Florence, Genoa City, Parma, Ragusa province, Turin, Varese Province, Venetian Region. Switzerland: Basel, Geneva, Neuchatel, St. Gall-Appenzell, Vaud, Zurich. France: Bas-Rhin, Calvados, Doubs, Haut-Rhin, Herault, Isere, Somme, Tarn. Germany: Saarland. Poland: Cracow City, Kielce, Lower Silesia. Spain: Asturias, Basque Country, Tarragona, Granada, Mallorca, Murcia, Navarra. Yugoslavia: Vojvodina.

Correlation of asbestos ban and annual percent changes

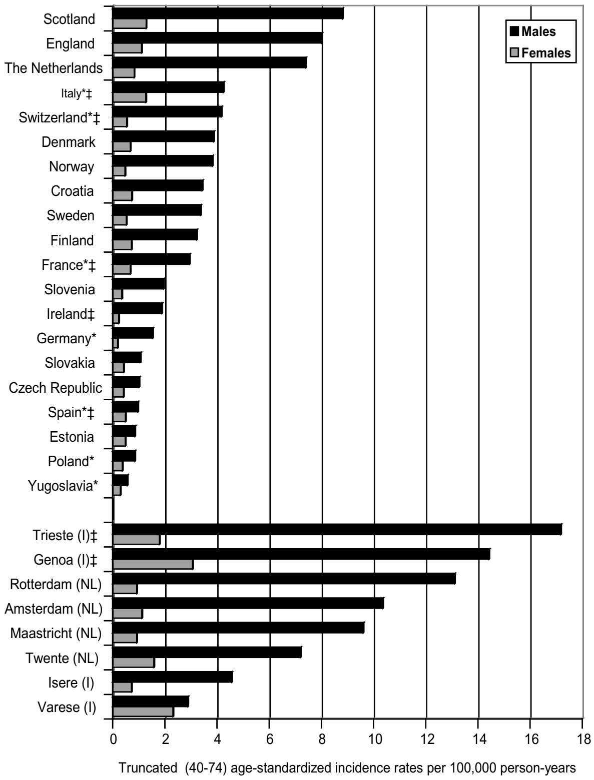
In order to describe the correlation between the EAPC in the most recent 10-year period and the year of the asbestos ban, a scatterplot was drawn incorporating a simple linear regression line, and its corresponding 95% CI.

Results

Pleural mesothelioma incidence in Europe

Table 1 provides some details with regards to the European cancer registries included in the EUROCIM database. The populations are sorted by descending magnitude of rates among males. Figure 1 shows $\mathrm{ASR}_{(40-74)}$ of PM by gender recorded in the most recent 5-year period in European cancer registries. There is a great deal of geographical variation in the rates of mesothelioma, ranging from 8.8 in Scotland, 8.0 in England and 7.4 in The Netherlands to rates lower than one in Spain (0.96), Estonia (0.85), Poland (0.85) and Yugoslavia, Vojvodina (0.56). In women, the ranking is similar to that observed in males, with female rates much lower than their male counterparts. The M:F ratios varied markedly across the populations studied, as reported in Table 1, from 1.8 in Estonia to 9.0 in The Netherlands. The M:F ratios also varied widely across the high incidence regional registries, with rates ranging from 1.2 in Varese to 14.2 in Rotterdam.

Figure 2 compares the $\mathrm{ASR}_{(40-74)}$ for PM in males (a) and females (b) between the two most recent 5-year periods (*i.e.* 1986–1990 and 1991–1995) in areas with the highest mesothelioma incidence rates. There were



Period = 1993-1997 (except for : see Table 1 for details).
* Selected areas only (see Table 1 for details).

Fig. 1. Truncated (age 40–74) age-standardized incidence rates per 100,000 (European Standard) of PM in European men and women.

comprehensive increases in the rates in European males over the decade, the SRRs ranging from 0.98 in Norway to 1.35 for England, where the only significant difference (95% CI: 1.28–1.42) between the two periods was observed. The $\mathrm{ASR}_{(40-74)}$ among females while lower were also increasing in most European populations, the exceptions being Denmark and Finland.

Time trends analysis

Figure 3 shows the observed and fitted rates based on log-linear regression on the $\mathrm{ASR}_{(40-74)}$ in men in the latest 10 years (in most populations, 1988–1997) *versus* the previous 10-year period (in most populations, 1978–1987), where available. Table 2 describes the EAPCs in each of the two periods, together with 95% CIs. During the first period, the EAPC significantly increased in all countries (excepting Denmark). During the latest 10 years the values of EAPC were evidently lower in comparison and a significant increase was detectable only in England and France. The analysis performed using *Joinpoint* did not reveal any significant changes, except for England, where a clear deceleration was detected in 1986. The rates of the selected regional registries are for the most part still on the increase, with exceptions being Rotterdam and Varese.

Figure 4 shows the observed and fitted rates on partitioning the populations into younger (40–64) and older (65–74) men. Table 3 shows the corresponding EAPCs by age group together with 95% CIs. The magnitude of recent trends in younger men is generally lower than those estimated for older men, in both national and regional cancer registry settings.

Asbestos ban and annual percent changes in mesothelioma incidence rates

The analysis of the correlation between changes in trend during the latest 10 years and the year of national asbestos ban for each country showed a positive, although weak, correlation (Figure 5), suggesting that countries where asbestos was effectively banned earlier convey more moderate increases relative to those for which bans were implemented subsequently.

Discussion

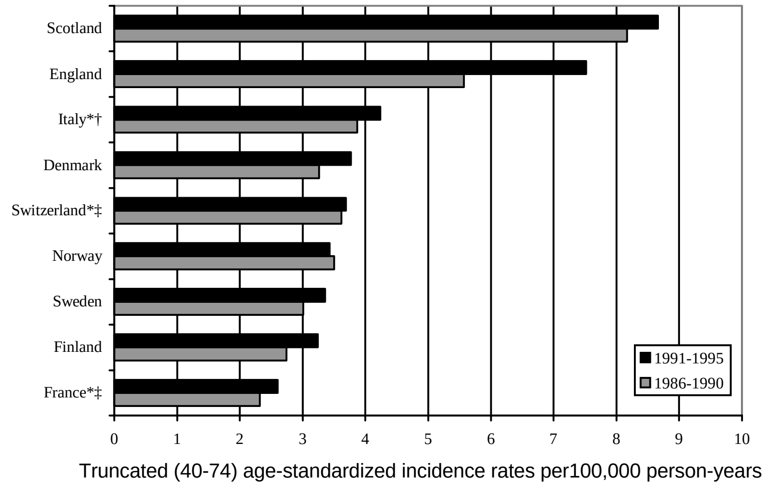
Mesotheliomas are malignant tumours of the mesothelium lining in serosal cavities, most often in the pleural cavity. Despite the scientific interest, the biology of mesothelioma is still not fully elucidated.

Risk factors for mesothelioma

The only well established risk factor for mesothelioma is an exposure to asbestos [27]. The association was confirmed for the first time in 1960 by Wagner *et al.* [28]. There are three main types of asbestos which are associated with induction of PM: crocidolite, amosite and chrysotile (known also as blue, brown and white asbestos, respectively). It is believed that different types of asbestos have different potency to cause mesotheliomas. It has been estimated, based on the observations from occupational cohort studies, that exposure specific risk of mesothelioma from those three main types of asbestos is approximately in the ratio 1:100:500 for chrysotile, amosite and crocidolite, respectively [29]. However, some researchers reported no differences between the risks of mesothelioma presented by different types of asbestos fibres [30].

Another type of asbestos, anthophyllite, has been extracted in Finland and exported in Europe, but data about its potential carcinogenity are poor [31]. Recently, it has been suggested by Roggli *et al.* [32] that also tremolite (hydrated calcium magnesium silicate) may play some role in the aetiology of mesothelioma.

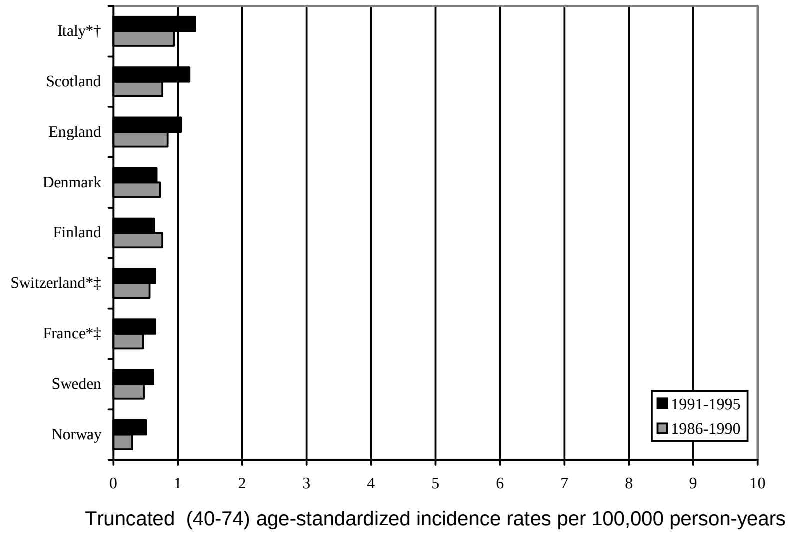
a) Males



SRR (95% CI)

1.06 (0.92 *to* 1.22)
1.35 (1.28 *to* 1.42)
1.10 (0.91 *to* 1.32)
1.16 (0.94 *to* 1.44)
1.02 (0.75 *to* 1.38)
0.98 (0.77 *to* 1.25)
1.11 (0.94 *to* 1.32)
1.18 (0.93 *to* 1.51)
1.12 (0.83 *to* 1.51)

b) Females



SRR (95% CI)

1.35 (0.98 *to* 1.88)
1.55 (1.06 *to* 2.26)
1.18 (0.93 *to* 1.51)
0.93 (0.59 *to* 1.46)
0.83 (0.52 *to* 1.30)
1.16 (0.57 *to* 2.36)
1.41 (0.78 *to* 2.55)
1.32 (0.89 *to* 1.95)
1.79 (0.88 *to* 3.62)

* Selected areas only–(see Table 1 fordetails).
† First period = 1987–1990.
‡ First period = 1988–1990.

Fig. 2. PM in areas with the highest incidence rates in Europe for the periods 1986–1990 and 1991–1995: truncated (age 40–74) age-standardized incidence rates per 100,000 (European Standard) and SRRs with 95% CI.

Although asbestos is considered to be the principal cause of mesothelioma, no exposure to asbestos fibres is detectable in a proportion of mesothelioma patients. It was estimated by Roggli *et al.* [33] that some 20% of mesotheliomas occur in persons with no history of asbestos exposure; however, we can not exclude that the long latency time may play a role in the masking of past exposures. Moreover, among people heavily exposed to asbestos, less than 10% develop mesothelioma [33]. The existing literature suggests that there might be other factors which contribute to the aetiology of this disease, such as radiation at high doses [34]. The role of genetic predisposition has not yet been clarified, however there is information which suggests that some mesothelioma cases may occur among individuals with a cancer-prone genotype susceptible to the toxic effect of asbestos [35, 36]. Another factor which has been suggested to contribute to the mesothelioma induction is infection by Simian virus 40 (SV40) [37]. Although the presence of SV40 in a fraction of mesothelioma cases has been

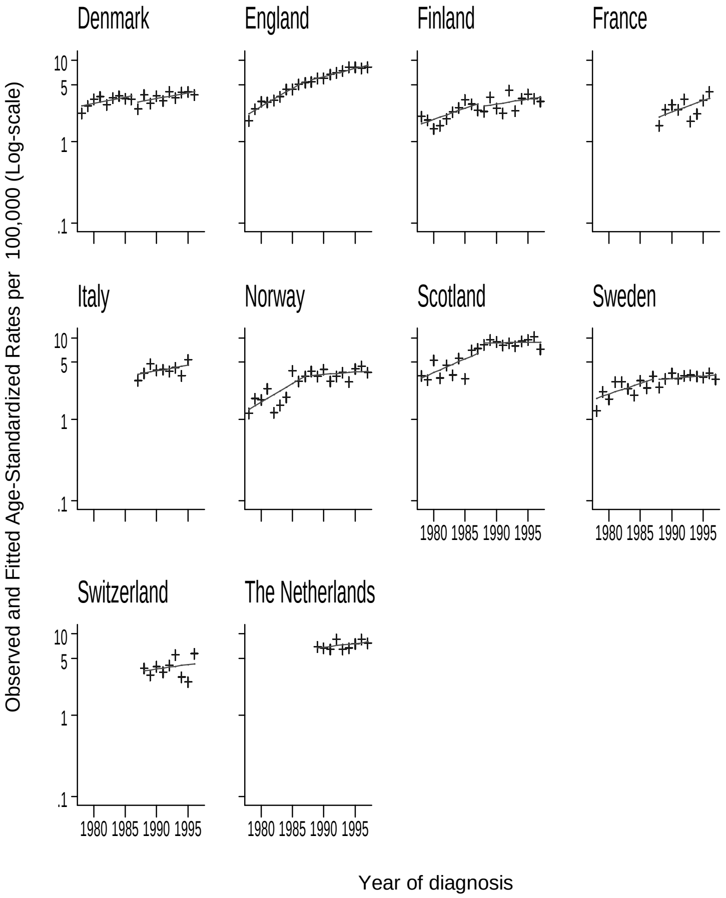


Fig. 3. Observed (+) truncated (age 40–74) age-standardized incidence rates per 100,000 and fitted rates (–) of PM among men in recent periods, where available. Models fitted separately for each period (about 1978–1987 and 1988–1997).

well documented, probably because of vaccination with contaminated poliovaccines [7, 8], some studies reported a lack of association [39–41]. In addition, some countries did not use those poliovaccines, such as Finland [42], whose high incidence rates are analysed here. A recent review tries to shed light on this point [43].

Past asbestos use in Europe

To understand the variations in trends, one must consider the temporal data on asbestos use and import in European countries. Europe has long been an important producer and consumer of asbestos. The major asbestos producer in Europe in 1986 was the Soviet Union, which produced 2,500,000 tons (93% of total European production), but significant production was also noted in Italy, Greece, Cyprus and Yugoslavia. Several European countries have stopped the asbestos mining, such as Finland (in 1975), Cyprus (in 1988), and Italy (in 1990) [27].

In 1986, the highest asbestos consumption per capita was in the former Soviet Union (7.8 kg per capita), much higher than in other parts of Europe. Significant consumption was observed also in Mediterranean countries (Portugal, Spain, Italy, Greece, Yugoslavia, Albania) – 1.9 kg/capita – and in Central European countries (Poland, Czechoslovakia, Hungary, Romania, Bulgaria) – 1.8 kg/capita. The lowest consumption was observed in Northern Europe (Denmark, Finland, Sweden) –0.7 kg/capita [27]. Consumption per capita decreased significantly up to 1994 in all regions of Europe.

In Denmark, asbestos use was considerable already in the 1930s, and after the Second World War there was a large increase until 1980, when import and use of crocidolite was abandoned and the use of the other types of asbestos was restricted [10]. In Finland, asbestos use began to increase during the early 1940s, reached its top in 1970s and then steeply declined [11]. In Sweden, asbestos import was already high in early 1950s, increased until 1960s then remained stable until 1975, when regulations limited its use [12]. In England, the

Table 2. EAPC and 95% CI of the truncated (age 40–74) age-standardized rates ($ASR_{(40-74)}$) for PM among males in two recent periods (where available)

Registry	First period	EAPC	(95% CI)	Second period	EAPC	(95% CI)
National cancer registries						
Scotland	1978–1987	7.7	(3.9 to 11.6)	1988–1997	0.2	(−2.5 to 3.0)
England	1978–1987	10.2	(5.8 to 14.6)	1988–1997	4.7	(1.6 to 7.8)
The Netherlands	N/A	–	–	1989–1997	2.1	(−1.5 to 5.6)
Italy[a]	N/A	–	–	1987–1995	3.2	(−1.5 to 8.0)
Switzerland[a]	N/A	–	–	1988–1996	2.5	(−2.3 to 7.4)
Denmark	1978–1986	3.5	(−1.9 to 8.9)	1987–1996	3.2	(−1.2 to 7.5)
Norway	1978–1987	10.5	(4.8 to 16.2)	1988–1997	1.3	(−3.0 to 5.5)
Sweden	1978–1987	5.9	(0.6 to 11.3)	1988–1997	1.4	(−3.1 to 6.0)
Finland	1978–1987	6.3	(0.8 to 11.8)	1988–1997	2.7	(−1.9 to 7.4)
France[a]	N/A	–	–	1988–1996	6.5	(0.6 to 12.4)
Regional cancer registries						
Genoa (I)	N/A	–	–	1986–1995	1.4	(−0.7 to 3.6)
Rotterdam (NL)	N/A	–	–	1989–1997	−1.1	(−3.6 to 1.5)
Amsterdam (NL)	N/A	–	–	1988–1997	2.3	(−0.3 to 4.9)
Maastricht (NL)	N/A	–	–	1988–1997	3.1	(0.4 to 5.8)
Twente (NL)	N/A	–	–	1989–1997	0.3	(−3.3 to 3.8)
Isere (F)	N/A	–	–	1988–1997	4.8	(0.8 to 8.8)
Varese (I)	N/A	–	–	1988–1997	−3.4	(−7.7 to 1.0)

Registries sorted by descending magnitude of the $ASR_{(40-74)}$, as reported in Table 1.

N/A = Period not available.

[a] Selected areas only (see Table 1 for details).

increasing use of asbestos started during the first two decades of the 20th century [44] and the maximum level of asbestos import was reached during the 1960s and it began to decline before the beginning of 1980s. In many European countries, the use of asbestos began to decrease only after the mid-1970s, due to perceived limitations in its use, firstly in crocidolite spraying (officially banned in UK in 1972 [Brewster D., 2002, personal communication], in Sweden in 1975 [12] and in Finland in 1976 [11]). Finally, it was progressively banned in many European countries in the 1980s and 1990s (Table 4) [45].

Previous time trend analyses of mesothelioma incidence rates

Another important issue when considering PM incidence and mortality time trends is a latency period (LP) between the first exposure to asbestos and the date of clinical diagnosis or death. It has been shown by Bianchi *et al.* [46] that the LP was different for different groups of asbestos-exposed individuals. The longest LP was found for maritime traders (56.2 years) and for domestic exposure (51.7), while the shortest LP was observed in insulators (29.6) and dock workers (35.4), the total mean being 48.7 years. This may influence time trends, since different type of asbestos exposure dominated in particular countries and regions. As a consequence of the strong cause–effect relationship, the incidence trends observed recently follow the asbestos exposure trends some 40 years ago. In fact, although preventive measures have been taken at different time points in Europe, European cancer registries have described constant increases in the incidence rates of PM in the last few decades. In Denmark, Andersson and Olsen [10] observed highly significant increases in the ASR of malignant mesothelioma from 1950s to 1970s, then the steepness of the rate increase began to decline. In Finland, the annual number of mesotheliomas rose steeply in the period 1975–1990, but it did not increase during the 1990s [11]. In Sweden, the annual incidence of PM has increased rapidly between 1960s and 1980s [12]. In The Netherlands, the incidence of mesothelioma remained stable over the time period 1989–1997 [47], but in the southern part of The Netherlands, the incidence rates for PM increased twofold between 1975–1979 and 1990–1994 [13]. In Genoa (Italy), the crude incidence rate for PM almost double between 1986–1987 and 1997–1998 [14].

Outside of Europe, US mesothelioma rates, after a significant increase during the period 1973–1980 [48], should likely have peaked by the end of the 20th century, as the birth cohort with the highest exposure was the 1925–1929 [49]. In New Zealand, mesothelioma incidence rates have increased progressively since the 1960s and reached 25 cases per million for men in 1995

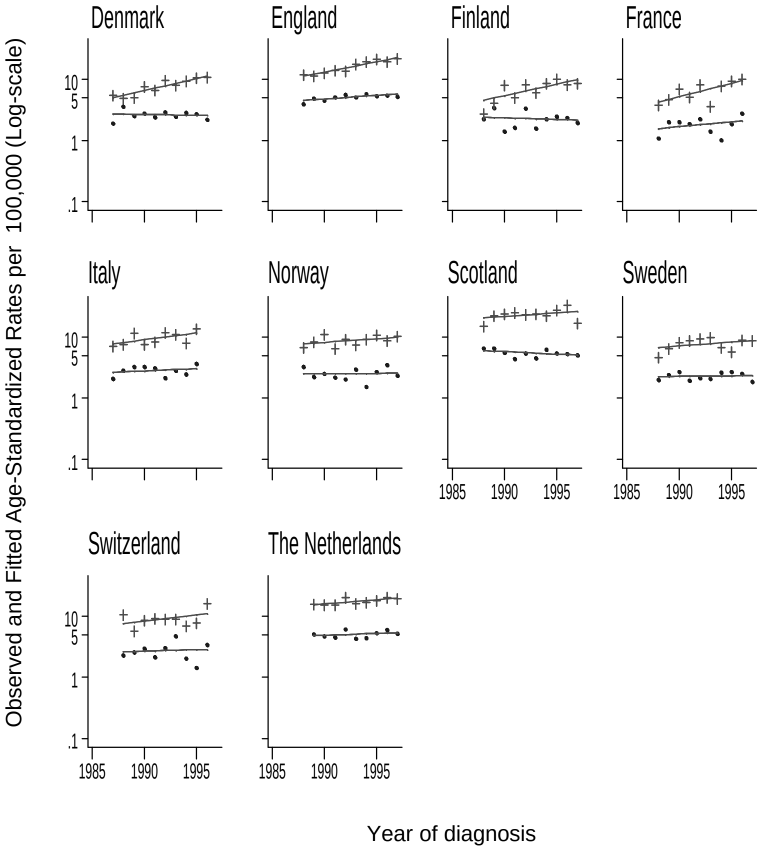


Fig. 4. Observed truncated age-standardized incidence rates per 100,000 among men aged 40–64 (•) and 65–74 (+) and fitted values (–) for pleural mesothelioma 1988–1997 in Europe.

[50]. In Australia, an important asbestos producer, mesothelioma incidence rates have been continually increasing and are amongst the highest reported rates in the world (59.8 per million among males aged 20+) [51].

PPT mortality as a surrogate of PM incidence

Recently, projections of future trends of PM have been performed using deaths from PPT (ICD-9 163) as surrogate for incidence of mesothelioma. The main advantage in using this indicator is the geographical availability (at national level) and the period of time covered (in most cases from the 1970s onwards), but some differences between countries in the ratio between PPT mortality rates and PM incidence rates are observed. In order to examine the extent of the misclassification, information on the registered cause of death for mesothelioma cases who died, and the diagnosis at registration (if there was a registration) of pleural cancer deaths is required. This topic was reviewed in Britain and France, where discrepancies between the two countries were found [16]. In Italy, Gorini *et al.* [52] found that 82% of all mesothelioma deaths were correctly coded primary pleural cancer (*i.e.*, ICD-9 163), while 60% of deaths coded 163 were included in the Mesothelioma Registry of Tuscany (period 1994–1999). Hence, the ratio of PM to pleural cancer was 0.73 (0.60/0.82). In another Italian study, the overall concordance between pathological diagnosis and death certification was 75% [53]. In the period 1980–1986, the Zurich cancer registry found a concordance tending to unity (0.80/0.78), as the 20% false positives cancelled each other out. [Schuler, 2002, personal communication]. It is therefore that changes in the coding of death over time may have a major impact on the underlying trends in mesothelioma mortality. Further work examining this relation is required.

Analyses on PPT mortality were performed by Peto *et al.* [16] and La Vecchia *et al.* [17] for Great Britain (see also [15]), Italy, France, Switzerland, Hungary, Germany and The Netherlands, suggesting that PM mortality

Table 3. EAPC and 95% CI of the truncated (ages 40–64 and 65–74) age-standardized rates for PM by age in the last available period among males in European cancer registries

Registry	Period	Age 40–64		Age 65–74	
		EAPC	95% CI	EAPC	95% CI
Scotland	1988–1997	−2.0	(−6.1 to 2.1)	2.6	(−0.5 to 5.8)
England	1986–1995	2.6	(−1.7 to 6.8)	7.8	(3.9 to 11.7)
The Netherlands	1989–1997	1.3	(−3.7 to 6.3)	3.1	(−1.2 to 7.4)
Italy[a]	1987–1995	1.8	(−4.9 to 8.5)	5.2	(−0.6 to 11.0)
Switzerland[a]	1987–1996	1.1	(−5.8 to 7.9)	4.5	(−1.4 to 10.4)
Denmark	1987–1996	−0.6	(−6.5 to 5.4)	9.1	(3.5 to 14.6)
Norway	1988–1997	0.2	(−5.9 to 6.2)	2.8	(−2.4 to 7.9)
Sweden	1988–1997	0.4	(−6.0 to 6.8)	2.9	(−2.6 to 8.4)
Finland	1988–1997	−1.2	(−7.6 to 5.2)	8.7	(2.8 to 14.6)
France[a]	1988–1996	3.6	(−4.8 to 12.1)	10.1	(3.0 to 17.2)
Regional cancer registries					
Genoa (I)	1986–1995	0.9	(−2.1 to 3.9)	2.2	(−0.5 to 4.9)
Rotterdam (NL)	1989–1997	−3.0	(−6.5 to 0.6)	1.8	(−1.4 to 5.0)
Amsterdam (NL)	1988–1997	0.5	(−3.4 to 4.4)	4.3	(1.3 to 7.2)
Maastricht (NL)	1988–1997	0.1	(−3.5 to 3.8)	7.5	(4.1 to 10.8)
Twente (NL)	1989–1997	1.1	(−4.0 to 6.2)	−0.8	(−5.0 to 3.5)
Isere (F)	1988–1997	−1.2	(−6.8 to 4.5)	13.0	(8.0 to 18.0)
Varese (I)	1988–1997	−0.8	(−7.0 to 5.5)	−6.7	(−11.9 to −1.5)

Registries sorted by descending magnitude of the $ASR_{(40–74)}$, as reported in Table 1.

[a] Selected areas only (see Table 1 for details).

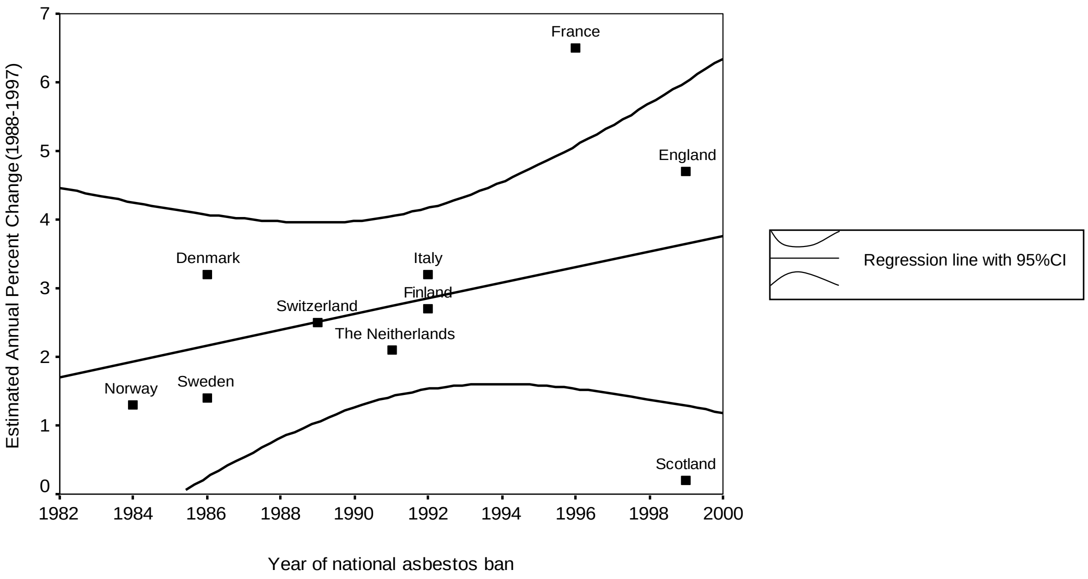


Fig. 5. EAPC of the truncated (age 40–74) age-standardized rates for PM among males in 1988–1997 in European cancer registries contrasted with year of national asbestos ban (regression line and 95% CI are reported).

rates will continue to increase in the next 20 years, when the cohorts of men born between 1940 and 1950 will reach the peak age for mesothelioma incidence. In France, the mortality from mesothelioma in men aged 50–79 will continue to increase, peaking around the years 2030–2040 [18, 19]. In Italy, the lifetime cumulative risk of dying from PPT is increasing up to the youngest birth cohorts, suggesting that likely the trend in male mortality from PPT will not peak until two or three decades [20].

Table 4. Details of national asbestos bans in Europe

Date	Event
1983	Iceland introduces ban (with exceptions) on all types of asbestos (updated in 1996)
1984	Norway introduces ban (with exceptions) on all types of asbestos (revised 1991)
1986	Denmark introduces ban (with exceptions) on chrysotile Sweden introduces the first of a series of bans (with exceptions) on various uses of chrysotile
1988	Hungary bans amphiboles
1989	Switzerland bans crocidolite, amosite and chrysotile (some exceptions)
1990	Austria introduces ban on chrysotile (some exceptions)
1991	The Netherlands introduces the first of a series of bans (with exceptions) on various uses of chrysotile
1992	Finland introduces ban (with exceptions) on chrysotile (came into force 1993) Italy introduces ban on all types of asbestos (some exceptions until 1994)
1993	Germany introduces ban (with minor exemptions) on chrysotile, amosite and crocidolite having been banned previously. The sole derogation remaining is for chrysotile-containing diaphragms for chlorine-alkali electrolysis in already existing installations. These will be banned as of 2011 Croatia bans crocidolite and amosite
1996	France introduces ban (with exceptions) on chrysotile Slovenia introduces ban on asbestos-cement
1997	Poland bans asbestos
1998	Belgium introduces ban (with exceptions) on chrysotile Lithuania issues first law restricting asbestos use; ban expected by 2004
1999	UK bans chrysotile (with minor exemptions)
2000	Ireland bans chrysotile (with exceptions)
2001	Latvia bans asbestos (exemption for asbestos products already installed however, they must be labelled)
2002	Spain and Luxembourg plan to ban chrysotile, crocidolite and amosite having been banned under earlier EU directives Slovak Republic expects to adopt EU asbestos restrictions banning all asbestos

(Source: Kazan-Allen, 2002 in http://www.ibas.btinternet.co.uk/index.htm, modified).

PM incidence and trends in national and regional cancer registries in Europe

From the analysis reported in this paper, it is clear that the incidence rates are still on the increase in European countries, but in most populations there is evidence of a slowing down in the mesothelioma epidemic. The relative magnitude of the trend in the last 10 years is less marked than that in the decade before, and recent trends in men aged 40–64 are less steep then those seen in older men (aged 65–74).

At a national level, Scotland, England and The Netherlands have the highest incidence rates in Europe, as expected [22]. In some regional registries, rates are notably high, as has been reported previously [14, 22]. The difference in rates between national and regional registries is not surprising, given that particularly elevated risks in some specific area will be diluted at the national level. In fact, regional registries cover local and small areas, where the risk can be very high. For instance, large shipbuilding plants, busy docks and industrial plants, where work related asbestos exposure was documented, are located in the areas of Trieste [54], Genoa [14, 55, 56] and Rotterdam [57], where the highest incidence rates have been detected. In Scotland, the higher incidence area corresponds substantially to the location of the shipbuilding industry in the past [58]. Similarly, Northern Ireland estimated very high rates for the period 1993–1999 among men ($\text{ASR} = 8.58$), clustering around the port of Belfast, where shipbuilding was a major industry (Gavin A, 2002, personal communication).

The low incidence rates observed in Eastern countries are somewhat surprising given that rather high asbestos exposure has been recently documented [27]. Eastern countries used mainly chrysotile imported directly from Russia. As far as mesotheliomas, chrysotile seems to be less carcinogenic than other types of asbestos [29], but this is unlikely to be the sole explanation. Other factors which might moderate the development of mesotheliomas, such as delay in asbestos exposure or competitive mortality from other causes among the exposed, are possible explanations. Problems with diagnosis or registration of mesothelioma cases cannot be discounted. The regression analysis of national time trends performed on incidence data provides some valuable insight. Although trends are still increasing, the scale of the increase in the late 1980s and 1990s is diminished in comparison to that observed in the previous decade. However, an additional analysis performed using *Joinpoint*, in order to detect and test for changes in the trend in the last 20 years, did not reveal any significant changes in the time trends, except for England, where a deceleration was detected in 1986. The degree of random variation in these trends may have affected the detection of joinpoints in the other registry datasets.

Asbestos ban and annual percent changes in mesothelioma incidence rates

The analysis of the correlation between changes in trend during the latest 10 years and the year of national asbestos ban (Figure 5) indicates that countries where asbestos was effectively banned earlier, have now lower EAPC than the others (with few exceptions). Obviously, due to the long latency time needed to develop mesothelioma, it will not be possible to draw any conclusion about ban effectiveness for many years. On the other hand, it could be possible that a weak, initial deceleration in rate growth could be detectable in recent trends, as a ban is usually preceded by many years of awareness and discussion. In some countries, limitations in the use of asbestos took place in the mid-1970s and, perhaps some precautions were taken before that the total ban was put in place. In Sweden, the first regulation was passed in 1964, recommending that asbestos should be replaced wherever possible [12]. In 1969, strict regulations were first released, in print in statutory instruments, making use of crocidolite unfeasible in the UK (initially, protection may have been more effective for manufacturers of asbestos rather than users in other industries) [Brewster D., 2002, personal communication].

In conclusion, PM incidence rates are still on the increase in Europe, but a deceleration has started in some countries, and a subsequent decrease may begin sooner than expected, considering data on asbestos exposure and the relatively recent ban on its use.

Appendix A

The personnel of the cancer registries contributing to the EUROCIM database, which makes comparative studies of cancer incidence such as this possible, are to be considered co-authors of present paper. They are:
Croatia – Croatian National Cancer Registry, Zagreb (Dr Marija Strnad).

Czech Republic – Czech National Cancer, Prague (Dr Marie Jechová).

Denmark – Danish Cancer Registry, Copenhagen (Dr Hans H. Storm).

Estonia – Estonian Cancer Registry, Tallinn (Dr Tiiu Aareleid).

Finland – Finnish Cancer Registry, Helsinki (Dr Timo Hakulinen)

France – Registre Bas-Rhinois des Cancers, Strasbourg (Dr Michel Velten); Registre Général des Tumeurs du Calvados, Caen (Dr Hacina Lefèvre); Registre des Tumeurs du Doubs, Besançon (Dr Arlette Danzon); Registre des Cancers du Haut-Rhin, Mulhouse (Dr Antoine Buemi); Registre des Tumeurs de l'Hérault, Montpellier (Prof. Jean-Pierre Daurès); Registre du Cancer de l'Isère, Meylan (Dr François Ménégoz); Registre du Cancer de la Somme, Amiens (Mme Nicole Raverdy); Registre des Cancers du Tarn, Albi (Dr Martine Sauvage).

Germany – Saarland Cancer Registry, Saarbrücken (Mr Hartwig Ziegler).

Ireland – National Cancer Registry, Cork (Dr Harry Comber).

Italy – Registro Tumori Toscano, Florence (Dr Eugenio Paci); Registro Tumori Ligure, Genova (Dr Marina Vercelli); Registro Tumori della Provincia di Parma, Parma (Dr Vincenzo De Lisi); Registro Tumori della Provincia di Ragusa, Ragusa (Dr Rosario Tumino); Piedmont Cancer Registry, Torino (Dr Roberto Zanetti); Registro Tumori Lombardia, Milano (Dr Franco Berrino); Trieste Cancer Registry, Trieste (Dr Giorgio Stanta).

Norway – Cancer Registry of Norway, Oslo (Dr Frøydis Langmark).

Poland – Cracow Cancer Registry, Cracow (Dr Jadwiga Rachtan); Cancer Registry of Kielce, Kielce (Mr Ryszard Mezyk); Lower Silesian Cancer Registry, Wroclaw (Mr Jerzy Blaszczyk).

Slovakia – National Cancer Registry of Slovak Republic, Bratislava (Dr Ivan Plesko).

Slovenia – Cancer Registry of Slovenia, Ljubljana (Dr Maja Primic-Zakelj).

Spain – Registro de Tumores del Principado de Asturias, Oviedo (Dr Alvaro Cañada Martínez); Basque Country Cancer Registry, Vitoria-Gasteiz (Dr Isabel Izarzugaza); Tarragona Cancer Registry, Reus (Dr Joan Borràs); Registro de Cáncer de Granada, Granada (Dr Carmen Martínez Garcia); Registro de Cáncer de Mallorca, Palma de Mallorca (Dr Isabel Garau); Registro de Cáncer de Murcia, Murcia (Dr Carmen Navarro Sánchez); Registro de Cáncer de Navarra, Pamplona (Dr E. Ardanaz Aicua).

Sweden – Swedish Cancer Registry, Stockholm (Dr Lotti Barlow).

Switzerland – Krebsregister Basel-Stadt und Basel-Land, Basel (Prof Joachim Torhorst); Registre Genevois des Tumeurs, Geneva (Dr Christine Bouchardy); Registre Neuchâtelois des Tumeurs, Neuchâtel (Dr Fabio Levi); Krebsregister St. Gallen Appenzell, St. Gallen (Dr Thomas Fisch); Registre Vaudois des Tumeurs, Lausanne (Dr Fabio Levi); Kantonalzürcherisches Krebsregister, Zürich (Dr Nicole Probst).

The Netherlands – Netherlands Cancer Registry, Amsterdam (Dr Otto Visser).

United Kingdom – Office of National Statistics, London (Dr Mike Quinn); Northern Ireland Cancer Registry, Belfast (Dr Anna Gavin); Scottish Cancer Intelligence Unit, Edinburgh (Dr David Brewster).

Yugoslavia – Cancer Registry of Vojvodina, Sremska Kamenica, (Dr Marica Mikov).

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