



Non-occupational exposure to asbestos and malignant mesothelioma in the Italian National Registry of Mesotheliomas

Dario Mirabelli, Domenica Cavone, Enzo Merler, et al.

Occup Environ Med 2010 67: 792-794
doi: 10.1136/oem.2009.047019

Updated information and services can be found at:
<http://oem.bmj.com/content/67/11/792.full.html>

	<i>These include:</i>
References	This article cites 10 articles, 1 of which can be accessed free at: http://oem.bmj.com/content/67/11/792.full.html#ref-list-1
Email alerting service	Receive free email alerts when new articles cite this article. Sign up in the box at the top right corner of the online article.

Notes

To request permissions go to:
<http://group.bmj.com/group/rights-licensing/permissions>

To order reprints go to:
<http://journals.bmj.com/cgi/reprintform>

To subscribe to BMJ go to:
<http://journals.bmj.com/cgi/ep>

Non-occupational exposure to asbestos and malignant mesothelioma in the Italian National Registry of Mesotheliomas

Dario Mirabelli,¹ Domenica Cavone,² Enzo Merler,³ Valerio Gennaro,⁴ Antonio Romanelli,⁵ Carolina Mensi,⁶ Elisabetta Chellini,⁷ Carmela Nicita,⁸ Alessandro Marinaccio,⁹ Corrado Magnani,¹⁰ Marina Musti²

► Additional table and appendix are published online only. To view these files please visit the journal online (<http://oem.bmj.com>).

¹Unit of Cancer Epidemiology, CeRMS and CPO-Piemonte, University of Turin, Turin, Italy

²Occupational Health Section "Ramazzini", Department of Internal Medicine and Public Health, University of Bari, Bari, Italy

³Veneto Mesothelioma Registry, Occupational Health Unit, Department of Prevention, Padua Local Health Authority, Padua, Italy

⁴Liguria Mesothelioma Registry, Department of Epidemiology and Prevention, National Cancer Research Institute (IST), Genoa, Italy

⁵Emilia-Romagna Mesothelioma Registry, Department of Public Health, Reggio Emilia, Italy

⁶Lombardia Mesothelioma Registry, Department of Occupational and Environmental Health, Fondazione IRCCS Policlinico, Mangiagalli, Regina Elena and Center EBPI, University of Milan, Milan, Italy

⁷Unit of Environmental and Occupational Epidemiology, Cancer Prevention and Research Institute (ISPO), Florence, Italy

⁸Cancer Registry, Hospital "M.P. Arezzo", Ragusa, Italy

⁹Unit of Epidemiology, Department of Occupational Medicine, Italian National Institute for Occupational Safety and Prevention (ISPESL), Rome, Italy

¹⁰Unit of Medical Statistics and Cancer Epidemiology, CPO-Piemonte, University of Eastern Piedmont, Novara, Italy

Correspondence to

Dr Dario Mirabelli, Unit of Cancer Epidemiology, Via Santena 7, 10126 Torino (TO), Italy; dario.mirabelli@cpo.it

Accepted 20 January 2010

ABSTRACT

Background Malignant mesotheliomas are strictly related to asbestos, but in a proportion of cases no exposure can be recalled. Published estimates of this proportion have important variations. Historical and geographical differences in the fraction of cancer due to any given exposure are to be expected, but incomplete identification of non-occupational exposures may have played a role.

Methods To assess the role of non-occupational exposures in causing malignant mesotheliomas in Italy, the exposures of cases registered by the national mesothelioma registry (ReNaM) were examined. ReNaM started in 1993 in five regions and currently covers 98% of the Italian population. Information on occupational and non-occupational exposures of cases is collected whenever possible.

Results From 1993 to 2001 ReNaM registered 5173 malignant mesothelioma cases, and exposures were assessed in 3552 of them. 144 and 150 cases with exposures limited to environmental (living in the neighbourhood of an industrial or natural source of asbestos) or familial (living with a person occupationally exposed to asbestos) circumstances, respectively, were identified, accounting for 8.3% of all cases.

Conclusions Geographical variations in the proportion of cases due to non-occupational exposures may be explained by the past distribution of asbestos-using industries.

INTRODUCTION

Malignant mesotheliomas are strictly related to asbestos exposure. Nonetheless, in a proportion of cases occupational exposures cannot be recalled.¹ The proportion of attributable cases depends on the past prevalence of an exposure, so historical and geographical differences are to be expected. However, some variation in estimates from different studies may stem from incomplete ascertainment of asbestos exposure, particularly of non-occupational exposures.

Investigating the risk associated with non-occupational exposure to asbestos has never been easy due to the overwhelming severity of occupational exposures, and the difficulty of defining which patterns of environmental exposure to an agent so ubiquitous could be relevant. Estimates of the dose-response relationship between asbestos and malignant mesothelioma at environmental levels of

What this paper adds

- It has long been recognised that non-occupational, presumably low-level, exposures to asbestos can cause malignant mesothelioma.
- We found that at least 8.3% of all mesothelioma cases occurring currently in Italy are due to non-occupational exposures. They are younger than average and are not entitled to compensation.
- The occurrence of these cases shows that "controlled use" of asbestos had never been achieved in Italy.
- Failure to recognise cases due to non-occupational exposures may lead to underestimation of the proportion of asbestos-related mesotheliomas.

exposure and of the risk due to environmental and household exposures are, therefore, recent.²⁻³

Italy has been a significant producer and user of asbestos.⁴ Furthermore, non-occupational exposures to asbestos have been an important cause of malignant mesothelioma in certain settings.⁵⁻⁹ But to what extent have they played a role in causing malignant mesotheliomas at a national level? A national mesothelioma registry (ReNaM) has operated since 1993 at the National Institute for Occupational Safety and Prevention (ISPESL).¹⁰ ReNaM runs a network of regional operating centres (CORs) maintaining a national database. We summarised data from the ReNaM database on cases with exposures classified as environmental (living in the neighbourhood of an industrial or natural source of asbestos) or familial (living with a person occupationally exposed to asbestos), to assess the relevance in Italy of past non-occupational exposures to asbestos.

SUBJECTS AND METHODS

CORs seek information from cases or a respondent (usually a next-of-kin) using a structured questionnaire supplemented by job-specific modules administered by trained interviewers. Life-long occupational and residential histories are collected, along with descriptions of the occupations held by the persons with whom the patients lived, of the materials used at home that could contain asbestos, and of other activities that could have involved asbestos exposure.

All these circumstances are assessed for asbestos exposure. To this purpose, raters supplement the description of exposure circumstances recorded in the questionnaires with information available from occupational health and safety units and regional environmental protection agencies. Ad hoc enquiries may also be carried out. Each circumstance is then classified according to the categories described in the online appendix. Since an individual may have incurred many exposure circumstances, each malignant mesothelioma case is assigned to his/her most severe exposure category, as an overall assessment. A conventional severity ranking is used (described in the online appendix). In particular, cases are classified as environmental malignant mesothelioma if (i) they are considered neither work-related nor due to familial exposures, and (ii) the patient lived near a source of asbestos pollution, taking into account the distance of their residence from the source, the amount of pollution produced and other factors such as wind direction, etc. As first-line criteria we used those described by Magnani *et al* in their appendix 1.³

We abstracted the records of all cases without occupational exposure and with either environmental or familial exposure, as defined in the online appendix, as categories 4 and 5. Their exposure assessment was revised for consistency with these definitions.

We computed standardised incidence rates for malignant mesotheliomas by sex and region, the proportion of cases with exposure classified as familial or environmental, and distribution by the industrial activity of their exposure circumstances. As cases could have multiple exposures, we considered only familial exposure circumstances for all individuals classified as familial cases, ignoring, if any, their environmental exposures. Cases classified as being environmental in origin by definition could not have familial exposures.

All calculations and statistical tests were carried out with the software package Stata 9.2.¹¹

RESULTS

Out of 5173 malignant mesothelioma cases (3746 men, 1427 women) registered between 1993 and 2001, exposure assessment was available for 3552 (2702 men, 850 women). For the remaining 1621 cases no interview, and thus no information on exposure, was available; women represented 35.5% of this group

compared with 23.9% of the group with exposure assessment ($p < 0.001$).

We found 294 cases (8.3% of those with exposure assessment) with at least one episode classified as environmental (144 cases) or familial (150 cases) exposure and without any evidence of occupational exposure. Their distribution by sex and region and the corresponding incidence rates are shown in the online supplementary table. There were major geographical differences in the proportion of malignant mesothelioma cases with exposure classified as environmental and familial (considered together), ranging from 24% in Piedmont to 2% in Tuscany. The male/female ratio ranged from 1:6.6 in Liguria to 1:1 in Sicily.

These patients were relatively young: 18% were less than 54 years old and 45% less than 64 years old. The average age at diagnosis was 65.0 years (95% CI 63.6 to 66.5), compared with 67.4 years for all ReNaM cases. Women represented 51% of all cases with environmental exposure, but 84% of those with familial exposure.

In table 1, the industrial activities assessed as having caused exposure are shown. As an individual may have had multiple exposures, 371 exposure circumstances were registered.

Environmental exposure assessment

There were multiple exposures, and 190 exposure circumstances were identified; more than one in three (74) were classified as due to residence in the neighbourhood of an asbestos-cement plant, in areas that were considered affected by its airborne emissions. The others were related to various activities, well recognised for their past use of asbestos or asbestos-containing materials.

Familial exposure assessment

Overall, 181 familial exposure circumstances were reported. Most often a close relative, a parent or a spouse, had been employed in activities or professions entailing exposure to asbestos.

DISCUSSION

Large geographical variations in the proportion of cases linked to environmental or familial exposures were observed. Specific areas where non-occupational cases constitute a substantial proportion of all malignant mesotheliomas had already been

Table 1 Malignant mesotheliomas from environmental and familial exposures, by industrial activity

Industrial activity	Environmental exposure		Familial exposure		Total	
	No.	(%)	No.	(%)	No.	(%)
Asbestos cement production	74	(39)	22	(12)	96	(26)
Asbestos textiles production	9	(5)	9	(5)	18	(5)
Asbestos mining	2	(1)	0	(0)	2	(1)
Shipyards	8	(4)	21	(12)	29	(8)
Railway carriage production/maintenance	4	(2)	11	(6)	15	(4)
Construction industry	0	(0)	18	(10)	18	(5)
Steel mills and iron foundries	9	(5)	9	(5)	18	(5)
Chemical/petrochemical plants, rubber industry	5	(3)	6	(3)	11	(3)
Power plants	1	(1)	6	(3)	7	(2)
Railways	11	(6)	8	(4)	19	(5)
Pipe fitting, heating system installation	0	(0)	11	(6)	11	(3)
Other activities	67	(35)	60	(33)	127	(34)
Overall number of exposure circumstances	190	(100%)	181	(100%)	371	(100%)
Overall number of cases	144		150		294	

Short report

recognised in Casale Monferrato, the Turin metropolitan area (Piedmont), Broni (Lombardia), La Spezia (Liguria) and Bari (Apulia), where important asbestos industries were located.^{3 5-9}

Italy exported some of the asbestos mined in Balangero (Piedmont) and imported Canadian and South African asbestos.⁴ Genoa (Liguria), Leghorn (Tuscany), Trieste (Friuli Venezia Giulia) and Venice (Veneto) were the busiest ports in the asbestos trade.¹²

Shipbuilding has been an important industry in Italy; it involved considerable use of asbestos and large numbers of exposed workers, as in many other countries.¹² Rolling stock production and repair also entailed use of asbestos, including crocidolite, and many exposed workers. Asbestos-cement production has been the main asbestos using industry. The first and largest Italian plant started in 1907 in Casale Monferrato (Piedmont), the second and second largest in Broni (Lombardy) in 1932, followed by many others; 37 plants were identified in a historical study on this trade (planned for publication elsewhere). The main shipyards, the number of railway carriage building and repair facilities and the number of asbestos-cement plants by region are reported in the supplementary online table.

Other industries producing asbestos-containing materials, such as asbestos textiles, linings for brakes and clutches, and asbestos cardboard and packing, were mainly located in Piedmont.

In this study the past distribution of major sources of asbestos pollution explains important variations in the occurrence of malignant mesothelioma due to non-occupational exposures. However, another source of variation might lie in differences across CORs in the quality of information (quality of interview) and/or in the application of criteria to identify non-occupational exposures. As quality control of interviews and of exposure assessment is conducted only at the COR level and no national panel is currently appointed for this purpose, we are unable to estimate the extent of this potential bias which could have increased inter-regional variations. We expect, however, that its main consequence would be underestimation of the number of environmental or familial cases of malignant mesothelioma, with those that are unrecognised falling into the category of 'unknown' aetiology. Another possible cause of underestimation of the proportion of environmental or familial cases is the over-representation of women among the cases for whom we lack information on exposures, considering that the prevalence of environmental or familial cases is highest among women. Lastly, all cases with at least one occupational exposure have been excluded from the present study; nevertheless, a definite and long lasting non-occupational exposure might be a more important contributory cause of malignant mesothelioma than a possible, but uncertain, occupational exposure (or a short or recent one). Therefore, it is likely that we underestimated the role of environmental and familial exposures in the aetiology of malignant mesothelioma. Despite these limitations, they explained 8.3% of all cases.

In conclusion, this is the first attempt to estimate the proportion of malignant mesotheliomas due to non-occupational exposures by direct enumeration rather than extrapolation from studies conducted in small populations with high exposures. Environmental and familial exposures accounted for a substantial proportion of all Italian malignant mesothelioma cases. Failure to recognise their aetiology would have led ReNaM

to underestimate the fraction of malignant mesotheliomas attributable to asbestos exposure.

Boffetta *et al* estimated that non-occupational cases might represent 11% of all malignant mesothelioma cases, but warned that this could be an over-estimate.¹³ Our findings are in general agreement with their results and are particularly disturbing in a country with a long industrial history. Moreover, non-occupational cases of malignant mesothelioma were younger than usual, unaware of the risks they were exposed to and have not hitherto been entitled to compensation. These features suggest that in Italy 'controlled' use of asbestos was not successful. Furthermore, non-occupational asbestos exposures may have continued until recently and may, in part, still continue today, sustaining the epidemic of malignant mesothelioma in Italy.

Acknowledgements We are indebted to Stefano Silvestri, Unit of Environmental and Occupational Epidemiology, Cancer Prevention and Research Institute (ISPO), Florence, Italy, who developed the criteria for exposure assessment, and to Massimo Nesti, Department of Occupational Medicine, Italian National Institute for Occupational Safety and Prevention (ISPESL), Rome, Italy, former director of ReNaM.

Funding ReNaM is financed by ISPESL. The units of epidemiology or occupational health hosting the regional operating centres belong to the national health service and are financed by their health authorities.

Competing interests None.

Contributors DM and DC wrote the article. AM conducted the analyses. All authors contributed data from their regional mesothelioma registries, discussed the results, and critically reviewed the manuscript.

Provenance and peer review Not commissioned; externally peer reviewed.

REFERENCES

1. Gardner MJ, Saracci R. Effects on health of non-occupational exposure to airborne mineral fibres. *IARC Sci Publ* 1989;375-97.
2. Hansen J, De Klerk NH, Musk AW, *et al*. Environmental exposure to crocidolite and mesothelioma. Exposure-response relationships. *Am J Respir Crit Care Med* 1998;157:68-75.
3. Magnani C, Agudo A, González CA, *et al*. Multicentric study on malignant pleural mesothelioma and non-occupational exposure to asbestos. *Br J Cancer* 2000;83:104-11.
4. Marinaccio A, Montanaro F, Mastrantonio M, *et al*. Predictions of mortality from pleural mesothelioma in Italy: a model based on asbestos consumption figures supports results from age-period-cohort models. *Int J Cancer* 2005;115:142-7.
5. Dodoli D, Del Nevo M, Fiumalbi C, *et al*. Environmental household exposures to asbestos and occurrence of pleural mesothelioma. *Am J Ind Med* 1992;21:681-7.
6. Magnani C, Dalmasso P, Biggeri A, *et al*. Increased risk of malignant mesothelioma of the pleura after residential or domestic exposure to asbestos: a case-control study in Casale Monferrato, Italy. *Environ Health Perspect* 2001;109:915-19.
7. Amendola P, Belli S, Binazzi A, *et al*. La mortalità per tumore maligno della pleura a Broni (Pavia), 1980-1997. [In Italian]. *Epidemiol Prev* 2003;27:86-90.
8. Musti M, Pollice A, Cavone D, *et al*. The relationship between malignant mesothelioma and an asbestos cement plant environmental risk: a spatial case-control study in the city of Bari (Italy). *Int Arch Occup Environ Health* 2009;82:489-97.
9. Ferrante D, Bertolotti M, Todesco A, *et al*. Cancer mortality and incidence of mesothelioma in a cohort of wives of asbestos workers in Casale Monferrato, Italy. *Environ Health Perspect* 2007;115:1401-5.
10. Nesti M, Marinaccio A, Chellini E. Malignant mesothelioma in Italy, 1997. *Am J Ind Med* 2004;45:55-62.
11. Stata 9.2 Statacorp Lakeway Drive, College Station, Texas 2007.
12. Mastrantonio M, Belli S, Binazzi A, *et al*. La mortalità per tumore maligno della pleura nei comuni italiani (1988-1997). [In Italian]. *Rapporti Istitisan* 02/12. <http://www.salute.gov.it/resources/static/primopiano/amianto/istisan.pdf> (accessed 30 Sep 2009).
13. Boffetta P, McLaughlin JK, La Vecchia C, *et al*. "Environment" in cancer causation and etiological fraction: limitations and ambiguities. *Carcinogenesis* 2007;28:913-15.