



ORIGINAL ARTICLE

Malignant mesothelioma due to non-occupational asbestos exposure from the Italian national surveillance system (ReNaM): epidemiology and public health issues

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ABSTRACT

Introduction Italy produced and imported a large amount of raw asbestos, up to the ban in 1992, with a peak in the period between 1976 and 1980 at about 160 000 tons/year. The National Register of Mesotheliomas (ReNaM, "Registro Nazionale dei Mesoteliomi" in Italian), a surveillance system of mesothelioma incidence, has been active since 2002, operating through a regional structure.

Methods The Operating Regional Center (COR) actively researches cases and defines asbestos exposure on the basis of national guidelines. Diagnostic, demographic and exposure characteristics of non-occupationally exposed cases are analysed and described with respect to occupationally exposed cases.

Results Standardised incidence rates for pleural mesothelioma in 2008 were 3.84 (per 100 000) for men and 1.45 for women, respectively. Among the 15 845 mesothelioma cases registered between 1993 and 2008, exposure to asbestos fibres was investigated for 12 065 individuals (76.1%), identifying 530 (4.4%) with familial exposure (they lived with an occupationally exposed cohabitant), 514 (4.3%) with environmental exposure to asbestos (they lived near sources of asbestos pollution and were never occupationally exposed) and 188 (1.6%) exposed through hobby-related or other leisure activities. Clusters of cases due to environmental exposure are mainly related to the presence of asbestos-cement industry plants (Casale Monferrato, Broni, Bari), to shipbuilding and repair activities (Monfalcone, Trieste, La Spezia, Genova) and soil contamination (Biancavilla in Sicily).

Conclusions Asbestos pollution outside the workplace contributes significantly to the burden of asbestos-related diseases, suggesting the need to prevent exposures and to discuss how to deal with compensation rights for malignant mesothelioma cases induced by non-occupational exposure to asbestos.

INTRODUCTION

Asbestos is a natural fibrous mineral of hydrate silicates, generally classified in amphiboles (actinolite,

What this paper adds

- ▶ Malignant mesothelioma is a rare tumour which can also occur after low levels of asbestos exposure.
- ▶ Epidemiological analytical studies have repeatedly reported a significant risk of mesothelioma for people exposed to asbestos in non-occupational settings.
- ▶ We documented that 10.2% of mesothelioma cases are due to non-occupational exposure to asbestos as suggested by the findings of a large epidemiological national surveillance system (15 845 cases and 12 065 individuals interviewed).
- ▶ The most significant source of risk is cohabitation with an occupationally exposed patient or residence near an asbestos cement plant; asbestos exposure during leisure activities is difficult to identify and probably underestimated.
- ▶ It is necessary to define policies and strategies for increasing prevention tools and for dealing with compensation rights for malignant mesothelioma cases induced by non-occupational exposure to asbestos.

amosite, anthophyllite, crocidolite and tremolite) and serpentine (chrysotile), showing different chemical and physical properties. It has unusual characteristics of plasticity and properties of high tensile strength, and thermal and chemical resistance.

Recently, the International Agency for Research on Cancer confirmed all forms of asbestos as carcinogenic for humans (group 1). There is sufficient evidence that asbestos causes mesothelioma and cancer of the lung, larynx and ovary. Positive associations have also been observed between exposure to all forms of asbestos cancer (malignant mesothelioma) and cancer of the pharynx, stomach,



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colon and rectum.¹ Malignant mesothelioma (MM) is a tumour arising from the serous membranes of the pleura and, less frequently, of the peritoneal and pericardial cavities and from the testis tunica vaginalis. Prognosis is poor and average survival is 9–12 months from diagnosis for pleural and even lower for peritoneal forms.

Many western countries are currently going through an MM epidemic, considering the extensive use of asbestos between the 1950s and the 1980s in several industrial applications and the long latency period (around 40 years) from the beginning of exposure. Moreover, asbestos is still extensively used in many countries in Asia, South America, Africa and in the former Soviet Union; at present, 125 million people have been estimated to be exposed to asbestos worldwide.²

In the countries that have banned asbestos, the majority of asbestos-related diseases are caused by occupational exposure that occurred in the past. Nevertheless, assessment of the spread and of the health effects of non-occupational asbestos exposure continues to be of great public interest because it is related to peculiar exposure circumstances like living with asbestos workers or close to asbestos mines or manufacturing plants, or naturally occurring asbestos fibres, or in asbestos-insulated buildings.³ In the past four decades, excesses of incidence of mesothelioma and cancer of the lung have been reported as a consequence of the natural presence of asbestos (or asbestos-like) material in rural areas in Turkey,⁴ Greece,⁵ Corsica in France,⁶ Biancavilla (Sicily) in Italy,⁷ New Caledonia,⁸ China⁹ and California in the USA.¹⁰ The increased risk of cancer for population groups resident in the vicinity of raw asbestos production sites (mines or mills), as well as for people living close to industrial manufacturing plants producing material containing asbestos, has been demonstrated.^{11–13}

In Italy, 3 748 550 tons of raw asbestos were produced up to the 1992 ban, with a peak between 1976 and 1980 at more than 160 000 tons/year; asbestos consumption decreased in Italy since 1980s only (around ten years later with respect to other industrialised countries).¹⁴ As environmental exposure related to residence near asbestos-cement plants has been repeatedly reported for Casale Monferrato,¹⁵ Bari,¹⁶ Broni¹⁷ and La Spezia,¹⁸ this usage pattern may have led to sustained non-occupational exposures. The contribution of different patterns of non-occupational exposures is most likely underestimated, due to their much lower level, which, however, is not negligible and is possibly sufficient to cause disease. A permanent surveillance system of mesothelioma incidence in Italy has been run since 2002 by the National Register of Malignant Mesotheliomas (ReNaM, “Registro Nazionale dei Mesoteliomi” in Italian) identifying cases and assessing asbestos exposure.¹⁹

The purpose of the present study is to present data about non-occupationally exposed MM case currently available in the ReNaM archive. The figure is discussed with respect to compensation and welfare system efficiency for people exposed in the past and to asbestos exposure prevention strategies for the present.

METHODS

The epidemiological surveillance of mesothelioma incidence is conducted in Italy by a specific register drawn up, by law, in 2002. ReNaM has a regional structure: a Regional Operating Centre (COR) has gradually been established in all Italian regions except the Molise region and an autonomous province of Bolzano, covering almost the whole country (98.5% of the Italian population). Each COR works applying the national standardised methods described in the specific guidelines.²⁰ They

actively search for MM cases by obtaining information from healthcare institutions that diagnose and treat cases (especially pathology units and lung care and chest surgery wards). Diagnostic coding criteria have been established by means of a grid according to three classes of decreasing level of certainty: certain, probable and possible MM. Occupational history, lifestyle and residential history are obtained using a standardised questionnaire, administered by a trained interviewer, to the patient or to the next of kin after informed consent expressed by the cases or their relatives at the beginning of the interview. CORs may consult local public health and safety agencies to gain supplementary information on occupational and/or residential exposure. In each COR, an industrial hygienist, or a panel of industrial hygienists, classifies and codes the exposure by examining the information collected. Moreover, an agreement between the Italian Workers' Compensation Authority (INAIL) and the Italian Social Security Institute (INPS) makes it possible to retrieve pension contributions from personal data. Therefore, in many cases, INAIL may provide CORs with information about occupational histories of mesothelioma cases, either as a confirmation of information obtained directly from the patient, or as a major information source when the interview is not available.

Occupational exposure classification can be assigned as definite, probable or possible. Definite occupational exposure refers to people whose work has involved the use of asbestos or materials containing asbestos. Probable occupational exposure refers to people who have worked in a firm where asbestos was certainly used, but whose exposure cannot be documented, and possible occupational exposure to people who have worked in firms in an economic sector where asbestos has been used. Further, specific codes are assigned to familial exposure (when patients have lived with a person occupationally exposed to asbestos), environmental (residence near a source of asbestos pollution without work-related exposure) and leisure activities. Modalities of exposure are assigned with an exclusive and hierarchical methodology: cases defined as ‘familial exposure’ had no occupational exposure, whereas cases having ‘environmental exposure’ had neither familial nor occupational exposure. Finally, cases classified as due to ‘leisure activities exposure’ had no other relevant circumstances of exposure. The data collected by each COR are then periodically sent to ReNaM and stored in a centralised database. All procedures and systems of classifications and codes are more extensively described in the aforementioned guidelines.

To date, ReNaM has collected cases with a diagnosis of MM in the period 1993–2008; the collection and analyses of data for the period of incidence 2009–2012 are ongoing. Italian regions did not contribute homogeneously during this period: Piedmont, Veneto, Tuscany and Apulia produced incidence regional data starting from 1993, Basilicata from 1995, Liguria, Emilia-Romagna and Marche from 1996, Sicily from 1998, Lombardy, Friuli-Venezia Giulia and Valle D'Aosta from 2000, Campania from 2001 and Umbria from 2006. The data from Calabria and Sardinia cannot be considered complete with regard to the incidence of the disease. Finally, Trentino Alto-Adige only collected data for the province of Trento (half of the resident people and territorial extension of the Region). The province of Bolzano and Molise region have still not contributed to the network. Standardised incidence rates have been calculated with the direct method for the territorial coverage of incidence data and with population at the national census at 2001 used as the denominator and for age standardisation. The exposure data analyses pertain to the whole ReNaM database

including data from regions with incomplete incidence figures. All statistical analyses were carried out with the SPSS software (V21.0).

RESULTS

In the period between 1993 and 2008, a list of 15 845 cases of MM were identified. The pleural site was reported in 93% (14 736 cases), while peritoneal cases accounted for 6.4% of the total number (1017 cases); pericardial and testicular cases accounted for 0.3% (41 and 51 cases, respectively). The male/female ratio was 2.6 among pleural cases, and 1.4 and 1.9 among peritoneal and pericardial ones, respectively. The mean age at diagnosis was 68.3 years (SD±10.6) in men and 69.8 (SD±11.6) in women. People aged less than 45 years were rare, accounting for 2.4% of all recorded MM cases. The standardised incidence rate for pleural mesothelioma (certain, probable and possible) in 2008 was 3.84 cases per 100 000 inhabitants for men and 1.45 for women; 0.26 and 0.12, respectively, for the peritoneal site and less than 1 case per million inhabitants for pericardial and tunica vaginalis testis forms. The modalities of exposure to asbestos fibres were investigated for 12 065 (76.1%) of the 15 845 cases collected. This percentage was not constant geographically and showed great variability (higher than 90% in Lombardy, Tuscany, Apulia, Umbria and the province of Trento; lower than 50% in Sicily, Campania and Calabria). For 8367 cases (69.3% of the 12 065 cases for which the exposure definition is available), the modalities of asbestos exposure were classified as occupational (definite, probable, possible); for 2466 cases (20.4%), we found no asbestos exposure.¹⁹

The list of cases defined as non-occupationally exposed includes 1232 individuals. We found 530 (4.4%) MM cases with familial exposure (they have lived with a person who was occupationally exposed), 514 MM cases (4.3%) with environmental exposure to asbestos (they lived near sources of asbestos pollution and have not been occupationally exposed) and 188 (1.6%) with exposure due to hobby-related or leisure activities. The proportion of MM cases due to non-occupational asbestos exposure (familial, environmental or related to leisure activities) was 10.2% at the national level with significant territorial variability and the highest values in Piedmont (24.4%), Trento autonomous province (15.6%), Puglia (14.4%) and Veneto (13.5%). The female/male ratio was 2.3:1 for the whole population with non-occupational exposure, but it reached the value of 5.9:1 focusing on MM cases with exclusively familial modalities of exposure.

Table 1 shows the demographic, diagnostic and personal history characteristics of the 1232 MM cases with non-occupational exposure to asbestos. As an individual may have had multiple exposure, 1427 causally relevant exposures were registered for the 1232 cases included in the analysis. Table 2 describes these 1427 modalities of exposures in detail. For the 530 cases classified as having familial aetiology, we considered only familial exposure circumstances, ignoring environmental exposures, if any. This choice is consistent with recent simulations of low-level exposed workers that show asbestos levels commensurate with background concentrations in those exposed domestically.²¹

In table 3, occupationally and non-occupationally exposed MM cases are compared with respect to selected epidemiological parameters. A statistically significant difference in mean age at diagnosis was found between occupationally and non-occupationally exposed cases (68.1 vs 67.2 years, $p<0.01$) and in non-occupationally exposed cases by gender (66 vs 68 years for men and women, respectively, $p<0.05$). The values range from

69.3 years (SD±11.01) for leisure exposed to 67.5 (SD±11.8) for familial and 66.1 (SD±13.6) for environmental, with a statistically significant difference by gender in familial cases ($p<0.0001$): 68 (SD±11.5) in women versus 63 (SD±12.6) years in men. Mean age at first exposure was lower among those with non-occupational exposure compared to the occupational cases (18.5 vs 22.5 years, $p<0.0001$). Latency time, defined as the time elapsing between the beginning of asbestos exposure and MM diagnosis, shows higher median values overall for non-occupational exposure than occupational exposure (46 years, SD±12): 51 years (SD±14) in familial exposures (although lower in women, 49.5 years, than in men, 55 years) and 49 years (SD±16) in environmental exposures (again lower in women, 47 years, than in men, 53 years). Conversely, in leisure activities, the median latency times is 43.5 years, significantly different by gender (48 vs 37 years, respectively, for men and women, $p<0.001$).

Figure 1 shows the geographical distribution of MM cases due to familial, environmental and leisure activities collected by

Table 1 MM cases (N, %) collected by the National Mesothelioma Register (ReNaM) due to familial, environmental and leisure activity exposure by gender, age, anatomical site, period of diagnosis, level of diagnostic certainty, morphology and modalities of interview (Italy, 1993–2008)

	Men		Women	
	N	Per cent	N	Per cent
Exposure modalities				
Familial	77	20.6	453	52.8
Environmental	217	58.0	297	34.6
Leisure activities	80	21.4	108	12.6
Pleural	348	93.0	801	93.4
Anatomical sites				
Peritoneum	23	6.1	56	6.5
Pericardium	0	0.0	1	0.1
Tunica vaginalis of the testis	3	0.8	–	–
Age classes				
0–44	24	6.4	36	4.2
45–64	147	39.3	276	32.2
65–74	93	24.9	274	31.9
+75	110	29.4	272	31.7
1993–1996	42	11.2	62	7.2
1997–2000	86	23.0	172	20.0
Period of diagnosis				
2001–2004	125	33.4	327	38.1
2005–2008	121	32.4	297	34.6
Diagnostic certainty				
MM certain	318	85.0	700	81.6
MM probable or possible	56	15.0	158	18.4
Morphology				
Epithelioid	226	60.4	523	61.0
Fibrous	40	10.7	50	5.8
Biphasic	46	12.3	93	10.8
MM NOS	36	9.6	107	12.5
Not available	26	7.0	85	9.9
Exposure detection				
Direct interview	200	53.5	392	45.7
Indirect interview	173	46.3	464	54.1
No interview, other information source	1	0.3	2	0.2
Overall	374	100.0	858	100.0

MM, malignant mesothelioma; NOS, not otherwise specified.

Table 2 Modalities of exposure of malignant mesothelioma (MM) cases (N, %) collected by the National Mesothelioma Register (ReNaM) disentangled by familial, environmental or leisure activity exposure categories and gender (Italy, 1993–2008)

	Men		Women	
	Number of exposures*	Per cent	Number of exposures*	Per cent
Familial: <i>cohabitation with</i> (530 MM cases)				
Parents	74	74.0	138	23.9
Husband/wife	3	3.0	354	61.4
Son/daughter	5	5.0	27	4.7
Other cohabitants	18	18.0	58	10.1
Overall	100	100	577	100
Environmental: <i>residence near</i> (514 MM cases)				
Asbestos cement plant	103	43.6	144	44.6
Railways	18	7.6	22	6.8
Rail stock building, repair and demolition plant	10	4.2	7	2.2
Docks	8	3.4	6	1.9
Shipbuilding and repair	8	3.4	7	2.2
Steel industry plants	2	0.8	12	3.7
Chemical or petrochemical plants	7	3.0	8	2.5
Mines or mills	7	3.0	9	2.8
Others	73	30.9	108	33.4
Overall	236	100	323	100
Use of asbestos materials containing asbestos†	29	34.5	92	80.7
Home masonry	25	29.8	3	2.6
Thermal insulation at home	9	10.7	2	1.8
Leisure activities (188 MM cases)				
Plumbing or electric repair at home	2	2.4	2	1.8
Car repair	4	4.8	—	—
Other activities	15	17.9	15	13.2
Overall	84	100	114	100

*The number of exposures exceeds the number of mesothelioma cases due to the possibility of multiple exposures for a single case.

†Including exposures due to the presence of asbestos in objects not used in a working context (eg, ironing boards, rural tool sheds).

ReNaM in the Italian territory. The map makes it possible to identify the areas of asbestos pollution contamination due to the presence of asbestos-cement industry plants (Casale Monferrato,

Broni and Bari), areas of shipbuilding and repair (Monfalcone, Trieste, La Spezia, Genova, Castellamare di Stabia, Livorno and Taranto) and areas of environmental exposure in Biancavilla

Table 3 Mean age at diagnosis.

	Number	Years (SD)	p Value
<i>Mean age at diagnosis</i>			
Occupational exposure	8367	68.1 (±10)	Ref
Non-occupational exposure	1232	67.2 (±12.3)	<0.01
Familial	530	67.5 (±11.8)	0.161
Environmental	514	66.1 (±13.6)	<0.001
Leisure activities	188	69.3 (±11.01)	0.108
<i>Mean age at first exposure</i>			
Occupational exposure	8367	22.5 (±8.3)	Ref
Non-occupational exposure	1232	18.5 (±15.6)	<0.001
Familial	530	17 (±14.3)	<0.001
Environmental	514	17 (±16.2)	<0.001
Leisure activities	188	27 (±14.5)	<0.001
<i>Median latency</i>			
Occupational exposure	8367	46 (±12)	Ref
Non-occupational exposure	1232	49 (±15)	<0.001
Familial	530	51 (±14)	<0.001
Environmental	514	49.5 (±16)	<0.001
Leisure activities	188	43 (±14.1)	<0.01

Mean age at first exposure and median latency period of malignant mesothelioma cases collected by the National Mesothelioma Register (ReNaM) by modalities of exposure (Italy, 1993–2008).

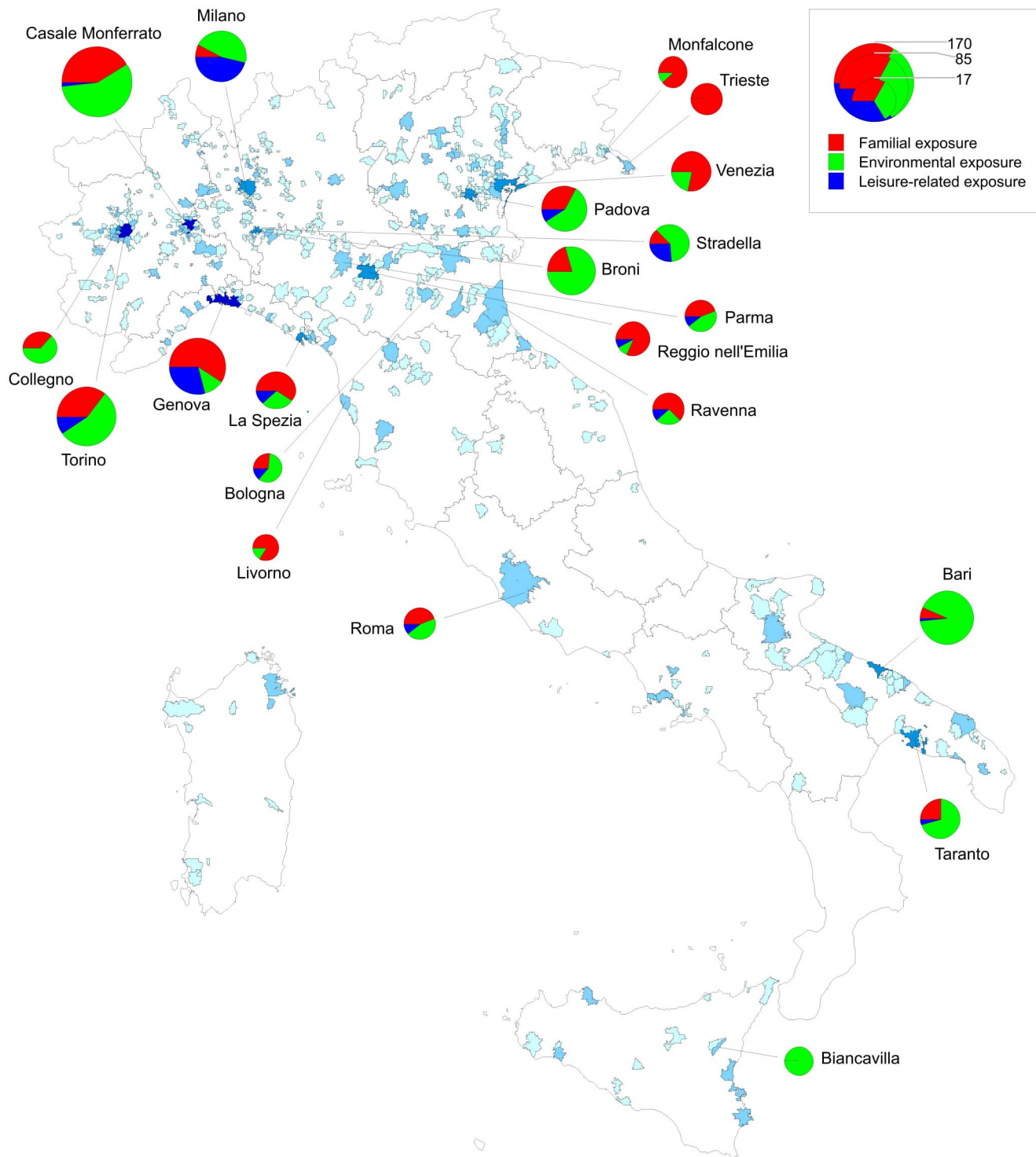


Figure 1 Geographical distribution of malignant mesothelioma (MM) cases due to environmental, familial, leisure activities collected by the National Mesothelioma Register (ReNaM) by municipalities of residence at diagnosis. Italy, 1993–2008. Labels and circle graphs are reported for municipalities with at least six MM cases with environmental (E, in green) or familial (F, in red) or leisure activities-related (L, in blue) exposure to asbestos. Selected municipalities are Casale Monferrato (92 MM cases due to environmental exposure in the period, 68 due to familial exposure, 4 leisure activities-related exposure), Torino (37, 25, 7), Collegno (7, 4, 0) in Piedmont; Genova (6, 32, 16), La Spezia (4, 9, 2) in Liguria; Milano (18, 3, 18), Broni (26, 7, 0), Stradella (9, 2, 4) in Lombardy; Padova (12, 7, 2), Venezia (4, 14, 0) in Veneto; Trieste (0, 9, 0), Monfalcone (1, 7, 0) in Friuli-Venezia Giulia; Reggio Emilia (1, 9, 1), Bologna (4, 2, 1), Parma (4, 4, 1), Ravenna (2, 5, 1) in Emilia-Romagna; Livorno (1, 5, 0) in Tuscany; Roma (4, 4, 1) in Lazio; Bari (42, 3, 1), Taranto (13, 5, 1) in Apulia; Biancavilla (7, 0, 0) in Sicily.

(Sicily) due to the local presence of fluoroedenite (an amphibole asbestiform mineral), a contaminating material massively used for construction and road paving in the area.

DISCUSSION

MM is a major public health issue considering the increasing incidence in many countries; the still complex and difficult

diagnosis, staging and treatment; the poor prognosis, which is not improving, and the implications for welfare and insurance systems due to the occupational origin for many patients. The close relationship with asbestos exposure has been demonstrated by a large amount of data, although the recognition of pathogenetic mechanisms is still incomplete. All forms of asbestos cause mesothelioma, prevalently of the pleura but also of the serous membranes of the peritoneum, lung, ovary and larynx cancers. A positive association has been reported for cancers of the colon and rectum, stomach and pharynx.¹ Asbestos has been banned in many industrialised countries but is still mined and used in a large part of the world.²² As a legacy of the massive use of asbestos, Italy is today one of the countries most involved in the monitoring, surveillance and control of asbestos-related diseases.²³ Similar experiences to the Italian mesothelioma incidence surveillance system, with regard to methods and extension, are scarce and, to the best of our knowledge, currently ongoing only in France²⁴ and Australia.²⁵

Critical limitations of the ReNaM data set have to be discussed preliminarily. Some regions of the Italian network were collecting incidence cases even before the beginning of the national register in 1993, but others started later or are not yet participating. Any evaluation of the trend of MM incidence is therefore strongly limited. The ability/effectiveness to identify the modalities of exposure is not fully consistent between regions and the percentage of patients interviewed varies between 45% and 95% depending on the available resources and knowledge. COR's activities began not at the same year, as started in Methods, and this could influence incidence and asbestos exposure findings. Although the coding and classifying systems (for diagnosis and exposure) such as the questionnaire for the anamnestic survey and the operative procedure are nationally established, nevertheless the possible lack of homogeneity among CORs in the practice is a crucial and real issue. The identification and assessment of the different asbestos exposure modalities actually represents a key factor of the ReNaM register that can help in defining the strategies to prevent the health risks/effects for the population and to guarantee a proper welfare protection. At present in Italy, the issue of insurance and welfare protection for mesothelioma cases due to non-occupational exposure to asbestos is under debate. Different modalities of non-occupational exposure to asbestos pose different concerns with respect to the welfare protection framework.

Environmental exposure from naturally occurring asbestos contamination of the soil has been documented in Turkey, where mesothelioma epidemics due to the presence of tremolite, chrysotile and erionite, belonging to the zeolite family, have been proved.²⁶ In Greece, a high frequency of pleural calcification was found in patients living in places where no industrial use of asbestos was documented in the past, but tremolite fibres have been found in the soil used to make whitewash that was commonly applied to homes in the affected areas.²⁷ Natural contamination of the soil with tremolite fibres has also been detected in Cyprus²⁸ and Corsica,⁶ as evidenced by occurrences of asbestos-related diseases without any asbestos use for industrial applications. Similarly, cases of pleural mesothelioma in New Caledonia have been signalled due to the use of a white-wash material primarily containing tremolite fibres,²⁹ and in Chinese rural areas they appear to be related to the presence of crocidolite outcrops.⁹ Cases of mesothelioma have been found in the town of Libby (Montana, USA), close to which there operated the world's largest vermiculite mine, vermiculite being extensively used in the surrounding residential zone,¹¹ and in the township of Wittenoom (Western Australia), where a

crocidolite mine was active from 1943 to 1966 with extensive use of the tailings to pave roads, footpaths and school playgrounds.³⁰ In Italy, three MM cases due to tremolite pollution in a rural area of Basilicata have been signalled,³¹ while in the area of Biancavilla Etnea (Sicily) an excess of mortality due to pleural tumours has been observed and subsequent analyses have confirmed the causal role of a mine in the neighbourhood extracting a fluoroedenite-contaminated material massively used for construction and road paving.⁷ The risk of mesothelioma associated with local industrial sources was clearly demonstrated for the neighbouring populations.^{32–33} The spatial variation in the mesothelioma risk in an area highly polluted by the asbestos-cement plant in Casale Monferrato has been discussed, adjusting for occupational and domestic exposures, highlighting the fact that the effect on the general population of pollution from industrial sources decreases with increasing distance from the factory.³⁴ Mesothelioma cases due to cohabitation with exposed people have been attributed to soiled work clothes brought home. An Italian cohort study of wives of Casale Monferrato asbestos-cement factory workers showed a large excess of pleural mesothelioma (standardised mortality ratio, SMR=18.00, 21 observed vs 1.2 expected).³⁵ Evidence is also accumulating about passive asbestos exposure in asbestos-containing buildings, such as public offices or schools, where the people involved have no awareness of direct physical contact with asbestos-containing material.³⁶

Estimates of the proportion of individuals non-occupationally exposed to asbestos, as well as of the relative contribution of non-occupational and occupational exposures to incidence, are rarely available,³⁷ although analyses of the incident trend for MM cases for different categories of exposure are reported.³⁸ Our study provides a reliable estimation of 10% (1232 cases) for MM cases due to non-occupational asbestos exposure based on more than 15 845 detected cases, of which 12 065 were individually interviewed. This estimate is strongly related to specific Italian patterns of exposure. The distribution of modalities of exposure shows that familial exposure is the most frequent in non-occupationally exposed cases, although it has to be considered that asbestos exposure during leisure activities is difficult to identify and probably underestimated. Residence near asbestos cement plants is largely predominant in the environmentally exposed patients. However, the analytical description of living conditions (historical residence) and habits (leisure time and hobby activities) involved in the risk of asbestos exposure remains of great value for primary prevention and public health policies.

The design of our study (an incidence surveillance system), the possible presence of competitive causes of death and the limited period of observation prevent statistical inferences on the association between exposure and time to event (age or latency).^{39–40} Non-occupational exposure exhibits some distinctive features that deserve special attention. One is that the individuals involved were especially likely to be unaware of their exposure or of the associated hazard, as in the case of people living around industrial sources of asbestos pollution and/or with asbestos workers. Another one is the considerably younger age at the start of exposure, which provides the opportunity for accruing a longer duration of exposure and latency.

According to our findings, asbestos pollution outside the workplaces significantly contributes to the burden of asbestos-related diseases. The evaluation of a framework for dealing with compensation rights for MM cases induced by non-occupational exposure to asbestos needs to be carefully undertaken from the economic, ethical and insurance points of view.

Finally, the identification of an environmental source of contamination, by means of a specialised surveillance system for MM incidence inclusive of individual exposure assessment, remains an important tool for primary prevention of risks.

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REFERENCES

- 1 IARC Working Group on the Evaluation of Carcinogenic Risks to Humans. Arsenic, metals, fibres, and dusts. *IARC Monogr Eval Carcinog Risks Hum* 2012;100(Pt C):11–465.
- 2 WHO. *Elimination of asbestos-related diseases*. Geneva: World Health Organization, 2006. http://www.who.int/occupational_health/publications/asbestosrelateddiseases.pdf
- 3 Goldberg M, Luce D. The health impact of non-occupational exposure to asbestos: what do we know? *Eur J Cancer Prev* 2009;18:489–503.
- 4 Bayram M, Dongel I, Bakan ND, et al. High risk of malignant mesothelioma and pleural plaques in subjects born close to ophiolites. *Chest* 2013;143:164–71.
- 5 Sakellariou K, Malamou-Mitsi V, Haritou A, et al. Malignant pleural mesothelioma from non occupational asbestos exposure in Mestovo (north-west Greece): slow end of an epidemic? *Eur Respir J* 1996;9:1206–10.
- 6 Boutin C, Viallat JR, Steinbauer J, et al. Bilateral pleural plaques in Corsica: a non-occupational asbestos exposure marker. *Eur J Respir Dis* 1986;69:4–9.
- 7 Bruno C, Comba P, Zona A. Adverse health effects of fluoro-edenitic fibers: epidemiological evidence and public health priorities. *Ann N Y Acad Sci* 2006;1076:778–83.
- 8 Goldberg M, Goldberg P, Leclerc A, et al. A 10-year incidence survey of respiratory cancer and a case-control study within a cohort of nickel mining and refining workers in New Caledonia. *Cancer Causes Control* 1994;5:15–25.
- 9 Luo S, Liu X, Mu S, et al. Asbestos related diseases from environmental exposure to crocidolite in Da-yao, China. I. Review of exposure and epidemiological data. *Occup Environ Med* 2003;60:35–41.
- 10 Pan XL, Day HW, Wang W, et al. Residential proximity to naturally occurring asbestos and mesothelioma risk in California. *Am J Respir Crit Care Med* 2005;172:1019–25.
- 11 Whitehouse AC, Black CB, Heppe MS, et al. Environmental exposure to Libby asbestos and mesotheliomas. *Am J Ind Med* 2008;51:877–80.
- 12 Mirabelli D, Calisti R, Barone-Adesi F, et al. Excess of mesotheliomas after exposure to chrysotile in Balangero, Italy. *Occup Environ Med* 2008;65:815–19.
- 13 De Klerk N, Alfonso H, Olsen N, et al. Familial aggregation of malignant mesothelioma in former workers and residents of Wittenoom, Western Australia. *Int J Cancer* 2013;132:1423–8.
- 14 Marinaccio A, Binazzi A, Di Marzio D, et al. Pleural malignant mesothelioma epidemic. Incidence, modalities of asbestos exposure and occupations involved from the Italian national register. *Int J Cancer* 2012;130:2146–54.
- 15 Magnani C, Dalmaso 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.
- 16 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.
- 17 Oddone E, Ferrante D, Cena C, et al. Asbestos cement factory in Broni (Pavia, Italy): a mortality study. *Med Lav* 2014;105:15–29.
- 18 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.
- 19 Marinaccio A, Binazzi A, Branchi C, et al. *Italian National Mesothelioma Register (ReNaM)—IV Report (in Italian)*. Monograph. Milan, Italy: INAIL, 2012. <http://www.ispesl.it/renam/Report.asp>
- 20 Nesti M, Adamoli S, Ammirabile F, et al. *Guidelines for the identification and definition of malignant mesothelioma cases and the transmission to IspeSl by Regional Operating centres*. Monograph. Rome, Italy: ISPEsl, 2003. <http://www.ispesl.it/dml/leo/download/RenamGuidelines.pdf>
- 21 Goswami E, Craven V, Dahlstrom DL, et al. Domestic asbestos exposure: a review of epidemiologic and exposure data. *Int J Environ Res Public Health* 2013;10:5629–70.
- 22 Sim MR. A worldwide ban on asbestos production and use: some recent progress, but more still to be done. *Occup Environ Med* 2013;70:1–2.
- 23 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.
- 24 Goldberg M, Imbernon E, Rolland P, et al. The French National Mesothelioma Surveillance Program. *Occup Environ Med* 2006;63:390–5.
- 25 Yeung P, Rogers A, Johnson A. Distribution of mesothelioma cases in different occupational groups and industries in Australia, 1979–1995. *Appl Occup Environ Hyg* 1999;14:759–67.
- 26 Berk S, Yalcin H, Dogan OT, et al. The assessment of the malignant mesothelioma cases and environmental asbestos exposure in Sivas province, Turkey. *Environ Geochem Health* 2014;36:55–64.

- 27 Langer AM, Nolan RP, Constantopoulos SH, *et al.* Association of Metsovo lung and pleural mesothelioma with exposure to tremolite containing whitewash. *Lancet* 1987;1:965–7.
- 28 McConnochie K, Simonato L, Mavrides P, *et al.* Mesothelioma in Cyprus: the role of tremolite. *Thorax* 1987;42:342–7.
- 29 Luce D, Billon-Galland MA, Bugel I, *et al.* Assessment of environmental and domestic exposure to tremolite in New Caledonia. *Arch Environ Health* 2004;59:91–100.
- 30 Reid A, Heyworth J, de Klerk N, *et al.* The mortality of women exposed environmentally and domestically to blue asbestos at Wittenoom, Western Australia. *Occup Environ Med* 2008;65:743–9.
- 31 Bernardini P, Schettino B, Sperduto B, *et al.* Three cases of pleural mesothelioma and environmental pollution with tremolite outcrops in Lucania. *G Ital Med Lav Ergon* 2003;25:408–11.
- 32 Kurumatani N, Kumagai S. Mapping the risk of mesothelioma due to neighborhood asbestos exposure. *Am J Respir Crit Care Med* 2008;178:624–9.
- 33 Tarrés J, Albertí C, Martínez-Artés X, *et al.* Pleural mesothelioma in relation to meteorological conditions and residential distance from an industrial source of asbestos. *Occup Environ Med* 2013;70:588–90.
- 34 Maule MM, Magnani C, Dalmaso P, *et al.* Modeling mesothelioma risk associated with environmental asbestos exposure. *Environ Health Perspect* 2007;115:1066–71.
- 35 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.
- 36 Binazzi A, Scarselli A, Corfiati M, *et al.* Epidemiologic surveillance of mesothelioma for the prevention of asbestos exposure also in non-traditional settings. *Epidemiol Prev* 2013;37:35–42.
- 37 Mirabelli D, Cavone D, Merler E, *et al.* Non-occupational exposure to asbestos and malignant mesothelioma in the Italian National Registry of Mesotheliomas. *Occup Environ Med* 2010;67:792–4.
- 38 Olsen NJ, Franklin PJ, Reid A, *et al.* Increasing incidence of malignant mesothelioma after exposure to asbestos during home maintenance and renovation. *Med J Aust* 2011;195:271–4.
- 39 Consonni D. Something is missing: what's wrong with using age at diagnosis/death or latency among cases. *Epidemiol Prev* 2013;37:85–8 [in Italian].
- 40 Andersen PK, Geskus RB, de Witte T, *et al.* Competing risks in epidemiology: possibilities and pitfalls. *Int J Epidemiol* 2012;41:861–70.