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# Health impact of exposure to asbestos in polluted area of Southern Italy

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Keywords

Bari • Asbestos • Contaminated town-site of national interest • Environmental exposure • Mesothelioma

Summary

*The three main sources of asbestos pollution in the city of Bari, Puglia, the former Fibronit asbestos factory, the Torre Quetta beach, the former Rossani barracks and the history of their reclamation are described. The results of cohort studies on factory workers and case-control studies on asbestos exposure to the resident population and the onset of mesothelioma are also reported. Finally, the data of the regional register of mesothelioma related to residents in the city of Bari and four new cases with environmental exposure due to the former Rossani barracks are presented.*

## Introduction

Environmental pollution is one of the most serious global challenges. It can induce effects on human health. In particular, some polluting substances (asbestos, polycyclic aromatic hydrocarbons, carbon monoxide, heavy metals, gases) can cause respiratory and oncological diseases in the general population [1-6]. Among these, asbestos is a naturally occurring fibrous mineral found in the ground and mines all over the world of which there are different mineralogical varieties (actinolite, amosite, antophyllite, chrysotile, crocidolite and tremolite) [7]. Because of its mechanical, electrical, chemical and thermal resistance characteristics, asbestos fibers are exploited in numerous commercial and industrial settings [8].

Since the 1960s, several studies have shown the relationship between asbestos and cancer [9, 10]. In 1964, the conference on the biological effects of asbestos organized by the New York Academy of Sciences unanimously recognized the carcinogenic effects of asbestos [11]. In 1973, the International Agency for Research on Cancer (IARC) classified all types of asbestos as carcinogenic to humans (Group 1) [12].

In contrast to other professional air pollutants (e.g. formaldehyde, wood and leather dusts) [13-15] that cause tumors mainly in the upper airways, asbestos fibers, when mechanically disturbing, tend to divide longitudinally, generating thinner fibers (fibrils) that can penetrate deeply into the lung and reach the pulmonary air spaces. Exposure to them can cause serious diseases such as fibrotic (asbestosis) and neoplastic processes [i.e. malignant mesothelioma (MM), lung cancer] [16-18]. These disorders are characterized by a long latency interval between the beginning of exposure and the onset of the disease (usually decades) [19].

In addition to occupational exposure, the risk of asbestos-related diseases is also linked to environmental exposure, both of human origin (i.e. pollution by industrial sites, presence of asbestos in buildings) or of natural origin (i.e. areas where there are natural outcrops of asbestos-like minerals) [20, 21].

Several studies have reported a significant risk of mesothelioma for environmental asbestos exposure. Other studies have shown an increased risk in the general population associated with relatively low exposure to asbestos [22, 23].

Environmental exposure is defined as a neighbourhood exposure based on residence close to industrial /mining sources of asbestos or residence in municipal or polluted areas. It is also described as any exposure that occurs during the period of residence in a city in which asbestos processing plants were located [24], nevertheless it can come from the presence of asbestos in buildings and from natural contamination of the soil [25].

In Italy, raw asbestos has been used in a wide range of industrial activities such as industrial production of asbestos-cement products, textile articles containing asbestos, shipbuilding, repair and\or demolition of railway rolling stock, construction and many other sectors. Therefore, the number of workers occupationally exposed is very significant [26].

Despite the Directive 2003/18/CE of the European Parliament and of the Council of 27 March 2003 that bans the use of asbestos, it is still used in developing countries and even in some of the twenty-five countries of the European Union [27].

In Italy, Law n. 257/1992 decreed the "cessation of asbestos use"; in particular, it prohibits the extraction, importation, exportation and use of asbestos and products containing asbestos. The law also provides measures to decontaminate and reclaim areas affected by asbestos pollution [28].

Although Italian legislation concerning asbestos is one of the most advanced in Europe, on national territory there are still present several million tonnes of compact materials containing asbestos and many tonnes of brittle asbestos in a large number of public and private and industrial sites [29].
According to World Health Organization, *contaminates sites* are defined as: "Localized areas hosting or having hosted large and / or hazardous industrial facilities, producing or with strong potential to produce environmental contamination resulting in health impacts" [30].
Despite in 2001, the municipality of Bari was included among Italian Polluted Sites, environmental remediation interventions only started in 2016, after fifteen years, and it is still in progress [31].
The area of Bari municipality, Apulia region of southern Italy, is one of the most contaminated sites nationwide and in 2001 was classified as site of national interest for remediation. The three main sources of asbestos pollution in the city of Bari are represented by the former Fibronit asbestos factory, the Torre Quetta beach and the former Rossani barracks.
Since the 1990s, several epidemiological studies have been conducted in exposed workers as well as in resident population. The aim of this review is to assess the impact on public health of exposure to asbestos in both occupationally and non-occupationally exposed individuals in the area of Bari municipality.

## Methods

The published literature was searched using MEDLINE, accessed via PubMed (the U.S. National Library of Medicine). Additional studies were also hand-searched from bibliographies of the selected studies. Key words included environmental pollution, asbestos (and specific fiber types, including crocidolite, amosite, and chrysotile), occupational exposure, municipality of Bari, health effects, mesothelioma, or asbestosis.
Analytical and descriptive epidemiologic studies were considered in this study, including cohort, case-control and case reports. The medical conditions of interest were pleural and peritoneal mesothelioma.
Information extracted from each study included first author, publication year, geographic area, study type, total number of cases, and controls, fiber type, industry type, measurement of asbestos, definition of asbestos exposure and/or period of employment/exposure and classification of outcome. The exposure studies reviewed included a variety of study types conducted in the area of Bari municipality, divided into 3 major groups:

1. SENTIERI Project - Epidemiological study of residents in national priority contaminated sites: incidence of mesothelioma.
2. Cohort studies - Occupational exposure assessment-Fibronit (Bari).
3. Environmental exposure.

The sites of interest are listed below.

### Fibronit asbestos cement factory

The former Fibronit placed close to a densely populated area, occupies a surface area of 39,000 square meters and it is composed of several industrial buildings and offices. The plant, with about 400 employees produced various products containing asbestos, from 1933 until 1985 [32, 33]. In particular, it manufactured pipes of various lengths, corrugated sheets and special pieces, such as square rods, ridges, sleeves or tanks, water tanks. The production cycle was divided into several phases which, until the beginning of the 1970s, were mostly dry and manually. The most common type of asbestos used in the factory was crysotile (80%), followed by crocidolite (15%) and amosite (5%).
The dusts initially sucked were carried to the outside generating a high environmental risk. Exhaust systems used in 1974 only partially had blast chillers.
The wards were cleaned with a shovel and a broom. The processing residues were accumulated on one side and once a week a company passed that took everything and took it away. Some of the waste material was in some cases thrown into natural troughs of soil existing in the Fibronit area and were then covered first with soil and then with asphalt. In Fibronit, there were no waste collection and disposal systems and no processing waste, other areas of the city outside the factory were repeatedly used as an illegal dump. There is no news of any use of personal protective equipment (PPE) by Fibronit workers who have testified that they returned home with clothes and hair soaked in dust.
From 1970 to 1974 some industrial hygiene surveys were carried out with measurement of the concentration of airborne fibers, in a range between 5 ff/l and 20 ff/l, with the highest values measured in the milling department and the monolithic tube and glass department. The first survey carried out by the National Institution for the Prevention of Accidents (ENPI) in 1970 revealed concentrations up to 20 ff/cc near the "molazza". In the second survey, carried out in 1972 by the Labor Inspectorate, the maximum concentrations reached were 10 ff/cc near the mullers and in the monolithic tube and glass department. Finally, in 1974, an expert opinion prepared by the judiciary carried out withdrawals on three consecutive days, finding concentrations that, where the most risky operations were performed, ranged from 4 to 19 ff/cc [32].
The operations that resulted with the greatest exposure to asbestos were emptying and rattling of the bags, milling, pipe turning and slab cutting. In the seventies, the ACGIH working exposure limit (TLV) was 5 ff / cc (fibers / cubic centimeter).
In 1975, the same year of the first complaints of the total non-existence of safety measures in the workplace, by the unions, the presence of dust was detected in the air not only of the factory, but also in the neighboring areas. Average concentration values equal to 16.06 x 10-4 "particles (< 5 microns in size) per cc of air" [34] were reported.
In 1994 the hygiene and public health service set up for Fibronit a work plan for the removal of some materials containing asbestos that had been piled up outside

the factory buildings since 1985 (cessation of the company's activities), there were high quantities of asbestos not only in outdoor sheds, but also in the basement of the plant and for several meters of depth. In the most serious cases, the contaminated areas also reached a thickness of 6 meters, for a total volume of about 90,000 cubic meters, even affecting the land on which the sheds are located. Even the underground utilities and the sewage system are contaminated by dust and asbestos processing residues.

From 1997 to 2001, provisional safety has started with the removal of shed roofs, the ground breach and with fixing paint to prevent asbestos fibers from continuing to disperse in the air.

In 2001, the Fibronit industrial area was included among Italian Polluted Sites (IPS) and in 2002 the Bari Public Prosecutor seizes the polluted area, still recognizing the presence of serious risks for public health.

After the closure of the factory in 1985, the work of partially securing the overpass was only completed in 2007. In 2011, the decision-making conference between the Ministries of the Environment, Health and Economic Development and the Apulia Region approves the project of putting Fibronit into permanent safety. To date, remediation activities are ahead. At the same time, the procedure for awarding the works for the construction of the park that will be built instead of the factory was started.

Currently, the area of the former Fibronit plant covers over ten hectares in a central area of the city of Bari. Nearby, there are both construction-free soils and densely built-up soils, as well as other areas with different destinations.

This area is defined as *brownfields* that is "sites that have been affected by the former uses of the site and the surrounding land; are derelict or underused; have real or perceived contamination problems; to bring them back to beneficial use" [35, 36].

### Torre Quetta Beach

Former workers have testified that the residues of processing were unloaded not only in the subsoil of the industrial area, but also in the surrounding areas and along the coastal strip, in particular on the coast south of the city "Torre Quetta", used as a landfill for waste and mixtures of asbestos processing.

At the beginning of 2001, a technical report by the Environmental Protection Agency of Apulia (ARPA) highlighted, in the stretch of the Bari coast of "Torre Quetta", the widespread presence of asbestos, both in the form of asbestos cement scrap embedded in the ground scattered everywhere, and in material friable with the presence of free asbestos fibers, present in the filling layers. The total amount of asbestos collected amounted to around 40,000 kilograms.

The materials had an absolutely peculiar typology, different from that of asbestos cement waste, which is often found in areas subject to uncontrolled waste dumping and deriving from building demolition, consisting of roof slabs, flues or fragmented downspouts. In 2004, the entire stretch of coast of "Torre Quetta" was precautionary seizure by the Judicial Authority.

For many years, Torre Quetta area has been used in public bathing and caused an unconscious exposure to asbestos in general population. As regards the permanent safety and reclamation of the area there are problems due to the continuous action of the sea, which over time has produced the erosion of the filling layers and the spread of asbestos materials on a very extensive stretch of coast [37].

### The Military Barrack "Rossani"

The military barracks "Rossani" were built in the early decade of the 20th century. The barracks, located near the central station – in the heart of city –, stands on a total area of 80,000 square meters of which 14,000 square meters of covered area. All the roofs and chimneys of the barracks buildings were constructed of asbestos. In 2001 the reclamation of asbestos roofing started, estimating the removal of about 5000 square meters of Eternit.

In 2004, an Inspection of the Environmental Protection Agency of Puglia (ARPA) suspended the first works for the removal of hazardous materials because the remains of the removal remained on the ground. In particular, the defaults would concern fragments of the dispersed artefacts, bags containing poorly kept asbestos, failure to use decontamination units and a pollution higher than that hypothesized in the operational program.

In 2005, despite the strong protests from citizens, the work resumes and were completed at the end of 2006 [38].

## Results

### SENTIERI Project

As part of the SENTIERI project, a national epidemiological study of the territories and settlements exposed to pollution risk, coordinated by the National Institute of Health, the mortality rate of IPS Bari-Fibronit relative to the years 1995-2002 was analyzed.

Among the main causes of death, there is an excess of mortality for all causes, for all tumors and for respiratory system diseases in both women and men. In women, there is an excess of mortality for diseases of the digestive system. Once adjusted for deprivation rate index, mortality is also higher than expected for cardiovascular diseases in both the genders, for digestive system in men and for genito-urinary system in women.

For causes of death for which there is an evidence sufficient or limited in association with the sources of environmental exposures of IPS, there is an excess for lung cancer in women. There is an excess for malignant pleural cancer among men and women.

Respectively among men and women, 49 and 17 deaths from pleural cancer with standardized mortality ratio (SMR) equal to 199 (confidence interval (CI) 90% 155-253) and 192 (CI 90% 122-287) [39].

## SENTIERI-ReNaM

The SENTIERI-ReNaM project described the incidence of mesothelioma in IPS in the period 2000/2011. In this period, 123 cases (88 men, 35 female) of MM were recorded in subjects residing in IPS. In men the average age at diagnosis was 66.4 (DS ± 11.4) and the median at 66.5; in women they were respectively 67.3 [standard deviation (SD) ± 12.4] and 70. The standardized incidence ratios (SIR) of MM (certain, probable, possible), for all the sites, were equal to 271 (CI 90% 228- 323) in men and 322 (CI 90% 244-426) in women [40].
The settlement, in the urban context, of the Fibronit factory for the production of asbestos cement has configured both direct asbestos exposure panels, airborne fibers during processing, and indirect exposure to environmental exposure. The cases of MM with environmental exposure, in the period considered, are 9 in men and 18 in women, with M/W ratio of 0.5. For these environmental cases, residence near the aforementioned Fibronit plant was established. In the only case with family exposure (female gender) it is an exhibition of cohabitants with employees in the manufacture of fiber cement products [40].

### Cohort studies - Occupational exposure assessment- Fibronit (Bari)

A first cohort study involved 233 Fibronit workers with disability pensions for asbestos on 12/31/1979. The data was retrieved from the National Institute of Occupational Accident Insurance (INAIL) archive. The mortality observed in the cohort was then compared with that expected based on mortality data from Apulia and was higher than expected, with significant excesses for asbestosis and for lung, pleural, mediastinal and peritoneal mesothelioma [41] (Tab. I).
Coviello et al. [32] analysed mortality in Fibronit workers present in the factory from 1972 to the closure of the same: the cohort included all male subjects, for a total of 417 people.
In terms of latency it is observed that, while the first cases of pulmonary neoplasia begin to appear already around 1975, the first case of pleural mesothelioma does not arise before 1990.

**Tab. I.** Fibronit cohort - National Institute of Occupational Accident Insurance – INAIL (Bari).

| | |
|---|---|
| Follow-up | 1980-1997 |
| Follow-up completed | 98,3% |
| Cause of death known | 96,6% of deaths |
| All deaths | SMR: 117 (87 deaths) |
| Pneumoconiosis | SMR: 11238 (14 deaths, p < 0.05) |
| Malignant tumors | SMR: 163 (38 deaths, p < 0.05) |
| Circulatory diseases | SMR: 64 (18 deaths, p < 0.05) |
| Lung tumors | SMR: 206 (17 deaths, p < 0.05) |
| Pleura and peritoneum tumors | SMR: 2551 (8 d., P < 0.05) |

In the investigated cohort, the average latency for pleural mesothelioma is about 42 years, with a minimum latency of 26 and a maximum of 52 years. The results of the study concerning the entire cohort of 417 workers show excess mortality for all causes, for pneumoconiosis, for all tumors, for malignant lung, pleura and peritoneum tumors [42] (Tab. II).
In 2016, the follow-up of 414 former Fibronit workers at 31 December 2012 was published. The subjects in the study, all male, number 414 (377 workers, 29 employees and 8 transacted from worker to employee duties), of which 325 (78%) were already present at February 1, 1972 in the Fibronit plant and 89 (22%) were hired later. No information is available about workers who left the job before the aforementioned date, which we define as baseline. The workers were hired in the factory between 1934 and 1982, with a median age at the first recruitment of 27.1 years [43] (Tab. III).
The analysis disaggregated by ten-year latency classes shows a significant excess for the lung tumor starting from the latency class 20-29 years, while the excess for the malignant tumor of the pleura occurs from the 30-39 year class and for peritoneum cancer from the 40-49 year class.
Among the non-neoplastic causes, pneumoconiosis shows extremely high values that are already evident starting from the 10-19 year latency class.
In the analysis along the latency axis, for lung cancer, we note an increase in SMRs up to the latency class 30-39 years, with subsequent decrease; in the case of pleural cancer the first cases appear 30 years after the beginning of the exposure with a growing SMR up to the latency class 50-59 years [43].

**Tab. II.** Fibronit cohort (1975-2000).

| | |
|---|---|
| Follow-up | 1972-1995 (105 deaths)<br>2000 (145 deaths) |
| All causes | 1995 SMR (CI 95%) 118 (97-143),<br>2000 SMR (CI 90%) 121 (102-142) |
| Asbestosis | 1995 SMR (CI 95%) 14.705 (9.519-21.708)<br>2000 SMR (CI 95%) 15.650 (11.010-22.250) |
| All tumors | 1995 SMR (CI 95%) 139 (100-189)<br>2000 SMR (CI 95%) 148 (114-191) |
| Lung tumors | 1995 SMR (CI 95%) 191 (116-294)<br>2000 SMR (CI 95%) 175 (116-259) |
| Pleural tumors | 1995 SMR (CI 95%) 1.578 (325-4.613)<br>2000 SMR (CI 95%) 2.963 (1.594-5.507) |
| Peritoneal tumors | 1995 SMR (CI 95%) 95 1667 (222-6018)<br>2000 SMR (CI 95%) 1165 (264-4.007) |

**Tab. III.** Fibronit cohort (1972-2012).

| | |
|---|---|
| Follow-up | 1972-2012 (232 deaths) |
| All causes | SMR (CI 95%) 120 (105-136) |
| Asbestosis | SMR (CI 95%) 13.268 (9.481-18.570) |
| All tumors | SMR (CI 95%) 194 (159-237) |
| Lung tumors | SMR (CI 95%) 201 (146-276) |
| Pleural tumors | SMR (CI 95%) 4.033 (2.541-6.401) |
| Peritoneal tumors | SMR (CI 95%) 2.945 (1.404-6.177) |

## Environmental exposure

In 2003 Bilancia et al. [44] analyze, with explorative methods based on geographical analysis, the relationship between the presence of the asbestos cement factory in the urban area of Bari and the mesothelioma cases that occurred between 1980 and 2001 among the residents. Subjects who have had a permanent residence in the city of Bari for a period of at least 20 years prior to the onset of the disease. The estimate of the SIR shows that within an area having a radius of approximately 1 km, centered on the industrial plant, the risk level was higher than expected. The data source of the 64 cases studied is the National mesothelioma Registry (ReNaM), the Regional Operations Center of Apulia (COR-Apulia). The data was analyzed with the S + SpatialStats software. Both the single data analysis and the exploratory geographical analysis showed an increase in the risk of disease among the people who lived near the asbestos cement factory: within an area centered on the location of the company and with a radius of about 1 km, the estimated risk was 2.38 times the normal level.

The impact of environmental exposure to asbestos, in neighborhoods bordering the production site, was also estimated with a case-control study that assessed the spatial distribution of 48 cases of mesothelioma of non-professional origin residing for more than 15 years time of diagnosis, from the data of the mesothelioma register of Puglia referring to the years 1993-2003, and of 273 controls also residing for over 15 years in the city of Bari. The complete residential histories of both cases and controls were analysed. The study compared the distribution of addresses between cases of MM with the corresponding distribution of controls, residents who died on the same calendar date as cases for causes other than mesothelioma. Residential history and distance from Fibronit has been considered as a proxy for environmental exposure to asbestos.

The disease risk was estimated using a logistic regression model, in which the probability of disease occurrence is expressed as a function of the distance classes from the Fibronit site. A non-parametric method was applied to estimate the total area of the risk relative. The study observed a significant increase in risk within the resident population within 500 meters of the plant [Relative Risk (RR) = 5.29 (95 CI: 1.18-23.74)] as the distance between the patients' home and the factory decreased. A cluster of six cases of MM has been identified east of Fibronit, near the urban beach "Torre Quetta", where unauthorized waste disposal occurred during 1950-70 years.

The results also show that the odds ratio (OR) for the lowest exposure group (in terms of distance from the plant, 1,500-2,000 m) is remarkably high but not significant (OR = 2.31, 95% CI: 0.88-6.06): a reasonable explanation is that this distance band includes the secondary cluster '' Torre Quetta" [33].

In the 2012 study [45] a high pulmonary fiber load is described in five mesothelioma cases, two women and three men, subjects who after an accurate reconstruction of the exposure circumstances were professionally unexposed but resident near Fibronit. The subjects of age at diagnosis between 36 and 65 years, diagnosed between 2005 and 2009, had lived in periods between 2 and 24 years, between 1960 and 1997, at distances between 200 and 2000 meters from the factory.

Lung tissue samples used to measure the pulmonary load of asbestos fibers were taken 10-38 years after the last residence (after the cessation of exposure). To provide information on the intensity of environmental exposure of asbestos, semi-quantitative and quantitative indices of cumulative environmental exposure to asbestos were calculated, based on the distance of the residence from the factory and its duration. The pulmonary load of fibers ranges from 110 000 to 2 300 000 fibers per gram of dry lung (f/g). In two cases, a 51-year-old woman and a 53-year-old man found concentrations greater than 1 000 000 f/g of amphibole fibers, a value proposed as a cut off to identify subjects with occupational exposure to asbestos, even when no evidence of such exposure is present in their work histories [46]. The semi-quantitative indices of asbestos exposure intensity assume that the intensity of exposure is proportional to the contamination of the environment surrounding the factory and that the contamination decreases with distance.

Amphiboles were found in the patients' lungs, presumably due to the slower clearance of amphiboles in the lungs. Considering the clearance of asbestos fibers and the average of 22.5 years of delay between the cessation of exposure and the collection of tissue samples, during exposure or immediately after the pulmonary load was probably much higher.

A linear relationship was observed between the pulmonary fiber load and the cumulative dose indices in the five subjects with environmental exposures. In the absence of systematic measurements of asbestos fiber concentrations in the Bari ambient air when the factory was active, these results provide information on past exposure to asbestos associated with contamination of the urban environment. Environmental exposure to a mixture of asbestos fibers can lead to a high pulmonary load of amphiboles even years after the cessation of exposure. The epidemiological data of an increased risk of mesothelioma for the general population of Bari, associated with asbestos contamination of the living environment, is confirmed [45].

In addition, from the data of COR Apulia on the years 1993/2015, there are 367 cases of mesothelioma among the residents of the city of Bari. 69% in males and 31% in females. For 70% of cases registered among residents (255) it was possible to reconstruct the exposure. 58% of reconstructed cases have occupational exposure, 3% family / domestic or extra-work exposure occurred as a result of leisure activities. 26% of the cases among the residents have environmental exposure, of these 45% are men and 55% are women. Among the cases resident in Bari, 107 occasions of environmental exposure were recorded due to Fibronit or Rossani. Among these cases, 62% was classified as environmental exposure in the absence of other exposures. On the contrary, for 38% of subjects who also had occupational exposure, despite having residences close to the two sources of exposure,

they were not classified as environmental exposures as they are multiple exposures.
Six family clans in blood relatives are present in the cases of COR Apulia related to occupational, family or environmental exposures due to Fibronit. Three sisters who lived inside the plant in the apartments available to employees [47]. Two brothers who worked in Fibronit and a couple, a father who worked in Fibronit and son with environmental exposure for residence near the plant for 36 years [48]. A mother and daughter couple both lived for 11 years near Fibronit [45]. A mother and son couple living near the plant for over 24 years, and a brother couple who worked in Fibronit and sister with family exposure, had washed his brother's suits for 11 years.
Recently from the regional registry data four new cases of MM emerged, one peritoneal and three pleural caused by environmental exposure to asbestos due to the presence of a military barracks located in a semi-central urban area [49, 50].

## Discussion

This study, consistent with literature, confirms the adverse health effects of asbestos environmental pollution in the Municipality of Bari resulting from the presence of the three contaminated sites in this area.
Since 1960, some authors showed the risk of pleural mesothelioma associated with asbestos exposure in South Africa, some of the cases reported have been attributed to environmental exposure [9].
Malignant mesothelioma cases found in the city of Bari are emblematic of unconscious environmental exposure in a large polluted city. In a recent review, Liu et al. [24] summarized the latest studies on the association between MM and environmental exposure to asbestos.
The role of non-occupational asbestos exposure (para-occupational, domestic or environmental) in the occurrence of MM has already been demonstrated in numerous studies. In a recent meta-analysis Marsh et al. [23] confirmed an increased risk of pleural MM from non-occupational exposure to asbestos RR = 6.9 (95% CI 4.2 to 11.4).
In this regard, IARC (2012, No. 100) [51] states that "In studies of asbestos concentrations in outdoor air, chrysotile is the predominantly detected fiber. Low levels of asbestos have been measured in rural areas (typical concentration, 10 fibers/m3 [f/m3]). Typical concentrations are about 10 fold higher in urban locations and about 1000 times higher in proximity of industrial sources of exposure (e.g. asbestos mine or factory, demolition site, or improperly protected asbestos-containing waste site)".
Moreover, when mesothelioma is due to environmental exposure, the M: F ratio is 1:1 and the median age at diagnosis is 60 years. The duration and intensity of exposure to asbestos are positively associated with the risk of MM [52, 53].
Because of the long latency period and the limited number of cases, the study of the environmental risk of MM is challenging [54]. Furthermore, considering that it is difficult to obtain an early diagnosis with radiological techniques alone, it is important to use biological indicators especially in the early stages [55]. Among these, mesothelin is one of the several well-know biomarkers used in the diagnosis of pleural malignant [56].
Other studies have found a significant risk of MM caused by residence near asbestos cement production plants without an occupational exposure [57, 58]. These studies highlight the importance of assessing the impact of exposure to asbestos not only among workers but also among their cohabiting family members and in the general population.
Orenstein and Schenker [59] studied the association between the distance of residence from the source of environmental exposure, the decrease in the duration of exposure and the risk of MM. Environmental exposure studies have shown that the increase in the distance from pollution sources is associated with a decreased MM risk [33, 60]. Furthermore, in 1989 Spurny established that fibers released from asbestos cement products have the same carcinogenic charge as standard chrysotile [61].
Regarding the four cases of MM selected from Apulia Regional Mesothelioma Register, all patients lived or worked at distances from 12 to 100 meters from the military barracks and from 200 to 1200 meters from Fibronit plant. In particular, patient n. 4 had an important exposure because he lived and worked closely with the two sources of pollution.
Instead, the patient n. 1 with peritoneal mesothelioma lived close to the source of pollution continuously from birth for 36 years and his long exposure, even if not professional, is in agreement with what was claimed by Hodgson and Darnton [62]. The patient was 36 at diagnosis. He was treated at a specialized center in France (Gustave Roussy Institute) where he underwent cytoreductive surgery (CRS) and hyperthermic intraperitoneal chemotherapy with oxaliplatin (HIPEC). An exposure to residential/environmental asbestos was ascertained: he had lived in a building less than 12 meters from the barracks for 36 years from birth: the apartment had overlooked the military barracks and since he was a child he had played to soccer in the camp of the barracks. Following a follow-up in April 2017, more than 18 years (221 months) after diagnosis and 216 months after treatment, the patient is alive and without recurrence. Currently, he has chronic diarrhea and chronic abdominal pain.
When the tumor occurs in younger people, generally, a genetic predisposition and environmental exposure to asbestos or other mineral fibers are implicated. Cytogenetic studies have shown chromosomal and genetic alterations in patients with MM could play an important role in the initial development and subsequent progression of tumor [63 64]. Molecular analysis with comparative genomic hybridization (CGH-array), performed on tumor samples embedded in paraffin, revealed multiple chromosomal anomalies (copy number alterations CNAs), with prevalent amplifications. Deletions have

been found in 1q21, 2q11.1 → 2q13, 8p23.1, 9p12 → 9p11, 9q21.33 → 9q33.1, 9q12 → 9q21.33 and 17p12 → 17p11.2. Chromosomes 3p21 (BAP1), 9p21 (CDKN2A) and 22q12 (NF2) were not affected. Such findings are rare in malignant peritoneal mesothelioma. Some chromosomal aberrations that in this case seem to be random, could justify the response to therapy and long survival, thus revealing useful prognostic factors in the peritoneum MM [50].

The authors report that peritoneal mesotheliomas increase with the square of cumulative exposure to asbestos and conclude that any further unit of exposure would have added lower risk for pleural MM and greater risk for peritoneal MM. Furthermore, Welch et al. [65], found a strong association (OR, 5.0; 95% CI: 1.2-21.5) between exposure in a population control case-study. of asbestos and peritoneal mesotheliomas in cases with relatively low exposures and conclude that intermittent or low asbestos exposure is associated with peritoneal mesothelioma. More recently, Dragon et al. [66] found that the difference in the incidence of pleural and peritoneal MM, in the same conditions of exposure to asbestos, is due to the different physiology of mesothelial cells in charge of a different inflammatory response.

This study, in agreement with the literature, confirms the negative health effects of environmental asbestos pollution in the city of Bari [33, 44]. Data on the environmental concentration of asbestos in the barracks and on the Fibronit site are not available. Fibronit fiber concentration measurements were only available with data limited to the 1970s. At that time up to 20 ff/cc of asbestos fibers in the air were measured (length > 5 µm and diameter> 0.3 µm). In 1972, up to 10 ff / cc and in 1974, after reclamation, concentrations ranging from 4 to 19 ff/cc were reported [32]. In the mid-1970s, environmental measurements near the plant in areas away from roads, without urban traffic pollution, reported average concentration values of 16.06 x 10-4 "particles (< 5 microns in size) per cc d 'air' [34], but were certainly not representative of the high level of pollution in previous decades.

The level of environmental pollution present at the time in the city of Bari, corresponding to the years of exposure in the cases discussed here, can also be estimated from the comparison with the currently recognized background levels. The exposure level at the background level corresponds to an average cumulative exposure of less than 0.1 fibers/mL-y, an average concentration of about 0.1 fibers/l, as reported by the monograph of the International Research Agency on Cancer (IARC) n. 100 (2012) [51]. Furthermore, the World Health Organization (WHO) has estimated that with continuous exposure at 0.4-1 fibers / l, the risk of MM would be from (4 to 10) × 100,000. The linear extrapolation to 0.1 fibers/l (the current background level) would correspond to an excess in the order of one case (from 0.4 to 2.5) of MM per 100,000 people [67].

The process of spreading asbestos fibers, both from the factory and from the military barracks, to the surrounding areas was favored by physical mechanisms and was confirmed by the history of urban expansion in the city of Bari around the two sites. Urban development and natural weather conditions have potentially contributed to release asbestos fibers into the environment. The wind direction influences the concentration of asbestos fibers in specific areas and the concentrations of asbestos in the air surrounding the point of emission depend on the direction and speed of the wind [68]. Furthermore, Abakay et al. [69] studied the risk of MM in relation to meteorological and geological conditions and the distance from the natural source of asbestos (naturally occurring asbestos – NOA) and found a greater risk near NOA and in the direction of the wind (downwind of the source). The study showed that the distance of a residence from a natural source of asbestos contamination and the prevailing wind conditions in the area can influence the risk of developing environmental mesothelioma. Other authors, Kurumatani, Kumagai [70] and Tarres et al. [71], also studied the effect of meteorological conditions on MM. In their studies, the dominant wind direction influenced the MM risk and therefore meteorological factors could be related to pleural MM deaths through environmental exposure. A high standardized mortality ratio (SMR) has been reported among people living in areas of relatively high concentration levels. Therefore, the authors conclude that a parameter that includes the meteorological conditions is a better *proxy* of the exposure dose than the distance of residence from the source of pollution and could be useful for a more accurate investigation of the effects of asbestos exposure between the residents [70]. Fazzo et al. [72], in a study on the incidence of tumors, reported that the highest values in the polluting sectors were consistent with the directions of the prevailing winds and confirmed that the air quality in the areas defined as "contaminated sites" (CS) is influenced by industrial atmospheric emissions.

In this study the meteorological data of the period of interest, from 1912 for the Rossani barracks and from 1933 for the Fibronit, were not available, so the meteorological data and the direction of the winds of the last years (1961-1990) were considered as in our previous study [33]. The diffusion of the wind does not seem to play an important role due to the absence of clearly dominant winds.

Furthermore, in the study conducted by Barbieri on the loading of asbestos fibers in the lungs of five patients who had lived in Bari (age at diagnosis from 36 to 65 years) and residence at distances ranging from 200 to 2000 m from Fibronit (from1960 to 1997), a linear relationship between the pulmonary load and the environmental exposure indices based on the distance between the residence and the factory has been demonstrated [2]. These results can provide information on the past exposure to asbestos associated with the contamination of the urban environment of Bari, in particular considering that the cases discussed lived at a distance between 200 and 1200 meters from Fibronit.

A systematic review of the quantitative relationship between MM and asbestos exposure was carried out for the second Italian Consensus Conference on Malignant Mesothelioma of the Pleura, in which it was documented that the MM incidence is increased with cumulative exposure to asbestos, the pulmonary fiber load and the duration of exposure [73]. In the study of the epidemiology of MM, the cumulative exposure is a proxy for the relevant exposure and the duration and intensity of the exposure are independent determinants of the appearance of MM [73]. The same conclusion was reported in the third Italian Consensus Conference on Malignant Mesotheliomas of the Pleura [74, 75]. Furthermore, a recent case-control study [76] explored the relationship between cumulative exposure and pleural MM after non-occupational exposure and studied the risk associated with asbestos materials in residential areas, with a cumulative exposure index for estimate exposure frequency, duration and intensity. The study showed a relationship between pleural MM risk and cumulative exposure after non-occupational environmental exposure (OR = 2.0 95% CI 1.2-3.2) and confirmed the quantitative relationship between MM incidence and cumulative exposure to asbestos, even at low levels of exposure due to non-occupational exposure (OR = 3.8 95% CI 1.3-11.1). The assessment of environmental exposure was based on the distance between the residence and the source of pollution.

ReNaM has documented that 10.2% of MM cases are due to unprofessional exposure to asbestos [77]. In particular, in our regional register, 10.9% of cases are due to environmental exposure [78]. These data confirm the difficulty in recognizing and attributing non-occupational exposure to asbestos even though this type of exposure is becoming increasingly common among new mesothelioma cases. Coherently with Armstrong, Driscoll [79], this can be defined as exposure to the "third wave". Indeed, Armstrong [76] defined "third wave exposure" as both occupational and non-occupational exposure to asbestos following repairs, renovations, demolition of buildings and environmental exposure to asbestos.

The history of these military barracks shows that the deterioration of asbestos in situ, the removal of asbestos and its exposure require careful control of the concentrations of asbestos fibers in urban air and in areas close to situations considered to be particularly dangerous, such as the renovation or demolition of houses and buildings constructed with asbestos cement products.

## Conclusion

In view of the official data available, the sources of asbestos pollution in the city of Bari and the impact on human health coming from asbestos exposure were highlighted.

The presence of the asbestos cement factory and military barracks in urban area is correlated with the increased risk of MM in resident population. The lack of recover and decontaminate of the two areas within the city was a serious public health problem.

According to the second government conference [80] and the national asbestos plan [81], environmental exposure to asbestos and risk of malignant mesothelioma are research priority for ReNaM and COR; the regions will have to commit the regional COR or other competent structures to investigate the degree of risk of mesothelioma related to non-professional exposure (environmental or para-occupational). Moreover, the scientific research, the establishment of the regional registry and the continuous confirmation of the effects of environmental exposure to asbestos have increased the risk awareness among the citizens of Bari and have led the authorities to plan the reclamation of contaminated sites to safeguard health public.

Epidemiological studies has shown that the risk of mesothelioma increases with the increase in exposure to asbestos fibers. There are no doubts regarding the proportional relationship between cumulative dose, and frequency of mesothelioma [73, 74, 82]. Furthermore, the most recent exposures have a lower weight, not a zero weight [83]. As with all carcinogens, however, there is no safety "threshold" below which the risk is zero [74].

Epidemiological surveillance of incident cases of mesothelioma is important to understand the damage to health due to exposure to asbestos, to identify exposure situations still present in the territory and to assess the evolution of asbestos exposure. In agreement with most of the data in the literature, both workers and their families should wear specific personal protective equipment devices to reduce the risk of adverse health effects [84-86].

The registration of mesothelioma cases is essential to epidemiological knowledge develop and to support research activities. It is an instrument of control and prevention of risks, an indicator to guide the choices and organization of health services in terms of public health and population needs [80, 87].

The risk associated with residual non-occupational and environmental exposure after the asbestos ban should not be underestimated. For environmental (residential) exposures the duration of exposure is the duration of the residence period and is a proxy for the cumulative dose to which residents have been exposed. It should be emphasized that in the work of Ferrante et al. [76], an increase in the risk of MM is observed with the increase in the cumulative exposure to asbestos. This increase is also observed when only those subjects who have had non-working exposure to asbestos are considered, as well as for the exposures to asbestos artefacts, including in particular the coverings, flooring materials and other asbestos cement materials in work (in situ). After the cessation of processing, the danger to public health is the presence of both large quantities of materials containing asbestos in a friable matrix, in civil and industrial buildings, in systems and means of transport (e.g naval), and in significant quantities of materials containing asbestos in a compact matrix whose progressive deterioration can cause the release of fibers and the consequent risk to health. Interventions are therefore required to remove even the residual environmental exposure [88] as demonstrated also by the data on the cases discussed here.

The experience of the city of Bari also shows that, being environmental exposures and taking into account the interest of citizens for the protection of public health, the timely identification of the most appropriate recovery decisions is essential in the risk management process. reclamation as well as the elaboration of specific communication interventions. Particularly important are the psychological support interventions in mesothelioma-affected communities [89]. The asbestos emergency in the city of Bari, which in this chapter was summarily reconstructed, also highlights the importance of EHL (Environmental Health Literacy), literacy on environmental health, which can be defined as the ability to search, understand , evaluate and use information on public health and the environment to encourage the adoption of informed choices, the reduction of health risks, the improvement of the quality of life and the environment. For this reason it is necessary to adopt a communication strategy that involves different stakeholders, health professionals, authorities, local communities, media, presenting results of environmental epidemiology research useful for health interventions and health promotion activities that actively involve the whole community in a participatory process [90, 91].

Public health can directly pursue the public good in terms of the maximum advantage for the greatest number of subjects, or it can have a privileged consideration for the worst situations [92]. It appears essential, in the light of current scientific knowledge, to adopt the precautionary principle to pursue the best solutions with respect to local priorities and the specific needs associated with reducing the health impact of involuntary exposure to asbestos through timely remediation, rehabilitation and surveillance on which the international scientific community agrees.

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## Conflict of interest statement

The authors declare no conflict of interest.

## Authors' contributions

LV, DC and GS developed and designed the study. FM and ESSC wrote the manuscript. LV, DC and AC revised it. LDM and MCD entered data. All authors read and approved the final manuscript.

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