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## Impact of an asbestos cement factory on mesothelioma incidence in a community in Italy

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### ABSTRACT

**Background:** Broni is a small town (9000 inhabitants) in the province of Pavia, Lombardy, north-west Italy, where the second largest Italian asbestos cement factory (Fibronit) was in operation between 1932 and 1993. Based on Lombardy Mesothelioma Registry (RML) data (2000–2011), we previously showed a high impact of asbestos exposure on malignant mesothelioma (MM) incidence among Fibronit workers, their families, and people living in Broni and in the nearby town of Stradella (11,000 residents). Given the great concern of the community, we have recently updated the data regarding 5 more years (2012–2016).

**Methods:** From the RML database we extracted subjects who ever worked in Fibronit, their family members, ever residents in Broni, and subjects living in Stradella and nearby towns at the time of diagnosis. For each type of exposure we calculated standardized incidence ratios (SIR = observed/expected cases).

**Results:** In the period 2000–2016 we registered 56 cases (2.52 expected, SIR = 22.2), 49 men (41 pleural, 8 peritoneal MM), 7 women (5 pleural, 2 peritoneal MM) with past occupational exposure in Fibronit. Among subjects never occupationally exposed and never exposed to extra-occupational sources unrelated to Fibronit, we counted 39 cases (4.24 expected, SIR = 9.2), 10 men (all pleural MM), 29 women (28 pleural, 1 peritoneal MM) in Fibronit workers' families, 91 pleural mesothelioma cases (7.43 expected, SIR = 12.2, 31 men, 60 women), ever residents in Broni, and 25 pleural mesothelioma cases (3.05 expected, SIR = 8.2, 6 men, 19 women) living in Stradella at the time of diagnosis. The overall number of excess cases was about 194 (211 against 17.24 expected). In the remaining adjacent (No. 8) and surrounding (No. 17) municipalities (32,000 people) there were 7 cases (1 men, 6 women, 8.85 expected).

**Conclusion:** The mesothelioma burden related to the asbestos cement factory is still high on factory workers, their families, and residents in Broni and Stradella towns.

### 1. Introduction

Many studies have investigated the effects of occupational exposure to asbestos among cohorts of workers. However, there have been few studies on the impact of asbestos exposure on their families (called familial, para-occupational, household, or domestic exposure) or among people who live near asbestos mines or factories (environmental exposure), and very few studies have examined those sources of exposure comprehensively (Barbieri et al., 2012; Boffetta and Stayner, 2006; Bourdes et al., 2000; Dalsgaard et al., 2019; Ferrante et al., 2007; IARC, 2012; Joubert et al., 1991; Magnani et al., 2001; Magnani et al.,

2013; Magnani et al., 1993; Musk et al., 2019; Musti et al., 2009; Rake et al., 2009; Ramos-Bonilla et al., 2019; Reid et al., 2008a; Reid et al., 2008b; Vianna and Polan, 1978).

Broni is a small town (about 9000 inhabitants) in the Province of Pavia, Lombardy region, north-west Italy, where the second largest Italian asbestos cement factory (Fibronit) was in operation between 1932 and 1993 (Luberto et al., 2019; Oddone et al., 2014, 2017). In the 1960s, the factory produced up to 100,000 tons/year of asbestos cement products (plain or corrugated sheets, pipes, others). Asbestos use was completely stopped in 1993 following the approval of the asbestos ban (Law 257/1992). The factory continued cement production until

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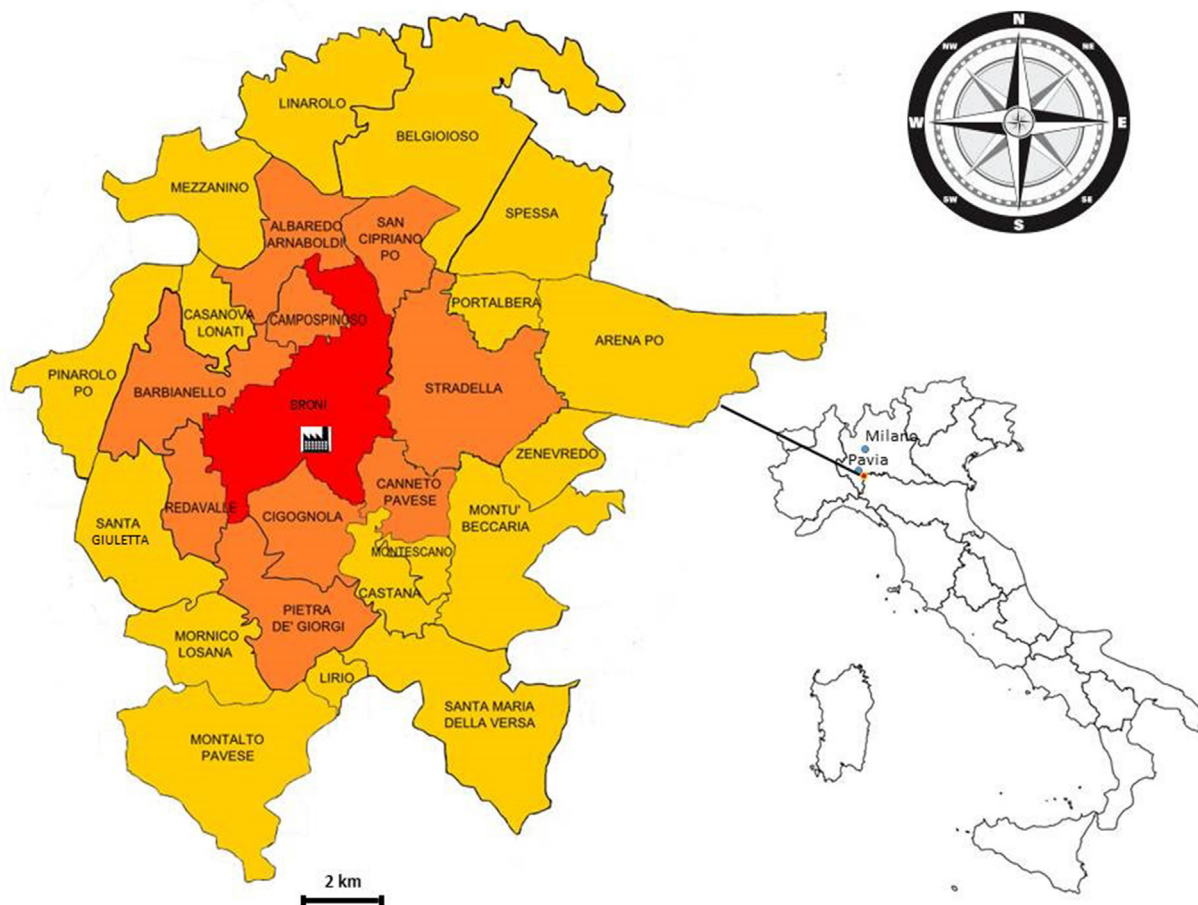


Fig. 1. Map of the area of Broni, province of Pavia, Lombardy, north-west Italy, showing the Fibronit asbestos cement factory, the town of Broni and 9 adjacent and 17 surrounding municipalities.

1997 and closed in 2000. The town of Broni was included by law 388/2000 in a government list of environmentally contaminated sites (*Siti di Interesse Nazionale*, SIN) (Pirastu et al., 2011). Remediation works in the factory area and in other parts of the town started after factory closure.

The occupational impact among Fibronit workers had been investigated for the period 1970–2004 (Oddone et al., 2014) and recently updated through 2014 (Oddone et al., 2017). Several studies have shown marked excesses of pleural cancer mortality and MM incidence among people living in the Broni area (Fig. 1) (Amendola et al., 2003; Binazzi et al., 2016, 2017; Di Paola et al., 2000; Fazzo et al., 2012a, 2012b; Magnani et al., 1994; Mensi et al., 2016a; Pirastu et al., 2011; Zona et al., 2019). However, these geographical studies were not able to distinguish sources of asbestos exposure.

Recently, using information on malignant mesothelioma (MM) cases collected by the Lombardy Mesothelioma Registry (*Registro Mesoteliomi Lombardia*, RML) we documented for the period 2000–2011 a high global impact (occupational, familial, and environmental) of the Fibronit factory on MM incidence in the area of Broni. In particular, we recorded 38 MM cases among Fibronit workers (occupational exposure), 37 cases among their cohabitants (familial exposure), 48 cases among people who had ever lived in Broni, and 16 cases in residents at the time of diagnosis in the nearby town of Stradella (about 11,000 inhabitants) (environmental exposure) (Mensi et al., 2015).

Recent projections in Lombardy indicate that large numbers of MM cases are to be expected in the forthcoming years (Mensi et al., 2016b). Given the great concern of the community and of several institutions in Lombardy (regional government and public health authorities) regarding the health impacts of asbestos exposure in the Broni area, in

this study we report updated results covering the period 2000–2016.

## 2. Methods

### 2.1. The Lombardy Mesothelioma Registry

The RML, established in 2000, is a population-based registry, part of a national network (*Registro Nazionale Mesoteliomi*, ReNaM) (Ferrante et al., 2016; Nesti et al., 2003; van Gerwen et al., 2019). It collects all MM cases diagnosed in people living in Lombardy (currently almost 10 million inhabitants) at the time of diagnosis from regional and extra-regional hospitals. Although compulsory by law, notification of known/suspected cases to the RML is incomplete. Therefore, completeness of reporting is periodically verified using several sources, including pathology, hospital admission, mortality, cancer registry, and the Italian Workers' Compensation Authority (*Istituto per l'Assicurazione contro gli Infortuni sul Lavoro*, INAIL) databases. The final clinical diagnosis is made on individual basis after examining the relevant clinical information, including chest X-rays and CT scan, and pathology reports. Verified MM cases are finally classified as definite, probable, or possible and included in the official database which is periodically transmitted to ReNaM. The presence of pleural plaques is also recorded. Pleural plaques are a recognised marker of asbestos exposure, and positive relationships between lung asbestos burden and both presence and extension of pleural plaques have recently been reported (Barbieri et al., 2019).

Subjects with confirmed MM or their next-of-kin are then interviewed (mostly face-to-face) by trained personnel using a standardized

questionnaire (Nesti et al., 2003) to collect lifetime occupational and residential history and various sources of extra-occupational exposures. Following ReNaM guidelines, lifetime asbestos exposure is then classified as “occupational” (definite, probable, possible) or (only for non-occupationally exposed cases) “extra-occupational”. The latter includes: familial (e.g., from contaminated clothes or hair of a family member); domestic or home-related (e.g. ironing on asbestos boards, small insulation works or repair activities in the house); environmental indoor (from presence of asbestos containing material within the house) and outdoor (residence near industries using asbestos). For subjects with multiple extra-occupational exposures the attribution is made on individual basis considering also the length of exposure to the various sources. Subjects with no evidence of asbestos exposure at interview are classified as non-exposed.

The information stored in the RML database allows the tracking of clusters of MM cases attributable to the same workplace, including Fibronit workers and subjects who had ever lived in Broni. For subjects never residing in Broni, only the last residence is stored in the RML database.

## 2.2. Classification of asbestos exposure associated with the Broni factory

In this study, we selected from the RML database all cases where the date of first diagnosis was between January 1, 2000 and December 31, 2016, the period in which case ascertainment and interview activities were completed. In this period 6226 cases (4048 men, 2178 women) were recorded, 4997 (80.3%) with definite, 480 (7.7%) with probable, and 749 (12.0%) with possible MM. We obtained an interview for 5835 (93.7%, 3841 men, 1994 women) individuals.

We classified exposure related to Fibronit in mutually exclusive groups as follows: 1) Occupational exposure, if the patient had ever worked in the factory (irrespective of possible exposure in other industries/jobs); 2) Familial exposure, if the patient has ever lived with a Fibronit worker; 3) Environmental exposure, if the patient has ever lived in Broni or was residing in Stradella at the time of diagnosis. We also analysed data on residents at the time of diagnosis in 8 towns adjacent to Broni and in 17 surrounding towns (Fig. 1). From the categories 2 and 3 above, we excluded patients with occupational exposure (in Fibronit or elsewhere) and with asbestos exposure from extra-occupational sources unrelated to Fibronit (i.e., familial or environmental exposure related to other factories, domestic or home-related activities, and indoor environmental exposures). In case of both familial and environmental exposure in Broni, we assigned exposure on a case-by-case basis, taking into account duration of exposure to either source. This is different from our previous work (Mensi et al., 2015), where we classified subjects exposed to both sources as “familial”, in line with national guidelines (Nesti et al., 2003). The 391 (6.3%, 207 men, 184 women) subjects without interview were excluded from analyses, because we could not assess exposure (either from Fibronit or from other sources).

## 2.3. Statistical analysis

Since there are no defined cohorts, we used approximations to calculate person-years and the expected number of MM cases. For the Broni factory, we considered 2012 workers (1840 men, 172 women) employed in Fibronit on January 1, 1950 or hired thereafter (Oddone et al., 2017), assuming (conservatively) that all workers were alive during the 17-year study period (2000–2016). For familial exposure we assumed that each worker in the Broni factory had been living with two family members ( $2012 \times 2 = 4024$ , equal number of men and women) (Mensi et al., 2015).

For environmental exposure, we used the sex- and age-specific population in every town provided by the Italian Network of Cancer Registries (*Associazione Italiana Registri Tumori*, AIRTUM) or downloaded from the Italian National Institute of Statistics website (*Istituto*

*Nazionale di Statistica*, ISTAT). For environmental exposure in Broni the population at risk is larger than that of Broni residents, because we counted also MM cases occurring among people who moved away from the town. Hence, we assumed a 10% yearly turnover of the population to take into account the changing (increasing) study base (Nelson et al., 2005).

We then applied to the above populations the average 2000–2016 regional MM incidence rates for people never exposed to asbestos, which were estimated as 1.4 (men) and 1.2 (women) per 100,000 person-years (Mensi et al., 2015). These rates were calculated using as numerators the number of non-exposed cases and as denominators the populations unexposed to asbestos in Lombardy; the latter were estimated by multiplying population figures by 0.678 (men) and 0.900 (women), which were the proportions of controls never exposed to asbestos in a population-based case-control study on lung cancer performed in Lombardy in 2002–2005 (De Matteis et al., 2012).

For environmental exposure in Broni and surrounding towns, we used sex- and age-specific (5-year classes) non-exposed reference rates. To analyse occupational and familial exposure, since the relevant age distributions are unavailable and the cohorts of workers and their cohabitants get older with time, we applied the average 2000–2016 regional incidence rates among never exposed subjects aged  $\geq 70$  years, which were 7.6 (men) and 4.8 (women) per 100,000 person-years.

To assess the impact of the approximations made to calculate person-years, we performed a sensitivity analysis in which we calculated expected cases in the way described above using national MM rates for the period 2000–2015 (year 2016 is not available yet). For all ages, the average rates were 3.9 (men) and 1.5 (women), while among those aged  $\geq 70$  years the rates were 18.1 (men) and 5.3 (women) per 100,000 person-years.

We calculated the standardized incidence ratio (SIR) as the ratio of observed and expected MM cases (Checkoway et al., 2004). Confidence intervals (CI) were calculated using the Poisson exact formula (Breslow and Day, 1987). We calculated 90% CIs in order to avoid a reductive interpretation of CIs as significance tests (Consonni and Bertazzi, 2017; Sterne and Davey Smith, 2001; Wasserstein et al., 2019). Statistical analyses were performed with Stata 15 (StataCorp, 2017).

## 3. Results

Overall, in the period 2000–2016, we identified 218 subjects (SIR: 8.4) with MM (207 pleural, 11 peritoneal), in the Broni area with asbestos exposure related to the Fibronit asbestos cement factory (Table 1). Men were 97 (SIR: 6.4) and women 121 (SIR: 11.1).

### 3.1. Occupational exposure in Fibronit

In 2000–2016 we recorded 56 MM cases among subjects ever exposed in Fibronit, 49 men (41 pleural, 8 peritoneal; SIR: 20.6) and 7 women (5 pleural, 2 peritoneal; SIR: 50.0). The average length of exposure at the Broni factory was 17.8 years, and the 25th, 50th, and 75th percentiles were 10, 19, and 24.5 years, respectively. Three male workers had been exposed for one year in Fibronit, the others for 3–37 years. Time since first employment in the factory in Broni (latency) ranged from 21 to 63 years (median: 47 years). Patients with pleural plaques were 26 (53.1%) in men and 4 (57.1%) in women.

Among the 49 men, 37 had been exposed to asbestos only within the Fibronit. Among the remaining 12 with exposure also in other industries, length of exposure in Fibronit exceeded that in other industries, except for 4 (3 employed for 1 year and 1 for 4 years in Fibronit). All the 7 affected women had been occupationally exposed to asbestos in Fibronit only.

### 3.2. Familial exposure

There were 39 subjects who had been cohabitants of Fibronit

**Table 1**

Malignant mesothelioma occurrence in subjects with exposure related to the Fibronit asbestos cement factory in the Broni area, province of Pavia, Lombardy, north-west Italy, 2000–2016. Numbers of expected cases were calculated using Lombardy region incidence rates among never exposed to asbestos (see Methods for details).

Exposure	Population at risk		Men			Women			Total		
	Male	Female	Obs	Exp	SIR (90% CI)	Obs	Exp	SIR (90% CI)	Obs	Exp	SIR (90% CI)
Total	62,033	74,519	97	15.18	6.4 (5.4–7.6)	121	10.91	11.1 (9.5–12.9)	218	26.09	8.4 (7.4–9.3)
Occupational <sup>a</sup>	1841	171	49	2.38	20.6 (16.0–26.1)	7	0.14	50.0 (23.5–93.9)	56	2.52	22.2 (17.6–27.8)
Familial <sup>b</sup>	2012	2012	10	2.60	3.8 (2.1–6.5)	29	1.64	17.7 (12.6–24.1)	39	4.24	9.2 (6.9–12.0)
Environmental											
Town of Broni <sup>c</sup>	11,848	13,385	31	3.83	8.1 (5.9–10.9)	60	3.60	16.7 (13.3–20.7)	91	7.43	12.2 (10.2–14.6)
Town of Stradella <sup>d</sup>	5340	5898	6	1.59	3.8 (1.6–7.4)	19	1.46	13.0 (8.5–19.1)	25	3.05	8.2 (5.7–11.4)
Other 8 adjacent towns <sup>d</sup>	3505	3627	0	1.16	0 (0.0–2.6)	1	0.97	1.0 (0.05–4.9)	1	2.13	0.5 (0.02–2.2)
17 surrounding towns <sup>d</sup>	12,161	12,775	1	3.62	0.3 (0.01–1.3)	5	3.10	1.6 (0.6–3.4)	6	6.72	0.9 (0.4–1.8)

Abbreviations: CI, confidence interval; Exp, expected; Obs, observed; SIR, standardized incidence ratio.

<sup>a</sup> We considered as population at risk the Fibronit workers at work on January 1, 1950 or hired thereafter (Oddone et al., 2017).

<sup>b</sup> Population at risk estimated assuming two family members (equal number of men and women) for each Fibronit worker.

<sup>c</sup> Population at risk estimated assuming a yearly 10% turnover of the Broni population (average 2000–2016 population: 4388 males and 4957 females).

<sup>d</sup> The average 2000–2016 population is shown.

workers: 10 men (all pleural MM; SIR: 3.8) and 29 women (28 pleural, 1 peritoneal; SIR: 17.7). On average, they had lived with a worker for 22.5 years (range 2–42 years), while the 25th, 50th, and 75th percentiles were 15, 24, and 28 years, respectively. Latency ranged from 33.5 to 75.5 years (median: 54.5 years). Subjects with pleural plaques were 3 (30.0%) in men and 13 (44.8%) in women.

### 3.3. Environmental exposure

All 123 subjects with environmental exposure, 38 men and 85 women, had pleural MM.

We identified 91 subjects who had ever lived in Broni, 31 men (SIR: 8.1) and 60 women (SIR: 16.7). At diagnosis, 48 patients (52.7%) were still living in Broni, 25 (27.5%) in the Broni area, and 18 (19.8%) elsewhere. The average length of residence in Broni was 32.4 years (range 1–77 years), and the 25th, 50th, and 75th percentiles were 18, 33, and 44 years. Time since first residence in Broni ranged from 14.5 to 84.5 years (median: 49.5 years). Subjects with pleural plaques were 7 (22.6%) in men and 7 (11.7%) in women.

There were 25 subjects with MM residing in the adjacent town of Stradella at the time of diagnosis, 6 men (SIR: 3.8) and 19 women (SIR: 13.0). No men and 4 women (21.1%) had pleural plaques.

In the other eight towns adjacent to Broni (about 7000 inhabitants), there was only a woman with MM. She was living in Canneto Pavese (average population: 686 men, 712 women) and had no pleural plaques.

In the 17 surrounding towns (about 25,000 inhabitants), there were 6 MM cases, 1 man (SIR: 0.3) living in Belgioioso (average population: 2867 men, 3084 women) and 5 women (SIR: 1.6), 2 living in Arena Po (average population: 801 men, 807 women), 1 in Belgioioso, 1 in Portalbera (average population: 718 men, 751 women), and 1 in Santa Giuletta (average population: 796 men, 852 women). The man and 1 woman (20.0%) had pleural plaques.

### 3.4. Sensitivity analysis

Using national rates, the total number of expected cases (men and women) was almost doubled (51.26) (Table 2) than when using regional non-exposed rates (26.09). Therefore, the overall SIRs were

roughly halved. The expected cases and SIRs in women were only slightly affected, while in men we observed substantially reduced SIRs, particularly for familial exposure and environmental exposure in Stradella.

## 4. Discussion

In this updated study we found a still high impact of past asbestos exposure from the asbestos cement factory Fibronit on workers, their families, and residents in the towns of Broni and Stradella, with a total of about 194 excess cases estimated in a 17-year period (211 cases against 17.24 expected). When we used national reference rates to calculate expected cases, the number of excess cases was still very high (177 excess cases, 211 against 33.97 expected). No clear excesses were found for residents in the other 8 adjacent and 17 surrounding towns.

The absolute impact from occupational exposure was larger in men (49 cases against 7 in women), while MM burden from familial (29 cases in women, 10 in men), and environmental (79 women and 37 men living in Broni and Stradella) exposure was higher in women. These gender differences are in part dependent on the hierarchical classification scheme used: in fact, subjects with both occupational and non-occupational asbestos exposure (mostly men) are assigned occupational exposure. In this work, the number of women with familial exposure is lower than in our previous paper (Mensi et al., 2015) for the reason explained in the Methods section.

This work was made possible by the high-quality population registry of MM patients (RML), which has recorded newly diagnosed MM cases among Lombardy inhabitants since 2000 (Mensi et al., 2007). In the RML, complete collection of clinical information and evaluation of MM cases is performed weekly. The good RML performance has been verified in comparison with Lombardy cancer registries (Nicita et al., 2014). The interview rate in 2000–2016 was high, 93.7% in Lombardy and 97.4% in the Province of Pavia.

This study has some limitations. First, subjects emigrated outside Lombardy are not covered by the RML. Second, only the last place of residence is stored in the database (except for residents in Broni). As a consequence, the number of MM cases related to exposure from Fibronit is probably underestimated. Third, in absence of defined cohorts we could only roughly estimate the population at risk of workers,

**Table 2**

Malignant mesothelioma occurrence in subjects with exposure related to the Fibronit asbestos cement factory in the Broni area, province of Pavia, Lombardy, north-west Italy, 2000–2016. Numbers of expected cases were calculated using national incidence rates 2000–2015 (see Methods for details).

Exposure	Population at risk		Men			Women			Total		
	Male	Female	Obs	Exp	SIR (90% CI)	Obs	Exp	SIR (90% CI)	Obs	Exp	SIR (90% CI)
Total	62,033	74,519	97	38.22	2.5 (2.1–3.0)	121	13.05	9.3 (7.9–10.8)	218	51.26	4.3 (3.8–4.8)
Occupational <sup>a</sup>	1841	171	49	5.66	8.7 (6.7–11.0)	7	0.15	46.7 (21.9–87.7)	56	5.82	9.6 (7.6–12.0)
Familial <sup>b</sup>	2012	2012	10	6.19	1.6 (0.9–2.7)	29	1.81	16.0 (11.5–21.8)	39	8.00	4.9 (3.7–6.4)
Environmental											
Town of Broni <sup>c</sup>	11,848	13,385	31	9.89	3.1 (2.3–4.2)	60	4.36	13.8 (11.0–17.1)	91	14.25	6.4 (5.3–7.6)
Town of Stradella <sup>d</sup>	5340	5898	6	4.12	1.5 (0.6–2.9)	19	1.78	10.7 (7.0–15.7)	25	5.90	4.2 (2.9–5.9)
Other 8 adjacent towns <sup>d</sup>	3505	3627	0	2.95	0 (0.0–1.0)	1	1.17	0.9 (0.04–4.1)	1	4.12	0.2 (0.01–1.2)
17 surrounding towns <sup>d</sup>	12,161	12,775	1	9.40	0.1 (0.05–0.5)	5	3.77	1.3 (0.5–2.8)	6	13.17	0.5 (0.2–0.9)

Abbreviations: CI, confidence interval; Exp, expected; Obs, observed; SIR, standardized incidence ratio.

<sup>a</sup> We considered as population at risk the Fibronit workers at work on January 1, 1950 or hired thereafter (Oddone et al., 2017).

<sup>b</sup> Population at risk estimated assuming two family members (equal number of men and women) for each Fibronit worker.

<sup>c</sup> Population at risk estimated assuming a yearly 10% turnover of the Broni population (average 2000–2016 population: 4388 males and 4957 females).

<sup>d</sup> The average 2000–2016 population is shown.

cohabitants, and Broni residents. However, the overall picture was confirmed in a sensitivity analysis: although SIRs in men were markedly reduced in men when using (higher) national rates to calculate expected cases, SIRs in women were only slightly affected. Moreover, changes were moderate in terms of excess cases.

Indirect evidence from two recent works suggests that the regional never exposed rates are probably a more adequate reference than national rates. Considering Fibronit workers, the number of expected cases we calculated using unexposed regional rates were 2.38 in men and 0.14 in women in a 17-year period. These figures are not so distant from those calculated in a recently updated mortality cohort study of Fibronit workers (see below), where the expected deaths from pleural or peritoneal cancers were 3.95 (men) and 0.35 (women), although over a longer period (45 years) (Oddone et al., 2017). Using national rates we calculated 5.66 expected for men (which seems overestimated) and 0.15 for women.

In a recent geographical study (see below) the crude incidence rates (2000–2012) were 21.3 (men) and 27.4 (women) times the average regional rates in Broni, while in Stradella the rates were 7.1 (men) and 17.4 (women) times higher (Mensi et al., 2016a). Compared to those figures, the SIRs we calculated using national rates (ranging from 1.5 to 13.8, Table 2), are probably underestimated.

#### 4.1. Asbestos exposure in the Fibronit factory and in the Broni area

No systematic measurements of asbestos levels were performed in the factory when production was highest, tasks were performed manually, and measures to reduce fibre dispersion were absent (Mensi et al., 2015). The elevated mortality from several asbestos-related diseases (asbestosis and lung, pleural, peritoneal, and ovary cancer) in the cohort of workers (Oddone et al., 2014, 2017) and the high frequency (> 50%) of pleural plaques in this study among affected workers suggest high asbestos exposures in the past.

Similarly, there are no environmental data on asbestos contamination among family members or residents in Broni or Stradella regarding periods of high activity of the Fibronit factory (Mensi et al., 2015). We are aware of only one recent study (still unpublished) on lung asbestos fibre lung burden in women in the Broni area. Although based on a few cases (six with familial and environmental exposure, two with

environmental exposure only), that study indicates elevated asbestos doses among wives of Fibronit workers and in Broni residents. In this study, the presence of pleural plaques in 30.0% of men and 44.8% of women with familial exposure is a further indication of important past asbestos exposure among members of Fibronit workers' families; also, one seventh of subjects resident in Broni and Stradella had pleural plaques.

#### 4.2. Asbestos exposure unrelated to Fibronit

In 2000–2016 the RML recorded 104 subjects with pleural MM (81 men, 23 women) who had been exposed to sources unrelated to Fibronit. Of these, 92 (77 men, 15 women), had been occupationally exposed in various sectors: construction, mechanic, transports, public administration and defense, food and beverage, non-asbestos textile, rubber, wood and furniture, rail-road equipment maintenance, energy production, and agriculture. Two very small asbestos cement factory had been operating in Arena Po (maximum 75 workers) and Portalbera (maximum < 50 workers): we found no cases employed in these two plants.

There was 1 woman with familial exposure (the husband has been working in a metal fusion plant). We identified 5 cases (2 men, 3 women) with environmental exposure: 1 man had been living in Casale Monferrato, Piedmont, which hosted the sadly famous largest asbestos-cement factory in Italy (Eternit); 1 man and 1 woman had been living near the asbestos cement plant in Portalbera; 1 woman lived near the asbestos cement factory in Arena Po; and 1 woman had been living in a house with an asbestos sheet located behind a radiator (environmental indoor exposure). Finally, there were 6 cases (2 men, 4 women) who had been performing activities at home involving asbestos exposure (construction/removal of asbestos sheets; ironing on asbestos boards).

#### 4.3. Comparison with other studies in the Broni area

Previous geographical studies have documented increased mortality from pleural cancer among residents in the Broni area (Amendola et al., 2003; Di Paola et al., 2000; Fazzo et al., 2012a, 2012b; Magnani et al., 1994; Pirastu et al., 2011) and increased mortality from pleural and peritoneal cancers among Fibronit workers (Oddone et al., 2014). We

refer to Table 2 in our previous paper for a review of those studies (Mensi et al., 2015). After that publication, other works regarding Fibronit workers and the Broni area were published (Binazzi et al., 2016, 2017; Mensi et al., 2016a; Oddone et al., 2017; Visonà et al., 2018; Zona et al., 2019).

The follow-up of the Fibronit workers has been updated by studying mortality among 2012 workers (1841 men and 171 women, at work on January 1, 1950 or hired thereafter). In the period 1970–2014 (1663 men, 165 women) the standardized mortality ratio (SMR) for pleural cancer was 25.28 in men (66 deaths observed) and 50.68 in women (8 deaths). SMRs for peritoneal cancer were 8.95 (12 deaths) in men and 10.53 (two deaths) in women. In men 17 deaths from asbestosis were recorded (Oddone et al., 2017).

A forensic autopsy study was performed on 188 subjects (124 men, 64 women) who died from asbestos related diseases in 2000–2017 in the Broni area, including 149 deaths from MM. Occupational exposure was more frequent in men, familial exposure in women (Visonà et al., 2018).

In a work on mesothelioma incidence (2000–2011) within the national project on Italian environmentally contaminated sites (SIN), among Broni residents there were 52 MM cases in men (47 pleural, 5 peritoneal; SIR: 12.89) and 43 in women (41 pleural, 2 peritoneal; SIR: 20.07) (Binazzi et al., 2016, 2017). The fifth report on Italian SINS documented clear excesses of deaths (2006–2013) from MM either in men (22 deaths, SMR: 13.31) or in women (27 deaths; SMR: 26.62) among Broni residents (Zona et al., 2019).

In a geographical study regarding the whole Lombardy region (2000–2012) Broni ranked first in terms of MM incidence rate (Mensi et al., 2016a). In Broni the crude incidence rate (per 100,000 person-years) was 100.0 in men (57 cases) and 68.4 in women (44 cases). Among residents in Stradella rates were 33.6 in men (23 cases) and 43.5 in women (33 cases). The crude incidence rates in the whole Lombardy Region were 4.7 (men) and 2.5 (women).

## 5. Conclusions

Using detailed information collected by the regional mesothelioma registry, this study provided evidence of a continuing large impact of the Fibronit asbestos cement factory in Broni in the local community. Given the still increasing incidence trend in the Lombardy region, in the forthcoming years we expect a large number of mesothelioma cases among former Fibronit workers, their families, and residents in Broni and Stradella.

The fact that three fourths of cases were attributable to familial or environmental exposure highlights the importance of a global assessment of the health effects of asbestos exposure in the community at large. Continuous monitoring of mesothelioma occurrence in this population is warranted.

## Authors contribution

Dario Consonni performed statistical analysis and drafted the manuscript. Sara De Matteis, Angela C Pesatori, contributed to interpretation and discussion of results. Barbara Dallari, Luciano Riboldi, Carolina Mensi participated in data collection, clinical and exposure evaluation, and contributed to interpretation and discussion of results. Carolina Mensi and Dario Consonni conceived the study. All authors read and approved the final manuscript.

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## Approval

As reporting of malignant mesothelioma to the National Mesothelioma Registry (ReNaM) is compulsory by law (277/1991 and 81/2008), ethics approval is not required.

## Declaration of competing interest

Dario Consonni and Carolina Mensi served as consultants for the court in trials concerning asbestos-related diseases.

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