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# Decade-long insights: tracking asbestos-related health impacts among formerly exposed workers in Palermo, Italy

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**Abstract**

***Background***. *Asbestos is a foremost occupational carcinogen globally. Despite the prohibition under Law 257/1992, Italy persists as one of the European nations most burdened by asbestos-related diseases (ARDs). This research assessed ARD cases in asbestos-exposed workers from the Province of Palermo, Italy, spanning 2010-2021.*
***Methods***. *Data acquisition utilized the epidemiological dataset from the 'Service of Prevention and Safety on Work Environment' under the Prevention Department of Palermo's Local Health Authority (LHA).*
***Results***. *Between 2010 and 2021, we identified 245 ARD instances, comprising 163 Asbestosis/Pleural plaques, 41 Lung Cancers, 38 Mesotheliomas, and 3 unspecified cases. Multivariate analysis indicated a notable decline in temporal exposure for mesothelioma (HR=0.933; 95% CI=0.902-0.965) and lung cancer (HR=0.93; 95% CI=0.90-0.978) relative to pleural plaques/asbestosis. Tobacco use displayed a pronounced correlation with lung cancer (smoker HR=64.520 95% CI=13,075-318.390; former smoker HR=20.917 95% CI=4,913-89.048). A significant link was observed between mesothelioma and pleural plaques/asbestosis in those employed in shipbuilding and repair (HR=0.371 95% CI=0.155-0.892).*

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***Conclusions***. *ARDs persist in clinical observations, even following the 1992 cessation of asbestos-related activities, emphasizing an enduring public health challenge. Enhancing prevention strategies is paramount, focusing on amplifying anamnestic and occupational data collection, thereby facilitating superior early diagnosis strategies for these maladies in the occupationally exposed cohort.*

## Introduction

Asbestos is a group of naturally occurring mineral silicate fibres of the serpentine and amphibole series (1). According to the European legal references, six naturally occurring asbestos types have been identified, inclusing serpentine mineal chrysotile (also known as "white asbestos") and five amphiboles (i.e. actinolite, amosite, anthophyllite, crocidolite, and tremolite) (1, 2). Since 1973, all forms of asbestos have been considered as carcinogenic, being classified as a Group 1 carcinogen (known to cause cancer in humans) by the International Agency for Research on Cancer (IARC) (3), while the EC Regulation 1272/2008 of the European Community nowadays considers asbestos as a Carcinogen of Group 1A (i.e. known to have carcinogenic potential for humans, classification largely based on human evidence) (2). The mechanisms by which asbestos causes disease are not fully understood (4). Currently, the unique fibrous morphology of the asbestos fiber appears to be the main factor in its promoting its health risks (5): because of their surface charge, asbestos fibers can adsorb to cellular macrophages and induce changes in macromolecules, ultimately leading to interference with the mitotic spindle and causing chromosomal damages, while the failing of alveolar macrophages in digesting asbestos figure lead to the release of reactive oxygen species from macrophages to the alveolar spaces (4). Amphiboles, with their needle-like structure, are especially hazardous due to their resilience and ability to deeply penetrate lung tissues, whereas the spiral structure of serpentine-asbestos tends to lodge in the upper respiratory tract (6).

Throughout the 20th century, and until the 1990s, Italy was among the world leading producers, exporters, and consumers of asbestos, both as raw asbestos fibers and asbestos containing products (APC) (2): in 2014, INAIL has estimated a total output from World War II to 1992 of 3,800,000 t of raw asbestos from the Italian mines of Emarese, Balangero and Val Malenco, with further 1,900,000 t of imported asbestos (7). The extensive use of asbestos led to the present-day significant burden of asbestos-related diseases (ARDs): lung carcinoma, malignant mesothelioma of the lung pleura (MPM), of pericardium, of the tunica vaginalis testis, as well as non-malignant but severe conditions (asbestosis). Even though in 1992 Italy became one of the first countries to ban extraction, import, marketing and production of all products containing asbestos (8, 9), ARD still occur. Data from the National Institute for Insurance against Accidents at Work (INAIL) reveal a persisting trend: between 2018 and 2022, an annual average of 1,329 ARD cases have been compensated by INAIL, for a total of 7,377 diagnoses from 6,643 workers (10), mostly of male gender (96.1%). With a pooled occurrence of 2,455 diagnoses, around 33.3% of compensated disorders pertains to mesothelial tissue and soft tissues (11), with further 2,107 disorders associated with other pleural conditions (28.6%). New diagnoses exhibit a clear geographic trend, with the highest percentages in the North-Western regions (31%), followed by North-Eastern regions (25%), Southern (20%), and Central regions (14%) (12).

Since 2003, taking into account the rising number of cases of ARD due the intensive use of asbestos in the past, and the fact that some countries still continued to use chrysotile asbestos, international organizations, such as the International Labor Organization (ILO) and the World Health Organization (WHO), recommended that special attention should be paid at global level, advocating for comprehensive national strategies targeting to the eradicating of ARDs (13-15). Their emphasis also encompasses the mitigation of health risks arising from previous exposures as asbestos-related malignant diseases have very long latency period (up to 40 years). Moreover, appropriate policies should be implemented for the appropriate managing of existing structures and materials containing asbestos (16).

Abundant evidence associates the exposure to all types of asbestos with MM, but also with cancers of the respiratory tract (mostly lung and larynx), and ovaries. More limited evidence has otherwise linked asbestos with gastrointestinal malignancies, including cancers of the pharynx, stomach, and colorectal regions, hinting at the potential systemic migration of asbestos fibers within the human body (17, 18). According to available estimates, 78% of occupational cancers recognized in EU member states can be related to previous asbestos exposure. Other recognized asbestos-induced conditions include pleural plaques, and interstitial disorders of the lung, ranging from aspecific fibrosis, and a pattern of interstitial fibrosis with characteristic asbestos bodies and ferruginous bodies also known as asbestosis (19).

MM is usually considered a rare malignancy in people not exposed to asbestos: with an estimated etiological fraction of 80% or more (20), it is usually acknowledged as a reliable indicator of previous asbestos exposure. Remarkably, even minimal asbestos exposure events, as seen in familial or residential contexts, can lead to MM, emphasizing the intricate role of genetic predisposition (21, 22). The prognosis for MM remains grim, averaging a life expectancy of merely ten months post-diagnosis (23). Concurrent tobacco and asbestos exposures amplify lung cancer risks, highlighting the synergy of these carcinogens. Notably, isolating lung cancers specific to either risk factor remains a challenge (24, 25).

As recently stressed by Catelan et al. (26), occupational settings remain the primary hub for asbestos exposure: in their study about a total of 6,226 MM cases (93.8% arising from lung pleura), 71.6% of males and 35.8% of females reported a work-related exposures to asbestos, with non-occupational, environmental exposures accounting for 2.1% of cases in males, and 4.9% in females, while 19.1% of male cases and 40.8% of female ones remained deprived of any documented exposure (16). No safe exposure limits can be acknowledged: not only, Italian Law n. 257 of March 27$^{th}$, 1992, categorically prohibited any activities involving asbestos, encompassing mining, import, export, sale, and manufacturing (27), but consistently with the Directive 2009/148/EC of 30 November 2009 on the protection of workers from the risks related to exposure to asbestos at work, Italian Legislative Decree 81/2008 currently mandates an Occupational Exposure Limit (OEL) for airborne asbestos exposure, i.e. 0.1 fibers per cubic centimeter averaged over an 8-hour workday (28, 29). Following the recent evaluation of the OEL by European Chemicals Agency and the subsequent statement that there is no threshold below which there is no risk (30, 31), more stringent OEL have been recently approved by the European Parliament: in the plenary session of October 3$^{rd}$, 2023, the OEL has been lowered from 0.1 to 0.01 fibres per cubic centimeter, without a transition period (32).

Despite the significance from a Public Health point of view, the actual burden of ARD has remained mostly uncertain, particularly in Italy. In order to improve registration and reporting of MM cases, a National Mesothelioma Registry (ReNaM) has been implemented since 2002 (33, 34), and diligently tracks incident cases of MM. According to the Seventh Report of ReNaM database, a total of 31,572 MM cases have been diagnosed between 1993 to 2018, and cataloged through extensive and systematic investigations of patients' occupational, residential, and familial histories (35, 36). Predominantly, MM manifests in the pleura (93.2%), with other sites like the peritoneum, pericardium, and tunica vaginalis of the testis being rarer. The average age of diagnosis hovers around 70 years, with males being affected more frequently, presenting a male to female ratio of 2.6 (37). Projections indicate that despite the 1992 asbestos ban, the MM epidemic in Italy might peak around 2024 for both genders (38).

Interestingly, Sicily (4,802,016 inhabitants according to 2023 census, i.e. 8.2% of total population) is among the most severely affected Italian regions (36). For instance, in 2022 alone 88 out of 939 diagnoses of ARD (9.4%) were associated with residents from this Region, including 16 out of 405 cases of malignant pleural mesothelioma (MM, 4.0%), and 60 out of 305 cases of respiratory tract neoplasia (19.7%) associated with exposure to asbestos fibers. In this study, we retrospectively analyze ARDs cases diagnosed in the province Palermo, the largest city of the region of Sicily, from 2010 to 2021. Additionally, we aim to discern the relationship between asbestos exposure and the onset of mesothelioma/lung cancer in workers across various asbestos-associated industries, with a specific focus on shipbuilding and the railway sector.

## Material and methods

*Study Area and Background*

Palermo, the fifth most populous city in Italy, boasts 630,733 inhabitants (39), while the encompassing Province of Palermo surpasses 1.2 million residents (39). The Palermo shipyard, established in 1984, stands as one of Italy's leading shipbuilding hubs and is among the most significant naval groups in Europe (40). The Palermo shipyard holds tripartite production missions: ship construction, repair, and conversion (41). The workforce count at Palermo's shipbuilding industry varies over the years, making it challenging to provide an exact number. Historically, Palermo has been a hub for industries, like shipbuilding and railways, known for their significant asbestos usage, a fact underscored by its ranking as the top Sicilian province for malignant mesothelioma cases (42).

*Data collection*

Data on asbestos-related diseases (ARDs) were extracted from an epidemiological registry that logs all diagnosed cases within the Province of Palermo. This registry, maintained by the 'Service of Prevention and Safety on Work Environment' of the Local Health Authority of Palermo, houses socio-demographic, occupational, and health-related information. The dataset encompasses data between January 2010 and December 2021, collected during occupational visits. The association between ARDs and occupational settings was categorized as "possible," "probable," or "highly probable," in line with the prevailing legal guidelines (43). In the following report, only either "probable" or "highly probable" cases were eventually included.

Analysts noted the following variables: Gender; Year of birth; Asbestos-related pathology type and its year of diagnosis; Age at diagnosis; Occupational exposure timeline (start-end years); Age at initial asbestos exposure;

Exposure duration; Average latency of disease onset; Company and job role; Smoking habits

For analytical purposes, the 'average latency of onset of the disease' signified the interval between initial asbestos exposure and ARD diagnosis. The "duration of exposure" represents the cumulative period a worker was involved in asbestos-associated tasks, either from their employment commencement to retirement or from the instigation of law 257/92. In data analysis, workers with asbestosis and pleural plaques, given their analogous pathogenesis and better prognosis, were grouped (44, 45). Conversely, mesotheliomas and lung cancer were treated as distinct categories.

*Statistical Analysis*

Data processing employed STATA® software. For every qualitative variable, both absolute and relative frequencies were determined. Quantitative variables, on the other hand, were reported as mean values ± standard deviation. The ANOVA test evaluated quantitative variables, while the chi-square test assessed frequencies. A p-value below 0.05 in a multinomial logistic regression model, using asbestosis-pleural plaques as a reference, denoted statistical significance for variables associated with asbestos-linked diseases.

## Results

This research undertook a systematic evaluation of data spanning over a decade from the province of Palermo.

Upon scrutinizing the 245 documented cases of asbestos-related diseases in Palermo and its surrounding province from 2010 to 2021, certain pronounced patterns emerge. The affected subjects had an average age of 72.5 years, underlining the late manifestation of these diseases, with a significant latency period averaging 49.3 years from the initial exposure (Table 1). This prolonged latency accentuates the insidious nature of asbestos-induced ailments. Most subjects started their exposure at a relatively young age, around 20.3 years, and the average duration of exposure was 30.1 years.

A remarkable 92.2% of these cases were affiliated with the shipbuilding sector, pointing to a potent locus of asbestos exposure, while only a minor 7.8% were associated with railways and other sectors. Alarmingly, a vast majority, 67.1%, reported not using any form of Personal Protective Equipment (PPE) during their occupational tenure, highlighting potential shortcomings in protective measures adopted in the past (Table 1).

The influence of personal habits, particularly smoking, revealed a trifurcated distribution: 7.7% active smokers, 46.5% non-smokers, and a significant 45.8% being ex-smokers. Respiratory complications further evidenced by 53.6% of the subject's reporting bronchitis. As for the specific asbestos-related diagnoses, Asbestosis and Pleural plaques were predominant at 66.6%. Mesothelioma cases accounted for 15.5%, lung cancer constituted 16.7%, and a small fraction (1.2%) remained undefined (Table 1).

Analyzing the univariable associations between various diagnoses of asbestos-related diseases and their demographic and occupational characteristics within the period from 2010 to 2021 in Palermo and its province, the following patterns can be discerned:

When comparing the average ages across three major diagnoses, individuals with Asbestosis or Pleural plaques, as illustrated in Table 2, were, on average, 72.7 years old (with a standard deviation of 5.8). This is slightly older than those diagnosed with Lung Cancer, who averaged 71.4 years (with a broader variability, SD: 8.5), but marginally younger than those with Mesothelioma, who had an average

Table 1 - Socio-demographic and occupational characteristics of the 245 cases of asbestos-related disease observed in Palermo and Province between 2010 and 2021.

| | n (%) |
|---|---|
| Age, average in years ± sd | 72.5 ± 6.6 |
| Latency, mean in years ± sd | 49.3 ± 8.1 |
| Exposure duration, average in years ± sd | 30.1 ± 7.6 |
| Age at start of exposure, mean in years ± sd | 20.3 ± 5.1 |
| Sector and production, n (%) | |
| - Shipbuilding | 226 (92.2) |
| - Railway and other sectors | 19 (7.8) |
| PPE use, n (%) | |
| - Yes | 79 (32.9) |
| - No | 161 (67.1) |
| Smoking habit, n (%) | |
| - Yes | 19 (7.7) |
| - No | 114 (46.5) |
| - Former smokers | 112 (45.8) |
| Bronchitis, n (%) | |
| - Yes | 127 (53.6) |
| - No | 110 (46.4) |
| Diagnosis, n (%) | |
| - Asbestosis/Pleural plaques | 163 (66.6) |
| - Mesothelioma | 38 (15.5) |
| - Lung Cancer | 41 (16.7) |
| - Not defined | 3 (1.2) |

age of 73.2 years (SD: 7.2). Yet, these age differences were not statistically significant, as evidenced by a p-value of 0.41 (Table 2).

The latency period, or the interval from exposure to the manifestation of the disease, presented a more pronounced divergence among the diagnoses. Those with Asbestosis or Pleural plaques had an average latency of 52.4 years, contrasting with Lung Cancer patients (47.5 years) and Mesothelioma patients (51.6 years). The differences here were statistically significant, with a p-value less than 0.001 (Table 2).

A similar trend was noticed in exposure duration: individuals with Asbestosis or Pleural plaques were exposed for an average of 30.9 years, which was relatively longer than Lung Cancer patients (29.3 years) and notably longer than Mesothelioma patients (26.9 years). Again, these differences were statistically significant, having a p-value less than 0.01 (Table 2).

The age at which individuals began their exposure to asbestos demonstrated minor variation, with Asbestosis/Pleural plaques patients starting at approximately 19.8 years, Lung Cancer patients at 22.3 years, and Mesothelioma patients at 20.5 years. However, these differences were not statistically significant (p-value: 0.28) (Table 2).

Smoking habits showcased distinct patterns. Only 4.3% of Asbestosis/Pleural plaques patients were active smokers, in contrast to a considerable 24.4% of Lung Cancer patients and 5.2% of Mesothelioma patients. This association was notably significant with a p-value less than 0.001 (Table 2).

The majority of the diagnosed individuals across all disease categories predominantly belonged to the shipbuilding sector. However, the proportion was highest for Asbestosis/Pleural plaques (95.7%), followed by Mesothelioma (89.5%), and then Lung Cancer (80.5%). This difference was statistically significant with a p-value less than 0.01 (Table 2).

Lastly, the utilization of Personal Protective Equipment (PPE) was not extensively adopted across the groups. Nonetheless, its use was most prevalent among the Asbestosis/Pleural plaques patients (37.3%), compared to Lung Cancer (26.3%) and Mesothelioma patients (23.7%). Still, this difference wasn't deemed statistically significant, with a p-value of 0.17 (Table 2).

Table 3 delineates the multivariable analysis

Table 2 - Univariable analysis between different diagnoses of asbestos-related diseases with demographic and occupational characteristics observed in Palermo and Province between 2010 and 2021.

| | Asbestosis/ Pleural plaques | Lung Cancer | Mesothelioma | p-value |
|---|---|---|---|---|
| Age, average in years (SD) | 72.7 ± 5.8 | 71.4 ± 8.5 | 73.2 ± 7.2 | 0.41 |
| Latency, average in years (SD) | 52.4 ± 6.6 | 47.5 ± 9.6 | 51.6 ± 7.4 | <0.001 |
| Exposure duration, average in years (SD) | 30.9 ± 6.4 | 29.3 ± 7.2 | 26.9 ± 11.8 | <0.01 |
| Age at start of exposure, average in years (SD) | 19.8 ± 4.3 | 22.3 ± 5.7 | 20.5 ± 6.7 | 0.28 |
| Tobacco smoking habit, n (%) | | | | |
| - Smoker | 7 (4.3) | 10 (24.4) | 2 (5.2) | <0.001 |
| - Non-smoker | 94 (57.7) | 2 (4.9) | 18 (47.4) | |
| - Former smoker | 62 (38) | 29 (70.7) | 18 (47.4) | |
| Sector and production, n (%) | | | | |
| - Shipbuilding | 156 (95.7) | 33 (80.5) | 34 (89.5) | <0.01 |
| - Other | 7 (4.3) | 8 (19.5) | 4 (10.5) | |
| PPE use, n (%) | | | | |
| - Yes | 60 (37.3) | 10 (26.3) | 9 (23.7) | 0.17 |
| - No | 101 (62.7) | 28 (73.7) | 29 (76.3) | |

examining the associations between sociodemographic and occupational parameters with distinct diagnoses of asbestos-related diseases, using Asbestosis/Pleural plaques as the reference category.

The adjusted hazard ratio (HR) for Mesothelioma and Lung Cancer, in relation to exposure duration, indicates a decrement in relative risk for both diseases compared to Asbestosis/Pleural plaques with each successive year of exposure. Specifically, for Mesothelioma, the HR stands at 0.933 (95% CI: 0.902-0.965), while for Lung Cancer, it is 0.939 (95% CI: 0.902-0.978).

Regarding smoking habits, active smokers exhibit a significantly elevated risk for Lung Cancer, with an HR of 64.520 (95% CI: 13,075-318,390). Their Mesothelioma risk yields an HR of 2.078, albeit with a wider CI of 0.418 to 10,319. Former smokers present an increased risk for Lung Cancer (HR: 20.917, 95% CI: 4,913-89,048), and for Mesothelioma, the HR is 1.857 (95% CI: 0.920-3.751).

Sectoral analysis reveals that individuals engaged in shipbuilding and repair manifest a diminished risk for both Mesothelioma and Lung Cancer. The HR for Mesothelioma in this sector is 0.448 (95% CI: 0.143-1.406), and for Lung Cancer, it is 0.371 (95% CI: 0.155-0.892).

Concerning PPE utilization, Mesothelioma risk among users is depicted by an HR of 1.009 (95% CI: 0.446-2.287). For Lung Cancer, the non-use of PPE slightly amplifies the risk, showcasing an HR of 1.220 (95% CI: 0.571-2.605).

## Discussion

Summary of main findings. The current study offers a follow-up perspective from a previous investigation conducted a decade earlier, which included a more limited cohort (46). Our retrospective study, a total of 245 cases of work-related claims for ARD were reported between 2010 and 2021, mostly from naval industry (92.2%), including 38 cases of MM (15.5%), and 41 cases of lung cancer (16.7%) with documented occupational exposure to asbestos, while the large majority of claims were associated with non-malignant disorders, that is pleural plaques and asbestos. Our analysis revealed a notably shorter latency period for the development of lung cancer compared to other asbestos-related diseases in the dataset, while the observed incidence of MM compared to asbestosis or pleural plaques aligns with recent findings in international literature (47). In multivariable analysis, when non-malignant disorders were assumed as the reference group, diagnoses of respiratory neoplasia were more frequently associated with smoking habit (HR 64.520, 95%CI

Table 3 - Multivariable analysis of sociodemographic and occupational variables associated with different diagnoses of asbestos-related diseases (reference group: non-malignant diseases, asbestosis/pleural plaques) (note: HR = hazard ratio; 95%CI = 95% confidence interval).

| Asbestosis/pleural plaques | Mesothelioma | | | Lung Cancer | | |
|---|---|---|---|---|---|---|
| | HR | 95%CI | | HR | 95%CI | |
| Exposure duration, average in years | **0.933** | **0.902** | **0.965** | **0.939** | **0.902** | **0.978** |
| Smoking habits | | | | | | |
| - no smoker | | | | 1.000 | | - |
| - smoker | 2.078 | 0.418 | 10,319 | **64.520** | **13.075** | **318.390** |
| - former smoker | 1.857 | 0.920 | 3.751 | **20.917** | **4.913** | **89.048** |
| Sector and production | | | | | | |
| - other | 1.000 | - | - | 1.000 | - | - |
| - shipbuilding and repair | 0.448 | 0.143 | 1.406 | **0.371** | **0.155** | **0.892** |
| PPE use | | | | | | |
| - yes | 1.009 | 0.446 | 2.287 | 1.000 | - | - |
| - no | 1.000 | - | - | 1.220 | 0.571 | 2.605 |

13.075 to 318.390 for current smokers; HR 20.917, 95%CI 4.913 to 89.048 for former smokers), while no substantial differences were identified for MM. Interestingly, the occurrence of claims for MM and non-malignant ARD in shipbuilding sector was similar (HR 0.448, 95%CI 0.143 to 1.406), while having worked in shipbuilding sector was less frequently reported in cases of respiratory neoplasia than in cases non non-malignant diseases (HR 0.371, 95%CI 0.155 to 0.892).

Interpretation and Generalizability. According to our results, shipbuilding, a cornerstone industry in the region and particularly in the province of Palermo, emerges as a potent nexus of exposure, thereby underscoring its critical role in occupational health concerns. The use of asbestos in shipbuilding was quite common (48-49), particularly from early 1930s to late 1970s, when naval and commercial shipyards did use hundreds of tons asbestos, to build and repair naval vessels for guaranteeing appropriate thermal insulation where needed (i.e. boliers, steam, and hot water pipes), fire protection, sound absorption etc (50, 51).

The high occurrence of ARS among workers from shipyards was similarly well documented, particularly in Italy. In 1979 and 2001, Puntoni et al. (52, 53) specifically inquired the mortality in workers employed at the shipyard of Genoa (Italy) employed or retired between 1960 and 1981 (last follow up in 1995), and their study reported an increased mortality for MM, but also for respiratory neoplasia (lung, larynx), and bladder cancer. In a more recent follow up the aforementioned studies, Merlo et al., reported on the mortality of 3,984 shipyard workers from the Genoa shipyard, including a total of 3,331 deaths (83.6%), with excess mortality for all cancers (Standardized Mortality Ratio [SMR] 1.27, 95%CI 1.20-1.34), pleural MM (SMR 5.75, 95%CI 4.69 to 6.97), cancers of the larynx (SMR 1.83, 95%CI 1.34 to 2.44) and of the lung (SMR 1.54, 95%CI 1.39 to 1.70) (54). Notably, Authors did report an increased occurrence deaths associated with non-malignant respiratory disorders of the lungs (SMR 1.27, 95%CI 1.14 to 1.41), and particularly asbestosis (SMR 22.77, 95%CI 15.25 to 32.70).

A similar study from the shipyard workers of Monfalcone (55) on 1,403 workers hired in 1950-1959 identified 35 diagnoses of MM between 1978 and 2012, with the highest percentage of cases occurring in people aged 14 to 19 years et the employment.

More recently, in a pool of 43 Italian asbestos cohorts, a total of 5,120 shipyard workers (99.6% of male gender) were documented (56), with a SMR 1.08, 95%CI 1.00 to 1.16 for the whole of sampled workers on all malignant neoplasm, and SMR 8.42, 95%CI 6.07 to 11.38 for pleural MM, SMR 1.18, 95%CI 1.03 to 1.34 for lung cancer. An increased mortality ratio was also associated with MM occurring in workers having performed ship furniture (SMR 8.26, 95%CI 3.78 to 15.69) and worked in dockyards (SMR 10.52, 95%CI 6.67 to 15.79), the latter also reporting increased SMR for cancers of the lungs (SMR 1.61, 95%CI 1.36 to 1.89).

The reasons for high occurrence of ARD and similarly increased mortality of shipyard workers can be explained not only through the likelihood of potential exposures to asbestos fibers due to the occupational tasks, but also to the specific settings of these exposures. Shipbuilding tasks require the workers to work in enclosed settings, where very high levels of asbestos exposure could be reached (57, 58). Moreover, as recently pointed out by Vimercati et al (59), only in recent years reliable substitute materials have been made available. Finally, vibration during sailing could release asbestos fibers from all asbestos containing materials, particularly from engine rooms, with resulting exposures of all workers involved in the maintenance of naval vessels even after the discontinuation of asbestos in naval industry.

While some of the aforementioned results were not unexpected, our results shed light on the occurrence of asbestos-related diseases in Palermo and its province over the studied period and the intricate interplay between socio-demographic characteristics, occupational settings, and individual habits. Most notably, our results underscores the inappropriate usage of PPE. Consistent use or neglect of personal protective equipment, might have substantial implications on the exposure levels and consequent health risks (60). Still, it should be stressed that the effectiveness of PPE in preventing ARD is affected by several factors that we were unable to properly track down because of the limited information retrieved by parent registry of the 'Service of Prevention and Safety on Work Environment' of the Local Health Authority of Palermo. First, PPE are effective only if properly worn, and workers have to be accurately and preventively trained (61). Assigned protection factors for the revised respiratory protection standard. www.osha.gov/sites/default/files/publications/3352-APF-respirators.pdf). Second, PPE have to be properly worn and removed in specifically designed rooms in order to avoid the potential contamination of workers' clothes. Third, PPE and/or their filters have to be changed regularly, and PPE repaired and replaced regularly or their efficacy is rapidly lost (62). Finally, as the potentially assessed timeframe ranged across 50 years or more, it is important to stress the very same industrial and legal requirements for PPE radically changed over time (63). As a consequence, while the low rate of workers reporting their accurate use cannot be underscored in any way, their potential preventive role should be carefully asseed.

Furthermore, personal habits, especially tobacco smoking, appeared to amplify the risk profile for respiratory cancers, suggesting that individual behavioral choices can act synergistically with occupational exposures to influence health outcomes. Again, these results were not unexpected (64). On the one hand, there is a vast body of research highlighting a strong correlation between lung cancer cases in the general populace and both occupational and environmental asbestos exposure (65). Our data on tobacco consumption further emphasizes the compounded health risks of smoking in combination with asbestos exposure. Previous studies have shown that smoking significantly augments lung cancer risks among those exposed to asbestos (46, 64), and some researchers suggest that the cellular damage caused by tobacco can be exacerbated by asbestos fibers, leading to a heightened risk of malignancy (64), particularly among individuals predisposed to asbestosis or pleural plaques (54). These results are reasonably due to the synergism between asbestos exposure and tobacco smoke in lung cancer causation at a biological level, resulting in the epidemiological evidence of a multiplicative model for the interaction effects of asbestos and smoking on the lung cancer risk, with no requirement for asbestosis. This observation was particularly pronounced for individuals employed within the shipbuilding and repair sector, who exhibited a heightened likelihood of developing asbestosis or pleural plaques over lung cancer, but again similar results previously documented and explained by the specific settings of naval yards (66).

In other words, as we delve deeper into the dynamics of these diseases, the patterns observed underscore the multifaceted nature of asbestos-related health risks and the imperativeness of a comprehensive approach to understanding and mitigation. This is particularly true when acknowledging gender disparities in the occurrence of ARD. As clearly documented by INAIL and ReNaM reports (19, 37), and recently pointed out by Mangone et al. (23) in their comprehensive review of MM cases documented by ReNaM of Emilia Romagna, ARD predominantly affect males, likely mirror patterns of occupational exposures, with the average age at diagnosis consistently exceeding 70 years (66). The influence of asbestos on male workers has been historically significant due to male-dominated occupations, especially in construction and shipbuilding (66).

Limits and strengths. Despite its potential interest and significance not only from an Occupational Health, but by a broader Public Health point of view, our study is affected by several shortcomings and substantial limits that should be accurately addressed. First of all, this observational study was designed to scrutinize the incidence and dynamics of asbestos-related diseases, which, despite advancements in clinical practice, continue to pose a significant public health challenge (47). Having been developed by the 'Service of Prevention and Safety on Work Environment', the service of the competent Local Health Authority of Palermo, the parent registry includes data that medical professionals are compulsorily required to share with Judicial Police bodies for Occupational Health and Safety when diagnosing diseases of either documented or alleged occupational etiology (67, 68). As a consequence, the present registry likely contains a more extensive set of data than corresponding estimates from pathology registries such as ReNaM (that only contains data on MM), but results are possibly inflated by inaccurate diagnoses from sentinel professional. However, it should be stressed that all cases were accurately reviewed by trained and highly skilled personnel, and only "probable" or "highly probable" cases were eventually included. Second, the present study was designed and performed as a single-center study. Despite its valuable insights, a multi-centric approach involving multiple regions or countries might offer a more comprehensive perspective on the global dynamics of asbestos-related diseases, offering a broader understanding of variations in incidence and practice (60), overcoming another noteworthy limitation of this investigation, that is its restricted sample size and the lack of a control group of healthy workers with similar asbestos exposure. Such a comparison would've enriched our understanding of the relative risks. Third, our report is affected by some significant gaps in the gathered data, and most notably the lack of analyses on non-occupational exposures and risk factors, including genetic ones, that could predispose individuals to asbestos-related malignancies, independent of any defined exposure threshold (69). Fourth, as previously stressed, we only dichotomously assessed the usage of PPE (ever vs. never): similar studies on the awareness and training about asbestos hazards in the Italian construction sector (60) have stressed that some degree of "fatigue" may affect actual usage of PPE, even among individuals used to employ these devices properly and accurately, while recall bias may have substantially affected the eventual estimates.

## Conclusions

Our study underscores the enduring public health challenge posed by asbestos-related diseases in Italy, even after its prohibition in 1992. The persistent emergence of these diseases is attributed to the extensive latency between exposure and onset of asbestos-related diseases (ARDs). Notwithstanding the limitations inherent in this research, the findings have potential implications for the Italian estimation of ARD incidences. As advocated by international entities and governing bodies, the pivotal role of epidemiological surveillance in addressing ARDs cannot be overstated. Such surveillance stands as a beacon guiding concerted efforts aimed at the eventual eradication of these diseases. The overarching objective in public health should pivot towards refining prevention strategies, bolstering care provisions - encompassing psychological assistance, and augmenting the compilation of detailed anamnestic and occupational data. This would include specifics on job roles, average duration of exposure, adherence to personal protective equipment, and smoking tendencies. Such comprehensive data collection is imperative for accurately gauging the true prevalence of these diseases, particularly among those with occupational exposures.

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**Riassunto**

***Valutazione dell'impatto di Salute delle patologie asbesto correlate in una coorte di lavoratori esposti professionalmente: un approfondimento decennale***

**Introduzione.** L'amianto è uno dei principali agenti cancerogeni professionali a livello globale. Nonostante il divieto previsto dalla legge 257/1992, l'Italia è una delle nazioni europee più gravate dal carico di malattie legate all'amianto (ARD). Il presente studio ha analizzato i casi di ARD nei lavoratori esposti all'amianto della provincia di Palermo, in Italia, nel periodo 2010-2021.

**Materiali e metodi.** L'acquisizione dei dati è stata effettuata durante l'attività di vigilanza del 'Servizio di Prevenzione e Sicurezza negli Ambienti di Lavoro' del Dipartimento di Prevenzione dell'Azienda Sanitaria Provinciale (ASP) di Palermo.

**Risultati.** Tra il 2010 e il 2021, abbiamo identificato 245 casi di ARD, comprendenti 163 casi di placche pleuriche, 41 tumori polmonari, 38 mesoteliomi e 3 casi di natura non specificata.

All'analisi multivariata il range temporale di insorgenza di mesotelioma (HR = 0,933; IC 95% = 0,902-0,965) e cancro polmonare (HR = 0,93; IC 95% = 0,90-0,978), rispetto alle placche pleuriche / asbestosi, è significativamente inferiore. L'abitudine tabagica è risultata significativamente associata con i casi d cancro al polmone (fumatore HR = 64.520 95% CI = 13.075-318.390; ex fumatore HR = 20.917 95% CI = 4.913-89.048). Infine si è osservata una correlazione statisticamente significativa tra i casi di mesotelioma e placche pleuriche/asbestosi nei soggetti impiegati nella cantieristica navale (HR = 0,371 IC 95% = 0,155-0,892).

**Conclusioni.** Nonostante la cessazione delle attività legate all'amianto nel 1992, le diagnosi di ARD persistono nelle osservazioni cliniche e della sorveglianza sanitaria degli ex lavoratori esposti, continuando a rappresentare una sfida per la Sanità Pubblica e la Medicina del Lavoro. L'attuazione di strategie di prevenzione e di diagnosi precoce nelle coorti professionalmente esposte, attraverso una adeguata raccolta di dati anamnestici e di esposizione, appare fondamentale per ancora diversi anni.

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