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Persistence burden and poor survival of pleural mesothelioma in central Italy, 2013–2022: a population-based study thirty years after asbestos ban

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Abstract

Background Pleural Mesothelioma (PM) is an asbestos-related cancer with poor prognosis. Despite the 1992 national asbestos ban, new cases continue to occur due to the long latency of the disease. The study aim was to evaluate incidence and survival trends of pleural mesothelioma in the Marche Region, central Italy, between 2013 and 2022.

Methods This population-based incidence study included adult residents of the Marche Region between 2013 and 2022. Incident PM cases were identified from the Cancer Registry of Marche Region. Incidence rates per 100,000 person-years (py) were calculated and stratified by sex, age, and province of residence. Temporal trend and covariates effect were assessed with Poisson regression. Overall survival was estimated using the Kaplan-Meier method and compared across subgroups; adjusted hazard ratios (HR) were obtained from multiple Cox regression model.

Results Between 2013 and 2022, there were 322 incident PM cases (82% male; median age 77 years). The crude incidence rate was 2.1 per 100,000 py (95% CI: 1.9–2.4), with no temporal change over the study period. The highest rates were observed in men, in age-group 75–79 years, and in the province of Ancona. One- and five-year survival rates were 48.8% and 8.3%, respectively. Older age and non-epithelioid histology were independently associated with higher mortality.

Conclusions The incidence of pleural mesothelioma in the Marche Region remained stable between 2013 and 2022, with a peak in 2018 requiring further observation to confirm it. The persistently high burden among men, older adults, and those living in industrialized coastal areas reflects the legacy of historical asbestos exposure. Continued population-based surveillance, integrated with follow-up of previously exposed workers, remains essential to monitor disease trends and support timely diagnosis and appropriate care pathways.

Keywords pleural mesothelioma, cancer, incidence, survival, cancer registry, epidemiology, secondary data

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Introduction

Pleural Mesothelioma (PM) is a rare but highly aggressive cancer affecting the pleura, the thin membrane lining the lungs and thoracic cavity. Its aetiology is primarily linked to asbestos exposure, which remains the main risk factor for the disease onset [1]. Although asbestos use has declined in many countries, cases related to past exposures continue to occur due to the disease's long latency period, which typically spans several decades and may exceed 40 years from the initial exposure [2–5].

Globally, the age-standardized incidence and mortality rates have shown a modest but consistent decline over the past three decades. According to Zhu et al. (2023), the global age-standardized incidence and mortality rates decreased respectively from 0.49 to 0.43 and from 0.46 to 0.40 per 100,000 between 1990 and 2019 [6]. Luan et al. (2025) reported a slight overall decline in incidence and mortality with a worldwide estimated annual percentage change of -0.20 (95% uncertainty intervals: -0.32 to -0.08) and of -0.23 (95% uncertainty intervals: -0.30 to -0.16), respectively. Despite these reductions, survival after diagnosis remains low, reflecting the disease's persistently poor prognosis despite therapeutic advances [7].

Italy, due to its extensive historical use of asbestos in various industries, has one of the highest PM incidence rates globally [8, 9]. In 2020, about 2,000 new diagnoses were estimated, with 75% of cases occurring in men. According to the Italian National Mesothelioma Registry (ReNaM), the crude incidence rate was 4.40 cases per 100,000 inhabitants per year in men and 1.41 in women as of 2019 [10]. Median survival following diagnosis is approximately 10 months, with a five-year survival rate of about 10% [11, 12]. While these national figures are informative, they may mask geographical heterogeneity. Mesothelioma clusters in Italy are associated with shipyards, asbestos-cement factories, and other localized sources of exposure [13]. However, few studies provide fine-grained incidence or survival data at the provincial or municipal level. Given the long latency and occupational origin of PM, residence at diagnosis may not reflect the location of exposure. Therefore, population-based cancer registry data without detailed exposure histories can only provide approximate indications of geographic disease patterns, making it difficult to identify local hotspots or guide targeted interventions.

In the Marche Region, a region of central Italy with a population of about 1.5 million, a report of the Cancer Registry documented an average of 31 new PM cases per year between 2013 and 2015, with a male-to-female ratio of 3.7:1 [14]. According to the Italian National Mesothelioma Registry (ReNaM) [10], 721 pleural mesothelioma cases were diagnosed among residents of the Marche Region between 1993 and 2021 (≈ 27 cases/year). Annual case counts increased from the mid-1990s, peaked in

the early 2010s, and remained relatively stable thereafter (with incomplete data for 2020–2021). In this Region, the province of Ancona is historically characterized by shipbuilding and industrial activities, highlighting the need for updated epidemiological data on asbestos-related diseases in the region.

This study aims to investigate the incidence and survival of Pleural Mesothelioma in the Marche Region, 20 to 30 years after the nationwide asbestos ban (Italian Law No. 257/1992), providing a comprehensive analysis of its epidemiological trends over the past decade.

Methods

Study design and population

This population-based incidence study focused on beneficiaries of the Italian National Health Service (INHS), residing in the Marche Region, older than 18 years between 2013 and 2022.

Data sources

Incident cases of PM were identified using the Cancer Registry of the Marche Region (CR), established by regional law in 2013 (*Deliberazione della Giunta Regionale* n. 1629 del 2/12/2013). Cases were selected using the International Classification of Diseases, 10th Revision (ICD-10) code C45.0 for diagnoses occurring between 2013 and 2022. The CR systematically collects data on all new cancer diagnoses, including basic demographic information and tumour characteristics. Data quality is ensured through validation using the Joint Research Centre-European Network of Cancer Registries Quality Check Software (JRC-ENCR QCS) and adherence to international cancer registration standards [15].

The Regional Beneficiaries database (RBD) of the Health Regional System was used to retrieve date of death and date of assistance end in Marche Region.

The two databases were linked using a deterministic procedure based on the beneficiary's identification code. This was a population-based study using secondary data sources; therefore, patients were not directly involved.

Statistical analysis

Continuous variables were summarized as medians and interquartile ranges (IQR), categorical variables were described using absolute and percentage frequencies, and stratified by sex.

Incidence rates of PM, with 95% confidence intervals (95% CI), were calculated per 100,000 person-years (py) for the overall study period (2013–2022) and for each calendar year, overall and stratified by sex. The numerator represented the total number of incident cases recorded in the CR, and the denominator corresponded the resident population of the Marche Region on January 1st of each year, as reported by the Italian National Institute of

Statistics (ISTAT) [16]. Age-standardized incidence rates (ASRs) were calculated using two standard populations: the EU-27 + EFTA (27 countries of European Union and European Free Trade Association) standard population (based on the 2011–20 Eurostat projections) [17] and the 2019 Global Burden Disease (GBD) world standard population from the Global Health Data Exchange [18]. Sex, age (< 65, 65–69, 70–74, 75–79, 80–84, 85 + years old), province of residence (Pesaro-Urbino, Ancona, Macerata, Fermo, Ascoli Piceno) incidence rates at diagnosis were estimated. In 2022, the resident population aged ≥ 18 years was 392,422 in Ancona, 296,572 in Pesaro-Urbino, 259,283 in Macerata, 173,789 in Ascoli Piceno, and 144,043 in Fermo [16].

Due to the small number of new diagnoses, two separate Poisson regression models were performed considering the PM incident cases as dependent variable and the annual population as offset. The first model was used to assess temporal trend using the year of diagnosis as a quantitative independent variable; a segmented analysis was applied to detect possible changes in the incidence trend. The second Poisson regression model was used to estimate incidence rate ratios (IRRs) and 95% CI considering sex, age-group and province of residence as covariates. The equidispersion assumption of the Poisson models were tested against the alternative hypothesis of overdispersion using the deviance and Pearson chi-square statistics [19].

Overall survival was estimated using the Kaplan-Meier method, and subgroups differences were evaluated using the log-rank test. Follow-up extended from the date of diagnosis to the date of death, date of assistance end in Marche, or December 31, 2023, whichever occurred first.

A multiple Cox proportional hazards model was used to estimate adjusted hazard ratios (HRs) for mortality by sex, age-group, province of residence, year of diagnosis, and histological subtype. The proportional hazards assumption was verified using Schoenfeld residuals.

Statistical analyses were performed using R (version 4.4.1). Effect estimates are reported with corresponding 95% confidence intervals and p-values.

Results

Characteristics of Incident Cases

Between 2013 and 2022, a total of 322 incident cases of PM were identified in the Marche Region. Most cases were males (82%), corresponding to a male-to-female ratio of 4.6:1. The median age at diagnosis was 77 years (IQR: 71–81), with the highest frequency (30.1%) observed among individuals aged 75–79 years. Regarding geographic distribution, more than half of the cases (51.9%) were residents in the Province of Ancona, followed by Pesaro e Urbino (18.0%), Macerata (13.7%), Fermo (9.3%), and Ascoli Piceno (7.1%). In terms of

histological subtypes, epithelioid mesothelioma was the most common (53.1%), followed by pleural mesothelioma not otherwise specified (25.8%), fibrous mesothelioma (11.5%), and biphasic mesothelioma (9.6%) (Supplementary Material Table S1).

Incidence of pleural mesothelioma over time

During the study period, the overall crude incidence rate was 2.1 (95% CI: 1.9–2.4) cases per 100,000 person-years (py), and was higher in males (IR: 3.6, 95% CI: 3.2–4.0) than in females (IR: 0.7, 95% CI: 0.6–1.0) (Supplementary Material Table S2). Annual incidence rates fluctuated slightly, ranging from a minimum of 1.5 (95% CI: 0.9–2.2) in 2014 to a maximum of 2.6 (95% CI: 1.9–3.6) cases per 100,000 py in 2018. ASRs calculated using the European and Global Burden of Disease (GBD) standard populations, were 2.0 and 1.2, respectively, over the decade.

As shown in Fig. 1, the annual incidence rates observed over the study period fluctuated around a line parallel to the x-axis, indicating no trend (IRR = 0.99; 95% CI 0.96–1.04; $p = 0.866$). The segmented analysis detected no breakpoints in the incidence trend.

Subgroup analysis of incidence

Marked differences in incidence were observed across demographic and geographic subgroups (Table 1).

Males exhibited a 6-fold higher incidence rate compared to females (IRR = 6.0, 95% CI: 4.5–8.0).

Individuals aged < 65 years showed the lowest incidence (Table 1). Rates rose progressively across age-groups, reaching 3.5 among those aged 65–69 years and 6.2 among those aged 70–74 years. The highest incidence was observed in the 75–79-year group, followed by 80–84 years and ≥ 85 years. Compared with individuals aged < 65 years, the incidence of PM increased more than ten-fold starting from 65 to 69 years (IRR = 11.0; 95% CI: 6.9–17.6) and peaked at 75–79 years (IRR = 43.2; 95% CI: 29.9–63.5), before slightly declining in the oldest age-groups.

When considering the province of residence, Ancona had the highest IR (3.5, 95% CI: 3.0–4.1). All the other provinces showed lower IRs than Ancona, with IRRs ranging from 0.3 (95% CI: 0.2–0.5) for Ascoli Piceno to 0.5 (95% CI: 0.3–0.7) for Fermo.

Survival analysis

During the follow-up period, a total of 295 deaths were observed among the 322 PM incident cases. The median survival time was 11.8 months (95% CI: 10.4–13.7), with a 1-year survival of 48.8% (95% CI: 43.6%–54.5%) and a 5-year survival of 8.3% (95% CI: 5.6%–12.3%).

As shown in Fig. 2, Females had higher survival probability than males as well as subjects with < 75 year at diagnosis than those with 75 or more years.

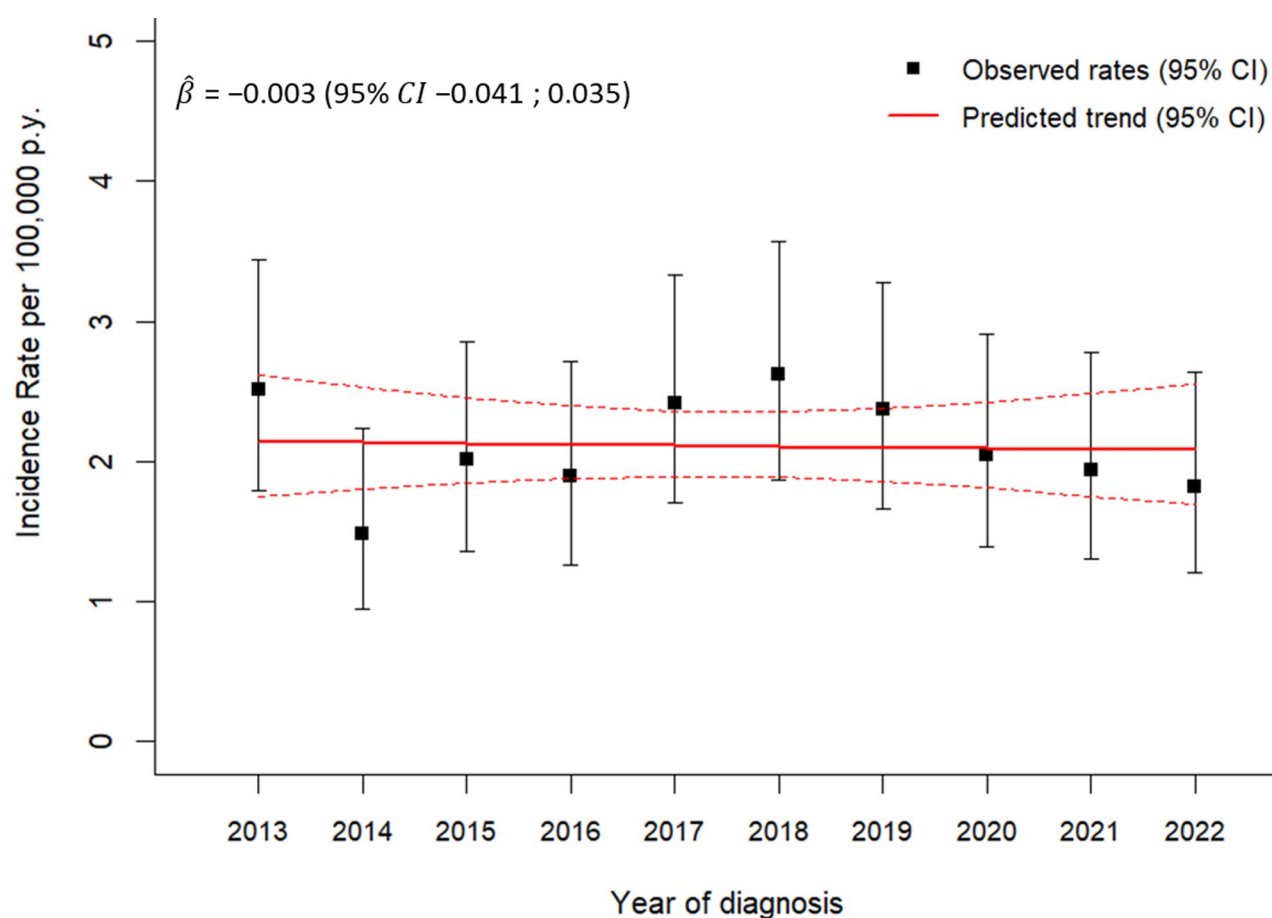


Fig. 1 Annual incidence rates of Pleural Mesothelioma per 100,000 person-years in the Marche Region between 2013 and 2022. Black squares represent observed rates with 95% confidence intervals, while the red line and dashed limits show the predicted trend of the Poisson model and its 95% confidence interval

Table 1 New cases of Pleural Mesothelioma and incidence rates per 100,000 py (95% CI) stratified by sex, age-group and province of residence. Incidence Rate Ratios estimated using multiple Poisson regression model

Variables	New cases	py	IR (95% CI)	IRR (95% CI) [#]
Sex				
Female	58	7,857,088	0.74 (0.56–0.95)	ref. cat.
Male	264	7,405,539	3.56 (3.15–4.02)	5.98 (4.53–8.03)
Age-groups				
< 65	38	11,528,611	0.33 (0.23–0.45)	ref. cat.
65–69	32	908,850	3.52 (2.41–4.97)	11.03 (6.85–17.63)
70–74	51	818,011	6.23 (4.64–8.20)	19.81 (13.05–30.33)
75–79	97	741,767	13.08 (10.60–15.95)	43.16 (29.93–63.53)
80–84	61	621,474	9.82 (7.51–12.61)	34.22 (22.93–51.72)
85 +	43	643,914	6.68 (4.83–9.00)	26.83 (17.32–41.71)
Province of residence				
Ancona	167	4,711,287	3.54 (3.03–4.12)	ref. cat.
Ascoli Piceno	23	2,081,937	1.10 (0.70–1.66)	0.30 (0.19–0.46)
Fermo	30	1,732,401	1.73 (1.17–2.47)	0.48 (0.32–0.69)
Macerata	44	3,151,817	1.40 (1.01–1.87)	0.39 (0.27–0.53)
Pesaro-Urbino	58	3,585,185	1.62 (1.23–2.09)	0.47 (0.34–0.62)

py Person-year (source: Italian National Statistics Institute, ISTAT), IR Incidence rate, 95% CI 95% Confidence interval, IRR Incidence Rate Ratios, ref. cat., reference category

[#] Estimates from the multiple Poisson regression model

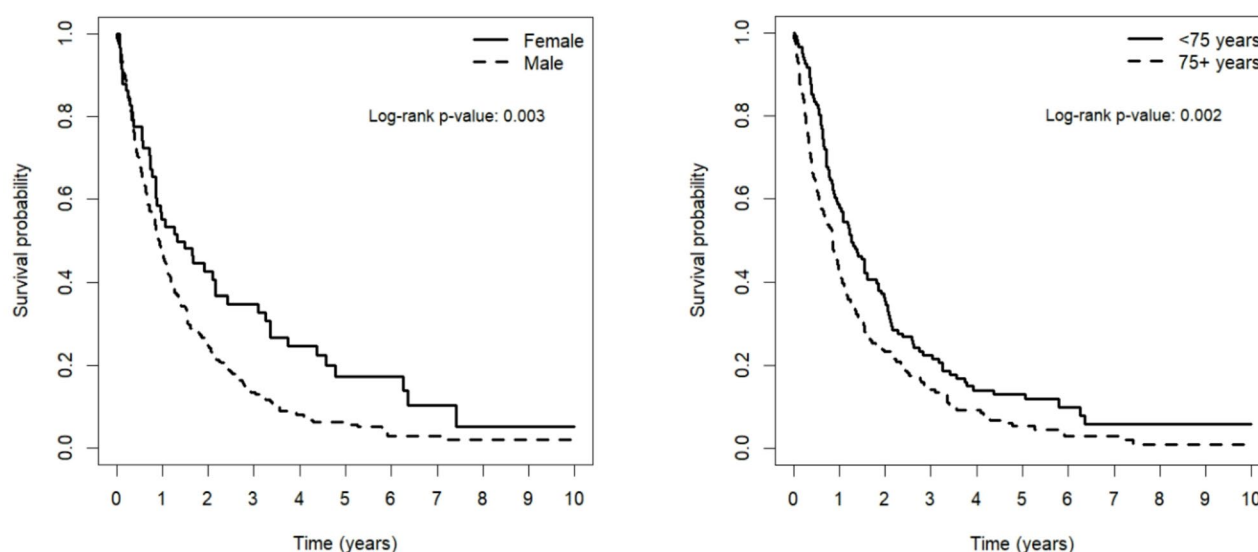


Fig. 2 Kaplan-Meier cumulative survival probability curves according to sex and age class

Table 2 Multiple Cox proportional hazard model for the risk of death according to demographic, geographic, temporal, and histological factors in patients with pleural mesothelioma, Marche Region

	Deaths/ Subjects at risk	HR (95% CI)
Sex		
Female	10/58	<i>ref. cat.</i>
Male	17/264	1.29 (0.93 - 1.79)
Age-group		
<65	8/38	<i>ref. cat.</i>
65-69	4/32	1.62 (0.95 - 2.74)
70-74	2/51	1.48 (0.92 - 2.37)
75-79	10/97	1.37 (0.89 - 2.13)
80-84	2/61	2.42 (1.53 - 3.82)
85 +	1/43	4.87 (2.91 - 8.15)
Province of residence		
AN	11/167	<i>ref. cat.</i>
AP	2/23	0.78 (0.49 - 1.24)
FM	5/30	0.85 (0.55 - 1.32)
MC	8/44	0.62 (0.43 - 0.89)
PU	1/58	1.21 (0.88 - 1.66)
Year of diagnosis		1.01 (0.96 - 1.05)
Histological subtypes		
9050/3 Mesothelioma, not specified	6/83	<i>ref. cat.</i>
9051/3 Fibrous mesothelioma	1/37	1.58 (1.04 - 2.38)
9052/3 Epithelioid mesothelioma	17/171	0.77 (0.58 - 1.02)
9053/3 Biphasic mesothelioma	3/31	1.74 (1.1 - 2.75)

HR Hazard Ratio, 95% CI 95% Confidence interval, *ref.cat.* reference category

Test the proportional hazards assumption $p = 0.085$

In Supplementary Material Table S3, one- and five-year survival probabilities are reported according to sex, age-group, province of residence and histological subtype. Survival declined markedly with increasing age. Across provinces, survival patterns were broadly consistent, though some variation was observed. One-year survival ranged from 43.7% (95% CI: 36.8–51.9) in Ancona to 60.9% (95% CI: 43.9–84.5) in Ascoli Piceno. The highest 5-year survival was observed in Macerata (17.3%; 95% CI: 8.6–34.8), followed by Ascoli Piceno (13.0%; 95% CI: 4.5–37.5), whereas other provinces had rates below 10%.

By histological subtype, the epithelioid form was associated with the most favourable outcomes, with 1-year survival of 61.4% (95% CI: 54.5–69.2) and 5-year survival of 9.1% (95% CI: 5.5–15.3). In contrast, patients with fibrous or biphasic mesothelioma had substantially lower 1-year survival (18.9% and 32.3%, respectively), and 5-year survival was around 5%.

In the multiple Cox proportional hazard analysis (Table 2), sex was not associated with the risk of death. Older ages at diagnosis showed an increasing effect on mortality risk. Compared with patients younger than 65 years, the risk of death progressively increased for those aged 80–84 years and for those aged ≥ 85 years. No differences in risk of death were observed across most provinces, although patients residing in Macerata showed a lower risk of death compared to Ancona (HR=0.6; 95% CI: 0.4–0.9). The year of diagnosis was not associated with mortality, indicating stable survival over the study period. The risk of death varied substantially according to histological subtype. Compared to unspecified pleural mesothelioma (ICD-O code 9050/3), both fibrous mesothelioma and biphasic were associated with higher mortality.

Discussion

This population-based study provides the first comprehensive analysis of pleural mesothelioma incidence and survival in a central Italian region with details on local areas, over the past decade, twenty to thirty years after the national asbestos ban.

Between 2013 and 2022, the overall crude incidence rate of 2.1 per 100,000 person-years aligns with national estimates reported by the Italian National Mesothelioma Registry-ReNaM (4.4 for men and 1.4 for women per 100,000 py in 2019) [10], and with data from European countries with similar occupational exposure histories [20].

In the analysed study period, a peak in the incidence of PM appears to have occurred around 2018, after which a decline in the incidence was observed, consistently with Italian age-period-cohort model predictions that incorporated historical asbestos consumption trends and anticipated a gradual reduction in cases after the peak of exposure [21, 22]. Additional years of observation are needed to confirm whether this decline represents a true downward trend in incidence. Indeed, it remains uncertain whether this observed decrease reflects the expected latency-related decline after the asbestos ban or may be due to the underdiagnosis or reporting delays associated with the COVID-19 pandemic, as previously observed by Smesseim and colleagues [23]. However, Italian data suggest that the overall impact of the pandemic on new mesothelioma diagnoses was limited, with fluctuations largely compatible with random variation [24], although regional differences cannot be excluded.

The marked predominance of male cases observed in this study is consistent with previous findings [1, 25, 26] and with national data from the Italian National Mesothelioma Registry during 1993–2021, according to which approximately 72% of cases occur in men and incidence rates are substantially higher than in women [10]. This reflects that men historically accounted for the majority of occupational asbestos exposures in high-risk sectors such as shipbuilding, construction, and asbestos-cement manufacturing. The highest incidence rate among individuals of the age-group 75–79 corresponds to those likely exposed before the 1992 ban, further confirming that the current burden of disease is largely driven by past exposures. This pattern aligns with the peaks in age-period-cohort mortality risk observed in a recent Italian study [27].

Our findings also revealed a geographical variability in the burden of the pleural mesothelioma within the region. The province of Ancona exhibited the highest incidence rate, likely reflecting its long-standing shipbuilding industry and for the presence of a national priority contaminated site due to a petrochemical refinery, for which an excess of PM cases had previously been

reported [28]. In contrast, incidence rates in the other provinces were comparable, suggesting relatively homogeneous exposure levels outside of the Ancona industrial area.

Our study confirmed a poor 1-year survival (48.8%), in line with Italian population-based data from the National Mesothelioma Registry, which reported a median survival of approximately 9–10 months in large national cohorts [12, 29]. Consistent with the general pattern of extremely poor prognosis observed in Italy and other European countries [30–32], the 5-year survival did not exceed 10%. Despite advances in treatment strategies, including multimodal and immunotherapeutic approaches [33], no improvement in survival was observed over the study decade. As previously suggested in Italian population-based analyses, access to hospitals with specialized thoracic services may influence survival estimates [12]; however, in our setting the major referral centre is located in Ancona's Regional Hospital, and we did not observe differences in case-mix or health-care availability that could clearly explain differences in survival (data not shown). These findings underscore the need for improving therapeutic approaches, but also the importance of standardized diagnostic work-up and care pathways. Italian evidence suggests substantial variability in diagnostic timelines and management patterns, highlighting the need to reduce inequalities in access to specialized multidisciplinary services and to strengthen regional coordination of care [34].

Although female patients in our study demonstrated higher crude survival, sex was not found to be an independent predictor of mortality in multiple analysis. However, a female advantage in survival has been documented elsewhere, with studies reporting a 15–30% lower risk of death among women compared to men [35–37]. Italian population-based data have reported a modest survival advantage for women, with slightly higher mortality risks observed in men ($HR \approx 1.1$), although no effect was observed after accounting for treatment factors [12]. Although these studies refer to similar contexts to Italy in terms of level of industrialization, the discrepancy of the sex predicting role may be due in part to the limited number of female cases observed in the Marche region.

Consistent with previous literature, in our study the epithelioid subtype was associated with the most favourable prognosis, whereas fibrous and biphasic subtypes showed higher mortality risks. This histological gradient in survival is well established [35, 38], also in terms of treatment response. Patients with epithelioid histology show better responses and longer survival than mixed or biphasic subtypes, with a median overall survival after first-line chemotherapy of 26.7 versus 15.0 months [39].

An unexpected finding was the lower mortality risk among patients residing in Macerata province compared with those in Ancona. This may suggest potential small-area differences in genetic, environmental or socio-economic factors not measurable in our study based on secondary data. Although direct comparisons are lacking in the mesothelioma literature, geographic variation in survival was documented across Italian regions [12] reflecting wide differences in terms of healthcare setting, specialties represented (i.e. thoracic surgery, radiotherapy) as well as technical and medical skills. Further clinical studies should explore whether differences in stage at diagnosis, treatment uptake, or healthcare capacity underlie this observed provincial variation.

Strengths and limitations

The main strengths of this study include the opportunity to use a population-based design and high-quality data, i.e. cancer registry data adherent to the international (JRC-ENCR) standards of completeness and accuracy. However, some limitations should be acknowledged. Information on occupational and environmental exposure was not available as well as lifestyle and clinical conditions, preventing direct linkage between incidence patterns and exposure history. Moreover, the relatively small number of cases, an inherent limitation of small-area studies, may have reduced the ability to detect subtle temporal, demographic, or geographic variations. Differences in case definition and morphology classification between cancer registries and specialized mesothelioma registries, as previously documented in Italy [40], could also influence incidence and survival estimates. Lastly, potential difficulties in accessing to proper diagnostic pathways across provinces could have influenced case ascertainment leading to an underestimation of the incidence.

Conclusions

In conclusion, the incidence of pleural mesothelioma in the Marche Region remained stable between 2013 and 2022. In this area of central Italy, a peak of new cases was observed in 2018, and a longer observational period is needed to confirm this finding. The persistently high burden among men, older adults, and residents of industrialized coastal areas reflects the lasting impact of historical asbestos exposure. Continuous local surveillance and targeted monitoring of high-risk populations, especially of previously exposed workers to ensure early diagnosis, are essential for tracking the disease burden that still persists 30 years after the law banning the use of asbestos in Italy, and guide diagnostic and therapeutic strategies.

Supplementary Information

The online version contains supplementary material available at <https://doi.org/10.1186/s12889-026-26903-6>.

Supplementary Material 1.

Supplementary Material 2.

Authors' contributions

Conceptualization: MB, ES; Methodology: MI, RG, ES; Statistical Analysis: MI; Data utilization authorization: MP, EP; Data curation: DS; Results interpretation: MI, ES; Writing-Original Draft Preparation: MI, ES; Writing-Review & Editing: MB, FC, MI, FM, RG, ES. All authors have read and agreed to the published version of the manuscript.

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Data availability

Restrictions apply to the availability of these data. The datasets generated and/or analysed during the current study are property of a third party that is the Regional Health Agency of Marche (ARSMarche) and, although they are anonymized, datasets are not publicly available due to the current regulation on privacy. The description of the administrative databases is available from the website [ARSMarche/Flussi](<https://www.regione.marche.it/ars/Aree-di-Attivita%C3%A0/Flussi-informativi-sanitari>). Other researchers can obtain access to the data through a formal request based on a research project to the Regional Health Agency of Marche.

Declarations

Ethics approval and consent to participate

This study was a population-based observational study conducted using anonymized secondary data from the Marche Regional Cancer Registry and regional administrative health databases. According to Italian regulations, studies based exclusively on anonymized registry and administrative data do not require approval from a local ethics committee or institutional review board, nor individual informed consent. The need for ethics approval was waived in accordance with national legislation and with the competent local ethics committee, the *Comitato Etico Territoriale (CET) delle Marche*, as no direct patient involvement or identifiable personal data were included in the study. All data were pseudonymized prior to analysis and handled in compliance with the General Data Protection Regulation (EU Regulation 2016/679). The study was conducted in accordance with the principles of the Declaration of Helsinki and its subsequent amendments.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

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