Mesothelioma among seamen: a systematic review and meta-analysis

Matteo Rota[a], Angelo Viscardi[b], Francesca Maghin[c,d], Donatella Placidi[b] and Adelaide Conti[c]

Objectives **Navy personnel and seafarers live and work 24 h per day in the shipboard environment and they are exposed to asbestos fibers released into the confined spaces aboard ships. We conducted a systematic review and meta-analysis to quantify the mesothelioma risk of seamen working aboard ships, either commercial or naval vessels, as compared to that of the general population.**

Methods **We carried out a literature search in MEDLINE through PubMed and EMBASE, from inception to 31 December 2021, of all studies on seamen working aboard ships, either commercial or naval vessels, characterized by exposure to asbestos and providing mesothelioma risk estimates. The Newcastle-Ottawa Scale was used to assess the quality of the studies included. The pooled standardized mortality ratio (SMR) was computed across eligible studies. The study protocol was registered on PROSPERO and reporting followed the preferred reporting items for systematic reviews and meta-analyses guidelines.**

Results **A total of 10 studies published from 1990 to 2020 were considered eligible and included in the systematic review and meta-analysis. All the included studies were of good quality, with a median score of seven out of nine. Overall, there were 235 mesothelioma cases/deaths in the included studies versus 115.6 expected, with a pooled SMR of 2.11 (95% confidence intervals, 1.70–2.62), in the absence of a significant between-study heterogeneity ($I^2 = 39\%$, $P = 0.11$).**

Conclusion **A more than double excess risk for mesothelioma among seamen working aboard ships emerged from our meta-analysis.** ***European Journal of Cancer Prevention*** **XXX: XXXX–XXXX Copyright © 2024 The Author(s). Published by Wolters Kluwer Health, Inc.**

European Journal of Cancer Prevention XXX, **XXX**:XXXX–XXXX

Keywords: asbestos, meta-analysis, mesothelioma, navy, seafarers

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Received 1 September 2023 **Accepted** 10 January 2024.

Introduction

Malignant mesothelioma is a highly fatal tumor arising from the pleural lining of the thoracic cavities. It is mainly caused by exposure to asbestos, a natural miner classified by the International Agency for Research on Cancer as 'carcinogenic to humans' based on its ability to cause mesothelioma and cancers of the lung, larynx and ovaries (IARC, 1987). Despite being banned since 2005 in the European Union, cancer cases due to exposure to asbestos in the past will continue to be detected (Nynäs *et al*., 2017; Alpert *et al*., 2020) given the long latency times that in some cases may reach up to 60–70 years (Bianchi *et al*., 1997). While mesothelioma incidence is extremely low in the general population, its incidence in workers professionally exposed to asbestos can vary between 0.5 and 25% (Robinson *et al*., 2005; Berman and Crump, 2008; Melaiu *et al*., 2018; Alpert *et al*., 2020).

Asbestos was used extensively in ship construction for insulation of ship structures, joiner bulkhead systems, fluid pipelines coverings, boilers, machinery parts, bulkhead panels, fire protection, sound absorption, soundproofing and individual protection during the carrying out of certain processes such as welding and many other uses. Navy personnel and seafarers live and work 24 h per day in the shipboard environment and they are exposed to asbestos fibers released into the confined spaces aboard ships (Dodge and Beck, 2016; Lemen and Landrigan, 2021).

Materials containing asbestos in naval engineering and on-board ships were 'friable' or 'compact'. Friable materials are to be considered all asbestos materials used for the insulation of the hot parts of the engine system (exhaust

Supplemental digital content is available for this article. Direct URL citations appear in the printed text and are provided in the HTML and PDF versions of this article on the journal's website (www.eurjcancerprev.com).

What is already known on this topic

Several cohort studies showed an increased risk of mesothelioma for Navy personnel and seafarers, but a comprehensive quantitative assessment is still missing.

What this study adds

This study describes a case of mesothelioma in a boiler mechanic of the Italian Navy and quantifies the mesothelioma standardized mortality ratio among seamen working aboard ships through a systematic review and meta-analysis. A more than double excess risk for mesothelioma emerged as compared to the general population.

How this study might affect research, practice or policy

As our case report shows, due to the long latency time it is still important to continuously monitor the hazard of seamen exposed to asbestos.

manifolds, fuel supply pipes, turbines, steam pipes and boilers) and as antinoise thermal insulation-fireproof bulkheads internal. Raw fiber, usually crocidolite, was used as a filling for thermal insulating cushions with an asbestos fabric casing, usually chrysotile, which was used for the thermal insulation of pipe coupling flanges and of the coupling flanges of large turbines, usually steam and in more limited numbers on gas. The thermal insulation of pipes was ensured with preformed cupels made of low-density materials such as asbestos fiber either pressed or inserted into very weak mineral matrices; these components gave these products poor mechanical resistance and a consequent high friability. Among the friable materials there are also fabrics (sheets, ribbons, ropes, threads and packings) with which metal pipes were covered for the transport of hot and even cold fluids; in the latter case the asbestos acted as an anticondensation agent. It has been estimated that the quantity of asbestos necessary for the insulation of the engine system of a turboship was approximately triple that necessary for the insulation of a diesel engine. Furthermore, in all ships the engine system has flame-retardant barriers that separate it from the rest of the ship (Bianchi and Bianchi, 2012a, 2012b; Marinaccio *et al*., 2021).

A recent published analysis of the Italian Mesothelioma Register (ReNaM) focusing on maritime workers concluded that the highest percentages of certain asbestos exposures are among naval engineers, motor mechanics, machine captains and sailors. Machine crew accounted for 49.3% of the cases, and deck crew for 27.6% (Vimercati *et al*., 2023).

We conducted a systematic review and meta-analysis to quantify the mesothelioma risk of seamen working aboard ships, either commercial or naval vessels, as compared to that of the general population.

Materials and methods

We conducted a systematic review and meta-analysis to identify studies investigating the association between exposure to asbestos of seamen working aboard ships, either commercial or naval vessels and mesothelioma risk.

Our systematic review and meta-analysis were conducted according to the preferred reporting items for systematic reviews and meta-analyses (PRISMA) guidelines (Page *et al*., 2021). The PRISMA checklist is provided in Supplementary Material 2, Supplemental digital content 1, *http://links.lww.com/EJCP/A447*. The study protocol was registered on PROSPERO (registration number: CRD42022306109).

Search strategy

We carried out a literature search in MEDLINE through PubMed and EMBASE, from inception (1946 and 1947, respectively) to 31st December 2021, of all studies on seamen working aboard ships, either commercial or naval vessels, characterized by exposure to asbestos and providing mesothelioma risk estimates. No language restrictions were applied. The full search strings are provided in Supplementary Material 1, Supplemental digital content 2, *http://links.lww.com/EJCP/A448*.

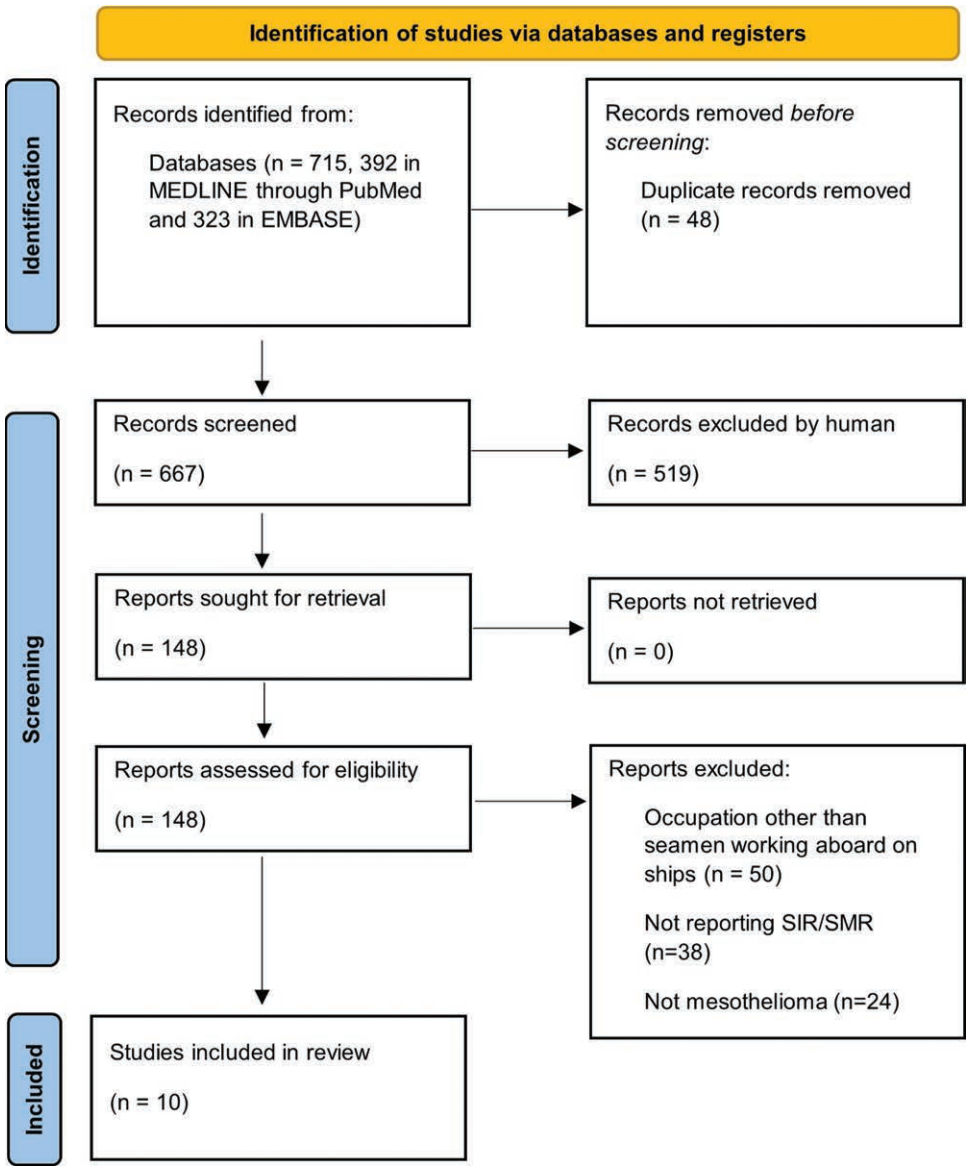
Study selection

The study selection process was carried out using a standardized Microsoft Excel (Microsoft Corporation, Redmond, Washington, USA) form to collect several study details as well as the title and abstract evaluation, and, when appropriate, full-text author evaluations.

After excluding duplicate articles, two authors (MR and AV) independently assessed the titles and abstracts of the retrieved references to exclude irrelevant ones. In case of disagreement, a third reviewer (FM) was consulted. The three authors are not from the same laboratory and they have different backgrounds [statistical (MR), technical (AV) and medico-legal (FM)]. Subsequently, the same two reviewers independently conducted the full-text screening of relevant articles in order to identify the studies that met the inclusion criteria. Any potential conflict was resolved through discussion between the three reviewers. For the sake of completeness, the references listed in the articles retained as relevant were reviewed to identify additional studies. The flowchart of the selection process is shown in Fig. 1.

Inclusion criteria were: (i) Design: cohort studies or nested case-control studies; (ii) Exposure to asbestos of seamen working aboard ships, either commercial or naval vessels and (iii) Outcome: incidence or

Fig. 1



PRISMA flowchart of study selection.

mortality due to mesothelioma as classified through the International Classification of Diseases (ICD) system used in that study (ICD-7 158, 162.2, 163–165; ICD-10 C450-459). Studies were included regardless of the methods used to ascertain mesothelioma disease status.

Exclusion criteria were: (i) Design: cross-sectional and case-control studies, case-reports or case-series, studies reporting results of economic analyses, qualitative studies, editorials or commentaries with no primary data, as well as studies on seamen working aboard ships that did not report mesothelioma risk estimates and (ii) Exposure: studies of workers exposed to asbestos in other occupational groups.

Outcome measures

Studies were considered eligible for the meta-analysis if they reported the standardized incidence ratio (SIR), or the standardized mortality ratio (SMR), comparing the observed number of mesothelioma cases/deaths of seamen working aboard ships, either commercial or naval vessels, compared to the expected numbers in the general population.

Data extraction

Data were extracted using a standardized form in Microsoft Excel (Microsoft Corporation, Redmond, Washington, USA). One reviewer (MR) performed the extraction, which was checked by a second reviewer

(AV). Any potential discrepancy was solved through discussion between the extractors and a third reviewer (FM). Data extracted from the selected studies included: subjects, country, study period, endpoints, relevant time period for exposure, main quantitative findings including the association measure (SMRs and SIRs) with the corresponding 95% confidence interval (CI) computed according to the Byar's formulae, and any other potentially relevant information on study methods and findings.

Evaluation of the quality of the studies

The Newcastle-Ottawa Scale (NOS) was used to assess the quality of the studies included in the systematic review and meta-analysis. The evaluation is based on eight items, which are categorized into three groups: selection of study groups, comparability of groups and ascertainment of exposure or outcome of interest. Stars are attributed to each item depending on the quality; a study can be awarded a maximum of one star for each of the items within the selection of study groups and ascertainment of exposures, while a maximum of two stars can be given for comparability. The NOS score is obtained by adding the stars of each item and it can range between 0 and 9. A study with an average NOS score of at least six stars out of nine is considered as having good quality.

Data synthesis

Pooled estimates were computed by using random-effects models in order to take into account the heterogeneity of risk estimates. Each study log(SMR) or log(SIR) was weighted by the inverse of its variance, which is mainly determined by the number of observed cases, plus the between-studies variance component τ^2 estimated through the moment estimator (DerSimonian and Laird, 1986). Considering that mesothelioma's lethality is among the highest of all forms of cancer, we summarized SIRs together with SMRs. Results were presented in a forest plot where individual study estimates are depicted by squares and their tips represent the 95% CIs, while the diamond is the pooled weighted SMR estimate.

We assessed between-studies heterogeneity using chi-square test and quantified the inconsistency using the I^2 statistic, which is the proportion of total variation contributed by between-studies variance (Higgins and Thompson, 2002). A leave-one-out-at-a-time sensitivity analysis was carried out to assess the influence of each study on the pooled estimate. Stratified analyses would be conducted to identify possible sources of heterogeneity.

A cumulative meta-analysis was carried out to assess time-varying evidence of mesothelioma among seamen working aboard ships. Briefly, in a cumulative meta-analysis studies were added one at a time according to publication year (earliest to the most recent) to assess the presence of a trend over time. The working hypothesis was that the presence of publication bias was assessed by visual examination of the funnel plot (Peters *et al*., 2008) and by applying the tests proposed by (Egger *et al*., 1997).

Results

Search strategy

The PRISMA flowchart describing the article selection process is reported in Fig. 1. The search identified 715 articles. After the identification of 48 duplicate research pieces, a total of 148 out of 669 unique papers were fully assessed for eligibility through full-text reading. The primary reasons for exclusion were the investigation of occupations other than seamen working aboard on ships (n = 50) and the lack of quantitative estimates of SMRs and SIRs (n = 38).

At the end of the screening process, a total of 10 papers (Darby *et al*., 1990; Rapiti *et al*., 1992; Pukkala and Saarni, 1996; Hemminki and Li, 2003; Rafnsson and Sulem, 2003; Sulem and Rafnsson, 2003; Strand *et al*., 2010; Mazurek *et al*., 2017; Ugelvig Petersen *et al*., 2018; Ugelvig Petersen *et al*., 2020) were considered eligible and included in the systematic review and meta-analysis.

Studies' main characteristics

The selected papers describe cohorts of seamen from USA and many European countries (UK, Iceland, Sweden, Norway, Denmark and Finland). The studies' characteristics are reported in Table 1.

Darby *et al*. (1990) investigated mortality in a cohort of 11 941 UK Royal Navy servicemen who served abroad in the 1950s and 1960s. A total of seven mesothelioma cases were observed, with a SMR of 3.4 (95% CI, 1.36–7.00).

A cohort of 2208 males enrolled as merchant marine seamen at the Civitavecchia harbor (Italy) from 1936 to 1975 (Rapiti *et al*., 1992) showed an excess mesothelioma mortality (3 observed deaths versus 0.51; SMR = 5.87; 95% CI, 1.18–17.19).

A cohort of 30 940 male and 11 529 female seafarers registered in the Finnish Seafarers' Pension Fund was followed up through the Finnish Cancer Registry for Cancer in 1967–92 (Pukkala and Saarni, 1996). Among males, there were nine mesothelioma cases out of a total of 1199 cancer cases, with SIR of 2.2 (95% CI, 1.03–4.27), while no cases were detected among women. The mesothelioma SIR for engine officers was 3.2 (95% CI, 0.7–9.5).

Hemminki and Li (2003) carried out a study to characterized time trends, regional, socioeconomic and occupational risk factors for mesothelioma in Sweden from 1961 to 1998. Among seamen, an excess incidence of mesothelioma was observed (11 cases observed versus 3.9 expected), with a SIR of 2.83 (95% CI, 1.41–5.06).

A population-based study of 6603 male marine engineers who ran and maintain engines on-board the vessels, with a

Table 1 **Main characteristics of the studies included in the systematic review and meta-analysis**

Study	Country and study period	Study design	Population characteristics	Main quantitative findings	NOS score
Darby *et al.* (1990)	UK (England and Wales) Employment between 1950 and 1969, with follow-up to 1 January 1984	PC	998 UK Royal Navy servicemen who served abroad in the 1950s and 1960s during nuclear tests in Australia and the Pacific Ocean	7 deaths from mesothelioma were recorded among Royal Navy servicemen of all services and ranks, with a SMR of 3.4 (95% CI, 1.36–7.00). SMR of mesothelioma among officers: 6.9 (95% CI, 1.7–27.6). SMR of mesothelioma among other ranks: 2.82 (95% CI, 1–2–6.8)	7
Rapiti *et al.* (1992)	Italy (Civitavecchia harbor) Employment between 1 January 1936 and 31 December 1975, with follow-up to 31 December 1989	PC	2267 registered male seamen, 948 of whom with at least one sailing	30 deaths from mesothelioma were recorded among male seamen with at least one sailing, with a SMR of 5.87 (95% CI, 1.2–17.2)	8
Pukkala and Saarni (1996)	Finland Employment between 1960 and 1980, with follow-up to 31 December 1992	PC	30 940 male seafarers and 11 529 female seafarers. Job category – deck officers: -3719 males; -45 females. Job category – engine officers: -3868 males; -17 females. Job category – radio officers: -676 males; -100 females. Job category – deck crew: -10 905 males; -141 females. Job category – engine crew: -7944 males; -37 females. Job category – other staff: -7585 males; -11 242 females	9 mesothelioma cases were observed among male seafarers, with a SIR of 2.2 (95% CI, 1.0–4.1). SIR of mesothelioma among male deck officers: 3.6 (95% CI, 0.8–10.6). SIR of mesothelioma among male engine officers: 3.2 (95% CI, 0.7–9.5). SIR of mesothelioma among male deck crew: 2.1 (95% CI, 0.3–7.6). SIR of mesothelioma among male engine crew: 1.1 (95% CI, 0.0–6.4). No mesothelioma cases were registered among female seafarers	7
Hemminki and Li (2003)	Sweden 1961 to 1998	RC	The Swedish Family-Cancer database includes all persons born in Sweden after 1931, totaling over 10.2 million individuals for whom occupational data was retrieved from the censuses of 1960 and 1970	11 mesothelioma cases observed in seamen, with a SIR of 2.83 (95% CI, 1.41–5.09)	7
Rafnsson and Sulem (2003)	Iceland 1955 to 1998	PC	6603 male marine engineers running and maintaining engines	4 mesothelioma cases, with a SIR of 2.8 (95% CI, 0.8–7.3). The SIR was 3.0 (95% CI, 0.8–7.7) when considering a 20-year lag time, and 4.8 (95% CI, 1.3–12.3) when considering a 40-year lag time	7
Sulem and Rafnsson (2003)	Iceland 1966 to 1998	PC	3874 male deck officers	No pleural cancer observed	7
Strand *et al.* (2010)	Norway Employment between 1950 and 1987, with follow-up to 31 December 2007	PC	28 345 officers and enlisted servicemen in the Royal Norwegian Navy potentially exposed to asbestos	22 mesothelioma cases, with a SIR of 1.65 (95% CI, 1.04–2.50). The SIR was 1.69 (95% CI, 0.68–3.49) in personnel with less than 2 years of service aboard the vessels, and 3.00 (95% CI, 1.44–5.51) for personnel aboard with 2 years or longer service. SIR of mesothelioma among personnel who served aboard in engine room for less than 2 years: 6.23 (95% CI, 2.51–12.18). SIR of mesothelioma among personnel who served aboard in engine room for more than 2 years: 6.49 (95% CI, 2.11–15.2)	8
Mazurek *et al.* (2017)	USA 1999 to 2015	RC	US Navy employers A database of the Centers for Disease Control and Prevention (CDC) including mesothelioma deaths from whom occupational data was retrieved from the National Occupational Mortality System (NOMS)	11 deaths from mesothelioma in US Navy employers, with a SMR of 2.0 (95% CI, 1.0–3.6). SMR among sailors and marine oilers: 3.4 (95% CI, 1.1–8.0)	7

(*Continued*)

Table 1
(*Continued*)

Study	Country and study period	Study design	Population characteristics	Main quantitative findings	NOS score
Ugelvig Petersen *et al.* (2018)	Denmark Employment between 1 April 1986–31 December 1999, with follow-up to 31 December 2015	PC	44 293 Danish seafarers, including 33 084 males and 11 209 females. Job category - machinists and engine room crew: -7345 males; -54 females. Job category - maintenance and other: -1166 males; -107 females	25 mesothelioma cases among male seafarers, with a SIR of 1.31 (95% CI, 0.88–1.94). No mesothelioma was diagnosed among female seafarers. SIR of mesothelioma among machinists and engine room crew: 2.31 (95% CI, 1.28–4.17). SIR of mesothelioma among maintenance and other: 1.68 (95% CI, 0.24–11.91)	8
Ugelvig Petersen *et al.* (2020)	Denmark, Finland, Iceland, Norway, Sweden 1961 to 2005	PC	81 740 male seafarers participating in the NOCCA (Nordic Occupational Cancer) project	143 mesothelioma cases among male seafarers, with a SIR of 2.17 (95% CI, 1.83–2.56)	7

CI, confidence intervals; RC, retrospective cohort study; RR, risk ratio; SMR, standardized mortality ratio.

follow-up from 1955 to 1998, showed an increased, but NS, risk of mesothelioma (SIR = 2.84; 95% CI, 0.76–7.26). The SIR was equal to 4.8 (95% CI, 1.3–12.3) when taking into account for a 40-year time lag (Rafnsson and Sulem, 2003).

No mesothelioma cases were observed in a cohort of Icelandic deck officers followed from 1966 to 1998 (Sulem and Rafnsson, 2003).

In a study carried out on a cohort of 28 300 military servicemen in the Royal Norwegian Navy, there were 22 mesothelioma diagnoses, with a SIR of 1.65 (95% CI, 1.04–2.50). A significantly increased risk of mesothelioma for engine room workers with <2 years (SIR = 6.23; 95% CI, 2.51–12.8) and ≥2 years (SIR = 6.49; 95% CI, 2.11–15.2) emerged (Strand *et al.*, 2010).

Mazurek *et al.* (2017) mapped mesothelioma mortality in the US during 1999–2015, showing 11 mesothelioma deaths among US Navy employers, corresponding to a SMR of 2.00 (95% CI, 1.00–3.58). An excess mortality emerged among sailors and marine oilers (SMR 3.4, 95% CI, 1.1–8.0).

There were 25 mesothelioma cases diagnosed in a Danish cohort of 33 084 male merchant seafarers followed up from 1986 to 2015, while no cases emerged among 11 209 female merchant seafarers (Ugelvig Petersen *et al.*, 2018). Although there was no significant excess incidence of mesothelioma in merchant seafarers (SIR = 1.31; 95% CI, 0.88–1.94), machinists and engine room crew experienced a more than double risk of mesothelioma (SIR = 2.31; 95% CI, 1.28–4.17) as compared to the general population.

A total of 143 mesothelioma cases were observed in a cohort of 81 740 seafarers followed in the Nordic Occupational Cancer (NOCCA) project, involving participants from population censuses in Denmark, Finland, Iceland, Norway and Sweden (Ugelvig Petersen *et al.*, 2020). An excess incidence of mesothelioma was found, with SIR of 2.17 (95% CI, 1.83–2.56).

Study quality

The risk of bias evaluation according to the NOS scale showed that all the included studies were of good quality, with a median score of seven out of nine.

Meta-analysis results

Overall, there were 235 mesothelioma cases/deaths in the included studies versus 115.6 expected, with a pooled SMR of 2.11 (95% CI, 1.70–2.62), in the absence of a significant between-study heterogeneity (I^2 = 39%; P = 0.11) (Fig. 2).

The leave-one-out sensitivity analysis showed that no studies have an influential role on the pooled estimate.

The limited number of studies, as well as the limited evidence of mesothelioma risk by seamen occupational subcategories, prevented us to carry out stratified analyses.

The cumulative meta-analysis (Fig. 3) showed a decreasing, although NS (P = 0.17), trend over time in the magnitude of mesothelioma risk.

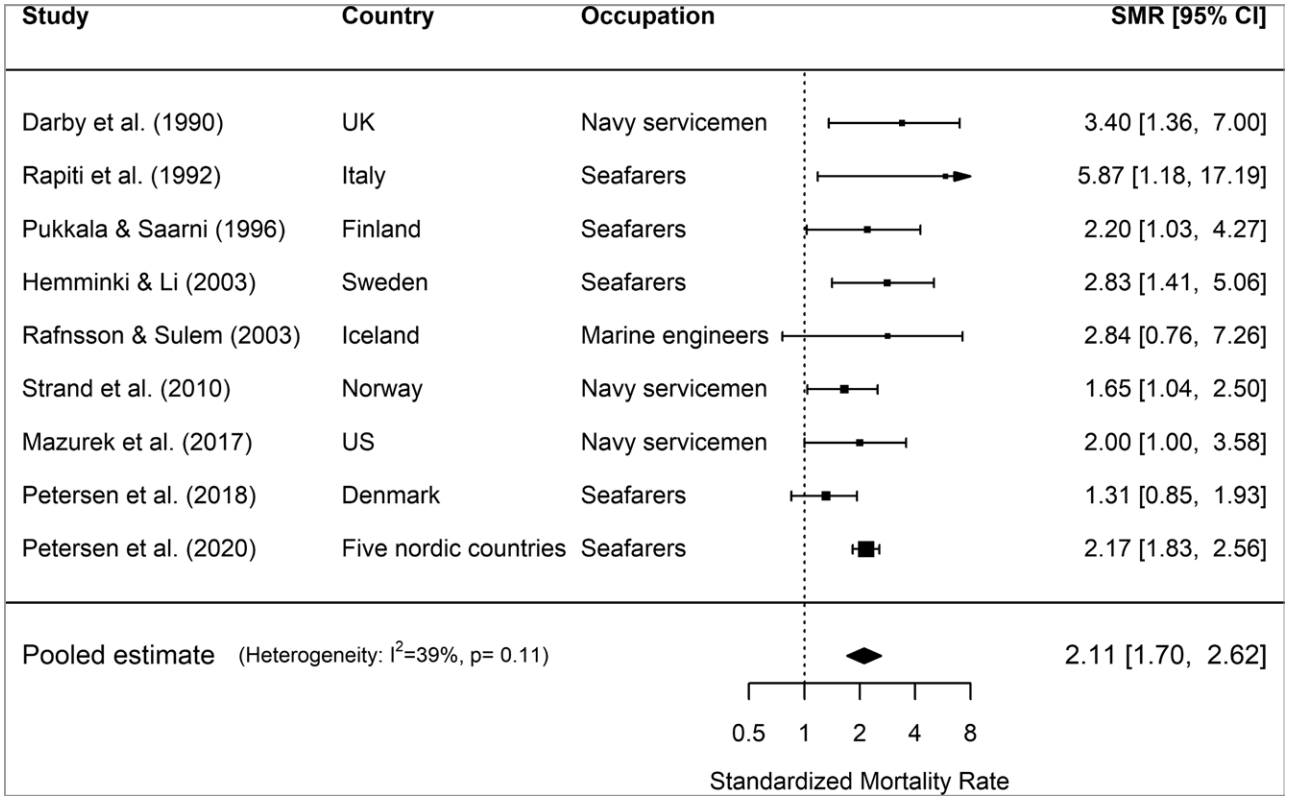
Assessment of risk of bias across studies

The funnel plot (Fig. 4) did not show any substantial asymmetry, and the Egger's test P was equal to 0.09, suggesting no evidence of publication bias.

Discussion

From late 1960s, the medical literature started to describe the asbestos hazards in shipbuilding and ship repairing in naval dockyards (Harries, 1968). The first reports of mesothelioma cases in less common occupational settings were published in the 1980s (Young *et al.*, 1981; Goldsmith, 1982), including the first reports on cancer in merchant seamen (Baksaas *et al.*, 1983). In 1991,

Fig. 2



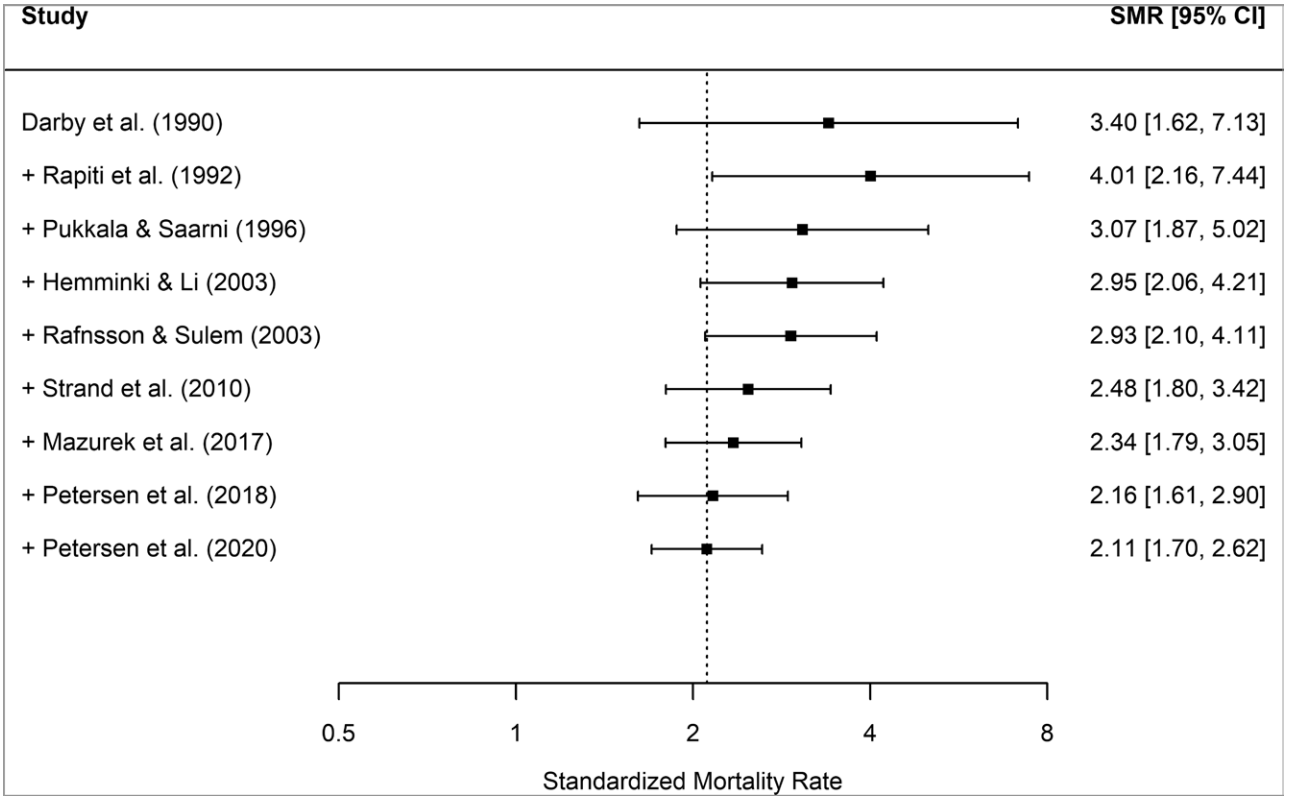
Forest plot of SMR estimates of mesothelioma mortality among seamen working aboard ships, either commercial or naval vessels, as compared to that of the general population.

Varouchakis *et al.* (1991) reported two case-reports of mesothelioma among merchant seamen, the first one in a 71-year-old male engineer employed for 35 years, and the second one in a 65-year-old male deck sailor employed for 25 years. More recently, Pesce *et al.* (2019) described the case of a 31-year-old man, who worked as merchant navy officer, diagnosed with malignant mesothelioma after presenting to the hospital with severe fatigue, unintentional weight loss over the last 6 months, and profuse night sweats with fever.

Recently, we experienced an investigation to determine the cause of death of a 57-year-old Italian man who worked as a boiler mechanic in the Italian Navy between 1982 and 1984, diagnosed with malignant mesothelioma in May 2019, who died in July 2020. The judicial autopsy documented a load of asbestos fibers equal to 2 100 000 per gram of dry tissue and a load of corpuscles equal to 12 000 per gram of dry tissue. The fibers were mainly composed of commercial amphibole asbestos (amosite and crocidolite) amounting to 2 000 000 and noncommercial calcium-amphibole asbestos (tremolite and actinolite) amounting to 100 000. Therefore, occupational exposure to crocidolite and amosite fibers was confirmed, which caused the onset of malignant pleural neoplasia and eventually led to the death of the man. This documented case report motivated us to carry out a systematic review and meta-analysis to highlight the translational use of the epidemiological literature in clinical practice, allowing us to recognize the causal role of asbestos in a seaman, with legal, epidemiological, social and individual consequences.

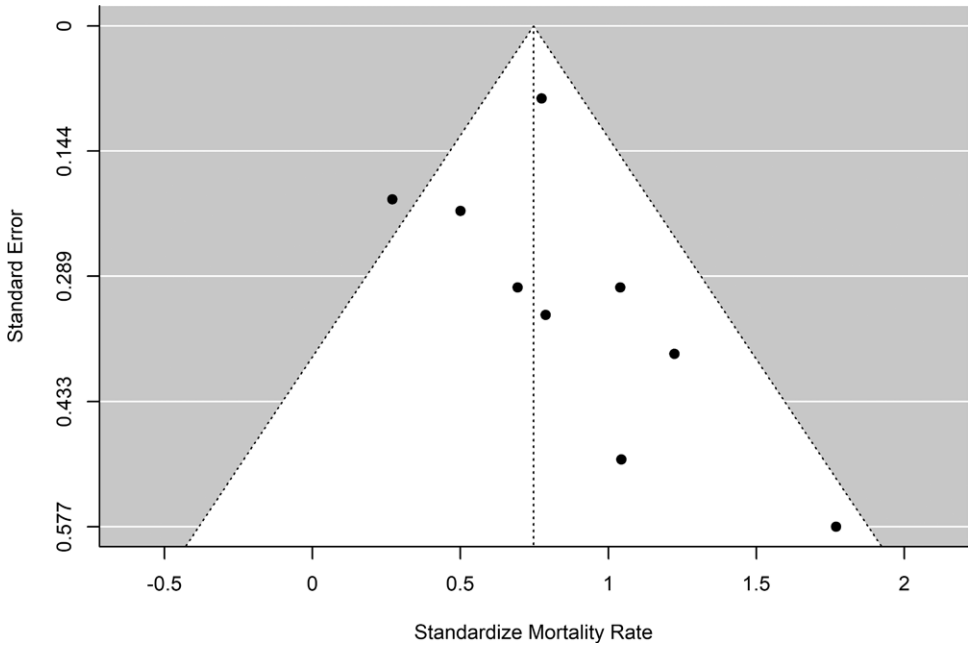
Asbestos is a known genotoxic carcinogen causing mainly (but not only) mesothelioma and lung cancer (Bourdès *et al.*, 2000; Nielsen *et al.*, 2014). The main determinants of asbestos toxicity are fiber size, biopersistence, chemical composition and particle surface characteristics (NIOSH, 2011a). When inhaled, asbestos fibers tend to deposit in the lung at the bronchiolar-alveolar duct bifurcations, setting off a variety of responses leading to inflammation, cell, and tissue damage, which can lead to malignant and nonmalignant diseases. From the lung, some fibers can migrate into the pleural space by different mechanisms (Institute of Medicine, 2006). The mechanisms by which asbestos causes disease are not fully understood, but there are three hypotheses to account for the pathogenicity of asbestos: direct interaction with cellular chromosomes, generation of reactive oxygen species and other cell-mediated mechanisms, especially inflammation (IARC, 2012).

Fig. 3



Cumulative meta-analysis results of mesothelioma mortality among seamen working aboard ships, either commercial or naval vessels, as compared to that of the general population.

Fig. 4



Funnel plot for publication bias assessment.

In addition to the aforementioned case report, we aimed to carry out a systematic review and meta-analysis to summarize the evidence and quantify the mesothelioma risk of seamen working aboard ships, either commercial or naval vessels, as compared to that of the general population. All the 10 included studies (Darby *et al*., 1990; Rapiti *et al*., 1992; Pukkala and Saarni, 1996; Hemminki and Li, 2003; Rafnsson and Sulem, 2003; Sulem and Rafnsson, 2003; Strand *et al*., 2010; Mazurek *et al*., 2017; Ugelvig Petersen *et al*., 2018; Ugelvig Petersen *et al*., 2020) showed an increased risk of mesothelioma, and the pooled meta-analytic risk of mesothelioma was 2.11 (95% CI, 1.70–2.62), in the absence of between-study heterogeneity. No publication bias emerged.

As compared to two recent published reviews (Dodge and Beck, 2016; Lemen and Landrigan, 2021) focused on measuring airborne asbestos on-board merchant ships and health outcomes of merchant seamen, the main strength of our investigation is the quantification of mesothelioma risk in seamen through a meta-analytic approach. Our systematic review was registered on PROSPERO, it was conducted according to the PRISMA guidelines, and it was based on a reproducible search that allowed to identify studies investigating several occupational groups potentially related to the one of our interests. In addition, for the sake of completeness, we screened the reference lists of included studies to be sure to include all the cohort studies summarizing the mesothelioma risk among seamen. We choose to include the 2020 study by Ugelvig Petersen *et al*. (2020), based on data derived from the NOCCA project, even though it may include subjects followed in other studies (Pukkala and Saarni, 1996Strand *et al*., 2010; Ugelvig Petersen *et al*., 2018). However, we assessed through the leave-one-out-at-a-time sensitivity analysis that the pooled estimate was not influenced.

Among the limitations, the lack of standardization in the reporting of malignant mesothelioma could represent a source of misclassification of the disease status. Since pleural mesothelioma was not identified as a distinct cancer until 1960 and peritoneal mesothelioma was not identified until 1964, it could be the case that in some of the included studies mesotheliomas were diagnosed as abdominal cancers or pleural metastatic adenocarcinomas. In addition, we were not able to quantify the risk of mesothelioma across different histological subtypes nor across occupational subcategories of seamen since only a few of the included studies gave such information (Pukkala and Saarni, 1996; Strand *et al*., 2010; Ugelvig Petersen *et al*., 2018). We did not screen the gray literature; anyway, we retained unlike that results of cohort studies reporting SMR estimates of mesothelioma as compared to the general population were unpublished. Last, since our systematic review was updated to December 2021, we may have missed the more recently published cohort studies investigating mesothelioma incidence among seamen.

As shown by Strand *et al*. (2010) in their investigation in the Royal Norwegian Navy, working in the engine room was shown to be a strong predictor of mesothelioma risk, with a more than six-fold increased significant risk. Ugelvig Petersen *et al*. (2018) showed that machinists and engine room crews had a more than two-fold increased significant risk of mesothelioma as compared to the general population. In a 1996 study by Pukkala and Saarni (1996), three cases of mesothelioma were observed among Finnish male engine officers versus 1 expected, with a 3.2-fold nonsignificant risk. Our results pointed out that the mesothelioma risk on ships is not confined to the engine room only, but several occupational subcategories are involved, as shown by a case series of 50 pleural mesothelioma in Italian men seafarers at the Trieste–Monfalcone area (Bianchi *et al*., 2005).

Although the risk of mesothelioma appears to be independent of smoking (IARC, 1987), we could not rule out residual confounding since the included studies did not keep into account smoking history nor data on other potential confounders. In addition, a lack of employment history did not allow to exclude exposures to asbestos during nonseamen occupations, as well as to ascertain the presence of a dose-response relationship.

The cumulative meta-analysis showed that the magnitude of mesothelioma risk among seamen is decreasing over time. However, although asbestos has been banned in 67 countries worldwide, the number of mesothelioma deaths has been increasing and the peak is not yet reached (Zhai *et al*., 2021) due to the long latency time, which ranges between 20 and 40 years on average. Although the mesothelioma risk of the youngest seamen cohorts will probably level off (Forsell *et al*., 2022), future studies are needed to ensure a continuous monitor of the health risks of seamen through better exposure assessments to occupational carcinogens and adequate follow-up times.

Conclusion

We carried out a systematic review and meta-analysis of the epidemiological evidence showing a more than double excess risk for mesothelioma among seamen working aboard ships.

Acknowledgements

All authors declare that they have no competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

All the primary data and analytic code are available from the first author on reasonable request.

Conflicts of interest

There are no conflicts of interest.

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