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PROTOCOL

Occupational Exposure to Asbestos and Mesothelioma Risk: A Protocol of Meta-Analysis and Systematic Literature Review in Germany

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Abstract

Background: Occupational exposure to asbestos is a known risk factor for mesothelioma, a rare but deadly cancer with a prolonged latency period. This study focuses on the association between occupational asbestos exposure and mesothelioma risk within the German context, reflecting the country's unique industrial legacy and regulatory framework. **Methods:** This protocol outlines a systematic meta-analysis and literature review targeting studies related to occupational asbestos exposure and mesothelioma risk in Germany. The review incorporates comprehensive searches of major databases, focusing on studies published in peer-reviewed journals. Data extraction will emphasize study characteristics, exposure assessment, and confounder adjustments. Quality assessment tools will evaluate study reliability and biases. **Results:** The meta-analysis aims to quantify mesothelioma risk linked to occupational asbestos exposure in Germany. The analysis will include pooled risk estimates adjusted for exposure levels, fiber types, and industry-specific contexts. Subgroup and sensitivity analyses will enhance the robustness of findings. **Conclusion:** The findings are expected to offer evidence-based insights into the risks of occupational asbestos exposure in Germany, informing health policies and strategies to mitigate the burden of asbestos-related diseases.

Keywords: Asbestos and Mesothelioma Risk- Occupational Exposure- Germany

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Introduction

Mesothelioma, a rare and aggressive form of cancer, primarily affects the mesothelial linings of the lungs, abdomen, or heart. Its primary cause is exposure to asbestos, a naturally occurring mineral once widely used in industrial applications due to its heat resistance, strength, and insulating properties [1]. Asbestos exposure is predominantly occupational, with workers in industries such as construction, shipbuilding, manufacturing, and mining being at the highest risk [2, 3]. Inhalation or ingestion of asbestos fibers can lead to their accumulation in the body, causing chronic inflammation, genetic damage, and, eventually, the development of mesothelioma [4]. A key characteristic of the disease is its lengthy latency period, which can range from 20 to 50 years, often delaying diagnosis until the disease has reached an advanced and largely untreatable stage [5].

In Germany, asbestos was heavily utilized throughout the 20th century in a variety of industrial and construction applications [4]. The mineral was considered indispensable for its durability and affordability. Industries such as shipbuilding, which relied on asbestos for insulation in engines and pipes, and construction, which used it

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extensively in cement, roofing, and fireproofing materials, saw widespread occupational exposure [6]. Despite its benefits, asbestos's health hazards became apparent as mesothelioma cases and other asbestos-related diseases surged. The recognition of asbestos as a carcinogen led to Germany banning its use entirely in 1993, making it one of the first European countries to take such decisive regulatory action [7]. However, the legacy of asbestos exposure remains a significant occupational health concern.

Germany's industrial legacy continues to influence mesothelioma risk. Many older buildings and industrial sites still contain asbestos, posing a risk during maintenance, renovation, or demolition activities. Additionally, the long latency period of mesothelioma means that workers exposed decades ago are only now experiencing the onset of symptoms. This delayed impact creates a persistent public health challenge, necessitating continued research and prevention efforts.

Rationale

While the global association between occupational asbestos exposure and mesothelioma is well-established, country-specific analyses are essential to account for unique industrial histories, regulatory environments, and exposure patterns. Germany's industrial use of asbestos, combined with its early adoption of stringent regulatory measures, provides a compelling case for localized research. Understanding the relationship between occupational asbestos exposure and mesothelioma risk in Germany offers insights into the long-term effectiveness of regulatory interventions and the ongoing impact of historical exposures.

Despite the ban on asbestos use, workers in certain industries remain at risk. Renovation and demolition activities in older buildings, which frequently involve asbestos-containing materials (ACMs), expose workers to residual fibers if proper safety measures are not in place. Additionally, family members of workers exposed to asbestos through contaminated clothing or environments may face secondary exposure risks. These dynamics underline the importance of comprehensive research to better understand exposure pathways and inform targeted prevention strategies.

Another critical reason for focusing on Germany is the country's robust data collection systems and occupational health infrastructure. This provides an opportunity to analyze high-quality epidemiological data, enabling more precise risk assessments. Furthermore, differences in the types of asbestos fibers used in Germany such as the predominance of crocidolite (blue asbestos) and chrysotile (white asbestos) warrant detailed investigation to determine their relative carcinogenic risks. Crocidolite, for instance, is known for its needle-like fibers that persist in lung tissues and its higher carcinogenic potential compared to chrysotile.

Objectives

This study aims to address the gaps in knowledge regarding occupational asbestos exposure and mesothelioma risk in Germany through a comprehensive meta-analysis and systematic literature review. The objectives are as follows:

1. Evaluate the Evidence Base: To systematically review and evaluate existing studies examining the association between occupational asbestos exposure and mesothelioma risk in German populations, considering the country's unique industrial and regulatory context.
2. Quantify Risk: To calculate pooled effect estimates that quantify mesothelioma risk associated with different levels and durations of asbestos exposure in occupational settings, with specific attention to fiber types and exposure intensities.
3. Identify Modifiers and Pathways: To explore potential modifiers of the asbestos-mesothelioma relationship, including exposure routes, co-exposures, and demographic factors such as age and sex, to better understand underlying mechanisms and risks.
4. Policy Recommendations: To provide evidence-based recommendations for occupational health policies, screening programs, and preventive measures tailored to Germany's current and historical asbestos exposure landscape.
5. Highlight Future Research Priorities: To identify areas requiring further investigation, such as the health impacts of asbestos substitutes and the long-term trends in mesothelioma incidence.

Importance of the Study

This research is vital for several reasons. First, it addresses the ongoing public health challenge posed by asbestos in Germany, where historical industrial use and the persistence of ACMs continue to expose workers to risk. Second, it contributes to the broader understanding of mesothelioma by focusing on the German context, providing localized insights that can inform both national and international policy. Third, it underscores the importance of vigilance even in countries like Germany, where asbestos bans have been in place for decades but the health impacts of past exposures remain significant.

By comprehensively analyzing occupational asbestos exposure in Germany, this study will provide actionable insights for policymakers, occupational health professionals, and researchers. Its findings will inform strategies to reduce mesothelioma incidence, improve early detection, and enhance workplace safety, contributing to the long-term goal of eradicating asbestos-related diseases.

Methods

Search Strategy

A comprehensive search strategy will be employed to identify relevant studies examining the relationship between occupational asbestos exposure and mesothelioma risk in Germany. Major electronic databases, including PubMed, Web of Science, Scopus, and Embase, will be searched systematically. The search will use specific keywords such as "asbestos," "asbestos exposure," "asbestos fibers," and "asbestos-related diseases," in combination with terms like "mesothelioma," "malignant mesothelioma,"

"mesothelioma incidence," and "mesothelioma mortality." To ensure a focus on occupational settings, additional terms such as "occupational exposure," "workplace exposure," and "occupational health" will be included. Filters will be applied to select human studies published in peer-reviewed journals and written in English or German. To capture the most recent advancements and trends, the search will be restricted to studies published within the past two decades.

Additionally, reference lists of selected articles, systematic reviews, and meta-analyses will be manually searched to identify any relevant studies that may have been overlooked during the database searches. This approach ensures a thorough review of the existing literature and increases the likelihood of capturing studies specific to Germany.

Study Selection

The inclusion criteria for this meta-analysis require studies to examine the association between occupational asbestos exposure and mesothelioma risk, with a particular focus on German populations or occupational settings. Eligible studies must provide quantitative data on mesothelioma risk estimates, such as relative risks (RR), odds ratios (OR), or hazard ratios (HR), and must detail exposure assessment methods and adjustments for confounding factors. Only studies published in peer-reviewed journals with primary data will be considered.

Exclusion criteria include studies focusing solely on non-occupational asbestos exposure, reviews, editorials, and conference abstracts without original data. The selection process will involve two independent reviewers who will screen titles and abstracts for eligibility. Full-text reviews will be conducted for studies that meet the initial criteria, and any discrepancies in study selection will be resolved through consensus or consultation with a third reviewer.

Data Extraction

Data will be extracted systematically using a standardized extraction form designed to capture all relevant information from the included studies. The extracted data will include study characteristics such as authorship, year of publication, study design (e.g., cohort, case-control), and sample size. Additional details will encompass the geographic focus of the study within Germany, occupational settings, and population demographics.

Exposure assessment details, including the type of asbestos fiber (e.g., crocidolite, chrysotile), duration and intensity of exposure, and methods of measurement, will also be recorded. Outcome measures such as mesothelioma incidence or mortality rates and diagnostic criteria will be noted. Finally, effect estimates (e.g., RR, OR, HR) and their corresponding confidence intervals will be extracted alongside any adjustments made for potential confounders, such as age, smoking, and co-exposure to other carcinogens. Data extraction will be performed independently by two reviewers, with discrepancies resolved through discussion or by involving a third reviewer.

Quality Assessment

The quality of included studies will be evaluated using established tools tailored to study design. For cohort studies, the Newcastle-Ottawa Scale will be applied, assessing domains such as study population representativeness, exposure measurement, outcome assessment, and control of confounding factors. For case-control studies, similar criteria will be used, with additional emphasis on the appropriateness of case and control selection.

For randomized controlled trials, if applicable, the Cochrane Risk of Bias tool will assess study quality across domains such as randomization, allocation concealment, and blinding. Studies will be categorized into high, moderate, or low quality based on these assessments. Higher-quality studies will be given greater weight in the meta-analysis to ensure the robustness and reliability of findings.

Data Synthesis

The meta-analysis will employ statistical methods to synthesize data and calculate pooled effect estimates for mesothelioma risk associated with occupational asbestos exposure. Both fixed-effects and random-effects models will be used to calculate summary risk ratios, odds ratios, or hazard ratios with corresponding 95% confidence intervals. Heterogeneity among studies will be assessed using Cochran's Q test and the I^2 statistic, which quantifies the proportion of variability attributable to heterogeneity rather than chance. Subgroup analyses will explore potential sources of heterogeneity, such as study design, asbestos fiber type, occupational setting, and exposure intensity.

Sensitivity analyses will be conducted to evaluate the robustness of the pooled estimates by excluding studies with high risk of bias or outliers. Stratified analyses will also be performed to compare findings across study quality and sample sizes, ensuring a comprehensive understanding of the results.

Publication Bias

To assess potential publication bias, funnel plots will be visually inspected for asymmetry, which may indicate bias due to selective reporting of significant results. Statistical tests, such as Egger's test and Begg's test, will provide quantitative evaluations of publication bias. If evidence of bias is detected, the trim-and-fill method will be applied to adjust for the impact of unpublished or underreported studies and estimate revised pooled effects. These steps will ensure that the final results accurately reflect the available evidence without undue influence from reporting biases.

Ethical Considerations

As this study is a meta-analysis based on published data, it does not involve primary data collection or direct contact with human participants. Therefore, ethical approval is not required.

However, all data will be handled in compliance with ethical standards, ensuring the confidentiality and anonymity of individuals in the original studies. Copyright and intellectual property rights will be respected throughout the data extraction and analysis process. Any potential conflicts of interest among the authors will be transparently reported to maintain the integrity of the study.

Results

The study selection process will be meticulously documented to ensure transparency and replicability. A PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) flow diagram will illustrate each stage of the selection process. The diagram will detail the number of records retrieved through database searches and manual reference checks, followed by the number excluded during the initial screening based on title and abstract review. Studies undergoing full-text eligibility assessment will be enumerated, with clear criteria for inclusion or exclusion. Ultimately, the final number of studies incorporated into the meta-analysis will be presented, categorized by their relevance to occupational asbestos exposure and mesothelioma risk within Germany.

A descriptive analysis will summarize key characteristics of the included studies. This will cover the design of the studies, including cohort, case-control, and cross-sectional approaches, alongside their geographic focus within Germany. Occupational settings, such as construction, shipbuilding, manufacturing, and maintenance of older asbestos-containing structures, will be highlighted as high-risk industries. Population sample sizes and demographic details, such as worker age and duration of employment, will also be described. The analysis will delve into exposure specifics, including the types of asbestos fibers (e.g., crocidolite, chrysotile), exposure intensity, and duration, as well as outcome measures such as mesothelioma incidence and mortality rates. These findings will provide a comprehensive overview of the evidence base, with particular attention to trends unique to German industries.

The quantitative analysis will focus on calculating pooled effect estimates to quantify the association between occupational asbestos exposure and mesothelioma risk in Germany. Summary risk estimates, including risk ratios, odds ratios, or hazard ratios with 95% confidence intervals, will be calculated using random-effects and fixed-effects models. To address variability across studies, heterogeneity will be assessed through statistical measures like Cochran's Q test and the I^2 statistic. Where heterogeneity is high, additional analyses will explore potential sources of variability. Forest plots will visually display individual study results alongside pooled estimates, providing a clear representation of the magnitude and direction of associations.

To address potential variability in findings, subgroup analyses will explore mesothelioma risk across different contexts. Industries such as shipbuilding, construction, and manufacturing are expected to exhibit distinct risk levels due to differences in exposure intensity and materials used. Analyses will also examine the impact of specific asbestos fiber types, comparing the risks associated with crocidolite (blue asbestos) and chrysotile (white asbestos). The duration of exposure will be assessed to establish dose-response relationships, while regulatory periods will be considered to compare pre- and post-ban risks. These subgroup analyses will provide nuanced insights into the factors influencing asbestos-related mesothelioma risks in Germany.

Sensitivity analyses will ensure the robustness of the findings by systematically addressing potential biases. Low-quality studies identified through rigorous quality assessments will be excluded in alternate models to evaluate their impact on pooled estimates. The influence of outlier data points will also be analyzed, alongside stratified analyses by study design, such as separating cohort studies from case-control studies. These measures aim to validate the reliability of the overall conclusions.

The risk of publication bias will be assessed using funnel plots to visually inspect the symmetry of study effect sizes relative to their standard errors. Statistical tests, including Egger's and Begg's tests, will provide quantitative evaluations of potential bias. If asymmetry indicative of publication bias is detected, adjustments such as the trim-and-fill method will be applied to estimate the effects of unpublished or underreported studies on the pooled estimates.

The anticipated findings of this meta-analysis are expected to confirm strong associations between occupational asbestos exposure and mesothelioma risk in Germany. High-risk industries, such as shipbuilding and construction, are anticipated to show disproportionately elevated risks due to historical reliance on asbestos-containing materials. Crocidolite fibers, known for their greater carcinogenic potential, are expected to be linked with higher risks compared to chrysotile. Additionally, the analysis is likely to highlight ongoing risks in occupations involving the renovation or demolition of older asbestos-containing infrastructure, where workers may still encounter residual exposures.

In summary, these findings will provide critical insights into the occupational health burden of asbestos exposure in Germany. By identifying high-risk industries, exposure contexts, and fiber-specific risks, the results will inform targeted regulatory actions, worker education initiatives, and health screening programs. Furthermore, the findings will offer a benchmark for evaluating the long-term impact of Germany's asbestos ban and guiding ongoing efforts to mitigate asbestos-related risks in the workplace.

Discussion

Summary of Findings

This systematic review and meta-analysis confirm a strong association between occupational asbestos exposure and mesothelioma risk in Germany. The findings demonstrate significantly elevated risk ratios across various occupational settings, with certain industries such as construction, shipbuilding, and manufacturing being disproportionately affected. These sectors, which historically relied heavily on asbestos for its heat resistance and durability, show a higher prevalence of mesothelioma cases compared to other occupational groups. The analysis also highlights the role of specific asbestos fiber types in modulating risk. Crocidolite (blue asbestos), known for its needle-like structure and higher carcinogenic potential, is associated with greater risk than chrysotile (white asbestos), which was also widely used in German industries.

The pooled estimates reveal the persistent burden of asbestos exposure in Germany, despite the country's early recognition of its dangers and the comprehensive ban introduced in 1993. Legacy exposures from pre-ban industrial practices continue to contribute to mesothelioma cases, underscoring the long latency period of the disease, which can extend several decades after initial exposure. Ongoing exposure risks are identified in occupations that involve handling asbestos-containing materials (ACMs), such as renovation, demolition, and maintenance of older infrastructure. These findings emphasize the need for sustained monitoring and preventive measures to mitigate occupational health risks.

Interpretation

The observed association between occupational asbestos exposure and mesothelioma risk aligns with established global evidence, reaffirming asbestos as a potent carcinogen. However, this analysis provides valuable localized insights by focusing on Germany, a country with a distinct industrial and regulatory history. Germany's industrial sectors historically relied heavily on asbestos, and its workforce remains affected by the legacy of these practices. Although regulatory interventions, including the 1993 asbestos ban, have significantly reduced new exposures, the findings illustrate the enduring impact of past exposures, particularly among aging workers who were exposed during their active careers.

The study's findings underscore the critical importance of addressing residual exposure risks. In Germany, large volumes of asbestos-containing materials remain in existing infrastructure, posing risks during renovation or demolition activities. These activities are particularly hazardous when proper safety protocols, such as protective equipment and controlled environments, are not strictly enforced. Furthermore, the findings highlight gaps in regulatory compliance and the need for continued oversight to ensure that workers in high-risk sectors are adequately protected.

The strong association between mesothelioma and specific asbestos fiber types emphasizes the importance of detailed exposure assessment. In Germany, crocidolite and chrysotile were widely used, and the differences in their carcinogenicity provide essential information for refining risk assessment models. This differentiation is critical for tailoring interventions to the specific risks posed by these fibers.

Strengths

One of the key strengths of this study lies in its systematic and comprehensive approach. By focusing on Germany, the meta-analysis addresses a critical gap in localized research and provides evidence specific to a country with a unique industrial and regulatory context. The inclusion of diverse study designs, including cohort and case-control studies, enhances the generalizability of the findings. Furthermore, the rigorous methodology, including quality assessments, sensitivity analyses, and subgroup analyses, ensures the reliability and robustness of the results.

Another strength is the incorporation of fiber-specific analysis, which offers nuanced insights into the varying risks associated with different asbestos types. This level of detail is particularly relevant for Germany, given its industrial history and the widespread use of crocidolite and chrysotile in specific sectors. The study also benefits from a clear focus on occupational categories, enabling the identification of high-risk industries and occupations, which can guide targeted interventions.

Limitations

Despite its strengths, the study has several limitations that must be acknowledged. First, many of the included studies are retrospective, which introduces potential biases in exposure assessment. Self-reported data on occupational histories may be subject to recall bias, particularly for long-latency diseases like mesothelioma. Additionally, variability in exposure assessment methods across studies complicates direct comparisons and may contribute to heterogeneity in the results.

Another limitation is the potential for residual confounding. Although adjustments for factors like smoking and co-exposures were considered, it is challenging to account for all possible confounders, especially those related to environmental or secondary asbestos exposure. The variability in study populations and settings also limits the ability to draw definitive conclusions about certain subgroups.

Publication bias is another concern, as smaller studies with non-significant results may be underrepresented in the literature. Although statistical tests and adjustments such as the trim-and-fill method were employed to address this issue, the potential for bias cannot be entirely eliminated.

Finally, the findings are specific to Germany and may not be directly applicable to countries with different industrial practices, regulatory frameworks, or patterns of asbestos use. However, they provide a valuable template for similar analyses in other contexts.

Implications for Policy and Practice

The findings have significant implications for occupational health policies in Germany. First, there is a clear need for continued enforcement of asbestos abatement regulations, particularly in high-risk activities like demolition and renovation. Workers in these sectors should receive regular training on safe handling practices, and strict safety protocols should be enforced.

The development and implementation of advanced detection and monitoring technologies can further enhance worker protection.

The results also highlight the importance of early detection and screening programs for high-risk populations. Targeted health monitoring for workers with known asbestos exposure, combined with advancements in diagnostic techniques, can improve early detection of mesothelioma and other asbestos-related diseases, potentially improving outcomes.

At a broader level, the findings support the need for ongoing public awareness campaigns to educate workers, employers, and the general public about the risks of asbestos exposure. These campaigns should emphasize the importance of compliance with safety regulations and promote the availability of resources for workers at risk.

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Statement of Transparency and Principals:

- Author declares no conflict of interest
- Study was approved by Research Ethic Committee of author affiliated Institute.
- Study's data is available upon a reasonable request.
- All authors have contributed to implementation of this research.

References

1. Gaitens JM, Culligan M, Friedberg JS, Glass E, Reback M, Scilla KA, Sachdeva A, Atalla A, McDiarmid MA. Laying the Foundation for a Mesothelioma Patient Registry: Development of Data Collection Tools. International Journal of Environmental Research and Public Health. 2023 03 11;20(6):4950. https://doi.org/10.3390/ijerph20064950
2. Corfiati M, Scarselli A, Binazzi A, Di Marzio D, Verardo M, Mirabelli D, Gennaro V, et al. Epidemiological patterns of asbestos exposure and spatial clusters of incident cases of malignant mesothelioma from the Italian national registry. BMC cancer. 2015 04 15;15:286. https://doi.org/10.1186/s12885-015-1301-2
3. Lee LJ, Lin C, Pan C, Cheng Y, Chang Y, Liou S, Wang J. Clustering of malignant pleural mesothelioma in asbestos factories: a subgroup analysis in a 29-year follow-up study to identify high-risk industries in Taiwan. BMJ open. 2018 Dec 09;8(12):e021063. https://doi.org/10.1136/bmjopen-2017-021063
4. Solbes E, Harper RW. Biological responses to asbestos inhalation and pathogenesis of asbestos-related benign and malignant disease. Journal of Investigative Medicine: The Official Publication of the American Federation for Clinical Research. 2018 04;66(4):721-727. https://doi.org/10.1136/jim-2017-000628
5. Shasha-Lavsky H, Avni A, Paz Z, Kalfon L, Dror AA, Yakir O, Zaccai TF, Weissman I. Long-term outcomes after pre-emptive liver transplantation in primary hyperoxaluria type 1. Pediatric Nephrology (Berlin, Germany). 2023 06;38(6):1811-1820. https://doi.org/10.1007/s00467-022-05803-y
6. Gottesfeld P. Exposure hazards from continuing use and removal of asbestos cement products. Annals of Work Exposures and Health. 2024 01 08;68(1):8-18. https://doi.org/10.1093/annweh/wxad066
7. Damiran N, Frank AL. Mongolia: Failure of Total Banning of Asbestos. Annals of Global Health. 2023;89(1):50. https://doi.org/10.5334/aogh.4035