Must countries shoulder the burden of mesothelioma to ban asbestos? A global assessment

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Handling editor Seye Abimbola

ABSTRACT

Introduction Mesothelioma is a key asbestos-related disease (ARD) but can be difficult to diagnose. Countries presumably ban asbestos to reduce future ARD burdens, but it is unknown if countries ban asbestos as a consequence of ARD burdens. We assessed if and to what extent mesothelioma burden has an impact on a country banning asbestos and obtaining targets for preventative strategies.

Methods We analysed the status of asbestos ban and mesothelioma burden during 1990–2019 in 198 countries. We assessed mesothelioma burden by age-adjusted mortality rates (MRs) estimated by the Global Burden of Disease Study (GBD) and mesothelioma identification by the WHO mortality database. For GBD-estimated mesothelioma MR, the pre-ban period in the asbestos-banned countries was compared with the 1990–2019 period in the not-banned countries. For mesothelioma identification, the 1990–2019 period was applied to both banned and not-banned countries.

Results The association of mesothelioma MR with ban status increased as the ban year approached. Logistic regression analyses showed that the odds of a country banning asbestos increased 14.1-fold (95% CI 5.3 to 37.9) for mesothelioma identification combined with a 26% (12% to 42%) increase per unit increase of mesothelioma MR (one death per million per year) during the period 1–5 years before the ban year (model p<0.0001).

Conclusion Mesothelioma burden had an impact on, and together with its identification, explained the banning of asbestos in many countries. Asbestos-banned countries likely learnt lessons from their historical policies of using asbestos because mesothelioma burden and identification follow historical asbestos use. Prevention targets for ARD elimination should combine asbestos ban with mesothelioma identification.

INTRODUCTION

Mesothelioma is a fatal malignancy with at least 80% attributable fraction to asbestos exposure.1 The disease can be difficult to diagnose and only approximately 50% of countries report mesothelioma deaths to the WHO.2 Nonetheless, due to its importance as a key asbestos-related disease (ARD), the burden of disease has been estimated for many countries of the world.3–5 The Global Burden of Diseases Study (GBD) recently

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ Six papers analysed the possible effect of a ban on the subsequent mesothelioma burden, that is, the post-ban effect: Four assessed individual countries and two studied the issue on a global scale.

⇒ Another two global assessment studies investigated the possible effect of pre-ban factors on subsequent asbestos bans: one included an analysis of mesothelioma burden and another assessed the ratification status of international conventions.

⇒ The former study had limited generalisability regarding the possible effect of mesothelioma on an asbestos ban because it covered relatively few countries using country-reported data in a study intertwined with several hypotheses.

WHAT THIS STUDY ADDS

⇒ Pre-ban mesothelioma mortality rates increased incrementally towards the ban year in asbestos-banned countries, and the difference to that of the not-banned countries widened as the ban year approached.

⇒ Asbestos bans can be explained by pre-ban mesothelioma burden and by mesothelioma identification, independently and in combination.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ Our study adds evidence that the burden and identification of mesothelioma are important drivers for banning asbestos.

⇒ Asbestos-banned countries likely learnt lessons from their historical policies of using asbestos because mesothelioma burden and identification follow historical use of asbestos.

⇒ International cooperation to eliminate asbestos-related disease should integrate technologies to identify mesothelioma in the roadmap to ban asbestos.
estimated that 29,300 people worldwide die each year from mesothelioma.\(^4\)

The WHO has been calling on countries to cease the use of asbestos in order to eliminate ARD.\(^6\) Since the mid-1980s, around 60 countries have adopted asbestos bans,\(^7\) but the pace of new bans has recently slowed.\(^8\) The current global consumption of raw asbestos lingers at around 1 million metric tonnes per year.\(^9\)

At the national level, the course of ARD burdens closely follows that of asbestos consumption after a period of several decades,\(^10-12\) which is reflected in geographical correlations between disease burdens and historical asbestos use.\(^13,14\) These relationships add to the scientific basis of policies to justify asbestos bans. In our recent literature review,\(^8\) we addressed the question of whether mesothelioma burdens decreased after asbestos bans and concluded that the timing of studies was too early to demonstrate the full effect of bans. Our review also emphasised the importance of asking the alternative question of whether high mesothelioma burdens preceded asbestos bans. This is part of a larger question as to why countries ban asbestos.

A series of articles aimed to elucidate how asbestos-banned countries transitioned from asbestos using to asbestos banned.\(^15\) A myriad of pathways was unravelled, involving wide variations in sociopolitical, juridical, cultural, scientific and technological conditions and the interplay of various stakeholders, for example, patients, non-governmental organisations, workers/employers, administrators and the health/scientific sectors. This raised the question: what common factor incentivised stakeholders to ultimately ban asbestos? We hypothesise this may be the ARD burden experienced by a country in the period preceding a ban.

Countries presumably ban asbestos for the purpose of eliminating the future ARD burden. However, it is unknown if countries ban asbestos as a consequence of the ARD burden. We believe this question merits thorough examination. Estimated burdens of mesothelioma are now available for a wide range of countries, and can be used to represent the ARD burden at a relevant time. Here, we aimed to determine if and to what extent mesothelioma burden has an impact on a country banning asbestos and obtaining targets for preventative strategies.

**METHODS**

We analysed the status of countries with data available for both the mesothelioma burden and asbestos ban. Due to limited reporting of mesothelioma burden by countries, we used widely referenced data estimated by the GBD, which analyses the global situation of diseases and injuries for a wide range of countries.

Recent GBD covers the period from 1990 to 2019 and includes estimated age-adjusted mortality rates (MRs) for mesothelioma.\(^4,16\) We employed the GBD-estimated age-adjusted MR of mesothelioma to represent the mesothelioma burden in each country. In the GBD and our study, mesothelioma was defined as C45 including all its subcategories in accordance with the International Classification of Diseases and Related Health Problems, 10th Revision\(^17\) (ICD-10). Our study subjects comprised 198 countries for which a GBD-estimated mesothelioma MR was available during our observation period of 1990–2019.

Mesothelioma MR data were downloaded from the global health data exchange of the Institute for Health Metrics and Evaluation,\(^16\) University of Washington, USA, which states that data ‘can be used, shared, modified or built on by non-commercial users via the Creative Commons Attribution-NonCommercial-NoDerivatives 4.0 International License’.\(^18\)

We calculated the average and median of mesothelioma MR during the period before asbestos ban (pre-ban) in asbestos-banned countries and during the entire observation period in not-banned countries. Note that the latter period represents the period during which asbestos was not banned despite the accumulation of mortality in the not-banned countries.

Six countries (Austria, Denmark, Iceland, Norway, Sweden and Switzerland) banned asbestos in or before 1990 (ie, ‘early banned’) and thus lacked data on the pre-ban mesothelioma MR. These countries were excluded from our main analysis of 198 countries and were instead analysed for their GBD-estimated mesothelioma MR during 1990–1994 (ie, the earliest period with available data on mesothelioma MR) to approximate pre-ban mesothelioma MR.

We defined mesothelioma identification as the entire process from clinical identification and attribution as cause of death to notification of statistics to the WHO. We refer to the country status of mesothelioma identification as ‘mesothelioma identified’ when data were present and ‘not-identified’ when data were absent from the WHO mortality database\(^19\) during the entire observation period for both banned and not-banned countries. The first year of mesothelioma identification for a particular country was defined as the year that data on mesothelioma deaths first appeared for that country in the WHO mortality database. Note that mesothelioma was introduced into the WHO mortality database for the first time in 1994 and the mesothelioma identification may have been initiated before or after the asbestos ban in banned countries.

We defined asbestos ban as a country’s banning of the production, import and new use of asbestos. We refer to a country’s asbestos ban status as ‘asbestos banned’ or ‘not-banned’ and the year of asbestos ban adoption based on the database of the International Ban Asbestos Secretariat.\(^7\)

\(\chi^2\) test was used to examine the association between the country status of asbestos ban and mesothelioma identification, each as a binary variable (yes/no). T-test and analysis of variance were used to compare the average MR between and across country groups, respectively. Logistic regression analysis was conducted to assess if and to what extent mesothelioma identification and MR explained asbestos ban. We calculated the variance inflation...
factor (VIF) using SAS and the VIF function in the car package of R to investigate collinearity between the explanatory variables. Microsoft Excel (Microsoft Corporation, Redmond, Washington, USA), SAS V.9.4 and R were used for data analysis. Stata software V.17.0 (Stata Corporation LLC, College Station, Texas, USA) was used to generate the box plot.

RESULTS

Table 1 shows the status of 198 countries in terms of asbestos ban and mesothelioma identification. Regarding asbestos ban, 54 (27%) of 198 countries banned asbestos and 144 (73%) did not. Regarding mesothelioma identification, 102 (52%) of 198 countries identified mesothelioma and 96 (48%) did not. When cross-stratified, 89% (48) of the 54 banned countries and 38% (54) of the 144 not-banned countries identified mesothelioma, and 48 (47%) of the 102 mesothelioma-identified countries and 6 (6%) of the 96 not-identified countries banned asbestos. Thus, asbestos ban and mesothelioma identification were closely associated (p<0.0001).

Table 2 shows mesothelioma MR by the status of asbestos ban and mesothelioma identification. The average MR was approximately two times as high in the asbestos-banned versus not-banned countries (5.14 vs 2.55 deaths per million per year, respectively; p=0.0004). The average MR was approximately 40% higher in the
null
Asbestos-banned countries were more likely to identify mesothelioma, and mesothelioma-identified countries were more likely to ban asbestos. Although cause and effect cannot be discerned because mesothelioma identification did not necessarily precede ban, we believe that an association between asbestos ban and mesothelioma identification is plausible, because a high burden of disease is likely to prompt practitioners and authorities to identify and notify the disease. However, this may depend on other factors that we did not examine, such as the level of knowledge of stakeholders regarding the relationship between asbestos and mesothelioma. Banned

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<td>1–5 years before (year of ban 2019)</td>
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See Methods for full definition of asbestos ban and mesothelioma identification.

*Six ‘early-banned’ countries that banned asbestos in or before 1990, that is, Austria, Denmark, Iceland, Norway, Sweden and Switzerland, are precluded from this analysis and are analysed separately in Table 4. See Methods for full explanation.

†) Period before the year of ban in asbestos-banned countries and period before 2019 in not-banned countries.
‡) Variance inflation factor (VIF) was used to assess collinearity between explanatory variable; VIF were 1.026 for mesothelioma identification and 1.025 for mesothelioma MR during 1–5 years before year of ban or 2019.

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See Methods for full definition of asbestos ban.
countries incurred higher pre-ban mesothelioma MR than not-banned countries. Notably, the incremental increases of MR in banned countries and of the difference in MR between banned and not-banned countries towards the ban year strengthen the notion that the preceding mesothelioma burden becomes increasingly important over time to ban asbestos. We speculate that mesothelioma burdens reinforce knowledge and raise concern of various stakeholders, culminating in a societal imperative to ban asbestos.

Logistic regression analyses showed that the odds of a country banning asbestos increased incrementally in response to pre-ban MR towards the ban year. Mesothelioma identification also explained asbestos ban in both the single-variate and two-variate models. The two-variate models were not impacted by collinearity between the explanatory variables of mesothelioma MR and mesothelioma identification. The ARD burden at a certain point in time includes a latent component (due to the latency between exposure and disease) which is not detectable until the latency period saturates. In our study, the pre-ban mesothelioma MR in asbestos-banned countries represented only the detectable component. In contrast, mesothelioma identification (defined for the period until 2019) reflected the detectable and latent components. Thus, it is reasonable that pre-ban mesothelioma MR and mesothelioma identification emerged as independent explanatory factors for countries to ban asbestos.

The fundamental strategy to eliminate ARD is to cease asbestos use. International cooperation for ARD emphasises the banning of asbestos to effectively prevent future disease burdens. Although the importance of asbestos bans cannot be understated, asbestos bans per se have no impact in alleviating the level of current ARD burden which result from historical asbestos use. Asbestos-banned countries likely learnt lessons from their historical policies of using asbestos via the mesothelioma burden and identification. International cooperation should thus integrate the theme of mesothelioma burden and identification, including the sharing of relevant technologies, in the roadmap to ban asbestos. The experience, expertise and technology acquired by the ‘banned and identified’ countries are valuable assets that can be used to support the global elimination of ARD. From a clinical standpoint, novel diagnostic tools are needed, such as easy-to-use kits for immunohistochemical staining, high-utility tissue and blood biomarkers and telepathology.

Many studies have featured themes of asbestos ban status or processes. Several studies reported higher mesothelioma burdens in asbestos-banned countries, relative to not-banned countries, based on straightforward, cross-sectional comparisons. Only a few previous studies have undertaken global assessment to identify factors that may subsequently promote asbestos bans. Seeking to explain ‘why some, but not all, countries banned asbestos’, Bahk et al.27 analysed the crude MR of mesothelioma as a factor that may lead to an asbestos ban. However, the Bahk et al study did not yield a definitive answer because the question was set in a larger framework of societal context interwoven with several hypotheses. Lin et al.28 identified two international conventions and government effectiveness as facilitators of asbestos bans. To our knowledge, our paper is the first to directly investigate if and to what extent mesothelioma burden has an impact on countries deciding to ban asbestos.

The association among pre-ban mesothelioma MR, mesothelioma identification and asbestos ban did not apply to certain countries. Relative to the MR of the ‘banned and identified’ countries, we found high MR in the ‘not-banned and not-identified’ countries of Andorra, Lesotho, Namibia, Eswatini and Botswana and in the ‘banned and not-identified’ country of Monaco (figure 1). These countries can learn from the policies of the ‘banned and identified’ countries, as such policies may ‘diffuse across countries of similar background’. Although the history of asbestos and ARD is unique to each country, several common patterns emerged regarding the relationship between the timing of a ban and the mesothelioma MR: (1) countries with high MR that banned asbestos early (eg, Netherlands, Italy and the UK and the six ‘early-banned’ countries—see below for the latter); (2) some countries without high MR that banned asbestos early (eg, Brunei and Kuwait); and (3) some countries with high MR that banned asbestos late (eg, Canada, South Africa and Turkey—historically asbestos-producing and asbestos-exporting countries) (online supplemental figure 1). Separately, political factors play important roles as typified by the EU Directive which effectively mandated all EU member states that had not yet banned asbestos to do so by January 2005. We did not include the six ‘early-banned’ countries in our main analysis because data on their pre-ban mesothelioma MR were not available in GBD. We thus substituted the pre-ban MR with the 1990–1994 MR in a separate analysis and found that the 1990–1994 MR of the ‘early-banned countries’ was compatible with the upper range of that of the ‘banned and identified’ countries (table 4). We speculate that the pre-ban MR of the ‘early-banned countries’ was also in the upper range of that of the ‘banned & identified’ countries. This speculation is supported by our observation that the pre-ban standardised incidence rates of male pleural mesothelioma in the early-banned countries of Denmark, Norway and Sweden were higher than or similar to that of Finland, which had an upper range pre-ban MR of the ‘banned and identified’ countries. Thus, the associations of asbestos bans with mesothelioma MR and identification found in this study would likely be strengthened if we could include the ‘early-banned’ countries in the main analysis.

A major strength of our study was that the national experiences of a wide range of countries were incorporated based on comparable data from international sources, enabling a global assessment. Another advantage was that distinct aspects of key variables were taken into consideration, that is, the level and identification of
the mesothelioma burden and the status and timing of ban. Also, the time sequence of mesothelioma burden and asbestos ban were adequately considered (the former variable was defined as preceding the latter). A major limitation of our study was our total dependence on GBD estimates which are prone to error particularly for developing countries due to uncertainties in the original information source as well as our narrow focus on the relationship between mesothelioma and bans. The dynamics leading to an asbestos ban are complex with many factors interacting in myriad ways. Thus, our approach may be oversimplified and may have overlooked important factors such as the level of stakeholders’ knowledge (as mentioned earlier), national economic status (eg, GDP) and political motives (eg, camouflage of mesothelioma status). We were unable to directly analyse data of the six ‘early-banned’ countries, which required a separate analysis. Furthermore, our study did not account for variations in completeness of asbestos ban. Finally, mesothelioma identification was not limited to the pre-ban period because the disease category was only first introduced into the WHO mortality database in 1994.

In conclusion, we herein report that mesothelioma burden had an impact on, and together with its identification, explained the banning of asbestos in many countries. These countries likely banned asbestos by taking lessons from their historical policies of using asbestos because the mesothelioma burden and its identification followed historical asbestos use. The identification of mesothelioma as a ‘signal tumour’ of the ARD burden is important to enhance the pace of asbestos bans. The world should adopt a comprehensive preventative strategy for ARD elimination that combines the banning of asbestos with the identification of mesothelioma.

References

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