*Title:* The Burden of Asbestos-Related Diseases due to Historical Asbestos Consumption Continues 15 Years Later: An Updated Ecological Study

*Authors:* Emma M Rath,1,2,3 Man Lee Yuen,2 Chimed-Ochir Odgerel,4,2 Ro-Ting Lin,5,2 Matthew Soeberg,2 Anna K Nowak,6,7,2 Ken Takahashi2,8,9

1. Giannoulatou Laboratory, Victor Chang Cardiac Research Institute, Sydney, Australia
2. Asbestos Diseases Research Institute, Sydney, Australia
3. School of Medical Sciences, University of New South Wales, Sydney, NSW 2052, Australia
4. Graduate School of Biomedical and Health Sciences, University of Hiroshima, Hiroshima, Japan
5. College of Public Health, China Medical University, Taichung, Taiwan
6. National Centre for Asbestos Related Diseases, University of Western Australia, Perth, Australia
7. Institute for Respiratory Health, Perth, Australia
8. School of Population and Global Health, University of Western Australia, Perth, Australia
9. University of Occupational and Environmental Health, Kitakyushu, Japan

*Corresponding Author:*

Professor Ken Takahashi, MD, PhD, MPH

Mail address: 577-3 Hara, Okagaki-machi, Onga-gun, Fukuoka Prefecture, Japan 811-4202

Email: 1) [ken.takahashi@uwa.edu.au](mailto:ken.takahashi@uwa.edu.au) 2) [ken.takahashi@adri.org.au](mailto:ken.takahashi@adri.org.au)

TEL: 1) +81 (Japan) 90 5087 5314 ; 2) +61 (Australia) 420 589 712

*Declarations of conflicts of interest:*

The authors have no declarations of conflict.

*Abstract:*

Background Asbestos-related diseases (ARD) are a growing concern, as many countries are experiencing the disease burden resulting from past asbestos use, while others continue to consume asbestos. In 2007, we reported a clear and plausible ecological association between the ARD burden and historical asbestos consumptions of countries. Now, a decade and a half later, we aimed to assess if and how this association may have changed. Methods We analyzed the sex-specific relationship of national data between the log-transformed age-adjusted mortality rates of mesothelioma and asbestosis for 2010-2014 and the per capita asbestos consumption of 1970-1979 and 1960-69, respectively, fit on a linear regression model. The previously analyzed (original) countries were included in the updated analysis and all countries with currently available data were included in the expanded analysis. Results The ecological associations were generally maintained in the original countries. The expanded analysis revealed positive associations, particularly for all and pleural mesothelioma in men, with 36-44% of the mortality variance explained by asbestos consumption. Conclusions The ecological associations were sustained, although the proportion of mortality variance explained in the association was lower than that found in the 2007 study. This is likely attributable to the addition of countries that recently started reporting ARD, many of which are economically developing. Our findings support the importance of eliminating asbestos consumption as a priority for ARD elimination. (223words)

Keywords: asbestos; mesothelioma, asbestosis, ecological study, international comparison

**Introduction**

Every year, about 230,000 people worldwide die from asbestos-related diseases (ARD).1,2 Of the several ARD types, malignant mesothelioma (“mesothelioma” hereafter) is the most fatal; it is almost invariably caused by occupational or environmental exposure to asbestos. Asbestosis, which is less fatal, is predominantly caused by occupational exposure to asbestos. The Global Burden of Disease study of 2019 estimated that about 29,250 and 3,570 annual deaths were due to mesothelioma and asbestosis, respectively.2 Individual countries shoulder ARD burdens of various levels and composition. Since 2003, international organizations such as the World Health Organization (“WHO” hereafter) and the International Labour Organization have been calling on countries to eliminate ARD by stopping the use (or consumption) of asbestos.3 Scientific organizations have been issuing calls along similar lines.4-6

The global situation regarding asbestos consumption is diverse and rapidly changing. Global asbestos consumption was recently estimated at about 1 million metric tons per year,7 and is clearly on a downward trend; however, the situation varies widely by country. Iceland totally banned asbestos in 1983. Since then, a total of 67 countries, many of which had historically consumed large amounts of asbestos, have adopted total bans.8 Asbestos consumption shifted from developed to developing countries beginning around the turn of the 21st century.9 Today, about 90 countries still import raw asbestos from a few asbestos-producing countries,10 mostly to manufacture asbestos-containing materials (ACM). Countries that do not manufacture ACM but lack an asbestos ban are likely to be importing and consuming ACM.

The causal relationship between asbestos exposure and mesothelioma in humans is well established, with an attributable fraction of 80-90%.11 Asbestosis, by definition, is caused by asbestos exposure. A long latency period is a unique characteristic of ARD, particularly mesothelioma, reaching 30 to 40 years or more between the first exposure and disease development.12 The latency period for other ARD, including asbestosis, is generally shorter than that of mesothelioma but longer than those of other diseases with known causes. It has been shown that the latency period of ARD in individuals can be reflected in population-level studies.13 Ecological studies, despite the widely acknowledged “ecological fallacy,” have the advantage of allowing researchers to study very large populations and utilize existing databases.14 Findings from ecological studies are based on the experience of populations, and add to the foundation of health policies.

In 2007, we reported clear and plausible ecological associations between deaths from mesothelioma and asbestosis and historical asbestos consumption.15 During the decade and half since then, while only a few countries have adopted asbestos bans,16 many countries continued to consume asbestos and ARD continued to take a toll in a range of countries. The WHO mortality database has been periodically updated: more data have accumulated for the originally analyzed countries and data are now available for some previously non-reporting countries that have started to report data. Regarding ARD, individual-level epidemiologic studies play a central role to establish causality. For public health policy, aggregate-level ecological studies can separately play an important role by elucidating the health consequences of asbestos use in populations and drawing implications on asbestos bans.

Thus, the objective of the present study was to assess the ecological relationship between recent ARD death burdens and historical asbestos consumption by updating the analyses for the originally reported countries and expanding the analyses to all countries with currently available data.

**Methods**

We studied the following ARD types: pleural mesothelioma (C45.0, as classified by the International Classification of Diseases, 10th revision [ICD-10]); peritoneal mesothelioma (C45.1, ICD-10); all mesothelioma; and asbestosis (J61, ICD-10). All mesothelioma was defined as mesothelioma (C45, ICD-10) as an independent category or a composite of any/all of its subcategories—i.e., pleural (C45.0), peritoneal (C45.1), pericardial (C45.2), other sites (C45.7), and unspecified (C45.9), as reported by the respective countries.

We extracted the yearly number of deaths for individual ARD by the sex and 5-year age category from the WHO mortality database.17 National population data were obtained from the United Nations (UN)18 and WHO,17 and prioritized for use in that order. For each country, sex-specific, age-specific mortality rates (deaths per million population per year) were calculated by dividing the number of sex-specific, age-specific deaths by the size of the corresponding sex-specific, age-specific national population, and then age-standardizing to the world standard population published in 2001.19 These death rates were then averaged for the study periods of 2000-2004 and 2010-2014.

The amount of historical asbestos consumption was defined as the average of the available yearly asbestos consumptions per capita (kg per capita per year): We used the average of 1960 and 1970 for the 1960-1969 study period and the average of 1970, 1975, and 1980 for the 1970-1979 study period. For each country, the volume of asbestos production, import, and export (in metric tons) was extracted from the report of the US Geological Survey.21 Consumption was defined as production plus import minus export, and the result was divided by the national population for that year.

For countries whose asbestos consumption data were available only as a subset of a larger entity, the country’s individual consumption was extracted as a proportion of the larger entity’s consumption using the first available asbestos consumption proportions (year 1995 for the former countries of USSR and Czechoslovakia and year 1998 for the former countries of Yugoslavia), or by country population proportions for the year of consumption (Belgium and Luxembourg, because the first available consumption proportion was from 2003 and deemed to be too distant). This strategy resulted in Slovenia being an outlier for whom it was plausible that the proportion of consumption could not be accurately determined by this method. Thus, Slovenia was excluded from further analysis. The ratio of economic activity, including asbestos consumption, in Slovenia in the 1960s and 1970s compared to other former Yugoslavia countries, was not expected to be similar to the situation in 1998 due to the involvement of the latter in a multi-year war in the 1990s.

For each category of ARD, linear regression analyses were carried out for each sex, with age-adjusted mortality rates of each ARD as the dependent variable and historical asbestos consumption as the independent variable. Analyses were carried out separately for all countries with currently available data, and for only the countries analysed in the 2007 report.15 Because several countries changed their practice of reporting mesothelioma deaths since the earlier analysis, e.g., some previously used C45.0 in 2000-2004 but used C45 in 2010-2014, the number of analyzed countries decreased in the updated analysis. National mortality rates were log-transformed to comply with the assumptions underlying the random errors in the regression model. Parameters in the regression model were estimated using the lm function of the R stats package20 and weighted by the size of sex-specific national populations of the median year of the consumption period. A p-value less than 0.05 was deemed to be statistically significant. QQ-plots and histograms of residuals were manually inspected and confirmed that the linear model is appropriate, including for data subsets that did not achieve statistical significance or whose adjusted-R2 value was negative or close to zero.

All statistical analyses and plots were carried out in R.20 We had used SAS version 8.02, not R, for the data analysis in our 2007 report. To ensure the compatibility of the two methods, we replicated our analysis of the original countries for the original time-frame using R. We confirmed good matches of the overall trend and p-values, and found only small differences (<5%) in a few specific parameters (B0, B1, R2), and thus proceeded with our current analyses using R. We attribute the small observed differences to updates in the WHO mortality data for the countries analyzed in the 2007 report.15

The R scripts used for the analyses reported in the present study are available in the Supplementary Information, as are RData files containing all analyzed data; the latter can be loaded into R with the command: load("filename.RData").

**Results**

Tables 1 and 2 show the sex-specific relationship of national data between the log-transformed age-adjusted mortality rates of individual asbestos-related diseases (ARD) and per capita historical asbestos consumption, fit on a linear regression model with the parameters, intercept B0 (i.e., expected mortality rate corresponding to zero asbestos consumption, or, the background mortality rate) and slope B1 (i.e., change in ARD mortality rates per unit change in asbestos consumption, or, incremental change in mortality rate), and adjusted R2 values. Table 1 updates the relationship reported in 2007 for the original set of countries by applying mortality rates of 2010-14 to probe subsequent changes (called updated analysis). Table 2 analyzes all currently available data from an expanded set of countries (called expanded analysis).

In the updated analysis (Table 1), the log-transformed mortality rates of 2010-14 were regressed on asbestos consumption from 1960-69 and 1970-79. When the log-transformed values are back transformed, all models showed positive slopes and small positive intercepts with variable statistical significance and R2 values: For the 1960-69 asbestos consumption, statistically significant positive associations were found for five of the eight ARD-sex combinations. The highest R2 value was found for asbestosis in men (R2=0.80), followed by all mesothelioma in men (R2=0.56) and peritoneal mesothelioma in women (R2=0.53); there was no statistically significant association for pleural mesothelioma in either sex or for asbestosis in women. For the 1970-79 asbestos consumption, statistically significant positive associations were found for seven of the eight ARD-sex combinations. The highest R2 value was found for asbestosis in men (R2=0.47), followed by peritoneal mesothelioma in women (R2=0.44) and all mesothelioma in men (R2=0.41); there was no statistically significant association for asbestosis in women.

In the expanded analysis (Table 2), the log-transformed mortality rates of 2010-14 were regressed on the asbestos consumption of 1970-79 for all countries now reporting ARD deaths. This included economically developing countries who recently started reporting these deaths. When the log-transformed values are back transformed, all models showed positive slopes and small positive intercepts with variable statistical significance and R2 values: Statistically significant positive associations were found for seven of the eight ARD-sex combinations but not for asbestosis in women. For all mesothelioma, the 1970-79 asbestos consumption was a highly significant positive predictor of the 2010-14 mortality with adjusted R2 values of 0.39 (p<0.0001) and 0.30 (p<0.0001) for men and women, respectively. The slope (B1) of the regression lines suggested that for an increment in asbestos consumption of 1 kg per capita in a population, men had a 2.4-fold (95%CI 1.8 to 3.0) (100.372×1 [95%CI 100.261 to 100.483]) increase and women had a 1.8-fold (1.4 to 2.2) (100.245×1 [95%CI 100.156 to 100.335]) increase in deaths from all mesothelioma. The intercepts (B0) were small at 10−0·251 =0.56 (0.31 to 1.01) for men and 10−0·456 = 0.35 (0.22 to 0.57), deaths per million population, respectively, for women (See also Table 3 for back-transformed values of the parameters).

For pleural mesothelioma, the 1970-79 asbestos consumption was a statistically significant positive predictor of the 2010-14 mortality rate for both men (R2=0.38, p<0.0001) and women (R2=0.24, p=0.0002). The slope suggested a 2.1-fold (1.6 to 2.7) (100.315×1 [100.202×1 to 100.429×1]) and 1.7-fold (1.3 to 2.1) (100.221×1 [100.110×1 to 100.332×1]) increase in pleural mesothelioma deaths for men and women, respectively, per 1 kg rise in asbestos consumption in the population.

For peritoneal mesothelioma, the relationships between the 2010-14 mortality rate and the 1970-79 asbestos consumption were statistically significant with positive slopes and small intercepts for both sexes (R2=0.36, p<0·0001, B1=0.17 [0.10 to 0.23] for men and R2=0.22, p=0·0006, B1=0.10 [0.05 to 0.15] for women). The slope suggested a 1.5-fold (1.3 to 1.7) (100.167×1 [100.101×1 to 100.233×1]) and a 1.3-fold (1.1 to 1.4) (100.099×1 [100.045×1 to 100.153×1]) increase in deaths from peritoneal mesothelioma in men and women, respectively, per 1 kg incremental rise in asbestos consumption in the population.

For asbestosis, the association was positive and statistically significant in men and yielded the highest adjusted R2 of all studied ARD (R2=0.44, p<0·0001, B1=0.30 [0.20 to 0.39]). The slope showed a 2.0-fold (1.6 to 2.4) (100.295×1 [100.201×1 to 100.389×1]) increase in deaths from asbestosis in men per 1 kg incremental rise in asbestos consumption in the population. However, the association was not significant in women.

Table 3 compares the parameters B0 (intercept or background mortality rate) and B1 (slope or incremental change in mortality rate) between the earlier study and the present expanded study, for which the log-transformed values were back transformed to allow a straightforward interpretation. Note that the earlier and present expanded study was based on the mortality rates of 2000-2004 and 2010-2014, respectively. Overall, these parameters changed only minimally: for all mesothelioma in men, the background mortality rate was 0.7 per million in 2000-2004 and 0.6 per million in 2010-2014 with incremental change in mortality rate at 2.4-fold in 2000-2004 and 2.4-fold in 2010-2014. For asbestosis in men, the background mortality rate was 0.06 per million in 2000-2004 and 0.10 per million in 2010-2014 with incremental change in mortality rate at 2.7-fold in 2000-2004 and 2.0-fold in 2010-2014.

The Figure shows the relationship as a scatterplot of countries for the expanded analysis in men (Table 2; men were chosen for having the higher adjusted R2 value). Country codes are shown next to the circles representing countries, whose size are proportional to the population sizes. These data points include more developing countries than the 2007 report. A positive linear association can clearly be seen between the log-transformed 2010-14 mortality rates and the 1970-79 asbestos consumption.

**Discussion**

Recent ARD mortality rates have remained closely associated with historical asbestos consumption. In the updated analysis, the 2010-14 mortality rates maintained a strong association between the two periods of asbestos consumption for 1960-69 and 1970-79, albeit somewhat reduced for mesotheliomas compared to the 2007 report.15 The relative strengths of the associations between the two asbestos consumption periods differed by ARD type, but the associations were strong for asbestosis in men and all mesothelioma in men for both periods. In the expanded analysis, the positive associations had modest R2 values but the patterns of association held across ARD types, with the strongest associations seen for asbestosis, all mesothelioma, and pleural mesothelioma, in men. In women, the associations were significantly positive for all ARD except for asbestosis. Associations were consistently stronger for men than for women.

In the updated analysis, lag times of 47.5 and 37.5 years (yr) were inherent between the mortality rates and asbestos consumption of 1960-69 and 1970-79, respectively. The latter model (with the 37.5-yr lag time) better reflected the consensus value for latency periods, and, compared to the former model (with the 47.5-yr lag time), showed clearer and more consistent associations with mortality rates, particularly for pleural mesothelioma in men. In contrast, the former model (with the 47.5-yr lag time) showed no association with pleural mesothelioma in either sex but showed significantly stronger association for peritoneal mesothelioma in both sexes. Our observations fit well with the findings by Reid et al.,12 who reported that as the time since first exposure extends past 40 years, the risk decreases for pleural mesothelioma, but not for peritoneal mesothelioma.

In the expanded analysis, we assessed the association between the 2010-14 mortality rates and the 1970-79 asbestos consumption in all countries with data. Historically, the world consumed the largest volume of asbestos in the 1970s, with 3.5 and 4.8 million metric tons consumed in 1970 and 1980, respectively.21 The year 1980 was the world’s historical peak. During the 1970s, the continental share of asbestos consumption was steady around 50 to 60% in Europe, decreased from 20% to 10% in North America, and increased from 15% to 20% in Asia.21 Thus, the 1970 decade for asbestos consumption, the 2010-14 half-decade for mortality rates and the 37.5-yr lag time provided an optimal setting to explore the ecological association on a global scale. The expanded analysis included more developing countries than the original analysis and thus improved the international representation.

Statistically, the regression models assumed a log-linear relationship between historical asbestos consumption and ARD mortality rates for which the slope (B1) of the regression line represented change in ARD mortality rates per unit change in asbestos consumption. With our model, mortality rates increased exponentially relative to asbestos consumption within the range of 1.3 and 2.4-fold per 1 kg incremental rise in per capita asbestos consumption. The intercept (B0) represented the expected mortality rate corresponding to zero asbestos consumption, i.e., the background mortality rate, which, with our model, ranged between 0.09 and 0.56 per million population. Thus, countries with little historical asbestos consumption experienced very low background levels of ARD. Since we reported this model in 2007,15 the GBD studies have used it to calculate global mortality rates due to mesothelioma in populations not exposed to asbestos.22 The sex-specific associations found in the present study (more consistent and stronger in men) are in line with findings from epidemiological studies conducted at individual levels,and can be explained by the dominance of men in asbestos-related occupations.23

The sex-specific statistical relationships enabled us to predict mortality rates corresponding to the mean consumption value. The male-to-female ratio could then be estimated for each ARD type. For all mesothelioma, the mortality rate predicted for the mean consumption value (1.82 and 1.86 kg per capita in men and women, respectively) was 2.66 (95%CI 2.45 to 2.89) in men and 1.00 (0.93 to 1.08) (per million people per year) in women. Thus, the male-to-female mortality rate ratio was estimated at 2.7. This value was within, but closer to the lower boundary, of the reported range of 2 – 10.23,24 The male-to-female mortality ratio was similarly estimated for pleural mesothelioma, peritoneal mesothelioma, and asbestosis at 3.5, 1.7, and 9.0, respectively (calculations not shown), which again were in line with the consensus values for these ARD types.23,24 However, the estimated ratio for asbestosis was not robust, given that the association for asbestosis was not statistically significant in women.

The majority of countries reported mesothelioma deathsto the WHO using disease subcategories. However, countries such as Finland and Serbia used only the C45 (all mesothelioma) category and so these countries did not contribute to the associations by subcategories. We note that there may be a reporting bias in how countries used the C45.9 (unspecified site) subcategory. For example, the USA, the UK, and Australia reported more than 70% of their total mesothelioma cases as C45.9 (unspecified site), compared to less than 15% for Germany, Italy and Japan. A predilection for C45.9 will cause a deficit in other subcategories. In our separate study of global mesothelioma deaths reported to the WHO, we speculated that there may be overlap between the pleura (C45.0) and unspecified site (C45.9) subcategories based on these subcategories having similar sex ratios and patterns of age-specific mortality rates.25 It is widely accepted that pleural mesothelioma outnumbers peritoneal mesothelioma by a factor of four or more.23,26 Thus, the mortality rates for pleural mesothelioma in the present study were likely underestimated due to this reporting bias.

Ecological studies are underappreciated mostly due to the “ecological fallacy,” which is the fallacy of drawing causal inference at the individual level based on population-level associations.14 This is a real constraint that warrants caution. However, neither the earlier nor present study attempted to draw a causal inference because there is sufficient evidence from human and animal studies that has enabled causality to be well established.23 Rather our studies approached the asbestos-ARD relationship from a different angle. While on missions of international cooperation, we have often heard policymakers of asbestos-using countries say that “… we have no ARD among our people, so there is no problem in using asbestos.” When causality is well established, ecological studies are informative because they provide a population perspective that individual-level epidemiological studies do not. They have the potential to impact policies by helping policymakers understand health-related phenomena in the context of country experiences. In relation to ARD, the pace of countries adopting asbestos bans is slow16 and the population at risk in the world remains high.Public health policy seeking the ultimate goal of asbestos ban warrants reinforcement from various perspectives including ecological studies.

Our independent variable was the volume of consumption of raw asbestos divided by the size of the national population, and thus represented the amount of asbestos consumed *per capita* in each country. Because we do not know whether and the extent to which this independent variable represents actual exposure amounts, our use of this independent variable was probably the largest limitation of our study. However, based on the wide application of this variable in descriptive and ecological studies,15,27,28 we judged it to be a reasonable surrogate. Also, a recent study applied the life cycle assessment methodology to assess the human toxicity and environmental impacts of ACM,29 the entire life cycle of which starts from *raw asbestos*. Other limitations of our study included the lack of distinction between fiber type (e.g., amphiboles, chrysotile) and the preclusion of population attributes that may have confounded the associations in question. Also, lung cancer, which is an important ARD, was not analyzed.

In both the 2007 and the present study, we analyzed all countries with data available *at the time*. Only the mortality data changed in the interim, with more countries reporting ARD deaths. Many of the newly included countries were developing countries that reported ARD for the first time, causing there to be more data points close to the origin (low consumption and low mortality). The expertise and infrastructure in developing countries are often insufficient to allow the diagnosis, recording and reporting of ARD.30 In addition, under-recognition and under-reporting may be more prevalent if the country in question has only just started to report ARD to the WHO. This may partly explain the lower R2 value obtained in the expanded analysis, relative to the 2007 study.

The main strength of our study was the incorporation of updated data for the original set of countries and the separate analysis of an expanded set of countries. This allowed us to observe how the associations changed (or held) after a further 15 years had elapsed. Other strengths of the study included the reliability and comparability of data obtained from authoritative and widely used global databases on death numbers (i.e., the WHO mortality database17) and asbestos consumption (i.e., the USGS data21), the application of sex-specific age-adjusted mortality rates, and the use of year-specific asbestos consumption rates per capita that enabled us to compare a wide range of countries. The long timeframe of our study also enabled us to compare the effect of two different latency times in the updated analysis.

Although lung cancer is an important ARD, it is not straightforward to assess lung cancer in the framework of an ecological study due to the known high attributable fraction of smoking. Future studies may address this problem by introducing a variable on historical tobacco consumption into the model. Addressing fiber type would also be expected to improve the future analyses and add findings. The challenge, however, will be to identify comparable data, such as data on historical tobacco consumption and fiber type, that can be feasibly analyzed. In 2013, the International Agency for Research on Cancer added cancers of the larynx and ovary to the list of ARD and commented that there were expert recommendations to include colorectal cancer.23,31 There are debates on the asbestos-relatedness of other cancers and health conditions31 for which ecological studies may be employed for exploratory purposes.

In conclusion, recent ARD burdens did not attenuate after 15 years and could be predicted from the amount of asbestos consumed by countries in the 1970s, particularly in men. In comparison to our 2007 study, the ecological associations remained strong and consistent, although somewhat reduced for mesothelioma, when data for the original countries were updated. The ecological associations held when data were expanded to more countries, including those of economically developing status starting to report ARD. Our updated and expanded results support the recommendation that eliminating asbestos consumption is a priority for ARD elimination.

Body of text excluding abstract = 3,980 words

**Country Codes for the Figure**

ARG=Argentina; AUS=Australia; AUT=Austria; BEL=Belgium; BGR=Bulgaria; BIH=Bosnia and Herzegovina; BRA=Brazil; CAN=Canada; CHE=Switzerland; CHL=Chile; COL=Colombia; CRI=Costa Rica; CYP=Cyprus; CZE=Czech Republic; DEU=Germany; DNK=Denmark; ECU=Ecuador; EGY=Egypt; ESP=Spain; EST=Estonia; FIN=Finland; FRA=France; GBR=United Kingdom; GRC=Greece; GTM=Guatemala; HKG=Hong Kong; HRV=Croatia; HUN=Hungary; IRL=Ireland; IRN=Iran; ISL=Iceland; ISR=Israel; ITA=Italy; JAM=Jamaica; JPN=Japan; KAZ=Kazakhstan; KGZ=Kyrgyzstan; KOR=South Korea; KWT=Kuwait; LKA=Sri Lanka; LTU=Lithuania; LUX=Luxembourg; LVA=Latvia; MAR=Mauritania; MDA=Moldova; MEX=Mexico; MKD=North Macedonia; MYS=Malaysia; NIC=Nicaragua; NLD=Netherlands; NOR=Norway; NZL=New Zealand; PAN=Panama; PER=Peru; PHL=Philippines; POL=Poland; PRT=Portugal; ROU=Romania; SAU=Saudi Arabia; SGP=Singapore; SLV=Slovenia; SRB=Serbia; SVK=Slovakia; SWE=Sweden; THA=Thailand; TUN=Tunisia; TUR=Turkey; URY=Uruguay; USA=United States; VEN=Venezuela; ZAF=South Africa

GBD 2017 Risk Factor Collaborators. 2018. Global, regional, and national comparative risk assessment of 84 behavioural, environmental and occupational, and metabolic risks or clusters of risks for 195 countries and territories, 1990-2017: a systematic analysis for the Global Burden of Disease Study 2017. Lancet 392:1923–94, PMID: [30496105](https://pubmed.ncbi.nlm.nih.gov/30496105/), <https://doi.org/10.1016/S0140-6736(18)32225-6>.

1. The Institute for Health Metrics and Evaluation. GBD Results Tool. <http://ghdx.healthdata.org/gbd-results-tool>
2. International Labour Organization and World Health Organization. 2007. Outline for the Development of National Programmes for Elimination of Asbestos-Related Diseases. [elim\_asbestos\_doc\_en.pdf (who.int)](https://www.who.int/occupational_health/publications/elim_asbestos_doc_en.pdf?ua=1),

(<https://www.who.int/occupational_health/publications/elim_asbestos_doc_en.pdf?ua=1>).

1. Takahashi K, Landrigan PJ, Ramazzini C. 2016. The global health dimensions of asbestos and asbestos-related diseases. Ann Glob Health 82:209, PMID: [27325079](https://pubmed.ncbi.nlm.nih.gov/27325079/), <https://doi.org/10.1016/j.aogh.2016.01.019>.
2. International Commission on Occupational Health. Asbestos ban. <http://www.icohweb.org/site/abestos-ban.asp>
3. Wael K Al-Delaimy. 2013. The JPC-SE Position Statement on Asbestos: A Long-Overdue Appeal by Epidemiologists to Ban Asbestos Worldwide and End Related Global Environmental Injustice. Environ Health Perspect 121(5):a144-a145, PMID: [23635993](https://pubmed.ncbi.nlm.nih.gov/23635993/), <https://doi.org/10.1289/ehp.1306892>.
4. U.S. Geological Survey. 2021. Mineral Commodity Summaries, January 2021. <https://pubs.usgs.gov/periodicals/mcs2021/mcs2021.pdf>, ISBN: 978-1-4113-4398-6, <https://doi.org/10.3133/mcs2021>.
5. Kazan-Allen L. 2019. List of national asbestos bans by country. [http://www.ibasecretariat.org/alpha\_ban\_list.php](http://www.ibasecretariat.org/alpha_ban_list.php%20) [accessed 3 January 2022].
6. Odgerel C-O, Arachi D, Driscoll T, Lin R-T, Takala J, Takahashi K. 2020. Burden of mesothelioma deaths by national income category: current status and future implications. Int J Environ Res Public Health Sep 21;17(18):6900, PMID: [32967259](https://pubmed.ncbi.nlm.nih.gov/32967259/), <https://doi.org/10.3390/ijerph17186900>.
7. Virta RL. 2009. Worldwide asbestos supply and consumption trends from 2003 through 2007. Circular 1298, U.S. Geological Survey: Reston, VA, USA. 2009. Available online: <https://pubs.usgs.gov/circ/2006/1298/c1298.pdf>, ISBN: 1-411-31167-1.
8. Mutti L, Peikert T, Robinson BWS, Scherpereel A, Tsao AS, de Perrot M, et al. 2018. Scientific advances and new frontiers in mesothelioma therapeutics. J Thorac Oncol 13(9):1269-1283.
9. Reid A, de Klerk NH, Magnani C, Ferrante D, Berry G, Musk AW et al. 2014. Mesothelioma risk after 40 years since first exposure to asbestos: a pooled analysis. Thorax, 69:843-850, PMID: [24842786](https://pubmed.ncbi.nlm.nih.gov/24842786/), <https://doi.org/10.1136/thoraxjnl-2013-204161>.
10. Nurminen M, Karjalainen A, Takahashi K. 2003. Estimating the induction period pleural mesothelioma from aggregate data on asbestos consumption. J Occup Environ Med 45(10):1107-1115, PMID: [14534453](https://pubmed.ncbi.nlm.nih.gov/14534453/), <https://doi.org/10.1097/01.jom.0000091682.95314.01>.
11. Walter SD. 1991. The ecologic method in the study of environmental health. I. Overview of the method. Environ Health Perspect 94:61-65, PMID: [1954942](https://pubmed.ncbi.nlm.nih.gov/1954942/), <https://doi.org/10.1289/ehp.94-1567938>.
12. Lin R-T, Takahashi K, Karjalainen A, Hoshuyama T, Wilson D, Kameda T, et a. 2007. Ecological association between asbestos-related diseases and historical asbestos consumption: an international analysis. Lancet 369:844-849, PMID: [17350453](https://pubmed.ncbi.nlm.nih.gov/17350453/), <https://doi.org/10.1016/S0140-6736(07)60412-7>.
13. Arachi D, Soeberg M, Chimed-Ochir O, Lin R-T, Takahashi K. Chapter 1. 2021. Trend in the Global Incidence of Mesothelioma: Is there Any Changing Trend After Asbestos Regulation and Ban? In: *Malignant Pleural Mesothelioma. Respiratory Disease Series: Diagnostic Tools and Disease Managements.* Nakano T, Kijima T, eds. Singapore: Springer Nature Singapore Pte Ltd, 3-13. . 2021. Malignant Pleural Mesothelioma. <https://doi.org/10.1007/978-981-15-9158-7_1>
14. World Health Organization (WHO). WHO Mortality Database: World Health Organization Statistical Information System (WHOSIS). <https://www.who.int/data/data-collection-tools/who-mortality-database> [accessed 1 July 2021].
15. United Nations (UN). World Population Prospects 2019. <https://population.un.org/wpp/Download/Standard/Population/> [accessed Jun 1, 2021].
16. World Health Organization (WHO). 2001. Age Standardization of Rates: A New WHO Standard. GPE Discussion Paper Series: No.31. Table 4. WHO World Standard Population Distribution (%), based on world average population between 2000-2025. <https://www.who.int/healthinfo/paper31.pdf> [accessed 1 July 2021].
17. R Core Team. 2018. R: A Language and Environment for Statistical Computing; R Foundation for Statistical Computing: Vienna, Austria.
18. Virta RL. 2006. U.S. Geological Survey - Worldwide asbestos supply and consumption trends from 1900 to 2000. Open-File Report 03-83. ISBN: 1-411-31167-1.
19. GBD 2019 Risk Factors Collaborators. 2020. Supplementary appendix 1. Supplement to: Global burden of 87 risk factors in 204 countries and territories, 1990–2019: a systematic analysis for the Global Burden of Disease Study 2019. Lancet 396:1223–49, PMID: [33069327](https://pubmed.ncbi.nlm.nih.gov/33069327/), <https://doi.org/10.1016/S0140-6736(20)30752-2>.
20. International Agency for Research on Cancer. 2012. IARC Monographs on the Evaluation of Carcinogenic Risks to Humans. Arsenic, Metals, Fibres, and Dusts. Volume 100C A Review of Human Carcinogens. Lyon, France: International Agency for Research on Cancer, 219-309 (Asbestos). ISBN: 978-92-832-1320-8.
21. Hillerdal G. 1999. Mesothelioma: cases associated with non-occupational and low dose exposures. Occup Environ Med 56:505-513. PMID: [10492646](https://pubmed.ncbi.nlm.nih.gov/10492646/), <https://doi.org/10.1136/oem.56.8.505>.
22. Delgermaa V, Takahashi K, Park E-K, Le GV, Hara T, Sorahan T. 2011. Global mesothelioma deaths reported to the World Health Organization between 1994 and 2008. Bull World Health Organ 89:716-724C. PMID: [22084509](https://pubmed.ncbi.nlm.nih.gov/22084509/), <https://doi.org/10.2471/BLT.11.086678>.
23. Australian Institute of Health and Welfare. 2021. Mesothelioma in Australia 2020. Cat. no. CAN 143. Canberra: AIHW. ISBN: 978-1-76054-912-1, <https://doi.org/10.25816/2g6c-8q81>.
24. Tossavainen A. 2004. Global use of asbestos and the incidence of mesothelioma. Int J Occup Environ Health 10:22-25. PMID: 15070022, <https://doi.org/10.1179/oeh.2004.10.1.22>.
25. Antao VCS, Pinheiro GA, Wassel JT. 2009. Asbestosis mortality in the USA: facts and predictions. Occup Environ Med 66:335-338. PMID: [19017689](https://pubmed.ncbi.nlm.nih.gov/19017689/), <https://doi.org/10.1136/oem.2008.039172>.
26. Pini M, Scarpellini S, Rosa R, Neri P, Gualtieri AF, Ferrari AM. 2021. Management of asbestos containing materials: a detailed LCA comparison of different scenarios comprising first time asbestos characterization factor proposal. Environ Sci Technol 55:12672-12682. PMID: [34468140](https://pubmed.ncbi.nlm.nih.gov/34468140/), <https://doi.org/10.1021/acs.est.1c02410>.
27. Carbone M, Adusumilli PS, Alexander HR, Baas P, Bardelli F, Bononi A, et al. 2019. Mesothelioma: Scientific clues for prevention, diagnosis and therapy. CA Cancer J Clin 69:402-429. PMID: [31283845](https://pubmed.ncbi.nlm.nih.gov/31283845/), <https://doi.org/10.3322/caac.21572>.
28. Finnish Institute of Occupational Health. 2014. Asbestos, Asbestosis, and Cancer - Helsinki Criteria for Diagnosis and Attribution 2014. Oksa P, Wolff H, Vehmas T, Pallasaho P, Frilander Heikki, eds. Finnish Institute of Occupational Health , 1-153.

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Table 1. Updated regression analyses\* on original set of countries for age-adjusted mortality rates† of asbestos-related diseases versus historical asbestos consumption‡ | | | | | | | | | | | | | | | | | |
|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
|  | | |  | n |  | Regression parameters | | | | | | | |  | Adjusted R2 |  | p value |
|  |  | B0 | (95%CI) | SE | p value | B1 | (95%CI) | SE | p value |  |  |
|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| †2010−14, ‡1960−69. | | | | |  |  |  |  |  |  |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
|  | All Mesothelioma | Male |  | 32 |  | 0.170 | (-0.050 to 0.389) | 0.108 | 0.1255 | 0.287 | (0.195 to 0.379) | 0.045 | <0.0001 |  | 0.560 |  | <0.0001 |
|  |  | Female |  | 31 |  | -0.155 | (-0.331 to 0.021) | 0.086 | 0.0827 | 0.173 | (0.099 to 0.247) | 0.036 | <0.0001 |  | 0.415 |  | <0.0001 |
|  | Pleural Mesothelioma | Male |  | 29 |  | -0.077 | (-0.525 to 0.371) | 0.218 | 0.7276 | 0.125 | (-0.063 to 0.312) | 0.091 | 0.1837 |  | 0.030 |  | 0.1837 |
|  |  | Female |  | 25 |  | -0.402 | (-0.819 to 0.015) | 0.202 | 0.0583 | 0.002 | (-0.172 to 0.175) | 0.084 | 0.9846 |  | -0.040 |  | 0.9846 |
|  | Peritoneal Mesothelioma | Male |  | 25 |  | -0.861 | (-1.039 to -0.682) | 0.087 | <0.0001 | 0.171 | (0.097 to 0.246) | 0.036 | 0.0001 |  | 0.451 |  | 0.0001 |
|  |  | Female |  | 27 |  | -1.038 | (-1.162 to -0.913) | 0.060 | <0.0001 | 0.126 | (0.075 to 0.178) | 0.025 | <0.0001 |  | 0.483 |  | <0.0001 |
|  | Asbestosis | Male |  | 27 |  | -1.149 | (-1.342 to -0.956) | 0.094 | <0.0001 | 0.404 | (0.323 to 0.486) | 0.040 | <0.0001 |  | 0.799 |  | <0.0001 |
|  |  | Female |  | 19 |  | -1.593 | (-1.808 to -1.379) | 0.102 | <0.0001 | 0.072 | (-0.017 to 0.160) | 0.042 | 0.1074 |  | 0.095 |  | 0.1074 |
|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| †2010−14, ‡1970−79. | | | | |  |  |  |  |  |  |  |  |  |  |  |  |  |
|  | All Mesothelioma | Male |  | 32 |  | 0.081 | (-0.110 to 0.272) | 0.094 | 0.3921 | 0.329 | (0.249 to 0.409) | 0.039 | <0.0001 |  | 0.691 |  | <0.0001 |
|  |  | Female |  | 31 |  | -0.181 | (-0.328 to -0.033) | 0.072 | 0.0183 | 0.179 | (0.117 to 0.241) | 0.030 | <0.0001 |  | 0.523 |  | <0.0001 |
|  | Pleural Mesothelioma | Male |  | 29 |  | -0.204 | (-0.588 to 0.180) | 0.187 | 0.2860 | 0.211 | (0.051 to 0.371) | 0.078 | 0.0119 |  | 0.183 |  | 0.0119 |
|  |  | Female |  | 25 |  | -0.546 | (-0.915 to -0.177) | 0.180 | 0.0053 | 0.077 | (-0.077 to 0.231) | 0.075 | 0.3141 |  | 0.002 |  | 0.3141 |
|  | Peritoneal Mesothelioma | Male |  | 25 |  | -1.120 | (-1.385 to -0.854) | 0.128 | <0.0001 | 0.239 | (0.129 to 0.349) | 0.053 | 0.0002 |  | 0.445 |  | 0.0002 |
|  |  | Female |  | 27 |  | -1.004 | (-1.154 to -0.853) | 0.073 | <0.0001 | 0.087 | (0.025 to 0.150) | 0.030 | 0.0079 |  | 0.213 |  | 0.0079 |
|  | Asbestosis | Male |  | 27 |  | -1.169 | (-1.409 to -0.929) | 0.116 | <0.0001 | 0.429 | (0.327 to 0.530) | 0.049 | <0.0001 |  | 0.743 |  | <0.0001 |
|  |  | Female |  | 19 |  | -1.395 | (-1.639 to -1.151) | 0.116 | <0.0001 | 0.050 | (-0.050 to 0.150) | 0.047 | 0.3030 |  | 0.007 |  | 0.3030 |
|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |

n = number of countries. B0 = intercept of regression line. B1 = slope of regression line

\*Regression model: log10(age-adjusted mortality rates of asbestos-related diseases) (deaths per million population per year) = B0 + B1 × historical asbestos consumption (kg per head per year)

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Table 2. New regression analyses\* on expanded set of countries for age-adjusted mortality rates† of asbestos-related diseases versus historical asbestos consumption‡ | | | | | | | | | | | | | | | | | | |
|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
|  | | |  | n |  | Regression parameters | | | | | | | | |  | Adjusted R2 |  | p value |
|  |  | B0 | (95%CI) | SE | p value |  | B1 | (95%CI) | SE | p value |  |  |
|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| †2010−14, ‡1970−79. | | | | |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
|  | All Mesothelioma | Male |  | 71 |  | -0.251 | (-0.507 to 0.004) | 0.128 | 0.0540 |  | 0.372 | (0.261 to 0.483) | 0.056 | <0.0001 |  | 0.385 |  | <0.0001 |
|  |  | Female |  | 69 |  | -0.456 | (-0.665 to -0.247) | 0.105 | <0.0001 |  | 0.245 | (0.156 to 0.335) | 0.045 | <0.0001 |  | 0.299 |  | <0.0001 |
|  | Pleural Mesothelioma | Male |  | 51 |  | -0.506 | (-0.785 to -0.228) | 0.139 | 0.0006 |  | 0.315 | (0.202 to 0.429) | 0.057 | <0.0001 |  | 0.376 |  | <0.0001 |
|  |  | Female |  | 49 |  | -0.870 | (-1.140 to -0.599) | 0.134 | <0.0001 |  | 0.221 | (0.110 to 0.332) | 0.055 | 0.0002 |  | 0.238 |  | 0.0002 |
|  | Peritoneal Mesothelioma | Male |  | 45 |  | -0.880 | (-1.044 to -0.715) | 0.081 | <0.0001 |  | 0.167 | (0.101 to 0.233) | 0.033 | <0.0001 |  | 0.361 |  | <0.0001 |
|  |  | Female |  | 46 |  | -0.961 | (-1.095 to -0.828) | 0.066 | <0.0001 |  | 0.099 | (0.045 to 0.153) | 0.027 | 0.0006 |  | 0.219 |  | 0.0006 |
|  | Asbestosis | Male |  | 50 |  | -1.024 | (-1.249 to -0.798) | 0.112 | <0.0001 |  | 0.295 | (0.201 to 0.389) | 0.047 | <0.0001 |  | 0.442 |  | <0.0001 |
|  |  | Female |  | 30 |  | -1.477 | (-1.705 to -1.248) | 0.111 | <0.0001 |  | 0.041 | (-0.049 to 0.131) | 0.044 | 0.3599 |  | -0.005 |  | 0.3599 |
|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |

n = number of countries. B0 = intercept of regression line. B1 = slope of regression line. See text for negative R2 value.

\*Regression model: log10(age-adjusted mortality rates of asbestos-related diseases) (deaths per million population per year) = B0 +B1 × historical asbestos consumption (kg per head per year)

Table 3. Parameters B0\* and B1† in the earlier‡ and present expanded§ study for which the log-transformed values were back transformed to enable straightforward comparison

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Table 3. Parameters B0\* and B1† in the earlier‡ and present expanded§ study for which the log-transformed values were back transformed to enable straightforward comparison | | | | | | | | | | | | | | | | |
|  |  |  | B0 Intercept | | | | |  | B1 Slope | | | | | |  |  |
|  | | | ‡earlier study | |  | §present expanded study | |  | ‡earlier study | |  | §present expanded study | |  |  |  |
|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| All Mesothelioma | Male |  | 0.733 | (0.473 to 1.135) |  | 0.561 | (0.311 to 1.010) |  | 2.410 | (1.991 to 2.918) |  | 2.354 | (1.823 to 3.038) |  |  |  |
|  | Female |  | 0.472 | (0.333 to 0.668) |  | 0.350 | (0.216 to 0.567) |  | 1.614 | (1.390 to 1.880) |  | 1.760 | (1.432 to 2.162) |  |  |  |
| Pleural Mesothelioma | Male |  | 0.391 | (0.175 to 0.873) |  | 0.312 | (0.164 to 0.592) |  | 1.807 | (1.282 to 2.547) |  | 2.068 | (1.591 to 2.687) |  |  |  |
|  | Female |  | 0.179 | (0.078 to 0.409) |  | 0.135 | (0.072 to 0.252) |  | 1.327 | (0.935 to 1.884) |  | 1.663 | (1.288 to 2.147) |  |  |  |
| Peritoneal Mesothelioma | Male |  | 0.033 | (0.017 to 0.067) |  | 0.132 | (0.090 to 0.193) |  | 2.153 | (1.603 to 2.891) |  | 1.468 | (1.261 to 1.710) |  |  |  |
|  | Female |  | 0.065 | (0.044 to 0.095) |  | 0.109 | (0.080 to 0.149) |  | 1.355 | (1.151 to 1.600) |  | 1.256 | (1.109 to 1.422) |  |  |  |
| Asbestosis | Male |  | 0.056 | (0.035 to 0.090) |  | 0.095 | (0.056 to 0.159) |  | 2.748 | (2.228 to 3.388) |  | 1.972 | (1.588 to 2.448) |  |  |  |
|  | Female |  | 0.031 | (0.019 to 0.049) |  | 0.033 | (0.020 to 0.056) |  | 1.122 | (0.920 to 1.365) |  | 1.100 | (0.893 to 1.351) |  |  |  |
|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |

\* intercept or background mortality rate

† slope or incremental change of mortality rate

‡ relationship between mortality rate of 2000−04 as the dependent variable and historical asbestos use of 1960−69 as the independent variable

§ relationship between mortality rate of 2010−14 as the dependent variable and historical asbestos use of 1970−79 as the independent variable

Diagram, schematic, scatter chart

Description automatically generated

Figure. Ecological relationship between current mortality rates\* of asbestos-related diseases and historical asbestos consumption†  
(A) All mesothelioma (males, n of countries = 71), (B) Pleural mesothelioma (males, n = 51), (C) Peritoneal mesothelioma (males, n = 45), (D) Asbestosis (males, n = 50). Circles are proportional to the size of sex-specific national populations. \*2010−14, †1970−79. See text for country codes.