

Recent Scientific Evidence Regarding Asbestos Use and Health Consequences of Asbestos Exposure

Manuela Valenzuela¹ · Margarita Giraldo¹ · Sonia Gallo-Murcia¹ · Juliana Pineda¹ · Laura Santos¹ · Juan Pablo Ramos-Bonilla¹

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Abstract To justify the continuous use of two million tons of asbestos every year, it has been argued that a safe/controlled use can be achieved. The aim of this review was to identify recent scientific studies that present empirical evidence of: 1) health consequences resulting from past asbestos exposures and 2) current asbestos exposures resulting from asbestos use. Articles with evidence that could support or reject the safe/controlled use argument were also identified. A total of 155 articles were included in the review, and 87 % showed adverse asbestos health consequences or high asbestos exposures. Regarding the safe/controlled use, 44 articles were identified, and 82 % had evidence suggesting that the

safe/controlled use is not being achieved. A large percentage of articles with evidence that support the safe/controlled use argument have a conflict of interest declared. Most of the evidence was developed in high-income countries and in countries that have already banned asbestos.

Keywords Asbestos · Safe/controlled use · Conflict of interest · Scientific evidence

Introduction

There are two main groups of asbestos fibers, amphiboles and serpentines [1–4]. Amphiboles include amosite, crocidolite, tremolite, actinolite, and anthophyllite [2–6]. Chrysotile is the only type of asbestos in the serpentine group [1–3, 5]. Asbestos has several physicochemical characteristics, including tensile strength and resistance to heat, fire, and corrosion, which result in multiple industrial applications [1, 7]. Therefore, asbestos has been and is still used in a large number of industrial products [1, 4, 6–8].

All forms of asbestos are carcinogenic to humans (Group 1) [1, 2, 9, 10]. Asbestos, including chrysotile, causes mesothelioma, cancer of the lung, larynx, and ovary [1, 2, 9, 10]. The scientific evidence suggests that there is no threshold for the carcinogenic effect of asbestos exposure [1, 4, 5, 9]. Because of its negative health effects, since the 1980s, different countries, especially high-income countries, began to restrict and ban the use of asbestos [2, 11]. The first country to implement a complete ban on asbestos was Iceland in 1983 [12], and by September 2015, 57 countries have banned the production and consumption of all forms of asbestos [13].

Asbestos has been used since ancient times [7], but its consumption markedly increased from the 1920s until the 1980s [2]. At the global scale, the highest level

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✉ Juan Pablo Ramos-Bonilla
jramos@uniandes.edu.co

Manuela Valenzuela
mm.valenzuela3195@uniandes.edu.co

Margarita Giraldo
mm.giraldo337@uniandes.edu.co

Sonia Gallo-Murcia
s-gallo@uniandes.edu.co

Juliana Pineda
ja.pineda920@uniandes.edu.co

Laura Santos
la-santo@uniandes.edu.co

¹ Department of Civil and Environmental Engineering, Universidad de los Andes, Cra 1^a Este No. 19A-40, Bogotá, Colombia

of asbestos consumption occurred in 1977, when approximately 4.7 million tons were reached [6, 11, 12]. Then, asbestos health risks triggered country-wide bans and stringent regulations, which resulted in a worldwide asbestos consumption decline until the late 1990s, when it leveled at two million tons, a consumption level that has been maintained since then with some minor fluctuations [2, 4, 6, 11, 12]. Most of the asbestos currently used is chrysotile (95–100 %) [1, 6, 7, 9], and low- and middle-income countries have a major share in the consumption and production of asbestos at a global scale [1, 2, 4, 9, 11]. Furthermore, in some parts of the world consumption is increasing, especially in Asia [2, 12, 14]. In 2012, 60 % of the global asbestos consumption was concentrated in China (26 %), India (25 %), and Brazil (9 %) [4]. It is estimated that 125 million people in the world are occupationally exposed to asbestos [3, 9], and each year 107,000 people die from asbestos related diseases (i.e., mesothelioma, lung cancer, and asbestosis) [2, 4, 11, 14].

One argument that has been used to justify the continued use of asbestos is that chrysotile asbestos is safe to use because it has a lower cancer potency compared to other asbestos types [15–18]. Although there is some evidence of a potency difference for mesothelioma [3, 4, 16, 19, 20], for lung cancer this potency difference is controversial [3, 5, 18, 19, 21, 22], and for both mesothelioma and lung cancer the potency difference has been strongly contended. Additional arguments to justify the use of chrysotile include that exposure is prevented because chrysotile-containing products are high-density (i.e., non-friable) [16] and that control interventions can be implemented to achieve a safe/controlled use [17, 18]. In many of the studies that argue in favor of a safe/controlled use of asbestos, conflicts of interest of the authors have been identified [1].

This review considers scientific publications over the last 5.5 years (Jan 2010 - Jul 2015), identifying studies that analyze health impacts associated with asbestos exposure, including studies that report no adverse health outcomes. The review also identifies studies that analyze asbestos exposures derived from the use of both asbestos and asbestos-containing products. The primary aim of this review is to determine among recently published scientific studies, how many studies show evidence of asbestos adverse health effects or high asbestos exposures compared to those that show no evidence of asbestos health effects or low asbestos exposures. The distribution of studies that either support or oppose the safe/controlled use argument is also identified. During the review process, for each study it was determined if a conflict of interest was reported and the income level of the country where the study was conducted.

Methods

The search process was conducted using PubMed. Keywords for the search were: asbestos + country name, safe use + asbestos, and controlled use + asbestos. Name of the countries were identified using the list of The World Bank income economy classification, consulted on December 1st, 2015. To be included in the review, articles should have been published between January 1st, 2010 and July 31st, 2015, and only articles written in English were considered. The search process of the keywords involving countries was finalized on January 22nd, 2016. The search process of the keywords involving safe and controlled use was conducted on March 15th, 2016. Once an article was identified, it was downloaded for free through multiple databases with which our institution, Universidad de los Andes, is affiliated.

From the list of titles of the articles that could not be accessed for free, articles that could be relevant for the review were selected. This list of articles was requested through Celsius Network, a software that, among other things, gives access to published articles in libraries that are member of Library Linkage. Because of budget constraints, articles that could not be accessed for free through Celsius Network were not included in the review. Furthermore, some articles that were requested through Celsius Network were not found by the system.

Articles identified in the search process by the country of origin were distributed based on this classification between six readers. There were no specific criteria for this distribution. Since sometimes PubMed classifies articles in a wrong country, the same article may have been included in more than one country and because of this some articles were read by more than one reader.

Since the purpose of the review was to identify empirical evidence regarding asbestos exposures resulting from asbestos use or health consequences derived from the use of asbestos, our readers classified the articles based on pre-established criteria. Three groups of studies were identified:

- 1) Epidemiological studies presenting evidence of the presence or absence of adverse health consequences in populations exposed to asbestos. In this category, studies addressing the following health outcomes were the only ones included: mesothelioma, asbestosis, pleural plaques, lung opacities and thickening, and cancer of the lung, larynx, and ovaries.
- 2) Exposure assessment studies that reported air asbestos concentrations or asbestos exposures resulting from the use of either asbestos or asbestos containing products. Regulatory compliance was also considered in this group of studies if it was explicitly discussed. In some studies, regulatory compliance was determined based on local regulations, which could be different from the

international reference value for asbestos air concentration of 0.1 f/cc.

- 3) Review articles and meta-analysis, if asbestos exposure was assessed in the study.

Articles focused on the following topics were excluded:

- Theoretical and simulation studies.
- Toxicological studies involving animals or in vitro studies.
- Studies analyzing the mode of action by which asbestos induce disease, including studies of genotoxicity.
- Studies presenting treatment options or prognostic methodologies for asbestos-related diseases (ARD).
- Studies that use projections to estimate future number of ARD cases.
- Studies stating that no exposure to asbestos occurred or that asbestos exposure could not be proven.
- Studies in which asbestos exposure was not assessed or determined.
- Studies involving environmental exposure produced by naturally occurring asbestos.
- Studies in which asbestos exposures occurred because of contamination of a material and not because of asbestos use (e.g., diamond mine, talc industry).
- Studies addressing multiple contaminants without individual conclusions for asbestos.
- Studies focused on methods for fiber counting.
- Studies that use information and surrogates constructed in countries or regions different from the one where the study was conducted, to estimate number of people occupationally exposed to asbestos.
- Studies analyzing potential and not validated biomarkers of disease presence or progression.
- Letters to the editor, editorials, responses, or commentaries.

For all the articles included, the following characteristics were determined: 1 – Country where the study was conducted, based on the geographical region of the study, and not the nationality of authors or institutions involved (i.e., if more than one country was involved, it was classified as either regional or global); 2 – Based on the World Bank country income classification (i.e., consulted on December 1st, 2015), the income level of each country was established (i.e., high, upper-middle, lower-middle, or low); 3 – Type of asbestos identified in the study; 4 – Conflict of interest reported by the authors of the study. If at least one author reported a conflict of interest, the article was classified as having a conflict of interest. Conflict of interest was solely determined based on what was reported by the authors in the article, and the researchers involved in this review made no changes on what was reported. If there was no specific report of either

presence or absence of conflict of interest, it was classified as *Not Reported* (NR).

Because of the extremely low number of studies identified in the initial search with evidence of either no asbestos health consequences or compliance of asbestos exposure limits (i.e., eight articles), an additional search was conducted using as keywords the names of some authors whose research has been sponsored by the industry. Three additional studies were identified. This search was conducted between March 27th and April 1st, 2016.

In some studies that complied with the inclusion criteria, it was difficult to define if the results could be used to determine elevated health risks or high air asbestos concentrations or exposures. In such cases, the study was classified as ambiguous.

We also tried to determine if the safe/controlled use concept could be assessed in some of the articles that complied with the inclusion criteria. In this case, studies included were not restricted to those that explicitly analyzed the presence or absence of a safe/controlled use. Thus, studies that did not have as explicit aim an analysis of the safe/controlled use were also included. For this, two types of studies were included in this classification:

- 1 Recent asbestos exposure studies (i.e., considering only asbestos sampling conducted after the year 2000) that found high asbestos concentrations resulting from asbestos use or absence of exposure controls (i.e., which can be considered evidence of lack of safe/controlled use), and recent studies that found no or low asbestos exposure (i.e., which support the safe/controlled use). When an exposure assessment article was not explicit about the year in which sampling was conducted, the corresponding author was contacted to confirm the year of the study.
- 2 Epidemiological studies of populations exposed to chrysotile, that found adverse health effects, not necessarily because of recent exposures, to take into consideration the latency of ARD (i.e., which argues against the safe/controlled use), and studies that, based on epidemiological data, concluded that chrysotile does not cause disease or is less toxicologically potent than amphiboles (i.e., which supports the safe/controlled use).

During a period of 10 weeks, weekly meetings were held between all readers to discuss studies that were difficult to classify, and to verify that the inclusion and exclusion criteria were consistently applied.

A final discussion of all the articles that were included in the review was conducted with all the readers, to verify one more time how each article was classified.

Results

A total of 1516 articles were identified through the search process. After applying the inclusion and exclusion criteria, 155 articles were included in the review. Looking at the consistency of the classification of articles that were read by two or more members of the research team (i.e., 231 articles), 206 articles with multiple readers were classified in similar groups (89 %). For the remaining 25 articles with unmatched classification (11 %), each article was discussed and a classification was determined by consensus.

Articles that were excluded from the review because they could not be accessed for free ($n = 44$), are included in Supplementary Material 1, Table S1. These 44 articles represent 3 % of the total number of articles initially identified.

Table 1 presents a classification of all the articles published between January 1st, 2010 and July 31st, 2015. Table 1 presents both epidemiological and exposure assessment studies as defined above, including all types of asbestos (i.e., amphiboles or chrysotile), and without restricting the moment in time when exposures occurred. Thus, Table 1 could include the analysis of morbidity or mortality of populations exposed to asbestos several decades ago, which is consistent with the latency period of many asbestos related diseases. Table 1 groups articles in three categories, based on asbestos health consequences (i.e., present or absent), asbestos exposure levels (i.e., compliant or non-compliant), and ambiguous when a study could not be classified based on the information it presented.

Most of the studies published in the period analyzed ($n = 134$; 87 %) present evidence of adverse health consequences resulting from asbestos exposures, or extremely high asbestos exposures of people using either asbestos or asbestos containing products. Only 11 (7 %) studies in the period analyzed presented evidence of no or reduced health consequences resulting from asbestos exposure or low asbestos concentrations associated with asbestos use. Ten studies were also classified as ambiguous. Regarding the conflict of interest, most of the studies (69 %) that report adverse health consequences or high asbestos exposures reported no conflict of interest, 8 % of the studies declared a conflict of interest, and 23 % of the studies do not report if there was a conflict of interest. For studies reporting no health effect or exposures in compliance with asbestos exposure limits, 70 % had a conflict of interest, 10 % reported no conflict of interest, and 20 % did not report if there was a conflict of interest.

There were also important differences in terms of the characteristics of the income levels of the countries that produced the scientific evidence. From the 155 articles included in the review, 63 % were conducted in countries with high economies, 21 % in countries with upper-middle economies, and less than 1 % were conducted in countries with lower-middle economies. In the period analyzed, no studies were

conducted in countries with low economies. Fifteen percent of the studies included more than one country, and for these studies an income-economy group could not be specified.

Analyzing in more detail the distribution of studies according to the income level of the countries, not considering studies classified as ambiguous, 145 studies were included in the review. From this, 22 studies were regional (i.e., Asia, Europe) or global, and could not be assigned to a specific country. Thus, 123 studies conducted in a specific country were identified. From these 123 studies, 91 (74 %) were conducted in countries with high economies, 31 (25 %) in countries with upper-middle economies, one (1 %) in a country with a lower-middle economy, and no studies were conducted in countries with low economies. Furthermore, 65 of the 123 studies (53 %) were conducted in countries that have already banned asbestos (i.e., Australia, Belgium, Denmark, Finland, France, Germany, Greece, Israel, Italy, Japan, Netherlands, New Caledonia, Poland, South Korea, Spain, Sweden, and the United Kingdom) [13]. Thus, only 58 studies were identified in countries that currently use asbestos, including 16 studies in the United States and eight studies in Canada, both high economy countries with stringent regulations for asbestos. Consequently, only 34 studies were identified over a period of more than 5 years in countries that use asbestos and do not have high economies. This is an extremely low number, considering that only 57 countries have banned asbestos. In Supplementary Material 2, Table S2 details the percent distribution of income levels of the countries where the studies were conducted.

Table 2 identifies and classifies studies depending on whether the evidence presented supports or not the safe/controlled use. Two types of studies were included in this classification, based on exposure assessment studies that presented evidence of high or low asbestos exposure (i.e., with samples collected after 2002), and epidemiological studies that presented evidence of presence or absence of health effects on populations exposed to chrysotile. All the studies shown in Table 2 were also included in Table 1. Table 2 does not include ambiguous studies.

As shown in Table 2, 44 studies had evidence that either supported or did not support the safe/controlled use argument. Thirty-six studies (82 %) had evidence against the safe/controlled use argument, and eight studies (18 %) had evidence that supported the safe/controlled use argument. Focusing on the studies that did not support the safe/controlled use argument, 11 % reported a conflict of interest, 64 % had no conflict of interest, and 25 % did not report if a conflict of interest was present. For the eight studies with evidence that support the safe/controlled use argument, four (50 %) had a conflict of interest, one (12 %) had no conflict of interest, and three (38 %) did not report if a conflict of interest existed. For studies that present recent evidence of asbestos exposure as a consequence of the use of either asbestos or

Table 1 Scientific evidence of asbestos health effects or asbestos exposures resulting from asbestos use

Income-Economy group	Country/Region	Evidence of presence of adverse asbestos health consequences or high/non-compliant asbestos exposures			Evidence of no asbestos health consequences or compliance of asbestos exposure limits			Ambiguous					
		#	% With conflict of interest		#	% With conflict of interest		#	% With conflict of interest				
			Yes	No		NR	Yes		No	NR	Yes	No	NR
High	Australia	3	[23–25]	-	67 %	33 %	0	-	-	0	-	-	-
High	Belgium	3	[26–28]	-	100 %	-	0	-	-	0	-	-	-
Upper-middle	Brazil	1	[29]	100 %	-	-	0	-	-	0	-	-	-
High	Canada	8	[30–37]	13 %	62 %	25 %	0	-	-	0	-	-	-
Upper-middle	China	14	[38–51]	-	93 %	7 %	0	-	-	0	-	-	-
Upper-middle	Colombia	3	[52–54]	-	67 %	33 %	0	-	-	0	-	-	-
High	Denmark	3	[55–57]	-	100 %	-	0	-	-	0	-	-	-
High	Finland	0	-	-	-	-	0	-	-	1	[58]	-	100 %
High	France	9	[59–67]	-	67 %	33 %	0	-	-	0	-	-	-
High	Germany	4	[68–71]	-	75 %	25 %	0	-	-	1	[72]	-	100 %
High	Greece	1	[73]	-	100 %	-	0	-	-	0	-	-	-
High	Hong Kong	2	[74, 75]	-	100 %	-	0	-	-	0	-	-	-
Lower-middle	India	1	[76]	-	-	100 %	0	-	-	0	-	-	-
Upper-middle	Iran	7	[77–83]	-	14 %	86 %	0	-	-	0	-	-	-
High	Israel	1	[84]	100 %	-	-	0	-	-	0	-	-	-
High	Italy	15	[85–99]	-	67 %	33 %	0	-	-	0	-	-	-
Upper-middle	Jamaica	0	-	-	-	-	0	-	-	1	[100]	-	100 %
High	Japan	6	[101–106]	-	83 %	17 %	0	-	-	0	-	-	-
Upper-middle	Malaysia	1	[107]	-	100 %	-	0	-	-	1	[108]	-	100 %
Upper-middle	Mexico	2	[109, 110]	-	-	100 %	0	-	-	0	-	-	-
Upper-middle	Mongolia	2	[111, 112]	50 %	50 %	-	0	-	-	0	-	-	-
High	Netherlands	2	[113, 114]	-	100 %	-	0	-	-	0	-	-	-
High	New Caledonia	0	-	-	-	-	0	-	-	1	[115]	-	100 %
High	Poland	2	[116, 117]	-	50 %	50 %	2	[118, 119]	-	100 %	1	[120]	100 %
High	South Korea	2	[121, 122]	-	100 %	-	1	[123]	-	100 %	0	-	-
High	Spain	1	[124]	-	100 %	-	0	-	-	0	-	-	-
High	Sweden	4	[125–128]	-	100 %	-	0	-	-	0	-	-	-
High	Taiwan, China	4	[129–132]	-	75 %	25 %	0	-	-	0	-	-	-
Upper-middle	Thailand	1	[133]	-	100 %	-	0	-	-	0	-	-	-
High	United Kingdom	2	[134, 135]	-	-	100 %	0	-	-	0	-	-	-
High	United States	12	[136–147]	34 %	58 %	8 %	4	[148–151]	100 %	2	[152, 153]	100 %	-

Table 1 (continued)

Income-Economy group	Country/Region	Evidence of presence of adverse asbestos health consequences or high/non-compliant asbestos exposures				Evidence of no asbestos health consequences or compliance of asbestos exposure limits				Ambiguous			
		#	Reference	% With conflict of interest		#	Reference	% With conflict of interest		#	Reference	% With conflict of interest	
				Yes	No			NR	Yes			No	NR
-	Asia	1	[14]	-	-	100 %	-	-	0	-	-	-	-
-	Europe	2	[154, 155]	-	100 %	-	-	-	0	-	-	-	-
-	Global	15	[2–6, 12, 19–22, 156–160]	13 %	80 %	7 %	[18, 161–163]	75 %	25 %	2	[164, 165]	100 %	-
Subtotal		134	-	8 %	69 %	23 %	-	64 %	9 %	10	-	40 %	20 %
Total		87 %				7 %				6 %			40 %

asbestos containing products, 15 studies (79 %) identified extremely high exposures that do not support the safe/controlled use concept. From these 15 studies, one reported a conflict of interest, seven had no conflict of interest, and seven did not report if a conflict of interest existed. Four studies (21 %) reported recent evidence of low or no asbestos exposures (i.e., supporting the safe/controlled use argument), in which two had a conflict of interest, and two did not report if a conflict of interest existed. Thus, there were no studies with recent evidence of low or no asbestos exposure with no conflict of interest.

In terms of the income level of the countries where the 44 studies were conducted (Table 2), 36 % were done in countries with high-economies, 55 % in countries with upper-middle economies, 2 % in countries with low-middle economies, and no studies were conducted in countries with low economies. Three of the studies involved multiple countries, and income level could not be determined. All the studies that had evidence to support the safe/controlled use argument were conducted in countries with either high economies (six; 75 %) or in multiple countries (two; 25 %). In Supplementary Material 2, Table S3 details the percent distribution of income levels of the countries where the studies were conducted.

Discussion and Conclusions

This review analyzed scientific studies published between January 1st, 2010 and July 31st, 2015, that presented empirical evidence of either health consequences associated with asbestos exposure or asbestos exposure assessments in occupational or general population settings in which asbestos or asbestos-containing products are used.

Overall, recent scientific evidence confirms once again the devastating effects of asbestos use in the health of populations at the global scale. Most of the studies included in the review had evidence of either adverse health effects or high asbestos exposures (Table 1). Furthermore, we identified 44 studies that had evidence that support or contradict the safe/controlled use argument (Table 2), and most of these studies presented evidence that did not support the achievement of a safe/controlled use of asbestos. Advocates of the safe/controlled use argument could debate that the health effects observed in some of the 44 studies included populations exposed to high asbestos concentrations, which would not comply with the conditions of a safe/controlled use. Thus, we did an independent analysis to identify articles with recent evidence of asbestos exposure resulting from the use of the material (Table 2), and most of them showed that there was no safe/controlled use of asbestos because of high exposures. There were five articles in this group in which the year of the sampling campaign was not explicit. We asked the corresponding authors about the year when sampling was

Table 2 Scientific publications with evidence that supports or rejects the safe/controlled use

Income-Economy group	Country/Region	Evidence of absence of asbestos safe/controlled use		Evidence of asbestos safe/controlled use		Recent low/No asbestos exposure		Evidence that supports asbestos safe/controlled use		
		#	Reference	#	Reference	#	Reference	#	Reference	
				% With conflict of interest		% With conflict of interest		% With conflict of interest		
				Yes	No	Yes	No	Yes	No	NR
High	Belgium	1	[28]	-	1	-	1	-	-	-
Upper-middle	Colombia	3	[52–54]	-	2	-	2	-	-	-
Lower-middle	India	1	[76]	-	-	-	-	-	-	-
Upper-middle	Iran	6	[77–82]	-	1	-	5	-	-	-
Upper-middle	Mongolia	1	[111]	1	-	-	-	-	-	-
High	Poland	0	-	-	-	-	-	-	-	1
High	South Korea	0	-	-	-	-	-	-	-	1
Upper-middle	Thailand	1	[133]	-	1	-	-	-	-	-
High	United States	1	[146]	-	1	-	-	2	[149, 150]	-
-	Global	1	[12]	-	1	-	-	-	-	-
Subtotal		15		1	7	7	7	2	0	2
Income-Economy group	Country/Region	Adverse health effects of chrysotile		Health effects of chrysotile revised/Questioned						
		#	Reference	#	Reference	#	Reference	#	Reference	
				% With conflict of interest		% With conflict of interest		% With conflict of interest		
				Yes	No	Yes	No	Yes	No	NR
High	Canada	1	[34]	-	-	-	-	-	-	-
Upper-middle	China	12	[38–46, 48, 49, 51]	-	12	-	-	-	-	-
High	Italy	1	[94]	-	-	-	1	-	-	-
Upper-middle	Mongolia	1	[112]	-	1	-	-	-	-	-
High	Poland	0	-	-	-	-	-	-	-	1
High	South Korea	1	[122]	-	1	-	-	-	-	-
High	United States	5	[136, 140, 141, 143, 144]	3	2	1	-	1	[151]	-
-	Global	0	-	-	-	-	-	1	[18, 163]	-
Subtotal		21		3	16	2	2	2	1	1
Total		# [%] of studies absence of controlled use	# [%] of studies that support controlled use	% With conflict of interest		% With conflict of interest		% With conflict of interest		
		36	82 %	11 %	64 %	25 %	64 %	50 %	12 %	38 %

conducted, and we received confirmation about the year of the study from four authors. Thus, for only one study [81] and based on the content of the article, we assumed that the asbestos exposure assessment was recent. Since occupational exposure limits can change between countries, exposures classified as in compliance in a country based on local regulations, could have been classified as not in compliance if the international standard of 0.1 f/cc had been used.

Among the 15 recent articles included in Table 2 that reported extremely high asbestos exposure, one article was from Belgium and included exposure to friable asbestos during a renovation of an old building in 2007 [28]. This would not correspond with the conditions of the safe/controlled use. However, Belgium has strict regulations for this type of job and is a high economy country with the financial and technical resources to enforce these regulations, and this study was included because it presents evidence of how difficult it is to control asbestos exposure resulting from the legacy of past asbestos use. This would be more critical in upper-middle, lower-middle, and low economies.

Some of the studies included in the review that analyzed incidence and prevalence of asbestos related diseases, estimated asbestos exposure using asbestos consumption or the location of the asbestos industry as surrogates. We recognize that this could lead to an ecological fallacy.

Most of the studies that presented evidence of no or little health effects resulting from asbestos exposure, or studies presenting low or no asbestos exposures, had a conflict of interest declared. Contrary to that, most studies presenting evidence of adverse health effects resulting from asbestos exposure or high asbestos exposures had no conflict of interest to declare (69 % vs. 9 %, Table 1). This has been observed in other areas of research. For example, two studies analyzing the association between sponsorship and research outcome in the development of new drugs and medical devices found that the results of studies funded by industry were more likely to favor the product of the sponsor, compared to studies with other funding sources [166, 167]. In a recent review of the potential effect of sponsorship in animal studies analyzing the effects of Atrazine, the authors found that studies that were not funded by industry were more likely (p -value 0.07) to conclude that atrazine had adverse effects compared to studies funded by industry [168].

We also identified some studies ($n = 4$) in which the authors declared they had no conflict of interest, but this declaration was followed by an acknowledgement of funding that clearly created a financial conflict of interest. For the purposes of this review, the declaration of the authors of the study (i.e., no conflict of interest) was maintained, but this is something that requires further discussion. A conflict of interest exists and must be declared if the authors have received funding that could potentially compromise the design and implementation of the study, as well as their judgment, recognizing that

declaring a conflict of interest does not necessarily mean that the study has been compromised. However, this is not a decision that the authors can make, and if a financial conflict of interest exists, it must be declared. The declaration of conflict of interest by authors should be verified with diligence by all journals, to prevent situations like the ones described above. Furthermore, from the original 155 articles identified, 38 did not report if a conflict of interest existed. All journals should have a mandatory requirement for a disclaimer of conflict of interest, especially in controversial topics like asbestos health consequences and use.

One concerning aspect of this review is the extremely low number of articles published in upper-middle, lower-middle, and low economy countries. Since most of the studies included in the review have been conducted in countries that have already banned asbestos or have stringent regulations on the material, exposure levels identified in this review could underestimate actual asbestos exposures occurring in low- and middle-income countries.

Regarding the countries that are the major producers (Russia, China, Brazil, Canada, Zimbabwe, Colombia) and consumers (China, India, Brazil, Russia, Indonesia, Kazakhstan, Thailand, Ukraine, Uzbekistan) of asbestos in the world [1, 2, 11], no studies were found for this review from Russia, Zimbabwe, Indonesia, Kazakhstan, Thailand, Ukraine, and Uzbekistan. Furthermore, three major players of the asbestos global trade, China, India, and Brazil, had what seems to be a rather low number of studies considering the volume of asbestos these countries produce and consume. Brazil and India only had one study each, and China had 14 studies. Thus, it is intriguing how with such a low number of scientific studies, especially in countries that use asbestos and in some cases in extremely large volumes, it could be argued that the material can be sold because there is a safe/controlled use. In fact, the majority of the little evidence that has been produced in countries that consume and produce asbestos suggests that a safe/controlled use of the material is not happening.

As authors we applied several quality control strategies to conduct the review. We specified in the framework of our aims clear inclusion and exclusion criteria. We held regular meetings to discuss those articles that were difficult to classify and the classification was reached by consensus. We had a percentage of articles (i.e., 231, 15 %) read by more than one person (i.e., blinded) to double check the way studies were classified, and for 89 % of the articles with two or more readers there was coincidence in the classification made. Finally, when closing the review, we did a group discussion, one by one, of the 155 articles included in the review. However, we acknowledge that there is always the possibility of human error in a review of this size. We may have missed articles that should have been included in the review, and we may have misclassified some articles in the process. Thus, we

invite other authors to build on the work we are presenting in the current review, to improve if necessary what we have done.

In closing, the scientific literature published in recent years confirms the negative consequences derived from the historical use of asbestos. Moreover, most of the studies that could be used to determine if a safe/controlled use of asbestos is being achieved suggest that current asbestos use is resulting in high asbestos exposures. We also found very few studies analyzing the use of asbestos containing construction products, which is one of the categories of asbestos products with the highest production and consumption at a global scale. The scientific literature does not seem to support the safe/controlled use concept, and we join other authors, once again, in a call for a global ban of asbestos.

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Compliance with Ethical Standards

Conflict of Interest Manuela Valenzuela, Margarita Giraldo, Sonia Gallo-Murcia, Juliana Pineda, Laura Santos, and Juan Pablo Ramos-Bonilla have no conflict of interest to declare.

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