Journal of Trace Elements in Medicine and Biology 71 (2022) 126948

Contents lists available at ScienceDirect

Journal of Trace Elements in Medicine and Biology

journal homepage: www.elsevier.com/locate/jtemb

Association between lead source exposure and blood lead levels in some lead manufacturing countries: A systematic review and meta-analysis

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ARTICLE INFO

Keywords:
Lead source exposure
Mean difference
Blood lead level
Meta-analysis

ABSTRACT

Lead is one of the 10 most toxic chemicals of greatest concern for its effects on public health. Predominantly, in undeveloped countries, high blood lead levels (BLLs) persist in the population. To develop intervention strategies that may reduce lead exposure in populations, it is a priority to know the sources of lead pollution. The objective of this critical review and meta-analysis is to assess whether there is an association between different sources of lead exposure and the mean difference in blood lead levels in people exposed. To identify the major lead source exposure, a statistical analysis was performed on selection studies. This investigation reveals the limited information available on the sources of lead in Mexico and other lead producer countries, such as Croatia, Ecuador, Brazil, South Korea, India, Nigeria, Turkey, and China. Meta-analysis could be performed only in battery, smelting mining, and glazed ceramic workers. Battery manufacturing workers have the highest mean difference level of lead in their blood worldwide. Mexico has the second highest mean difference BLL in battery workers in the world. An interesting difference between the mean difference in BLL in mining workers from uncontrolled industry (−39.38) and controlled industry (−5.68) was found. This difference highlighted the success of applying strict control of lead sources and community education to reduce BLL and its potential harmful effects on human health and the environment. Children living near mining sites have the highest mean difference BLL (−11.1). This analysis may aid in assessing the source of lead exposure associated with a range of BLLs in people. Furthermore, this review highlights several social and cultural patterns associated with lead exposure and lead levels in control populations. These results could help to develop international lead regulations and appropriate public health guidelines to protect people around the world.

1. Introduction

Lead is a heavy metal widely used to manufacture paints, lead acid batteries, solders, glazed ceramics, cosmetics, and traditional medicines, and in refining and smelting. The International Lead and Zinc study group reported that, in 2018, worldwide lead production and consumption had increased 0.4% and 0.2%, respectively, compared with 2017 [1], with approximately 80% of produced lead used to make batteries. Industrial wastes containing lead pollute the air, soil and water, resulting in extensive worldwide lead environmental contamination [2].

Exposure has neurotoxic effects in children and nephrotoxic, cardiovascular and carcinogenic effects in adults [3]. In addition, lead is stored in human bones for approximately 15 years [4]. The Institute for Health Metrics and Evaluation estimated that exposure to lead accounted for 1.06 million deaths and 24.4 million years of healthy life lost in 2017 [5].

Because of its widespread use, extensive environmental contamination and public health concerns, lead has been classified by the World Health Organization (WHO) as one of the top 10 hazardous chemicals in the world. Lead pollution remains a serious problem in lead-producing countries such as Mexico.

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https://doi.org/10.1016/j.jtemb.2022.126948
Received 14 October 2021; Received in revised form 5 February 2022; Accepted 8 February 2022
Available online 11 February 2022

The identification of sources of lead exposure can establish appropriate public health guidelines. Isotopic analysis can determine sources of lead exposure only in some specific conditions. The associations between mean blood lead level (BLL) and sources of lead exposure have not been determined.

Two types of studies have assessed BLL in human populations. In one type, the source of lead exposure is known. The other type involves the general population, in which the source of lead has not been clearly determined. This meta-analysis of selected studies assessed whether different sources of lead exposure were associated with differences in BLL in exposed populations.

The determination of associations between lead sources and BLL ranges can enable the identification of sources of lead exposure.

2. Methodology

2.1. Search and selection of literature

This research was carried out following the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) Statement [6]. The English literature search was conducted using the PubMed and Web of Science databases. Additionally, Google Scholar was consulted to include secondary sources of information not available in those databases of the following nature: Mexican and foreign regulations, book chapters, old nonindexed publications, journalistic notes, and scientific bulletins (19, in total). The period covered by the search for articles was from October 30th, 1975, to October 6th, 2021, with the participation of five independent authors who argued and selected them. Research terms (search keywords) kept a similar or derived format from the phrase "lead exposure", followed by the country or source of exposure, such as: Lead exposure Mexico People, lead exposure glazed ceramic, lead exposure acid battery, lead exposure-based paint, lead exposure toys, lead exposure folk remedies. However, the last two terms of “smelter and mines” resulted in an exception from the previous style due to ambiguity and little precision of the same that resulted in many records. Therefore, it was decided to change the search term to "blood lead levels in" after “smelter and mines”.

This systematic review uses the following eligibility criteria for articles chosen: 1) Studies that specifically evaluate the outcomes of populations exposed to sources of lead; 2) Assessment of lead exposure by the blood lead biomarker; 3) Investigations with other biomarkers or other metals if they report blood lead; 4) Publications with populations of more than 10 participating individuals (exception was a family with 5 individuals [7]). Lead studies, in vivo and in vitro experimentation, toxicity mechanisms, standardisation of analytical techniques, determinations in environmental samples and unrelated searches (off topic) were excluded.

2.2. Data extraction and quality of evidence

Five of the coauthors independently examined each publication to extract data on first author, year of publication, study location, type of study, type of exposure, occupation (working time), sex, age (children or adults), lead quantification methods, and blood lead level (geometric mean or arithmetic mean, interval). For the meta-analysis, in addition to the mean value of the biomarker, the standard deviation and the total number of participants in the experimental and control populations were extracted. To assess the quality of the selected studies, the Strengthening the Reporting of Observational Studies in Epidemiology-Molecular Epidemiology (STROBE-ME) criteria were adopted, which consider 28 elements to evaluate [8]). Among the most important are the following: specification of the biomarker, study design, statistical analysis method, distribution of the biomarker and interpretation. The methodology includes a scoring scale for the degree of the information found: 0 (not reported), 0.5 (partially reported) and 1 (complete). Furthermore, according to the number of total points obtained in the evaluated publications, quality intervals were established: 0–10 points, 11–19 points, and 20–28 points corresponded to low quality, medium quality, and high quality, respectively.

2.3. Statistical Analysis

The meta-analysis was carried out in RevMan software version 5.4 (Review Manager, Copenhagen: The Nordic Cochrane Center, The Cochrane Collaboration, 2011) and aimed to find the mean BLL of workers according to their source of lead exposure to compare with others. For this reason, the mean comparison test was used under a random effects model, followed by the report of their respective 95% CI (confidence interval) and the representation in forest plots. Heterogeneity was calculated using the I2 statistics. A p value < 0.05 was considered to establish significant differences in the analysis performed.

3. Results

The initial phase of identification in the databases yielded a total of 4008 records, including 743 duplicates, whose purification yielded 3265 publications with scannable titles and abstracts (see Fig. 1 "Prism Graph"). After applying the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE-ME) criteria [8], in this systematic procedure, 80 review reports were selected. An additional 19 references corresponding to ancient text, legal rules of regulation, newspaper articles, web pages or articles were included. For the meta-analysis section, 69 reports were included from the 80 selected by STROBE-ME. We included 50 case studies for meta-analyses of exposed lead workers and 19 for children exposed to lead sources. In another way, the percentage of the quality of the publications was 73.87% high quality (82/111) and 26.12% medium quality (29/111) in the systematic review. It should be noted that studies of high-quality nature differ very little from those within the medium range, only by including a greater number of statistical measurement models and evaluating more biomarkers that slightly increase the final weighting, but in the end, both kinds contribute the necessary data to carry out the meta-analysis itself. (See 3. A Appendix).

3.1. Historical lead uses

In ancient Mexico, the Aztecs were acquainted with lead, which was known as Tnetzili (moonstone) [9]. Ancient ceramic shows a low lead concentration in pre-Hispanic Mexican pottery. The extended and excessive use of lead in Mexico did not occur until the introduction of lead glazing during the 16th century, which offered an alternative option to the burnished ceramic method (still employed today) [10]. In the world, the use of lead dates to ancient civilisations such as the Egyptian or the Sumerian who were unaware of the toxicity of this metal. It was not until the 2nd century B.C. that Nicander of Colophon described the first clinical manifestations resulting from exposure to lead minerals such as Litharge and Cerussite. At the end of the Middle Ages and during the Renaissance, lead poisoning was already considered a disease particular of goldsmiths, painters and miners, and the first “epidemics” of lead poisoning were recorded. Analysis of the Greenland ice sheets has shown lead deposits comprising a total of approximately 400 tons. These findings are attributed to the mining and smelting of lead ore that took place at the time of the Roman civilisation [11]. The first Mexician study, “Envenenamiento lento por plomo en los habitantes de Oaxaca”, was published in 1878. This study describes the considerable health risks of salts used in the glazing of ceramics and warns of the need for regulatory policies on their use [12]. Last century, a description of saturnism (lead poisoning) in ceramic artisans in a small town in Mexico was published [13].

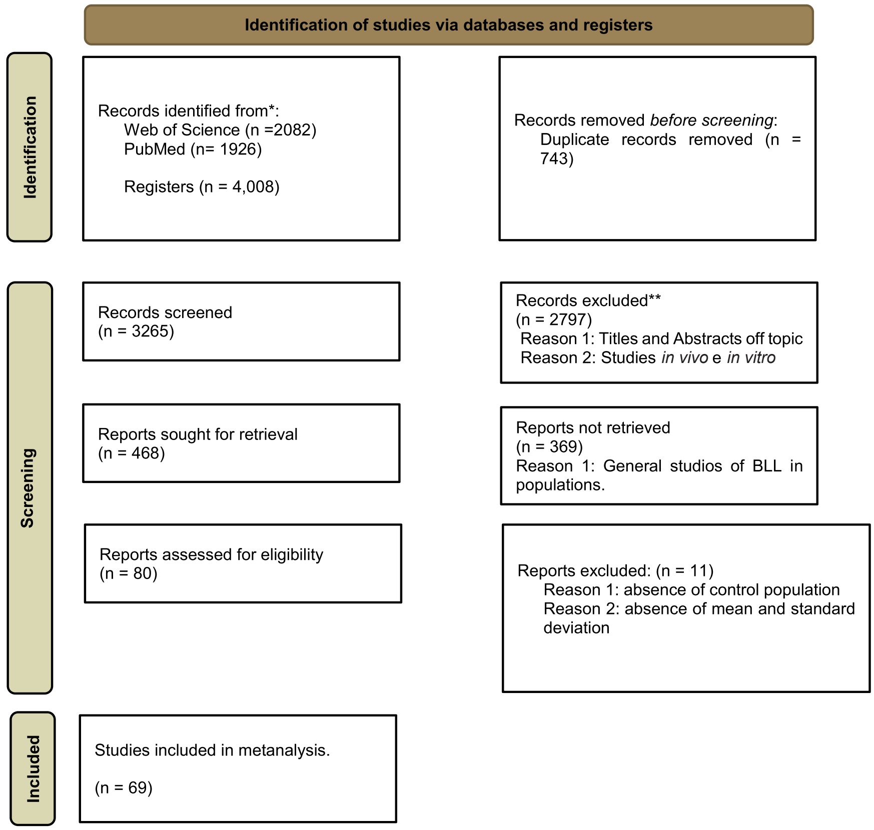

Fig. 1. Diagram of the report identification and screening process (PRISMA).

3.2. Current sources of lead exposure

3.2.1. Glazed ceramics

This lead source exposure is the most documented exposure in Mexico, and traditional cooking utensils consist of glazed clay pottery (GCP). The glaze is made by applying lead oxide. Cooking at high temperature and acid meals detaches lead particles from the enamel. This results in lead concentrations up to 2300 mg/kg in food [14].

The use of glazed ceramic is constant in Mexico. In 1991, approximately 30% of Mexico's urban population used GCP for cooking and storing food, and 22% of this population showed a BLL > 15 μg/dl [15]. Recently, one study showed that 34.5% of participants reported having used GCPs, and 21.8% of this population showed a BLL higher than ≥ 5 μg/dl; this value is still considered dangerous [16].

Studies in Mexico of populations exposed to lead due to the use of glazed ceramic over a period of 30 years are not included in our meta-analysis (1989–2019). Since they do not accomplish the statistical requirements for it. However, important points need to be considered. High variability is observed among the BLL values found in the studies. The investigations were conducted in areas of Mexico City, Oaxaca, and Morelos, whose populations reported the use of GCP to prepare or serve food. We can see that a high BLL was measured in Mexico City's children before the ban of lead usage in gasoline. The recorded values of BLL went from an arithmetic mean of 24.3 μg/dL [17] and 15.2 μg/dL [18] for two children's studies prior to 1997–8.4 μg/dL [19] and 8.6 μg/dL [20] for similar studies.

A reduction in BLL in children is correlated with a reduction in the lead level in the air. The proportion of BLL > 5 μg/dL decreased from 92% in 1998–8% in children aged 1–5 years in 2015 [21].

However, after 1998, BLL measurements remained constant over the years for different regions.

In the state of Morelos, the arithmetic mean reported in two cross-sectional studies performed 11 years apart showed a constant mean BLL in children: 8.20 μg/dL in 2003 and 7.23 μg/dL in 2014 [22]. In Oaxaca state, another investigation reported childrenś BLL with a geometric mean (GM) of 10.5 μg/dL [23]. In the same region, 15 years later, another report showed a BLL geometric mean (GM) of 13 μg/dL, showing similar values after the last study [24].

There is a difference between the prevalence of 21.8% in children with BLL > 5 μg/dL, [16] and 8% in other children [21]. This is probably due to the population sample studied and the prevalence of GCP usage outside of Mexico City.

For adults using glazed ceramic in Mexico, only studies before the official removal of lead in gasoline in 1997 were found. The mean BLL is not higher than 20 μg/dL in ceramic users [25,26].

The problem of the use or manufacture of GCPs spreads outside Mexico. Lead poisoning from a beverage stored in a lead-glazed earthenware jug was reported in France [27]. In Ecuador, 53 children with BLL levels of 4.2–94.3 μg/dL indicative of acute intoxication were investigated; the source of lead exposure was found to be GCP [28].

3.2.1.1. Glazed ceramics workers meta-analysis. In this section, a meta-analysis was performed on selected studies to assess the effect on BLL in people exposed to lead from working with glazed ceramics worldwide. Only three countries have enough studies for meta-analysis.

Running the meta-analysis found a mean difference in BLL summary of − 21.97 for a total of 819 GC workers. Interestingly, the mean BLL of Ecuador workers was higher (−28.8) than that of Mexican workers (−17.47). This result is due to the high mean BLL in the control Mexican group (> 20 μg/dL). However, this difference was not statistically significant due to the overlap between the studied groups (considering a 95% interval) (Fig. 2).

3.2.2. Batteries

Approximately 85% of the worldś lead consumption is due to the production of lead-acid batteries (LABs), and the automotive industry is

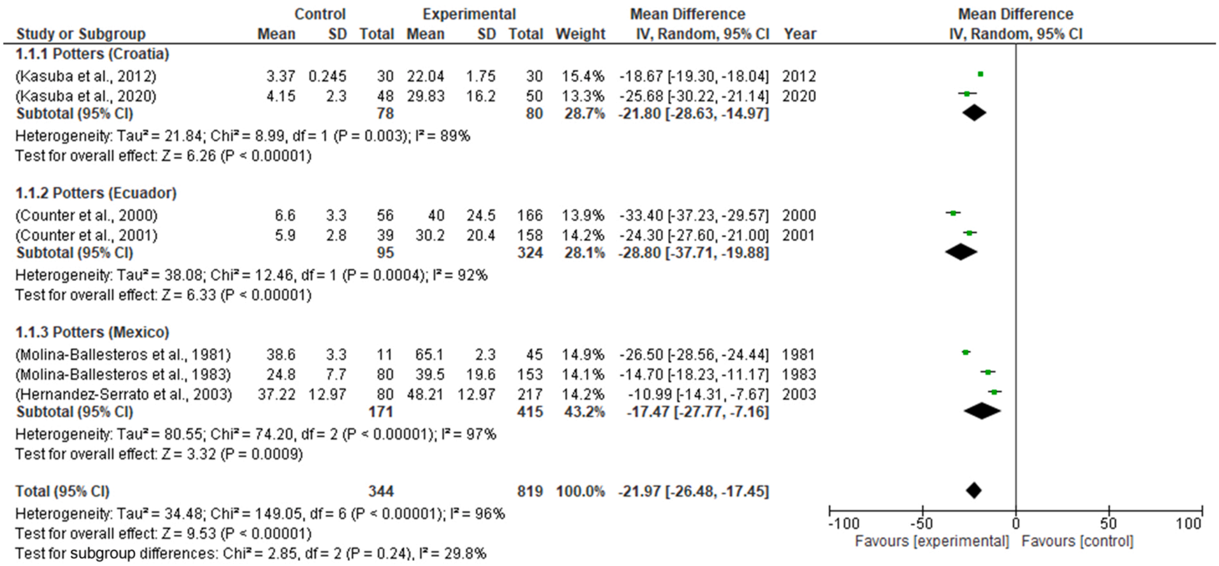

Fig. 2. Forest plot graph showing the effect of lead exposure on the mean difference in blood lead levels of pottery workers from Croatia (1.1.1), Ecuador (1.1.2) and Mexico (1.1.3).

increasing its demand. The most common system for recycling LAB in developed countries is collecting and transporting LAB to smelting plants in reverse distribution; the spent units are collected by the manufacturer and sent to a secondary lead smelter for recycling. This process is enclosed and reduces toxic emissions. In underdeveloped countries, most batteries are collected in rural areas or through small family businesses. Lead and sulphuric acid content in electrolyte solution release into the air usually results in contamination of water, soil, homes and food [2].

Battery production is cheaper in developing countries than in developed countries due to low local wages and unchecked environmental regulations [29,30]. We found HIGH environmental lead levels associated with the LAB industry in developing countries. In Mexico, high levels of lead in the soil of specific sites, at least 1000 mg/kg at a lead battery factory site in Monterrey [31] and over 40,000 mg/kg at a lead battery recycling site in Tepetlaoxtoc [32]. In other parts of the world, the same pollution problem is found; in Nigeria, a study of discharges from a battery manufacturing plant found high levels of lead in the soil, 102 mg/kg. [33]. In Ghana, airborne lead levels range from 522.83 μg/m^3 to 2 820.3 μg/m^3 [34]. All lead levels figure above the recommended international standards [2].

Differences between the arithmetic means of the BLL in LAB industry workers from developing countries (64 μg/dL) and developed countries (25 μg/dL) are found. Informal recycling in low- and middle-income countries causes 495,550 deaths per year [2].

In our analysis, in a few reports of LAB workers, the mean BLL was below 25 μg/dL, one in Barbados [35] and three in China [36–38]. In other studies, people who were not workers, such as children, showed BLL below 25 μg/dL [39–42]. Some studies with BLLs above 25 μg/dL come from battery workers from developed countries [43–45] at different times. However, most of them come from undeveloped countries where the mean BLL of workers is higher than 45 μg/dL [46–49]. Few studies are on children, for example, a case of a family who lived in a place that was once an LAB work site [7].

Massive lead poisoning was reported in a LAB recycling community in Senegal; eighteen children died from lead encephalopathy, and BLL in the population studied had a GM of 129.5 μg/dL [47]. In Vietnam, a study showed that for 109 children from family businesses involved in lead recycling, 72% had BLL between 26.3 and 44.9 μg/dL, while 28% had BLL $\geq$ 45 μg/dL [50].

To assess the mean difference in BLL among LAB workers in some countries, a meta-analysis was performed on studies that had statistical requirements.

3.2.2.1. Battery workers meta-analysis. Fig. 3 shows that the highest mean difference BLL value was for Turkey (−81.59), followed by Mexico (−64.42), among the countries under study. Moreover, there is no significant difference between these two countries since interval values overlap. These countries have higher mean difference BLL than the mean global of six countries which is − 46.35. India is the country with more studies included in this kind of statistical analysis and with higher heterogeneity. Nigeria has a low mean difference in BLL due to high BLL in the control population studied, and the mean control BLL is at least 40 μg/dL [51].

The heterogeneity between the groups was similar and high (>75%), except for Mexico. This country has 0% heterogeneity with a very similar mean difference in BLL over the years.

In the world, the most studied group for health lead effects is children. However, some studies show the adult's health effect for lead exposure. One data study spanning 1925–1976 suggests that high BLL could be a factor behind an excess of deaths from renal disease and stroke in lead workers [52]. A more recent study found an association between blood lead levels and respiratory, gastrointestinal and musculoskeletal morbidities among 391 workers at a lead-acid battery factory [53]. In addition, genotoxic effects have been documented by comet, micronucleus and chromosomal aberrations in buccal epithelial cells of battery recycling workers [54]. Such health risks are significant for communities living near battery industries. The introduction of measures to control these activities should be a priority in these countries.

3.2.3. Smelting

The smelting industry is an important source of lead risk worldwide; however, few studies have been conducted to address this issue. In Mexico, an investigation of the population living within 1 km of a lead smelter located in the city of Torreon gave a mean BLL of 17. 3 μg/dL for 98 children [55]. A recent report at the same site found that for 50.6% of children living within 3.5 km of the smelter, the BLL was greater than 10 μg/dL [56]. A similar study in another Mexican region of 50 children living near a mining area found that their mean BLL was 9.4 g/dL [57].

China is one of the largest producers and consumers of lead in the world. Ninety percent of the childrens BLL levels exceeded the WHO standard (< 5 μg/dL). Other health effects, such as renal damage and

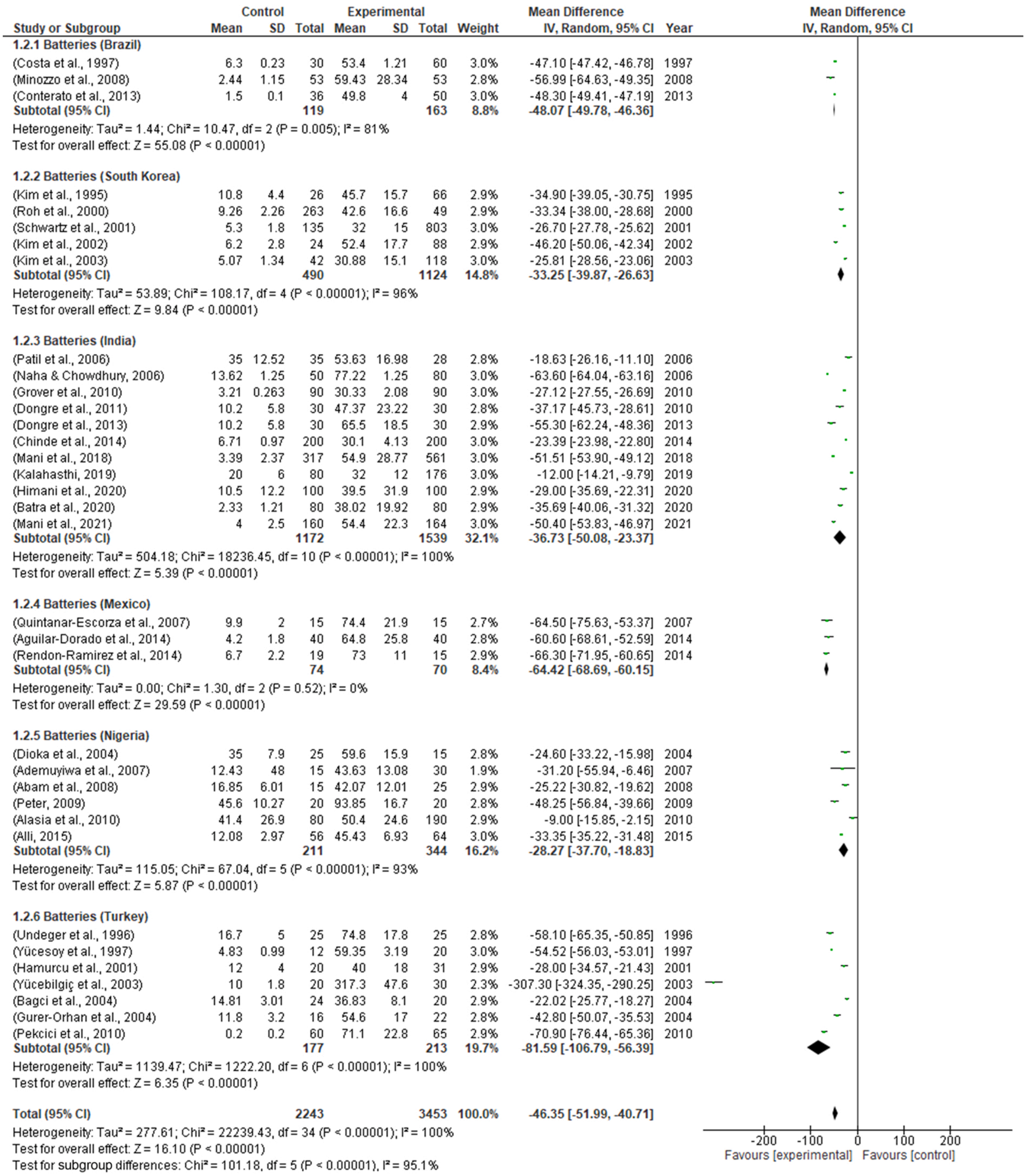

Fig. 3. Forest plot effect of battery industry sources on the mean difference in BLL in exposed workers worldwide.

relatively complex cancers, were reported [58]. In South Africa, where mining is one of the main economic activities, the impact of lead on children has been investigated. A study found a mean BLL of 15.9 μg/dL and lower school performance in children living in a mining town [59]. An Armenian study by Grygoryan et al. assessed BLL in children living in three communities adjacent to metal mining and smelting industries; the authors found geometric means of 6.0 μg/dL, 6.4 μg/dL, and 6.8 μg/dL for these communities, indicating an urgent need to promote and enforce safe industrial practices and stricter environmental regulations in these areas [60].

3.2.3.1. Smelting meta-analysis. For the meta-analysis of BLL on smelting mining workers, two subgroups were made: regulated (control) and nonregulated industries. These exclusion criteria were clearly explained in the studies about safety measures in industries. Lower mean differences in BLL were found in the control industry. In this case, (Fig. 4), no overlap in the examined groups was observed. A statistically significant difference was found between them. Additionally, for the regulated mining and smelting industry, the mean difference BLL is lower.

3.2.4. Meta-analysis of lead workers exposed to glazed ceramic, battery, and mining

Meta-analysis was performed on 8525 individuals: 5223 lead-

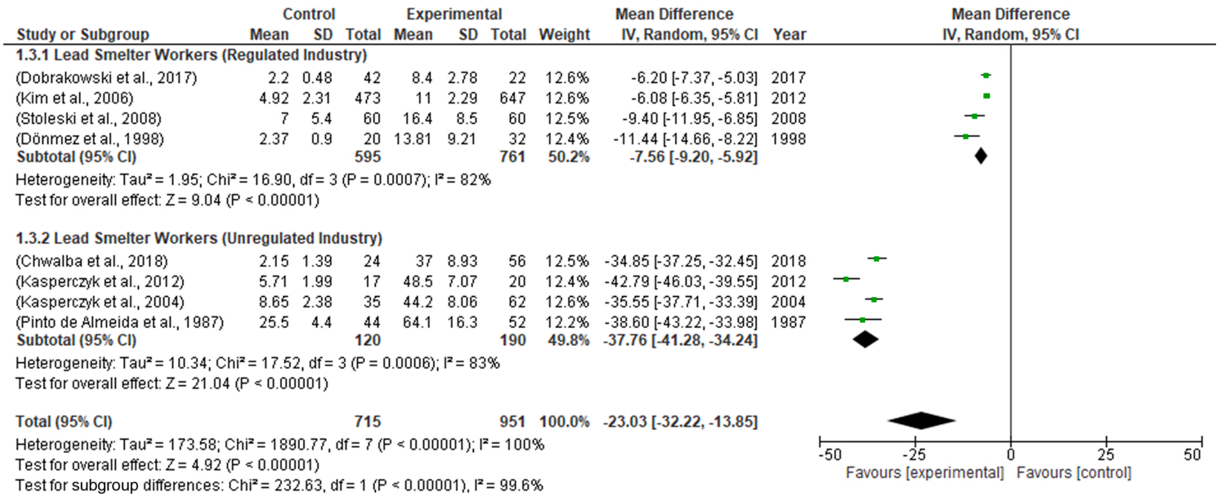

Fig. 4. Forest plot graph that expresses the comparison between the mean difference in blood lead levels of mining smelter workers (regulated industry) and mining smelter workers (nonregulated industry).

exposed workers and 3302 controls. We used data only from battery-, glazed ceramic- and mining-exposed workers since we found studies with the requirements needed for statistical testing in this group of workers. The results (Fig. 5) show that battery workers have the highest mean BLL with a − 46.35 difference. This group has a higher number of studies found and analysed for meta-analysis. High heterogeneity was found due to different dates and countries that were analysed. Nevertheless, in this group, only two studies had lower values (−12 and- 9), and most of the studies had higher BLL than the other worker groups analysed. Most of the lead extracted in the world is used in the battery industry, and it is important to conduct more studies in countries such as Mexico, Turkey and Africa to obtain control measurements.

Another important point is the mean BLL difference between the nonregulated and regulated mining industries (−37.76) vs. (−7.56), respectively. This difference highlights the importance of taking measurements to reduce toxic exposure in industry. For the GC group, the analysis is difficult. Due to the high BLL in the control in the first three old studies, the group results in a lower mean difference in BLL in workers. Nonetheless, this lead source exposure is very important worldwide, with a mean control difference of BLL − 21.97.

3.2.4.1. Meta-analysis of lead children exposed to glazed ceramic, battery and mining. Only a small number of studies have the requisites to be included in meta-analysis for lead children exposed. A lower mean BLL difference was found in comparison to exposed adult workers. In contrast to workers, in this group, children living near mining smelting sites had the highest mean BLL (−11.1). Children living in mine tailings (−6.83) have lower mean difference BLL than those who live near mining smelting sites, probably this waste material from the mine process has low lead concentration. Children exposed to lead living near the battery industry or with relatives working in this industry have the second highest mean BLL difference (−9.43) of all the analysed groups. For children exposed to GCP used for cooking and to store food at home, the mean BLL was − 6.02. There was an overlap in the mean difference in BLL in children for all groups (Fig. 6).

3.2.5. Paint and pigments

There are few studies about BLL in paint workers. A former study of 25 building painters not exposed to an alternative source of lead found that their average BLL was 10.48 μg/dL [61]. In the U.S., a recent analysis of BLL in painters showed that BLL increased 10 μg/dL two months after initial exposure, and 11% of workers after 4 months of paint exposure had BLL higher than 30 μg/dL [62]. In India, 35 paint workers with 5–12 years of employment show a mean BLL of 21.64 μg/dL [63]. However, there is no correlation reported between lead content in paint and BLL in any study to date.

Lead compounds (lead chromate, lead oxides, and basic lead carbonate) are used in paint as primers, pigments and driers. In countries such as China and the United States, the regulatory limit of LBP is 90 ppm [64]. A recent review shows that the lead content in enamel paint in Mexico is the highest in Latin America at 51,860 mg/kg; in contrast, Uruguaýs lead content in this paint is 9.8 mg/kg. The same study found that paint produced and sold in developing countries contains thousands of times more lead than in developed countries [65]. In a US report, it was found that eating paint is a risk factor in children for lead poisoning (BLL of 45 μg/dL) [66]. However, the risk of lead exposure in homes painted with lead-based paint is due to paint deterioration that contaminates dust and soil. However, information on BLL in people living in these homes is limited.

3.2.6. Toys

In addition to paint, lead is added to polyvinyl chloride (PVC) used in toys to give stability, brightness and flexibility. The smallest kids are more vulnerable to lead intoxication because of their habits of biting and chewing toys.

The International Organization for Standardization establishes that the acceptable limit for lead migration in toys is 90 ppm. This limit is similar in many countries, such as Mexico [67], Australia and Canada [68] and the United States [69].

Despite this regulation, the Consumer Product Safety Commission (CPSC) in the U.S. found excessive levels of lead in the paint of Mexican toys [70]. In the world, a wide interval of lead levels in toys is found. China is the largest exporter of toys in the world; approximately 80% of the world's toys come from China. In Nigeria, 25 samples of toys imported from China have lead levels of 36.1 to − 106 mg/kg. [71]. Another analysis of Chinese plastic toys found that 27 out of 72 analysed exceeded the lead level of 100 mg/kg [72]. Similar results were found on a sample from the three largest online shopping platforms in China; toys from two of them were found to have an average lead concentration of 25 mg/kg and 32 mg/kg, while the third measured 219 mg/kg [73].

In India, 97 samples of toys were analysed, and lead levels were above permissible limits in 22 of 97 samples [71,74]. An investigation of toys sold in Bogota, Colombia analysed 116 samples of paint of the samples, and only 8 presented lead levels between 244 and 47,600 ppm [75].

Globally, high lead levels in toys have been reported in many countries, such as China (860,000 ppm), South Africa (145,000 ppm), the United States (22,500 ppm), Palestine (6036 ppm), Thailand

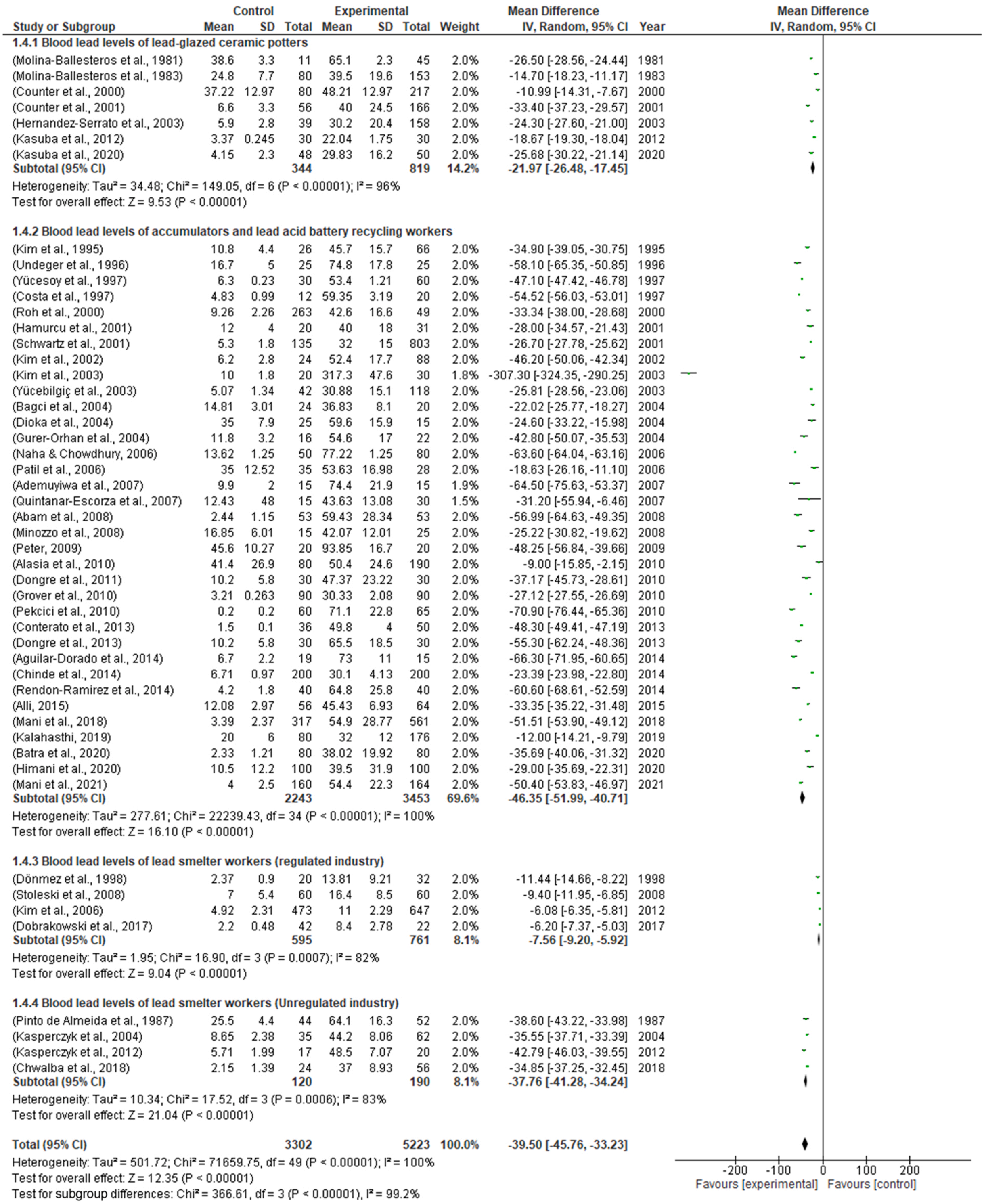

Fig. 5. Forest plot shows the comparison between the mean difference levels of lead in blood from the workers of lead acid batteries, glazed ceramic, mining-foundry (Regulated and Unregulated) industries.

(4486 ppm) and India (2104 ppm) [76].

In the world, a surveillance programme to monitor lead content in childrenś toys and other items used by children is lacking. Moreover, BLL in children using these toys is not known; consequently, the severity of the problem is not well known.

3.2.7. Folk medicine

The scarce economic resources and cultural reasons in some regions of Mexico make traditional medicine the first medical option. “Azarcon” (lead oxide) is added in small portions to childrenś bottles; cases of Azarcon poisoning have been reported in children between nine months and five years old [77]. In other rural communities in Baja California, Mexico, intestinal or stomach illnesses are generally treated with azarcon [78].

The use of folk remedies containing lead extends to other parts of the world. Ayurvedic medicine, a traditional Chinese system practised

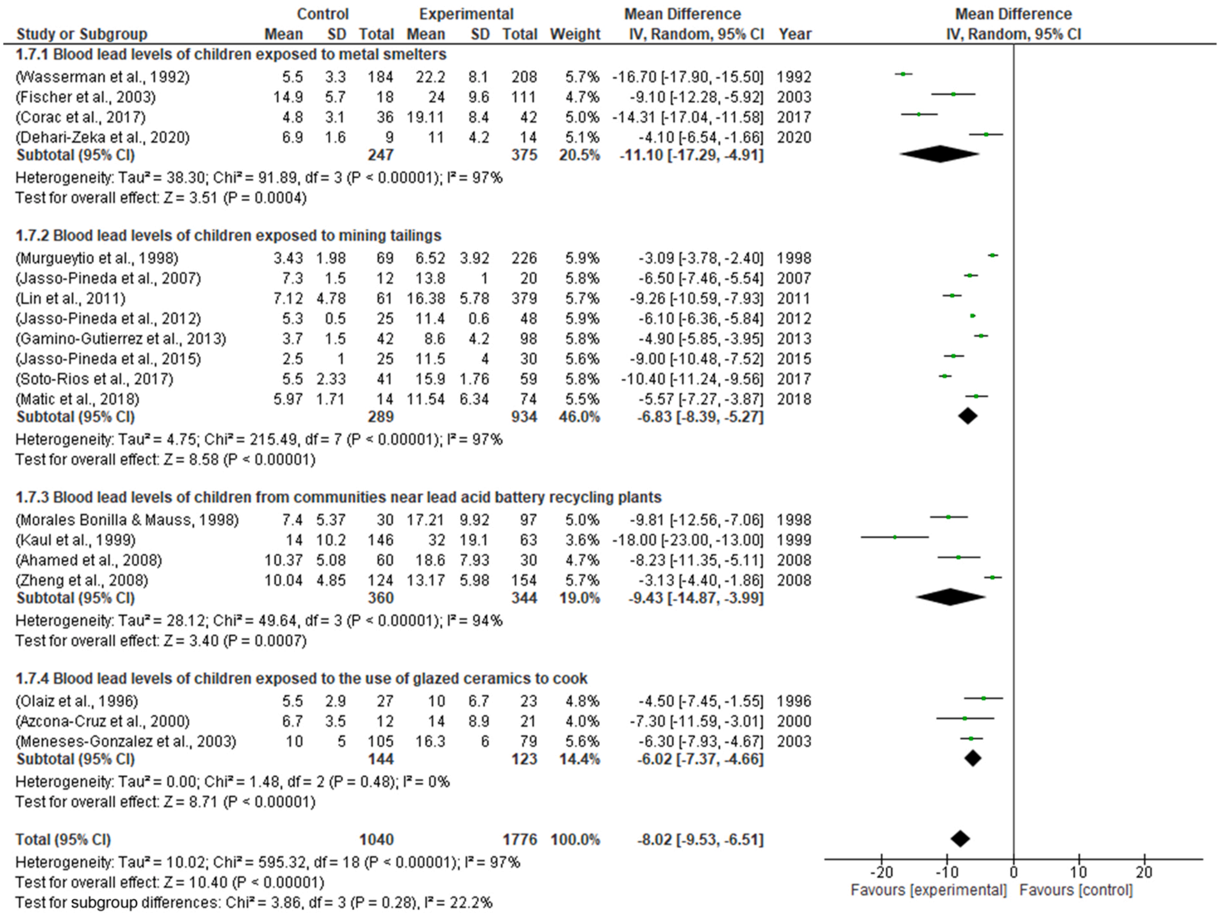

Fig. 6. Forest plot graph for comparison between sources of lead exposure and mean difference of blood lead levels in children.

mainly in India, includes lead in its remedies. Used by up to 80% of the Hungarian population, [79]. In Australia, herbal medicines, particularly Indian Ayurvedic preparations, as well as those of Chinese origin, are also sources of lead risk for Australian adults [80].

Only in lead poisoning cases is the BLL reported; for folk remedies, users' ID is not known. Child lead poisoning associated with lead-based folk remedies has been reported in the United States, mostly among immigrants: Hispanic, Mexican, South Asian, Chinese and Indian [81]. In China, 213 (41.4%) of the 515 cases of lead poisoning recorded in a paediatric lead specialty clinic were caused by folk medicine. Most patients exhibit nonspecific symptoms, such as hyperactivity, attention difficulty, aggressiveness, constipation and anorexia [82]. In India, a retrospective study (2005–2013) of 786 patients with unexplained abdominal pain showed that 75 patients (9.5%) presented lead intoxication (BLLs > 25□ g/dL). These patients had a history of Ayurvedic medication with high levels of lead [83]. A noncommercial Malaysian folk diaper powder was identified as a source of lead exposure in a 9-month-old infant with 18 μg/dL BLL [84].

3.2.8. Gasoline

Until 1970, all gasoline in the world contained lead. Today, many countries have eliminated the use of leaded gasoline. Mexico eliminated lead in gasoline in 1997 [85], while Japan did so in 1980. Other countries that have eliminated the use of gasoline include Austria and Canada in 1993, Sweden and Denmark in 1995 and the USA in 1996 [86]. Therefore, the average BLL level in the population has decreased in many countries.

3.2.9. Candies

In Mexico, a reduction in the concentration of lead in candies was reported [87]. The association between candy consumption and BLL in children is unclear [88]. In the rest of the world, there is insufficient epidemiological evidence to associate candy and chocolate consumption with BLL in individuals. A study conducted in Nigeria found high levels of lead, chromium and cadmium in these products [89].

3.2.10. Cosmetics

Lead is found in cosmetics; lead chromates can be found in lipsticks and eye liners or in shadows as pigments. The US Food Drug & Cosmetic Act establishes a maximum lead concentration of 20 μg/g. In a review of 46 papers published from 1989 to 2013, the lead contents found in cosmetics in Nigeria and China were 130 μg/g and 58.7 μg/g, respectively [90]. Kohl is an eye cosmetic used in Asia and Africa; a recent European investigation on the content of Kohl found the presence of lead in it with concentrations ranging from a few mg/kg to over 400, 000 mg/kg [91]. Kohl is used for children; in a study of 69 children in India, the mean BLL measured was 29.6 μg/dL [92]. Research on the content of the metal in cosmetics and the BLL in users is scarce.

4. Discussion

Our systematic review provides evidence that high BLL persists in undeveloped countries such as Mexico. The prevalence of children from 1 to 4 years of age with BLL higher than 5 μg/dL is 21.8%, in comparison with the U.S., where children of the same age have a prevalence of 3.1% [16]. Nigeria has 36% of children (<15 years old) with BLL > 10 μg/dL [93]. In addition, in most of the studies included in the meta-analysis, the BLL of control individuals was higher than 5 μg/dL.

The aim of this study was to assess whether there is an association between different sources of lead exposure and the mean difference in blood lead levels in exposed people. This study found evidence of an association between lead source exposure and BLL in lead-*exposed industrial labourers*. In the case of home lead sources, information was limited to carry out meta-analysis.

Based on meta-analysis results from 50 studies of lead-exposed workers, there is a mean difference in BLL between different industry workers.

The highest mean difference in BLL was found in people working in battery production and smelter mining noncontrolled industries. This was followed by glazed ceramic pottery and smelter mining controlled industries.

For the battery industry, there is considerable information available about it as well as a world report by the WHO. Senegal, Dominican Republic and Vietnam are analysed in this report [2]. In our meta-analysis, other countries were studied: Brazil, south Korea, India, Mexico, Nigeria, and turkey. From publications made from 1995 to 2021. The mean difference in BLL was higher than 25 μg/dl in exposed workers. In Turkey, Mexico and Brazil, the high mean difference BLL of battery workers has remained constant over the last 20 years. For example, in México after 63 years, the mean BLL in battery workers is still high. In two studies not included in the meta-analysis, due to a lack of a control group, the BLL was similar. In the first study, the BLL was > 60 μg/dL in 30% of workers [94], and in a recent study, the BLL measured in battery industry workers was higher (69.9 μg/dL) [95]. In these countries, no definite actions have been taken to reduce the high BLL in the battery industry, despite its importance due to the high BLL in workers and children exposed to this lead source. In contrast, for India and Korea, a reduction in the mean difference BLL is observed.

The noncontrolled smelter industry is the second lead source with a mean BLL of − 37.76 μg/dL in the world for meta-analysis. Nevertheless, worldwide, there are not enough epidemiological studies about mining areas to analyse the effects of lead in humans and its effect on the environment. Several studies have shown a BLL of 40 μg/dL for populations living in certain mining areas [55,56,60,96].

At this point, it is important to consider that the mean BLL in controlled smelter workers is − 7.56 μg/dL. This difference is due to the measurement of the control lead exposure of workers in these industries. Notably, the difference between the mean BLL in the controlled mining and noncontrolled mining industries is an example: Enforcing safe industrial practices with pollutant emission control would reduce the environmental and human impact.

Glazed ceramics are the third leading exposure source in the world, considering the mean BLL of − 21.97 μg/dL in GC workers. The BLL values for people working glazed ceramics showed an important reduction over the years.

In general, for adult studies considered in the meta-analysis, high heterogeneity was found due to different dates and countries of the studied cases. Most of the subjects in all worker studies were men between 20 and 55 years old. Limitations of this study come from different relevant variables, such as years of work in the industry, work conditions, and bioaccessibility of lead compounds. However, large met-analyses such as this (8525 individuals) are likely to be more valid [97].

In a meta-analysis of children, the mean difference in BLL was different compared to workers. The highest mean difference in BLL was for children living near mining smelting sites, followed by those close to battery and mining tailings. The lowest mean difference in BLL was for children using glazed ceramic to cook and serve food. Glazed ceramic people exposed studies come from Mexico. In Mexico, the BLL measured in children exposed to GCP has been constant, with a GM between 7.23 μg/dL and 10.5 μg/dL for the last 15 years [16]. For the rest of the world, the number of reports about this subject is scarce.

In this case, children have lower BLL than adults due to factors that need to be considered: the longtime of exposure and the direct exposure to the source. It is important to note the high BLL in the overall children control group for the battery exposure group. An overlap in the mean difference BLL is observed for all lead sources in children. In contrast, workers meta-analysis showed a clear difference between the analysed groups.

Our systematic review provides evidence of the lack of studies analysing the relationship between lead sources such as paint, folk medicine, candies, toys, colour pencils and cosmetics and BLL in exposed people. Further studies are needed to establish their role as a source of lead in humans. Some studies suggest that these are important lead sources in the general population. Paint is a general lead source exposure, and high levels are found for many countries. High levels of lead in paint have been reported around the world [76]. In a national Mexican report where 118 samples were analysed, 53 of them had more than 10, 000 ppm lead [98]. This is a potential source of lead poisoning for children [76]. Toys lead concentration is regulated in many countries. Recent reports, however, indicate that high lead levels are still found in toys [76]. Some folk medicines include lead in their prescriptions and represent a source of lead poisoning worldwide [78]. Few reports are found on this subject; a review of 28 publications reported 82 incidents of lead poisoning in children [99].

5. Conclusions

In this meta-analysis, direct evidence between the mean difference in BLLs and lead sources in lead-exposed workers was found. The highest BLL was found in battery industry workers. Limitations to this meta-analysis may be due to heterogeneity and could be improved in a larger meta-analysis, as this one involved 8525 individuals (5223 lead-exposed workers and 3302 controls).

Further efforts must be aimed at linking the lead sources at home, such as cosmetics, folk medicine, paint, candies, and toys, with the BLL in people exposed to them. However, there is no direct evidence of a link between those home lead sources and BLL in users. It will be important to know the contribution of lead sources home in the BLL. Lead bioavailability, metal speciation, and time of exposure are factors that determine the BLL in lead-exposed users. Protection of lead-exposed populations and monitoring their BLL are necessary. Additionally, adequate periodical surveillance for lead sources should be required worldwide to reduce environmental lead pollution.

Declaration of interest statement

The authors report no conflict of interest. Each author participated in the review process and preparation and writing of this paper. Authors involved in the preparation of this review did not receive any compensation from any source. The conclusions drawn reflect only the professional work product of the authors. The affiliations of the authors are shown on the cover page.

Acknowledgements

The authors thank the anonymous reviewer whose comments and suggestions helped to improve and clarify this manuscript. The first author, Chavez-Garcia J. Adolfo, is thankful to the National Council for Science and Technology (CONACYT) for a scholarship awarded as an SNI level 3 research assistant of Prof. Juvencio Robles (CVU CONACYT 1006121).

Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.jtemb.2022.126948.

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