Blood lead levels in low-income and middle-income countries: a systematic review

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Summary

Background Since the global phase-out of leaded petrol, reports have suggested that lead exposure remains substantial or is increasing in some low-income and middle-income countries (LMICs). However, few studies have attempted to systematically assess blood lead levels over the full range of LMICs. We aimed to describe values for blood lead level in LMICs.

Methods In this systematic review, we searched PubMed for studies published between Jan 1, 2010, and Oct 31, 2019, that reported blood lead levels in the 137 countries in World Bank LMIC groupings. Studies were reviewed for inclusion if they contained blood lead level data from human populations residing in any given country; comprised at least 30 participants; presented blood lead level data derived from venous, capillary, or umbilical cord samples of whole blood; had data that were collected after Dec 31, 2004; and were published in English. Data on blood lead level were extracted and pooled, as appropriate, to make country-specific estimates of the distribution of background blood lead levels among children and adults, along with information on specific sources of exposure where available. This study is registered with PROSPERO, number CRD42018108706.

Findings Our search yielded 12 695 studies, of which 520 were eligible for inclusion (1100 sampled populations from 49 countries comprising 1 003 455 individuals). Pooled mean blood lead concentrations in children ranged from 1·66 µg/dL (SD 3·31) in Ethiopia to 9·30 µg/dL (11·73) in Palestine, and in adults from 0·39 µg/dL (1·25) in Sudan to 11·36 µg/dL (5·20) in Pakistan. Background values for blood lead level in children could be pooled in 34 countries and were used to estimate background distributions for 1·30 billion of them. 632 million children (95% CI 394 million–780 million; 48·5%) were estimated to have a blood lead level exceeding the US Centers for Disease Control's reference value of 5 µg/dL. Major sources of lead exposure were informal lead acid battery recycling and manufacture, metal mining and processing, electronic waste, and the use of lead as a food adulterant, primarily in spices.

Interpretation Many children have a blood lead level exceeding 5 µg/dL in LMICs, despite leaded petrol phase-outs. Given the toxicity of lead, even at low amounts of exposure, urgent attention is required to control exposures and to expand population-based sampling in countries with no or scant data.

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Introduction

Naturally occurring levels of lead in the Earth's crust are below applicable human health guidelines, with exposure resulting primarily from anthropogenic contamination.[1] The greatest historical source of lead exposure was the use of tetraethyl lead as an anti-knocking agent in petrol, beginning in the early 20th century, which resulted in the dispersion of at least 9 million tonnes of lead into the environment.[2] The global phase-out of leaded petrol constitutes one of the major success stories of environmental health science, influencing policies worldwide for public good. Beginning with the USA in 1975, the phase-out was progressively adopted by high-income countries (HICs) in the 1980s and 1990s. As a result, the average level of lead in the blood for people aged 1–74 years in the USA decreased by 78%, from 12·8 µg/dL to 2·8 µg/dL between 1976 and 1991.[3] Similar decreases were noted in other HICs, such as Sweden and Germany.[4,5] Phase-outs were slow to be adopted in low-income and middle-income countries (LMICs); however, by the end of 2005, nearly all LMICs had eliminated use of leaded petrol in automobiles.[6]

Despite phase-outs of leaded petrol, reports in LMICs suggest that average blood lead levels in the general population are substantially higher than that in HICs. This finding is troubling, particularly because research continues to show the adverse effects of lead at progressively decreasing amounts of exposure. The relationship between increased blood lead levels in children and decrements in intelligence quotient does not appear to have a threshold, with an impact seen at a level as low as 1 µg/dL. Decrements continue at higher

Research in context

Evidence before this study

Few studies have systematically reviewed the data on blood lead level in low-income and middle-income countries (LMICs). Existing studies have included only a partial assessment of the available data, resulting in an incomplete characterisation of the burden of lead toxicity and exposure sources in LMICs. We searched the PubMed database with the keywords "blood", "lead", and "[country name]" for the 137 countries in World Bank LMIC country groupings, yielding 12 695 studies published between Jan 1, 2010, and Oct 31, 2019.

Added value of this study

This study considerably expands existing knowledge of blood lead levels in LMICs. 520 unique studies from 49 countries were included, compared with fewer than 100 studies in previous efforts covering similar periods of time. The results, which include a review of sources, might present more robust national estimates.

Implications of all the available evidence

Blood lead level seems to remain higher in LMICs than in high-income countries. Given the lifelong adverse impacts of lead exposure, urgent attention is required to address the greatest sources of exposure.

amounts of lead exposure, albeit with proportionally less impact.[7–9] As for adults, analyses have found that the relationship between blood lead level and increased risk of cardiovascular morbidity and mortality is also seen at a level as low as 1 µg/dL.[10,11]

There have been several efforts to systematically review or estimate blood lead levels in populations living in LMICs on the basis of reports in peer-reviewed literature. In 2013, Horton and colleagues[12] did a systematic review of 76 studies published in English between 2000 and 2012 containing blood and urine concentrations of metals in children (aged ≤18 years) in ten emerging market countries, including six LMICs (as defined by 2018 World Bank income groupings). In most cases, the blood lead level identified exceeded the US reference amount of 5 µg/dL; however, most studies reviewed were investigations done at known contaminated sites.[12] In 2017, Olympio and colleagues[13] reviewed 56 papers published between 2000 and 2014 reporting the blood lead level of children (aged ≤18 years) in 16 Latin American and Caribbean countries. A high prevalence of blood lead level exceeding 5 µg/dL and 10 µg/dL was found, but only two of the 16 countries (Peru and Mexico) had values from population-based studies, as opposed to studies of identified hotspots of exposure (ie, heavily contaminated areas). In 2013, Attina and Trasande[14] calculated the economic costs associated with paediatric lead exposure in LMICs on the basis of data extracted from 68 articles published between 2000 and 2012. Studies reporting lead exposure in heavily contaminated areas or occupational exposures were excluded, except for studies with a control population not residing in the contaminated area. However, because the focus of the analysis was economic costs, country-specific estimates of blood lead level were not reported.

The Institute for Health Metrics and Evaluation (IHME) does a literature review of blood lead level as the basis of their annual Global Burden of Disease (GBD) calculations. From 2010 to 2017, 88 studies from 27 LMICs were found to have been done on people who were construed to be reasonably representative of the associated country's age-specific general population (ie, not individuals in hotspots) and were, therefore, used in the 2017 GBD assessment.[15] The published values for blood lead level were pooled and then adjusted for covariates (eg, traffic, urbanicity, sex, leaded petrol phase-out date) to estimate national values and the attributable disease burden in disability-adjusted life-years and deaths. Where no studies that met the GBD's eligibility criteria were available, estimates were made on the basis of data from neighbouring countries and the identified covariates.[16] However, in its published work, IHME does not report country-level estimates for blood lead level, making it difficult to ascertain their reliability. Furthermore, the reliance on the use of leaded petrol in estimating blood lead levels in countries with no data might lead to bias if other sources of exposure are not considered.

Overall, the published work on blood lead levels in LMICs does not provide a clear picture of current lead exposure. Additionally, a preliminary evaluation done by our team suggested that many studies were not included in each of these analyses that, if subjected to a comprehensive and standardised assessment, could further enrich our understanding of lead exposure in LMICs. We aimed to expand the scope of the literature review to a larger set of studies and to describe values for blood lead level that are representative examples of the probable experience in each country.

Methods

Search strategy and selection criteria

For this systematic review, we searched PubMed between Nov 11 and Nov 29, 2019, using the search terms "[country name]" (all fields, Medical Subject Heading [MeSH] terms, abstract text), "blood" (subheading, all fields, MeSH terms), and "lead" (all fields, MeSH terms) for studies published between Jan 1, 2010, and Oct 31, 2019. LMIC names (n=137) were taken from World Bank

groupings.[17] Studies were reviewed for inclusion if they contained blood lead level data from human populations residing in any given country; comprised at least 30 participants; presented blood lead level data derived from venous, capillary, or umbilical cord samples of whole blood (serum and plasma samples were excluded); had data that were collected after Dec 31, 2004; and were published in English. At least two reviewers independently searched PubMed with the defined search terms.

Titles were reviewed for relevance as a first screening step and selected studies were then subject to review of associated abstracts. When a study did not meet the inclusion criteria, it was excluded and a justification was provided by the reviewer. Each reviewer independently completed all steps in the review process, with all unique studies being combined in a comprehensive list. Any potential conflicts were resolved between reviewers through discussion with a third collaborator.

Data analysis

A bias assessment was done following guidance provided by the US Office of Health Assessment and Translation Handbook.[18] The tool is comprised of 11 possible questions addressing different types of bias. Studies are assessed against the applicable questions and ranked according to tier, with tier one indicating a low risk of bias and tier three indicating an unacceptable (ie, high) risk of bias. Each study was reviewed against seven relevant questions to assess study design, data analysis and interpretation, and the presentation of results. The full text of these seven questions is attached in appendix 1 (p 3). Only studies in tier one and tier two were included in the analysis.

The following information was extracted by individual reviewers in duplicate from studies that met the inclusion criteria: title, author, year, location, population characteristics (eg, sex and age), statistics on blood lead level (eg, central tendency, dispersion, sample size), sources of exposure, analysis method, and the nature of exposure (ie, background, occupational, non-occupational).

Population subsamples were coded to different subgroups on the basis of the severity of their exposure. Subsamples with an identifiable high risk of exposure not representative of the general population (eg, living near a known hazardous waste site or applying contaminated cosmetics) were coded to the non-occupational subgroup. Those subsamples drawn from general populations or used as controls in case-control studies were coded to the background subgroup and were assumed to be representative of general exposure. Subsamples drawn from worker populations exposed to lead were coded to the occupational subgroup.

Where possible, blood lead levels were separated into adult or child subsamples, and coded as such. Where this was not possible, the subsample was coded as both. A child was defined as aged 18 years or younger, consistent with the UN Convention on the Rights of the Child.[19] Subsamples were disaggregated by occupation and source of exposure where those data were available. Subsamples were disaggregated by sex only when a sample with both sexes was unavailable. If sex was not specified, subsamples were coded to the so-called both subgroup.

Studies were also flagged as to whether or not probable sources of exposure were identified, such as communities living near contamination hotspots or adjacent to industrial areas, occupational exposures, or those with significant associations between blood lead level and an environmental assessment or questionnaire. Studies carried out of populations in cities with significant industrial activity that the authors linked to lead exposure were also categorised as probable. Studies that evaluated blood lead level in a given population and that provided possible sources of exposure on the basis of a review of the literature, rather than an assessment of exposure in situ, were coded to the so-called possible subgroup. Studies that did not define an exposure source were coded to the undefined subgroup. To deal with data duplication, we first compared study titles, then the unique PubMed identifier (ie, PMID or EntrezUID).

Multiple studies did not provide statistical information sufficient for the pooling of data. Specifically, arithmetic mean and SD in µg/dL were required to pool data in the methods used in this systematic review. Where these data were unavailable, various methods were used to impute the missing values. The selection of the appropriate approach was guided by recommendations set out by Weir and colleagues,[20] whereby widely used methods for imputing missing data were evaluated (appendix 2 pp 1–3).

See Online for appendix 2

Mean background blood lead levels were calculated at the country level for children and adults following methods described by Fewtrell and colleagues[21] and by Attina and Trasande.[14] In this method, means were transformed into their natural logarithms before being weighted by sample size. Specifically, the log-transformed sample means were multiplied by their respective sample sizes and summed. The sum was then divided by the sum of the sample size to attain the average. The natural anti-logarithm of the average was then taken. Thus, the population arithmetic mean for each country was calculated as follows:

See Online for appendix 1

$$\mu = \mathrm{e}\,\frac{\sum \ln(\overline{x})n}{\sum n}$$

where μ is population arithmetic mean and $\overline{x}$ is the subsample mean. The population SD was calculated by taking the weighted average of the sample variances as follows:

$$\sigma = \sqrt{\frac{\sum_{i=1}^{k}(\mathrm{n}_i-1)s_i^2}{\sum_{i=1}^{k}(\mathrm{n}_i-1)}}$$

where σ is the population standard deviation and s is the SD of the subsample.

Once the mean blood lead level and SD were estimated for the population within each country, we calculated the

For the **protocol** see www.crd.york.ac.uk/PROSPERO

	Titles returned by PubMed	Abstracts reviewed	Studies included in analysis	Cohorts included in analysis	Total population of reviewed cohorts
Bangladesh	74	22	10	15	5437
Brazil	1066	65	36	67	12 834
China	4128	410	149	281	676 886
Egypt	306	26	14	34	2134
India	1402	62	41	94	230 864
Iran	897	61	40	68	7203
Mexico	402	94	45	92	24 205
Nigeria	167	52	20	36	3685
Pakistan	203	57	30	162	11 102
South Africa	277	30	10	14	4133
Thailand	215	21	11	15	3579
Turkey	919	60	23	43	3133
Other LMICs with eligible cohorts*	1650	161	91	179	18 260
Other LMICs without eligible cohorts†	989	11	0	0	0
Total	12 695	1132	520	1100	1 003 455

LMICs=low-income and middle-income countries. *Armenia, Benin, Bolivia, Bosnia and Herzegovina, Cameroon, Colombia, Democratic Republic of the Congo, Ecuador, Ethiopia, Ghana, Grenada, Haiti, Indonesia, Iraq, Jamaica, Jordan, Kenya, Kosovo, Lebanon, Malaysia, Mongolia, Morocco, Nepal, North Macedonia, Palestine, Peru, Romania, Russia, Senegal, Serbia, Sri Lanka, Sudan, Tanzania, Tunisia, Uganda, Ukraine, Vietnam. †Afghanistan, Albania, Algeria, American Samoa, Angola, Azerbaijan, Belarus, Belize, Bhutan, Botswana, Bulgaria, Burkina Faso, Burundi, Cape Verde, Cambodia, Central African Republic, Chad, Comoros, Republic of the Congo, Costa Rica, Cuba, Djibouti, Dominica, Dominican Republic, El Salvador, Equatorial Guinea, Eritrea, Eswatini, Fiji, Gabon, The Gambia, Georgia, Guatemala, Guinea, Guinea-Bissau, Guyana, Honduras, Côte d'Ivoire, Kazakhstan, Kiribati, North Korea, Kyrgyzstan, Laos, Lesotho, Liberia, Libya, Madagascar, Malawi, Maldives, Mali, Marshall Islands, Mauritania, Mauritius, Federated States of Micronesia, Moldova, Montenegro, Mozambique, Myanmar, Namibia, Nauru, Nicaragua, Niger, Papua New Guinea, Paraguay, Philippines, Rwanda, Saint Lucia, Saint Vincent and the Grenadines, Samoa, São Tomé and Príncipe, Sierra Leone, Solomon Islands, Somalia, South Sudan, Suriname, Syria, Tajikistan, Timor-Leste, Togo, Tonga, Turkmenistan, Tuvalu, Uzbekistan, Vanuatu, Venezuela, Yemen, Zambia, Zimbabwe.

Table 1: **Results of the literature review**

	Subsamples	Total sample size	Background subsamples	Non-occupational subsamples	Occupational subsamples
Automobile repair	13	781	2	2	9
Battery manufacture or recycling	118	11 912	4	38	77
Bullets	8	1277	2	5	1
Ceramics	13	1485	5	5	4
Contaminated sites	4	1676	0	4	0
Diet	15	2533	10	5	0
Dumpsite	5	410	2	2	2
Electronic waste	35	6366	5	23	7
Industry (lead)	8	818	0	3	5
Industry (other)	69	7988	24	12	34
Lead-based paint	7	940	4	0	3
Mining	31	4588	1	30	3
Other	35	3464	10	18	6
Petrol	7	1252	4	0	3
Smelting	52	21 778	10	21	22
Tobacco products	58	3771	7	51	0

Data are n. Data are from 478 subsamples with probable sources of exposure of the 1100 total subsamples.

Table 2: **Sources of lead exposure in background, non-occupational, and occupational settings**

number of children with a level above particular threshold values at the national level. The US Centers for Disease Control and Prevention (CDC) currently uses a reference value of 5 µg/dL for lead in children, which was revised downward from the previous reference value of 10 µg/dL in 2012.[22] An estimate of the number of children (aged 0–14 years) with a level above each of these values was calculated with age distribution data provided by the IHME and the means and SDs calculated as described previously.[23] Given that blood lead level tends to be log-normally distributed, the distribution of a population with a concentration above a threshold was calculated in Microsoft Excel 2018 with the following syntax: =1–(NORM.DIST(LN([threshold]),LN([mean]),LN([sd]),TRUE)). Sensitivity testing was done to assess the relative influence of imputation methods by use of the leave-one-out approach. In this case, imputation methods were reviewed sequentially, with subsamples associated with each method successively removed or reinserted in each run. Thus, subsamples with arithmetic means imputed with one method were removed in the first run, although reinserted in the second, when those imputed with a second method were removed and so on. Variability in the results was assessed through a series of one-way ANOVA tests against the full dataset. Sensitivity testing was only carried out on background subsamples of blood lead level among adults and children. The relative influence of capillary lead level measurements was similarly assessed.

Data were aggregated, organised, and analysed in Microsoft Excel 2018. ANOVA tests and forest plots were done with Stata statistical software (version 15.1).

This systematic review was listed with the PROSPERO International prospective register of systematic reviews maintained by the UK National Institute for Health Research on Sept 13, 2018. The protocol is available online (CRD42018108706).

Role of the funding source

The funding sources restricted research to lead exposure in LMICs, although they otherwise had no role in study design, data collection, data analysis, data interpretation, writing of the report, or the decision to submit for publication.

Results

Our search identified 12 695 studies, of which 11 563 papers (91%) were excluded on the basis of reviewing titles for relevance, leaving 1132 studies. During abstract review and data extraction, an additional 612 studies were excluded. Therefore, the final dataset for analysis comprised 520 studies covering 1100 sampled populations (ie, subsamples) with a total population of 1 003 455 people from 49 countries (table 1). Detailed results of the literature review, including the exclusion justification and the results of the bias assessment, are provided in appendix 2 (pp 3–4).

Background blood lead levels were available in 300 subsamples from 34 countries for children and in 358 subsamples from 37 countries for adults. For non-occupationally exposed people, blood lead levels were available in 156 subsamples from 23 countries for children and in 106 subsamples from 16 countries for adults. Studies of occupationally exposed people, including six child subsamples from Egypt and one from Pakistan, were available in 191 subsamples from 24 countries.

Probable sources of exposure were identified for 478 (43%) of 1100 subsamples. An additional 80 subsamples (7%) were associated with possible sources of exposure. These sources were then sorted into 16 different exposure categories (table 2). Detailed results of the imputation methods for missing data are provided in appendix 2 (pp 1–3).

Pooled mean blood lead levels in children ranged from 1·66 µg/dL (SD 3·31) in Ethiopia to 9·30 µg/dL (11·73) in Palestine, and in adults from 0·39 µg/dL (1·25) Sudan to 11·36 µg/dL (5·20) in Pakistan (table 3). The figure shows mean background blood lead levels in children for the 34 countries where data were available. The equivalent figure for mean background blood lead levels in adults is available in appendix 2 (p 8). The results for non-occupational and occupational subgroups are provided in appendix 2 (pp 6–9). The average blood lead levels among both occupational and non-occupational subgroups were elevated compared to the background subgroups. The blood lead levels in both of these groups were highly variable due to the heterogeneous study populations and the diversity of contributing sources.

	Children			Adults		
	Sub-samples	Total sample size	Pooled mean blood lead level, µg/dL (SD)	Sub-samples	Total sample size	Pooled mean blood lead level, µg/dL (SD)
Bangladesh	7	3460	7·87 (5·69)	4	1290	3·90 (2·57)
Benin	3	1092	5·27 (3·02)	4	351	4·56 (5·80)
Brazil	17	3921	2·65 (3·07)	24	6292	3·43 (3·52)
Cameroon	1	147	8·70 (3·90)	..	..	..
China	86	591 043	4·17 (4·54)	81	358 009	3·47 (3·33)
Colombia	3	866	3·06 (0·60)	1	381	0·98 (0·36)
Democratic Republic of the Congo	3	314	7·46 (4·03)	2	80	5·82 (1·87)
Ecuador	1	69	3·17 (2·54)	..	..	..
Egypt	11	1100	8·24 (4·78)	13	747	10·36 (8·17)
Ethiopia	1	132	1·66 (3·31)	3	208	3·92 (5·07)
Ghana	..	..	..	4	110	1·45 (4·40)
Grenada	..	..	..	1	52	1·17 (3·31)
Haiti	1	273	6·00 (2·38)	..	..	..
India	22	5593	5·22 (6·66)	41	222 353	4·42 (3·44)
Indonesia	3	387	5·20 (3·00)	2	51	2·11 (1·04)
Iran	8	928	3·62 (4·62)	26	1814	6·03 (5·98)
Iraq	1	207	5·30 (1·90)	2	666	8·47 (3·20)
Jamaica	5	651	2·90 (2·98)	2	130	0·83 (1·17)
Jordan	..	..	..	3	93	3·16 (1·38)
Kosovo	1	53	2·3 (0·07)	1	21	1·70 (0·70)
Lebanon	..	..	..	2	116	4·35 (0·54)
Malaysia	..	..	..	1	136	2·60 (2·10)
Mexico	45	4509	3·62 (3·46)	25	6342	3·39 (2·74)
Mongolia	2	338	3·82 (2·55)	1	100	3·10 (3·31)
Morocco	12	770	4·57 (3·14)	5	193	4·80 (4·60)
Nepal	1	312	6·69 (4·22)	5	173	4·44 (3·97)
Nigeria	6	844	7·67 (5·89)	12	626	7·76 (2·82)
North Macedonia	..	..	..	2	119	2·41 (1·44)
Pakistan	33	2382	9·27 (3·17)	45	4627	11·36 (5·20)
Palestine	2	1883	9·30 (11·73)	..	..	..
Romania	2	144	2·60 (2·61)	..	..	..
Russia	4	1088	5·17 (4·18)	2	30	1·56 (0·55)
Senegal	1	32	8·22 (3·16)	..	..	..
Serbia	1	54	7·80 (4·27)	3	119	1·27 (5·96)
South Africa	4	2185	5·59 (3·61)	5	1553	1·57 (1·63)
Sri Lanka	..	..	..	3	284	4·37 (2·39)
Sudan	..	..	..	1	15	0·39 (1·25)
Tanzania	1	43	2·26 (0·96)	1	24	4·71 (1·62)
Thailand	5	1813	5·12 (3·03)	6	1219	4·89 (4·75)
Tunisia	..	..	..	1	20	9·36 (3·31)
Turkey	4	462	3·23 (2·53)	22	971	2·51 (3·11)
Uganda	2	263	6·68 (4·43)	..	..	..
Ukraine	..	..	..	1	61	1·96 (1·64)
Vietnam	1	311	4·97 (5·50)	1	51	3·90 (2·20)

Background individuals were drawn from the general population or from controls in case-control studies.

Table 3: **Pooled mean background blood lead levels for adults and children in the 44 low-income and middle-income countries where data were available**

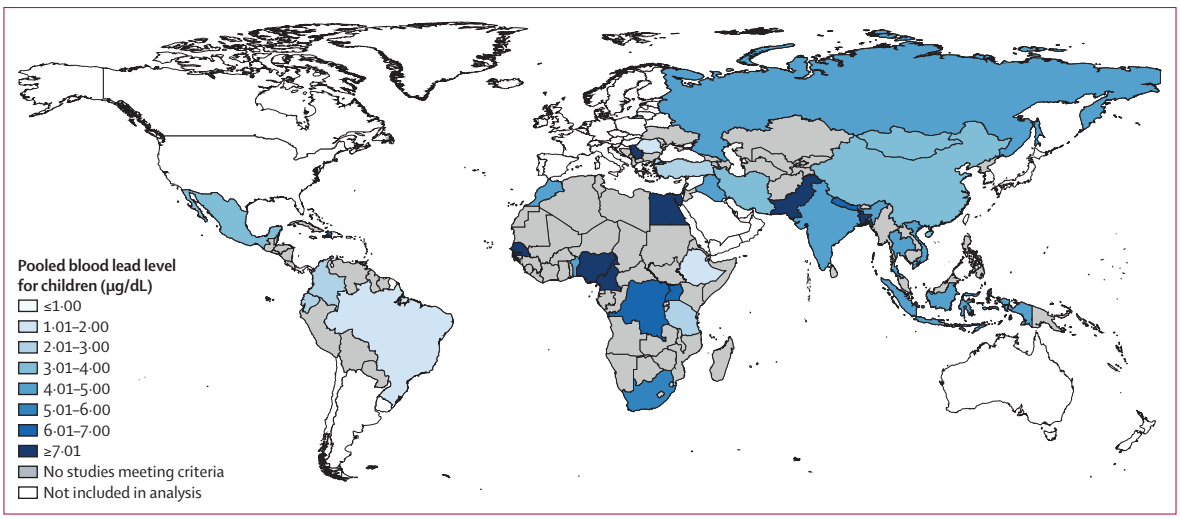

Figure: **Pooled mean background blood lead levels in children in 34 low-income and middle-income countries with available data**

Of the 1·30 billion children (aged 0–14 years) living in the 34 LMICs with acceptable data on background blood lead levels in children, approximately 632 million (95% CI 394 million–780 million; 48·5%) were estimated to have a level exceeding the CDC reference value of 5 µg/dL, and 413 million (236 million–551 million; 31·7%) were estimated to exceed the previous reference value of 10 µg/dL (table 4).

In the sensitivity analyses, ANOVA tests of the full dataset and versions with sequentially removed imputed values did not result in significant differences in the findings (p>0·05), nor did the removal of capillary samples (n=28 capillary samples).

Discussion

This systematic review of published values of blood lead level in LMICs had three major findings. The first finding is that there is a paucity of rigorous data on lead exposure in the general populations of LMICs. In the 137 countries classified as LMICs by the World Bank, only 44 countries (32%) had data on background blood lead level that were judged to be of adequate quality to be included in this analysis. Fewer countries had data on blood lead levels of adequate quality for children (34 countries [25%]) and adults (37 countries [27%]) from the general population, and fewer still had such data based on more than one subpopulation (23 countries [17%] for children and 27 countries [20%] for adults). In terms of geographical distribution, most of the LMICs in Africa and many in central Asia and Latin America did not have any studies that met our criteria.

The second finding is that, among the 44 countries with background data that were analysed, the average blood lead level of the general population appears to be higher in LMICs than in HICs, most importantly in children. Of the 34 countries with background data for children, more than 632 million (95% CI 394 million–780 million; 48·5%) of 1·28 billion children were estimated to have a blood lead level exceeding the CDC reference value of 5 µg/dL, among whom 413 million children (236 million–551 million; 31·7%) were estimated to have a blood lead level above 10 µg/dL. These figures might be underestimates of global LMIC exposure because they represent only 34 of 137 LMIC countries. Additionally, the subsamples used here were chosen in studies as control populations specifically because they represented an absence of identifiable sources of exposure. By excluding non-occupational exposures, this study presents a more conservative picture of lead exposure in LMICs.

The contrast between LMICs and HICs is stark. In the USA, for example, 2017 CDC National Childhood Blood Lead Surveillance Data showed that less than 2% of children (aged 0–5 years) had blood lead levels exceeding 5 µg/dL (40 122 of 2 014 208 sampled children).[24] In Sweden, a general population-based longitudinal survey of 2440 children found a geometric mean blood lead level of 1·3 µg/dL in 2007.[25] An international study of large-scale population-based prospective birth cohort studies found that mean blood lead level in the cohorts from France, Germany, and Japan were all below 1 µg/dL.[26]

There are few similar national-level estimates in LMICs, with which the accuracy of the results presented in this systematic review can be gauged. In 2020, Yan and colleagues[27] pooled 95 studies representing 297 000 Chinese children, finding a mean blood lead level of 5·34 µg/dL (SD 3·09), compared with that of 4·17 µg/dL (4·54) derived from a population of 591 043 in this study. In 2019, Téllez-Rojo and colleagues[28] studied 1457 urban Mexican children aged 1–4 years. The authors do not present an indication of central tendency, although a median blood lead level of 3·3 µg/dL can be derived from the statistics presented.[28] This systematic review reviewed the blood lead level of 4509 Mexican children and found a pooled value of 3·62 µg/dL (SD 3·46). These

	Pooled mean blood lead level, µg/dL (SD)	Population (aged 0–14 years)	Children with blood lead level of >5 µg/dL (95% CI)	Children with blood lead level of >10 µg/dL (95% CI)
Bangladesh	7·87 (5·69)	47 334 000	28 546 129 (20 301 826–32 860 429)	21 078 848 (13 331 165–25 722 107)
Benin	5·27 (3·02)	4 621 600	2 397 101 (849 390–3 194 555)	1 298 635 (292 490–2 076 538)
Brazil	2·65 (3·07)	47 840 000	13 655 022 (4 779 097–20 592 640)	5 653 344 (1 375 281–10 237 658)
Cameroon	8·70 (3·90)	9 991 800	6 574 477 (1 265 141–8 072 622)	4 588 727 (492 446–6 404 146)
China	4·17 (4·54)	233 220 000	105 535 665 (89 820 897–118 236 768)	65 741 080 (52 856 196–76 916 508)
Colombia*	3·06 (0·60)	11 736 900	..	..
Democratic Republic of the Congo	7·46 (4·03)	35 681 400	21 872 694 (12 417 870–26 242 163)	14 869 639 (6 681 374–19 714 269)
Ecuador	3·17 (2·54)	4 698 000	1 467 093 (0–3 287 669)	510 395 (0–1 938 945)
Egypt	8·24 (4·78)	29 971 900	18 738 259 (15 591 686–20 804 541)	13 511 034 (10 414 599–15 760 082)
Ethiopia	1·66 (3·31)	41 251 000	7 351 289 (0–27 150 752)	2 745 463 (0–17 805 193)
Haiti	6·00 (2·38)	3 617 279	2 109 151 (229 084–2 924 773)	1 006 891 (36 312–1 916 890)
India	5·22 (6·66)	378 590 000	192 734 783 (133 373 944–226 395 076)	138 537 342 (86 418 991–171 623 893)
Indonesia	5·20 (3·00)	71 208 000	36 604 831 (12 572 936–49 057 554)	19 629 034 (4 232 044–31 690 506)
Iran	3·62 (4·62)	18 565 000	7 734 728 (976 729–10 778 070)	4 707 899 (354 544–7 454 404)
Iraq	5·30 (1·90)	14 924 000	8 001 759 (537 674–12 255 453)	2 407 230 (29 799–6 513 431)
Jamaica	2·90 (2·98)	696 180	214 699 (3058–372 607)	89 137 (394–203 434)
Kosovo*	2·30 (0·07)	293 579	..	..
Mexico	3·62 (3·46)	35 052 000	13 932 644 (10 523 851–16 667 032)	7 245 601 (4 896 118–9 386 785)
Mongolia	3·82 (2·55)	828 950	320 587 (991–547 019)	125 658 (65–307 402)
Morocco	4·57 (3·14)	9 356 800	4 383 200 (2 854 797–5 449 313)	2 308 439 (1 238 107–3 232 101)
Nepal	6·69 (4·22)	9 352 200	5 425 152 (0–7 263 909)	3 648 335 (0–5 707 054)
Nigeria	7·67 (5·89)	80 444 000	47 898 934 (30 881 172–55 950 677)	35 441 624 (19 809 092–44 080 315)
Pakistan	9·27 (3·17)	66 339 000	46 678 635 (44 144 422–48 814 430)	31 431 002 (28 606 378–33 961 287)
Palestine	9·30 (11·73)	1 882 010	1 128 370 (0–1 404 414)	918 992 (0–1 220 401)
Romania	2·60 (2·61)	3 042 000	753 121 (0–1 793 885)	242 950 (0–941 734)
Russia	5·17 (4·18)	22 644 000	11 532 142 (3 191 286–15 100 570)	7 297 600 (1 342 601–10 840 485)
Senegal	8·22 (3·16)	6 598 700	4 402 364 (1 426 853–5 419 254)	2 853 029 (545 430–4 121 946)
Serbia	7·80 (4·27)	1 444 180	895 993 (0–1 141 872)	623 880 (0–909 304)
South Africa	5·59 (3·61)	14 552 700	7 778 383 (3 548 364–9 901 018)	4 729 807 (1 579 499–6 860 937)
Tanzania*	2·26 (0·96)	24 083 400	..	..
Thailand	5·12 (3·03)	11 950 400	6 075 112 (3 121 660–7 823 838)	3 262 620 (1 231 670–4 903 766)
Turkey	3·23 (2·53)	19 756 800	6 302 619 (402 459–11 002 659)	2 211 761 (51 761–5 401 056)
Uganda	6·68 (4·43)	18 894 400	10 906 029 (1 288 429–13 916 296)	7 427 880 (477 489–10 698 277)
Vietnam	4·97 (5·50)	21 598 500	10 768 832 (0–16 189 076)	7 361 977 (0–13 068 374)
Total	..	1 302 060 678	632 719 797 (394 103 618–780 610 933)	413 505 854 (236 293 846–551 619 231)

*No children were estimated to be above these thresholds.

Table 4: **Estimated number of children (aged 0–14 years) exceeding 5 µg/dL and 10 µg/dL blood lead concentrations in 34 low-income and middle-income countries covered by the analysis**

results seem to indicate that the findings of this study are generally consistent with other efforts.

The third main finding of the study is that the sources of exposure in LMICs appear to be distinct from those in HICs. The decrease in average blood lead level in HICs has been most commonly attributed to the phase-out of tetraethyl lead used in petrol, with remaining pockets of high exposure due to the continued presence of lead-based enamel paints in residential settings in countries such as the USA.[29] The sources of lead exposure in LMICs seem to be different. For example, with regard to lead-based paint, relatively few LMICs have legislatively banned this source of exposure for use in residential settings.[30] However, despite the absence of bans in most countries, lead-based paint does not appear to be a major source of lead exposure in LMICs. This conclusion is similarly supported by a 2019 assessment of homes and preschools in Jakarta, Indonesia, which showed a low risk of exposure despite lead-based paint being readily available in stores.[31] Instead, key sources of lead exposure in LMICs identified in this systematic review include informal lead acid battery recycling and manufacture, metal mining and processing, electronic waste, and the use of lead as a food adulterant, primarily in spices. In

one country in particular, Mexico, lead-based ceramic glazes were a significant source of exposure.[28]

This study expands on previous reviews in an effort to develop a more comprehensive assessment of blood lead levels in people in LMICs. The data aggregated here could form the basis of future studies to help to improve the surveillance of blood lead levels, the establishment of an international registry housed in an academic institution or international organisation, or both. Researchers could be encouraged to register the anonymised results of their studies into the database and to follow basic quality assurance and control methods. Measurement of blood lead levels in fresh and archived samples should also be encouraged throughout the course of large population-based cohort studies that include children, the initiations of which have been steadily increasing in LMICs.[32] Given that nearly all testing of blood lead level in LMICs is done by individual academics, such efforts could greatly improve current knowledge.

A limitation of this study relates to the pooling of discrete reports to calculate a nationally representative value of blood lead level. In most cases, the data were not collected for this purpose and typically represent a small geographical area or subsection of the population. The relative influence of the results of any one study is somewhat diminished when pooled with others; however, only a single subsample could be identified in 11 of the 34 countries for which data meeting our criteria were available on children and in ten of the 37 countries for such data on adults.

These limitations are shared by preceding efforts of other researchers who, by comparison, reviewed fewer studies than the 520 studies used in this systematic review. For example, in 2013, Attina and Trasande based their global estimates on a review of 68 studies.[14] Likewise, in their 2018 GBD report, IHME used 88 studies from LMICs for the period 2010–17.[15]

Regarding the inclusion criteria, it is worth noting that income is not a static category. 11 countries were LMICs at one point during the decade covered by this study, but were HICs during the year that einclusion criteria were developed (2018). Furthermore, the exclusive use of studies published in English in the PubMed database is likely to have resulted in the exclusion of a large amount of available data.

In conclusion, this systematic review of 520 studies indicates that blood lead level seems to remain elevated in LMICs, despite phase-outs of leaded petrol. The primary sources of exposure appear to be related to industrial emissions, although reviewed studies were not fully amenable to a quantitative assessment. Approximately 632 million children (95% CI 394–780 million; 48·5%) were found to have a blood lead level exceeding the CDC reference value of 5 µg/dL. The true global burden is no doubt considerably larger, given that these estimates derive from only 44 countries with adequate data on background levels from a total of 137 LMICs. An international registry could be established to house the anonymised results of testing carried out by researchers and to improve surveillance of blood lead level in LMICs.

Contributors

BE conceptualised and designed the study. BE did the literature review, data extraction and synthesis, contributed to the bias assessment, and served as the primary author of the manuscript. EN, GF, and JS did the literature review and data extraction. GF did the bias assessment. MPT contributed to the writing of the manuscript and provided guidance on the approach. HH contributed to the interpretation of data and writing of the manuscript. All authors had full access to all the data in the study and had final responsibility for the decision to submit for publication.

Declaration of interests

BE, EN, JS, and GF were all employed by Pure Earth (New York, NY, USA) at periods during the authoring of this study. Pure Earth is a non-governmental organisation with a focus on lead exposure in LMICs, including exposures resulting from industrially contaminated sites. Pure Earth receives financial support from private and public donors including the Clarios Foundation and the Trafigura Foundation. Financial support from the Clarios Foundation began after the submission of this article. Pure Earth also receives in-kind advice and support from individuals employed at private environmental consulting firms and the International Lead Association. MPT is affiliated with Broken Hill Lead Reference Group (NSW, Australia), LEAD Group (NSW, Australia), and NSW Environment Protection Authority's Broken Hill Environmental Lead Program, and reports undertaking paid and non-paid work for the NSW Environment Protection Authority's Broken Hill Environmental Lead Program in relation to the assessment and management of environmental lead contamination in Broken Hill, NSW, Australia. MPT has also provided advice in relation to lead exposure matters to various law firms, relating to mining and smelting lead contamination and human exposures in Australia and Africa, including accepting personal fees from Leigh Day for an investigation of lead contamination in Zambia. MPT also reports managing two community-orientated programmes in Australia that provide advice about lead contamination from garden soils and household dusts with support from Macquarie University. MPT also reports compensated and uncompensated work for the Australian Building Codes Board, the Australian Federal Government, and the US non-governmental organisation Pure Earth. HH reports that he has served at times as an expert witness consultant in litigation involving lead exposure and health impacts.

Data sharing

All data used in the study have been uploaded in appendix 1.

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