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Effects of blood lead levels <10 µg/dL in school-age children and adolescents: a scoping review

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Abstract

Context: Lead exposures among school-age children are a major public health issue. While the harmful effects of lead exposure during the first years of life are well known, there is not as much understanding of the effects of low levels of lead exposure during later childhood.

Objective: To review the effects of blood lead levels (BLLs) <10 µg/dL in school-age children and adolescents

Data Sources: We searched Medline, Embase, Global health, CINAHL, Scopus, and Environmental Science Collection databases between January 1, 2000, and May 11, 2023.

Study Selection: We included peer-reviewed English-language articles that presented data on the effects of BLLs <10 µg/dL in individuals ages 5 through 18 years.

Data Extraction: Data on country, population, analytic design, sample size, age, BLLs, outcomes, covariates, and results were extracted.

Results: Overall, 115 of 3,180 screened articles met the inclusion criteria. The reported mean or median BLL was <5 µg/dL in 98 articles (85%). Of the included articles, 89 (77%) presented some evidence of an association between BLLs <10 µg/dL during school age and detrimental outcomes in a wide range of categories. The strongest evidence of an association was for the outcomes of intelligence quotient (IQ), and attention-deficit/hyperactivity disorder (ADHD) diagnoses or behaviors.

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Contributors Statement

Audrey Pennington designed the data abstraction instrument, screened articles for inclusion, abstracted article data, coordinated and supervised data collection, and drafted the manuscript. Madison Smith, Cheryl Cornwell, and Stella Chuke screened articles for inclusion, abstracted data, and critically reviewed and revised the manuscript. Joseph Courtney conceptualized the study, screened articles for inclusion, and critically reviewed and revised the manuscript. Paul Allwood critically reviewed and revised the manuscript. All authors approved the final manuscript as submitted and agree to be accountable for all aspects of the work.

Conflicts of Interest Disclosures

The authors have no conflicts of interest relevant to this article to disclose

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Limitations: Few articles controlled for BLLs at age younger than 5 years, limiting conclusions about the relation between later BLLs and outcomes

Conclusions: BLLs <10 μg/dL in school-age children and adolescents may be associated with negative outcomes. This review highlights areas that could benefit from additional investigation.

Article Summary

This scoping review summarizes the current literature on the effects of blood lead levels <10 μg/dL in school-age children and adolescents.

Introduction

Lead is a toxic element present in the Earth's crust and human activities.[1] It is ubiquitous in both indoor and outdoor environments. Children are particularly susceptible to the harmful effects of lead due to their behavior and the essential development that occurs during childhood. Recently, there has been increased activity in programs aiming to test and remediate lead hazards in schools to reduce lead exposures among school-age children.[2,3] Potential sources of lead exposure in schools include lead-contaminated water, lead-based paint in older school buildings, lead-contaminated soil, and lead-containing playground equipment and surfacing.[4,5]

While there has been a particular focus on lead exposures among children under the age of 6 due to their rapid development and known vulnerability to lead,[6] there is not as much understanding of the effects of lead exposure, particularly at low to moderate levels, during later childhood. As children grow, they ingest fewer environmental toxins per kilogram of body weight.[7] Older children often outgrow hand to mouth behaviors and spend less time on the floor and ground, which can result in a reduction in lead exposure. Development also differs between younger and older children. For example, the brain grows most rapidly in the first years of life and reaches 90% of its adult size by age 6.[8] The brain is particularly susceptible to the effects of toxins during this period of rapid development.[9] A better understanding of the effects of low to moderate blood lead levels (BLLs) during school age could inform current initiatives focused on lead. To support public health programs and decision-making, we conducted a scoping review on the effects of BLLs <10 μg/dL in school-age children and adolescents.

Methods

We searched Medline, Embase, Global Health, CINAHL, Scopus, and Environmental Science Collection databases for articles published between January 1, 2000, and May 11, 2023. Search criteria included key words and medical subject headings (MeSH) related to lead (e.g., lead exposure, blood lead, lead poisoning), school-age children and adolescents (e.g., child, pediatric, school age), and outcomes of interest (e.g., cognition, academic performance, crime). Full search criteria are included in Supplemental Table 1. We identified additional relevant studies by screening the references of included articles and review articles on lead.

We included peer-reviewed articles available in English that presented data on the effect of BLLs <10 μg/dL in individuals between the ages of 5 and 18 years. The outcome studied could be at any age after the BLL was tested. We excluded articles if they did not include an estimate of the association between individual BLL and an outcome, or if they did not report the BLLs in the sample. For example, studies that examined aggregated measures of BLLs and outcomes, for instance at the census tract level, were excluded. Studies that included children or adolescents with BLLs >10 μg/dL, or individuals under the age of 5 years or over the age of 18 years, were only included if they presented some results that met inclusion criteria (i.e., restricted to children with BLLs <10 μg/dL drawn between the ages of 5 and 18 years). Studies that did not list a maximum BLL in the sample were excluded if, based on the parameters presented, it seemed likely that the distribution included values >10 μg/dL (e.g., a sample with a mean BLL of 8.0).

We first screened titles and abstracts of database search results. Next, we screened the full texts of relevant articles to determine if they met inclusion criteria. For selected articles, we abstracted data on country, population, analytic design, sample size, age range, BLL, outcomes, covariates, and results. For analytic design, we abstracted the design of the analysis that met our inclusion criteria, not necessarily of the overall study. If a prospective cohort study only had results on BLLs and an outcome that were measured concurrently, we listed it as a cross-sectional analytic design. We used the study results and perceived likelihood of bias to classify the strength of the evidence in each article as no evidence of an association, some evidence of an association, and strong evidence of an association. To ensure the accuracy of the data abstraction, data were abstracted from each article twice (AP, MS, CC, SC contributed to the abstractions).

We followed the PRISMA extension for scoping reviews (PRISMA-ScR) guidelines.[10] This activity was reviewed by the Centers for Disease Control and Prevention (CDC) and was conducted consistent with applicable federal law and CDC policy.

Results

The database searches resulted in 3,094 non-duplicate references (Figure 1). We identified an additional 86 references to screen from the reference lists of included articles and from review papers on lead. Of the 3,180 reviewed papers, 2,578 were excluded after title and abstract review. We reviewed the full texts of 602 papers. Of these papers, 487 were excluded because they did not meet inclusion criteria. Common reasons for exclusion after full text review were no reported measures of blood lead during school age (n=50), no reported outcomes at age 5 years or older (n=18), no analytic results restricted to the ages and BLLs of interest (n=268), not an original research study (n=48), and not available in English (n=43). Ultimately, 115 articles met the inclusion criteria.

Studies were conducted in 28 different countries and most frequently took place in the United States (n=36), the Republic of Korea (n=21), China (n=13), and Russia (n=6) (Supplemental Table 2). There was a wide range in the types of populations included in studies. It was most common for studies to include children and adolescents with no known environmental exposure to lead. Some studies were conducted among specific ethnic or cultural groups such as studies among Inuit children in the Canadian Arctic or children from the Akwesasne Mohawk Nation.[11–14] Thirty-five studies were conducted among, or included, children or adolescents with potential industrial exposures to lead, such as children living near lead smelters or mines.[15–49] The most common analytic design was cross-sectional (n=94, 82%); fewer analyses were from case-control studies (n=13, 11%) or prospective cohort studies (n=14, 12%) (Table 1).

The reported mean, geometric mean, or median BLL was <5 μg/dL in 98 articles (85%); of which it was <2 μg/dL in 58 articles (Supplemental Table 2). Almost all outcomes examined could be categorized into one of 15 general groups (Table 1). The outcome group with the greatest number of studies was Intelligence Quotient (IQ) (n=25, 22%), followed by neurocognitive and neurobehavioral function other than IQ (n=24, 21%), and attention-deficit/hyperactivity disorder (ADHD) diagnoses and behaviors (n=22, 19%). The examined outcomes of gut microbiome,[50] insulin-like growth factor 1 (IGF-1),[34] and toxocariasis[51] did not fit into any of the larger categories. We did not identify any articles that looked at the outcomes of crime or juvenile detention even though they were included in the search terms.

When classifying the strength of evidence in an article, articles classified as providing strong evidence of an association typically presented elevated effect estimates adjusted for important covariates accompanied by confidence intervals excluding the null value. Some of the articles in the strong evidence category also presented a dose-response relationship between BLL and the examined outcome.

Of the 115 included articles, 89 (77%) presented findings that provided some evidence of a potential association between BLL <10 μg/dL during school age and detrimental outcomes and 20 (17%) provided strong evidence of an association. There was some evidence suggesting a detrimental impact of lead for each of the 15 outcome categories examined. The strongest evidence of an adverse association was for the outcome categories of IQ and ADHD diagnoses or behaviors. Out of the 25 articles with results on IQ, 8 (32%) presented strong results of an association with school-age lead[16, 23, 41, 47, 52–55] while the remaining articles presented either some or no evidence of an association. A prospective cohort study by Skerfving and colleagues examined the association between lead exposure at ages 7–12 years and IQ at ages 18–19 years in 3,176 children.[47] When adjusting for covariates, and restricting the sample to children with BLL <5 μg/dL, they observed a negative association between BLL and IQ. Out of the 22 articles with results on ADHD diagnoses or associated behaviors, 5 (23%) presented strong evidence an association with school-age lead.[19, 56–59] For example, using data on 2,588 children and adolescents from the U.S. National Health and Nutrition Examination Survey (NHANES), Froehlich and colleagues observed a dose response relationship between BLLs among adolescents ages 8 to 15 years and ADHD diagnoses.[57] They found that compared to adolescents with BLL 0.2–0.8 μg/dL, the odds of receiving an ADHD diagnosis were 1.7 times greater among adolescences with BLL 0.9–1.3 μg/dL (95% Confidence Interval [CI]: 1.0, 2.9), and 2.3 times greater among adolescences with BLL >1.3 μg/dL (95% CI: 1.5, 3.8) when adjusting for covariates.

The outcome of behavior had a single study demonstrating strong evidence of an association and the outcome of neurocognitive and neurobehavioral function other than IQ had 2 studies demonstrating strong evidence of an association. However, for both outcomes a high proportion of studies provided some results suggesting an association (78% and 63%, respectively). As an example of one of the studies providing some evidence of an association, a study conducted by Joo and colleagues among 271 Korean children observed evidence of an association between low BLLs and behavioral problems when adjusting for covariates, but only among girls and not among boys.[60] There was less evidence of an association with school-age lead levels for the other outcome categories, either due to fewer studies examining the outcomes in the category (i.e., 5 or fewer studies) or fewer studies with evidence of an association (i.e., 45% or more of studies providing no evidence of an association).

Common threats to the quality of included articles were lack of control for BLL in early life, which are known to be related to many of the outcomes examined, and inability to determine the temporal sequence between exposure and outcome. Only 3 studies (3%) took into account in their analysis the effects of lead exposure before the age of 5 (e.g., BLLs measured at ages 2–3).[52, 61, 62] The majority of articles (n=99, 86%) did adjust results for other potential confounders like sex, age, and parental characteristics such as parental IQ or education. Only 14 of the included studies (12%) had any measurements of BLL and the outcome of interest at different timepoints.[34, 38–40, 43, 47, 61, 63–69] All other studies determined the exposure and outcome concurrently so were unable to determine whether the documented BLLs preceded the outcome.

Discussion

The articles identified in this review indicate that low to moderate BLLs in school-age children and adolescents may be associated with detrimental effects on a breadth of outcomes. Outcomes with the strongest evidence for an association were IQ and ADHD diagnoses and behaviors. This review suggests that preventing exposure to lead, even at low levels, continues to be important throughout later childhood and adolescence.

A strength of the literature on this topic is the study variety. Articles in this review sampled children and adolescents of different ages and backgrounds from diverse populations in 28 different countries. Given the large number of included studies and the wide range of outcomes examined, we classified outcomes into 15 groups to facilitate describing the overall results of studies. These groups are heterogeneous and thus there is likely heterogeneity in the association between BLLs and the specific outcomes in any one outcome grouping. Additionally, the specific age window of susceptibility for different outcomes may vary. The details in Supplemental Table 2 can aid readers seeking more detail for specific outcomes. Likewise, the threshold for what we considered to be a study providing “some evidence” of an association between BLLs and an outcome of interest was low. For example, a study examining 10 different subscales or domains for a given outcome could easily observe associations between BLLs and one or two subscales by chance alone. We encourage readers to draw their own conclusions about the state of the evidence in the articles compiled in this review.

One topic that was absent from the included studies was investigation into the main routes of low lead exposure among school-age children. Some of this is due to lack of data availability, for example large national surveys are unable to complete environmental investigations for all study participants. However, smaller studies could conceivably ask questions or complete investigations related to sources of lead exposure. Information on the main sources of lead exposure among school-age children with low BLLs could be helpful for prioritizing remediation activities in communities.

BLLs most closely represent recent lead exposure and are not good estimates of cumulative lead doses over a longer period of time.[70] A single measure may poorly reflect longer-term exposure patterns. There is no way to establish from a cross-sectional study whether the detected BLL caused, or even preceded, the outcome of interest. Likewise, a child with an undetectable BLL during school age may have had a higher BLL in early life that may be related to their current condition. These considerations are most relevant for outcomes that develop over a long period of time such as the timing of puberty or a child's anthropogenic measurements. It is also possible that certain outcomes may increase the likelihood that a child consumes lead by changing a child's behavior, such as pica. Such reverse causality is unidentifiable in a study where exposure and outcome are measured concurrently. These nuances emphasize the importance of longitudinal data, including data on BLLs during the first years of life, to disentangle these complicated relationships. Although there is a large body of literature on the impact of BLLs during school age on a wide range of outcomes, there is limited literature that can establish temporality between BLLs and outcomes of interest.

This review has limitations to consider. First, although our search terms included a wide range of outcomes, it is unlikely that they include every outcome that could possibly be related to lead. We may have missed certain groups of publications due to missing key words in our search criteria. Second, 268 articles were excluded because, although they assessed the impact of low to moderate BLLs in school-age children, they did not present results that combined the BLLs and ages of interest specified in our inclusion criteria. We did not contact the authors of these studies to inquire about the availability of additional analyses or data that may have met the inclusion criteria. The reference list of these publications is available from the authors upon request for any researchers aiming to complete meta-analyses on this topic. Lastly, while we assessed specific characteristics that influence study quality, we did not quantitatively assess and present results on the study quality of each of the included articles. This was partly due to the heterogeneity between study outcomes and their differences in availability of objective measurements. Studies including a more limited scope of outcomes could address these issues more comprehensively.

This articles in this review can help support initiatives focused on reducing lead exposure among school-age children and adolescents. Future research on this topic could better control for the known effects of early-life lead exposure and better determine the temporality between BLLs and outcomes of interest. Understanding the impact of lead among school-age children and adolescents can help us protect them from the harmful effects of lead.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Abbreviations

ADHD	attention-deficit/hyperactivity disorder
ASD	autism spectrum disorder
BLL	blood lead level
CI	confidence interval
IQ	intelligence quotient

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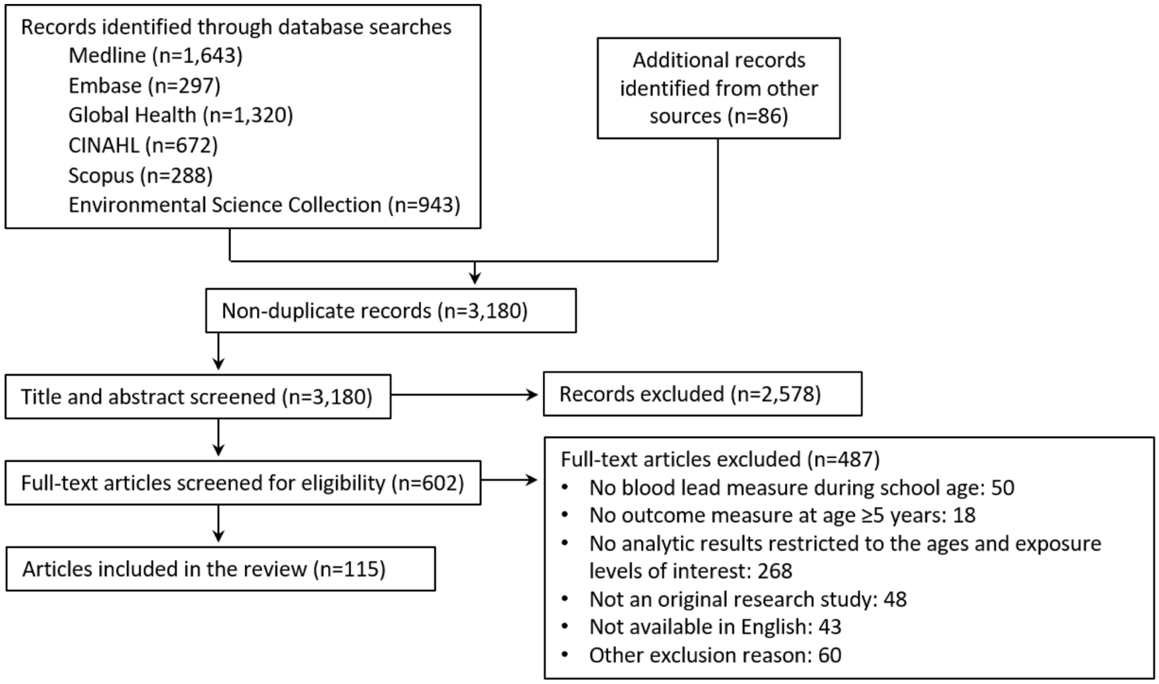

Figure 1.

Flow chart of selected studies

Table 1.

Characteristics of included studies (n=115)

Characteristic	n (%)	References
Sample Size		
<100	9 (8%)	
100–500	63 (55%)	
501–1,000	18 (16%)	
>1,000	25 (22%)	
Analytic Design[a]		
Case-control study	13 (11%)	
Cross-sectional analysis	94 (82%)	
Prospective cohort study	14 (12%)	
Outcome Category[b]		References
ADHD diagnoses and behaviors	22 (19%)	14, 19, 48, 54, 56–59, 62, 64, 71–82
Allergic outcomes	3 (3%)	83–85
Anthropometry	5 (4%)	31, 65, 69, 86, 87
ASD diagnoses and behaviors	4 (3%)	66, 73, 88, 89
Behavior	14 (12%)	14, 22, 24, 43, 48, 56, 60, 62, 63, 67, 68, 88, 90, 91
Cardiovascular outcomes and risk factors	11 (10%)	88, 92–101
Genetic (e.g., gene expression)	2 (2%)	26, 41
Immune function	2 (2%)	32, 46
IQ	25 (22%)	15–17, 23, 26, 27, 35, 36, 41, 45, 47, 49, 52–55, 59, 61, 62, 89, 102–106
Metabolism, vitamin, or protein-related outcomes	4 (3%)	15, 29, 107, 108
Neurocognitive and neurobehavioral function (other than IQ)	24 (21%)	13, 18, 20, 21, 36, 37, 42, 44, 45, 48, 49, 62, 71, 77, 88, 89, 102, 105, 109–114
Oral health	3 (3%)	28, 115, 116
Organ function (e.g., renal, kidney)	7 (6%)	15, 25, 30, 97, 117–119
Puberty onset and reproductive hormones/function	12 (10%)	11, 12, 33, 38–40, 120–125
School performance and learning disabilities	5 (4%)	47, 56, 77, 78, 126
Other[c]	3 (3%)	34, 50, 51

ADHD=attention-deficit/hyperactivity disorder, ASD=autism spectrum disorder, IQ=intelligence quotient

[a]Percentages do not add up to 100 because some articles reported analyses in >1 category. Analytic design was determined by analysis type and not study design. For example, some analyses from prospective cohort studies were classified as cross-sectional if the exposure and outcome from the analysis that met the inclusion criteria were determined concurrently.

[b]Percentages do not add up to 100 because some articles reported outcomes in >1 category

[c]Includes gut microbiome, insulin-like growth factor 1 (IGF-1), and toxocariasis