Eco-Environment & Health 4 (2025) 100127

Contents lists available at ScienceDirect

Eco-Environment & Health

journal homepage: www.journals.elsevier.com/eco-environment-and-health

Perspective

A more scientific blood lead reference value urgently needs to be updated in China: From a national and international insight

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ARTICLE INFO

Keywords:
Blood lead level
Blood lead reference value
Update
Lead exposure
Children

ABSTRACT

Although blood lead levels (BLLs) in children have significantly decreased compared to two decades ago, incidents of lead poisoning and elevated BLLs among children continue to occur frequently. This trend suggests that China's current hygienic regulations are not sufficiently effective in managing children's lead exposure. This study analyzed the revision processes of blood lead reference values (BLRVs) in children from various countries, the current BLLs and their changing trends in China, potential sources of lead pollution and exposure, the requirements for managing and protecting children's health, as well as the national measures and strategies for lead emission management and control. The study also explored the necessity and urgency of updating China's BLRVs in children. Based on the specific conditions in China, a proposed BLRV of 50 μg/L was deemed more reasonable and was suggested for implementation, with the potential to yield substantial economic benefits through improved IQ outcomes should the updated BLRV be adopted.

1. Does childhood lead exposure remain a critical public health issue?

There is overwhelming evidence that lead exposure poses a significant threat to human health, with children being particularly vulnerable when exposed to lead at high or low levels [1–3], and children's lead exposure remains a critical global concern [3–5] due to its substantial toxicity and harmful effect [6]. Among the 88 risk factors contributing to the global burden of diseases, lead stands out as the only heavy metal in the top 25, increasingly impacting disability-adjusted life-years [7]. The United Nations has issued a warning that one in three children suffers from lead poisoning, which happens overwhelmingly in Asia [8]. According to recent reports from the United Nations Children's Fund, lead exposure is responsible for 1.5% of annual global deaths, around 900,000 fatalities, and up to approximately 800 million children whose blood lead levels (BLLs) were 5 μg/L or higher. Each year, over 5 million children aged 0–14 die from diseases linked to environmental factors, including lead exposure [9], predominantly in developing nations [10,11] Alarmingly, BLLs in children in low- and middle-income countries remain dangerously high [6]. In China, a significant number of children aged 3–5 (3.7 million, 2.7%) and 6–11 (3.0 million, 1.8%) have BLLs exceeding 50 μg/L [12], which are significantly higher than those observed in the USA and many European countries [13,14]. Thus, the control and prevention of lead exposure in children continue to be a formidable and crucial public health challenge, particularly in China.

2. How to control blood lead levels in the pediatric population?

A scientific BLRV is essential for crafting effective public health policies that regulate BLLs in children. Such BLRV can serve as a foundational and effective policy tool for the prevention of lead exposure in children. The BLRV for children does not function as a clinical threshold that delineates an acceptable range of BLLs. Instead, it is utilized to pinpoint children with elevated BLLs, typically those at the upper echelon of the population's blood lead distribution. This identification facilitates targeted preventive measures and the evaluation of their

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https://doi.org/10.1016/j.eehl.2024.10.003
Received 4 August 2024; Received in revised form 21 October 2024; Accepted 30 October 2024
Available online 29 November 2024
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effectiveness. The BLRV functions as a statistical indicator based on the distribution of lead content in the blood, classifying individual results as "elevated" or "not elevated". Thus, many countries have adjusted their BLRVs to enhance child health protection, considering both current BLLs in children and the urgency of the matter. For instance, the USA lowered its BLRV for children aged 1–5 from 50 μg/L in 2010 to 35 μg/L in 2018, marking the top 2.5% of children aged 1–5 with elevated BLLs, as determined by NHANES [13]. Similarly, France has set a reference intervention level of 50 μg/L for children aged 0.5–6 [15], Japan at 40 μg/L for children aged 1–6 [16], Germany at 35 μg/L for children aged 3–5 [17], and South Korea at 22.5 μg/L for children aged 3–5 [18], to protect the majority of the population. The rationale behind these downward adjustments in high-income countries is the observed decline in BLLs, as depicted in Fig. 1. Adopting a lower BLRV could significantly benefit a considerable number of children by facilitating early intervention and management of lead exposure from diverse sources, as evidenced by the case study in North Carolina [19]. Accordingly, certain health benefits associated with lead exposure can be obtained, such as a decrease in disability-adjusted life-years in the USA from 4.38 in 1999 to 3.41 in 2019 and a 19.19% decrease in the age-standardized disability-adjusted life-years rates of idiopathic developmental, intellectual disability attributable to lead exposure in high-income regions of North America [20,21].

3. Are the current BLRV for children in China effective in controlling the health risks of childhood lead exposure?

While most children in China now have BLLs lower than the current BLRV of 100 μg/L [4,12], signifying the existing BLRV may not be effective in protecting children's health and might warrant revision. Over the past two decades, BLLs in children have declined significantly because of the phasing out of leaded gasoline. However, there has been a trend of slight increase or plateauing in BLLs observed after 2015 [22]. A comparison with the current BLRV of 100 μg/L for children of all ages in China [23] revealed that only 0.5% (0.7 million) of children aged 3–5 years and 0.1% (0.1 million) of children aged 6–11 years old were found to have BLL exceeding 100 μg/L [12]. This indicates that the majority of children have BLLs that are considered relatively low and not elevated, thus not in need of case management based on experiences from blood lead control in China and other developed countries. Paradoxically, the current average BLLs in Chinese children remain higher than those in the USA and European countries [13,14,24]. Additionally, lead exposure ranked 14th and 15th among the risk factors contributing to mortality and disability-adjusted life-years in China in 2017 [25]. Furthermore, although the prevalence of lead poisoning incidents among children

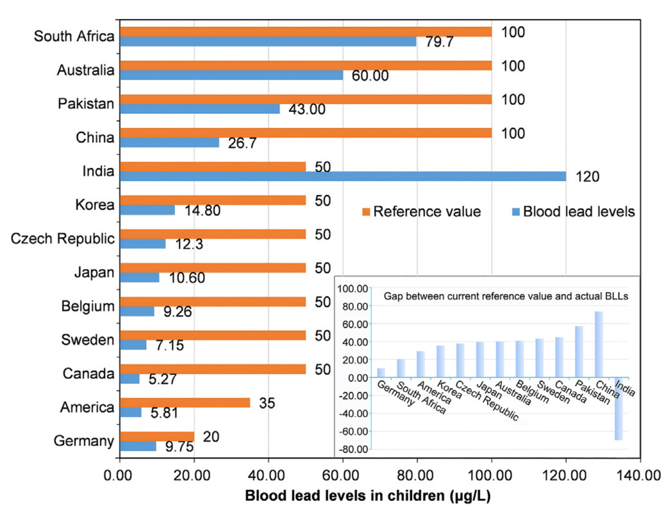

Fig. 1. Blood lead levels and its reference value in children from different countries.

generally declined from 2009 to 2019, certain regions such as Guizhou [26], Gansu [27] and Hunan Province [22], home to lead-related industrial activities like smelting and mining communities, coking plants, e-waste recycling, and coal-fired power plants, continue to face severe environmental lead pollution and high levels of lead exposure for children [28–30]. Notably, neurotoxic effects have been documented even at the lowest lead concentration, making it impossible to establish a safe exposure threshold [3]. Therefore, current evidence suggests a continued need for vigilance, highlighting a significant gap between the management of BLLs in children based on the current BLRV and the actual adverse effects of lead exposure. Consequently, the absence of scientifically sound and efficient regulations and management tools, such as an updated BLRV, could potentially heighten the risk of lead exposure among the population [6].

The poor compatibility of environmental standards with the current hygienic guidelines in lead exposure management poses a significant challenge in protecting children's health in China, implying that the existing BLRV for children may be inadequate. We assumed that Pb concentration in each environmental medium complies with the minimum or maximum thresholds set by the current environmental quality standard. Using the exposure factors related to various exposure pathways [31,32], the Integrated Exposure Uptake Biokinetic (IEUBK) model and health risk assessment model developed by the US EPA were applied to calculate the BLLs and non-cancer risks of children, respectively, as detailed in the Supplementary Information (SI). Our analysis revealed that when the lead concentration was at the minimum threshold of each environmental quality standard, 0.6% of children had elevated hazard quotient (HQ) and 4.1% had BLL exceeding 100 μg/L. Conversely, if the lead content reached the maximum threshold of each standard, these proportions rose to 33.2% and 75.3%, respectively, as presented in the SI. While these two scenarios may not capture all the real-world complexities and are subject to certain uncertainties in estimation, the findings suggest substantial variations in the population at high risk of lead exposure on the basis of current BLRV of 100 μg/L and the thresholds set in environmental quality standards. This discrepancy underscores a lack of coordination and consistency between the BLRV and environmental quality standards, compromising efforts to safeguard children's health from lead exposure. Therefore, the absence of scientifically sound and efficient regulations and management tools, such as an updated BLRV, could potentially increase the risk of lead exposure among children.

4. How should we set a more scientific BLRV for children, and what are the benefits?

A much lower and scientific BLRV of children in China could be modified by relevant hygiene authorities, informed by the BLLs obtained from the China National Human Biomonitoring (CNHBM) in 2017 and recent improvements in environmental quality. Data from the CNHBM revealed that the 97.5th percentiles of the BLL distribution were 50.95 μg/L and 45.87 μg/L, respectively, for the children at 3–5 and 6–11 years old [12]. In terms of the successful experience of lead control measures [33] and BLRV revision in developed countries like France and the USA, the US CDC has lowered the BLRV from 50 μg/L to 35 μg/L, in order to identify children with BLLs in the top 2.5%, which are significantly higher than the majority, based on the latest two rounds of the NHANES and Morbidity and Mortality Weekly Report [13]. Thus, a BLRV of 50 μg/L in China could serve as a public health benchmark to pick out the ones in the highest 2.5% of children from the blood lead testing, which would be conducive to either maintaining or reducing the BLLs of children in the future. Considering the decreasing trend in BLLs among Chinese children from 2006 to 2022, with an average BLL of 17.01 μg/L and an estimated 6.7 million children aged 3–11 having BLLs above 50 μg/L in 2018 [12], alongside the reduction in environmental pollution such as national $PM_{2.5}$ pollution and exposure during 2013–2020 [34], aligning with the national goals of "Beautiful China" "Healthy China" and "Carbon peaking and carbon neutrality", it is time to renew the BLRV for children in China. Therefore, some scholars have proposed revising the BLRV for Chinese children to 50 μg/L based on these data, including the proportions exceeding 50 μg/L (6.0%) in 2018, as well as the associated disease burden of BLLs over 50 μg/L (0.41 million person-years) [12]. On the other side, the gaps between actual BLLs of children and their relative BLRV in typical developed countries range from 10.2 to 44.7 μg/L with a mean value of 34 μg/L (Fig. 1). If China adopts a BLRV of 50 μg/L for children under age 6, the 33 μg/L gap between actual BLLs in 2018 and the updated BLRV would align with observations in other developed countries that have successfully reduced children's BLLs. However, the updated BLRV would likely reveal inequalities and disparities in BLLs at regional and provincial levels, as well as a rise in the percentage of children who have BLLs exceeding the BLRV. It was reported that approximately 6.7 million children had BLLs above the value of 50 μg/L [12], mostly in the regions with lead or zinc mineralization belts and heavy industries (especially non-ferrous metallurgy, which would release a large amount of non-ferrous metals during the process of smelting with raw materials such as ores and concentrates), and could be intervened through national industrial restructuring [35].

The identification of approximately 6.7 million Chinese children aged 3–11 years with BLLs above this cut-off value of 50 μg/L should stimulate targeted lead education, environment assessments, and enhanced medical surveillance. The potential health benefits from the regulation of children's BLL following an updated BLRV are substantial. Scholars have postulated that a reduction of 10 μg/L in blood lead concentration can enhance cognitive function, with improvements in IQ points ranging from 0.185 to 0.323. Each incremental increase in IQ points correlates with a productivity boost of 1.76%–2.38% in the workforce [36,37]. For instance, the socioeconomic benefits from BLL reductions among 3-to-5-year-old children between 2000 and 2018 were estimated by evaluating the productivity gains resulting from cognitive enhancements, as illustrated in SI. According to the China Statistical Yearbook of 2019, the average annual wage in China was 82,413 yuan. Taking into account a 5% discount rate over a 40-year working lifespan, the cumulative and discounted economic benefits per child in the future could amount to 9.96 million yuan. The economic loss of childhood lead exposure has notably diminished due to the considerable decline in BLLs from 2000 to 2018. When these findings are extrapolated to the 35,424,119 children aged 3–5 years, according to the Seventh National Population Census, the potential annual economic gain could range from 7.03 trillion to 16.59 trillion yuan.

5. Is the updated BLRV for children enforceable and implementable?

The scientific identification of pollution sources is essential for the prevention and management of lead exposure, particularly among the top 2.5% of the population with elevated blood lead levels, and is especially relevant when employing the updated BLRV. Humans can be exposed to lead through various environmental media, including air, water, food, soil, dust [30,38–40], and other sources such as lead-based paint [41]. Lead accumulating in the above environments is mainly from coal combustion [38], the use of lead-containing products, and lead-related manufacturing [42]. Source apportionment of lead exposure, using reliable methods like isotope techniques, has revealed that industrial emissions, the use of raw materials, and fuel combustion are the main sources of exposure for children living in specified areas with the aforementioned lead-related industrial activities [28,38]. Historically, leaded gasoline and lead-based paint were the predominant sources of lead in the environment and human body worldwide before the twentieth century [43,44], as a substantial body of evidence has indicated that the decrease in BLLs in children was related to the reduction in the use of these products [35,45,46]. In high-income countries such as the USA, Australia, and France, following the phase-out of leaded gasoline, the main sources of lead exposure have shifted to older houses, paints, imported ceramics, cosmetics, and so on [45,47]. In China, lead-based paint is not extensively used in the housing stock, and most residents live in dwellings constructed after the ban on lead-based paint [12]. Although the use of "folk remedy" containing lead powders (litargirio, litharge, PbO, Pb_3O_4) for children's skincare and oral ulcers has been strongly associated with the BLLs in children, it only occurred in some rural areas in the north-eastern and southeastern parts of China.

Household coal combustion, alongside non-ferrous smelting and coal-fired power plants, has become a significant contributor to atmospheric lead emissions [48,49]. Lead-bearing substances like biomass fuels and coal are predominantly used as domestic fuels in rural regions, with a utilization rate of 31% in rural versus 13% in urban settings [31,32,50]. Our literature review indicates that Chinese coal exhibits a relatively high level of lead, with an arithmetic mean of 27.05 μg/g and a weighted mean of 14.03 μg/g, due to its uneven distribution of reserve heterogeneity (see SI). These fuels are usually burned in inadequately ventilated spaces and stoves, resulting in reduced thermal efficiency and increased lead emission [51]. Thus, following the prohibition of leaded gasoline in 2000, there was a substantial 98% reduction in Pb emissions from motor vehicle gasoline combustion in China. However, Pb emissions from non-ferrous metal smelting and coal combustion have significantly risen by 387% and 536% in all categories, respectively, from 2000 to 2018 [22]. The substantial volume of lead emissions emanating from these sources can be enriched in various environmental matrices, such as soil, dust, water, and food [52–54], and eventually, some of them enter the human body. Nationwide, children's BLLs are significantly correlated with Pb emissions from non-ferrous metals smelting ($R^2 = 0.92$) and coal combustion ($R^2 = 0.84$) [22,55]. In general areas such as Yunnan [27,30] and Gansu [38], with a combination of traffic, industries, as well as coal use, lead in children's blood was mainly sourced from coal-fired ash after leaded gasoline was phased out instead of vehicle exhaust, paint dust, and metallurgic dust. Furthermore, a slight upward trend was observed in children's BLLs from 2015 to 2018, which was in accordance with the growth of lead emissions from coal burning and non-ferrous metals smelting [22]. The co-existence of low-level environmental lead exposure but relatively high BLLs, along with fluctuant temporal and uneven spatial distribution of children's BLLS in China, could be partly due to the distribution of coal combustion and non-ferrous metal smelting activities. Therefore, unraveling the sources, production, and utilization of coal resources and non-ferrous metals in China, as well as identifying the sources of lead exposure in the human body, will help to implement the updated BLRV and take effective management of lead exposure in children, particularly for those living in areas with lead-related industrial activities.

Under the national goal of mitigating pollution and reducing carbon, the decrease in coal consumption presents an opportune and essential moment to implement the updated BLRV in the foreseeable future. By apportioning the sources of children's lead exposure, the trajectory of BLLs can be forecasted for specific timeframes, such as by 2030 or 2060, based on energy consumption plans and lead emissions from potential sources. Utilizing lead emission coefficients from various industries [22], atmospheric lead emissions were calculated and predicted from 2009 to 2030, aligning with China's targeted peak year for carbon emission (for details, refer to SI). As illustrated in

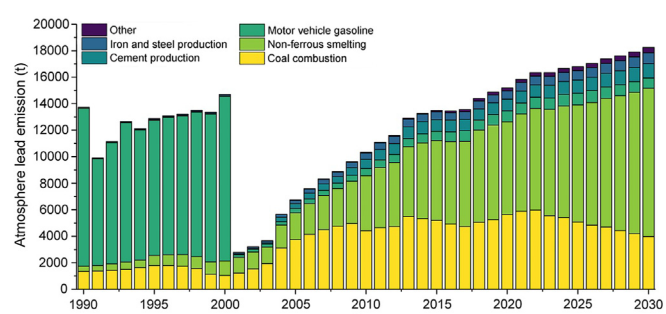

Fig. 2. Estimated atmospheric lead emission in China from 1990 to 2030.

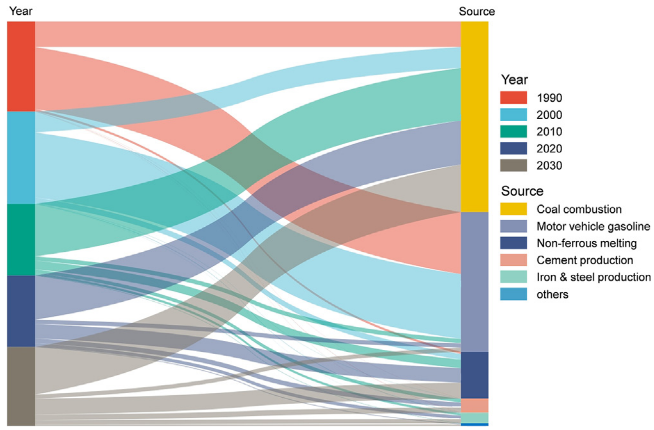

Fig. 3. The comparison of sources of atmospheric lead emissions from 1990 to 2030.

Fig. 2, atmospheric lead emissions exhibit a pattern of initial decline followed by an increase or stabilization at a certain level, with a peak occurring between 2018 and 2023, significantly surpassing pre-2000 levels. The anticipated surge in atmospheric lead emissions is primarily attributed to coal combustion and non-ferrous metal smelting, which are expected to remain substantial. In terms of exposure source of lead for children, coal combustion has played a predominant role in most regions in China [12,28], while Pb emission from non-ferrous smelting dominates in specific areas with heavy non-ferrous smelting activities [30,35,38]. In order to protect the ecosystem and public health, numerous initiatives and objectives have been formulated in recent years, such as Healthy China Action Plan and Carbon Peaking and Carbon Neutrality Goals. A key strategy to achieve these objectives involves restructuring the energy sector and optimizing industrial layouts, such as formulating a series of technical specifications for the application and issuance of emission permits in the non-ferrous smelting industry and updating pollutant discharge standards in coal-related industries. Moreover, in accordance with the China and Global Energy Outlook Report [56], coal consumption is projected to decrease by 12% in 2030 compared to 2020 (Fig. 3 and Fig. S2) in the case of coordinated development of society, economy, and ecological environment. By 2039, coal consumption is anticipated to return to the levels of 2009. Given the higher lead content in coal, along with its low thermal efficiency and higher lead release [51,57], lead exposure among Chinese children remains a critical concern in the near future. Therefore, it is imperative and reasonable to update the BLRV to 50 μg/L to regulate children's BLLs through a variety of approaches, such as policy tool formulation and pollution source management.

There is no doubt that the implementation and enforcement of lead control laws and policies are crucial efforts and effective ways of controlling children's BLLs in China. Research emphasizes that stringent legal environmental enforcement targeting emissions from coal combustion and nonferrous metals is essential, in addition to successfully phasing out lead in gasoline, paint, and other sources [22]. A comprehensive approach is necessary to minimize children's exposure to lead. Apart from updating the BLRV, conducting targeted and periodic lead testing of populations that may be at risk for lead poisoning could also be a cost-effective way to identify and monitor exposure levels. Such measures are crucial for early detection and intervention, ensuring the protection of children's health from the detrimental effects of lead exposure.

CRediT authorship contribution statement

Xiaoli Duan: Writing – original draft, Supervision, Project administration, Methodology, Funding acquisition, Conceptualization. **Suzhen Cao:** Validation, Investigation, Data curation. **Jiacheng Guan:** Visualization, Data curation. **Ligang Hu:** Writing – review & editing, Validation, Methodology. **Chengye Sun:** Writing – review & editing, Validation, Methodology. **Chonghuai Yan:** Writing – review & editing, Methodology, Investigation. **Xiaoli Zhao:** Writing – review & editing. **Fengchang Wu:** Writing – review & editing.

Declaration of competing interest

The views expressed in this manuscript are solely of the authors and do not necessarily reflect those of the funding agencies. Additionally, we declare that we have no financial and personal relationships with other organizations that can inappropriately influence our work.

Acknowledgements

This work was supported by the National Key Research and Development Program of China (2022YFC3701303, 2022YFC3702604), National Natural Science Foundation of China (41977374), Chinese Academy of Engineering Strategic Research and Consulting Project (2024-XZ-42).

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.eehl.2024.10.003.

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