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# Probabilistic modeling of aggregate lead exposure in children of urban China using an adapted IEUBK model

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## HIGHLIGHTS

- A probabilistic method based on IEUBK model was developed under data limitations.
- Sensitivity analysis was performed to explore influence of parameters.
- Source allocation for lead exposure in Chinese urban children was estimated.

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## ABSTRACT

Lead, a ubiquitous pollutant throughout the environment, is confirmed to be neurotoxic for children by pulmonary and oral routes. As preschool children in China continue to be exposed to lead, we analyzed the available biomonitoring data for preschool children in urban China collected in the period 2004–2014 through a literature review. To identify apportionment of lead exposure sources for urban children in China, we modified the IEUBK model with a Monte Carlo module to assess the uncertainty and variability of the model output based on limited available exposure data and compared the simulated blood lead levels with the observed ones obtained through literature review. Although children's blood lead levels in urban China decreased statistically over time for the included studies, changes in blood lead levels in three economic zones and seven age groups except for two age-specific groups were no longer significant. The GM-predicted BLLs and the GM-observed BLLs agreed within 1 μg/dL for all fourteen cities. The 95% CIs for the predicted GMs and the observed distribution (GM ± GSD) overlapped substantially. These results demonstrated the plausibility of blood lead prediction provided by the adapted IEUBK model. Lead exposure estimates for diet, soil/dust, air, and drinking water were 12.01 ± 6.27 μg/day, 2.69 ± 0.89 μg/day, 0.20 ± 0.15 μg/day, and 0.029 ± 0.012 μg/day, respectively. These findings showed that the reduction of lead concentrations in grains and vegetables would be beneficial to limit the risk of dietary lead exposure for a large proportion of preschool children in urban China.



## 1. Introduction

Lead is a ubiquitous pollutant throughout the environment and a confirmed neurotoxin, which is mainly absorbed by pulmonary and oral routes in humans. Blood lead levels (BLLs) of children have reduced sharply over the last three decades in developed countries due to the success of environmental policies (Schulz et al., 2007; U.S. CDC, 2013; Etchevers et al., 2014). Although the BLLs in Chinese children 0–18 years of age reduced substantially from 9.05 μg/dL in 1993 to 5.76 μg/dL in 2011, this reduction was slightly lower and fluctuant compared with U. S. and European children (Li et al., 2014b). An estimated 12.6% of Chinese children has BLLs above 5 μg/dL (Li et al., 2014b), suggesting that a relevant fraction of children is still experiencing a significant lead exposure.

Information on site- and age-specific BLLs in the general population of preschool children in China need to be carefully reviewed for children since BLLs have profound effect on the main burden of IQ loss (Lanphear et al., 2005). It is therefore important to gain a deep understanding of exposure conditions and to screen situations with potential for significant exposure. As leaded gasoline hazard is controlled or eliminated from on-road vehicles in China since 2000s, other lead sources, including leaded-paint, soil and household dust, and tap water, assume a greater importance in determining the total lead exposure (Lin et al.,

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2009; Chen et al., 2012a). Previous studies were performed in regions with significant point sources such as battery plants and coking plants (Chen et al., 2012b; Cao et al., 2014; Li et al., 2016). Identifying apportionment of lead exposure sources is essential to design prevention strategies and to control environment exposure also in contexts where contamination hot-spots are not present but exposure might be anyway significant, such as the general urban environment of Chinese cities.

One of the prerequisites for developing policies aimed at reducing the overall exposure to lead and eliminating elevated BLLs (BLLs ≥10 μg/dL) is an accurate assessment of the contribution from multiple exposure sources. Lead isotopic fingerprinting technique seems to be promising as it can provide high-precision measurements for source identification and apportionment of pollution sources from a relatively small number of samples. However, due to its high cost and labor-intensive nature, the use of isotopic fingerprinting is often restricted (Smith et al., 1996). Moreover, isotopic fingerprinting is limited in the cases where potential lead sources have widely different isotopic signatures or are relatively weak (Cheng and Hu, 2010). Biokinetic models have been applied to predict potential risks to human from chemical exposure, to establish chemical remediation levels, and to develop future scenarios for decision makers (Griffin et al., 1999a; Buur et al., 2008). Four biokinetic models have been commonly used to predict BLLs from lead exposure through multiple environmental media, including: (1) the Integrated Exposure Uptake Biokinetic (IEUBK) model (White et al., 1998); (2) the International Commission on Radiological Protection (ICRP) model (Leggett, 1993); (3) the O'Flaherty model (O'Flaherty, 1998); and (4) the MERLIN-Expo model (Fierens et al., 2016). Previous studies have compared and evaluated these models (U.S. EPA, 2006).

The IEUBK model can easily be recoded and developed to be a probabilistic model for quantifying the impact of variability and uncertainty in input parameters as the model source code is available to the users (U.S. EPA, 1994b). The IEUBK model was empirically validated in the U.S. young children with BLLs below 30 μg/dL (U.S. EPA, 1994a; Hogan et al., 1998). However, the IEUBK model is not widely used in China probably because of discrepancies in the exposure parameters between U.S. and Chinese children (Wang et al., 2011; Li et al., 2016). In addition, the model output can be strongly affected by errors caused by input uncertainties, boundary conditions, and initial conditions among site-specific data and exposure parameters. Much attention has been focused on the parameter uncertainty issues in IEUBK model and their effects on model performance (Goodrum et al., 1996; Dong and Hu, 2011). Monte Carlo-based method is a technique for randomly sampling from a probability distribution, and was implemented in IEUBK model to quantify parameter uncertainties (Goodrum et al., 1996; Griffin et al., 1999b). Furthermore, Dong and Hu (2011) utilized Markov Chain Monte Carlo simulation to assess parameter uncertainties in combination with Bayesian inference by estimating the true posterior distribution for model parameters conditioned on observations from literature. The recent availability of new data about children exposure parameters in China offers an opportunity to reassess children exposure to lead particularly after the dietary habits changed in recent years (Wang et al., 2016). The assessment of probability distributions for key model parameters and parameter uncertainty analysis in the modeling of lead exposure and biokinetics is currently desirable and useful to gauge the reliability and precision of predicted BLLs for Chinese children. In the present study we provided a systematic review of epidemiological studies on blood lead screening for specific age group of preschool children in Chinese urban areas since the removal of lead from gasoline. We also reviewed data on external exposure to lead corresponding to the selected subgroups. We performed analyses of children BLLs in selected subgroups defined by geographic region and age. Ultimately, we examined the relationship between external exposure and biomonitoring data by using a probabilistic IEUBK model, and estimated the contribution of multiple pathways to the overall lead exposure among Chinese children aged 0–7 years, considering uncertainty and variability of available exposure data and updated population exposure parameters.

## 2. Materials and methods

### 2.1. Biomonitoring data

We conducted a systematic literature search of China National Knowledge Infrastructure (CNKI) and Web of Science to identify epidemiologic studies of BLLs of children aged 0–7 years old in China. It took nearly four years for Chinese government to completely remove leaded gasoline nationwide since 2000 (Yan and Shen, 2008). For evaluating exposure levels and sources after the introduction of lead-free gasoline, we limited our search to studies published between January 2005 and January 2016. We selected only studies based on a stratified sampling scheme with sample size larger than 500. Studies were included when measurements were performed in capillary or venous blood under stringent quality assurance and quality control. Preference was given to results reporting detailed statistical information suitable to calculate geometric mean (GM) and geometric standard deviation (GSD) of BLLs. Epidemiological studies carried out in rural areas were excluded because of the differences in exposure conditions between rural and urban children. Where multiple publications included overlapping populations in the same region, we included the publication that considered the largest sampling size. A total of 28 studies were eligible to be included in this study. The full list of selected references is available in Table S1 of Supplemental Materials.

The BLLs from each individual study were assumed to follow the lognormal distribution (Billick et al., 1979). Accordingly, the GM and GSD were taken to represent BLLs distribution in each subpopulation, which are determined by the relationships among parameters of the lognormal distribution (as reported in Supplemental Materials). Data were then combined to one by taking sample-size weighted geometric mean and geometric standard deviation as representative of BLL for each city or region (for details see Supplemental materials).

### 2.2. Characterization of different exposure pathways

We also performed a search in the databases CNKI and Web of Science to collect lead concentrations measured in environment media corresponding to the selected biomonitoring data. The lead isotope ratios of children BLLs in China were closer to those of food, drinking water and air (Cao et al., 2014). Moreover, considering the limited data availability, we decided to focus on four pathways in this study: air, soil and dust, diet including grain and vegetable, drinking water. The selection criteria for the exposure data were similar to those for biomonitoring data, including a sound sampling design, adequate sample size, stringent quality control, the availability of enough statistical information (e.g., arithmetic mean and standard deviation), and where applicable, a sampling period comparable with the biomonitoring data. Only for 14 out of 28 cities it was possible to find data on lead concentration for air, soil, grain and vegetable, which are presented by survey site in Supplemental Materials (Table S2 to S5).

Monitoring data of environmental samples commonly approximate a lognormal distribution (Ikeda et al., 1989; Zhang et al., 1997; Hsu et al., 2006; Xia et al., 2011). Few studies included in this work gave an insight into the structure or distribution of environmental monitoring data. Thus, to facilitate calculation, we fitted the lead concentrations of environmental media in each individual study to a lognormal distribution. We collected annual mean concentration of air-borne lead in 14 cities and GM was estimated to be in the range of 0.006–0.539 $\mu g/m^3$ (Table S2 in Supplemental materials). GM of lead concentration in soil was in the range of 9.33–95.68 mg/kg, with samples being collected mostly from soils in residential areas or otherwise from generic "urban soils" (Table S3 in Supplemental materials). We considered