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ORIGINAL PAPER

Concurrent Assessment on Blood Lead in Young Children and Toy Lead in Shanghai

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Abstract

Since toys are potential sources of lead contamination for young children, we aim to explore potential correlations between blood-lead-levels (BLLs) of young children and toy-lead contamination using two concurrent investigations. In investigation-1, a total of 2249 children under 7 years old were studied using stratified-cluster-sampling in 6 districts of Shanghai, parents completed questionnaires and children's whole-blood was collected, and then BLLs were measured using tungsten-atomizer-absorption-spectrophotometer. In investigation-2, a total of 288 toys made of different materials (plastic, wooden, metals, and stuffed cloth) were collected in 6 great supermarkets/toy-stores and toy-lead-levels were measured by a portable X-ray-fluorescence instrument. The geometric-mean of BLLs was 2.02 μg/dL. Adjusting for related confounders, playing with plastic toys was a significant risk factor ($\beta = 0.067$, $P < 0.05$) for BLL-increment. Plastic toys accounted for the highest proportion (154/288, 53.47%) and had the highest rates exceeding toy-lead-standards (the over-standard rates of ≥ 300/600 mg/kg, plastic toys: 3.90%/1.30%; other toys: 0.00%/0.00%). Children's BLLs in the three (Pudong-suburban, Xuhui, and Yangpu) districts and toy-lead over-standard rates in the neighboring stores were compared, the highest BLLs and over-standard rates were both found in Pudong-suburban district and similar BLLs and over-standard rates were observed between Yangpu and Xuhui districts (Pudong-suburban vs. Xuhui vs. Yangpu: 2.07 vs. 1.55 vs. 1.50 μg/dL for the medians of BLLs, $P < 0.001$; 1.67% vs. 0.00% vs. 0.00% for the over-standard rates of ≥ 600 mg/kg). This study raised the possibility that lead contamination in toys (especially in low social-economic-status areas) might be associated with BLLs in young children. Lead contamination from plastic toys needs cautions for preventing children from lead exposure.

Keywords Child · Blood lead · Toy lead · Plastic toys

Background

There is no 'safe threshold' for lead exposure, and even 'low' levels of lead exposure in young children are associated with neurodevelopmental deficits (Bellinger 2008; Cai et al. 2021; Lanphear et al. 2005). Although a significant decline in children's blood lead levels (BLLs) has occurred in recent 20 years (Yan et al. 2013), children's exposure to lead still exists in many developing countries. A national investigation conducted during 2016–2020 in China showed that the geometric-mean of BLLs among Chinese children and teenagers (aged 1–18 years old) was 2.73 μg/dL, and children of 1–6 (especially 4–6) years old had higher BLLs than children in other age ranges (Wang et al. 2021a). Another national study in China measured BLLs among 31,373 children aged 0–84 months old from 2013 to 2015, and reported that the geometric-mean of the BLLs was 2.67 μg/dL (Ji et al. 2011). These findings suggest that although significant progress has been made in decreasing children's BLLs, investigations on the environmental sources of lead contamination and interventions to further decrease

Extended author information available on the last page of the article

children's lead exposure are still warranted, especially among children under 7 years old.

Previous studies have reported the potential sources of lead contamination for young children. Significant transition of lead contamination sources from industrial exposure to non-industrial exposure has occurred in recent 20 years (Hon et al. 2017). The lead contamination in toys in developing countries needs to be concerned (Njati and Maguta 2019; Shen et al. 2018; Yazdanfar et al. 2022). Hand-to-mouth activity peaks among children under 7 years old, especially among toddlers. Children of all ages love toys, and toy-biting is a common behavior in young children. Once toys are bitten, or toy pieces are ingested, lead in toys may become bioavailable, induce high BLLs in children and do harm to children's health (Gulson et al. 2009; Horton et al. 2013). Ingestion of lead in low-cost toys may induce children's extremely high BLLs, and even child death (Centers for Disease and Prevention 2006; VanArsdale et al. 2004). However, evidence is scarce concerning children's exposure to lead via toys.

In different countries, different regulatory thresholds are established for lead contents in toys. The regulatory thresholds for total lead and soluble lead in toys are 600 mg/kg and 90 mg/kg in China, respectively (GB24613-2009). The European-Union (EU) threshold for migratable lead concentrations in toys is 130 mg/kg [EU Toy Safety Directive (2009/48/EC)], while American regulatory threshold values allowed for surface coatings and total lead in toys is 90 mg/kg and 300 mg/kg, respectively (USCPSC, 2011). Lead compounds may be used as ingredients of toys, or in the leaded-paint, metal and plastic parts of toys. The industries of both paints and polyvinyl-chloride (PVC) toys are growing every year. Therefore, the worry is that children's lead exposure due to contact with toys may increase if lead is contained in paints of toys or PVC toys. Asian countries are leading in the paint production. From 2012 to 2017, the trend on toy sales portrayed a steady increase worldwide and China was the leading country in toy export, accounting for 46.1% of the worldwide toy export business (Njati and Maguta 2019). Thus, investigations on lead levels in toys and blood among young children in China are warranted. We speculate that toy-biting may be a potential source of lead pollution if toys are contaminated by lead.

Therefore, this study focused on children under 7 years old who are most susceptible to lead exposure, and aimed to evaluate BLLs and toy-play behaviors in young children in Shanghai using strict stratified-random sampling, and evaluate total lead levels in toys sold in great supermarkets/toy-stores close to the home addresses of the study children, so as to explore the potential association between BLLs and lead levels in toys among young children. This study may help to explore the potential sources of lead exposure and develop related strategies to prevent young children from lead contamination.

Methods

Investigation 1: The Epidemiological Study on the Association Between Children's Toy-Play Behavior and Their BLLs

Study Design and Sampling Method

A cross-sectional investigation was conducted in Shanghai, China, from June 2013 to July 2014, and children under 7 years old (84 months) were recruited using a multi-stage stratified clustered random sampling based on the area (urban/suburban)-district-neighborhood method. The sampling sites were shown in Fig. 1. In urban and suburban areas, we selected three districts in each area (the 3 out of the 8 administrative districts for urban areas: Xuhui, Yangpu, and Jing'an districts; the 3 out of the 9 administrative districts for suburban areas: Pudong-suburban, Chongming, and Jiading districts). A probabilistic proportional to size sampling method was used to select districts based on the population numbers at administrative districts. Within each selected district, children were recruited from 1 to 2 neighborhoods by the simple-random-sampling method. In the selected areas, children's gender and age were the stratification factors. We calculated the sample size for each stratification. Finally, a total of 2249 children aged from 0 to 84 months old were enrolled.

Written informed consents were obtained from each child's parent. The study was approved by the Medical Ethics Committee of Xinhua Hospital affiliated to Shanghai Jiao Tong University School of Medicine.

Questionnaire

Parents of the study children completed a 30 min interview questionnaire collecting information on child age and sex, yearly family income level, maternal educational level, materials of children's toys (plastic, wooden, metal, stuffed cloth, and others), frequencies of toy-biting behavior and finger-biting behavior (never: less than twice per year; sometimes: less than twice per month; often: more than twice per week; always: more than twice per day).

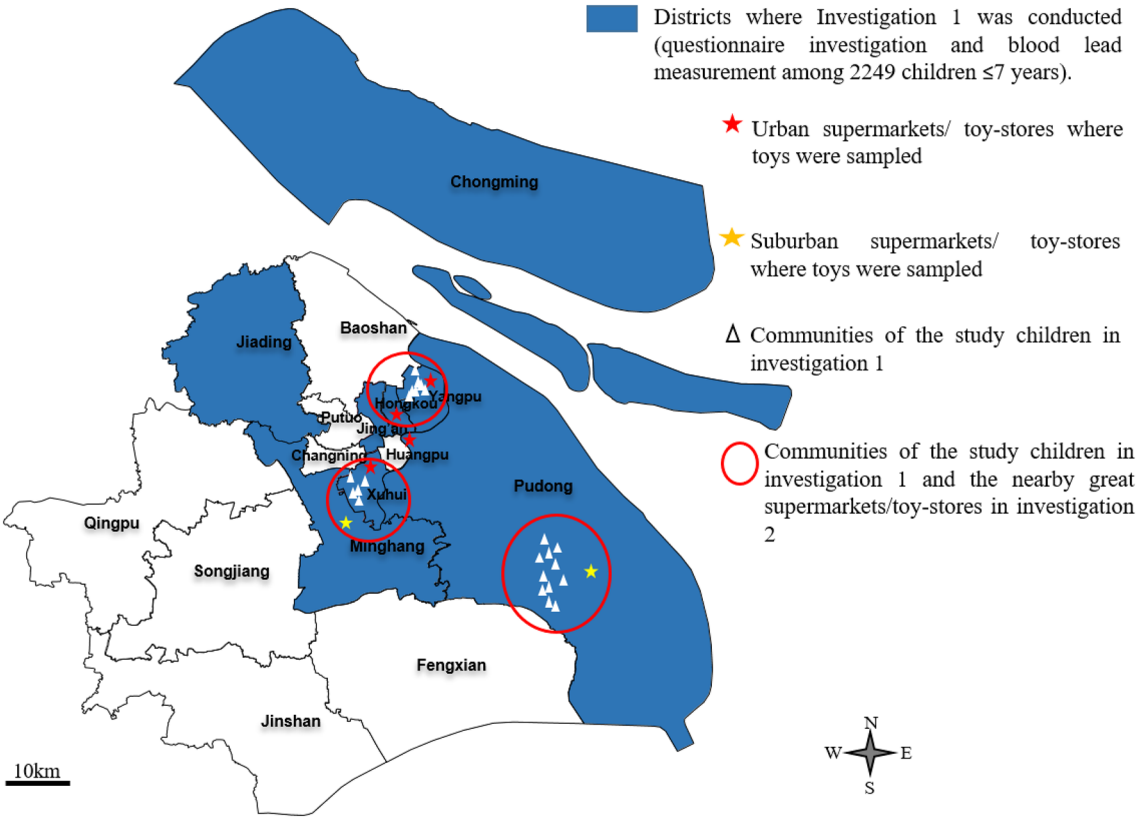

Fig. 1 The distributions of the investigation 1 and investigation 2 in Shanghai in this study. Districts where only Investigation 1 was conducted (questionnaire investigation and children's blood lead measurement among 2249 children ≤ 7 years) were labeled blue. Urban supermarkets or toy-stores where toys were sampled were labeled by red stars, suburban supermarkets or toy-stores where toys were sampled were labeled by yellow stars. Communities of the study children in investigation 1 were labeled by white triangles. The communities of the study children in investigation 1 and the nearby great supermarkets/toy-stores in investigation 2 were circled by red circles

Blood Lead Measurement

Children's whole blood was collected in a clean room without any known lead contamination. The procedure for children's arm decontamination before blood sampling included three stages—preparation (washing children's arm with soap and water), drying and disinfection (with 75% alcohol). Three-milliliters of venous blood were collected using EDTA vacutainer tubes. BLLs were analyzed by a tungsten atomizer absorption spectrophotometer (PinAAcle900Z, USA). Quality control was performed using a standard laboratory protocol. Five levels of standard products (from low to high lead levels) were used to form the daily calibration curves (1–50 μg/dL; agreement < 5%). Each sample was analyzed twice and the mean value was used. A blank sample was analyzed every 50 measurements to prevent inter-sample contamination. The limit of detection (LOD) was 0.1 μg/dL for BLLs, and actually no sample had a BLL below the LOD.

Investigation 2: Measurement on Total Lead in Toys in the Great Supermarkets/Toy-Stores

Another cross-sectional investigation was conducted on total lead in the toys sold in the 6 great supermarkets/toy-stores in Shanghai from June 2014 to July 2014. A total of 4 supermarkets (2 Auchan and 2 Carrefour supermarkets) and 2 toy-stores (Toys'R'Us) were investigated including 4 urban and 2 suburban supermarkets/toy-stores (Fig. 1). Considering that the Pudong district had a large area extending from urban to suburban areas, we investigated two stores in Pudong district including one supermarket in the suburban area and one toy-store in the urban area. Carrefour and Auchan were both the top 10 retailers in the world, and were local toy top-selling mass-markets. Toys'R'Us was a well-known toy retailer. Finally, a total of 288 toys made of plastic, stuffed cloth, wooden, and metal materials were measured, and the material proportion of the study toys matched the material proportion of the toys laid out in the study supermarkets/toy-stores.

Lead concentrations in toys were measured with a portable X-ray Fluorescence (XRF) instrument (Thermo-Fisher Scientific, Niton XL3t GOLDD+). We cleaned the surface of the toys with alcohol swabs to remove any contamination. Then, we placed the device above the most flatted surfaces of the toys. Each sample was analyzed with a 3 min measurement.

A blank control (silicon powder) was used to ensure that the XRF was calibrated before use in the field and the XRF device was calibrated annually to assure result integrity. The XRF was calibrated using a set of NIST standards (NIST 2709a and NIST 2579) and plastics with known concentrations of metals. The calibration normalization to the Compton scattering peak of the silver anode characteristic x-ray production should explain most variations in thickness between a few millimeters and infinitely thick as seen by the XRF, which would correspond with 1–2 cm of thickness in most plastics. The XRF measured about 1 cm^2 area of the sample. We used a 50 kV max energy with our Ag anode which optimized the energy for measurements in elements with emissions in the 8–15 keV range.

Then the data were analyzed using the standard procedure of previous studies (Specht et al. 2019, 2014, 2022; Zhang et al. 2021). Our fitting deconvolution algorithm utilized alpha and beta peaks for most elements with K, L, and M shell measures in the appropriate energy ranges. The net counts from Pb derived from the calibration standards were used to identify the Pb concentration of each sample. The limit of detection (LOD) depended on the thickness of the samples. We used the square root of the uncertainty values to replace the values of less than LOD.

Statistical Analyses

Statistical analyses were performed using SPSS Statistics Software (Version 22.0) and $P < 0.05$ was considered statistically significant. The results were expressed as frequencies or geometric means or medians (interquartile ranges) according to the data type. The BLLs with a skewed distribution were logarithmically transformed and analyzed using multiple linear regression models. The Chi-square test or Fisher's exact test with Bonferroni post hoc test was used to compare the rate differences among the toys of different materials. Among the 6 stores, the 5 stores were great supermarkets/toy-stores close to the communities of the study children living in Yangpu, Xuhui, and Pudong-suburban districts in investigation 1 (Fig. 1), and it was very likely for parents of the children living in Yangpu, Xuhui, and Pudong-suburban districts to buy toys for their young children in these 5 stores. Therefore, we compared the BLLs of the children living in these three districts in investigation-1 and rates exceeding toy-lead-standards in toys sold in the 5 neighboring stores in investigation-2. The Kruskal–Wallis test with Bonferroni post hoc test was used to compare the differences in BLLs and lead levels in toys.

Results

From Investigation 1: Characteristics of the Study Children

The characteristics of the 2249 children from the 6 districts of Shanghai were presented in Table 1. The percentages of boys and girls were 53.40% ($n = 1201$) and 46.60% ($n = 1048$), respectively, and the percentages of children aged 0–12, 12–36, and 36–84 months old were 9.41%, 23.65%, and 66.83%, respectively. More than half of the families had yearly income of more than 100,000 RMB. Approximately half of the mothers (45.15%) had educational levels at the university/college level or above. Only a few children (16.94%) had the fingernail-biting behavior.

A total of 53.58% of the participants usually/often played with toys with only one type of material, while other children usually/often played with toys with two or more types of materials. Surprisingly, there were 3.33% of participants hardly played with any toys. Of the enrolled children, 83.28% played with plastic toys, 33.79% played with stuffed cloth toys, 31.35% played with wooden toys and only 10.40% played with metal toys.

About the frequency of the toy-biting behavior during the last year: approximately half of the study children hardly bit toys (less than twice per year), and 37.38% of the participants bit toys less than twice per month. However, there were still 10.05% of the participants having toy-biting behavior for more than twice per week and even 1.82% of the participants bit toys for more than twice per day. Boys and younger age were the risk factors for more toy-biting behavior while family yearly income level and maternal educational level had no significant associations with the frequencies of children's toy-biting behavior. (Supplementary Tables 1–4).

The geometric mean and median of the BLLs were 2.02 μg/dL and 2.00 μg/dL, respectively. In addition, 3.51% (79/2249) of the study children had BLLs above 5 μg/dL and 0.22% (5/2249) had BLLs above 10 μg/dL. As shown in Supplementary Table 5, the children in Chongming, Jiading, Jing'an and Pudong districts had higher BLLs than the children in Xuhui and Yangpu districts did ($P < 0.01$). The children aged 36–84 months old had the highest BLLs, followed by the children aged 12–36 and 0–12 months old ($P < 0.01$). Boys had higher BLLs than girls did ($P < 0.01$).

Table 1 Characteristics of the study children (n = 2249)

Characteristics	*N* (%)	Characteristics	*N* (%)
District		Plastic	1873 (83.28)
Chongming	392 (17.44)	Stuffed cloth	760 (33.79)
Jiading	390 (17.34)	Metal	234 (10.40)
Jingan	336 (14.94)	The other	99 (4.40)
Pudong	389 (17.30)	The number of toys' materials played by one child	
Xuhui	344 (15.30)		
Yangpu	398 (17.70)	0	75 (3.33)
Sex		1	1205 (53.58)
Male	1201 (53.40)	2	537 (23.88)
Female	1048 (46.60)	3	343 (15.25)
Age (months)		4	82 (3.65)
0–12	214 (9.41)	5	7 (0.31)
12–36	532 (23.65)	Bite toys	
36–84	1503 (66.83)	Never	1094 (49.75)
Yearly family incomes (RMB)		Sometimes	822 (37.38)
		Often	243 (10.05)
< 30,000	108 (4.99)	Always	40 (1.82)
30,000–50,000	287 (12.83)	Bite fingernail	
50,000–100,000	591 (27.29)	Never	1858 (83.51)
≥ 100,000	1189 (54.89)	Sometimes	367 (16.49)
Maternal educational levels		Often	0
≤ primary school	144 (6.44)	Always	0
Junior high school	615 (27.49)	Blood Pb levels (μg/dL)	
Senior high school	468 (20.92)	Median (interquartile range)	2.00 (1.44, 2.90)
University, college level or above	1010 (45.15)		
		Geometric mean	2.02
Toy materials		Pb > 5 (*N*, %)	79, 3.51%
Wooden	705 (31.35)	Pb > 10 (*N*, %)	5, 0.22%

Never less than twice per year, *sometimes* less than twice per month, *often* more than twice per week, *always* more than twice per day

Table 2 The association between the toys' materials and blood lead levels

Toys' materials	Not playing with toys made of this material[a]	Playing with toys made of this material	
		*β** (95%CI)	*P**
Plastic	Reference	0.067 (0.011, 0.124)	< 0.05
Wooden	Reference	− 0.022 (− 0.070, 0.027)	0.386
Metal	Reference	− 0.058 (− 0.129, 0.014)	0.112
Stuffed cloth	Reference	0.015 (− 0.033, 0.063)	0.541

Multiple linear regression models were applied

The blood lead levels were logarithmic transformed

[a]"Not playing with toys made of this material" was used as the reference group

*Models were adjusted for children's age, sex, family income levels, maternal educational levels, toy-biting frequencies and playing with toys made of other materials or not

From Investigation 1: The Association Between Materials of Toys Played by the Study Children and Their BLLs

Adjusted linear regression analyses showed significant association between materials of toys played by the study children and logarithmically transformed BLLs (Table 2). After adjusting for related confounders (children's age, sex, family income levels, maternal educational levels, frequencies of toy-biting and playing with toys of other materials or not), playing with plastic toys (*vs*. not playing with plastic toys) was a significant risk factor for BLL increment ($\beta = 0.069$, $P < 0.05$), while playing with wooden (vs. not playing with wooden toys), metal (vs. not playing with metal toys) and stuffed cloth (vs. not playing with cloth toys) toys had no significant associations with the BLLs.

Table 3 Comparisons of the lead concentrations in toys made of different materials

Toys' materials	Sample size	Lead concentrations (mg/kg)				
		Max	% above LOD	% above 90	% above 300	% above 600
Plastic	154 (53.47%)	624.45	21.43%	8.44%	3.90%	1.30%
Wooden	40 (13.89%)	58.76	7.50%[a]	0.00%	0.00%	0.00%
Metal	28 (9.72%)	275.10	42.86%[a]	7.14%	0.00%	0.00%
Stuffed cloth	66 (22.92%)	235.94	13.64%[a]	7.58%	0.00%	0.00%

The Chi-square test or Fisher's exact test with Bonferroni post hoc test was used to compare the over-standard rates in toys of different materials

LOD the limit of detection of the method, *SE* standard error

[a]Bonferroni multiple-comparison tests found no significant differences among the groups (Wooden, Metal and Stuffed cloth toys)

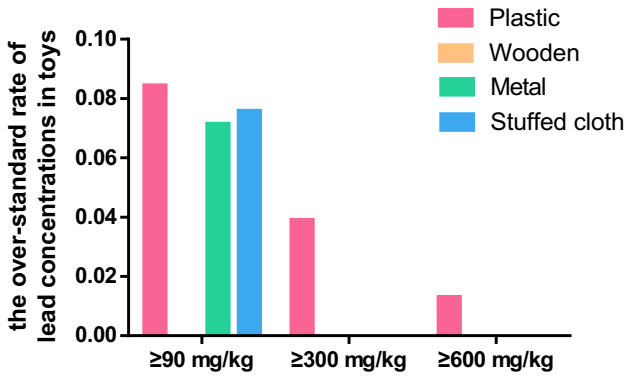

Fig. 2 The over-standard rates of total lead in the toys made of different materials. A total of 288 sampled toys (154 plastic toys, 40 wood toys, 28 metal toys, 66 stuffed cloth toys) were measured total lead levels. Among all the measured toys, the plastic toys had the highest over-standards rates of lead levels, with a total of 8.44% plastic toys having the lead levels over 90 mg/kg, 3.90% over 300 mg/kg, and 1.30% over 600 mg/kg. No wooden toys had the lead levels over 90 mg/kg. Among the metal toys, a total of 7.14% toys had the lead levels over 90 mg/kg while no metal toys exceeded the standards of 300 mg/kg and 600 mg/kg. Among the stuffed cloth toys, a total of 7.58% toys had the lead levels over 90 mg/kg while no stuffed cloth toys exceeded the standards of 300 mg/kg. The Chi-square test or Fisher's exact test was used to compare the differences in the rates among toys made of different materials

From Investigation 2: The Association Between Lead Levels in Toys and Materials of Toys

We tested 288 toys from the 6 supermarkets/ toy-stores (Fig. 1). As shown in Table 3 and Fig. 2, among the measured toys, plastic toys accounted for 53.47% (154/288) of the study toys, followed by stuffed cloth (66/288, 22.92%), wooden (40/288, 13.89%), and metal (28/288, 9.72%) toys. The maximum lead concentration was found to be 624.45 mg/kg in plastic toys. All the measured toys met the Chinese toy lead regulatory threshold (600 mg/kg) except plastic toys. Metal toys had the highest lead detection rate (12/28, 42.86%), followed by plastic (33/154, 21.43%), stuffed cloth (9/66, 13.64%), and wooden (3/40, 7.5%) toys. No wooden toys exceeded US total lead regulatory threshold (300 mg/kg) and Chinese total lead standard (600 mg/kg). However, the plastic toys had the highest over-standard rates of lead levels, a total of 3.90% plastic toys exceeded US total lead regulatory threshold (300 mg/kg) and 1.30% exceeded the Chinese standard (600 mg/kg). When we compared lead levels in toys with the same material among different district stores, we found that the highest lead concentration (624.45 mg/kg) and over-standard-rates (13.79% for the standard of 90 mg/kg, 6.90% for the standard of 300 mg/kg and 3.45% for the standard of 600 mg/kg) of lead levels were both observed in plastic toys in Pudong-suburban store. In addition, relatively high median lead levels were found in metal toys in Hongkou (median = 10.03 mg/kg, very close to Yangpu) and Minhang (median: 9.59 mg/kg, very close to Xuhui) stores (Supplementary Tables 7 and 8).

Comparisons of the BLLs Among Children in the Three Districts and Over-Standard Rates of Lead Levels in Toys in the Neighboring Supermarkets/Toy-Stores

According to the reports of Chinese online trading in 2013 and 2014, the online trading accounted for a small part of the whole trading (7.9% for 2013 and 10.6% for 2014) (CNNIC 2014, 2015). Most parents tended to buy toys in the supermarkets/toy-stores close to their home. Therefore, we matched the children in investigation 1 with the supermarkets/toy-stores in investigation 2, and compared the BLLs of the children in the three (Xuhui, Yangpu, and Pudong-suburban) districts and toy-lead over-standard rates in toys sold in the neighboring supermarkets/toy-stores. The average distances between the neighboring supermarkets/toy-stores and the home addresses of the children were 3.4 km for the

Table 4 Comparisons of the lead concentrations in toys in different districts

District	Sample Size	Lead concentrations (mg/kg)				
		Max	% above LOD	% above 90	% above 300	% above 600
Xuhui	91	403.18	17.58%	6.59%	1.10%	0.00%
Yangpu	134	521.83	15.67%	6.72%	2.24%	0.00%
Pudong-suburban	60	624.45	25.00%	6.67%	3.33%	1.67%

The Chi-square test or Fisher's exact test with Bonferroni post hoc test was used to compare the differences in the over-standard rates among toys in different districts

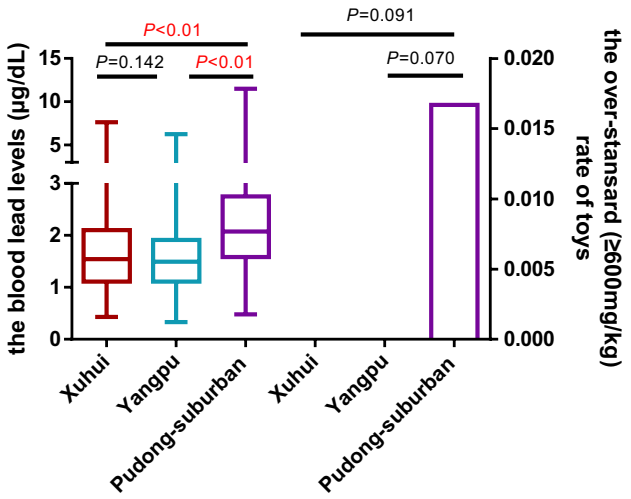

Fig. 3 Comparisons of the blood lead levels (BLLs) and over-standard rates of toy lead in different districts. We compared BLLs of the children in the three districts and total lead levels in toys in the neighboring great supermarkets/toy-stores. The BLLs of the children from Pudong-suburban district ($n=389$, median = 2.07 ug/dL) were significantly higher than those from Xuhui ($n=344$, median = 1.55 ug/dL, $P<0.01$) and Yangpu ($n=398$, median = 1.50 ug/dL $P<0.01$) districts. Among the measured districts, the highest over-standards rate of toy lead levels (1.67% above 600 mg/kg) was found in Pudong-suburban district while no measured toys in Xuhui or Yangpu districts exceeded the Chinese total lead standard (600 mg/kg). The BLLs were on the left side of the diagram and the over-standard rates of lead concentrations in toys were on the right side. The BLLs were expressed as the median and interquartile range. The Kruskal–Wallis test with Bonferroni post hoc test was used to compare the BLLs among different districts. The Chi-square test or Fisher's exact test was used to compare the differences in the rates among toys of different districts

Pudong-suburban children, 2.3 km for the Yangpu children, and 3.7 km for the Xuhui children, so as to ensure that these supermarkets/toy-stores were the main stores where parents bought toys for children. As Table 4 showed, the measured toys in Pudong-suburban district had the highest over-standard rates of total lead levels (3.33% above 300 mg/kg, 1.67% above 600 mg/kg), followed by the Yangpu (2.24% above 300 mg/kg, 0.00% above 600 mg/kg) and Xuhui (1.10% above 300 mg/kg, 0.00% above 600 mg/kg) districts. And the toys which exceeded the Chinese total lead standard (600 mg/kg) were only found in Pudong-suburban district.

As Fig. 3 showed, the BLLs of the children from Pudong-suburban district (median: 2.07 ug/dL) were significantly higher than those from Xuhui (median: 1.55 ug/dL, $P<0.01$) and Yangpu (median: 1.50 ug/dL, $P<0.01$) districts, and the BLL median in the Xuhui children in was similar as the BLL median in the Yangpu children. The trend of over-standard rates after toy lead comparison was consistent with the trend of the BLL comparison. The over-standard rates of lead concentrations in toys for Pudong-suburban children (3.33% above 300 mg/kg, 1.67% above 600 mg/kg) were relatively higher than those for Yangpu (2.24% above 300 mg/kg, 0.00% above 600 mg/kg) and Xuhui (1.10% above 300 mg/kg, 0.00% above 600 mg/kg) children (Table 4). These findings suggested that the areas with higher children's BLLs seemed to have higher over-standard rates of lead levels in toys sold in the neighboring supermarkets/ toy-stores, which raised the possibility that lead contamination in toys might be associated with children's BLLs.

Discussion

In this study with two concurrent investigations, we investigated 2249 children aged 0–7 years old and the total lead levels in 288 toys. We found that the plastic toys accounting for a highest proportion (156/288, 53.06%) among the study toys had the highest over-standard rate of lead levels compared with toys of other materials, and playing with plastic toys was a significant risk factor for BLL-increment among children under 7 years old. Together with the findings of the BLLs and over-standard rates of lead concentrations in toys in the neighboring supermarkets/ toy-stores, we suggest the possibility of the potential association between higher over-standard rates of lead levels in toys and higher BLLs in children under 7 years old.

In this study, we found that the geometric mean of the BLLs in children aged 0–7 years old in shanghai from 2013 to 2014 was 2.02 μg/dL, lower than the level shown by another concurrent study conducted in China nationwide among children in the same age group (Yan et al. 2020). However, compared with concurrent studies on BLLs in children of similar ages, the BLLs reported in this study were still higher than the levels reported in developed

countries, but lower than the levels reported in most of the developing countries. The geometric mean of the BLLs of children aged 1–5 years old in USA from 2013 to 2014 was 0.78 μg/dL (Wang et al. 2021b), and the median of the BLLs of children aged 3–5 years old in Korea from 2012 to 2014 was 1.34 μg/dL (Burm et al. 2016). In Kashmir of India, the mean of the BLLs of children aged 2–4 years old was 4.71 μg/dL around 2018 (Rashid et al. 2019). In Enugu of southeastern Nigeria, the mean of the BLLs of children aged 0–5 years old in 2011 was 7.5 μg/dL (Ugwuja et al. 2014). However, in São Paulo of Brazil, the geometric mean of the BLLs of children aged 1–4 years old in 2013 was only 2.16 μg/dL (Olympio et al. 2018).

Consistent with other investigations, we found that plastic toys had the highest over-standard rates of lead levels. Previous studies unveiled that PVC plastic toys and metallic jewelry toys usually had very high lead concentrations (Greenway and Gerstenberger 2010; Hillyer et al. 2014; Njati and Maguta 2019; Sanders et al. 2013; Shen et al. 2018). This may be because that PVC toys contain lead and cadmium additives, acting as plasticizers so as to make PVC soft and pliable. The PVC plastic toys accounted for a considerable part of plastic toys. According to Joseph A's survey, 27.1% of the tested plastic toys were made of PVC plastics (Greenway and Gerstenberger 2010). In light of our findings, 83.28% of the study children played with plastic toys, and plastic toys accounted for a substantial proportion of the measured toys. Therefore, high lead levels in plastic toys may explain why playing with plastic toys was a significant risk factor for BLL increment in young children and worth attention.

We compared children's BLLs and over-standard rates of lead levels in toys in the neighboring stores, and proposed the possibility that the district with higher over-standard rates of lead levels in toys might have higher BLLs in young children. These findings suggested that lead contamination in toys might be a significant contributing factor for children's BLL increment. Previous studies showed that mouthing behavior played an important role in children's exposure to environmental contaminants (Tulve et al. 2002). Children are increasingly likely to mouth non-food items since 6 months old, and a high frequency of mouthing hands or objects begins to moderate between 2 and 3 years old (Firestone et al. 2007), then becomes less frequent after 3 years old (Xue et al. 2010). Mouthing of lead contaminated toys may cause the release of lead in toys via contacting toys with saliva, and ingestion of toy pieces may result in the release of lead into digestive fluids, simulating saliva extraction and gastro-intestinal digestion (Guney and Zagury 2013; Weidenhamer et al. 2011).

This study had some strengths and limitations. This study analyzed the adjusted association between children's BLLs and the materials of children's toys using epidemiological investigation by strict stratification-random sampling, and compared the BLLs in young children and the lead levels in toys sold in the neighboring stores. Previous studies measured either lead levels in toys or children's BLLs. Few studies combined these two issues and analyzed potential correlations between them, and fewer studies compared lead levels among toys made of various materials. However, this study also had some limitations. First, we didn't collect the information on where parents usually bought toys for their children in the questionnaire. The comparisons of the BLLs and lead levels in toys were based on the speculation that parents tended to buy toys from the supermarkets/ toy-stores close to their home. Although online shopping was rare in 2013–2014 in China, it was still possible that, in some conditions, parents might buy toys from other supermarkets/ toy-stores far away from their home. Second, in investigation 2, we didn't measure toy lead levels in all the 6 districts involved in investigation 1 where children's BLLs were tested. It would be better if we could directly test the lead levels in toys used by the study children. However, the preliminary findings of this study also provided clues for the potential association of children's BLLs and materials of toys. Third, because this study was a cross-sectional investigation, the findings can only imply that there may be a potential association of children's BLLs with materials of toys but not meaning causality. It needs prospective studies to further explore the cause-and-effect relationship between BLLs and materials of toys. Fourth, although various important confounders were adjusted, there is still a possibility that other potential confounders may be missing. Fifth, in this study, we cannot rule out the possibility that lead contamination in metal toys may not be fully disclosed in this study because of small sample size of metal toys. Due to these limitations, we consider that the inconclusive but suggestive evidence shown by this study needs further confirmation by future researches.

Conclusion

The present study explored the potential correlation of BLLs in young children with lead contamination in toys in nearby stores in 2013–2014 in Shanghai, China. We suggest that playing with plastic toys was a significant risk factor for BLL-increment and plastic toys which accounted for the highest proportion in the toy market tended to have high over-standard rates of lead levels. In addition, comparisons of children's BLLs and over-standard rates of lead levels in toys in the surrounding stores suggested that lead contamination in toys may be associated with high BLLs in young children. These findings highlight the concern about lead contamination in toys, especially in plastic toys in low social-economic-status areas, and stricter supervision on

toy market or toy trade may be considered to prevent young children from potential lead exposure.

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Data Availability The datasets used in this study are available from the corresponding author on reasonable request.

Declarations

Conflict of interest The authors have no relevant financial or non-financial interests to disclose.

Ethics Approval and Consent to Participate The study was approved by the Medical Ethics Committee of Xinhua Hospital affiliated to Shanghai Jiao Tong University School of Medicine (approval no. XHEC-C-2012-007). Written informed consents were obtained from each child's parent.

Consent to Publish All authors declare they have given consent to publish this article.

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Supplement Table 1: The comparison of the toy-biting behavior among different age groups.

Age group	Total	Never	Sometimes	Often	Always	χ^2 test	
						χ^2 value	*P* value
0-1y	207	37 (17.87%)[c]	58 (28.02%)[a]	93 (44.93%)[c]	19 (9.18%)[a,c]		
1-3y	524	163 (31.11%)[b]	253 (48.28%)[a,b]	98 (18.70%)[b]	10 (1.91%)[a]	528.21	<0.01
3-7y	1468	894 (60.90%)[b,c]	511 (34.81%)[b]	52 (3.52%)[b,c]	11 (0.75%)[c]		

The Chi-square test or Fisher's exact test with Bonferroni post hoc test was used to compare the differences in the rates among different age groups.

[a]: 0-1y vs 1-3y, $P<0.05$; [b]: 1-3y vs 3-7y, $P<0.05$; [c]: 0-1y vs 3-7y, $P<0.05$.

Supplement Table 2: The comparison of the toy-biting behavior between girls and boys.

Sex groups	Total	Never	Sometimes	Often	Always	χ^2 test	
						χ^2 value	*P* value
Boys	1181	556 (47.08%)[a]	450 (38.10%)	148 (12.53%)[a]	27 (2.29%)[j]	12.14	<0.01
Girls	1018	538 (52.85%)[a]	372 (36.54%)	95 (9.33%)[a]	13 (1.28%)		

The Chi-square test or Fisher's exact test with Bonferroni post hoc test was used to compare the differences in the rates between girls and boys.

[a]: male vs female, $P<0.05$.

Supplement Table 3: The comparison of the toy-biting behavior among different family incomes groups.

Family income groups(¥)	Total	Never	Sometimes	Often	Always	χ^2 test	
						χ^2 value	*P* value
<10,000	21	9 (42.86%)	8 (38.10%)	4 (19.05%)	0 (0)	15.17	0.232
10,000-30,000	86	35 (40.70%)	33 (38.37%)	17 (19.77%)	1 (1.16%)		
30,000-50,000	271	136 (50.18%)	110 (40.59%)	23 (8.49%)	2 (0.74%)		
50,000-100,000	577	281 (48.70%)	217 (37.61%)	69 (11.96%)	10 (1.73%)		
⩾100,000	1169	590 (50.47%)	426 (36.44%)	127 (10.86%)	26 (2.22%)		

The Chi-square test or Fisher's exact test with Bonferroni post hoc test was used to compare the differences in the rates among different family income groups

Supplement Table 4: The comparison of the toy-biting behavior among different maternal educational levels.

Maternal educational levels	Total	Never	Sometimes	Often	Always	χ^2 test	
						χ^2 value	*P* value
⩽primary school	139	70 (50.36%)	52 (37.41%)	16 (11.51%)	1 (0.72%)		
Junior high school	603	285 (47.26%)	250 (41.46%)	60 (9.95%)	8 (1.33%)		
Senior high school	459	222 (48.37%)	175 (38.13%)	56 (12.20%)	6 (1.31%)	12.99	0.163
University, college	987	511 (51.77%)	341 (34.55%)	110 (11.14%)	25 (2.53%)		

The Chi-square test or Fisher's exact test with Bonferroni post hoc test was used to compare the differences in the rates among groups with different maternal educational levels.

Supplement Table 5: The comparison of the BLLs.

Parameter	Variables	Sample Size	BLL (ug/L) median (interquartile range)	*P* value
District	Chongming	392	2.61 (1.73, 3.61)[a]	<0.01
	Jiading	390	1.88 (2.45, 2.94)[a]	
	Jingan	336	1.53 (2.62, 34.9)[a,b]	
	Pudong	389	1.59 (1.07, 2.75)[b]	
	Xuhui	344	1.13 (1.55, 2.11)[c]	
	Yangpu	398	1.12 (1.50, 1.92)[c]	
Age (months)	0-12	214	1.11 (1.62, 2.52)	<0.01
	12-36	532	1.36 (1.95, 2.76)	
	36-84	1503	1.52 (2.07, 2.96)	
Sex	Male	1201	1.50 (2.08, 2.95)	<0.01
	Female	1048	1.38 (1.91, 2.81)	

The Mann-Whitney U test or Kruskal-Wallis test with Bonferroni post hoc test was used to compare the differences among different groups.

[a, b, c]: Bonferroni multiple-comparison tests found no significant differences among the groups labeled with same letters and significant differences between any two groups labeled with different letters.

Supplement Table 6: The number of toys' materials played by one child.

The number of toys' materials played by one child (sample size)					
0 (75)	1 (1205)	2 (537)	3 (343)	4 (82)	5 (7)
	Plastic (941)	Plastic+ Stuffed cloth (248)	Plastic+Stuffed cloth+Wooden (258)	Plastic+Wooden+Metal+ Stuffed cloth (78)	Plastic+Wooden+Metal+ Stuffed cloth+the other (7)
	Stuffed cloth (109)	Plastic+Wooden (205)	Plastic+Wooden+Metal (51)	Plastic+Wooden+Metal+the other (4)	
	The other (69)	Plastic+Metal (48)	Plastic+ Stuffed cloth+Metal (27)		
	Wooden (65)	Wooden+ Stuffed cloth (27)	Plastic+Wooden+the other (7)		
	Metal (20)	Wooden+Metal (5)			
		Plastic+the other (4)			

Supplement Table 7: The comparisons of toy lead levels among different districts with the same material.

Toys' materials	District	Sample Size	Lead concentrations (mg/kg)				
			median (interquartile range)	Max	% above 90	% above 300	% above 600
Plastic	Hongkou	39	2.76 (2.36, 8.80)	521.83	7.69%	5.13%	0.00%
	Minhang	35	2.41 (2.10, 3.49)	403.18	8.57%	2.86%	0.00%
	Pudong-suburban	27	2.23 (1.89, 21.07)	624.45	13.79%	6.90%	3.45%
	Pudong-urban	2	-	1.81	0.00%	0.00%	0.00%
	Xuhui	13	2.25 (2.09, 2.44)	2.63	0.00%	0.00%	0.00%
	Yangpu	38	2.69 (2.27, 3.29)	307.65	5.26%	2.63%	0.00%
Wooden	Hongkou	10	2.68 (2.32, 3.73)[a]	5.19	0.00%	0.00%	0.00%
	Minhang	10	2.28 (1.95, 27.31)	58.76	0.00%	0.00%	0.00%
	Pudong-suburban	10	1.92 (1.87, 2.19)[a]	2.64	0.00%	0.00%	0.00%
	Yangpu	10	2.28 (2.05, 2.98)	3.65	0.00%	0.00%	0.00%
Metal	Hongkou	4	10.03 (2.97, 16.06)	16.48	0.00%	0.00%	0.00%
	Minhang	10	9.59 (3.74, 36.73)	275.10	20.00%	0.00%	0.00%
	Pudong-suburban	11	2.70 (1.65, 9.39)	61.36	0.00%	0.00%	0.00%
	Yangpu	3	-	5.66	0.00%	0.00%	0.00%
Stuffed cloth	Hongkou	16	2.93 (2.35, 4.24)	109.00	12.50%	0.00%	0.00%
	Minhang	13	2.69 (2.33, 3.10)	99.95	7.69%	0.00%	0.00%
	Pudong-suburban	12	2.37 (2.25, 2.59)	7.24	0.00%	0.00%	0.00%
	Pudong-urban	3	-	2.37	0.00%	0.00%	0.00%
	Xuhui	10	2.78 (2.63, 3.50)	3.87	0.00%	0.00%	0.00%
	Yangpu	12	2.63 (2.29, 3.15)	235.94	16.67%	0.00%	0.00%

The Kruskal-Wallis test with Bonferroni post hoc test was used to compare the differences among groups.

[a]: Hongkou vs Pudong, $P<0.05$.

Supplement Table 8: The comparisons of toy lead levels among the different materials within the same district.

District	Toys' materials	Sample Size	Lead concentrations (mg/kg)				
			median (interquartile range)	Max	% above 90	% above 300	% above 600
Hongkou (very close to Yangpu)	Stuffed cloth	16	2.93 (2.35, 4.24)	109.00	12.50%	0.00%	0.00%
	Metal	4	10.03 (2.97, 16.06)	16.48	0.00%	0.00%	0.00%
	Wooden	10	2.68 (2.32, 3.73)	5.19	0.00%	0.00%	0.00%
	Plastic	39	2.76 (2.36, 8.80)	521.83	7.69%	5.13%	0.00%
Minhang (very close to Xuhui)	Stuffed cloth	13	2.69 (2.33, 3.10)	99.95	7.69%	0.00%	0.00%
	Metal	10	9.59 (3.74, 36.73)[a]	275.10	20.00%	0.00%	0.00%
	Wooden	10	2.28 (1.95, 27.30)[a,b]	58.76	0.00%	0.00%	0.00%
	Plastic	35	2.41 (2.10, 3.49)[b]	403.18	8.57%	2.86%	2.86%
Pudong-suburban	Stuffed cloth	12	2.37 (2.25, 2.59)	7.24	0.00%	0.00%	0.00%
	Metal	11	2.70 (1.65, 9.39)	61.36	0.00%	0.00%	0.00%
	Wooden	10	1.92 (1.87, 2.19)	2.64	0.00%	0.00%	0.00%
	Plastic	27	2.23 (1.89, 21.07)	624.45	13.79%	6.90%	3.45%
Pudong-urban	Stuffed cloth	3	-	2.37	0.00%	0.00%	0.00%
	Plastic	2	-	1.81	0.00%	0.00%	0.00%
Xuhui	Stuffed cloth	10	2.78 (2.63, 3.50)[b]	3.87	0.00%	0.00%	0.00%
	Plastic	13	2.25 (1.09, 2.44)[b]	2.63	0.00%	0.00%	0.00%
Yangpu	Stuffed cloth	12	2.63 (2.29, 3.15)	235.94	16.67%	0.00%	0.00%
	Metal	3	-	5.66	0.00%	0.00%	0.00%
	Wooden	10	2.28 (2.05, 2.98)	3.65	0.00%	0.00%	0.00%
	Plastic	38	2.69 (2.27, 3.29)	307.65	5.26%	2.63%	0.00%

The Kruskal-Wallis test with Bonferroni post hoc test was used to compare the differences among groups.

[a]: Stuffed cloth vs Metal, $P<0.05$, [b]: Wood vs Plastic, $P<0.05$, [c]: Stuffed cloth vs Plastic, $P<0.05$.