



HHS Public Access

Author manuscript

Environ Int. Author manuscript; available in PMC 2020 January 01.

Published in final edited form as:

Environ Int. 2019 January ; 122: 310–315. doi:10.1016/j.envint.2018.11.031.

Lead exposure during childhood and subsequent anthropometry through adolescence in girls

Andrea L. Deierlein^a, Susan L. Teitelbaum^b, Gayle C. Windham^c, Susan M. Pinney^d, Maida P. Galvez^b, Kathleen L. Caldwell^e, Jeffery M. Jarrett^e, Ryszard Gajek^c, Lawrence H. Kushi^f, Frank Biro^g, Mary S. Wolff^b, and Breast Cancer and Environment Research Program

^aDepartment of Epidemiology, College of Global Public Health, New York University, NY, NY, USA

^bDepartment of Environmental Medicine and Public Health, Icahn School of Medicine at Mount Sinai, NY, NY, USA

^cEnvironmental Health Investigations Branch, California Department of Public Health, Richmond, CA, USA

^dUniversity of Cincinnati College of Medicine, Department of Environmental Health, Cincinnati, OH, USA

^eNational Center for Environmental Health, Centers for Disease Control and Prevention, Atlanta, GA, USA

^fDivision of Research, Kaiser Permanente, Oakland, CA, USA

^gDivision of Adolescent Medicine, Cincinnati Children's Hospital Center, Cincinnati, OH, USA

Abstract

Introduction—Cross-sectional studies suggest that postnatal blood lead (PbB) concentrations are negatively associated with child growth. Few studies prospectively examined this association in populations with lower PbB concentrations. We investigated longitudinal associations of childhood PbB concentrations and subsequent anthropometric measurements in a multi-ethnic cohort of girls.

Methods—Data were from The Breast Cancer and the Environment Research Program at three sites in the United States (U.S.): New York City, Cincinnati, and San Francisco Bay Area. Girls were enrolled at ages 6–8 years in 2004–2007. Girls with PbB concentrations collected at 10 years old (mean 7.8 years, standard deviation (SD) 0.82) and anthropometry collected at 3 follow-up visits were included (n=683). The median PbB concentration was 99 ug/d (10th percentile= 0.59 ug/dL and 90th percentile= 2.00 ug/dL) and the geometric mean was 1.03 ug/dL (95% Confidence Interval (CI): 0.99, 1.06). For analyses, PbB concentrations were dichotomized as <1 ug/dL (n=342) and ≥1 ug/dL (n=341). Anthropometric measurements of height, body mass index (BMI), waist circumference (WC), and percent body fat (%BF) were collected at enrollment and follow-

Corresponding Author: AL Deierlein.

Publisher's Disclaimer: This is a PDF file of an unedited manuscript that has been accepted for publication. As a service to our customers we are providing this early version of the manuscript. The manuscript will undergo copyediting, typesetting, and review of the resulting proof before it is published in its final citable form. Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

up visits through 2015. Linear mixed effects regression estimated how PbB concentrations related to changes in girls' measurements from ages 7-14 years.

Results—At 7 years, mean difference in height was -2.0 cm (95% CI: $-3.0, -1.0$) for girls with ≥ 1 ug/dL versus <1 ug/dL PbB concentrations; differences persisted, but were attenuated, with age to -1.5 cm (95% CI: $-2.5, -0.4$) at 14 years. Mean differences for BMI, WC, and BF% at 7 years between girls with ≥ 1 ug/dL versus <1 ug/dL PbB concentrations were -0.7 kg/m² (95% CI: $-1.2, -0.2$), -2.2 cm (95% CI: $-3.8, -0.6$), and -1.8% (95% CI: $-3.2, -0.4$), respectively. Overall, these differences generally persisted with advancing age and at 14 years, differences were -0.8 kg/m² (95% CI: $-1.5, -0.02$), -2.9 cm (95% CI: $-4.8, -0.9$), and -1.7% (95% CI: $-3.1, -0.4$) for BMI, WC, and BF%, respectively.

Conclusions—These findings suggest that higher concentrations of PbB during childhood, even though relatively low by screening standards, may be inversely associated with anthropometric measurements in girls.

Keywords

lead; childhood; girls; height; body fat

1. Introduction

Lead is an environmental toxin capable of interfering with neurodevelopment, endocrine function, and growth in children.^{1,2} The main sources of lead exposure tend to be lead paint, consumer products, air pollution, water, and food packaging.²⁻⁵ Despite implementation of numerous policies, which have drastically reduced childhood lead exposures in the United States (U.S.), detectable blood lead (PbB) concentrations persist, with approximately half of children ages 1-5 years having PbB ≥ 1 ug/dL.⁶ No level of PbB is considered safe and there is evidence to support lasting detrimental health effects with PbB concentrations <10 ug/dL.¹

Studies of prenatal lead exposure suggest that fetal exposure to increasing maternal PbB concentrations is associated with premature birth, low birth weight, and smaller gains in height and weight during infancy and childhood.⁷⁻¹⁰ Postnatal PbB concentrations are also negatively associated with anthropometry in children.^{9,11-15} Among children, ages 7 years and younger, participating in the second and third National Health and Nutrition Examination Surveys (NHANES II, 1976-1980 and III, 1988-1994, mean PbB concentrations were ~ 15 and 4 ug/dl, respectively), height was strongly negatively correlated with PbB concentration; with 1.2 - 1.6 centimeters (cm) shorter heights per 10 ug/dL increase in PbB concentrations.^{11,12} A decrease in weight of 1.1 kilograms (kg) per 10 ug/dL increase in PbB concentrations was also observed.¹¹ However, no^{10,16,17} and positive¹⁸ associations have also been reported.

Many of the previous studies were based on cross-sectional data and/or had sample populations with mean PbB concentrations above the Centers for Disease Control and Prevention reference level of 5 ug/dL (the level at which public health actions should be initiated).^{11,12,19} There remains limited epidemiological investigation of lower postnatal

PbB concentrations (<5 ug/dL) and children's health, particularly anthropometry. The objective of the current study was to investigate associations of childhood PbB concentrations and subsequent anthropometric measurements among a multi-site, multiethnic cohort of girls with PbB concentrations reflective of the low environmental lead exposure levels observed in the general U.S. population.²⁰

2. Materials and Methods

2.1. Study Population

The Breast Cancer and Environment Research Program included a prospective puberty cohort funded by the National Institute of Environmental Health Sciences and National Cancer Institute. The study and recruitment process have been described previously.²¹ Girls ages 6-8 years were enrolled in 2004-2007 at three sites (baseline, n=1,239): Icahn School of Medicine at Mount Sinai, which recruited in East Harlem, New York (New York City); Cincinnati Children's Hospital/University of Cincinnati (Cincinnati), which recruited from schools in the Cincinnati metropolitan area and through the Breast Cancer Registry of Greater Cincinnati; and Kaiser Permanente health care system in Northern California, which recruited in the San Francisco Bay Area (San Francisco). In addition to age, inclusion criteria required that girls have no underlying endocrine medical conditions, be of black or Hispanic race/ethnicity (New York City site only), and have been born in the Kaiser Permanente system (San Francisco). The study was approved by the institutional review board at each site and the Centers for Disease Control and Prevention (CDC). There were 881 girls with PbB concentrations collected at some time point in the study (baseline or at a follow-up visit); 795 had anthropometric measurements collected at 3 biannual or annual follow-up visits, of which 683 had PbB concentrations collected at age 10 years (120 months) or younger.

2.2. Blood lead measurements

Blood lead analysis was conducted at the CDC or California Department of Public Health Laboratory using inductively coupled plasma mass spectrometry.²² Both laboratories are CLIA compliant. Detection limits were 0.07 µg/dL and results for all samples were above that concentration. The median PbB concentration was 0.99 ug/dL (mean (SD) = 1.16 (0.67) ug/dL, range=0.18, 5.40, 10th percentile= 0.59 ug/dL and 90th percentile= 2.00 ug/dL) and the geometric mean (GM) was 1.03 ug/dL (95% Confidence Interval (CI): 0.99, 1.07). We initially categorized PbB concentrations as: <1 ug/dL (n=342, reference group), 1-<2 ug/dL (n=272), and ≥ 2 ug/dL (n=69), to examine the highest levels in our sample). In these analyses, associations were similar for PbB concentrations in the 1-<2 ug/dL and ≥ 2 ug/dL categories, compared to <1 ug/dL category. Therefore, PbB concentrations were dichotomized and included in final analyses as <1 ug/dL (n=342, mean (SD)= 0.73 (0.16) and GM=0.70; 95%CI, 0.69-0.72) and ≥ 1 ug/dL (n=341, mean (SD)= 1.61 (0.70) and GM=1.50; 95%CI, 1.45-1.56).

The final analytic sample was limited to those girls with PbB concentrations collected at age 10 years (n=683). There were 112 girls (16%, n=106 girls were from the New York City site) who had PbB concentrations collected after age 10 years (mean age= 11.7 years) who

were excluded. We chose the cut-point of 10 years because it is an age when girls are experiencing increases in height and it precedes peak height velocity by approximately 1 year.^{23,24} Inclusion of girls with PbB concentrations collected at older ages (>10 years, mean age=11.7 years) may skew the results since these girls are contributing anthropometric data within a shorter (older) age range and at ages when growth, particularly height, may begin to slow. Sensitivity analyses including all girls (n=795) were conducted for comparison. In these analyses, predicted mean differences in all measurements were attenuated but were not substantively different in magnitude or precision from the final analytic sample, so they are not presented.

2.3. Anthropometric measurements

Weight (kilograms, kg), standing height (cm), and umbilical waist circumference (cm) were collected at baseline and at biannual (Cincinnati) or annual (New York City and SFBA) follow-up visits by trained interviewers using a standard protocol.²⁵ Children wore light clothing and no shoes. All anthropometric measurements were taken twice, recorded to the nearest 0.1 cm or 0.1 kg, and averaged for analyses. Measurements were taken a third time (and averaged) only if the absolute difference between the previous two measurements exceeded the tolerance level (1 cm or 0.3 kg). BMI was calculated as weight divided by squared height (kg/meters²). Percent body fat was estimated using bioelectrical impedance analysis (Tanita). Only anthropometric measurements taken at the time of PbB concentrations collection and the follow-up visits thereafter were included in analyses. The median number of times that anthropometric measurements were taken for each girl during the follow-up period was 9 (range, 3-15 collection times). BMI percentile, waist circumference, and percent body fat were correlated in this population ($r=0.75$ for BMI and waist circumference; $r=0.79$ for BMI and percent body fat; and $r=0.88$ for waist circumference and percent body fat).

2.4. Covariates

Data regarding sociodemographic and other characteristics were completed by the girls' mothers (or caregivers) via self-administered (Cincinnati) or interviewer-administered questionnaires, conducted in English or Spanish. Race/ethnicity was identified as Black, Hispanic, White, and Asian. Highest education level of either parent was used as a proxy of socioeconomic status and was categorized as high school graduate or less, some college/college graduate, and graduate or professional degree.

2.5. Statistical analysis

Statistical analyses were performed using Stata 15 (College Station, Texas). Confounders were selected a priori based on a conceptual model and a review of the previous literature. Linear mixed effects models with an unstructured correlation matrix assessed the relationship between dichotomous PbB concentrations (measured at baseline) and girls' height, BMI, waist circumference, and percent body fat, separately, from ages 7 through 14 years.²⁶⁻²⁸ This age range was selected due to the smaller numbers of girls with measurements at younger and older ages. Final models included dichotomous PbB concentrations, age (at anthropometric measurement, centered and rounded to the nearest tenth of a year), age squared (accommodates non-linearity in growth), race, an interaction

term between age and PbB concentrations, an interaction term between age squared and PbB concentrations, and an interaction term between race and age (allows for differences by race in girls' measurements over time). These models were used to generate predicted differences (and 95% confidence intervals, CI) in each of the anthropometric outcomes comparing 1 ug/dl to <1 ug/dl PbB concentrations at each integer age using the *pwcompare* command. Additional adjustment of final models for caregiver education slightly strengthened but did not appreciably alter the observed associations. An interaction term between race and blood Pb concentrations was also tested in final models, but was not statistically significant ($p>0.10$ in all models).

3. Results

3.1. Study population characteristics

In the final analytic sample, average age at collection of blood PbB concentrations was 7.8 years (SD=0.82) and approximately half of the sample had PbB concentrations ≥ 1 ug/dl ($n=341$). The mean (SD) BMI percentile, height percentile, waist circumference, and percent body fat at collection of PbB concentrations were 61.0 (29.6)%, 55.6 (28.7)%, 59.2 (7.8) cm, and 16.8 (8.8)%, respectively. Unadjusted geometric means of PbB concentrations by selected sociodemographic characteristics of the girls are presented in Table 1. PbB concentrations were similar across categories of characteristics with the exception that higher PbB concentrations were observed among Black girls compared to those of other race/ethnic groups, among girls at the New York City and Cincinnati sites compared to those in San Francisco, and among girls whose caregivers had achieved a high school education or less compared to those with more educated caregivers. However, by category of PbB concentration, only distributions of race/ethnicity statistically significantly varied ($p<0.05$, Table 1). We also examined the distributions of baseline characteristics of girls who were missing blood Pb concentrations or anthropometric measurements. Compared to girls with complete data, those with missing data were more likely to be older (age 9 years and older), from the New York City site, black or Hispanic, overweight or obese, and have a less educated caregiver ($p<0.05$ for all comparisons).

3.2. Association of PbB concentrations with height

PbB concentrations ≥ 1 ug/dL were consistently negatively associated with anthropometric measurements throughout the study period (Tables 2 and 3). Table 2 shows the predicted mean differences in height between girls with PbB concentrations ≥ 1 versus <1 ug/dL from ages 7 through 14 years. At 7 years, girls with PbB concentrations ≥ 1 ug/dL were -2.0 cm (95% CI: $-3.0, -1.0$) shorter than girls with PbB concentrations <1 ug/dL. The predicted mean differences in height between girls with high and low PbB slightly decreased with age and at 14 years, girls with PbB concentrations ≥ 1 ug/dL were -1.5 cm (95% CI: $-2.5, -0.4$) shorter than girls with PbB concentrations <1 ug/dL.

3.3. Association of PbB concentrations with BMI, waist circumference, and percent body fat

Table 3 shows the predicted mean differences in BMI, waist circumference, and percent body fat between girls with PbB concentrations <1 ug/dL versus ≥ 1 ug/dL from ages 7

through 14 years. PbB concentrations ≥ 1 ug/dL were consistently inversely associated with each of the anthropometric measurements across the follow-up period. Between 7 to 14 years, differences in BMI, waist circumference, and percent body fat ranged from -0.7 to -0.9 kg/m², -2.2 to -3.0 cm, and -1.7 to -2.2% , respectively.

4. Discussion

This study prospectively examined the influence of childhood PbB concentrations on anthropometry among a cohort of young, multi-ethnic U.S. girls. PbB concentrations in these girls were representative of the low exposure levels commonly observed in the US (e.g. NHANES 2003-2006 the geometric mean of PbB concentrations was 1.03 (SE=0.02) among children 3-19 years old.²⁰ We found that PbB concentrations at ages 6-10 years were negatively associated with subsequent anthropometric measurements collected over ~7 years. Girls with PbB concentrations ≥ 1 ug/dL were shorter and had lower BMI, waist circumference, and percent body fat than those with PbB concentrations <1 ug/dL at baseline and throughout the follow-up period.

There are several biological mechanisms through which lead may influence children's physical growth and body composition. Lead may interfere with bone cell function, metabolism, and bone mineralization.^{29,30} For example, lead may alter circulating levels of 1,25-dihydroxyvitamin D₃ (a hormone required for bone development and maintenance), as well as the ability of bone cells to respond to hormonal regulation, leading to impaired bone formation. Lead may also have endocrine-disrupting capabilities by reducing responses to hormones that are necessary for growth, such as insulin-like growth factor and growth hormone, and inhibiting the hypothalamic-pituitary-growth axis.^{31,32}

Many, mostly cross-sectional, epidemiological studies report that PbB concentrations measured during childhood are associated with shorter height.^{11,12,14,15,33-39} These studies have included children within a wide range of ages, from infancy through adolescence, and mean PbB concentrations, from ~ 2 to >20 ug/dl. Reported heights in these studies were approximately 1-3 cm shorter per 10 ug/dl increase in lead concentrations;^{11,12,14,34,36} this range includes the predicted mean differences in height observed in the current study of ~ 1.5 -2 cm for girls with high versus low PbB concentrations. Collectively, these results suggest that the association of lead and height may be robust to a range of PbB concentrations.

Negative associations of lead and BMI are less consistently reported. Similar to the current study, several studies observed lower BMI or weight with higher PbB concentrations.^{11,13,20,34,37,40,41} For example, Scinicariello et al. examined cross-sectional associations of PbB concentrations and BMI z-score among US children ages 3-19 years (NHANES 1999-2006) with PbB concentrations comparable to those of girls in the current study (the geometric mean was 1.03 ug/dl in both studies).²⁰ Compared to children in the first quartile of PbB concentrations (PbB concentrations ≤ 0.70 ug/dl), those in the third (1.10-1.60 ug/dl) and fourth (≥ 1.16 ug/dl) quartiles had lower BMI z-scores (-0.15 (SE=0.06) and -0.33 (SE=0.07), respectively), and lower odds of overweight and obesity.²⁰ However, other studies reported null^{10,15-17,36} or positive¹⁸ associations. Among Korean children, ages 5-13

years, with relatively low mean PbB concentrations (2.4 ug/100ml, SD=0.7), Min and colleagues found an inverse association for height (B=-1.45 cm, SE 0.64), but no association with weight or BMI³⁶ In another study, dentin (but not bone) lead levels were weakly, positively associated with BMI in cross-sectional analyses at ages 6-9 years (B=1.02, SE=1.02) and at follow-up at ages 19-22 years (B=2.65, SE=1.16); however, loss to follow-up in this study was nearly 75%.¹⁸ BMI is often used as an indicator of adiposity in population-based studies; however, since it is an index of weight relative to height, it is highly correlated with both fat mass and fat-free mass in young children.⁴² In the current study, measurements of waist circumference (estimates central adiposity or visceral fat) and percent body fat (differentiates fat-free mass from fat mass), in addition to BMI, were included to assess changes in girls' body composition.⁴³ We observed inverse associations of higher PbB concentrations with all three measurements (BMI, waist circumference, and percent body fat), which remained fairly consistent throughout the study period and did not substantially vary with increasing age. These findings suggest that PbB concentrations are associated with lower BMI, which may be attributed to shorter height, as well as reduced body fat. Given that our study is the first, to our knowledge, to consider alternative assessments of body composition and PbB concentrations, replication of these findings is warranted.

Strengths of this study include its longitudinal design with repeated anthropometric measurements in a large, multi-ethnic sample of girls from childhood through early adolescence, which represents a period of physiological and physical changes related to growth and development. In addition to height, we considered three distinct, indirect estimations of adiposity: BMI, waist circumference, and percent body fat. These measurements are correlated but also complementary but also allowed for a varied assessment of how lead exposure may influence girls' body composition. This study was limited to a one-time measurement of PbB concentrations. PbB concentrations have low within-child variability and reflect lead exposure over the previous several months⁴⁴⁻⁴⁶; therefore, they may be indicative of relatively recent or possibly more constant exposures. Given that sources of lead are likely to be consistent in the environment, e.g. air and water pollution, PbB concentrations in this study may be representative of lead exposures occurring even earlier in childhood. This may explain the observed inverse associations of PbB concentrations and anthropometric measurements at baseline. For the most part, these associations persisted through early adolescence, which could be a consequence of continued lead exposure but cannot be determined due to the one-time blood measurement. Still, reverse causality cannot be ruled out. It is plausible that PbB concentrations may be diluted by body size, such that taller girls have lower PbB concentrations relative to shorter girls (which may also be age-related). We attempted to reduce this possibility by limiting analyses to younger girls at sample collection (≤ 10 years) when rates of growth are likely slower compared to older ages, for most girls.^{23,24} PbB concentrations were also categorized (<1 and 1 ug/dl) and there were no differences at baseline in the distributions of age, height percentiles, or BMI percentiles between PbB categories (Table 1), suggesting that dilution by body size did not solely influence our results. Lastly, we cannot exclude the possibility of unmeasured confounding by genetic, dietary, or other factors that may be associated with both lead exposure (or metabolism) and childhood growth.

5. Conclusions

This is the first prospective, longitudinal epidemiological study to examine the relationship between PbB concentrations during childhood and anthropometric measurements in girls over approximately 7 years of follow-up. The findings suggest that PbB concentrations 1 ug/dl are inversely associated with height and body composition in girls throughout early adolescence. These associations were observed at relatively low PbB concentrations that are below screening standards and relevant to exposure levels occurring in the U.S. and other countries.

Acknowledgements:

The authors thank the collaborators at the centers involved in this research including Jessica Montana, Dr. Nancy Mervish, Dr. Cheryl Stein, Rochelle Osborne, Lisa Boguski, Dr. Joel Forman, and Dr. Barbara Brenner (Mount Sinai School of Medicine); Gayle Greenberg, Peggy Monroe, Banita Bailey, Kathy Ball, Dr. Bob Bornschein (Cincinnati); Dr. Robert Hiatt, Dr. Louise Greenspan, Dr. Julie Deardorff, Janice Barlow (Kaiser Permanente).

Funding: This publication was made possible by the National Institutes of Environmental Health (NIEHS) R00ES023474; Breast Cancer and the Environment Research Program (BCERP) award numbers U01ES012770, U01ES012771, U01ES012801, U01ES019435, U01ES019453, U01ES019454, and U01ES019457 from NIEHS and the National Cancer Institute (NCI); P01ES009584, P30ES023515, and P30ES006096 from NIEHS; and UL1RR024131, CSTA-UL1RR029887, and CSTA-UL1RR026314 from the National Center for Research Resources (NCRR). We also gratefully acknowledge support from the California Department of Public Health (CDPH) and Avon Foundation for this research. Its contents are solely the responsibility of the authors and do not necessarily represent the official position of the National Institutes of Health, the Centers for Disease Control and Prevention, or the CDPH.

Abbreviations

PbB	blood lead
BMI	body mass index
WC	waist circumference
BF%	percent body fat

References

1. Program NT. NTP Monograph on Health Effects of Low-level Lead. 2012 <https://ntp.niehs.nih.gov/pubhealth/hat/noms/lead/index.html>. Accessed April 1, 2018.
2. Prevention CDCa. Preventing lead poisoning in young children. 2005 <http://www.cdc.gov/nceh/lead/publications/PrevLeadPoisoning.pdf>. Accessed April 1, 2018.
3. Yoo SS, Lee S, Jeon DH, Kwack I, Lee KH. Analysis of metals from recycled papers and paper products for food packaging. *Food Science and Biotechnology*. 2001;10(2): 178–182.
4. Lanphear BP, Matte TD, Rogers J, et al. The contribution of lead-contaminated house dust and residential soil to children's blood lead levels: a pooled analysis of 12 epidemiologic studies. *EnvironRes*. 1998;79(1):51–68.
5. Levin R BM, Kashtock ME, Jacobs DE, Whelan EA, Rodman J, Schock MR, Padilla A, Sinks T. Lead exposures in U.S. Children, 2008: implications for prevention. *Environ Health Perspect*. 116(10): 1285–1293. [PubMed: 18941567]
6. Bellinger DC, Chen A, Lanphear BP. Establishing and achieving national goals for preventing lead toxicity and exposure in children. *JAMA pediatrics*. 2017;171(7):616–618. [PubMed: 28505218]
7. Renzetti S, Just AC, Burris HH, et al. The association of lead exposure during pregnancy and childhood anthropometry in the Mexican PROGRESS cohort. *EnvironRes*. 2017;152:226–232.

8. Shukla R, Bornschein RL, Dietrich KN, et al. Fetal and infant lead exposure: effects on growth in stature. *Pediatrics*. 1989;84(4):604–612. [PubMed: 2780121]
9. Schell LM, Denham M, Stark AD, Parsons PJ, Schulte EE. Growth of infants' length, weight, head and arm circumferences in relation to low levels of blood lead measured serially. *American Journal of Human Biology*. 2009;21(2):180–187. [PubMed: 18991336]
10. Dallaire R, Dewailly E, Ayotte P, et al. Growth in Inuit children exposed to polychlorinated biphenyls and lead during fetal development and childhood. *EnvironRes*. 2014;134:17–23.
11. Schwartz J, Angle C, Pitcher H. Relationship between childhood blood lead levels and stature. *Pediatrics*. 1986;77(3):281–288. [PubMed: 3951909]
12. Ballew C, Khan LK, Kaufmann R, Mokdad A, Miller DT, Gunter EW. Blood lead concentration and children's anthropometric dimensions in the Third National Health and Nutrition Examination Survey (NHANES III), 1988-1994. *JPediatr*. 1999;134(5):623–630. [PubMed: 10228299]
13. Little B, Spalding S, Walsh B, et al. Blood lead levels and growth status among African-American and Hispanic children in Dallas, Texas–1980 and 2002: Dallas Lead Project II. *AnnHumBiol*. 2009;36(3):331–341.
14. Kafourou A, Touloumi C, Makropoulos V, Loutradi A, Papanagioutou A, Hatzakis A. Effects of lead on the somatic growth of children. *Archives of Environmental Health: An International Journal*. 1997;52(5):377–383.
15. Vivoli G, Fantuzzi G, Bergomi M, et al. Relationship between low lead exposure and somatic growth in adolescents. *Journal of exposure analysis and environmental epidemiology*. 1993;3:201–209. [PubMed: 9857305]
16. Huzior-Bałajewicz A, Pietrzyk J, Schlegel-Zawadzka M, Piatkowska E, Zachwieja Z. The influence of lead and cadmium environmental pollution on anthropometric health factors in children. *Przegląd Lekarski*. 2001;58(4):315–324. [PubMed: 11450360]
17. Lamb MR, Janevic T, Liu X, Cooper T, Kline J, Factor-Litvak P. Environmental lead exposure, maternal thyroid function, and childhood growth. *EnvironRes*. 2008; 106(2): 195–202.
18. Kim R, Hu H, Rotnitzky A, Bellinger D, Needleman H. A longitudinal study of chronic lead exposure and physical growth in Boston children. *EnvironHealth Perspect*. 1995; 103(10): 952.
19. Prevention ACoCLPPCfDCa. Low level lead exposure harms children: A renewed call for primary prevention. 2012 https://www.cdc.gov/nceh/lead/acclpp/final_document_030712.pdf. Accessed April 1, 2018.
20. Scinicariello F, Buser MC, Mevissen M, Portier CJ. Blood lead level association with lower body weight in NHANES 1999–2006. *ToxicolApplPharmacol*. 2013;273(3):516–523.
21. Biro FM, Galvez MP, Greenspan LC, et al. Pubertal assessment methods and baseline characteristics in a mixed longitudinal study of girls. 2010;126(3):e583–e590.
22. Gajek R BF, She J. Determination of essential and toxic metals in blood by ICP-MS with calibration in synthetic matrix. *Anal Methods*. 2013;5:2193–2202.
23. Abbassi V. Growth and normal puberty. *Pediatrics*. 1998;102(Supplement 3):507–511. [PubMed: 9685454]
24. McCormack SE, Cousminer DL, Chesi A, et al. Association between linear growth and bone accrual in a diverse cohort of children and adolescents. *JAMA pediatrics*. 2017; 171(9):e171769–e171769. [PubMed: 28672287]
25. Kuczumarski RJ. CDC growth charts; United States. 2000.
26. Harville DA. Maximum likelihood approaches to variance component estimation and to related problems. *Journal of the American Statistical Association*. 1977;72(358):320–338.
27. Ware JH. Linear models for the analysis of longitudinal studies. *American Statistician*. 1985;39(2): 95–101.
28. Laird NM, Ware JH. Random-effects models for longitudinal data. *Biometrics*. 1982;38(4):963–974. [PubMed: 7168798]
29. Pounds JG, Long GJ, Rosen JF. Cellular and molecular toxicity of lead in bone. *EnvironHealth Perspect*. 1991;91:17.

30. Mushak P, Davis JM, Crocetti AF, Grant LD. Prenatal and postnatal effects of low-level lead exposure: integrated summary of a report to the US Congress on childhood lead poisoning. *EnvironRes.* 1989;50(1): 11–36.
31. Berry JW, Moriarty CM, Lau Y-S. Lead attenuation of episodic growth hormone secretion in male rats. *International journal of toxicology.* 2002;21(2):93–98.
32. Fleisch AF, Burns JS, Williams PL, et al. Blood lead levels and serum insulin-like growth factor 1 concentrations in peripubertal boys. *EnvironHealth Perspect.* 2013;121(7):854.
33. Frisancho AR, Ryan AS. Decreased stature associated with moderate blood lead concentrations in Mexican-American children. *AmJClinNutr.* 1991;54(3):516–519.
34. Ignasiak Z, Sławińska T, Rojek K, Little B, Malina R. Lead and growth status of schoolchildren living in the copper basin of south-western Poland: Differential effects on bone growth. *AnnHumBiol.* 2006;33(4):401–414.
35. Rahman A, Maqbool E, Zuberi HS. Lead-associated deficits in stature, mental ability and behaviour in children in Karachi. *Annals of tropical paediatrics.* 2002;22(4):301–311. [PubMed: 12530279]
36. Min K-B, Min J-Y, Cho S-I, Kim R, Kim H, Paek D. Relationship between low blood lead levels and growth in children of white-collar civil servants in Korea. *IntJHygEnvironHealth.* 2008;211(1-2):82–87.
37. Zeng X, Xu X, Qin Q, Ye K, Wu W, Huo X. Heavy metal exposure has adverse effects on the growth and development of preschool children. *Environmental geochemistry and health.* 2018:1–13. [PubMed: 27921191]
38. Selevan SG, Rice DC, Hogan KA, Euling SY, Pfahles-Hutchens A, Bethel J. Blood lead concentration and delayed puberty in girls. *N Engl J Med.* 2003;348(16): 1527–1536. [PubMed: 12700372]
39. Yang H, Huo X, Yekeen TA, Zheng Q, Zheng M, Xu X. Effects of lead and cadmium exposure from electronic waste on child physical growth. *Environmental Science and Pollution Research.* 2013;20(7):4441–4447. [PubMed: 23247522]
40. Little B, Snell L, Johnston W, Knoll K, Buschang P. Blood lead levels and growth status of children. *American Journal of Human Biology.* 1990;2(3):265–269. [PubMed: 28520290]
41. Kamel N, Ramadan A, Kamel M, Mostafa Y, Abo Re-N, Ali A. Impact of lead exposure on health status and scholastic achievement of school pupils in Alexandria. *The Journal of the Egyptian Public Health Association.* 2003;78(1-2): 1–28. [PubMed: 17219908]
42. Nyström CD, Henriksson P, Ek A, et al. Is BMI a relevant marker of fat mass in 4 year old children? Results from the MINISTOP trial. *Eur J Clin Nutr.* 2018:1.
43. Brambilla P, Bedogni G, Moreno LA, et al. Crossvalidation of anthropometry against magnetic resonance imaging for the assessment of visceral and subcutaneous adipose tissue in children. *Int J Obes.* 2006;30(1):23.
44. Duggan MJ. The uptake and excretion of lead by young children. *Archives of Environmental Health: An International Journal.* 1983;38(4):246–247.
45. Sexton K, Adgate JL, Fredrickson AL, Ryan AD, Needham LL, Ashley DL. Using biologic markers in blood to assess exposure to multiple environmental chemicals for inner-city children 3–6 years of age. *EnvironHealth Perspect.* 2006; 114(3):453.
46. Sexton K, Ryan AD. Using exposure biomarkers in children to compare between-child and within-child variance and calculate correlations among siblings for multiple environmental chemicals. *Journal of Exposure Science and Environmental Epidemiology.* 2012;22(1): 16. [PubMed: 22008795]

Highlights

- Few studies prospectively examined association of childhood lead and anthropometry
- This study included a multi-ethnic US population of girls with low lead concentrations
- Anthropometric measurements were taken 3 times during follow-up
- Lead concentrations ≥ 1 ug/dl were negatively associated with anthropometry at ages 7-14 years
- Future research should include investigation of low blood lead concentrations

Table 1.

Blood lead (PbB) concentrations by selected sociodemographic characteristics of girls participating in the Breast Cancer Environment and Reproduction Program (final analytic sample, n=683).*

	N (%)	PbB (ug/dL)		Mean (SD)	Range	PbB<1 ug/dL (n=342)	PbB 1 ug/dL (n=341)
		GM	95% CI			N (%)	N (%)
Site	683						
New York	30 (4)	1.17	0.98, 1.39	1.29 (0.63)	0.44, 3.20	12 (4)	18 (5)
Cincinnati	326 (48)	1.12	1.06, 1.18	1.28 (0.79)	0.34, 5.40	153 (45)	173 (51)
San Francisco Bay Area	327 (48)	0.93	0.89, 0.98	1.04 (0.51)	0.18, 3.73	177 (52)	150 (44)
Race/Ethnicity	683						
Black	192 (28)	1.29	1.20, 1.37	1.45 (0.80)	0.42, 5.40	60 (18)	130 (39)
Hispanic	103 (15)	1.01	0.92, 1.11	1.13 (0.57)	0.39, 3.65	48 (14)	55 (16)
Asian	42 (6)	0.84	0.74, 0.95	0.91 (0.37)	0.36, 2.19	26 (8)	16 (5)
White	346 (51)	0.93	0.89, 0.98	1.05 (0.59)	0.18, 5.30	208 (61)	138 (40)**
Age at PbB Collection (years)	683						
6-< 7	121 (18)	1.04	0.95, 1.14	1.19 (0.70)	0.19, 4.40	62 (18)	59 (17)
7-< 8	283 (41)	1.06	1.00, 1.12	1.19 (0.66)	0.38, 5.40	132 (39)	151 (44)
8-< 9	207 (30)	1.00	0.94, 1.07	1.15 (0.70)	0.18, 5.30	110 (32)	97 (28)
9 - 10	72 (11)	0.96	0.86, 1.06	1.06 (0.54)	0.34, 3.20	38 (11)	34 (10)
BMI Percentile	683						
<50th	254 (37)	1.05	0.99, 1.12	1.20 (0.69)	0.18, 4.30	117 (34)	137 (40)
50 - <85th	230 (34)	1.02	0.96, 1.08	1.15 (0.67)	0.34, 5.30	120 (35)	110 (32)
85 - <95th	104 (15)	1.01	0.91, 1.12	1.17 (0.77)	0.29, 5.40	54 (16)	50 (15)
95th	95 (14)	1.02	0.93, 1.10	1.11 (0.52)	0.41, 2.80	51 (15)	44 (13)
Height Percentile	683						
<25th	134 (20)	1.02	0.94, 1.10	1.13 (0.61)	0.43, 4.20	61 (18)	73 (21)
25 th - <50 th	150 (22)	1.09	1.01, 1.18	1.23 (0.69)	0.19, 5.30	66 (19)	84 (25)
50 th - <75 th	176 (26)	1.03	0.96, 1.11	1.17 (0.64)	0.18, 4.70	92 (27)	84 (25)
75 th	223 (33)	0.99	0.93, 1.06	1.14 (0.71)	0.29, 5.40	123 (36)	100 (29)
Caregiver Education	666						
High School or Less	265 (40)	1.09	1.03, 1.16	1.24 (0.70)	0.29, 4.70	122 (36)	143 (43)
College	257 (39)	1.00	0.94, 1.06	1.14 (0.67)	0.18, 5.30	137 (41)	120 (36)
Graduate School	144 (22)	0.95	0.89, 1.01	1.03 (0.49)	0.34, 4.30	77 (23)	67 (20)

GM, geometric mean; 95%CI, 95% Confidence Interval; BMI, Body Mass Index

* Sociodemographic characteristics of girls were assessed at the time of collection of PbB concentrations

** chi-squared test, $p < 0.05$

Author Manuscript

Author Manuscript

Author Manuscript

Author Manuscript

Table 2.

Predicted mean differences* in height among girls from ages 7 through 14 years with ≥ 1 ug/dl versus <1 ug/dl blood lead (PbB) concentrations (n=683).

Age (years)	Height (cm)	95% CI	P
7	-2.0	-3.0, -1.0	<0.001
8	-1.9	-2.8, -0.9	<0.001
9	-1.7	-2.7, -0.8	<0.001
10	-1.6	-2.6, -0.7	0.001
11	-1.6	-2.5, -0.6	0.002
12	-1.5	-2.5, -0.5	0.004
13	-1.5	-2.5, -0.5	0.004
14	-1.5	-2.5, -0.4	0.01

* Linear mixed-effects models included dichotomous PbB concentrations, age (at anthropometric measurement, centered and estimated to the nearest tenth of a year), age squared, race, an interaction term between age and PbB concentrations, an interaction term between age squared and PbB concentrations, and an interaction term between race and age.

Table 3.

Predicted mean differences* in body mass index (BMI), waist circumference (WC), and percent body fat (BF) among girls ages 7 through 14 years with ≥ 1 ug/dl versus <1 ug/dl blood lead (PbB) concentrations (n=686).

Age (years)	BMI (kg/m ²)	95% CI	P	WC (cm)	95% CI	P	BF (%)	95% CI	P
7	-0.7	-1.2, -0.2	0.005	-2.2	-3.8, -0.6	0.01	-1.8	-3.2, -0.4	0.01
8	-0.8	-1.3, -0.3	0.001	-2.5	-3.8, -1.1	<0.001	-2.0	-3.3, -0.7	0.003
9	-0.9	-1.4, -0.4	0.001	-2.7	-4.0, -1.4	<0.001	-2.1	-3.4, -0.8	0.001
10	-0.9	-1.4, -0.4	0.001	-2.9	-4.3, -1.4	<0.001	-2.2	-3.4, -0.9	0.001
11	-0.9	-1.5, -0.3	0.002	-3.0	-4.5, -1.4	<0.001	-2.1	-3.4, -0.9	0.001
12	-0.9	-1.5, -0.3	0.005	-3.0	-4.7, -1.3	0.001	-2.1	-3.4, -0.8	0.002
13	-0.8	-1.5, -0.2	0.02	-3.0	-4.8, -1.1	0.002	-1.9	-3.2, -0.6	0.003
14	-0.8	-1.5, -0.02	0.05	-2.9	-4.8, -0.9	0.005	-1.7	-3.1, -0.4	0.01

* Linear mixed-effects models included dichotomous PbB concentrations, age (at anthropometric measurement, centered and estimated to the nearest tenth of a year), age squared, race, an interaction term between age and PbB concentrations, an interaction term between age squared and PbB concentrations, and an interaction term between race and age.