EPA/600/R-23/061
March 2023
www.epa.gov/isa

United States Environmental Protection Agency

Integrated Science Assessment for Lead

Appendix 2: Exposure, Toxicokinetics, and Biomarkers

External Review Draft

March 2023

Health and Environmental Effects Assessment Division
Center for Public Health and Environmental Assessment
Office of Research and Development
U.S. Environmental Protection Agency

DISCLAIMER

This document is an external review draft for peer review purposes only. This information is distributed solely for the purpose of predissemination peer review under applicable information quality guidelines. It has not been formally disseminated by the Environmental Protection Agency. It does not represent and should not be construed to represent any agency determination or policy. Mention of trade names or commercial products does not constitute endorsement or recommendation for use.

DOCUMENT GUIDE

This Document Guide is intended to orient readers to the organization of the Lead (Pb) Integrated Science Assessment (ISA) in its entirety and to the sub-section of the ISA at hand (indicated in bold). The ISA consists of the Front Matter (list of authors, contributors, reviewers, and acronyms), Executive Summary, Integrated Synthesis, and 12 appendices, which can all be found at https://cfpub.epa.gov/ncea/isa/recordisplay.cfm?deid=357282.

Front Matter

Executive Summary

Integrative Synthesis

Appendix 1. Lead Source to Concentration

Appendix 2. Exposure, Toxicokinetics, and Biomarkers

Appendix 3. Nervous System Effects

Appendix 4. Cardiovascular Effects

Appendix 5. Renal Effects

Appendix 6. Immune System Effects

Appendix 7. Hematological Effects

Appendix 8. Reproductive and Developmental Effects

Appendix 9. Effects on Other Organ Systems and Mortality

Appendix 10. Cancer

Appendix 11. Effects of Lead in Terrestrial and Aquatic Ecosystems

Appendix 12. Process for Developing the Pb Integrated Science Assessment

CONTENTS

LIST OF TABLES

LIST OF FIGURES

ACRONYMS AND ABBREVIATIONS

μ-SRXRF	microbeam synchrotron radiation X-ray fluorescence
100LL	100 octane, low lead
AALM	All-Ages Lead Model
AAS	atomic absorption spectroscopy
AERMOD	American Meteorological Society/Environmental Protection Agency Regulatory Model
AF	absorbed fraction
AHHS	American Healthy Homes Survey
ALAD	δ-aminolevulinic acid dehydratase
ALF	artificial lysosomal fluid
AQCD	Air Quality Criteria Document
AQS	Air Quality System
ASV	anodic stripping voltammetry
BLL	blood lead level
BLRV	blood lead reference value
BMI	body mass index
Cal EPA	California Environmental Protection Agency
CDC	Centers for Disease Control and Prevention
CR	creatine
CSMR	chloride to sulfate mass ratio
DoD	Department of Defense
DOE	Department of Energy
DOHMH	Department of Health and Mental Hygiene (New York City)
DWSD	Detroit Water and Sewage Department
δ-ALA	δ-aminolevulinic acid
EBLL	elevated blood lead level
FDA	Food and Drug Administration
FWSC	Flint Water Service Center
GFR	glomerular filtration rate
GI	gastrointestinal
GM	geometric mean
GSD	geometric standard deviation
HA	Housing Authority
HC	hydrocarbons
HFE	hemochromatosis
ICP-AES	inductively coupled plasma atomic emission spectroscopy
ICP-MS	inductively coupled plasma mass spectrometry
ICRP	International Commission on Radiological Protection
IDF	Israeli Defense Force
IEUBK	Integrated Exposure Uptake Biokinetic
IMPROVE	Interagency Monitoring of Protected Visual Environments
IRLs	interim reference levels
ISA	Integrated Science Assessment
IVBA	in vitro bioaccessibility
KXRF	K-shell X-ray fluorescence
LA-ICP-MS	laser ablation inductively coupled plasma mass spectrometry
LOD	limit of detection
LSL	lead service line
LTC	loading to concentration
MG	Mahayogaraj Guggulu
MMB	multimedia biomarker
mo	month, months
NAAQS	National Ambient Air Quality Standards
NATA	National Air Toxics Assessment
NR	not reported
N.D.	not detected
NHANES	National Health and Nutrition Examination Survey
NHEXAS	National Human Exposure Assessment Survey
OSHA	Occupational Safety and Health Administration
PAH	polycyclic aromatic hydrocarbon
Pb	lead
PbA	air Pb concentration
PbB	blood Pb concentration
PIR	poverty-to-income ratio
PM	particulate matter
PUFA	polyunsaturated fatty acids
RBA	relative bioavailability
RBCs	red blood cells
RSD	relative standard deviation
SAB	Scientific Advisory Board
SD	standard deviation
SES	socioeconomic status
SHEDS	Stochastic Human Exposure and Dose Simulation
SLL	soil lead level
TDS	Total Diet Study
TRI	Toxics Release Inventory
TSP	total suspended particles
VA	Veterans Affairs

WQS	weighted quantile sum	XRF	X-ray fluorescence
WWEIA	What We Eat in America	yr	year, years

APPENDIX 2 EXPOSURE, TOXICOKINETICS, AND BIOMARKERS

The purpose of this appendix is to review exposure, toxicokinetic, and biomarker information relevant to human lead (Pb) exposure, with a focus on scientific literature from 2011 onwards. Section 2.1 reviews pathways of Pb exposure, exposure assessment methodologies, exposure studies by various pathways, co-exposures, and exposure disparities for specific populations. Section 2.2 reviews absorption, distribution and metabolism, and elimination of Pb from the body. Section 2.3 reviews methodologies for biomarker measurement and the relationships between blood Pb and Pb in bone and soft tissues. Section 2.4 reviews studies of biomarker levels, including trends in Pb biomarker levels over time. Sections 2.5 and 2.6 review empirical models and biokinetic models of Pb exposure – Pb blood relationships, respectively. Section 2.7 presents overall conclusions on the scientific evidence reviewed within this appendix.

2.1 Exposure

The purpose of this section is to review studies, with a focus on recent literature, that provide information about human exposure to Pb through the environment. Because Pb body burden is often used to estimate exposures (e.g., Pb concentrations in blood, bone, etc.), and because air-related Pb exposure may occur through inhalation or ingestion of materials that have been contaminated by Pb originally found in ambient air, this appendix evaluates the evidence for total Pb exposures, including inhalation exposures and exposures from ingestion of food, water, dust and soil, and other materials. Lack of data makes it a challenge to trace Pb to air in biomarker studies using speciation or isotopic signatures.

The information in this chapter builds on conclusions from the 2013 Pb Integrated Science Assessment (ISA) (U.S. EPA, 2013), which found that air Pb concentrations and blood Pb levels (BLLs) have continued to decrease over the past 45 years. The phasing out of leaded gasoline and reductions in point source Pb emissions have been important contributors to this decline. Section 1.5.2 of this current ISA reports the national median of the annual maximum 3-month average Pb concentration declined by 88% from 2010 to 2021. Section 1.5.2 contains more details on national Pb air concentration temporal trends (https://cfpub.epa.gov/ncea/isa/recordisplay.cfm?deid=357282).

As described in detail in Section 2.4.1, there has been a decline in BLLs from 1976 to 2018 in all birth cohorts. The geometric mean (GM) BLL across all subjects surveyed in the 1999–2000 National Health and Nutrition Examination Survey (NHANES) cycle was 1.66 µg/dL (95% CI: 1.60, 1.72). The GM BLL across all subjects surveyed in the 2017–2018 NHANES cycle was 0.753 µg/dL (95% CI: 0.723, 0.784). BLLs have decreased among all age and race/ethnicity groups. GM BLL differences between non-Hispanic black children and other racial/ethnic groups have also lessened over time.

Despite the drop in air Pb concentrations and human BLLs over time, sources of Pb still remain. This section discusses exposure to Pb in air and other environmental media, including soil, dust, and water. It also discusses Pb exposure through other pathways, including diet, consumer products, ammunition, and occupational exposures. Co-exposures and exposures in specific populations are also briefly discussed.

2.1.1 Overview of Pathways for Pb Exposure

Since the publication of the 2013 Pb ISA (U.S. EPA, 2013), the environmental pathways for Pb exposure have remained consistent, whereas the amounts of Pb from various sources have changed. Pb has multiple point and nonpoint sources and passes through various environmental media, including air (the focus of this assessment), soil, or water. The Venn diagram (Figure 2-1) below depicts the various pathways that Pb can take through the environment to reach a human being.

The "air/soil/water" arrows in the diagram show humans, plants, and animals can be exposed to Pb through contact with Pb-containing media. These exposures are considered air-related if Pb passed through the air compartment at any point prior to plant, animal, or human contact. For example, air-related Pb exposure may occur through inhalation or ingestion of food, water, dust and soil, or other materials that have been contaminated by Pb originally in ambient air. Additionally, organisms can also be exposed to Pb directly through contact with air that contains Pb. Non-ambient air-related exposures include those from an occupation, hand-to-mouth contact with Pb-containing consumer goods, hand-to-mouth contact with dust or chips of peeling Pb-containing paint, or ingestion of Pb in drinking water conveyed through Pb pipes. Pb body burden is an aggregation of all of these different exposures.

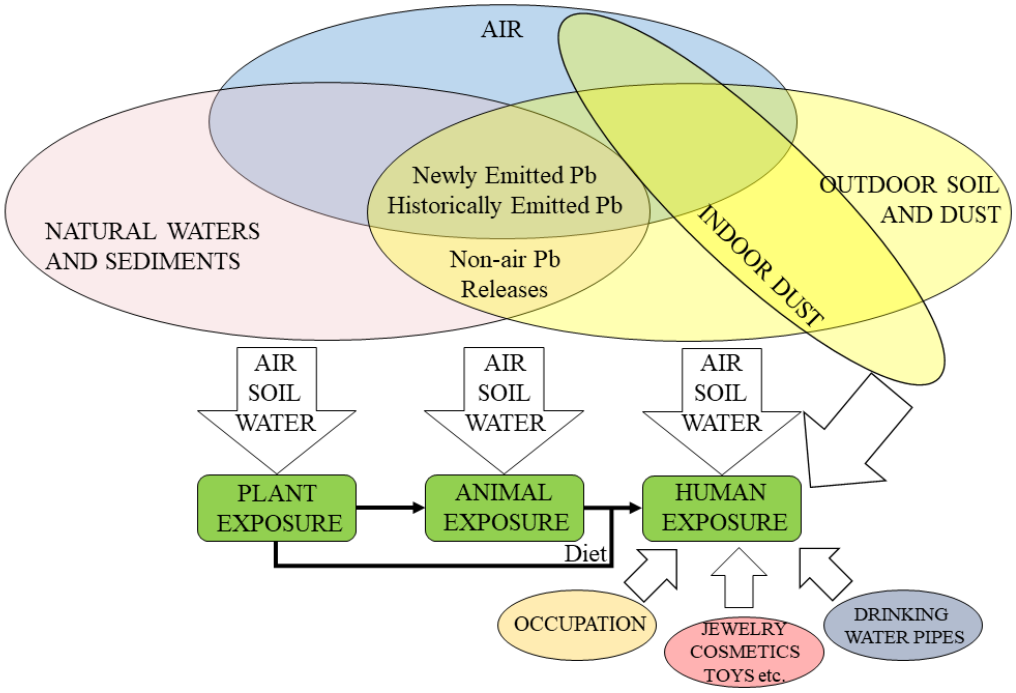


Figure 2-1 Conceptual model of multimedia Pb exposure.

Concentrations of Pb in an individual's microenvironment and that individual's time spent doing different activities can influence their exposure. The importance of different sources and pathways of Pb exposure varies across the U.S. population and is situation specific. As an example, Pb in soil was found to likely be a key pathway of exposure for children in pre- and post-Katrina New Orleans, whereas Pb-contaminated drinking water was a key contributor to elevated BLLs (EBLLs) during the Flint Water Crisis (Gómez et al., 2018; Mielke et al., 2017; Zahran et al., 2017b; Kennedy et al., 2016). Evidence points to incidental ingestion of Pb dust by hand-to-mouth activity as a leading exposure route for young children (Mielke et al., 2017; von Lindern et al., 2016; U.S. EPA, 2013).

Frank et al. (2019) performed a meta-analysis looking at Pb measured in multiple environmental media over the last 20 years. The mean estimate of Pb in urban residential soils was three times higher than in rural residential soils. The infrastructure in urban centers tends to be older than rural residential communities, and those urban centers are closer to Pb sources including dense traffic networks, industrial emissions, and brownfield sites. Data were limited for most environmental media, with soil and dust being the most robust in terms of the amount of available literature. More comparisons across environmental media with consistent sampling methodology would be worthwhile to understand the contribution of each environmental pathway to exposure.

2.1.2 Environmental Exposure Assessment Methodologies

Various monitoring techniques are used to estimate exposure to Pb from the environment. The 2013 Pb ISA (U.S. EPA, 2013) contains brief descriptions of some of these techniques, and the 2006 Pb Air Quality Criteria Document (AQCD) (U.S. EPA, 2006a) contains more detailed information. To understand the contributions of particular pathways to overall Pb exposures, measurements in air, soil, and dust are performed. Ambient air monitoring techniques are described in detail in Section 1.4 (https://cfpub.epa.gov/ncea/isa/recordisplay.cfm?deid=357282). Four national monitoring networks (State or Local Air Monitoring Stations, Chemical Speciation Network, Interagency Monitoring of Protected Visual Environments [IMPROVE], and National Air Toxics Trends Station) collect data on Pb concentrations and report data to EPA's Air Quality System (AQS) (U.S. EPA, 2019a). National Ambient Air Quality Standards (NAAQS) compliance must be determined using Federal Reference Methods or Federal Equivalent Methods that measure Pb in total suspended particles (TSP). In some studies, indoor and personal monitoring of Pb have also been performed to understand these Pb concentrations' relationships to outdoor air and possible exposure (e.g., (Stevens et al., 2014)).

Pb in soil can be measured using inductively coupled plasma atomic emission spectroscopy (ICP-AES) of a nitric acid digested sample (Wharton et al., 2012) or inductively coupled plasma mass spectrometry (ICP-MS) (Yu et al., 2022). It has also been measured by EPA method 6200, which uses portable X-ray fluorescence (XRF) (Obeng-Gyasi et al., 2021). Dust samples for Pb analysis are collected using wipe sampling and vacuum sampling as described in the 2013 Pb ISA (U.S. EPA, 2013), and these techniques have not drastically changed since they were first formalized.

The multiple pathways by which individuals are potentially exposed to Pb can make it challenging to determine the primary Pb source causing an individual's BLL to become elevated. The ratio of three isotopes (^{206}Pb, ^{207}Pb, and ^{208}Pb) in human biomarkers can be compared with those found in indoor, outdoor, and occupational sources to provide supporting evidence of where Pb originated (Jaeger et al., 1998). Becker et al. (2022) used isotope ratios (^{208}Pb/^{206}Pb and ^{206}Pb/^{207}Pb) to apportion the sources of blood Pb in five children (ages 1–6 years) living in urban areas of Kansas City, MO, who were screened for EBLLs (>5 µg/dL). Indoor dust samples were collected in play areas where the children spent significant time. One child's blood Pb was isotopically similar to Pb in both indoor dust and yard soil, which likely contributed to the indoor dust Pb based on the similarity in their isotopic ratios. Turmeric, indoor dust, and paint chips were each individually identified as a dominant source of Pb in blood for three other children. For a child having the highest BLL, nearly 13 µg/dL, the isotopic Pb ratios in blood were dissimilar to the Pb ratios in yard soil, indoor dust, and paint chips. This suggests that another unsampled Pb source in the home or elsewhere was causing this child's EBLL.

Xue et al. (2022) developed a generalizable approach to identify locations of hotspots for Pb exposure based on childrens' elevated BLLs and analyzed Pb models or indices as surrogates of exposure in those locations. A case study was used to apply the approach. BLL data (1,930,943 samples) for children <6 years of age were obtained from the Michigan Department of Health and Human Services for

the 2006-2016 period. The BLL data (half venous, half capillary samples) was well correlated (r=0.58) between venous and capillary samples within person and year. These BLL data were geocoded to Michigan census tracts. A top 20-percentile method and geospatial cluster analysis method were both used to identify census tracts with high %EBLLs. In addition, U.S. EPA's EJSCREEN 2017 Pb Paint EJ Index, modeled BLLs of Schultz et al. (2017), and the U.S. Department of Housing and Urban Development's Deteriorated Paint Index were used as Pb models/indices for analyzing old housing data and sociodemographic variables. These were analyzed and mapped at census tract resolution with model-to-model comparison by analyzing the models against one another and modeling them against %EBLL data to see if they are useful as surrogates in absence of BLL data. The percentage of census tracts in Michigan with an exceedance rate > 10% for BLLs > 5 µg/dL decreased from 14.8% in 2006-2007 to 4.1% in 2014-2016. The three Pb models/indices had high statistical convergence, indicating high similarity between them. Both the geospatial clustering approach and the 20-percentile method had moderate statistical convergence with %EBLLS from 2014-2016. The method was found to be able to inform hotspot identification for Michigan, however, the authors acknowledged that this method may miss some locations as the methods did not identify all areas of EBLLs in this study and should be verified by available blood Pb data and information about local Pb sources and exposures. Zartarian et al. (2022) provides a broader state-of-the-science overview of Pb geospatial mapping approaches including links to publicly available BLL data from 32 state health departments, a multimedia environmental sources data table, and a summary of available Pb exposure indices and their data.

In addition to using measurements of Pb concentrations in environmental media and biomarkers, various modeling strategies have been used to estimate Pb exposure. Air dispersion models estimate the spread of Pb releases throughout the air in a certain region. For example, the American Meteorological Society/Environmental Protection Agency Regulatory Model (AERMOD) is a steady-state plume model that considers short-range dispersion from stationary industrial sources in the planetary boundary layer over both simple and complex terrain (Cimorelli et al., 2005; Perry et al., 2005). Several studies have used AERMOD to estimate air Pb concentrations around industrial facilities (e.g., Moody and Grady (2017) in Detroit, MI). The RISK Screening Environmental Indicators-Geographic Microdata model, which models transport and dispersion of air emissions using AERMOD, has been used to model chemical-specific Toxics Release Inventory (TRI) releases and air Pb concentrations around point sources, based on what is known about environmental fate and transport (e.g., Hill et al. (2021) in Syracuse, New York) (U.S. EPA, 2022).

Biokinetic models have been developed at EPA that estimate levels of Pb in blood given information on potential exposure to Pb in environmental media. The Integrated Exposure Uptake Biokinetic (IEUBK) model was first created in the late 1980s and early 1990s to help evaluate Pb exposure in children at potential Superfund sites. It was designed to allow users to predict whether BLLs for children from birth to seven years over periods no less than a month exceed a target BLL based on a GM BLL predicted from available information about exposure to Pb (SRC, 2020). The All-Ages Lead Model (AALM) was developed to extend biokinetic modeling capability beyond the age of seven, include

intermittent exposures, and model additional (e.g., bone) tissue concentrations of Pb. Both of these models are described in detail in Chapter 4 of the 2006 Pb AQCD (U.S. EPA, 2006a), and recent updates are described in Section 2.6 of this document. Sections 2.2, 2.3, and 2.4 discuss toxicokinetics, biomarker measurements, and biomarker trends, respectively.

The Stochastic Human Exposure and Dose Simulation (SHEDS)-Multimedia model is an EPA probabilistic model for estimating environmental exposures through inhalation, ingestion, and dermal routes. Estimates of exposure are based on human activity recorded in the Consolidated Human Activity Database, dietary consumption surveys, and modeled or observed levels of a contaminant in environmental media, food, and surfaces. Zartarian et al. (2017) and Stanek et al. (2020) used the SHEDS-Multimedia model in combination with an approximation of IEUBK to estimate drinking water Pb contributions to blood Pb in U.S. children. The Zartarian et al. (2017) analyses included a comparison of the coupled SHEDS-IEUBK methodology against CDC's national-scale NHANES blood lead level data and an exposure pathway contribution analysis. Stanek et al. (2020) used the SHEDS-IEUBK methodology to evaluate various drinking water scenarios' relationship to BLL. NORMTOX and Modeling Environment for Total Risk are other models used for estimating environmental exposures to Pb, described in the 2013 Pb ISA (U.S. EPA, 2013).

2.1.3 Exposure Studies

The following sections describe research on Pb exposure through various environmental media, dietary sources, consumer products, and ammunition.

2.1.3.1 Airborne Pb Exposure

Airborne Pb exposure occurs through inhalation of Pb in air and can be measured most accurately for an individual through personal air exposure monitoring. Although the 2006 AQCD (U.S. EPA, 2006a) contained limited data on personal exposure monitoring of airborne Pb, the 2013 Pb ISA (U.S. EPA, 2013) expanded upon this issue. The 2013 Pb ISA (U.S. EPA, 2013) contains detailed information on studies that show how outdoor, indoor, and personal Pb particulate matter (Pb-PM) concentrations were correlated and varied by local conditions in studies ranging from 1999 to 2010 (Table 2-1 reproduced below).

Table 2-1 Comparison of personal, indoor, and outdoor Pb-PM measurements from several studies included in the 2013 Pb ISA.

Study	Location	Pb Metric	Sampling Period	Personal Pb	Indoor Pb	Outdoor Pb
Clayton, 1999, 14003@@author-year}	IL, IN, MI, MN, OH, WI	Med. Pb-PM_{50} (ng/m^3)	July 1995–May 1997	13	6.6	8.5
Adgate, 2007, 156196@@author-year}	Minneapolis-St. Paul, MN	Avg. Pb-$PM_{2.5}$ (ng/m^3)	Spring, Summer, Fall 1999	6.2	3.4	2.0
Molnár, 2007, 156774@@author-year}	Stockholm, Sweden	Avg. Pb-$PM_{2.5}$ (ng/m^3)	December 2003–July 2004		Homes: 3.4 Schools: 2.5 Preschools: 1.8	Homes: 4.5 Schools: 4.6 Preschools: 2.6
Tovalin-Ahumada, 2007, 190165@@author-year}	Mexico City, Mexico	Med. Pb-$PM_{2.5}$ (ng/m^3)	April–May 2002		26	56
	Puebla, Mexico	Med. Pb-$PM_{2.5}$ (ng/m^3)	April–May 2002		4	4
Pekey, 2010, 667712@@author-year}	Kocaeli, Turkey	Avg. Pb-$PM_{2.5}$ (ng/m^3)	May–June 2006, December 2006–January 2007		Summer: 34 Winter: 85	Summer: 47 Winter: 72
		Avg. Pb-PM_{10} (ng/m^3)	May–June 2006, December 2006–January 2007		Summer: 57 Winter: 125	Summer: 78 Winter: 159
Rasmussen, 2007, 91084@@author-year}	Windsor, Ontario, Canada	Med. Pb-$PM_{2.5}$ (mg/kg)	April 2004	311	124	221

Pb = lead; PM = particulate matter

Past studies have shown personal Pb-PM concentrations to be higher than indoor or outdoor concentrations. The National Human Exposure Assessment Survey (NHEXAS) study (Clayton et al., 1999) cited in the 2006 Pb AQCD (U.S. EPA, 2006a), which sampled Pb in multiple exposure media across six states in EPA Region 5, found personal air Pb concentrations to be significantly higher than indoor or outdoor Pb concentrations. Adgate et al. (2007) found average personal Pb-$PM_{2.5}$ concentrations to be roughly three times higher than outdoor Pb-$PM_{2.5}$ concentrations and roughly two times higher than indoor Pb-$PM_{2.5}$ concentrations.

The Detroit Exposure and Aerosol Research Study measured personal, indoor, and outdoor $PM_{2.5}$ mass components in six Detroit, Michigan neighborhoods over a 3-year period from 2004 to 2007 during winter and summer (Stevens et al., 2014). As mentioned in Williams et al. (2009), which contains details of the design and implementation of the study, daily monitoring was performed from Tuesday to Sunday and integrated over a 24-hr time period from 9:00 a.m. to 9:00 a.m. the next day. In contrast to previous studies, which found higher personal Pb concentrations, the authors found personal Pb-$PM_{2.5}$ concentrations were slightly less than indoor or outdoor concentrations at most sites. High relative standard deviation (RSD) values associated with PM mass components in personal measurements (Pb mass concentration RSD ranged from 66% to 270%, depending on site) indicated high spatial and temporal variability across sites, pointing to possible influence by personal activities and microenvironments.

Table 2-2 shows outdoor, indoor, and personal Pb-$PM_{2.5}$ collected by season across six sites (Stevens et al., 2014). Sites were selected according to their proximity to suspected PM sources, including industry (Sites 1, 4, 5), diesel truck traffic (Site 3), automotive traffic (Sites 4 and 6) and results from pilot testing of measurements of PM, carbon monoxide, and polycyclic aromatic hydrocarbon (PAH) concentrations at those sites. Site 7 had very low concentrations of measured PM determined to be due only to regional influences. Site 5 was in a heavily industrialized area and also showed the highest concentrations of other elements measured in the study, including Fe, Mn, and Ca. Higher concentrations of Pb in outdoor, indoor, and personal air measurements at Site 5 suggest that industrial emissions contributed to Pb not only in outdoor air but also air that infiltrated homes and microenvironments. Personal monitoring used active and passive monitors attached to a nylon vest, whereas indoor and outdoor monitoring used similar monitors but with weather shielding. The overall Pb-$PM_{2.5}$ mass concentration ratio of personal to indoor air during summer and winter was 1.1 and 0.9, respectively. Our literature search and screening did not capture other recent literature containing personal Pb-PM concentration measurements. Section 2.5 explores BLLs and their relationship to Pb in air and in other environmental media.

Table 2-2 Pb-$PM_{2.5}$ concentrations across six sites in Detroit, Michigan.

Site[a]	Season	Outdoor – Mean (ng/m^3)	Indoor – Mean (ng/m^3)	Personal – Mean (ng/m^3)
1	Summer	14.0	12.0	11.0
	Winter	9.0	6.0	6.0
3	Summer	9.0	8.0	8.0
	Winter	8.0	5.0	6.0
4	Summer	4.0	4.0	4.0
	Winter	5.0	3.0	3.0

Site[a]	Season	Outdoor – Mean (ng/m^3)	Indoor – Mean (ng/m^3)	Personal – Mean (ng/m^3)
5	Summer	15.0	12.0	11.0
	Winter	42.0	14.0	13.0
6	Summer	6.0	4.0	5.0
	Winter	5.0	2.9	3.0
7	Summer	5.0	2.0	4.0
	Winter	4.0	3.0	3.0

[a]Site 2 was originally considered for inclusion; ultimately, however, its characteristics were deemed similar to some of those already involved.

Data sourced from Stevens et al. (2014).

Indoor air Pb concentrations can vary with outdoor air Pb concentrations because of infiltration rates, indoor and outdoor Pb sources, and meteorology. As seen in Table 2-1 and Table 2-2 above, although the majority of studies showed higher outdoor Pb-PM concentrations than indoor Pb-PM concentrations, some studies have recorded higher indoor Pb-PM concentrations. Indoor dust containing Pb may be disturbed and released into indoor air environments, contributing to indoor Pb-PM concentrations. Resuspension rates due to foot traffic may be affected by walking behavior, type of floor surface (e.g., carpet, vinyl), and particle size (U.S. EPA, 2013). Williamson et al. (2021) measured Pb in PM at a high school in Texas by taking thirteen samples each integrated over 2–6 days for a period of 2 months. Elemental analysis showed an average Pb indoor-outdoor mass concentration ratio in $PM_{10-2.5}$ to be 2.1, suggesting the presence of indoor sources.

The infiltration of outdoor Pb-PM can play a role in the relationship between indoor and outdoor concentrations and is affected by multiple factors. A subsequent multivariate fixed effects analysis of the NHEXAS-MD data (Clayton et al., 1999) by Egeghy et al. (2005) found Pb levels measured in indoor air were significantly associated with log-transformed outdoor air Pb levels, ambient temperature, number of hours in which windows were open, whether the home was built before 1950, and fireplace usage frequency. Molnár et al. (2007) measured $PM_{2.5}$ in homes, preschools, and schools in Stockholm, Sweden and found a net infiltration rate of ~0.6. As shown in Table 2-2, Stevens et al. (2014) found overall ratios of indoor to outdoor Pb during summer and winter to be 0.7 and 0.2, respectively, suggesting that outdoor air had greater infiltration during summer.

Ambient Pb concentrations can vary spatially across urban centers because of point (e.g., industrial facilities, airports) and nonpoint (e.g., roadway networks) sources, as well as the meteorology (wind strength and direction) that disperses Pb. Section 1.5.3 of this ISA (https://cfpub.epa.gov/ncea/isa/recordisplay.cfm?deid=357282) contains studies that examined spatial variability of Pb air concentrations at several urban centers, such as Los Angeles, CA and St. Louis, MO and were attributed to a wide variety of sources including nearby chat piles, abrasive vehicle emissions, and a previously operating Pb smelting plant (Li and McDonald-Gillespie, 2020; Yadav and Turner, 2014; Pakbin et al., 2011). Emissions from aviation gas can also contribute to Pb concentrations at and

around airports, as discussed in Section 1.2.1 of this ISA (https://cfpub.epa.gov/ncea/isa/recordisplay.cfm?deid=357282). These concentrations have the potential to be inhaled by those on airport grounds or in surrounding neighborhoods. These emissions can also deposit into soil surrounding airports or mix with suspended soil Pb concentrations in air. Some studies, discussed in Section 2.4.1, have associated BLLs with proximity to airports that use avgas Zahran et al. (2017a); Miranda et al. (2011). Resuspension of Pb deposited from historical sources may also contribute to Pb exposures. Section 2.4 discusses the relationship of BLLs to various Pb sources.

The size of Pb particles that someone may be exposed to can vary due to source type and proximity to those sources. The size distributions of soil and house dust particles tend to be larger than ambient air particles (Siciliano et al., 2009; U.S. EPA, 1990; Hee et al., 1985). Particles that are either ultrafine or coarse may be affected by particle dynamics that limit their contribution to exposure. Before ultrafine Pb-PM reaches a person, these particles may aggregate into larger sizes (Hays et al., 2011). On the other end of the size distribution spectrum, coarse particles have higher settling velocities than fine and ultrafine particles, meaning that exposure to these larger particles will likely be more spatially and temporally heterogeneous than fine particles, which can travel farther across urban centers (U.S. EPA, 2013). Studies examining the size distributions of Pb-PM are discussed in more detail in Section 1.5.5 (https://cfpub.epa.gov/ncea/isa/recordisplay.cfm?deid=357282).

Airborne Pb-PM from motor vehicle combustion tends to be smaller than that emitted by industrial sources, resuspended soil, and tire/brake wear (U.S. EPA, 2013; Schauer et al., 2006). Cho et al. (2011) found that published literature after 1986 indicated a shift in the primary particle size mode of airborne Pb particles from below 2.5 µm to between 2.5 and 10 µm, attributed to a shift away from the use of Pb in motor vehicle gasoline. There is also evidence that Pb particles in emissions from piston-engine aircraft are smaller than those emitted from an automobile engine using the same leaded fuel. The addition of tetraethyl Pb in both aviation and motor vehicle gasoline results in exhaust containing Pb dibromide particles. Previous studies of motor vehicle exhaust showed that these particles range in size from around 20 to 100 nm in diameter with a mean of 50 nm (NASEM, 2021). Griffith (2020) tested 100LL (100 octane, low Pb) aviation fuel in a 1959 model aircraft and a 1957 model automobile. Exhaust samples from the piston-engine aircraft were found to be 13 nm in average diameter, whereas those from the automobile were 35 nm in average diameter. Both exhausts contained Pb dibromide beads in a hydrocarbon matrix; however, the motor vehicle exhaust particles contained 5–10 beads or more, whereas those in the aircraft exhaust were found to contain 1–2 beads.

2.1.3.2 Exposure to Pb in Soil and Dust

As described in detail in Section 1.3.2 (https://cfpub.epa.gov/ncea/isa/recordisplay.cfm?deid=357282), Pb can be found in soil and dust as a result of deposition of atmospheric Pb, past combustion of leaded gasoline, automobile parts (e.g., wheel

weights), aviation, industrial activities, or Pb-based paint. This Pb can be further transported through resuspension in dust back into ambient air or tracked indoors and resuspended into indoor air environments. Pb in soil can contribute to exposure through ingestion (i.e., hand-to-mouth activity) or inhalation of resuspended dust. As described in the following paragraphs, elevated Pb concentrations have been found in a wide variety of outdoor soil locations, including residential properties, near roads, on or near airports, playgrounds, urban gardens, and in house dust.

2.1.3.2.1 Outdoor Pb

Resuspended soil and dust can contribute to outdoor Pb-PM concentrations. Section 1.2.6 of this current document (https://cfpub.epa.gov/ncea/isa/recordisplay.cfm?deid=357282) contains detailed information on recent research investigating the contribution of resuspended soil to airborne concentrations. Laidlaw et al. (2012) analyzed the contribution of resuspended soil Pb to air Pb in Birmingham, AL; Chicago, IL; Detroit, MI; and Pittsburgh, PA. Using the IMPROVE soil estimation calculation and data from one sampling location in each city over different time periods, the authors found atmospheric Pb strongly correlated with atmospheric soil concentrations. Using a mixed effects model, the predicted percent increase in atmospheric Pb for each percent increase in atmospheric soil was 0.709 (95% CI: 0.535, 0.882) in Pittsburgh, 0.848 (95% CI: 0.724, 0.973) in Detroit, 0.710 (95% CI: 0.573, 0.847) in Chicago, and 0.922 (95% CI: 0.812, 1.033) in Birmingham.

Pb in soil has been found above background levels in both major urban centers and smaller cities (Clark and Knudsen, 2013). A study of 170 homes in Appleton, WI found a range of Pb concentrations between 47 and 32,483 µg Pb/g among soil around homes of various types. Soil next to homes built before 1960 had significantly ($p < 0.001$) higher GM Pb concentrations than homes built after 1960, and spatial sampling of soil next to a subset of 71 homes found a general decreasing trend in Pb concentrations with increasing distance away from each home (Clark and Knudsen, 2013). Pavilonis et al. (2020) measured Pb concentrations in soil from 34 parks across New York City; concentrations were found to range from 7.8 mg Pb/kg to 6,300 mg Pb/kg, with a median concentration of 161 mg Pb/kg. Parks in areas with the highest population growth between 2010 and 2017, greatest manufacturing density, most new building construction, and greatest street density had the highest Pb concentrations; however, how much these individual factors contributed was not resolved. Wang et al. (2022) captured 99 surface (2–3 cm of the mineral-soil surface excluding overlying organic materials) soil samples in Durham, NC. Mean total concentrations (± standard deviation) of Pb were found to be 2,281 mg/kg (±2,868 mg/kg, n = 31) in house foundation soils, 321 mg/kg (±533 mg/kg, n = 42) in urban streetside soils, 42.1 mg/kg (±25.0 mg/kg, n = 19) in city park soils, and 15.9 mg/kg (±3.58 mg/kg, n = 7) in suburban streetside soils. By using isotopic signatures, the authors found that house foundation soils had significant input of legacy Pb-based paint, whereas urban streetside soils had a mixed origin made up predominantly of legacy leaded gasoline and atmospheric deposition.

The distribution of soil Pb concentrations in New Orleans has been particularly well documented. Between 1989 and 2015, four surveys of soil Pb were carried out. For each survey, soil samples were collected from street sides, near home foundations, and from vacant properties and parks as far as possible from house sides and streets, and data were stratified by census tract. Due to the effects of Hurricanes Katrina and Rita in 2005, Surveys 2 and 3 examined fewer census tracts than previous surveys but stratified data according to the census boundaries established in Survey 2 for continuity. Because many of the tracts not sampled in Surveys 3 and 4 were outlying areas with relatively low Pb concentrations, comparison to the full data set from Survey 2 would not be appropriate. The results of these surveys are summarized in Table 2-3, including average median Pb concentrations for the full data set from each survey, as well as subsets of data from Survey 2 corresponding to only those census tracts included in Surveys 3 and 4 for comparison. Key outcomes of these surveys are discussed below.

Table 2-3 Median soil Pb concentrations in New Orleans census tract level surveys.

Survey Number	Yr	Number of Tracts	Number of Samples	Full Data Set Median Conc. (mg/kg)	Subset Median Conc. (mg/kg)
1	1989–1992	283	4,011	134	
2	1998–2000	286	4,388	100	329[a], 280[b]
3	2005–2006	46	1,748	203	
4	2013–2015	176	3,320	132	

[a]Average median soil Pb concentration across the 46 census tracts included in Survey 3
[b]Average median soil Pb concentration across the 176 census tracts included in Survey 4
Data sourced from Mielke et al. (2005), Zahran et al. (2010), and (Mielke et al., 2016).

Mielke et al. (2005) first reported data from Surveys 1 and 2. In Survey 1, 71 of 286 census tracts had median soil Pb that exceeded the EPA regulatory standard for certain residential properties of 400 mg/kg[1], and 10 census tracts had a median soil level of ≥1,000 mg/kg. In general, Pb concentrations in outlying suburbs decreased moderately from Survey 1 to Survey 2. However, the authors note this decline was a result of moderate decreases in suburban soil Pb concentrations, and inner-city areas actually increased. (Mielke et al., 2011b) further examined a subset of samples from Survey 2. This study includes 224 soil samples collected from ten Housing Authority (HA) public properties and 363 soil samples collected from residential private properties within an 800 m radius of the centroids of the HA properties. Six HA properties were located within the inner city, and the other four were located in the

[1] As defined in the Code of Federal Regulations (40 CFR 745), a soil-Pb hazard is bare soil on residential real property or on the property of a child-occupied facility that contains total Pb equal to or exceeding 400 ppm (µg/g) in a play area or an average of 1,200 ppm of bare soil in the rest of the yard based on soil samples.

outlying areas of New Orleans. As observed in the full data set, samples retrieved from both HA properties and private residences had higher Pb concentrations in inner-city locations compared with those from outlying areas. However, Pb concentrations in soil taken from HA locations were significantly lower (about half or less) than Pb concentrations taken from nearby private residences. The authors attribute this difference to the fact that HA properties had unpainted brick facades, whereas private properties were painted wood. Altogether, these results highlight the importance of legacy inputs of Pb from leaded automobile gas and Pb paint on soil Pb concentrations.

Zahran et al. (2010) examined soil Pb concentrations from Survey 3 compared with soil Pb concentrations in those census tracts from Survey 2. In 29 of 46 neighborhoods examined, median soil Pb declined between surveys. In Survey 3, 6 of 46 census tracts had soil Pb levels of $\geq$ 400 mg/kg, compared with 15 of 46 neighborhoods exceeding this standard in Survey 2. (Mielke et al., 2016) compared Pb concentrations in soil from Survey 4 to those measured in the same census tracts in Survey 2. Median soil Pb levels across sampled census tracts dropped significantly, which the authors attribute to factors associated with Hurricane Katrina rather than reduction in inputs. Specifically, they cite removal of Pb-painted drywall and woodwork during renovations and sequestration of Pb-contaminated soil beneath low-Pb sedimentary material from outside the city, which was moved in both intentionally during reconstruction and unintentionally during levee breaches associated with the storm (Mielke et al., 2000). They theorized that addition of clean soil may provide an effective means of mitigating the impact of Pb exposure. This method was further explored by (Walsh et al., 2018) and (Egendorf et al., 2018) and found to be effective. However, the findings of Rabito et al. (2012) indicate that elevated Pb concentrations persist in many areas of New Orleans. This study used a different sampling strategy than the census tract studies, focusing solely on Pb concentrations in soil samples taken near homes. Of the 109 homes sampled in 2009, Pb concentrations were often still high; nearly half had elevated soil Pb, and 27% of those homes had soil Pb greater than 1,200 ppm.

Pb has also been found present in children's playground soils, which is a concern for accidental ingestion by children (U.S. EPA, 2013). Mielke et al. (2011a) found Pb soil concentrations ranged from 14 to 3,692 mg/kg with a median soil concentration of 558 mg/kg on playground soils at 11 daycares and community centers in New Orleans. Almansour et al. (2019) found, among 28 randomly sampled playgrounds in Boston, a median Pb soil concentration of 65.7 mg/kg. This number was typical for soils in Massachusetts based on U.S. Geological Survey data, indicating this was likely background Pb instead of Pb originating from anthropogenic sources (Smith et al., 2013).

Human uptake of Pb through soil exposure can also occur during gardening as a result of unintentional soil and dust ingestion. Gardeners may not wear protective equipment or properly wash off soil when finished with gardening, and they may eat or drink while working or track soil into the home (Schmeltz et al., 2020; Spliethoff et al., 2016). However, exposure to soil Pb in urban gardens can be lower than in other gardens as a result of clean soil being brought in for gardening beds (Spliethoff et al., 2016). The 2013 Pb ISA (U.S. EPA, 2013) evaluated studies that previously looked at Pb in urban garden

soil, including Clark et al. (2006), who tested the soil in 103 urban gardens in two Boston neighborhoods. Using isotopic analysis, the authors found that Pb-based paint contributed 40 to 80% of Pb in the urban garden soil samples, with the rest coming from historical Pb emissions. Furthermore, Clark et al. (2006) estimated that Pb consumption from urban gardens could be equivalent to 10 to 25% of the exposure to Pb from drinking water for children living in the Boston neighborhoods studied. Spliethoff et al. (2016) investigated bed soil (508 samples, where plants were being grown) and non-bed soil (54 samples, where no growing was occurring) of urban gardens in New York City and found bed soil had a median of 96 mg Pb/kg, whereas non-bed soil had a median of 181 mg Pb/kg. The authors also estimated mean dust-Pb concentration due to soil tracking at 72 mg Pb/kg. In a separate study, Cheng et al. (2015) found a median value of 355 mg Pb/kg in 1,652 urban garden soil samples around New York City. Three percent of community garden samples and 18% of home garden samples were found to exceed 1,200 mg Pb/kg, a level of contamination not recommended for vegetable gardening (U.S. EPA, 2014). A small pilot study of urban gardens in New York City found a mean value of 372 ppm Pb in the 18 soil samples taken (Schmeltz et al., 2020).

In urban gardens, there can be spatial variability across Pb concentrations at the surface. A study in Terre Haute, IN collected 1,061 surface soil samples from a 1.25-acre (54,450-sq. ft.) urban garden at high spatial resolution. All samples were collected from the top several inches of soil and stored in sample bags for analysis using handheld XRF. The authors found there was high variability across the garden, ranging from background Pb levels to concentrations above 800 ppm (Latimer et al., 2016). A smaller study of an urban garden in southern Detroit, MI, which collected 80 samples, found a mean value of 151 mg Pb/kg among all samples. However, there was also high variability across samples taken, with a minimum of 17 mg Pb/kg and a maximum of 882 mg Pb/kg found (Bugdalski et al., 2014).

Soil and dust transfer can be an important exposure route for Pb. This is especially true for children who may play outside, close to the ground (Moya and Phillips, 2014). The updated EPA Exposure Factors Handbook (U.S. EPA, 2017) reviewed soil/dust ingestion studies and based on that literature recommends, for use in general population modeling or risk assessment, a daily soil and dust ingestion rate made up of a combination of soil and settled dust of 40 mg/day (<6 months old), 70 mg/day (6 months to <1 year), 90 mg/day (1 to <2 years), 60 mg/day (2 to <6 years), 80 mg/day (1 to <6 years), 60 mg/day (6 to <12 years), and 30 mg/day (12 years through adult) (U.S. EPA, 2017). Ingestion rates through hand-to-mouth transfer can be important for determining exposure to soil and dust particles. In a review of studies examining soil and dust ingestion rates in children, Moya and Phillips (2014) noted mean daily ingestion rates varied by quantification method, each of which has specific limitations. Studies that used the tracer element method, biokinetic model comparison method, and activity pattern method reported mean daily soil and dust ingestion rates of 26–470, 110, and 10–1,000 mg/day, respectively. von Lindern et al. (2016) estimated soil and dust ingestion rates for multiple age groups of children (<10 years of age) by using BLL data, age-specific biokinetic slope factors, and estimated Pb uptake. Mean ingestion rates ranged from 50 to 154 mg/day across all age groups and scenarios.

Two recent studies have used the Stochastic Human Exposure and Dose Simulation Soil and Dust (SHEDS-Soil/Dust) model to estimate distributions of soil and dust ingestion rates in children and adults. Özkaynak et al. (2022) reported arithmetic mean ingestion rates (dust plus soil) of approximately 40 mg/day for children <1 year of age, 50 mg/day for 1 to <3 years, 60 mg/day for 3 to <11 years, 40 mg/day for 11 to <16 years, and 20 mg/day for adolescents 16 to <21 years. A notable contribution of this work was the consideration of the season of the year and the time individuals spent outside. For children <1 year of age, ingestion was from dust only due to an assumed negligible amount of time outside. For other age groups, daily soil-only ingestion rates were approximately doubled (based on Tables S7–S10 of the paper) in the summer relative to other seasons, increasing from 9 to 15 mg/day for children 1 to <2 years of age, 20 to 47 mg/day for 2 to <3 years, 23 to 57 mg/day for 3 to <11 years , 17 to 40 mg/day for 11 to <16 years, and 9 to 20 mg/day for 16 to <21 years. (Hubbard et al., 2022) reported that for adults (≥21 years), daily average ingestion rates of soil and dust could range from 7 to 123 mg/day for the general population to high occupational exposures, respectively. This study also showed soil ingestion rates were increased in the summer relative to other seasons. Dust ingestion rates were only minimally affected by seasonality.

The properties of soil, including size and humidity, can affect the adherence of soil particles to hands. Ruby and Lowney (2012) suggests particle adherence occurs below 150 µm. Finer soil particles (<63 µm in diameter) tend to adhere to human hands more efficiently than larger particles. Soil with higher moisture content results in slightly larger particles (<100 µm in diameter) having selective adherence to hands (U.S. EPA, 2017). Approximately 90% of the cumulative mass of soil adhered to children's hands is <150 µm in size. Smaller particles are more mobile than larger particles and are more likely to accumulate in the indoor environment as a result of deposition of wind-blown soil or track-in transport of soil on clothes, shoes, pets, toys, and other objects, providing additional opportunity for exposure to this particle size fraction (Stalcup, 2016).

2.1.3.2.2 Indoor Pb

Both the 2006 Pb AQCD (U.S. EPA, 2006a) and the 2013 Pb ISA (U.S. EPA, 2013) recognize house dust as a pathway for Pb exposure. Table 3-5 of the 2013 Pb ISA (U.S. EPA, 2013) contains studies that measured indoor Pb dust concentrations between 2006 and 2011. Median Pb dust concentrations ranged from 63 mg/kg (Zota et al., 2011) to 470 mg/kg (Spalinger et al., 2007), although locations sampled within buildings (e.g., floors, windowsills) and sampling procedures varied by study.

The 2013 Pb ISA (U.S. EPA, 2013) discusses how Pb in house dust can be present as a result of infiltration from outdoors. Pb-containing dust may enter a building through infiltration in the air or on the surfaces of objects and persons who enter the building. Proximity to historic and active metals mining and smelting sources has been linked to increased levels of Pb in house dust (Zota et al., 2011; Gaitens et al., 2009; Spalinger et al., 2007). Tu et al. (2020) estimated contributions of yard soil to indoor dust by collecting indoor residential dust and soil surrounding homes in eight communities near former mining or

smelting operations. Mass soil-to-dust transfer coefficients with good to moderate fit were found to range from 0.14 to 0.47 for Pb.

Pb can be released from housing materials, often linked to older homes that may have Pb-based paint (Mielke and Gonzales, 2008). Dietrich et al. (2022) found that among 434 sampled homes around the United States, exterior paint peeling, interior paint peeling, and older housing were predictors of higher Pb dust concentrations. Pb-containing dust can be present in carpet and on other flooring material (Wilson et al., 2007; Yu et al., 2006). The second American Healthy Homes Survey (AHHS II) concluded in June 2019 and sampled 703 homes in 37 states for Pb-based hazards. Results from the AHHS II estimate that 34.6 million homes have Pb-based paint somewhere in the building, a decrease from both AHHS I, which estimated 37.1 million homes, and the National Survey of Lead and Allergens in Housing, which estimated 37.9 million homes. The AHHS II also estimates that 29.0 million homes had a dust Pb hazard present, defined as a dust Pb level ≥10 µg/ft^2 or a windowsill dust Pb level ≥100 µg/ft^2 (U.S. EPA, 2020). Sowers et al. (2021) used X-ray absorption spectroscopy on a small subset of dust and soil samples collected from homes used in the AHHS I and found that Pb-based paint contributed strongly to house dust. A study of 102 homes in Rochester, NY with unenclosed painted porches found that 92% tested positive for Pb-based paint (≥1 mg/cm^2). The GM on the tested components was 1.1 mg/cm^2 (95% CI: 0.88 mg/cm^2, 1.141 mg/cm^2) (Wilson et al., 2015).

In another study, over 100 homes in Philadelphia, many within 0.5 miles of a legacy Pb point source (industrial facilities, Pb-based paint), were found in 2014 to have median front door floor dust, mean child play area floor dust, and child bedroom windowsill dust Pb levels of 17.7 µg/ft^2, 13.9 µg/ft^2, and 31.2 µg/ft^2, respectively (Dignam et al., 2019). A small study of 35 homes in the United States found that Pb concentrations in floor varnish were correlated with pre-1930s housing during refinishing exercises (Schirmer et al., 2012). Matt et al. (2021) investigated the contribution of tobacco smoke to Pb dust concentrations in the homes of 60 multiunit housing residents in San Diego, using wipe and vacuum floor dust samples. Vacuum dust nicotine loading was found to be significantly ($p = 0.0012$) associated with Pb dust loading; however, vacuum dust nicotine was not found to be associated with Pb concentrations in surface wipes from floors or windows. Floor wipe samples of nicotine concentrations were also not associated with Pb measured in vacuum dust or surface wipe samples.

Dust-Pb concentration values are important for calculating estimates of Pb intake or as input to blood Pb models (e.g., IEUBK), whereas dust-Pb loading values can be compared with dust-Pb loading regulatory values and can serve as another representation of exposure (Bevington et al., 2021). However, of the many dust-Pb monitoring studies that exist, only some report both dust-Pb concentration and dust-Pb loading values (i.e., the dust-Pb concentration multiplied by the total dust loading on a surface). EPA previously combined data from three studies to create a dust-Pb loading to dust-Pb concentration (LTC) model based on empirical data (U.S. EPA, 2019d). Bevington et al. (2021) developed an LTC model by pairing 2,174 dust-Pb loading and dust-Pb concentration values across five studies (each with $n > 200$ homes), incorporating data from an additional two studies not used in the EPA model (Clayton et al.,

1999; Lanphear et al., 1996). The authors evaluated 17 different versions of the LTC model across a wide range of dust-Pb loadings (0.1–10,000 µg/ft^2) using evaluation data from 32 studies and found there was relatively good agreement between the LTC models and data sets for central tendency values of dust-Pb concentrations. The model with the most agreement, model 16, had slope (0.413), y-intercept (5.291), and R^2 values (0.578) that were overall most similar to the evaluation dataset slope (0.440), y-intercept (5.511), and R^2 values (0.473) among the different LTC models tested. At high-dust Pb loadings, the predicted values for dust-Pb concentrations were overestimated; however, the highest dust-Pb loading values came from intervention studies in which dust-Pb loading was likely higher than would occur in homes found in the general population.

2.1.3.3 Dietary

Possible sources of Pb in food include introduction during processing or preparation with Pb-contaminated drinking water, preparation in Pb-glazed cookware, deposition of Pb onto raw food materials, uptake from soil by fruit and vegetable crops, and Pb exposure in livestock that produce dairy or meat ingredients (U.S. EPA, 2013). Pb in commonly consumed food items purchased from grocery stores in the United States is measured and reported on an ongoing basis by the Food and Drug Administration (FDA) Total Diet Study (TDS). These data have been combined with food consumption data from What We Eat in America (WWEIA), the food consumption section of NHANES, to model dietary Pb intake (Gavelek et al., 2020; Spungen, 2019). Because of the high risk of Pb poisoning associated with low body mass, dietary Pb in infants and children is a particular concern and the FDA has issued updated interim reference levels (IRLs) for dietary Pb intake of 2.2 µg/day for children and 8.8 µg/day for women of childbearing age (Flannery and Middleton, 2022).

The 2006 Pb AQCD (U.S. EPA, 2006a) stated that according to the TDS data for surveys conducted between 1982–1984 and 1994–1996, estimates of Pb intake from food dropped across all age groups (U.S. EPA, 2006a). This was attributed to a general decline in food Pb concentrations resulting from regulations, such as a ban on Pb soldering in food cans and the ban on Pb additives in automobile gasoline, which reduced contamination in crops and livestock. However, the 2013 Pb ISA (U.S. EPA, 2013) summarized results of the 2008 TDS, which found a range of Pb concentrations in foods, with the highest levels (>65 µg/kg) measured in noodles, carrots in baby food, and oatmeal in baby food (U.S. EPA, 2013). The document also summarized the results of Manton et al. (2005), which suggested that some dietary Pb in children 0–12 months may originate from Ca salts used in some baby formula. These findings demonstrate that although concentrations of Pb in food have generally fallen, there is considerable variability, underscoring the importance of considering individual behavior when assessing risk associated with dietary Pb exposure.

Zartarian et al. (2017) investigated dietary Pb exposure based on 2007–2013 TDS data and found diet may still be a major contributor to BLLs for some individuals. The study used a combined SHEDS-

IEUBK multimedia model and data for children's activity patterns, Pb concentrations in media, exposure factors, and biokinetic dose factors from a variety of sources that were intended to simulate exposure conditions for 2009–2014 NHANES data and NHEXAS Region 5 data. The authors found ingestion of soil/dust, food, and water were major contributors to BLLs. However, results varied depending on the age of the participant and BLL percentile. For 1 to <2-year-olds soil/dust ingestion was the dominant pathway above the 80th percentile, but food intake was a major contributor below the 70th percentile, accounting for half of blood Pb values and contributing ~0.6 µg/dL on average across all percentiles. Water contributed ~10–15% of the BLL, depending on the percentile, or ~0.2 µg/dL on average.

In addition, two studies used Pb concentrations reported in the 2014–2016 TDS surveys with 2009–2014 WWEIA food consumption data to model potential dietary Pb intake for specific groups. Gavelek et al. (2020) estimated dietary Pb exposure in male and female children 7–17 years (n = 4,906), female children 16–49 years (n = 4,562), and men and women 18+ years (n = 14,614). Spungen (2019) estimated dietary exposures for male and female children 1–6 years of age (n = 3,103) and two subgroups of ages 1–3 (n = 1,717) and 4–6 years (n = 1,386). In both studies, lower-bound Pb concentrations were calculated by setting all Pb values less than the limit of detection (LOD) to zero, and upper-bound Pb concentrations were calculated by setting all Pb values less than the LOD to the LOD. In addition, "hybrid" mean Pb concentrations were calculated by setting Pb values less than the LOD to zero if there were no detected levels of Pb in food from 2009 to 2016; if Pb was detected in food at least once from 2009 to 2016, Pb values less than the LOD were set to half the current LOD. Table 2-4 below shows estimated mean and 90th percentile dietary Pb exposures for each population considered. For all groups with children, the upper bound values on the mean and 90th percentile estimates for dietary Pb intake exceed the current IRL for dietary Pb intake. In addition, the "hybrid" and lower-bound values on the 90th percentile estimates also exceed the current IRL. Notably, most food groups with the highest contributions were related to highest consumption rather than highest Pb concentration in those foods.

Table 2-4 Dietary exposures to Pb based on FDA Total Diet Study (2014–2016) and What We Eat in America (2009–2014) food consumption data.

		Dietary Pb Exposure (µg/day)					
		Mean			90th Percentile		
Reference	Population	Lower Bound[a]	Upper Bound[b]	Hybrid[c]	Lower Bound[a]	Upper Bound[b]	Hybrid[c]
(Gavelek et al., 2020)	Male and Female 7–17 yr	1.4	4	2.2	2.3	5.8	3.4
	Female 16–49 yr	1.6	4.6	2.4	2.8	6.7	4

		Dietary Pb Exposure (µg/day)					
		Mean			90th Percentile		
(Spungen, 2019)	Male and Female 18+ yr	1.7	5.3	2.7	3.2	7.8	4.5
	1–6 yr	1.2	3.2	1.8	2	4.6	2.9
	1–3 yr	1.0	3.0	1.7	1.8	4.4	2.6
	4–6 yr	1.3	3.4	2.0	2.1	4.8	3.1

yr = year(s).
[a]Values less than LOD set to zero.
[b]Values less than LOD set to LOD.
[c]Values less than LOD set to zero if there were no detections from 2009 to 2016; otherwise, values less than LOD set to 0.5 × LOD.

Both Gavelek et al. (2020) and Spungen (2019) limited the scope of their analyses to data collected from 2014 onwards because FDA started using ICP-MS in 2014 to measure elemental concentrations, as opposed to atomic absorption spectroscopy (AAS), which was used previously. ICP-MS has a lower LOD and limit of quantification than AAS (Gray and Cunningham, 2019), making these measurements difficult to compare directly to past TDS results. Despite this change, 74% of samples measured in the 1994–1996 TDS were below the detection limit for Pb, whereas in the new 2018–2020 TDS, this value increased to 85% of samples, further demonstrating an overall decrease in food Pb concentrations. In addition, Spungen (2019) found there may have been some decline in children's lower-bound mean Pb exposure from 2004–2008 to 2014–2016, with 0.11 µg/kg bw/day for 2-year-olds changing to 0.08 µg/kg bw/day for 1 to 3-year-olds, respectively.

While FDA TDS is a valuable tool for monitoring Pb in foods, the study design does have inherent limitations. First, because sampling for this program is meant to be broadly representative rather than comprehensive, more detailed studies may be valuable to fully describe Pb concentrations in food items consumed primarily by children and women of childbearing age. For instance, a study carried out by Gardener et al. (2019) presented data on Pb concentrations from an extensive sampling of baby foods. Of the 564 U.S. baby food samples, Pb was detected in 37% of samples (median = non-detect, max = 183.6 µg/kg), but none exceeded FDA consumption guidelines. In addition, because the TDS focuses on commonly consumed food items purchased at supermarkets, dietary Pb exposure from foods not purchased from supermarkets may be overlooked. Small farms, home agriculture, and game meats also present Pb exposure risk from dietary sources not captured in the TDS. Consumption of game meat hunted with Pb ammunition may increase dietary Pb exposure risk due to inadvertent consumption of ammunition fragments as previously described in detail in the 2013 Pb ISA (U.S. EPA, 2013).

Spliethoff et al. (2014) investigated Pb in eggs of chickens raised in New York City community gardens. Median Pb concentrations were found to be below the detection limit of 10 µg/kg, less than Pb

found in chicken eggs in previous studies (Van Overmeire et al., 2009; Trampel et al., 2003). Leibler et al. (2018) investigated Pb in backyard-produced chicken eggs and modeled their contribution to children's (younger than 7 years) BLLs using the IEUBK model. They found Pb egg concentrations were correlated with surrounding soil amounts. Contributions to BLLs based on the IEUBK tested over four different scenarios and different simulated ages ranged from 0.1 µg/dL to 1.5 µg/dL, depending on the frequency of consumption and age of the child. In addition, Lupolt et al. (2021) measured Pb concentrations in 13 commonly consumed produce items sampled from 104 urban farm and community garden sites in Baltimore, MD. Pb concentrations (ppb) measured in collards (58.3 ± 48.3), kale (58.3 ± 32.5), lettuce (68.0 ± 121.0), cucumbers (23.6 ± 26.0), and peppers (51.7 ± 49.4) grown in the urban farms and gardens were significantly higher ($p < 0.05$) than concentrations measured in store-bought, commercially grown produce of the same type.

The 2013 Pb ISA (U.S. EPA, 2013) previously reported on Pb uptake and bioaccumulation in agriculture. Uptake of Pb has been shown to occur in potted plants (Del Río-Celestino et al., 2006), vegetable crops (Lima et al., 2009), grasses (Vandenhove et al., 2009), and wild mushrooms (Sesli et al., 2008). Pb contamination can occur from atmospheric deposition (Uzu et al., 2010) and from treatment of crops with compost produced from wastewater sludge (Cai et al., 2007) and from fertilizer (Chen et al., 2008). Egendorf et al. (2021b) investigated the relative importance of Pb accumulation through roots, splash, and atmospheric deposition in lettuce grown in soil with high (~1,200 mg/kg) and low (~90 mg/kg) Pb concentrations in New York City and Ithaca, NY. In low-Pb soils, splash and atmospheric deposition accounted for 84% and 78% of lettuce Pb grown in New York City and Ithaca, respectively. In high-Pb soils, splash and atmospheric deposition accounted for 88% and 93% of Pb in lettuces, with splash being the dominant mechanism. The authors also show soil covers, such as mulch, were significantly ($p < 0.05$) correlated with lower Pb concentrations in lettuce compared with the bare soil treatment due to reduced contamination from splash. Pb accumulation in agricultural crops is covered in greater detail in Appendix 11.

2.1.3.3.1 Drinking Water

Drinking tap water is a pathway to Pb exposure. Several recent studies have been conducted that focus on broad scale surveys of Pb concentrations in drinking water across a region and provide insight on the subject. Sansom et al. (2019) looked at the exposure to Pb-contaminated drinking water in 13 residences of a Houston ship channel community. Pb concentrations above detection limits were found in 4 of the 13 homes studied, ranging from 0.6–2.4 ppb. Gleason et al. (2019) analyzed water systems used in New Jersey in two distinct time periods: 2000–2004 and 2010–2014. Among all the water systems analyzed for Pb, 443,936 had Pb concentrations between 0 µg/L and 2 µg/L, and 7,845 had Pb concentrations over 2 µg/L. DeSimone et al. (2020) analyzed 500 tap water samples from 72 Tennessee schools in 2017 and 3,428 samples from 160 Tennessee schools in 2019. Pb concentrations detected across all samples ranged from <0.5 (elementary schools, 2017) to 18,800 g/L (elementary schools,

2019), with medians ranging from 3.0 (middle schools, 2017) to 227 µg/L (elementary schools, 2019) among all samples. Nearly 90% of the schools tested (n = 205) had a Pb concentration higher than 1 µg/L; 50 schools had a Pb concentration higher than 15 µg/L. The average ages of the elementary, middle, and high school buildings were >50 years old.

One of the primary factors driving the observed variability in drinking water Pb concentrations is the corrosion of Pb plumbing components found in some homes and/or distribution systems; this can include Pb service lines (LSLs), Pb-soldered joints, and Pb brass faucets and fixtures. Although new LSLs were banned in 1986, drinking water infrastructure built prior to 1986 may still contain Pb components, putting people residing in older homes and communities at greater risk. A 2016 survey of infrastructure found that between 15 and 22 million people in the United States are served by community water systems with full or partial LSLs (Cornwell et al., 2016). This represents a significant reduction from earlier surveys because of efforts to replace LSLs with safer alternatives. However, jurisdictional issues sometimes make full replacement of LSLs impossible, resulting in implementation of a partial replacement strategy in some areas. Trueman et al. (2016) evaluated the effects of full and partial replacement of LSLs on Pb concentrations in drinking water in 45 single family homes. Prior to line replacement, 90th percentile Pb concentrations in the first four L of water collected, beginning with the first draw following a minimum 6-hour standing period, ranged from 16.4 to 44 µg/L. For homes with full replacement of LSLs, 1 month after replacement, 90th percentile Pb concentrations in tap water samples ranged from 2 to 12 µg/L. On the other hand, Pb concentrations in tap water collected from homes with partial replacement of LSLs increased substantially in the first month and did not show a significant reduction in concentration over the 6-month period of study. This is attributed to galvanic corrosion at the interface between new copper plumbing and existing Pb pipes, which increases release of Pb to drinking water. Similar results have been observed for BLLs associated with partial replacement of LSLs. Brown et al. (2011) conducted cross-sectional analyses to determine whether children residing in houses with LSL or partial replacement of LSL in Washington, DC had higher BLLs compared with children residing in houses with no LSLs in Washington, DC. Between 2004 and 2006, children living in houses with partially replaced LSLs were more likely to have a higher BLL compared with children living in houses with no LSLs (OR = 1.9 [95% CI: 1.5, 2.3] for a BLL between 5 and 9 µg/dL; OR = 3.3 [95% CI: 2.2, 4.9] for a BLL ≥10 µg/dL; relative to a BLL of <5 µg/dL).

Many factors control the degree of corrosion in plumbing components and resulting Pb mobilization to tap water. These include water treatment chemicals, pH, types and amounts of minerals found in the water, age of Pb plumbing components, and water temperature. Corrosion control in LSLs often involves developing an insoluble scale of Pb minerals that limits mobilization to water. This process is facilitated by low temperature, high pH conditions with significant chlorine residuals from disinfection. Orthophosphate-based corrosion control inhibitors may also be added to sequester Pb in a less soluble mineral phase. In recent years, water treatment plants in many municipalities have discontinued the use of chlorine for disinfection due to the formation of carcinogenic byproducts. Commonly, chloramines are used instead but may lead to greater mobilization of Pb to water due to the formation of more soluble Pb

minerals at a neutral pH (Renner, 2006; Vasquez et al., 2006). Because water quality depends on many factors, EPA recommends new water treatment systems be optimized for corrosion control and any subsequent change in treatment or raw water quality be assessed for potential increases in Pb concentrations (U.S. EPA, 2003b).

Gibson et al. (2020) analyzed and merged the BLLs of 59,483 children in North Carolina with demographic data and drinking water source (private wells or regulated water utility). The authors found that among the children (n = 7,709) who drank from private wells, there was an increased chance of higher BLL (mean = 1.75 µg/dL for private wells versus 1.59 µg/dL for water utilities). Adjusting for all other variables, the odds of an EBLL (defined as >5 µg/dL in this study) was 2.1% for private well drinkers versus 1.7% for water utility drinkers. These findings suggest that Pb released through corrosion in private well systems may lead to increased BLLs as private wells are not covered under the Safe Drinking Water Act and owners of private wells may not be using proper corrosion control (Knobeloch et al., 2013). Past studies have found higher levels of Pb concentrations in private well water (Stillo and MacDonald Gibson, 2018; Pieper et al., 2015).

Pb contamination in drinking water due to not implementing correct corrosion control methods occurred in Flint, MI. Between 1967 and 2014, the city purchased treated water from the Detroit Water and Sewage Department (DWSD), originating from Lake Huron. During this period, the Flint Water Service Center (FWSC) was maintained as a backup treatment facility, treating water from the Flint River only two to four times a year for a few days at a time and then discarding the treated water. However, in 2014, city officials made the decision to stop purchasing DWSD water and instead distribute water from the Flint River with treatment at the FWSC. The DWSD water, originating from Lake Huron, was optimized for corrosion control and treated with phosphate corrosion control inhibitors. However, the FWSC was not optimized; the facility had difficulty maintaining chlorine residuals throughout the distributions system for some periods and did not add corrosion inhibitors, both of which likely contributed to destabilization of Pb scales (Masten et al., 2016). In addition, because of a switch from sulfate to chloride-based coagulants, the chloride to sulfate mass ratio (CSMR) increased from 0.45 to 2.04 (Pieper et al., 2017). For water with alkalinity observed at the Flint facility (<50 mg/L), a CSMR over 0.5 indicates very high risk for corrosion (Masten et al., 2016). Water from the Flint River was treated and distributed from April 2014 to October 2015. Independent studies found high concentrations of Pb in drinking water taken from homes. Pieper et al. (2017) tested a home termed "Ground Zero" and found Pb concentrations in water were well above actionable limits, ranging from 217–13,200 µg/L in April 2015. The same group carried out a larger study, examining Pb concentrations in tap water from 2015 to 2017 (Pieper et al., 2018). In August 2015, the median Pb concentration in first draw water samples from the 156 homes sampled was 3.5 µg/L, with 17% of samples exceeding 15 µg/L and a maximum measured concentration of 158 µg/L. Samples taken after the reintroduction of DWSD-treated water had lower median Pb concentrations in first draw water samples, at 1.9 µg/L in March 2016 and 1.2 µg/L in July 2016. However, while Pb concentrations in most homes decreased after reintroduction of DWSD water, some remained anomalously high, either because of scouring of loose Pb deposits from

pipes or galvanic corrosion of partially replaced LSLs. Pb concentrations in drinking water for these homes did not fall below 10 µg/L until full replacement of LSLs (Mantha et al., 2020).

It is important to note between-study variation in the sampling and analytic methodologies may reduce the comparability of Pb concentrations in tap water across studies. Factors including water sample volume collected, stagnation, spacing of Pb within piping, and sampling protocol can all affect measurements of Pb within tap water (Triantafyllidou et al., 2021). Riblet et al. (2019) compared different sampling protocols including different rates of flushing and stagnation after flushing in 21 households. The authors found Pb concentrations in tap water ranged from 5.5 to 14.0 µg/L, depending on the sampling protocol used.

2.1.3.3.2 Breast Milk

Breast milk has been identified in prior reviews as a potential dietary source of Pb exposure for infants (U.S. EPA, 2013, 2006a). Table 2-5 shows the contribution of maternal blood Pb to Pb in breast milk over the past 40 years in populations in the United States, Mexico, and Europe, as estimated from data reported in papers. Gulson et al. (1998a) cautioned that studies reporting >1.5 µg/L milk Pb per µg/dL blood Pb are likely due to contamination of samples (e.g., contamination due to Pb on hands of women as they collect their milk). Trends in breast milk Pb concentrations with time postpartum generally show no temporal relationship or a slight decline (Ettinger et al., 2006; Sowers et al., 2002; Gulson et al., 1998a). Statistically significant Spearman correlations between breast milk Pb and both whole blood Pb ($r = 0.44$, $n = 81$) and plasma ($r = 0.31$, $n = 81$) have been observed (Ettinger et al., 2014). In a study of healthy infants (97 males, 113 females; median age: 11.4 months; range: 8–23 months) conducted from July 2014 to June 2016 in Seoul, Korea, duration of breastfeeding was correlated ($r = 0.427$, $p < 0.001$) with the infants' BLLs (Choi et al., 2017). Breastfed infants had significantly ($p < 0.001$) elevated blood Pb (median: 1.12 µg/dL; interquartile range: 0.77, 1.63) compared with mixed fed infants' blood Pb (median: 0.81 µg/dL; interquartile range: 0.51, 1.11) and formula fed infants' blood Pb (median: 0.62 µg/dL; interquartile range: 0.39, 0.82). Several recent studies and reviews have investigated the effect of maternal Pb exposures and risk factors on breast milk Pb (e.g., Rebelo and Caldas (2016) and Cherkani-Hassani et al. (2019)). These factors likely predominately reflect effects on maternal blood Pb and are not further considered here.

Table 2-5 Contribution of maternal blood Pb to breast milk at 1–3 months postpartum.

Milk Pb/ Blood Pb	Milk Pb[a] (µg/L)	Blood Pb[a] (µg/dL)	n[b]	Location Sample Yr	Reference
0.10	0.8 ± 0.7	7.7 ± 4.0	81	Mexico City, Mexico	Ettinger et al. (2014)

Milk Pb/ Blood Pb	Milk Pb[a] (µg/L)	Blood Pb[a] (µg/dL)	n[b]	Location Sample Yr	Reference
				1997–1999	
0.15	1.4 ± 1.1	9.3 ± 4.5	310, 367[c]	Mexico City, Mexico 1994–1995	Ettinger et al. (2006)
0.16	1.5 ± 1.2	9.4 ± 4.5	255	Mexico City, Mexico 1994–1995	Ettinger et al. (2004a)
0.16	0.5 ± 0.3	3.1 ± 0.7	35	Holmsund, Sweden 1990–1992	Hallén et al. (1995)
0.24	2.8 ± 1.6	11.9 ± 9.4	39, 62[c]	Tucson, Arizona yr not reported	Rockway et al. (1984)
0.25	0.73 ± 0.70	29 ± 8	9	Migrated to Australia yr not reported	Gulson et al. (1998a)
0.28	0.9 ± 0.4	3.2 ± 1.0	39	Röännskär, Sweden 1990–1992	Hallén et al. (1995)
1.35	1.74 ± 11.5	1.29 ± 0.60	51, 75[c]	Szczecin, Poland 2007–2008	Baranowska-Bosiacka et al. (2016)
3.3	4 (median)	1 (median)	80	West Bank, Palestine 2017–2018	Shawahna (2021)
4.4	6.1 ± 1.0	1.4 ± 0.2	15	Camden, New Jersey 1997–2000	Sowers et al. (2002)

yr = year

[a]Mean ± Standard Deviation unless otherwise reported.

[b]Paired milk Pb and blood Pb samples unless otherwise indicated.

[c]Number of milk Pb samples, number of blood Pb samples, which includes additional subjects.

Ettinger et al. (2014) reported infant BLLs at 3 months postpartum were increased by 1.8 µg/dL per 1 µg/L milk Pb at 1 month postpartum ($p < 0.0001$, $r^2 = 0.3$). However, milk Pb only accounted for 30% of the variability in the infants' blood Pb concentrations (PbB). Using the IEUBK v2.0, a maximum blood Pb contribution of 0.3 µg/dL is predicted due to milk Pb at 5 months of age using a water Pb concentration of 1.0 µg/L (to mimic milk exposure) and an upper percentile (mean + 2SD; i.e., the 98th percentile) intake rate of milk of 1 L/day for infants <12 months of age based on Chapter 15 of the U.S. EPA Exposure Factors Handbook U.S. EPA (2011). The importance of hand Pb contamination to BLL was investigated by Simon et al. (2007), who found BLLs of 13 infants decreased for 30–90 days after birth before beginning to gradually increase along with hand-wipe Pb concentrations (which increases the likelihood of ingestion during hand-to-mouth behavior) of the infants. The infants' BLLs were correlated with hand-wipe Pb concentrations of both the infants ($r^2 = 0.72$, $p < 0.01$) and mothers ($r^2 = 0.62$,

$p < 0.01$). Thus, the contribution of breast milk Pb itself to infants' blood Pb may be overestimated by Ettinger et al. (2014) due to exposure by other pathways such as the hand-to-mouth behavior of infants.

2.1.3.4 Exposure to Pb in Consumer Products

Consumer products have been identified as a source of Pb exposure in previous reviews (U.S. EPA, 2013, 2006a). This subsection builds upon discussions from the 2013 Pb ISA (U.S. EPA, 2013), highlighting consumer products found in the recent literature, detailing their corresponding Pb content, and further summarizing trends since that ISA (U.S. EPA, 2013).

Table 2-6 shows Pb content found in several consumer products, including spices, traditional medicines, cosmetics, toys/baby products, pottery, and tobacco. This table is an update of Table 3-7 in the 2013 Pb ISA (U.S. EPA, 2013).

Although products purchased in the United States have been found with detectable Pb content, most consumer products identified with detectable Pb content originate in countries abroad (Table 2-6). In many cases, these products were purchased outside the United States and brought into the country by the consumer. For example, in an analysis of 1,496 of the consumer products sampled by the New York City Department of Health and Mental Hygiene (DOHMH) between 2008 and 2017, Hore et al. (2019) reported 45% of spices purchased abroad had Pb content above 2 ppm, as opposed to 13% of sampled spices purchased in the United States. The 2-ppm threshold is the permissible limit in food additives that is used by DOHMH as a guidance limit (Hore et al., 2019).

Table 2-6 Pb content in various consumer products.

Product Category	Product	Location of Purchase	Country of Origin	Pb Content (units)	Reference
Cosmetics	Lipsticks	United States (California)		Average: 0.36±0.39 µg/g; Maximum: 1.32 µg/g	Liu et al. (2013)
	Costume cosmetics	United States (California)	China, United States, Taiwan	N.D. to 27 mg/kg	Perez et al. (2017)
	Lip products (lip balms, lip glosses, lipsticks)	Online; China (Harbin)	NR	2.48–18.22 mg/kg	Gao et al. (2018b)
	Lipsticks	Iraq	NR	0.45–48.59 µg/g	Sayyadi and Ioannidu (2015)
Pottery	Glazed containers	Mexico		0.026–68.6 mg/kg	Bahéna et al. (2017)

Product Category	Product	Location of Purchase	Country of Origin	Pb Content (units)	Reference
Spices	Georgian saffron	United States (New York), Georgia	Georgia	Geo Mean: 240.1 µg/g	Hore et al. (2019)
Tobacco	Cigarettes (filler tobacco, filter, and ash)	Ireland		0.378–1.16 µg/cigarette	Afridi et al. (2015)
	Cigarettes	Nigeria	Nigeria	Filler Tobacco: 17.21–74.78 µg/g; Filter: 4.09–13.78 µg/g	Benson et al. (2017a)
	Cigarettes	Portugal	NR	0.44–0.72 (mean: 0.55) (µg/g)	Pinto et al. (2017)
	Dried tobacco leaves	United States	Thailand	36.12 ppm (µg/g)	El Zahran et al. (2018)
	Cigarettes	China	China	Mean: 2.7718 µg/g	Li et al. (2020)
Toys and Baby Products	Teethers and feeding teats	Europe (Unspecified, products were made in China)		N.D. to 27.31 µg/g	Aboel Dahab et al. (2016)
	Diaper powder	United States		620,000–639,500 µg/g	Karwowski et al. (2017)
	Children's toys and jewelry (metallic toys and jewelry, plastic toys, paper/wood toys, brittle/pliable toys, and paint coating from toys)	China (Nanjing)	NR	0.08–860,000 mg/kg	Cui et al. (2015)
Traditional Medicine	Ayurvedic medications: Mahayogaraj Guggulu (MG), Bruhat Vata Chintamani Rasa (BVCR)	United States (Wisconsin); Produced in India and purchased online		MG: 48,700 mg/kg; BVCR: 16.4 mg/kg	Meiman et al. (2015)
	Kajal (eye cosmetic)	Afghanistan, brought into United States	Afghanistan	540,000 µg/g	CDC (2013)
	Daw Tway	Not specified: Myanmar or United States	Myanmar	Median: 520 µg/g	Ritchey et al. (2011)

Product Category	Product	Location of Purchase	Country of Origin	Pb Content (units)	Reference
	Oral Ayurvedic medications (Pregnita, Vatvidhwansan Ras, Kankayan Bati (Gulma), Garbhaoal Ras, Ovarin, Garbha Dharak Yog, Laxmana Louh, Garbha Chintamani Ras (Vrihat) (Swarna Yukt), Pigmento)	United States (New York)		7.3–24,000 µg/g	Hore et al. (2012)
	Sindoor	United States (New Jersey); India	India	U.S. Samples: Geo mean (SD): 5.4 (1.6) Max: >300,000; India samples: 28.1 (32.4) Max: >300, 000 (µg/g)	Shah et al. (2017)

BVCR = Bruhat Vata Chintamani Rasa; MG = Mahayogaraj Guggulu; N.D. = not detected; NR = not reported; SD = standard deviation

Research evidence has shown exposure to cigarette smoke through use of cigarettes or secondhand smoke can lead to increased BLLs. Richter et al. (2013) analyzed BLLs of NHANES data from 1999 to 2008 for participants 3 years and older who responded to questions about smoking (n = 43,627). The authors found the BLLs were higher for smokers and nonsmokers exposed to secondhand smoke even after controlling for age of housing and occupational exposure to Pb. Apostolou et al. (2012) analyzed BLLs and demographic information of 6,830 subjects aged 3–19 years old using NHANES data from 1999–2004. The authors found participants in the highest quartile of serum cotinine (≥0.44 µg/L), a biomarker indicator of recent smoke exposure, had 28% higher BLLs than those in the lowest quartile (<0.03 µg/L). In addition, those living with one or two smokers had 14% and 24% higher BLLs, respectively, than those living without smokers. Higher BLLs have also been found in studies of Swedish smokers (Almerud et al., 2021; Wennberg et al., 2017). A study of the relationship between BLLs and smoking status in an elderly population of Koreans found higher BLLs among smokers (GM: 2.09, geometric standard deviation [GSD]: 1.93 for smokers; GM: 1.90, GSD: 1.66 for nonsmokers), but it was not statistically significant (p = 0.2597) (Lee et al., 2017).

Electronic cigarettes are also a potential source of Pb exposure. Hess et al. (2017) measured Pb concentrations in liquid cartridges from five brands of e-cigarettes. Pb concentrations were highly variable, even among samples from the same brand, with median values for each brand ranging from 1,970 µg/L to 4.98 µg/L. Olmedo et al. (2018) and Zervas et al. (2020) also provided evidence that Pb may be transferred from the heating coil in e-cigarettes to vapor, adding a potential source of Pb exposure from these devices.

2.1.3.5 Occupational Exposure

Engagement in the workplace is a common source of Pb exposure. Although its use in many industries has decreased over time, as of 2011, it accounted for 95% of BLLs ≥25 µg/dL in adults CDC (2011). This section builds upon previous reviews and briefly summarizes recent studies that examine modern occupational Pb exposure in the United States. Information on the specific Pb exposure-blood Pb relationship in occupational cohorts can be found in Section 2.5.1.

The 2013 Pb ISA (U.S. EPA, 2013) states that operations involving Pb-containing materials in various industries are a source of occupational Pb exposure. This occurs in many industry sectors, including construction, manufacturing, wholesale trade, transportation, remediation, and recreation. Pilots may be exposed to avgas through preflight fuel checks in which 75,000 to 175,000 gallons of avgas are discarded on the ground annually. Start-up and idling of planes at high fuel-to-air ratios, along with venting of avgas from production, transport, distribution, and storage, create additional opportunities for exposure (NASEM, 2021). In an investigation conducted by the Wisconsin State Health Department between 2015 and 2016, Weiss et al. (2018) found 171 (73.7%) shipyard workers had BLLs greater than 5 µg/dL.

Ammunition is another source of occupational Pb exposure. Pb exposure occurs through inhalation or ingestion of Pb in dust and skin contact with leaded bullets. Numerous studies have shown the connection between EBLLs and ammunition, particularly in indoor and outdoor shooting ranges. The Occupational Safety and Health Administration (OSHA) has standards in place for firing ranges OSHA (2020), and the Department of Energy (DOE) has set guidelines for range design to mitigate airborne Pb exposure (DOE, 2012). Recently, a Department of Defense (DoD)-commissioned U.S. National Academy of Sciences report (NRC, 2013) on health effects of Pb exposure at firing ranges concluded the OSHA standard of 40 µg/dL is insufficient, which led to a DoD technical report on new health-based blood Pb guidelines (U.S. APHC, 2014). A few recent studies examining the relationship between shooting ranges and Pb exposure are highlighted below.

Greenberg et al. (2016) took blood Pb and continuous personal airborne Pb measurements of 175 soldiers across four infantry units of the Israeli Defense Force (IDF) in a cross-sectional study. BLL measurements were taken before and after basic and advanced training courses conducted in outdoor shooting ranges. Soldiers (n = 174) were found to have nondetectable BLLs before basic and advanced training courses. The percentage of soldiers with detectable BLLs increased from 21% after the basic training course to 89% after the advanced training course. Weber et al. (2020) conducted a study to characterize Pb exposure during five training tasks of a 45-day advanced urban assault class conducted in both 2014 and 2016. Pb-free ammunition was used in the 2016 class, and that significantly reduced air sampling and BLL measurements. However, mean and maximum personal air measurements were found to be above the OSHA permissible exposure limit of 0.050 mg/m^3 in both years. The authors suggest this may be due to influences of other sources of Pb exposure, such as residual Pb present in weapons or resuspension of Pb present in range soil due to historical usage.

In addition to personal exposure, working with Pb-containing materials or in a Pb-contaminated work setting may also result in take-home exposures, where a worker contaminates their home environment with Pb originating from the workplace and potentially exposes other members of the household. Several CDC reports have found evidence of take-home Pb exposures. In 1998, an investigation of Pb poisoning in six furniture workers and their families was performed. A father working for a company that refinished antique furniture had a BLL of 46 µg/dL, while the 18-year-old child and 4-month-old daughter had BLLs of 26 µg/dL and 24 µg/dL, respectively. Among the families of the total of six workers investigated, five of the six family members aged 7-12 did not have EBLLs but a 7-month-old infant whose father's BLL was above 40 µg/dL had a BLL of 16 µg/dL, and it was 15 µg/dL 30 days later. Workers' BLLs decreased on average by 15 µg/dL in about 3 months after an occupational Pb safety program was put in place. In one case, a wipe sample of the carpet where a worker played with his children was 30 µg/ft^2 but was reduced to 14 µg/ft^2 after steam cleaning; however, the 4-month-old's BLL only decreased steadily after Pb-painted surfaces within the home were remediated (CDC, 2001).

From 2010-2011 it was determined that among 78 families of workers in a battery recycling facility, 11 children (16% of 68 children <6 years of age) had confirmed BLLs ≥10 µg/dL, and 39 children (57%) had BLLs ≥ 5 µg/dL. 85% of vehicle dust samples and 49% of house dust samples were ≥ 40 µg/ft^2. Children's BLLs decreased 9.9 µg/dL on average after EPA began clean-up of employee homes and vehicles. In addition, the company was required to setup shower facilities, shoe washes, and clean changing areas, and children with BLLs ≥5 µg/dL were enrolled in case management (CDC, 2012). In 2008, 55 new cases of EBLLs (≥15 µg/dL) in venous samples among children <6 years were identified in Maine. No Pb-based paint or elevated Pb levels were found in the homes of six children. It was found that these children were exposed to high Pb levels in the vehicles and child safety seats, likely as a result of household contacts who worked in environments with high-risk to Pb exposure (CDC, 2009).

Ceballosa et al. (2021) examined the relationship between sociodemographic-, work-, and home-related factors and Pb concentrations in house dust sampled from the homes of 23 construction, five janitorial, and two autobody workers in Boston, MA. Factors from all 3 categories were found to be associated with Pb in house dust, pointing to overlapping vulnerabilities. Pb in homes' dust ranged from 20-8,310 ppm, with those in construction workers' homes on average higher and more variable (mean: 775 ppm, median: 264 ppm, max: 8,300 ppm) than the homes of autobody and janitorial workers (mean: 296 ppm, median: 303 ppm, max: 579 ppm) suggesting that some construction workers were at risk for take-home exposure. Other specific factors that were predictive of greater Pb concentrations in house dust were not having a locker at work, not changing clothes after work, not washing hands after work, washing clothes at a laundromat, and having a house built before 1978.

Other literature have also studied the link between take-home exposures and BLLs in house occupants. Newman et al. (2015) linked a case of child Pb poisoning to a father's take-home occupational exposure at an e-scrap recycler company. In June 2010, a male 1-year-old child and female 2-year-old child had EBLLs of 18 µg/dL and 14 µg/dL, respectively, while the father's BLL was measured as

25 µg/dL. The father did not wear personal protective equipment (PPE) at work and the family reported that he often had visible dust in his hair upon returning home. In addition, a lead risk assessment found detectable Pb dust on the floor of the home, but no Pb paint was found. The father left his occupation after the EBLLs were recognized, and the children's BLLs dropped to 8.7 µg/dL (male) and 7.9 µg/dL (female), respectively, over the course of 3 months. Rinsky et al. (2018) characterized BLLs among employees at a lead oxide manufacturing facility and children living in their households. Among those who worked in the manufacturing area, average maximum BLLs consistently ranged from 40-59 µg/dL. Of the 17 children examined, three had BLLs 5-9 µg/dL and two had BLLs 10-19 µg/dL. The researchers found many inconsistencies in adherence to PPE use and personal hygiene protocols which likely resulted in both occupational exposure in workers and take-home exposure in household members. Becker et al. (2022) found no association of BLLs with paraoccupational Pb samples from dust on the father's workpants and work shoes when using isotopic ratio analysis. Instead, other sources were identified including paint chips, soil, house dust, turmeric, or another unknown source, depending on the household. However, this study did not focus on occupations known to have a high risk of Pb exposure.

2.1.4 Co-Contaminants Commonly Present with Pb

Pb is commonly present in the environment with other contaminants, but the quantity and species of these contaminants depend on the source type and environmental media in which Pb is contained. For example, exposure to Pb associated with avgas may occur either through contact with liquid fuel and fluid vapors during aircraft fueling operations or through inhalation of piston-engine aircraft exhaust. Exposure to co-contaminants found in avgas is expected to differ between unused fuel and exhaust as combustion changes the chemical properties of the fuel. Lovestead and Bruno (2009) investigated the composition of 100LL aviation gas and found that in addition to tetraethyl Pb, the fluid was composed of various branched and linear alkanes (largely isomers of hexane and pentane) and a small amount of toluene. This result was similar to the composition disclosed by the manufacturer in the Material Safety Data Sheet. Turgut et al. (2020) provided data on the gaseous and PM_{10} emissions from a single reciprocating engine aircraft fueled by 100LL avgas. A total of 70 PM samples were analyzed for concentrations of 48 trace elements using ICP-MS. The PM samples were composed of 24 ± 12.8% trace metals, with the remaining mass likely composed of black or organic carbon. Regardless of test condition, Pb was by far the most abundant trace element (median 4.6×10^6 ng/m^3), followed by Na, which was 40 times less abundant (1.1×10^5 ng/m^3). Other elements measured were reported in groups based on median ranges as shown in Table 2-7. In the gaseous phase, CO_2, CO, total hydrocarbons (HC), and NO_X were sampled. In general, there was an increase in NO_X emissions with increasing engine speed and a decrease in CO and HC emissions.

Emissions from some ongoing industrial activities (e.g., metal working, mining, Pb acid battery manufacturing and recycling, glass and cement manufacturing) and resuspended PM deposited by historical activity may contain Pb and other metals. Zota et al. (2011) examined concentrations of Pb, Zn,

Cd, As, and Mn in dust samples taken from homes near a mining-impacted superfund site in Oklahoma. Reported concentrations of Pb in house dust were 109 ± 138 µg/g; co-contaminant concentrations may be found in Table 2-7. Mixed metal particles measured from the emissions stack of a steel manufacturing plant were found to be composed of Pb, Zn, K, and Na (Reinard et al., 2007). Machemer (2004) also investigated the composition of airborne particles originating from the basic oxygen furnace of iron and steel manufacturing facilities. The <38 µm size fraction (used as a proxy for the respirable fraction) of particles was largely composed of Fe, Al, Ca, Mg, Mn, and Si. In addition, the particles contained Pb at concentrations ranging from 200–220 mg/kg and significant quantities of other potentially toxic metals are reported in Table 2-7. The authors also note the particles had a strongly alkaline, potentially corrosive, pH of 12.4.

Pb remobilized by wildfires may have a variety of inorganic and organic co-contaminants. Odigie and Flegal (2014) measured trace metal contents in ash collected from the 2012 Williams fire in Los Angeles, CA. In addition to Pb (7 to 42 µg/g), they measured Co, Cu, Ni, and Zn (concentrations shown in Table 2-7). Ghetu et al. (2022) investigated PAH concentrations in air during wildfire events across the western United States between 2018 and 2020. They found 12 PAHs in air associated with wildfires (reported in Table 2-7).

Road dust commonly consists primarily of organic carbon and crustal elements (S, Al, Fe, Ca, K, Na, Mg); other, less abundant components commonly observed are related to brake and tire wear (Cu, Zn, Sb, Ba, Pb, and S) and catalytic converters (Pt, Rh, Pd) (O'Shea et al., 2021; Hays et al., 2011; Lough et al., 2005). Hays et al. (2011) also noted ten metals listed as EPA air toxics (Mn, Cr, Sb, Ni, Pb, As, Co, Cd, Se, and Be) were generally enriched in $PM_{0.1}$, and several biologically antagonistic suites of metals (Cd, Cu, and V) were found in multiple PM size modes. Similarly, Pb along with crustal elements such as Fe, Si, Ca, K, Mn, and Zn were observed in resuspended soil and dust, along with other potentially toxic or antagonistic components (Cr, As, Cu, V), which varied spatially depending on local sources (Kundu and Stone, 2014).

Table 2-7 Co-contaminants in Pb sources.

Source	Co-contaminants	Concentration	Reference
Piston-Engine Aircraft Exhaust	In < Sn < S < Ca < Al	[2.3–11.2] × 10^4 ng/m^3	Turgut et al. (2020)
	Cr < Zn < Ba < As < Sm < Se < V < Mg	[1.3–12.3] × 10^3 ng/m^3	
	Sr < Mn < Cd < Ge < Ti < Ni < Cu	[1.2–9.4] × 10^2 ng/m^3	
	La < Ag < Ga < Zr	7.6–33.8 ng/m^3	
	Cr	1,500 mg/kg	Machemer (2004)

Source	Co-contaminants	Concentration	Reference
Iron and Steel Manufacturing	Mn	18,000 mg/kg	
	Zn	5,500 mg/kg	
Wildfire Ash	Co	3–11 µg/g	Odigie and Flegal (2014)
	Cu	15–69 µg/g	
	Ni	6–15 µg/g	
	Zn	65–500 µg/g	
Wildfire Emissions	dibenzo[e,l]pyrene, 6-methylchrysene,	Concentrations not Reported	Ghetu et al. (2022)
	7,12-dimethylbenz[a]anthracene, anthanthrene		
	5-methylchrysene, benzo[a]chrysene		
	naphtho[2,3-x]pyrene, naphtho[1,2-b]fluoranthene		
	coronene, perylene, dibenzo[a,l]pyrene		
House Dust Near Chat Piles	Zn	876 ± 627 µg/g	Zota et al. (2011)
	Cd	4.3 ± 6.8 µg/g	
	As	6.3 ± 9.9 µg/g	
	Mn	143 ± 98 µg/g	

Many studies that investigate Pb exposure by using biomarkers do not include other contaminants in their analysis. However, Shim et al. (2017) analyzed NHANES blood and urine biomarker data for a U.S. population 6 years of age or older from 2007 to 2012 to understand co-exposures of Pb with three other metals: As, Cd, and Hg. For all metals, only measurements above the LOD were used. All possible unique combinations of the metals were then selected wherein each metal concentration was at or above the population median in blood, urine, or both. The weighted creatine-adjusted median values found in urine were 7.91 µg/L (As), 0.2 µg/L (Cd), 0.44 µg/L (Hg), and 0.5 µg/L (Pb). The weighted median values found in blood were 0.27 µg/L (Cd), 0.76 µg/L (Hg), and 1.07 µg/dL (Pb). Table 2-8 below shows the prevalence of As, Cd, Pb, and Hg detected at or above median concentrations. The most commonly occurring combinations were Cd/Pb (8.4%), Cd/Hg/Pb (10.6%), and As/Cd/Hg/Pb (22.1%).

Table 2-8 Specific unique combinations of As, Cd, Pb, and Hg detected at or above the respective median concentrations in urine or blood among the U.S. population 6 years and older, NHANES 2007–2012 data.

Metal Combination[a]	Sample N[b]	Prevalence[c] – Weighted %	Prevalence[c] – 95% Confidence Interval
None	590	8.4[d]	7.0, 9.7
Pb	347	3.6	3.1, 4.2
As/Pb	236	2.2	1.8, 2.7
Cd/Pb	632	8.4	7.3, 9.5
Pb/Hg	294	3.7	3.1, 4.3
As/Cd/Pb	381	4.4	3.7, 5.1
As/Hg/Pb	448	5.7	4.9, 6.5
Cd/Hg/Pb	696	10.6	9.3, 11.9
As/Cd/Hg/Pb	1,671	22.1	20.3, 23.9

[a]As and Hg represent total As and Hg.

[b]All participants (n = 7,408) were tested for urinary and blood Cd, Pb, and Hg, as well as urinary As.

[c]Detected in blood and/or urine specimens at or above median concentrations.

[d]In 8.4% of the U.S. population 6 years and older, none of the four metals were detected at or above their respective population medians in urine or blood.

Data sourced from Shim et al. (2017).

2.1.5 Exposure Disparities for Specific Populations

The 2013 Pb ISA (U.S. EPA, 2013) noted elevated or differential Pb exposure and biomarker levels (such as blood Pb) have been shown to be statistically related to several population characteristics, including age, sex, race and ethnicity, socioeconomic status (SES), proximity to Pb sources, and residential factors. The 2013 Pb ISA (U.S. EPA, 2013) evaluated past research on these population characteristics' relationship to Pb exposure and biomarker levels, including biological or intrinsic (e.g., age, sex) and nonbiological or extrinsic (e.g., SES) factors. Evidence for increased exposure in this section primarily relies on studies that measured BLLs. BLLs and other biomarkers are further explored in Sections 2.3 and 2.4.

2.1.5.1 Proximity to Pb Sources

The 2006 AQCD (U.S. EPA, 2006a) found proximity to industrial sources likely contributes to higher Pb exposures. The 2013 Pb ISA (U.S. EPA, 2013) stated the highest air Pb concentrations measured using Pb-TSP monitoring were measured at monitors located near sources emitting Pb. Additional evidence has shown EBLLs as a result of proximity to sources that emit Pb. Jones et al. (2010) found neonates born near a Pb-contaminated hazardous waste site had significantly higher umbilical cord BLLs (median: 2.2 µg/dL, 95% CI: 1.5, 3.3 µg/dL) compared with a reference group of neonates not living near a potentially contaminated site (median: 1.1 µg/dL, 95% CI: 0.8, 1.3 µg/dL) but did not analyze covariation between exposure and maternal characteristics, meaning that maternal characteristics may have confounded results.

Benson et al. (2017b) assessed the relationship between airborne Pb sources and BLLs in children aged 1 to 5 years. The authors used annual average ambient air Pb levels modeled by the EPA National Air Toxics Assessment (NATA) for 2005 and industrial Pb releases obtained from the EPA TRI. For TRI industrial releases, inverse distance squared weighted exposure, defined as the sum of pounds of Pb released by each facility divided by the distance between each child and each industrial facility squared, was calculated for each child to estimate Pb exposure from industrial releases. The estimated median annual average ambient air Pb level was 1.77 ng/m^3, and the median inverse distance squared weighted exposure from Pb TRI facilities was 1,748 lb/mi^2. Univariate analysis of unadjusted data found Pb exposure from industrial releases was not significantly associated with children's BLLs, whereas annual average ambient concentrations were significantly related ($p < 0.01$); odds ratios indicated a 1.37 to 2.63% increase in BLLs for every 1 ng/m^3 increase in annual average ambient air Pb concentration. However, after adjusting for demographic covariates, including sex, race, age in months, education level, percentage pre-1950 housing, poverty-income ratio, region, and survey cycle, NATA estimated annual average ambient air Pb was no longer significantly related to BLLs, whereas a significant association was found for industrial Pb releases ($p = 0.001$). In the adjusted model, a 10,000 lb/mi^2 increase in inverse distance squared weighted exposure was associated with an estimated 1.13% (95% CI: 0.45%, 1.81%) increase in BLL. Brink et al. (2013) analyzed the relationship between air Pb concentration and children's BLLs. BLL data were obtained from the Centers for Disease Control and Prevention (CDC) Healthy Homes and Lead Poisoning Prevention Branch for 1,508 of the 3,220 U.S. counties from 2000 to 2006. Modeled ambient concentrations of annual average airborne Pb at the county level were obtained from 2005 NATA data. They found the highest 10% of estimated annual average air Pb concentration included counties with total concentrations >0.00297 µg/m^3, whereas the lowest 10% was <0.000526 µg/m^3. The proportion of tested children with BLLs ≥10 µg/dL was 1.24% in the counties with the highest 10% of estimated air Pb concentration, whereas the proportion with BLLs ≥10 µg/dL was 0.36% in counties with the lowest 10% of estimated air Pb. They also carried out a multivariate negative binomial regression and found estimated air Pb concentration was significantly associated ($p = 0.017$) with BLLs (% ≥10 µg/dL) after adjusting for percentage of pre-l950 housing, rural classification, and percentage of black children by county. Brink et al. (2016) carried out a more detailed analysis to examine the link between 2005

NATA-estimated annual average air Pb concentration and the BLLs of children within 105 contiguous counties in Kansas. BLL data for children under 36 months was provided through the Kansas Environmental Public Health Tracking Network for 2000–2005. It was found that the mean estimated annual average Pb concentration was 0.00177 μg/m^3 in the 13 counties with at least one resident child with BLL over 10 μg/dL, and the mean Pb concentration was 0.00064 μg/m^3 in the counties with no children with BLLs over 10 μg/dL. No relationship between estimated NATA air Pb concentration and mean BLL by census tract or county was found. However, a multilevel model to predict BLL using distance from a Pb-emitting TRI site, adjusting for child's age in months, poverty rate, and pre-1950 housing at the census tract level, found a significant ($p < 0.001$) inverse relationship between mean BLL and distance from TRI site (i.e., higher BLL with decreasing distance).

Klemick et al. (2020) analyzed the impact of Superfund cleanup on children's BLLs by using BLL data from the mid-1990s to mid-2010s for children aged 6 months to 5 years old residing within 5 km of at least one Superfund site in six states. They also used cleanup milestone dates from EPA's Superfund Enterprise Management System to identify when construction was complete, which included 87 Superfund sites where Pb was identified as a contaminant. The results of their model showed that prior to the start of cleanup, the rate of BLLs >3 μg/dL was 4–8% higher for children living within 2 km of Pb-contaminated Superfund sites than those living 2–5 km away, and the difference was significant ($p < 0.01$).

2.1.5.2 Age

In the 2013 Pb ISA (U.S. EPA, 2013), children were concluded to have higher risk of Pb exposure compared with adults because of hand-to-mouth contact, crawling, and poor hand washing. As discussed in Section 2.3, children also have a higher rate of bone turnover, a higher percentage of total body burden found in the bloodstream, and a lower overall body mass (Barry, 1975). Wang et al. (2021) analyzed the BLLs of 68,877 participants using NHANES data from 1996 to 2016. The authors analyzed the data both by cross-sectional analysis and birth cohort analysis. BLL data for each NHANES cycle displayed a "U" shaped curve, with the highest BLLs among young children (1–5 years) and older adults (≥70 years), and the lowest BLLs among individuals 12–19 years old. When data were stratified into birth cohorts, BLLs were highest in young children (age 1–5) and decreased monotonically with age. However, the authors note that from 1999 to 2016, the 1990s cohort BLLs declined faster than other cohorts observed; in addition, they found the rate of BLL decrease was faster before the ages of 13–17 years than after, which may be due to the fast growth of blood volume within children, which can dilute blood Pb concentrations.

Jones et al. (2009) evaluated trends in 1- to 5-year-old children's BLLs based on 1988–2004 NHANES data. Their model indicated 1- to 2-year-old children were significantly more likely ($p < 0.0001$) to have BLLs ≥10 μg/dL than those in the 3- to 5-year age range after adjusting for

percentage of non-Hispanic black, having a poverty-to-income ratio (PIR) of ≥1.3, and living in a moderate-risk [built ~1950–1977] or high-risk [built before 1950] house. For the most recent NHANES cycle included in the study (1999–2004), 2.4% (95% CI: 1.4, 3.5) of children 1–2 years old and 0.9% (95% CI: 0.4, 1.5) of children 3-5 years old had BLLs ≥10 µg/dL. This result implies there is a shift in distribution of BLLs as young children age, likely due to differences in exposure, including behavioral influences as well as the previously discussed age-related changes in physiology.

Senior populations may have elevated lifetime Pb exposures due to exposures that occurred prior to the removal of leaded gasoline and broader Pb regulation. NHANES data for 2009–2010 presented in the 2013 Pb ISA (U.S. EPA, 2013) revealed that BLLs were higher for participants 60 years or older compared with younger adults and adolescents. Several studies found statistically significant relationships between age and blood or bone Pb (Miranda et al., 2010; Theppeang et al., 2008; Nriagu et al., 2006). Jain (2016) investigated the BLLs of men and women over 65 years old using NHANES data from 2003–2012. The authors found that those over 65 had higher BLLs than 20–64-year-olds (i.e., 28% higher unadjusted GM, 26% higher adjusted GM). Vearrier and Greenberg (2012) analyzed 2,168 BLLs of people over 80 from NHANES data between 1999–2010 and measured the BLLs of 76 people 80 years or older who presented to an inner-city emergency department. GMs of NHANES-obtained BLLs ranged from 2.66 µg/dL (1999–2000) to 1.98 µg/dL (2009–2010), with a decreasing trend overall. The GM of inner-city subjects was 1.72 µg/dL. The authors acknowledge that decreasing Pb exposure over time may have led to lower BLLs in the more recent data from older subjects.

2.1.5.3 Immigrant Populations

Both premigration and postmigration factors may contribute to EBLLs among U.S. immigrant populations. Commonly identified premigration factors include immigration from areas with a high risk of Pb exposure and use of cultural products with high Pb content (see Section 2.1.3.4). Postmigration BLL increases are commonly caused by continued use of high-Pb cultural products as well as household exposure to Pb in peeling paint and drinking water. BLLs in refugee children are particularly well studied because testing is included in medical screenings conducted within 90 days of arrival to the United States and may be followed up with a repeat exam several (typically 3–6) months later. Balza et al. (2022) conducted a systematic review of 13 studies published between 2011 and 2021 that reported BLLs in refugee children (≤18 years of age) and compared these to either BLLs measured in the general population or the CDC reference value. The percentage of refugee children with EBLLs reported in the 13 studies is summarized in Table 2-9. Twelve of the studies used data from entrance and/or follow-up medical exams, whereas Ritchey et al. (2011) reported BLLs for refugees with varying time since immigration as well as children born in the United States to refugee parents. In addition, 11 of the studies reported BLLs from refugees originating from many countries, whereas Ritchey et al. (2011) reported BLLs from only Burmese refugees and Seifu et al. (2020) focused solely on Cuban refugees. Other important variations between the studies were limits for children's age, which ranged from <6 years to

<19 years; reference levels at which BLLs were considered elevated (either 5 or 10 µg/dL, although some studies reported both); and sampling method (i.e., venous versus capillary). There is evidence that capillary blood samples may be at a higher risk of contamination and biased higher compared with venous samples. This is discussed in detail in Section 2.3.2.

Table 2-9 Prevalence of elevated blood Pb levels in refugee children.

Study	Age	n	Study Yr	EBLL Reference Value	Initial EBLL (%)	Follow-up EBLL (%)	Other EBLL (%)*	Sampling Method
(Ritchey et al., 2011)[c]	<6	197	2009	5 µg/dL 10 µg/dL			37% 7.1%	Capillary; positives confirmed with venous draws.
(Eisenberg et al., 2011)	<7	1,148	2000–2007	10 µg/dL	16%			5% of initial samples and 32% of follow-up samples were capillary.
(Williams et al., 2012)[c]	<6	257	2008–2011	5 µg/dL 10 µg/dL		39% 9%		Not reported.
(Raymond et al., 2013)[a]	<16	1,007	1995–2010	10 µg/dL	22.7%			Both venous and capillary used. Capillary confirmed with second test.
(Yun et al., 2016)	<19	8,148	2006–2012	5 µg/dL	21.1%			Not reported.
(Sandell et al., 2017)[b]	<18	225 199	2007–2009, 2013	9 µg/dL	5.6% 7.8%			Not reported.
(Kotey et al., 2018)	<15	1,950	2012–2016	5 µg/dL	11.2%			Not reported.
(Geltman et al., 2019)[c]	<7	3,054	1998–2015	5 µg/dL 10 µg/dL	41.9% 7.9%			Venous only.
(Shakya and Bhatta, 2019)[c]	<18	5,661	2009–2016	5 µg/dL 10 µg/dL	22.3% 2.1%			Capillary; positives confirmed with venous draws.
(Pezzi et al., 2019)	<16	27,284	2010–2014	5 µg/dL	19.0%	22.7%		28% of initial samples and 24% of follow-up samples were capillary.
(Lupone et al., 2020)[c]	<16	705	2012–2017	5 µg/dL 10 µg/dL	17%			Venous only.

Study	Age	n	Study Yr	EBLL Reference Value	Initial EBLL (%)	Follow-up EBLL (%)	Other EBLL (%)*	Sampling Method
(Seagle et al., 2020)[c]	<16	1,178	2010–2015	5 µg/dL 10 µg/dL	8% 0.8%			Not reported.
(Seifu et al., 2020)[d]	<16	301	2003–2016	5 µg/dL 10 µg/dL	41.9% 7.9%			Venous only.

EBLL = elevated blood lead level

*"Other EBLL (%)" includes data from studies that did not use BLLs from entrance or follow-up medical exams.

[a]Study measured BLLs in Manchester, NH (n = 639) and Providence, RI (n = 368).

[b]Study followed two cohorts of children during two different time periods (2007–2009 and 2013).

[c]Study reported data for both 5 µg/dL and 10 µg/dL reference values.

[d]Study reported BLL as elevated at 10 µg/dL for testing done prior to June 2012 and 5 µg/dL for testing done afterwards.

Only two studies, Seagle et al. (2020) and Sandell et al. (2017), reported a prevalence of EBLLs in refugee children that was <10% of total tested children. Reported values in other studies ranged from 11.2 to 41.9%. Seven studies examined prevalence of EBLLs in refugee populations compared with a nonrefugee comparison group. In all instances, the percentage of refugees with EBLLs was significantly larger than the comparison group, ranging from 6 to 31 times the percentage of nonrefugee population with EBLLs.

Several of the included studies examined the relationship between prevalence of EBLL and the refugee's country or region of origin. Eisenberg et al. (2011) reported the prevalence of EBLLs for children from Africa was 3.8 times that of children from Europe/Central Asia (reference group) and 5.6 times that of West African children specifically. In addition, children born in the Near East and South Asia region had a 3.6 times greater prevalence of EBLLs than children from Europe/Central Asia. Geltman et al. (2019) reported immigrating from Africa (OR 2.49), East Asia and the Pacific (OR 1.98), and South-Central Asia (OR 2.47) was associated with increased risk of EBLL compared with Europe or Eurasia. Lupone et al. (2020) reported the majority of children in their study with EBLLs arrived from countries in Africa (55.0%), and the prevalence of EBLLs was 30% for children from the Middle East, 14.2 % for children from Southeast Asia, and 0.8% for children from Eastern Europe. Yun et al. (2016) reported prevalence of EBLLs for children from Bhutan (26.8%), Burma (via Thailand) (1.9%), Burma (via Malaysia) (10.5%), the Democratic Republic of the Congo (25%), Ethiopia (13.1%), Iraq (19.9%), and Somalia (19.8%). (Shakya and Bhatta, 2019) reported a high prevalence of EBLLs in children from South Asia, including Afghanistan (56.2%), Nepal (44%), Bhutan (32.8%), and Burma (31.8%). Pezzi et al. (2019) reported a high prevalence of EBLLs for children from India (57.9%), Afghanistan (55.1%), Burma (37.2%), Nepal (27.5%), and Syria (22.7%).

In two of the studies, time away from the country of origin correlated with lower BLLs. Kotey et al. (2018) reported an inverse association between length of time from resettlement to testing and EBLL, and Shakya and Bhatta (2019) also reported a decrease in BLL with increased time since arrival.

However, time away from country of origin did not result in lowered BLLs for all children observed. Williams et al. (2012) focused on BLLs measured during follow-up tests conducted several months post immigration. They reported 22 children experienced a 2 µg/dL or more increase in BLLs between two screens. Eleven of these children had relocated to a secondary housing placement since their initial screening test, and they attribute the increased BLLs to exposures at the new address. However, the remaining 11 children experienced an increase in their BLLs while remaining at their initial housing placement. Three children experienced a BLL increase above 10 µg/dL (one from 20 to 25 µg/dL). The remaining eight children experienced an increase in BLLs, but the results of the screening test remained below 10 µg/dL. Additional studies in the review also looked at correlations to housing and found similarly mixed results. Eisenberg et al. (2011) found that residing in a census tract with older housing was associated with higher BLL increases after resettlement, and (Kotey et al., 2018) reported a 10-year increase in the age of housing was associated with a 27% increase in the odds of an EBLL. However, Ritchey et al. (2011) did not identify Pb paint or other environmental factors as significantly related to BLLs, and Raymond et al. (2013) did not find a significant association between age of housing and BLLs in refugees residing in either Manchester, NH or Providence, RI. However, they did find BLLs were generally higher for refugee children than nonrefugee children living in the same buildings in Manchester but did not find this in Providence.

Disparities in prevalence of EBLLs and increase of BLL after immigration to the United States may be partly explained by differences in lifestyle habits and use of cultural products among refugee populations. Ritchey et al. (2011) examined EBLLs among children of Burmese refugees in Indiana, including U.S.-born children. They found EBLL in this population was significantly predicted by daily use of thanakha and Daw Tway, a culturally specific cosmetic and digestive remedy, respectively. Laboratory testing confirmed high concentrations of Pb (median 520 ppm) in Daw Tway. Differences between nonrefugee immigrant populations have also been observed. Kaplowitz et al. (2016) investigated a population of U.S.-born children in Michigan and compared BLLs in children with immigrant mothers to BLLs in children with U.S.-born mothers. After controlling for individual, family, and neighborhood characteristics, only children of South Asian-born mothers had BLLs statistically significantly higher than children of U.S.-born mothers, whereas children of African- and Latin American-born mothers had BLLs that did not statistically differ from children of U.S.-born mothers.

2.1.5.4 Race/Ethnicity

Both SES and race/ethnicity have been reported as correlated with BLLs. In some cases, these factors may be linked, such as in the case of racial/ethnic minorities and those of low SES being more likely to live in older housing (Leech et al., 2016). The 2006 Pb AQCD (U.S. EPA, 2006a) and the 2013 Pb ISA (U.S. EPA, 2013) found higher blood and bone Pb levels among African Americans.

Campanella and Mielke (2008) found differences in potential exposure between racial/ethnic groups in metropolitan New Orleans. In census blocks where surface soil Pb levels were less than 20 mg/kg, the population was 36% black, 55% white, 3.0% Asian, and 6.0% Hispanic, based on the 2000 census. In contrast, they found that for census blocks in which soil Pb levels were between 1,000 and 5,000 mg/kg, the population was 62% black, 34% white, 1% Asian, and 4% Hispanic. Cassidy-Bushrow et al. (2017) measured Pb levels in tooth-matrix biomarkers among 71 children born between September 2003 and December 2007 in Detroit, MI. They found African-American children had 2.2 times higher Pb levels in the second and third trimesters ($p < 0.001$) and 1.9 times higher Pb levels postnatally in the first year of life ($p = 0.003$) than white children. More information on using tooth-matrix biomarkers can be found in Section 2.3.4.2.

NHANES data in Section 2.4.1 show on a national scale that non-Hispanic black people had higher BLLs than the average BLLs for all groups from 2011 to 2018 but were lower than non-Hispanic whites in some years. Asians were the racial/ethnic group with the highest BLLs from 2011 to 2018. Jones et al. (2009) found, using 1988–1991 and 1999–2004 NHANES data that although the differences of percentage BLLs ≥2.5 µg/dL between racial/ethnic groups dropped between the two sets of years, non-Hispanic black children still had higher percentages with BLLs ≥2.5 µg/dL compared with non-Hispanic whites and Mexican Americans, with large observable differences for BLLs between 2.5 and <10 µg/dL. More recent data have shown that although average BLLs for children of all racial/ethnic groups have continued to drop, there still exists a gap between non-Hispanic white children and minority children. Teye et al. (2021) investigated the BLLs of 6,772 children using NHANES data from 1999 to 2016 and found that although BLLs declined for all racial/ethnic groups over time, BLLs of non-Hispanic black children were statistically significantly ($p < 0.05$) higher than non-Hispanic white children from 1999 to 2014. However, the authors also show that from 1999 to 2016, this gap decreased (a difference of 0.92 µg/dL in 1999–2000 versus 0.15 µg/dL in 2015–2016 data). Egan et al. (2021) analyzed BLLs of 27,122 children from NHANES data spanning 1976–2016. The authors found that among children 1–5 years old and 6–11 years old, non-Hispanic white children had GM BLLs lower than Mexican American or non-Hispanic black children for most years. The authors also show that this gap has decreased over time.

Aelion and Davis (2019) analyzed BLL data of approximately 177,000 South Carolina children less than 6 years of age, reported between January 2011 and December 2016. Other demographic variables including age and sex were recovered at the individual and census-block level, and the child's residence at the block group level was also used. The mean BLL for urban block groups was found to be statistically significantly higher than rural block groups ($p < 0.0001$; 2.21 versus 2.11 µg/dL). Rural children <1 year of age had lower BLLs than urban children of the same age (1.50 versus 2.10 µg/dL). Black children had statistically significantly higher mean BLLs in the urban block group ($p < 0.0001$; 2.23 µg/dL) than black children in the rural block group (2.08 µg/dL). Past research has supported the idea that urban areas will have higher exposures than rural areas due to proximity to point and nonpoint

sources. However, the authors acknowledge further research is needed to identify the differential sources that contribute to Pb exposure in early life.

Moody et al. (2016) examined disparities in children's BLLs related to race and socioeconomic characteristics of place of residence. This study used 216,101 BLL records obtained from a statewide database for children <1 month old to 16 years of age, taken between 2006 and 2010 in Detroit, MI. Using bivariate regression, they determined there was an increase in mean BLLs as neighborhood SES declined for all races. In addition, they found race was a factor regardless of SES as evidenced by higher mean BLLs for black children compared with white children residing in the same neighborhoods. Lynch and Meier (2020) conducted a similar investigation, which focused on the intersectional effect of poverty, home ownership, and racial/ethnic composition on childhood Pb exposure. This study analyzed 48,393 BLLs of children ≤6 years of age obtained from the Wisconsin Department of Health Services from 2014 to 2016. The samples were aggregated by 215 Milwaukee census tracts, with 225 individual childhood blood Pb observations contributing to census tract-level means on average. They found that EBLLs were significantly ($p < 0.0001$) related to predominantly low home ownership, high poverty, and majority non-white census tracts. Further, their model showed children residing in neighborhoods with all three factors had a 1.78 µg/dL (95% CI: 1.44, 2.11, $p < 0.0001$) higher mean BLL than those in high home ownership, low poverty, and majority white census tracts, after adjusting for average census tract housing age and number of children. Nriagu et al. (2011) found the mean BLL among a population of 6-month- to 15-year-old Arab-American and African-American children in Michigan in 2007–2008 was 3.8 ± 2.3 µg/dL (range: 1–18 µg/dL) with 3.3% of the children having BLLs above 10 µg/dL, which was higher than the statewide average of 1.1% of children <6 years old in 2008.

2.1.5.5 SES

The 2006 Pb AQCD (U.S. EPA, 2006a) found negative associations between income or other SES metrics and blood Pb, although these relationships were not always statistically significant. Nriagu et al. (2006) analyzed BLLs from 934 African-American heads of households ranging from 14 to over 55 years of age in Detroit with household income below the 200th percentile of the federal poverty level in 2003. They found education ($p < 0.001$), income ($p < 0.001$), and employment status ($p = 0.04$) were all statistically significant predictors of BLLs, with blood Pb decreasing with some scatter as education and income level increased. On a national level, the difference in BLLs that has historically been seen between different income levels has been decreasing. Jones et al. (2009) evaluated the relationship between BLLs reported for 1- to 5-year-old children in 1988–2004 NHANES data and the family's PIR, defined as the ratio of total family income to the poverty threshold for the year of the interview. The results of their multivariate logistic regression model found children from families with a (PIR) ≤1.3 (low income) were significantly associated with BLLs ≥10 µg/dL. However, for the most recent NHANES cycle included in the study (1999–2004), although the percentage of 1- to 5-year-old children having

BLLs ≥10 μg/dL was higher for PIR ≤1.3 than for PIR >1.3 (1.8% versus 0.8%), this difference was not statistically significant.

Wheeler et al. (2019b) investigated reasons for EBLLs (>5 μg/dL) among children <6 years old across 1,208 census tracts in Maryland from 2005–2015. They found the three statistically strongest community predictors of EBLL in order of importance were percentage of pre-1940 housing, percentage of African Americans in the population, and inverse median household income (meaning larger values in disadvantaged areas) in the past 12 months. In a follow-up study on the same population, Wheeler et al. (2022) examined the relationship between EBLLs and temporally varying neighborhood characteristics. There were clear temporal trends in the blood Pb test data, with the percentage of EBLLs peaking in 2006 at 11% and then gradually declining to a low of 2% in 2015. As in the previous study, which did not account for temporal variation, the percentage of pre-1940 housing and the inverse median household income in the past 12 months were statistically important predictors of EBLL. However, this follow-up study found the percentage of African Americans in the population was a much less important predictor of EBLL risk than the investigators had previously observed. They also note the relationship between these factors and risk of EBLLs remains positive and significant over the entire time period but generally diminished over time, indicating a decline in exposure disparities. Wheeler et al. (2019a) also investigated EBLL risk among children <6 years old in 1,332 census tracts in Minnesota from 2011 to 2015. Using a weighted quantile sum (WQS) regression model, the five variables most significantly correlated to children's BLLs (in order of most to least by estimated WQS index weight) were percentage of houses built prior to 1940 (0.32), percentage not using Social Security income (0.18), percentage of housing that was renter occupied (0.12), percentage unemployed (0.09), and percentage of African Americans in the population (0.08). Six of the 15 variables tested were not found to be significantly predictive, including percentage below the federal poverty level, percentage receiving public assistance income, and percentage receiving public assistance food stamps.

2.2 Kinetics

The 2013 Pb ISA (U.S. EPA, 2013) contains previously available information on the empirical basis for understanding Pb toxicokinetics in humans. The following sections serve as an update to that information. This empirically based information has been incorporated into mechanistic biokinetic models that support predictions about the kinetics of Pb in blood and other selected tissues. The following sections emphasize discussion of inorganic Pb because it comprises the dominant forms of Pb to which humans in the United States are exposed as a result of releases of Pb to the atmosphere and historic surface deposition of atmospheric Pb. A more detailed discussion of the toxicokinetics of organic Pb can be found in the 2006 Pb AQCD (U.S. EPA, 2006a).

2.2.1 Absorption

The major exposure routes of Pb in humans are ingestion and inhalation. Three terms that are commonly used to aid in understanding Pb's uptake into the body are absorption, bioavailability, and bioaccessibility. Absorption refers to the uptake of Pb ingested or inhaled into the blood from the respiratory or gastrointestinal (GI) tract. Bioavailability is the fraction of the amount of Pb ingested or inhaled that enters systemic circulation. If properly measured (e.g., time-integrated blood Pb), under most conditions, Pb bioavailability is equivalent (or nearly equivalent) to Pb absorption. The time-integrated blood Pb (i.e., the integral of blood Pb over time) provides a useful measure of bioavailability because it reflects both recent Pb absorption as well as contributions from Pb sequestered in soft tissue and bone. Bioaccessibility is a measure of the physiological solubility of Pb in the respiratory or GI tract. Pb must be bioaccessible for absorption to occur. Processes that contribute to bioaccessibility include physical transformation of Pb particles and dissolution of Pb compounds into forms that can be absorbed (e.g., Pb^{2+}). Bioaccessibility is typically assessed by measuring the fraction of Pb in a sample that can be extracted into a physiological or physiological-like solution (e.g., gastric juice or solution similar to gastric juice).

2.2.1.1 Inhalation

Systemic absorption of Pb deposited in the respiratory tract is influenced by particle size and solubility, as well as by the pattern of regional deposition within the respiratory tract. Particles <1 μm deposited in the bronchiolar and alveolar region can be absorbed after extracellular dissolution or can be ingested by phagocytic cells and transported from the respiratory tract. Larger particles (>2.5 μm) that are primarily deposited in the ciliated airways (nasopharyngeal and tracheobronchial regions) can be transferred by mucociliary transport into the esophagus and swallowed, thus being absorbed in the GI tract. For a detailed discussion of factors affecting particle deposition and retention in the human respiratory tract, the reader is referred to Chapter 4 of 2019 PM ISA (U.S. EPA, 2019c). Section 4.2.4 of that document specifically addresses biological factors affecting particle deposition, such as activity level and age with an emphasis on children. The sections below provide information on bioaccessibility of inhaled Pb in the lung and GI tract as a function of exposure source and particle size. Empirical estimates of blood Pb – air Pb slopes for various populations, derived from epidemiologic studies, are summarized in Section 2.5.1.

2.2.1.1.1 Experimental Human Exposures

Inhaled Pb-laden particles depositing in the lower respiratory tract seem to be absorbed equally and totally, regardless of chemical form (Morrow et al., 1980; Chamberlain et al., 1978; Rabinowitz et al., 1977). Absorption half-times have been estimated for radon decay progeny in adults who inhaled aerosols

of Pb and bismuth isotopes generated from decay of ^{220}Rn or ^{222}Rn. The absorption half-time for Pb from the respiratory tract to blood was estimated to be approximately 10 hours in subjects who inhaled aerosols having an activity median particle diameter of approximately 160 nm (range 50–500 nm) (Marsh and Birchall, 1999) and approximately 68 minutes for aerosols having diameters of approximately 0.3–3 nm (Butterweck et al., 2002). Given the submicron particle size of the exposure, these rates are thought to represent, primarily, absorption from the bronchiolar and alveolar regions of the respiratory tract.

2.2.1.1.2 Occupational Exposures

In consideration of occupational exposures, the ICRP (2017) classifies the absorption of materials from particles deposited in the respiratory tract as Type F (fast), M (moderate), and S (slow). These rates of absorption affect how much deposited material enters the blood. For Type F Pb-laden particles, nearly all Pb moves rapidly (within an hour) into the blood. For the Type M and S Pb-laden particles, Pb is slowly absorbed into the blood over years and decades, respectively. For the Type M and S particle forms, much of the deposited Pb is cleared from the respiratory tract before it can be absorbed into the blood. Most material cleared from the respiratory tract is swallowed, and subsequent absorption (10–20%) may occur in the GI tract. The ICRP (1995) recommends most elements be classified as Type M because it is the least likely to excessively over- or underestimate dissolution and absorption into the blood.

In consideration of the experimental evidence, the ICRP (2017) recommended classifying most forms of inhaled Pb (i.e., Pb dichloride, dibromide, difluoride, hydroxide, nitrate, and oxide) as having Type F absorption; dissociation of Pb from particles occurs at a rate of 100 day^{-1} (10-minute half-time). Type M classification for Pb was recommended in Table A17 of ICRP (2002b). The ICRP (2017) has no specific Pb forms recommended for Type M. However, a Type S classification is recommended for mineral dusts containing Pb with dissociation of Pb from particles at a rate of 0.0001 day^{-1} (7,000-day half-time). There is a specific recommendation for radon progeny with 10% dissociation at a rate of 100 day^{-1} (10-minute half-time) and 90% at a rate of 1.7 day^{-1} (10-day half-time). For particles that have cleared from the respiratory tract to the GI tract, ICRP (2017) recommends absorption fractions of 0.2 (radon and Type F) and 0.002 (Type S).

Two physiologically based models have been developed for assessment of occupational exposures to Pb (Sweeney, 2021; CalEPA, 2013). The California Environmental Protection Agency (CalEPA) assumes inhaled Pb particles deposited in the alveolar region of the lung are completely absorbed into the blood within a day. Particles deposited in the head and tracheobronchial region were assumed to be cleared to the GI tract, where their absorption fraction was 0.15. On the basis of its model simulations using measured aerosol size distributions of Pb in occupational scenarios, CalEPA found that based on the patterns of deposition and subsequent absorption, it was appropriate to assume an overall absorption fraction of 0.30 for inhaled Pb-laden particles. Developed for the DoD, Sweeney (2021) adopted the absorption fraction of 0.30 for inhaled Pb-laden particles used by CalEPA (2013). In review

of the DoD modeling, NASEM (2020) supported an absorbed fraction (AF) of 0.3 from inhaled Pb as a health-protective estimate.

Occupational studies show AFs of Pb from inhaled Pb-laden particles are varied. Lach et al. (2015) reported Pb particle diameters were generally in the range of 0.1 to 10 µm at an indoor firing range. Applying the approach and parameters of CalEPA (2013), NASEM (2020) estimated an AF of only 0.231 for Pb aerosols at the indoor firing range. A study of battery workers suggests absorption fractions should be far greater. Using personal particle samples (open-face sampler) collected on battery workers, Dartey et al. (2014) found bioaccessibility of Pb from particles in simulated gastric fluid was 90% (median, n = 30) and bioaccessibility in an artificial lung lining fluid (Hatch solution) was 5.2% (median, n = 27). Assuming the particle size distribution (mass median aerodynamic diameter, 14.1 µm; geometric standard deviation, 1.5) and particle deposition fractions in the respiratory tract (head, 0.971; tracheobronchial, 0.026; alveolar, 0.006) for battery workers from Table B-3 of CalEPA (2013), an absorption fraction of 0.8 (i.e., 0.9×(0.971+0.026) + 0.15×0.006) of Pb from inhaled particles is predicted. In this case of battery workers, assuming an absorption fraction of 0.3 could underestimate Pb absorption by 2.5 times. Thus, it is important to consider absorption in the lung and GI tract to the extent possible to assure accurate assessment of the risk to the exposed.

2.2.1.1.3 Urban Exposures

A few studies have quantified the bioaccessibility in the GI tract of Pb in atmospheric particles, based on various in vitro extraction methods. In a study of PM_{10} and $PM_{2.5}$ samples collected in February–March 2006 from downtown Vienna, Austria, Falta et al. (2008) used synthetic gastric juice to investigate the bioaccessibility of metals, including Pb. The Pb concentrations associated with the PM_{10} and $PM_{2.5}$ samples were almost identical, indicating most of the Pb was associated with fine particles. The percentage extracted by synthetic gastric juice was, on average, 86% and 83% Pb for $PM_{2.5}$ and PM_{10} fractions, respectively. In a similar study, Gao et al. (2018a) collected PM_{10} and $PM_{2.5}$ samples in Harbin, China in the summer (July, August 2014) and winter (October, November 2014). These authors evaluated total GI bioaccessibility of Pb from particles in simulated salivary, gastric, and intestinal fluids. For the winter samples, ambient air Pb concentrations between PM_{10} and $PM_{2.5}$ samples were quite similar, again indicating most of the Pb was associated with fine particles. The total percent in fluid extracts (i.e., bioaccessible) was, on average, 22% and 23% Pb for $PM_{2.5}$ and PM_{10} fractions, respectively. However, for the summer samples, ambient air Pb concentrations were 2.8 times greater in PM_{10} than $PM_{2.5}$ samples, and the extracted fractions were quite low (4% and 1% Pb for $PM_{2.5}$ and PM_{10} fractions, respectively).

Several studies have examined the bioaccessibility of airborne Pb-laden particles in the lung. Two common extraction fluids are used to simulate bioaccessibility. Gamble's solution is used to mimic the neutral conditions (pH 7.4) of epithelial/interstitial fluids. Artificial lysosomal fluid (ALF) is used to mimic cellular conditions that exist following an immune response in the lung, associated macrophage

activity, and acidic (pH 4.5) conditions. Wiseman and Zereini (2014) collected PM_{10}, $PM_{2.5}$ and PM_1 samples between June 2009 (summer) and November 2010 (autumn) in Frankfurt, Germany at an area affected by four-lane traffic. For PM_{10}, $PM_{2.5}$, and PM_1, the average bioaccessible fraction of Pb in ALF was 0.96, 0.84, and 0.78, respectively; in Gamble's solution, it was 0.26, 0.04, and 0.05, respectively. da Silva et al. (2015) assessed the pulmonary bioaccessibility in simulated lung fluid (Gamble's solution) of PM_{10} samples collected at four sampling stations during winter (June–July 2010) in Rio de Janeiro, Brazil. In general, all sampling stations were in mixed residential/commercial areas with intense automotive traffic. Similar to the fraction of 0.26 for PM_{10} reported by Wiseman and Zereini (2014), the overall mean lung bioaccessible fraction of PM_{10} in Gamble's solution was 0.22 (range: 0.11–37). Niu et al. (2010) determined the bioaccessibility of Pb in fine (0.1–1.0 µm) and ultrafine (<0.1 µm) urban airborne PM from two sites in 1992–1993 and 1999–2000 within Ottawa, Canada. The bioaccessibility was based on Pb extraction in ammonium acetate (pH = 7 to simulate the neutral lung environment). The nano fraction accounted for 33% of Pb mass, the fine fraction was 42% of Pb mass, and the remaining 25% was associated with particles >1 µm in size. Although the Pb concentration declined by 7% for fine and 13% for nano particles between the initial and later sampling periods, increases in bioaccessibility increased potentially absorbed Pb by 1.2 times (fine) and 1.5 times (nano). For the 1999–2000 sampling phase, the bioaccessibility fraction showed clear increase with decreasing particle size (fraction, size; 0.15, 1 µm; 0.20, 0.2 µm; 0.28, 0.06 µm).

Considering possible resuspension and human inhalation, Dean et al. (2017) measured the bioaccessibility of urban street dusts collected from five northern U.K. cities: Durham, Edinburgh, Liverpool, Newcastle upon Tyne, and Sunderland. Twenty-one samples were collected, dried, disaggregated, and sieved to <125 µm and then <10 µm (particle sizes likely to be inhaled by pedestrians). Bioaccessibility was assessed in a synthetic epithelial lung fluid having a pH of 7.4. Dusts were added to the synthetic fluid, shaken, and maintained at 37°C for 96 hours. The authors found a bioaccessible fraction of 4.2 ± 2.2% (range 1.2–8.8%). These low bioaccessible fractions are consistent with low bioaccessible fractions of 0.26, 0.04, and 0.05 reported for PM_{10}, $PM_{2.5}$, and PM_1, respectively, in Gamble's solution by Wiseman and Zereini (2014).

2.2.1.1.4 Smelting and Mining Exposures

Goix et al. (2016) reported the Pb bioaccessibility in ALF and Gamble's solution of $PM_{0.5}$ samples collected from areas of smelting and mining in Oruro, Bolivia. $PM_{0.5}$ samples represented 79% and 71% of $PM_{2.5}$ mass in the smelting and mining area samples, respectively. The bioaccessibility fractions of $PM_{0.5}$ from smelting samples were 0.70 (ALF) and 0.32 (Gamble's solution). Considerably lower bioaccessibility fractions were reported for mining at only 0.07 (ALF) and 0.02 (Gamble's solution). Gastric bioaccessibility of dust samples was also greater in the smelting than mining areas. Li et al. (2016) assessed changes in Pb bioaccessibility in ALF and Gamble's solution of $PM_{2.5}$ samples collected before (June–July), during (August), and after (September–October) the 2014 Youth Olympic

Games in Nanjing, China. Two important Pb sources in $PM_{2.5}$ from urban sites of Nanjing are coal emissions and smelting activities, the latter of which were shut down during the Olympics (but the former continued for electricity production). Pb bioaccessibility in ALF was lower (61 ± 4.3%, n = 9) during the games than before (66 ± 6.4%, n = 10) or after (78 ± 4.6%, n = 13). The lower bioaccessibility in ALF during the games may reflect the importance of the normally occurring smelting operations. Interestingly, the average Pb bioaccessibility based on Gamble's solution was higher (20%) during games than before (10%) or after (11%).

Xing et al. (2020) examined both ALF and gastric bioaccessibility of dust samples collected from the exterior windowsill (i.e., the trough) of the 1st through 9th floors of buildings in Jiyuan City, Henan Province, northern China, an area affected by Pb smelting and other industries. Trough dusts are generally assumed reflective of outside air and exterior contamination that runs down windows with rain to collect in the trough area. Dusts were size fractioned into <10, 10–45, and 45–125 μm, which are reflective of the size distribution of the dust and not the airborne particle sizes that were transported and deposited on the troughs or higher building surfaces. On the basis of isotopic ratios, the authors concluded higher floors were more affected by smelting and lower floors more by resuspension of soils. At the four sample sites most affected by smelters, the bioaccessible fractions in ALF (0.835) and gastric fluid (0.812) were nearly identical. This suggests bioaccessibility in ALF may be a reasonable substitute for gastric bioaccessibility for smelting dusts.

2.2.1.1.5 Organic Pb Exposures

Alkyl Pb compounds can exist in ambient air as vapors. Inhaled tetraalkyl Pb vapor is nearly completely absorbed following deposition in the respiratory tract. As reported in Section 4.2.1 of the 2006 Pb AQCD (U.S. EPA, 2006b), a single exposure to vapors of radioactive (^{203}Pb) tetraethyl Pb resulted in 37% initially deposited in the respiratory tract, of which ~20% was exhaled in the subsequent 48 hours (Heard et al., 1979). In a similar experiment conducted with ^{203}Pb tetramethyl Pb, 51% of the inhaled ^{203}Pb dose was initially deposited in the respiratory tract, of which ~40% was exhaled in 48 hours (Heard et al., 1979).

Estimation of bioavailability of tetraethyl Pb following combustion is relevant to some aviation exposures (e.g., persons exposed to leaded gasoline used in piston-engine aircraft). Chamberlain et al. (1975) suggested 35% of inhaled combustion products of tetraethyl ^{203}Pb fuel [likely to have been a mixture dominated by inorganic Pb halides but may also have included alkyl Pb species (U.S. EPA, 2006a)] are deposited and then retained in adult lungs with a half-life of 6 hours. Fifty percent of that ^{203}Pb was detectable in the blood within 50 hours of inhalation, and the rest was found deposited in bone or tissue. Chamberlain et al. (1975) estimated a 1 μg/dL increment in blood Pb could result from continuous inhalation over a period of months of a Pb-laden aerosol at a concentration of 1 μg Pb/m^3 generated by vehicle engine combustion of fuel containing tetraethyllead.

2.2.1.2 Ingestion

The extent and rate of GI absorption of ingested inorganic Pb are influenced by physiological states of the exposed individual (e.g., age, fasting, nutritional calcium (Ca^{2+}) and iron (Fe) status, pregnancy) and physicochemical characteristics of the Pb-bearing material ingested (e.g., particle size, mineralogy, solubility). Pb absorption in humans may be a capacity-limited process, in which case the percentage of ingested Pb that is absorbed may decrease with increasing rate of Pb intake. Numerous observations of nonlinear relationships between blood Pb concentration and Pb intake in humans provide support for the likely existence of a saturable absorption mechanism or some other capacity-limited process in the distribution of Pb in humans (Sherlock and Quinn, 1986; Sherlock et al., 1984; Pocock et al., 1983; Sherlock et al., 1982). While evidence for capacity-limited processes at the level of the intestinal epithelium is compelling, the dose at which absorption becomes appreciably limited in humans is not known.

2.2.1.2.1 Physiologic Factors

In adults, estimates of absorption of ingested water-soluble Pb compounds (e.g., Pb chloride, Pb nitrate, Pb acetate) range from 3 to 10% in fed subjects (Maddaloni et al., 1998; Watson et al., 1986; James et al., 1985; Heard and Chamberlain, 1982; Rabinowitz et al., 1980). The absence of food in the GI tract increases absorption of water-soluble Pb in adults. Reported estimates of soluble Pb absorption range from 26 to 70% in fasted adults (Maddaloni et al., 1998; James et al., 1985; Blake et al., 1983; Heard and Chamberlain, 1982; Rabinowitz et al., 1980). Reported fed:fasted ratios for soluble Pb absorption in adults range from 0.04 to 0.2 (James et al., 1985; Blake et al., 1983; Heard and Chamberlain, 1982; Rabinowitz et al., 1980).

Limited evidence demonstrates GI absorption of water-soluble Pb is higher in children than in adults. Estimates derived from dietary balance studies conducted in infants and children (ages 2 weeks to 8 years) indicate ~40–50% of ingested Pb is absorbed (Ziegler et al., 1978; Alexander et al., 1974). Experimental studies provide further evidence for greater absorption of Pb from the gut in young animals compared with adult animals (Aungst et al., 1981; Kostial et al., 1978; Pounds et al., 1978; Forbes and Reina, 1972). The mechanisms for an apparent age difference in GI absorption of Pb have not been completely elucidated and may include both physiological and dietary factors (Mushak, 1991). To further investigate the effects of the presence of food in the GI tract on Pb absorption, children (3–5 years old) who ate breakfast had lower BLLs compared with children who did not eat breakfast (Liu et al., 2011). This difference persisted after controlling for nutritional variables (blood iron [Fe], calcium [Ca^{2+}], copper [Cu], magnesium [Mg], and zinc [Zn]). This observation may be explained by lower GI absorption of Pb ingested with or in close temporal proximity to meals. Direct evidence for meals lowering GI absorption of Pb has also been reported for adults (Maddaloni et al., 1998; James et al., 1985).

Nutritional interactions of Pb with dietary elements (e.g., Fe, Ca^{2+}, Zn) are complex. Pb competes with other elements for transport and binding sites that can result in adjustments of homeostatic regulators to absorb and retain needed elements. Additionally, low levels of macronutrients may alter Pb bioaccessibility in the GI tract. Genetic variation in absorption and metabolism may modify all of the above.

Children who are iron deficient have higher blood Pb concentrations than similarly exposed iron-replete children, suggesting iron deficiency may result in higher Pb absorption or, possibly, other changes in Pb biokinetics that contribute to altered blood Pb concentrations (Schell et al., 2004; Marcus and Schwartz, 1987; Mahaffey and Annest, 1986). Studies conducted in animal models have provided direct evidence for interactions between iron deficiency and increased Pb absorption, perhaps by enhancing binding of Pb to iron-binding proteins in the intestine (Bannon et al., 2003; Morrison and Quarterman, 1987; Barton et al., 1978b). An analysis of data from a sample of 448 women (ages 20 to 55 years) did not find a significant association between iron body stores (indicated from serum ferritin concentration) and blood Pb concentrations, although depleted irons stores (serum ferritin of <12 µg/L) were associated with higher blood concentrations of cadmium (Cd), cobalt (Co), and manganese (Mn) (Meltzer et al., 2010). Healthy infants (97 males, 113 females; median age: 11.4 months; range: 8–23 months) underwent iron-deficiency screenings from July 2014 to June 2016 in Seoul, South Korea (Choi et al., 2017). The infants had no intake of herbal medicine, iron, or zinc supplements in the prior 3 months. Iron deficiency was associated ($p < 0.001$) with an increased median blood Pb concentration of 1.24 µg/dL (interquartile range: 0.84, 1.64) relative to no deficiency, wherein blood Pb concentration was 0.75 µg/dL (interquartile range: 0.51, 1.10). The presence of iron-deficiency anemia was associated ($p < 0.001$) with a further increase in median blood Pb to 1.44 µg/dL (interquartile range: 1.14, 1.80) relative to its absence, wherein blood Pb was 0.79 µg/dL (interquartile range: 0.51, 1.14). In a Norwegian study (Meltzer et al., 2016) of smoking women ($n = 267$; mean age = 38.3 years, range: 21–55 years), no correlation was observed between blood Pb and blood iron concentrations with either original data values ($r = –0.01$) or log-transformed data ($r = 0.00$). The effects of iron nutritional status on blood Pb include changes in blood Pb concentrations in association with genetic variation in genes involved in iron metabolism. For example, genetic variants in the hemochromatosis (HFE) and transferrin genes are associated with higher blood Pb concentrations in children (Hopkins et al., 2008). In contrast, HFE gene variants are associated with lower bone and BLLs in elderly men (Wright et al., 2004).

Several studies have suggested dietary Ca^{2+} may have a protective role against Pb by decreasing absorption of Pb in the GI tract and by decreasing the mobilization of Pb from bone stores to blood. In experimental studies of adults, absorption of a single dose of Pb (100,300 µg Pb chloride) was lower when the Pb was ingested together with Ca^{2+} carbonate (0.2 g Ca^{2+} carbonate) than when the Pb was ingested without additional Ca^{2+} (Blake and Mann, 1983; Heard and Chamberlain, 1982). A similar effect of Ca^{2+} occurs in rats (Barton et al., 1978a). Similarly, an inverse relationship was observed between dietary Ca^{2+} intake and blood Pb concentration in children, suggesting children who are Ca^{2+} deficient may absorb more Pb than Ca^{2+}-replete children (Elias et al., 2007; Schell et al., 2004; Mahaffey et al.,

1986; Ziegler et al., 1978). These observations suggest Ca^{2+} and Pb share and may compete for common binding and transport mechanisms in the small intestine, which are regulated in response to dietary Ca^{2+} and Ca^{2+} body stores (Fullmer and Rosen, 1990; Bronner et al., 1986). However, animal studies have also shown multiple aspects of Pb toxicokinetics are affected by Ca^{2+} nutritional status. For example, feeding rats a Ca^{2+}-deficient diet is associated with increased Pb absorption, decreased whole-body Pb clearance, and increased volume of distribution of Pb (Aungst and Fung, 1985). These studies suggest associations between Ca^{2+} nutrition and blood Pb that have been observed in human populations may not be solely attributable to effects of Ca^{2+} nutrition on Pb absorption. Other potential mechanisms by which Ca^{2+} nutrition may affect blood Pb and Pb biokinetics include effects on bone mineral metabolism and renal function.

Blood Pb concentrations in young children have also been shown to increase in association with lower dietary Zn levels (Schell et al., 2004). Mechanisms for how Zn affects blood Pb concentration, (i.e., whether it involves changes in absorption or changes in distribution and/or elimination of Pb) have not been determined.

2.2.1.2.2 Mineralogical Factors

Dissolution of Pb from the soil/mineralogical matrix in the stomach appears to be the major process that renders soil Pb bioaccessible for absorption in the GI tract. Absorption of Pb in soils and dust has been most extensively studied in the in vivo swine model. Gastric function of swine is thought to be sufficiently similar to that of humans to justify use of swine as a model for assessing factors that may affect GI absorption of Pb from soils in humans (U.S. EPA; Juhasz et al., 2009; U.S. EPA, 2007a; Casteel et al., 2006; Casteel et al., 1997). Other practical advantages of the swine model over rodent models have been described and include absence of coprophagia; ease with which Pb dosing can be administered and controlled; and higher absorption fraction of soluble Pb (e.g., Pb acetate) in swine, which is more similar to humans than rats (Smith et al., 2009). The swine studies measure blood and/or tissue Pb (e.g., kidney, liver, bone) concentrations following oral dosing of swine with either Pb-laden soil or with a highly water-soluble and fully bioaccessible form of Pb (e.g., Pb acetate). A comparison of the internal concentrations of Pb under these two conditions provides a measure of the bioavailability (i.e., absorption) of Pb in soil relative to that of Pb acetate, which is typically referred to as relative bioavailability (RBA). RBA measured in the swine assay is equivalent to the ratio of the AF of ingested dose of soil Pb to that of water-soluble Pb acetate (e.g., RBA = $AF_{Soil\ Pb}/AF_{Pb\ acetate}$).

U.S. EPA (2021b) provides a review of published studies conducted in swine to assess Pb RBA in 41 different soil or "soil-like" test materials. Table 2-10 summarizes RBA data for varied forms and sources of Pb. The mean of RBA estimates from 31 soils was 0.54 (±0.32[SD]), the median was 0.60, and the 5th to 95th percentile range was 0.11 to 0.97. RBA estimates for soils collected from eight firing ranges were approximately 1.0 (Bannon et al., 2009). The relatively high RBA for the firing range soils may reflect the high abundance of relatively unencapsulated Pb carbonate (30–90% abundance) and Pb

oxide (160%) in these soils. Similarly, a soil sample (low Pb concentration) mixed with a National Institute of Standards and Technology paint standard (55% Pb carbonate, 44% Pb oxide) also had a relatively high bioavailability (0.72) (Casteel et al., 2006). A somewhat lower RBA has been reported for a variety of paints having an average RBA of 0.61 ± 0.24 with a large RBA range from 0.35 to 1.1 (Hunt, 2016). Samples of smelter slag, or soils in which the dominant source of Pb was smelter slag, had relatively low RBA (0.14–0.53, three sites), as did a sample from a mine tailings pile (RBA = 0.06–0.40, two sites) and a sample of finely ground galena mixed with soil (RBA = 0.01) (U.S. EPA, 2021b). U.S. EPA (2021b) recommended a central tendency RBA of 0.6 (60%) for Pb in soils that are not associated with firing ranges. This is consistent with a separate meta-analysis of soil Pb data (Dong et al., 2016).

Table 2-10 Relative bioavailability for varied Pb forms and sources.

Relative Bioavailability	Pb Form
Low (<10% RBA)	Anglesite (Pb sulfate), Fe/Pb sulfate, Galena (Pb sulfide), Pb-related sulfosalts
Medium (20–55% RBA)	Fe/Pb oxide, Fe/Pb silicate, Mine tailings, Dust and soil (mining associated), PbO, Pb phosphate, Slag, Zn/Pb silicate
Elevated (55<RBA<90%)	Pb-based paint, Dust and soil (smelter associated), Urban soil (legacy leaded gasoline and atmospheric deposition)
High (>90% RBA)	Pb ammunition (Pb shot), Cerussite (Pb carbonate), MnPb Oxide

RBA = relative bioavailability
Source: (Wang et al., 2022; U.S. EPA, 2021b; Dong et al., 2016; Goix et al., 2016; Bannon et al., 2009; Casteel et al., 2006).

Drexler and Brattin (2007) developed an in vitro bioaccessibility (IVBA) assay for soil Pb that uses extraction fluid composed of glycine, deionized water, and hydrochloric acid at a pH of 1.50 that is combined with sieved test material (<250 μm) for 1 hour. The assay was tested for predicting in vivo RBA of 18 soil-like test materials that were assayed in a juvenile swine assay (Casteel et al., 2006). A regression model relating IVBA and RBA was derived based on these data (Equation 2-1):

$$RBA = (0.878 \times IVBA) - 0.028$$

Equation 2-1

where RBA and IVBA are expressed as fractions (i.e., not as percent). The weighted r^2 for the relationship (weighted for error in the IVBA and RBA estimates) was 0.924 ($p < 0.001$). The IVBA assay reported in Drexler and Brattin (2007) has been identified by EPA as a validated method for predicting RBA of Pb in soils for use in risk assessment (U.S. EPA, 2015, 2007b). A review of soil Pb RBA estimates made using the IVBA assay described above and Equation 2-1 identified 270 estimates of Pb RBA in soils obtained from 11 hazardous waste sites. The mean for the sitewide RBA estimates (n = 11

sites) was 0.57 (SD 0.15), the median was 0.63, and the 5th to 95th percentile range was 0.34 to 0.71. The use of the IVBA assay for predicting in vivo RBA for soils that have been treated with amending agents that alter the solubility or mobility of Pb, such as those that have been treated with high levels of phosphate (e.g., 1% phosphoric acid w/w), is not recommended (U.S. EPA, 2015).

Equation 2-1 cannot be reliably extrapolated to other in vitro assays that have been developed for estimating Pb bioaccessibility without validation against in vivo RBA measurements made on the same test materials. Comparisons of outcomes among different in vitro assays applied to the same soil test materials have found considerable variability in IVBA estimates (Juhasz et al., 2011; Smith et al., 2011; Saikat et al., 2007; Van de Wiele et al., 2007). This variability has been attributed to differences in assay conditions, including pH, liquid:soil ratios, inclusion or absence of food material, and differences in methods used to separate dissolved and particle-bound Pb (e.g., centrifugation versus filtration). Smith et al. (2011) found that algorithms for predicting RBA based on two different IVBA assays did not yield similar predictions of RBA when applied to the same material. Given the dependence of IVBA outcomes on assay conditions, in vitro assays used to predict in vivo RBA should be evaluated against in vivo RBA estimates to quantitatively assess uncertainty in RBA predictions (U.S. EPA, 2007b).

Absorption of Pb in house dust has not been rigorously evaluated quantitatively in humans or in experimental animal models. The RBA for paint Pb mixed with soil was reported to be approximately 0.72 (95% CI: 0.44, 0.98) in juvenile swine, suggesting paint Pb dust reaching the GI tract may be highly bioavailable (Casteel et al., 2006). The same material yielded a bioaccessibility value (based on IVBA assay) of 0.75 (Drexler and Brattin, 2007), which corresponds to a predicted RBA of 0.63, based on Equation 2-1. A review of indoor Pb RBA estimates made using the IVBA assay and Equation 2-1 identified 100 estimates of Pb RBA in dusts obtained from two hazardous waste sites. Mean Pb RBAs for the Herculaneum site were 0.47 (SD 0.07, 10 samples) for indoor dust and 0.69 (SD 0.03, 12 samples) for soil. At the Omaha site, mean Pb RBAs were 0.73 (SD 0.10, 90 samples) for indoor dust and 0.70 (SD 0.10, 45 samples) for soil. Yu et al. (2006) applied an IVBA method to estimate bioaccessibility of Pb in house dust samples collected from 15 urban homes. Homes were selected for inclusion in this study based on reporting to the state department of health of at least one child with a blood Pb concentration >15 µg/dL, and Pb paint dust may have contributed to indoor dust Pb. The mean IVBA was 0.65 (SD 0.08, age: 52.5 to 77.2 months).

The above results, and the IVBA assays used in studies of interior dust, have not been evaluated against in vivo RBA estimates for dust samples. Although expectations are that a validated IVBA methodology for soil would perform well for predicting RBA of interior dust, this validation has not actually been experimentally confirmed. Factors that may affect in vivo predictions of RBA of interior dust Pb could include particle size distribution of interior dust Pb and the composition of the dust matrix, which may be quite different from that of soil.

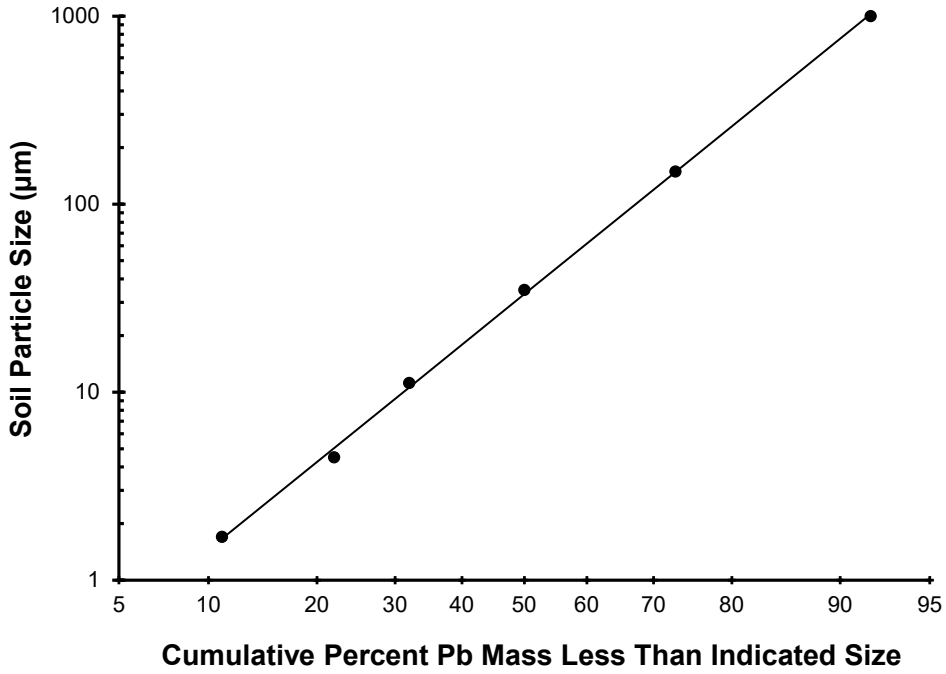
2.2.1.2.3 Particle Size

Several studies have shown Pb concentrations in soil, bioavailability, and particle adherence to the hands (which affects the probability of incidental ingestion) all depend on particle size. In past reviews, studies showed GI absorption of Pb from larger Pb-containing particles (>100 µm) tended to be lower than from smaller particles (Healy et al., 1992; Barltrop and Meek, 1979). Stalcup (2016) reviewed literature (January 2000–December 2011) on the relationship between particle size and dermal adherence and between particle size and Pb enrichment. Particle size distribution of metals in shooting ranges, incinerators, mine tailings and associated background soil samples from three mining sites, as well as urban soils and dusts, demonstrated consistent enrichment in particle size fractions smaller than <150 µm (Juhasz et al., 2011; Kim et al., 2011; Luo et al., 2011; Madrid et al., 2008; Ljung et al., 2007; Pye et al., 2007; Ljung et al., 2006; Momani, 2006; Weiss et al., 2006; Tawinteung et al., 2005). The importance of particle size as it relates to dermal adherence, consequent ingestion, and variance in contaminant levels may also apply to other metals, PAHs, or other contaminants in soil and dust (Beamer et al., 2012; Ruby and Lowney, 2012; Bergstrom et al., 2011; Siciliano et al., 2009; Yamamoto et al., 2006). More recent studies continue to support Pb enrichment in smaller particle sizes and provide bioaccessible data as a function of particle size.

Logiewa et al. (2020) examined metal content of road dust samples collected in three industrial and mining towns in southern Poland. The concentration of Pb generally increased with decreasing particle size and was greatest in particles <2 µm. Figure 2-2 illustrates the cumulative distribution of Pb mass in the dust samples. Of note, the figure shows 73% of Pb mass is associated with particles <150 µm and 80% with particles <250 µm. This suggests the recently developed sieving recommendations (Stalcup, 2016) will not negatively affect the mass of soil sampling required or the validity-established IVBA methodology. Karna et al. (2017) specifically examined the effect of sieving <150 µm versus <250 µm on the determination of IVBA. They examined bioaccessibility of Pb in soils dried and sieved into several size fractions (<250 to >150, <150 to >75, <75 to >38, and <38 µm) using a validated IVBA technique (Stalcup, 2016; U.S. EPA, 2007b). Of the four soil types examined, only one showed an increasing trend (r = 0.012) in IVBA Pb with decreasing soil-size fraction. The authors concluded that sieving to <150 µm rather than <250 µm would not undermine currently validated IVBA protocols in future bioavailability studies.

Goix et al. (2016) reported gastric bioaccessibility of dust samples collected from areas of smelting and mining in Oruro, Bolivia using an in vitro method validated against the in vivo juvenile swine technique. The bioaccessible fraction was greater in dusts associated with smelting (0.63) than mining (0.13), but no clear effect of particle size on bioaccessibility was observed. In a study of 16 soil samples contaminated by Pb from varied sources (e.g., shooting range, incinerator, smelting/mining), Juhasz et al. (2011) also examined the effect of particle size on bioaccessibility. In six of the 16 samples, bioaccessibility increased with progression to finer particle sizes (<50 versus <100 versus <250 µm) with the largest changes being about a 25% increase (e.g., from 38 to 63%) going from <250 to <50 µm

particles. However, the largest bioaccessibility change was in the opposite direction from soil collected at a shooting range, where bioaccessibility increased from about 69 to 99%, going from <50 to <250 µm particles. Overall, among studies, there are no consistent changes in IVBA as a function of particle size.



Source: Points are data derived from Tables 4 and 5 of Logiewa et al. (2020). The solid line is a log normal fitted to the data with a median of 33 µm and a geometric standard deviation of 11.5. Not illustrated in the figure is the 8% of Pb mass that was found associated with particles between 1 and 2 mm.

Figure 2-2 Distribution of Pb in road dust samples collected in three industrial and mining towns located in southern Poland.

2.2.2 Distribution and Metabolism

A simple conceptual representation of Pb distribution is that it contains a fast turnover pool, comprising mainly soft tissue, and a slow pool, comprising mainly skeletal tissues (Rabinowitz et al., 1976). The highest soft tissue concentrations in adults occur in liver and kidney cortex (Gerhardsson et al., 1995; Oldereid et al., 1993; Gerhardsson et al., 1986; Barry, 1975; Gross et al., 1975). Pb in blood (i.e., plasma) exchanges with both of these compartments.

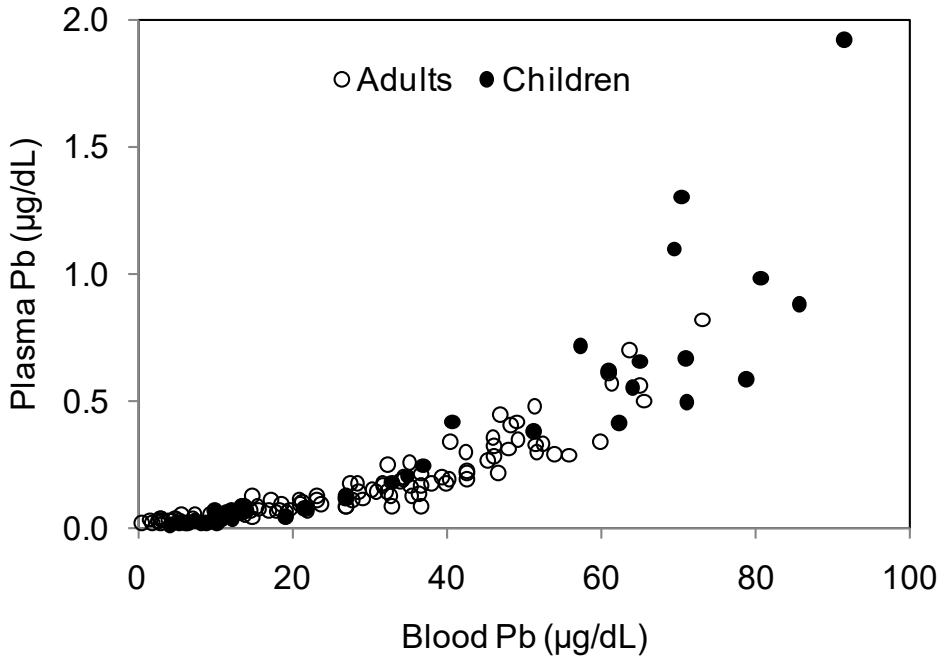
2.2.2.1 Blood

Blood comprises ~1% of total Pb body burden. Pb in blood is found primarily (>99%) in the red blood cells (RBCs) (Smith et al., 2002; Manton et al., 2001; Bergdahl et al., 1999; Bergdahl et al., 1998; Hernández-Avila et al., 1998; Bergdahl et al., 1997a; Schütz et al., 1996). Delta-aminolevulinic acid dehydratase (ALAD) is the primary binding ligand for Pb in erythrocytes (Bergdahl et al., 1998; Xie et al., 1998; Bergdahl et al., 1997a; Sakai et al., 1982). Two other Pb-binding proteins have been identified in the RBC, a 45 kDa protein (K_{max} 700 µg/dL; K_d 5.5 µg/L) and a smaller protein band having a molecular weight of <10 kDa (Bergdahl et al., 1998; Bergdahl et al., 1997a; Bergdahl et al., 1996). Of the three principal Pb-binding proteins identified in RBCs, ALAD has the strongest affinity for Pb (Bergdahl et al., 1998) and appears to dominate the ligand distribution of Pb (35 to 84% of total erythrocyte Pb) at BLLs below 40 µg/dL (Bergdahl et al., 1998; Bergdahl et al., 1996; Sakai et al., 1982). Pb binding to ALAD is saturable; the binding capacity was estimated to be ~850 µg/dL RBCs (or ~40 µg/dL whole blood), and the apparent dissociation constant has been estimated at ~1.5 µg/L (Bergdahl et al., 1998). Hematocrit is somewhat higher in the neonate at birth (51%) than in later infancy (35% at 6 months), which may lead to a decrease in the total binding capacity of blood over the first 6 months of life that results in a redistribution of Pb among other tissues (Simon et al., 2007).

The primary binding ligand for Pb in RBCs is encoded by a single gene that is polymorphic in two alleles (ALAD1 and ALAD2). These can be co-dominantly expressed. Thus, three different genotypes are possible (ALAD 1-1, ALAD 1-2, and ALAD 2-2). In the 2013 Pb ISA (U.S. EPA, 2013), many studies showed individuals with the ALAD-2 gene had higher BLLs. However, there was also evidence showing there was no difference in BLLs between ALAD-1 or ALAD-2 carriers or even lower BLLs for ALAD-1-2/2-2 carriers. Despite further research on the subject, results are still mixed across the literature. Mani et al. (2018) investigated the effect of ALAD polymorphisms on 561 occupationally Pb-exposed and 317 nonoccupationally Pb-exposed subjects in India. The mean BLL levels for the occupationally exposed group were 57.69 ± 29.1 (ALAD 1-2/2-2) and 53.97 ± 28.62 µg/dL (ALAD 1-1), whereas for the nonoccupationally exposed group, BLLs were 3.83 ± 2.65 (ALAD 1-2/2-2) and 3.25 ± 2.26 µg/dL (ALAD 1-1). Sobin et al. (2011) investigated the association of BLLs and ALAD polymorphisms in 306 minority children in Texas. Heterozygous boys with ALAD-2 present had a mean BLL of 3.5 µg/dL, whereas those without had a mean of 2.7 µg/dL. Heterozygous girls with ALAD-2 present had a mean BLL of 2.6 µg/dL, whereas those without had a mean of 2.7 µg/dL. Kayaaltı et al. (2016) studied placental Pb levels in a small sample of 97 pregnant women in Turkey and found those with ALAD 1-1, ALAD 1-2, and ALAD 2-2 polymorphisms had median values of 7.54 µg/kg, 11.78 µg/kg, and 18.53 µg/kg, respectively. In another small study of 81 brain tumor patients in Egypt, mean BLLs for those with the presence of only ALAD-1 and those with an ALAD-2 allele were found to be 25.93 µg/dL ± 12.73 and 34.39 µg/dL ± 17.87, respectively. In contrast, Warrington et al. (2015), using Australian and U.K. cohorts, found no statistically significant association of BLLs with ALAD 1-2. Leroyer et al. (2013) studied ALAD polymorphism and BLLs in 204 French men, finding no statistically significant difference between those with ALAD 1-1, ALAD 1-2, or ALAD 2-2 polymorphisms.

Saturable binding to RBC proteins contributes to an increase in the plasma/blood Pb ratio with increasing PbB and curvature to the blood Pb–plasma Pb relationship (Rentschler et al., 2012; Kang et al., 2009; Jin et al., 2008; Barbosa et al., 2006a; Smith et al., 2002; Manton et al., 2001; Bergdahl et al., 1999; Bergdahl et al., 1998; Bergdahl et al., 1997b; deSilva, 1981). An example of this is shown in Figure 2-3. Saturable binding of Pb to RBC proteins has several important consequences. As blood Pb increases and the higher affinity binding sites for Pb in RBCs become saturated, a larger fraction of the blood Pb is available in plasma to distribute to the brain and other Pb-responsive tissues. This change in distribution of Pb contributes to a curvature in the relationship between Pb intake (at constant absorption fraction) and blood Pb concentration. Plasma Pb also exhibits faster kinetics. Following exposures of five adults that resulted in relatively high blood Pb concentrations (56–110 µg/dL), the initial (fast-phase) elimination half-time for plasma Pb (38 ± 20 [SD] days) was approximately half that of blood (81 ± 25 days) (Rentschler et al., 2012).

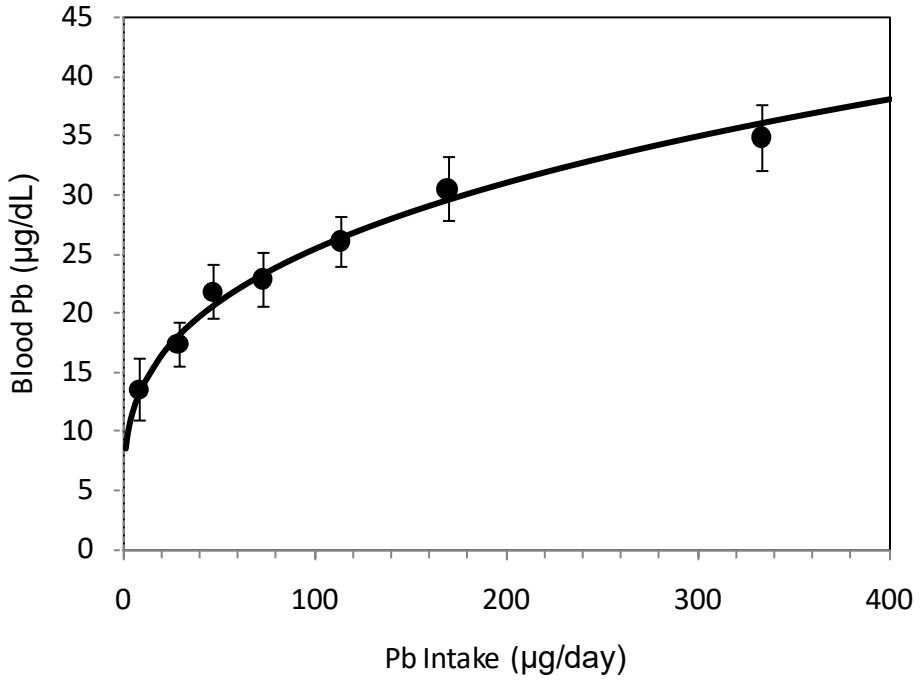
Typically, at blood Pb concentrations <100 µg/dL, only a small fraction (<1%) of blood Pb is found in plasma (Marcus, 1985; Manton and Cook, 1984; deSilva, 1981). However, as previously noted, plasma Pb may be the more biologically labile and toxicologically effective fraction of the circulating Pb. Approximately 40–75% of Pb in the plasma is bound to proteins, of which albumin appears to be the dominant ligand (Al-Modhefer et al., 1991; Ong and Lee, 1980). Pb in serum that is not bound to protein exists largely as complexes with low molecular weight sulfhydryl compounds (e.g., cysteine, homocysteine) and other ligands (Al-Modhefer et al., 1991).



Source: Adapted with permission of Elsevier Publishing and the Finland Institute of Occupational Health, Bergdahl et al. (1999); Bergdahl et al. (1997b).

Figure 2-3 Plot of blood and plasma Pb concentrations measured in adults and children.

As shown in Figure 2-3, the limited binding capacity of Pb-binding proteins in RBCs produces a curvilinear relationship between blood and plasma Pb concentration. The limited binding capacity of RBC binding proteins also confers, or at least contributes, to a curvilinear relationship between Pb intake and blood Pb concentration. A curvilinear relationship between Pb intake and blood Pb concentration has been observed in children (Sherlock and Quinn, 1986; Lacey et al., 1985; Ryu et al., 1983). Data from Sherlock and Quinn (1986) are illustrated in Figure 2-4; although the blood Pb is limited to >13 µg/dL, the relationship becomes approximately linear at relatively low daily Pb intakes (i.e., <50 µg/day) and blood Pb concentrations <22 µg/dL.

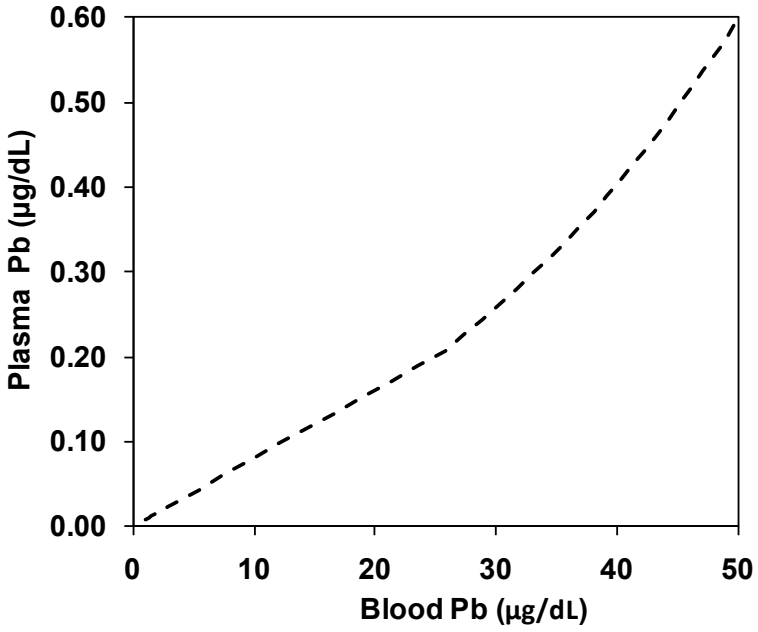


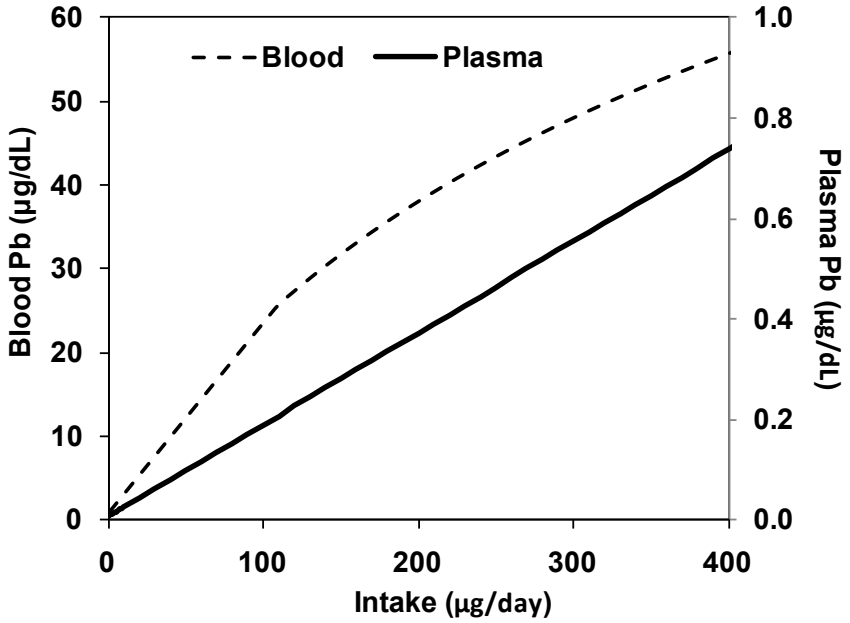
Data represent mean and standard errors for intake; the line is the regression model (blood Pb = 3.9 + 2.43 (Pb intake [µg/week]$^{1/3}$). Source: Adapted with permission of Taylor & Francis Publishing, Sherlock and Quinn (1986).

Figure 2-4 Relationship between Pb intake and blood Pb concentration in infants (n = 105, age 13 weeks, formula fed).

Figure 2-5 shows the predicted relationship between quasi-steady state blood and plasma Pb concentrations in a 4-year-old child using the International Commission on Radiological Protection (ICRP) model (Pounds and Leggett, 1998; Leggett, 1993). The ICRP model is a mechanistic model of Pb biokinetics that consists of a systemic biokinetics model (Leggett, 1993) and absorption factors for inhaled Pb (ICRP, 1995) (see Section 2.6 for a brief description). The abrupt inflection point that occurs

at approximately 25 µg/dL blood Pb is an artifact of the numerical approach to simulate the saturation of binding using discontinuous first-order rate constants for uptake and exit of Pb from the RBC. A continuous function of binding sites and affinity, using empirical estimates of both parameters, yield a similar but continuous curvature in the relationship (Bergdahl et al., 1998; O'Flaherty, 1995). Nevertheless, either approach predicts an approximately linear relationship at blood Pb concentrations below about 25 µg/dL, which, in this model, corresponds to an intake of about 100 µg/day (absorption rate ≈ 30 µg/day) (upper panel). An important consequence of the limited Pb-binding capacity of RBC proteins is the plasma Pb concentration will continue to grow at a linear rate above the saturation point for RBC protein binding. One implication of limited RBC binding capacity is a larger fraction of the Pb in blood will be "free" in plasma and available to distribute to the brain and other tissues as blood Pb increases. This process could potentially contribute to nonlinearity in dose-response relationships in studies in which blood Pb is the used as the internal dose metric.





Note: Model simulations are for a 4-year-old having from birth a constant Pb intake of between 1 and 400 µg/day. Simulation based on ICRP Pb biokinetics model (Leggett, 1993).

Figure 2-5 Simulation of quasi-steady state blood and plasma Pb concentrations in a child (age 4 years) associated with varying Pb ingestion rates.

Studies conducted in swine provide additional evidence in support of RBC binding kinetics influencing distribution of Pb to tissues. In these studies, the relationship between the ingested dose of Pb and tissue Pb concentrations (e.g., liver, kidney, bone) was linear, whereas the relationship between dose and blood Pb was curvilinear with the slope decreasing as the dose increased (Casteel et al., 2006). Saturable binding of Pb to RBC proteins also contributes to a curvilinear relationship between blood Pb and both plasma Pb and urinary Pb, whereas Pb in plasma and urine are linearly related (Bergdahl et al., 1997b).

2.2.2.2 Bone

The dominant compartment for Pb in the body is in bone. In human adults, more than 90% of the total body burden of Pb is found in the bones, whereas bone Pb accounts for just under 60% of the body burden in infants less than a year old and just over 70% of the body burden in older children (Barry, 1975). Bone is composed of two main types, cortical (or compact) and trabecular (or spongy or cancellous). The proportion of cortical to trabecular bone in the human body varies by age but is about 80 to 20% in adults (O'Flaherty, 1998; Leggett, 1993; ICRP, 1973). It should be recognized that cortical and trabecular bone coexist within the same bone. For example, the tibia is generally considered a cortical bone with less than 1% trabecular bone at its midshaft but is 55–75% trabecular bone toward the ends of

the bone [see ¶38 of ICRP (1996)]. In totality, the tibia is 74–83% cortical and 17–26% trabecular. Compact cortical bone is found along the shaft (diaphysis) of long bones, whereas the spongy, more highly perfused trabecular bone is found toward the ends (metaphysis) of the bones where growth is occurring and further out (epiphysis) toward the ends of the bones (ICRP, 2002a).

Pb distribution in bone includes uptake into cells that populate bone (e.g., osteoblasts, osteoclasts, osteocytes) and exchanges with proteins and minerals in the extracellular matrix (Pounds et al., 1991). Pb forms highly stable complexes with phosphate and can replace calcium in the calcium-phosphate salt, hydroxyapatite, which comprises the primary crystalline matrix of bone (Meirer et al., 2011; Brès et al., 1986; Miyake et al., 1986; Verbeeck et al., 1981). Several intracellular kinetic pools of Pb have been described in isolated cultures of osteoblasts and osteoclasts, which appear to reflect physiological compartmentalization within the cell, including membranes, mitochondria, soluble intracellular binding proteins, mineralized Pb (i.e., hydroxyapatite) and inclusion bodies (Long et al., 1990; Pounds and Rosen, 1986; Rosen, 1983). Approximately 70–80% of Pb taken up into isolated primary cultures of osteoblasts or osteocytes is associated with mitochondria and mineralized Pb (Pounds et al., 1991).

The composition of bones changes with age (ICRP, 2002a). In infants, compact cortical bone is highly vascular with a large portion of bone surfaces showing formation (calcification) and reabsorption. By adolescence, the cortical bone is more stable in structure and uniform in appearance. By later adulthood, cortical bone begins to become porous. For trabecular bone, there appears to be a rapid increase during infancy that may continue more gradually through childhood followed by a slow decline thereafter. There may be changes in trabecular bone after bone growth has ceased in response to mechanical stress on the bone. With the changes in bone composition, the density of hydrated bone increases from birth to adulthood, but then decreases beyond about 40 years of age.

Pb accumulates in bone regions having the most active calcification at the time of exposure. In the 2006 Pb AQCD (U.S. EPA, 2006a) and 2013 Pb ISA (U.S. EPA, 2013), Pb accumulation is thought to occur predominantly in cortical bone during childhood and in both cortical and trabecular bone in adulthood. However, considering the changes in bone composition early in life, a rigid dichotomy between accumulation of Pb in trabecular versus cortical bone during childhood is complicated. With continued exposure, Pb concentrations in bone may increase with age throughout the lifetime beginning in childhood, indicative of a relatively slow turnover of Pb in adult bone (Park et al., 2009; Barry and Connolly, 1981; Barry, 1975; Gross et al., 1975; Schroeder and Tipton, 1968). The cortical and trabecular bones have distinct rates of turnover and Pb release, which is about 1.5–1.7 times greater in adults for trabecular than cortical bone in terms of both volume and grams calcium per day [see Table 20 of ICRP (1996)].

A high bone formation rate in early childhood results in the rapid uptake of circulating Pb into mineralizing bone; however, bone Pb is also recycled to other tissue compartments, back to bone, or excreted in accordance with a high bone resorption rate (O'Flaherty, 1995). Thus, most (60–65%) of the Pb acquired early in life is not permanently fixed in the bone (O'Flaherty, 1995; Leggett, 1993; ICRP,

1973). However, some Pb accumulated in bone may persist into later life. McNeill et al. (2000) compared tibia Pb levels and cumulative blood Pb indices in a population of 19- to 29-year-olds who had been highly exposed to Pb in childhood from the Bunker Hill, ID smelter; they concluded Pb from exposure in early childhood had persisted in the bone matrix until adulthood.

Additional discussion of the Pb in bone and its mobilization are provided in other sections of this chapter. Maternal mobilization of Pb from the bone to the fetus is discussed in Section 2.2.2.4. The relationship between Pb in blood and bone is discussed in Section 2.3.5.

2.2.2.3 Soft Tissues

Most of the Pb in soft tissue is in the liver and kidney (Gerhardsson et al., 1995; Oldereid et al., 1993; Gerhardsson et al., 1986; Barry, 1981; Barry, 1975; Gross et al., 1975). Presumably, the Pb in these soft tissues (i.e., kidney, liver, and brain) exists predominantly bound to protein. High-affinity cytosolic Pb-binding proteins have been identified in rat kidney and brain (DuVal and Fowler, 1989; Fowler, 1989). The Pb-binding proteins in rats are cleavage products of α2μ globulin, a member of the protein superfamily known as retinol-binding proteins that are generally observed only in male rats (Fowler and DuVal, 1991). Other high-affinity Pb-binding proteins (K_d ~14 nM) have been isolated in human kidney, two of which have been identified as a 5 kDa peptide, thymosin 4 and a 9 kDa peptide, acyl-CoA binding protein (Smith et al., 1998). Pb also binds to metallothionein but does not appear to be a significant inducer of the protein in comparison with the inducers Cd and Zn (Waalkes and Klaassen, 1985; Eaton et al., 1980).

The liver and kidneys rapidly accumulate systemic Pb ($t_{1/2}$ = 0.21 and 0.41 hours, respectively), which amounts to 10–15% and 15–20% of intravenously injected Pb, respectively (Leggett, 1993). A linear relationship in dose-tissue Pb concentrations for kidney and liver has been demonstrated in swine, dogs, and rats (Smith et al., 2008; Casteel et al., 2006; Casteel et al., 1997; Azar et al., 1973). In contrast to bone, which accumulates Pb with continued exposure in adulthood, concentrations in soft tissues (e.g., liver and kidney) are relatively constant in adults (Treble and Thompson, 1997; Barry, 1975), reflecting a faster turnover of Pb in soft tissue relative to bone.

2.2.2.4 Fetus

Evidence for maternal-to-fetal transfer of Pb in humans is derived from cord blood Pb to maternal blood Pb ratios (i.e., cord blood Pb concentration divided by mother's blood Pb concentration). Group mean ratios range from about 0.7 to 1.0 at the time of delivery for mean maternal BLLs ranging from 1.7 to 8.6 μg/dL (Röllin et al., 2017; Amaral et al., 2010; Kordas et al., 2009; Patel and Prabhu, 2009; Carbone et al., 1998; Goyer, 1990; Graziano et al., 1990). The relationship for individual mother-child pairs is variable but well correlated (Pearson r = 0.79); in a predominantly young, low-income, urban

population (n = 159), factors associated with higher cord BLL compared with maternal BLL included maternal elevated blood pressure and alcohol consumption, whereas factors associated with relatively lower ratios of cord blood Pb to maternal blood Pb included maternal increased hemoglobin levels and sickle cell trait (Harville et al., 2005). Calcium intake and physical activity were not associated with differences between cord blood Pb and maternal blood Pb. Consistent with other studies, the ratio of mean cord blood Pb (1.64 µg/dL) to mean maternal blood Pb (1.93 µg/dL) was 0.85. The similarity of isotopic ratios in maternal blood and in blood and urine of newly born infants provides further evidence for placental transfer of Pb to the fetus (Gulson et al., 1999).

Transplacental transfer of Pb may be facilitated by an increase in the plasma/blood Pb concentration ratio during pregnancy (Montenegro et al., 2008; Lamadrid-Figueroa et al., 2006). Maternal-to-fetal transfer of Pb appears to be related partly to the mobilization of Pb from the maternal skeleton. Evidence for transfer of maternal bone Pb to the fetus has been provided by stable Pb isotope studies in cynomolgus monkeys exposed during pregnancy. Approximately 7–39% of the maternal Pb burden transferred to the fetus was derived from the maternal skeleton, with the remainder derived from contemporaneous exposure (O'Flaherty, 1998; Franklin et al., 1997). The upper value in the range (39%) represented the one monkey with historical Pb exposure from a brief 4-month exposure period in 1990 with ^{204}Pb acetate trihydrate (nominally 1,500 µg Pb/kg/day) but received only small amounts of environmental Pb exposure during pregnancy; for the monkeys that received high doses of Pb during pregnancy (1,500 µg Pb/kg/day; 7 days/week), the range was lower (7–25%) (O'Flaherty, 1998; Franklin et al., 1997).

2.2.2.5 Organic Pb

Information on the distribution of Pb in humans following exposures to organic Pb is extremely limited. However, as reported in the 2006 Pb AQCD (U.S. EPA, 2006b), the available evidence demonstrates near complete absorption following inhalation of tetraalkyl Pb vapor and subsequent transformation to trialkyl Pb metabolites. One hour following brief inhalation exposures to ^{203}Pb tetraethyl or tetramethyl Pb (1 mg/m^3), ~50% of the ^{203}Pb body burden was associated with liver and 5% with kidney; the remaining ^{203}Pb was widely distributed throughout the body (Heard et al., 1979). The kinetics of ^{203}Pb in blood showed an initial declining phase during the first 4 hours (tetramethyl Pb) or 10 hours (tetraethyl Pb) after the exposure, followed by a reappearance of radioactivity back into the blood after ~20 hours. The high level of radioactivity initially in the plasma indicates the presence of tetraalkyl/trialkyl Pb. The subsequent rise in blood radioactivity, however, probably represents water-soluble inorganic Pb and trialkyl and dialkyl Pb compounds that were formed from the metabolic conversion of the volatile parent compounds (Heard et al., 1979).

Alkyl Pb compounds undergo oxidative dealkylation catalyzed by cytochrome P450 in the liver and, possibly, other tissues. Trialkyl Pb metabolites have been found in the liver, kidney, and brain

following exposure to the tetraalkyl compounds in workers (Bolanowska et al., 1967); these metabolites have also been detected in brain tissue of nonoccupational subjects (Nielsen et al., 1978).

2.2.3 Elimination

The rapid phase (30 to 40 days) of Pb excretion in adults accounts for a varied fraction of absorbed Pb (Chamberlain et al., 1978; Rabinowitz et al., 1976; Kehoe, 1961a, b). The fraction of absorbed Pb that is rapidly eliminated generally decreases with increasing exposure duration. This rapid phase of Pb excretion is followed by slower phases of Pb clearance from soft tissues and bone. Due to the long half-life of Pb in bone, it can serve to maintain BLLs long after external exposure has ceased. Absorbed Pb is excreted primarily in urine and feces, with sweat, saliva, hair, nails, and breast milk being minor routes of excretion (Kehoe, 1987; Chamberlain et al., 1978; Rabinowitz et al., 1976; Griffin et al., 1975; Hursh et al., 1969; Hursh and Suomela, 1968).

Approximately 30% of intravenously injected Pb in humans (40–50% in beagles and baboons) is excreted via urine and feces during the first 20 days following administration (Leggett, 1993). The kinetics of urinary excretion following a single dose of Pb is similar to that of blood (Chamberlain et al., 1978), likely due to the fact that Pb in urine derives largely from Pb in plasma. Evidence for this is the observation that urinary Pb excretion is strongly correlated with the rate of glomerular filtration of Pb (Araki et al., 1986) and plasma Pb concentration (Rentschler et al., 2012; Bergdahl et al., 1997b) (i.e., glomerular filtration rate × plasma Pb concentration), and both relationships are linear. While the relationship between urinary Pb excretion and plasma Pb concentration is linear, the plasma Pb relationship to blood Pb concentration is curvilinear (as described in Section 2.2.2.1 and demonstrated in Figure 2-3). This relationship contributes to an increase in the renal clearance of Pb from blood with increasing blood Pb concentrations (Chamberlain, 1983). Similarly, a linear relationship between plasma Pb concentration and urinary excretion rate predicts a linear relationship between Pb intake (at constant absorption fraction) and urinary Pb excretion rate, whereas the relationship with blood Pb concentration would be expected to be curvilinear (Section 2.3.6).

Estimates of urinary filtration of Pb from plasma range from 13 to 22 L/day, with a mean of 18 L/day (Araki et al., 1986; Manton and Cook, 1984; Manton and Malloy, 1983; Chamberlain et al., 1978), which corresponds to half-time for transfer of Pb from plasma to urine of 0.10 to 0.16 days for a 70 kg adult who has a plasma volume of ~3 L. The rate of urinary excretion of Pb was less than the rate of glomerular filtration of ultrafilterable Pb, suggesting urinary Pb is the result of incomplete renal tubular reabsorption of Pb in the glomerular filtrate (Araki et al., 1986); however, net tubular secretion of Pb has been demonstrated in animals (Victery et al., 1979; Vander et al., 1977). On the other hand, estimates of blood-to-urine clearance range from 0.03 to 0.3 L/day with a mean of 0.18 L/day (Diamond, 1992; Araki et al., 1990; Berger et al., 1990; Koster et al., 1989; Manton and Malloy, 1983; Ryu et al., 1983;

Chamberlain et al., 1978; Rabinowitz et al., 1973), consistent with a plasma Pb to blood Pb concentration ratio of ~0.005–0.01 L/day (U.S. EPA, 2003a).

More recently, Diamond et al. (2019) estimated blood-to-urine clearance in adolescents (12 to <20 years; n = 1,269) and adults (20 to 80 years; n = 6,356) using paired blood Pb, urine Pb, serum creatinine, and urine creatinine concentration data in individual subjects from 2009–2016 NHANES data. The median (5th, 95th percentile range) blood-to-urine clearance rates were 0.043 (0.008, 0.132) L/day in adolescents and 0.040 (0.009, 0.118) L/day in adults. Linear regression, including age, gender (NHANES variable was self-identified sex), body weight for adults, body height for adolescents, and serum creatinine clearance (a metric of the glomerular filtration rate, GFR) explained 67–68% of the variability in blood-to-urine clearance. Serum creatinine clearance (i.e., GFR) accounted for 95–98% of the explained variance in blood-to-urine clearance. On the basis of the above differences, urinary excretion of Pb can be expected to reflect the concentration of Pb in plasma and variables that affect delivery of Pb from plasma to urine (e.g., glomerular filtration and other transfer processes in the kidney).

Ho et al. (2022) investigated an index of blood-to-urine clearance in adolescents (12 to 18 years; 1,542 males and 1,383 females) using paired blood Pb, urine Pb, serum creatinine, and urine creatinine concentration data of individual subjects from 1999–2012 NHANES data. The authors normalized urine Pb for dilution by dividing by urine creatinine. The authors observed the ratio of normalized urine Pb to blood Pb was 30% lower in males than females. On the basis of this observation, the authors suggested differences in renal elimination contributed to a greater body burden (as indicated by blood Pb) in males relative to females. However, the normalized urine Pb to blood Pb ratio used by the authors is not a measure of urinary Pb elimination. Urinary Pb elimination requires using a measure of total urine flow as conducted by Diamond et al. (2019), who found the ratio of urinary Pb elimination rate to blood Pb was very similar between males and females.

The value for fecal:urinary excretion ratio (~0.5) was observed during days 214 following intravenous injection of Pb in humans (Chamberlain et al., 1978; Booker et al., 1969; Hursh et al., 1969). This ratio is slightly higher (0.7 to 0.8) with inhalation of submicron Pb-bearing PM due to ciliary clearance and subsequent ingestion. The transfer of Pb from blood plasma to the small intestine by biliary secretion in the liver is rapid (adult $t_{1/2}$ = 10 days) and accounts for 70% of the total plasma clearance (O'Flaherty, 1995).

Organic Pb absorbed after inhalation of tetraethyl and tetramethyl Pb is excreted in exhaled air, urine, and feces (Heard et al., 1979). Fecal:urinary excretion ratios were 1.8 following exposure to tetraethyl Pb and 1.0 following exposure to tetramethyl Pb (Heard et al., 1979). Occupational monitoring studies of workers exposed to tetraethyl Pb showed it is excreted in the urine as diethyl Pb, ethyl Pb, and inorganic Pb (Vural and Duydu, 1995; Zhang et al., 1994; Turlakiewicz and Chmielnicka, 1985).

2.3 Pb Biomarkers

The 2013 Pb ISA (U.S. EPA, 2013) contains background information on Pb in various biomarkers and their relationships. This section explores recent advances in the biological measurements of Pb that act as indicators of exposure or body burden and the relationships between those biomarkers, including bone and blood Pb. Although the following sections look at Pb in different biomarkers individually, body burden can be represented by multiple biomarkers at the same time. Levin-Schwartz et al. (2020) proposed the concept of a multimedia biomarker (MMB) for Pb. In their study, they developed a weighting of multiple biomarkers, including blood Pb, to represent body burden. They found blood Pb and the developed MMB best correlated with IQ scores for 251 Italian adolescents.

2.3.1 Bone-Pb Measurements

Because mineralized tissues within the body act as long-term Pb storage sites with a half-life measured in decades, measurement of Pb within these tissues is important to understand overall body burden. Bone measurements of Pb are conducted through a variety of methods that can be invasive or noninvasive. The 2013 Pb ISA (U.S. EPA, 2013) contains a comprehensive list of invasive methods that measure Pb concentration in excised bone, including flame AAS and anodic stripping voltammetry (ASV). Noninvasive in vivo measurements can be done using XRF. As the 2013 Pb ISA (U.S. EPA, 2013) noted, the rise in the popularity of XRF as a measurement tool for bone Pb has eclipsed other methods because of its ease of use. K-shell XRF (KXRF) has been used widely to conduct in vivo measurements of both trabecular and cortical bone (Specht et al., 2016).

XRF is now incorporated into portable technologies (Nie et al., 2011). Zhang et al. (2021) evaluated a portable XRF device against a traditional KXRF instrument using the mid-tibia bone in 71 people of three Indiana communities. The correlation between the portable XRF and KXRF instruments for all participants was r = 0.48 (95% CI: 0.27, 0.64). However, correlation was much higher r = 0.78 (95% CI: 0.61, 0.87) for those with minimal soft tissue thickness (>5 mm). Portable XRF works most accurately on bones with minimum tissue thickness such as the skull and tibia (Specht et al., 2019a). Given the shallow penetration depth (0.2 mm) of portable XRF and the fact that all bone is covered in a cortical shell, it is likely that any portable XRF measurements are of cortical bone.

New developments are allowing for Pb to be spatially resolved. Pemmer et al. (2013) found, using XRF spatial mapping of 14 human bone samples from individuals with osteoporotic femoral neck fractures, that levels of Pb accumulated in the cement lines of samples was roughly two times more than the surrounding bone matrix. Specht et al. (2019a) used portable XRF along the skulls and tibias of 31 cadavers, finding no real change in Pb levels, matching previous studies of the skull and tibia.

2.3.2 Blood-Pb Measurements

The 2013 Pb ISA (U.S. EPA, 2013) details common methods and their limitations for screening Pb in blood, including AAS, graphite furnace atomic absorption spectrometry, ASV, ICP-AES, and ICP-MS. Blood measurements can be taken through venous blood samples or capillary blood samples. Capillary blood samples are commonly collected due to their ease of collection (i.e., a finger prick) versus venipuncture for venous blood samples. Point-of-care instruments using ASV offer low-cost, "in office" results within minutes (ACCLPP, 2013). Anderson et al. (2007) examined false positive capillary blood samples in 0- to 5-year-old children between 2002 and 2003 in Maine. Defining a false positive as a capillary BLL ≥10 µg/dL with a confirmatory venous BLL <10 µg/dL, they found a 73% false positive rate. False positive capillary samples were most frequent for BLL between 10 and 14 µg/dL (i.e., just in excess of the former CDC blood Pb action level). Using 2011–2017 Minnesota data for 0- to 6-year-old children, Wang et al. (2019) reported 60% false positives, defined as having a capillary BLL ≥5 µg/dL followed by a venous BLL <5 µg/dL. False positive capillary samples were most frequent for BLL between 5 and 6.9 µg/dL (i.e., just over the CDC's 2012 blood Pb reference value, BLRV). False positive capillary BLLs are due to a positive bias in capillary sample measurement and contamination of the fingertips where samples were collected (Wang et al., 2019; Anderson et al., 2007).

There are challenges to measuring BLLs at low values, especially as average blood Pb concentrations become lower as a result of reductions in exposure. At lower BLLs, contamination of equipment also becomes a larger issue. Pb contamination can occur in laboratory reagents and supplies and during sample collection. Laboratories have had to update equipment to measure at lower limits of detection from flame absorption spectroscopy in the 1970s to newer methods of ICP-MS analysis used today. Caldwell et al. (2017) presents data from the Lead and Multi-Element Proficiency program, which evaluated the performance of BLL measurements in approximately 180 laboratories between 2011 and 2015. Although the study found most U.S. laboratories can measure BLLs at ±2 µg/dL (≤20 µg/dL), the authors noted the current acceptability criteria for BLL measurements is ±4 µg/dL or ±10%, whichever is greater. Measurement precision of laboratories was quantified in terms of an RSD, which increases with decreasing BLL. For four BLL samples sent to 50 labs (205 total labs) and consensus mean BLLs ranging from 1.1 to 1.5 µg/dL (average 1.3 µg/dL), the RSD ranged from 37 to 70% (average 49%). For five BLL samples sent to 50 labs (247 total labs) and consensus mean BLLs ranging from 4.15 to 5.15 µg/dL (average 4.7 µg/dL), the RSD ranged from 10 to 19% (average 17%). On the basis of these data and assuming a linear trend, RSD is estimated to be about 28% and 14% for 3.5 and 5 µg/dL, respectively. For a single blood Pb measurement from a child, the 95% CI are 1.6–5.4 µg/dL and 3.7–6.3 µg/dL for the actual BLLs of 3.5 and 5 µg/dL. While a measured value of 5 µg/dL showed a child's BLL was over 3.5 µg/dL, a measured BLL of 3.5 µg/dL should not necessarily be clinically interpreted as showing the child has a BLL of <5 µg/dL. In a subsequent CDC study, Caldwell et al. (2019) reported laboratory precision ranged from 0.26 µg/dL for ICP-MS to 1.50 µg/dL for ASV.

Haque et al. (2021) proposed a method for measurement of Pb in the archived clotted erythrocyte fraction of whole blood. A Pearson correlation coefficient of 0.90 and 0.89 were found for acid digestion and alkaline dilution, respectively.

2.3.3 Urine-Pb Measurements

The 2013 Pb ISA (U.S. EPA, 2013) summarizes issues related to using urine Pb as a biomarker. Briefly, the concentration of Pb in urine is a function of urinary Pb excretion and flow rate. Urine samples can be collected as timed or untimed samples, with untimed samples needing correction to account for variation in urine flow, which can vary by a factor of more than 10. Urine-Pb concentration measurements provide little reliable information about exposure or body burden unless they can be adjusted to account for unmeasured variability in flow rate. Urine-Pb concentration reflects concentration of Pb in blood, representing both recent and past exposures to Pb, and thus cannot distinguish between a long-term low level of exposure or a higher acute exposure. The literature search and screening for this appendix did not capture any significant new advancements in methodology for urine-Pb measurements. A discussion of urinary Pb elimination is provided in Section 2.2.3.

2.3.4 Pb in Other Biomarkers

The 2006 Pb AQCD (U.S. EPA, 2006a) contains detailed discussion on using Pb biomarkers other than blood Pb or bone Pb as indicators of exposure. The 2013 Pb ISA (U.S. EPA, 2013) contains additional summaries of what is known regarding the use of teeth, hair, saliva, and serum δ-aminolevulinic acid (δ-ALA) and ALAD as biomarkers of Pb exposure. These other biomarkers have not been established to the same extent as blood and bone Pb. Below are summaries of recent literature containing information on advances in methodology for measurement of these biomarkers.

2.3.4.1 Teeth

As discussed in the 2013 Pb ISA (U.S. EPA, 2013), researchers have advocated use of sections of the enamel and dentine to obtain more information on Pb exposure rather than using the whole tooth. Two popular analytical techniques, among others, are laser ablation inductively coupled plasma mass spectrometry (LA-ICP-MS) and microbeam synchrotron radiation X-ray fluorescence (μ-SRXRF). Both of these techniques have been proposed for measurement of sections of teeth rather than the whole tooth to understand timing of exposure as the tooth develops. Teeth are composed of several tissues formed pre- and postnatal. Therefore, if a child's Pb exposure during the years of tooth formation varied widely, different amounts of Pb would be deposited at different rates (Rabinowitz et al., 1993). The neonatal line formed in deciduous teeth during birth can be used to distinguish between prenatal and postnatal dentine

and enamel (Hodgson et al., 2015). Shepherd et al. (2012) and Shepherd et al. (2016) used LA-ICP-MS across two small samples of deciduous teeth to reconstruct histories of exposure.

Arora et al. (2014) proposed measuring Pb in prenatal, postnatal, and secondary dentine of 34 incisors, 25 canines, and 26 molars naturally shed from children using LA-ICP-MS. They found strong association between birth dentine Pb and maternal cord blood Pb with a weaker association as the child aged. Johnston et al. (2019) also used this technique to assess the correlation of prenatal tooth Pb and postnatal tooth Pb with surrounding soil Pb levels in 43 child subjects in Los Angeles, CA. After adjusting for maternal education and batch, positive associations were observed between teeth Pb concentration per 100 mg/L increase in soil Pb concentration for both prenatal teeth (statistically significant) and postnatal teeth ($p = 0.056$). Wang et al. (2017b) applied μ-SRXRF to one incisor and two molars. The authors were able to successfully resolve Pb concentrations at the micrometer scale.

2.3.4.2 Hair

The 2006 Pb AQCD (U.S. EPA, 2006a) discusses the applications, methodological limitations (e.g., external contamination), and lack of empirical basis for using hair Pb as a biomarker of Pb exposure. The 2013 Pb ISA (U.S. EPA, 2013) summarizes this information. Although several studies have used hair as a biomarker for Pb exposure since 2011, there have been no major methodological advancements, and there are still major limitations present (Skröder et al., 2017). Hair Pb measurements may be contaminated at the surface by environmental Pb or artificial hair treatments. They are also a poor predictor of blood Pb (U.S. EPA, 2013). Pb concentrations have been found to vary along the hair shaft (Jursa et al., 2018).

2.3.4.3 Saliva

Sampling salivary Pb is an attractive alternative to blood Pb sampling because of its ability to be noninvasive. The 2013 Pb ISA (U.S. EPA, 2013) summarizes earlier literature on salivary Pb measurements. It indicates older reports of salivary Pb showed strong correlation between blood Pb and salivary Pb but reports between 2006 and 2011 showed weak or inconsistent associations. Both Barbosa et al. (2006b) and Nriagu et al. (2006) found significant but weak associations between blood Pb and salivary Pb in adults from two different populations. These differences in outcomes may be a result of exposure history, dental health, and/or the methods for determining Pb in saliva.

Staff et al. (2014), when collecting saliva and whole blood from 105 U.K. workers, noted that refrigerated blank saliva run through the saliva collection device resulted in significant Pb contamination from the device itself that was also highly variable. Additionally, their review of the literature found the correlation between salivary Pb and blood Pb was much stronger at higher Pb levels than low exposure levels, with their own study having a Pearson's r of 0.457 between log(salivary Pb) and log(blood Pb).

When testing 407 oral fluid samples of children aged 6 months to 5 years, Gardner et al. (2016) found a Pearson's r of 0.687 between blood Pb and salivary Pb samples. Given currently available data and lack of uniform testing methods and conditions, it is unclear whether salivary Pb can be a more reliable testing method than blood Pb measurements.

2.3.4.4 Serum δ-ALA and ALAD

The 2013 Pb ISA (U.S. EPA, 2013) concluded blood ALAD activity and serum δ-ALA could potentially be used as biomarkers for Pb exposure. Inhibition of erythrocyte ALAD by Pb results in a rise of the ALAD substrate δ-ALA in plasma. Huang et al. (2020) investigated the threshold of ALAD activity reduced by Pb exposure by using BLL and polymorphism data from 121 Pb workers and 117 nonexposed workers in Taiwan. Using a generalized additive model and multiple regressions, the authors found BLLs above 10 µg/dL resulted in significantly inhibited ALAD enzyme activity. On the basis of the different ranges of BLLs studied, the authors recommend a range of 5–10 µg/dL as an inflection point for declining ALAD activity among adults. This is similar to La-Llave-León et al. (2017), who found, among 633 pregnant women in Mexico, that ALAD activity was reduced for BLLs between 2.2 and 10 µg/dL.

2.3.5 Relationship between Pb in Blood and Pb in Bone

The kinetics of elimination of Pb from the body reflects the existence of multiple pools of Pb in the body. The dominant washout phase of Pb from the blood, exhibited shortly after a change in exposure occurs, has a half-life of ~20–30 days (Leggett, 1993; Rabinowitz et al., 1976) in adults. Studies of a limited number of adults (four individuals with hip or knee replacement, a married couple, and 10 female Australian immigrants) in which the Pb exposure was from historical environmental sources (i.e., minimal current Pb exposure relative to past Pb exposure) have found bone Pb stores can contribute as much as 40–70% to blood Pb (Smith et al., 1996; Gulson et al., 1995; Manton, 1985). Bone Pb burdens in adults are slowly lost by diffusion (heteroionic exchange) as well as by bone resorption (O'Flaherty, 1995). Half-times for the release of Pb in bone are dependent on age and intensity of exposure. Bone compartments are much more labile in infants and children than in adults as reflected by half-times for movement of Pb from bone into the plasma (e.g., cortical $t_{1/2}$ = 0.23 years at birth, 1.2 years at 5 years of age, 3.7 years at 15 years of age, and 23 years in adults; trabecular $t_{1/2}$ = 0.23 years at birth, 1.0 years at 5 years of age, 2.0 years at 15 years of age, and 3.9 years in adults) (Leggett, 1993). Slow transfer rates for the movement of Pb from nonexchangeable bone pools to plasma are the dominant transfer process determining long-term accumulation and elimination of bone Pb burden.

Pb transferred from bone and other body compartments to plasma, as well as newly absorbed Pb from the GI and respiratory tracts, is, in part, transferred to bone surfaces. The exchange of Pb from plasma to the bone surface is a rapid process. On the basis of Leggett (1993), the half-time for movement

of Pb from plasma to trabecular bone surface is 11 minutes in an adult and 17 minutes in a 1-year-old. The half-time for movement of Pb from plasma to cortical bone surface is 14 minutes in an adult and 4 minutes in a 1-year-old. The major deposition fractions of Pb from plasma in the Leggett (1993) model are to extravascular fluids (70–74%) and RBCs (20–24%). Slightly greater than the transfer from plasma to soft tissues (8–9%), which is minimally affected by age, the transfer from plasma to bone is 8% in adults and 14% for a 1-year-old (Leggett, 1993). Of the transfer from plasma to bone, trabecular bone is expected to receive 56% of the Pb depositing in bone of adults and only 20% of the Pb depositing in bone of 1-year-olds. Conversely, cortical bone receives 44% and 80% of Pb deposited in bone from plasma in adults and 1-year-olds, respectively. Thus, the rates of transfer from plasma to bone and compartmentalization between cortical and trabecular bone both vary with age.

When blood Pb concentrations are monitored in individuals over periods of years following a cessation or decrease in exposure, the decrease in blood Pb concentration exhibits complex kinetics that can be disaggregated into components having faster and slower rates. The slower rates of clearance of Pb from the blood over months and years following the cessation or reduction in exposures is thought to primarily reflect elimination of Pb stores in bone. Nilsson et al. (1991) reported a tri-exponential decay in the blood Pb concentrations of 14 individuals having a median occupational exposure period of 26 years. Thirteen individuals had been temporarily removed from work because of excessive exposures (blood levels ≥70 µg/dL or high urinary δ-aminolevulinic acid levels). Representing 22% of blood Pb, the fast compartment had a clearance half-time of 34 days. The intermediate compartment, 27% of blood Pb, had a clearance half-time of 1.12 year. The slow compartment, 50% of blood Pb, had a clearance half-time of 13 years. The authors attributed the fast, intermediate, and slow compartment clearance to elimination of Pb from blood and some soft tissues, from trabecular bone, and cortical bone, respectively. Rentschler et al. (2012) also observed a slow terminal phase of Pb elimination from blood in five adults who had Pb poisoning due to either occupational or nonoccupational exposures that ranged from approximately 1 month to 12 years and resulted in blood Pb concentrations of 70–110 µg/dL. In this study, the blood Pb monitoring period extended from 1 to 74 days following cessation of exposure to approximately 800 days following the diagnosis of poisoning; however, it was not of sufficient duration to estimate the terminal half-time. When the terminal half-time estimated by Nilsson et al. (1991) was used (13 years) to fit data for these Pb poisoning cases to a two-component exponential decay model, the initial faster phase represented approximately 80% of the blood Pb and the half-time was estimated to range from 60 to 120 days. The relatively longer fast phase half-time reported by Rentschler et al. (2012) compared with Nilsson et al. (1991) may reflect the relatively high blood Pb concentrations in these poisoning cases that resulted in temporary anemia and subsequent reestablishment of normal erythrocyte levels. In addition, the use of a two-compartment model, with an assumed slow half-time of 13 years, as well as uncertainty about the actual time of cessation of exposure may have prevented discerning a third, faster elimination compartment in these data.

The longer half-life of Pb in bone compared with blood Pb, allows a more cumulative measure of long-term Pb exposure. Pb in adult bone can serve to maintain BLLs long after external exposure has

ceased (Fleming et al., 1997; Inskip et al., 1996; Smith et al., 1996; Kehoe, 1987; O'Flaherty et al., 1982), even for exposures that occurred during childhood (McNeill et al., 2000). The more widespread use of in vivo XRF Pb measurements in bone and indirect measurements of bone processes with stable Pb isotopes have enhanced the use of bone Pb as a biomarker of Pb body burden.

Several studies have found a stronger relationship between patella Pb and blood Pb than tibia Pb and blood Pb (Park et al., 2009; Hu et al., 1998; Hernandez-Avila et al., 1996; Hu et al., 1996). Hu et al. (1998) suggest that trabecular bone is the predominant bone type providing Pb back into circulation under steady-state and pathologic conditions. The stronger relationship between blood Pb and trabecular Pb compared with cortical bone is probably associated with the larger surface area of trabecular bone allowing for more Pb to bind via ion exchange mechanisms and more rapid turnover making it more sensitive to changing patterns of exposure. Relationships between Pb in blood and bone in children and adults are discussed in greater detail below (Sections 2.3.5.1, and 2.3.5.2).

2.3.5.1 Children

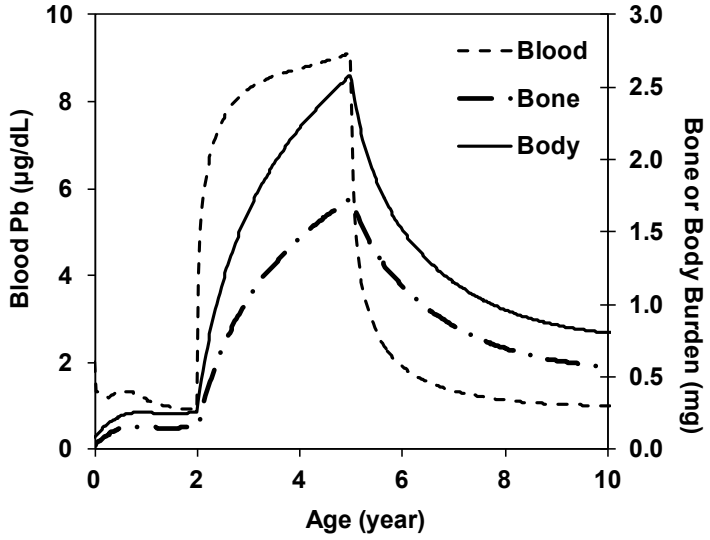
As discussed in Section 2.2.2.2, bone growth in children contributes to accumulation of Pb in bone, which comprises most of the Pb body burden. As a result, bone Pb more closely reflects Pb body burden than blood Pb. However, changes in blood Pb concentration in children (i.e., associated with changing exposures) are thought to more closely parallel changes in total body burden than such changes in adults. Figure 2-6 shows a biokinetics model simulation of the temporal profile of Pb in blood and bone in a child who experiences a period of constant Pb intake (from ages 2 to 5) via ingestion (µg Pb/day) followed by an abrupt decline in intake. The figure illustrates several important general concepts about the relationship between Pb in blood and bone. While blood Pb approaches a quasi-steady state after a period of a few months with a constant rate of Pb intake (as demonstrated by the vertical dashed line), Pb continues to accumulate in bone with continued Pb intake after the quasi-steady state is achieved in blood. The model also predicts the rate of release of Pb from bone after a reduction in exposure is faster than in adults. This difference has been attributed to accelerated growth-related bone mineral turnover in children, which is the primary mechanism for release of Pb that has been incorporated into the bone mineral matrix.

Several studies have examined blood Pb in children following changes in exposure. Children (n = 3) removed from a relatively brief exposure to elevated environmental Pb exhibited faster slow-phase kinetics than children (n = 3) removed from exposures that lasted several years, with half-times of 10 and 20–38 months, respectively (Manton et al., 2000). The longer half-times measured under the latter conditions reflect the contribution of bone Pb stores to blood Pb following a change in exposure. However, the children exposed for the longer period (studied from ages 30 to 60 months) were older than those exposed for a brief period (studied from ages 8 to 30 months), which may account for a portion of the longer retention since bone remodeling decreases rapidly with age. Another study examined the time

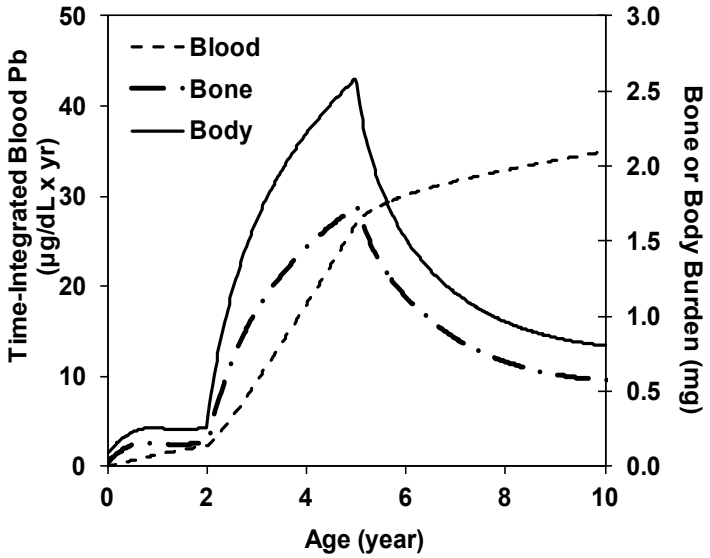
for blood Pb to decrease below 10 µg/dL in a large group of children (n = 579) having peak blood Pb at an average age of 33 months (Roberts et al., 2001). Children were grouped into four categories by their peak blood Pb (10 to <15, 15 to <20, 20 to <25, and 25 to <30 µg/dL). The average time for the children's blood Pb to decrease below 10 µg/dL was 9.2, 14.3, 20.9, and 24 months, respectively. On the basis of the mid-points of each blood Pb range and the time to reach 10 µg/dL, the apparent half-time[1] for clearance from blood can be estimated at 29 months in the lowest blood Pb group and 16–18 months in the other three groups. The increased half-life for the lowest blood Pb group suggests the lowest blood Pb group may have experienced a longer duration of elevated Pb exposure than the three higher blood Pb groups.

A couple of studies investigated the relationship between blood and bone Pb in Pb-poisoned and non-Pb-poisoned children recruited through Xinhua Hospital, Shanghai Jiaotong University, China (Specht et al., 2019b; Specht et al., 2016). This discussion focuses on Specht et al. (2019b) and not their preliminary results from fewer children (Specht et al., 2016). K-shell XRF tibia bone Pb was well correlated with blood Pb ($r^2 = 0.59$; n = 157). The correlation between K-shell XRF and blood Pb improved ($r^2 = 0.95$, n = 24) by the time of a third chelation treatment. The authors attributed stronger correlation between bone and blood Pb following the third chelation to a reduced effect in continued environmental Pb intake. Figure 2-7 illustrates the half-times for blood Pb in children reported in the study. Thirty-five percent of the variability in half-times is attributable to the children's ages; sex was not influential. Children (9 females, 7 males) under the age of 3 had a fast half-time of only 6.4 days (SD: 3.5 days) that was significantly ($p < 0.001$) less than observed in older children (8 females, 26 males; half-time: 19.2 days; SD: 13.9).[2] This study shows an equilibrium between Pb in bone and blood compartments in children such that both are likely associated with total Pb body burden when continued environmental Pb intake has been minimized or eliminated.

[1] Half-time (months) = [Ln(1/2)×(Time to 10 µg/dL)] / Ln[(10 µg/dL)/(midpoint blood Pb)]
[2] These data were computed from supplemental data and differ slightly from values reported by the authors in their paper. This difference appears to be due to the data of a 3.1-year-old boy being grouped by the authors in data for children <3 years of age.



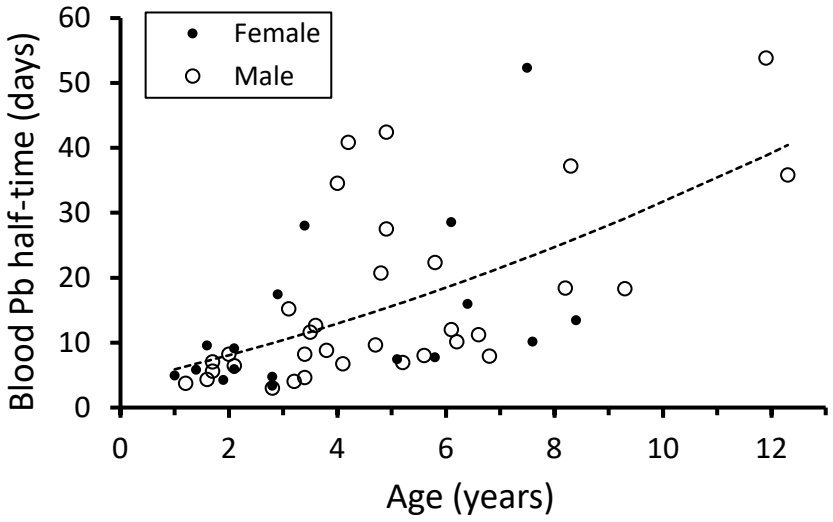
1



2

Note: Blood Pb concentration is thought to parallel body burden more closely in children than in adults, due to more rapid turnover of bone and bone-Pb stores in children (upper panel). Baseline Pb intake is 3.2 µg/day from birth until age 2, followed by a period of increased intake (38.2 µg/day) from age 2 until age 5, with a return to baseline intake of 3.2 µg/day at age 5. The time-integrated blood Pb concentration increases over time (lower panel). Simulation based on ICRP Pb biokinetics model (Leggett, 1993).

Figure 2-6 Simulation of relationship between blood Pb concentration and body burden in children, with an elevated constant Pb intake from age 2 to 5 years.



Note: A quadradic fitted to the data is included to illustrate the trend in blood Pb half-times as a function of age. Linear and quadradic functions both fit the data well (r^2 = 0.35) and differ mainly in their intercepts of 1.7 and 3.9 days, respectively.
Source: Data for 50 children are from supplemental table of Specht et al. (2019b).

Figure 2-7 Half-times of Pb in blood as reported by Specht et al. (2019b).

2.3.5.2 Adults

In adults, where a relatively large fraction of the body burden residing in bone has a slower turnover compared with blood, a constant Pb uptake (or constant intake and fractional absorption) gives rise to a quasi-steady state blood Pb concentration, whereas the body burden continues to increase over a much longer period, largely because of continued accumulation of Pb in bone. This pattern is illustrated by hypothetical simulations in Figure 2-8, wherein a low exposure to a constant baseline GI intake of 20 µg/day occurs through the first 30 years of life. Subsequently, there is a 20-year period of increased intake, wherein simulations show a relatively rapid increase in blood Pb concentration from a baseline of approximately 2 µg/dL to a new quasi-steady state, achieved in ~75-100 days (i.e., approximately 3–4 times the blood elimination half-life). In contrast to the rapid increase in blood Pb, the bone and body burden exhibit a steady increase across the full exposure 20-year period of enhanced exposure intake.

Following cessation of the 20-year enhanced exposure period at age 50, blood Pb concentration declines rapidly compared with the slower decline in bone and body burden. There is a rapid drop in blood Pb within a year from 9 to 3 µg/dL (67% decrease) for the lower intake and from 90 to 40 µg/dL (55% decrease) for the higher intake exposure. Careful examination of the simulations shown in Figure 2-8 reveals the accumulation and elimination phases of blood Pb kinetics are not symmetrical; elimination is slower than accumulation as a result of the gradual release of bone Pb stores to blood. This response, known as the prolonged terminal elimination phase of Pb from blood, has been observed in retired Pb workers and in workers who continued to work after improved industrial hygiene standards reduced their

exposures. These simulations in Figure 2-8 illustrate how a single blood Pb concentration measurement or a series of measurements taken over a short time span could be a relatively poor index of Pb body burden.

The drop in blood Pb concentrations following cessation of elevated exposure in Figure 2-8 is well described (r = 0.996) by a tri-exponential decay function having the half-times of 30 days, 5 months, and 8 years for the fast, intermediate, and slow compartments, respectively. For the low level of Pb intake illustrated in the top panel of Figure 2-8, the fast, intermediate, and slow clearance compartments represent 66%, 19%, and 15% of blood Pb, respectively. For the high level of Pb intake illustrated in the bottom panel of Figure 2-8, the fast, intermediate, and slow clearance compartments represent 35%, 19%, and 46% of blood Pb, respectively. The higher exposure resulted in more accumulation of Pb in bone relative to the lower exposure scenario. This bone accumulation is reflected in the blood Pb clearance kinetics by a larger slow compartment and smaller fast compartment for the high exposure.

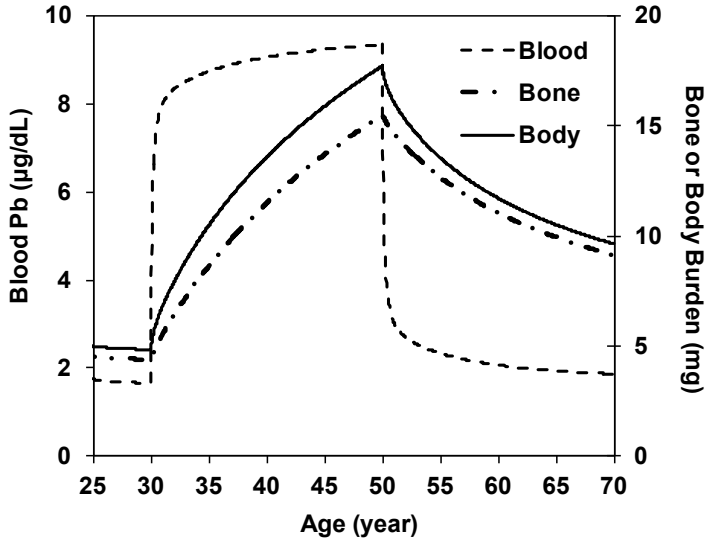
One important potential implication of the profoundly different kinetics of Pb in blood and bone is that, for a constant Pb exposure, Pb in bone will increase with increasing duration of exposure and, therefore, with age. In contrast, blood Pb concentration will achieve a quasi-steady state. As a result, the relationship between blood Pb and bone Pb will diverge with increasing exposure duration and age. This divergence can impart different degrees of age-confounding when either blood Pb or bone Pb is used as an internal dose metric in dose-response models. In a review of epidemiologic studies that evaluated the associations between blood Pb, bone Pb, and cognitive function, the association was stronger for bone Pb than blood Pb (particularly for longitudinal studies) for older individuals with environmental Pb exposures and low BLLs (Shih et al., 2007). In contrast, occupational workers with high current Pb exposures had the strongest associations for BLLs with cognitive function, thus providing evidence for this divergence (Shih et al., 2007).

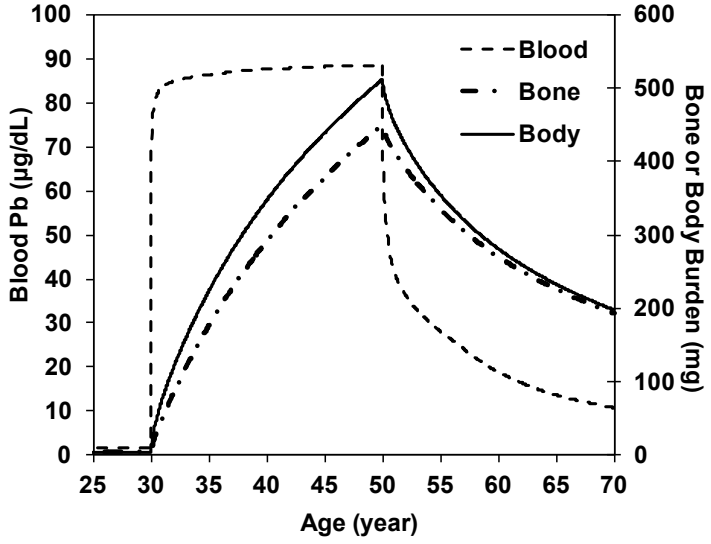
The expectation for an increase in bone Pb and body burden with age applies to scenarios of constant exposure but not necessarily to real-world populations in which individual and population exposures have changed over time. Longitudinal studies of blood and bone Pb trends have not always found strong dependence on age (Nie et al., 2009; Kim et al., 1997). Kim et al. (1997) found bone Pb levels increased with increasing age in elderly adults (age 52–83 years) only when the data were analyzed cross-sectionally. When analyzed longitudinally, the trend for individual patella Pb was a 23% decrease over a 3-year period (approximate $t_{1/2}$ of 8 years), whereas tibia Pb levels did not change over the same period. Therefore, although older individuals tended to have higher bone Pb levels, the 3-year temporal trend for individuals was a loss of Pb from the more labile Pb stores in trabecular bone. Nie et al. (2011) observed longitudinal observations of blood and bone Pb in elderly adults did not show a significant age effect on the association between blood Pb and bone Pb (patella and tibia), when the sample population (n = 776) was stratified into age tertiles (mean age 62, 69 or 77 years).

Although differences in kinetics of blood and bone Pb degrade the predictive value of blood Pb as a metric of Pb body burden, within a population that has similar exposure histories and age demographics, blood and bone Pb may show relatively strong associations. A recent analysis of a subset of data from the

Veterans Affairs (VA) Normative Aging Study (an all-male cohort) showed cross-sectional measurements of blood Pb concentration accounted for approximately 9% (tibia) to 13% (patella) of the variability in bone Pb levels. Inclusion of age in the regression model accounted for an additional 7–10% of the variability in bone Pb (Park et al., 2009).

In addition to changes in exposure (discussed above), there are physiological processes in adults during different life circumstances that can increase the contribution of bone Pb to blood Pb. These life circumstances include times of physiological stress associated with enhanced bone remodeling, such as during pregnancy and lactation (Hertz-Picciotto et al., 2000; Silbergeld, 1991; Manton, 1985), menopause or in the elderly (Silbergeld et al., 1988), extended bed rest (Markowitz and Weinberger, 1990), hyperparathyroidism (Kessler et al., 1999) and severe weight loss (Riedt et al., 2009).





Note: A constant baseline intake of 20 µg/day from age 0–30 results in a quasi-steady state blood Pb concentration and body burden. An increase in Pb intake to a relatively low intake of 120 µg/day (top panel) or a high intake of 4,020 µg/day (bottom panel) from age 30 to 50 gives rise to a relatively rapid increase in blood Pb to a new quasi-steady state and a slower increase in body burden. At age 50, intake returns to the baseline of 20 µg/day. There is a rapid drop in blood Pb within a year from 9 to 3 µg/dL (67% decrease) for the lower intake and from 90 to 40 µg/dL (55% decrease) for the high intake. Following the long period of high Pb intake, there is a rapid decline in blood Pb over the first year followed by a more gradual decline in blood Pb. Simulation based on ICRP Pb biokinetics model (Leggett, 1993).

Figure 2-8 Simulation of relationship between blood Pb concentration, bone Pb, and body burden in adults.

During pregnancy, bone Pb can serve as a Pb source as maternal bone is resorbed for the production of the fetal skeleton (Gulson et al., 2003; Gulson et al., 1999; Franklin et al., 1997; Gulson et al., 1997). Increased blood Pb during pregnancy has been demonstrated in numerous studies, and these changes have been characterized as a "U-shaped" pattern of lower blood Pb concentrations during the second trimester compared with the first and third trimesters (Lamadrid-Figueroa et al., 2006; Gulson et al., 2004; Hertz-Picciotto et al., 2000; Gulson et al., 1997; Lagerkvist et al., 1996; Schuhmacher et al., 1996; Rothenberg et al., 1994). The U-shaped relationship reflects the relatively higher impact of hemodilution in the second trimester versus the rate of bone Pb resorption accompanying Ca^{2+} releases for establishing the fetal skeleton. In the third trimester, fetal skeletal growth on calcium demand is greater, and Pb released from maternal skeleton offsets hemodilution. Gulson et al. (1998b) reported that during pregnancy, blood Pb concentrations in the first immigrant Australian cohort (n = 15) increased by an average of about 20% compared with nonpregnant migrant controls (n = 7). Skeletal contribution to blood Pb, based on the isotopic composition of the immigrant subjects, increased in an approximately linear manner during pregnancy. The mean increases for each woman during pregnancy varied from 26 to 99%. Interestingly, the percent change in blood Pb concentration was significantly greater during the post pregnancy period than during the second and third trimesters. This is consistent with Hansen et al. (2011), who demonstrated the greatest BLLs at 6 weeks postpartum compared with the second trimester in 211 Norwegian women. Increased calcium demands of lactation (relative to pregnancy) may contribute to the greater change in blood Pb observed post pregnancy compared with the second and third trimesters. The contribution of skeletal Pb to blood Pb during the post pregnancy period remained essentially constant at the increased level of Pb mobilization.

Gulson et al. (2004) observed calcium supplementation was found to delay increased mobilization of Pb from bone during pregnancy and halved the flux of Pb release from bone during late pregnancy and postpartum. In another study, women whose daily Ca^{2+} intake was 850 mg per day showed lower amounts of bone resorption during late pregnancy and postpartum than those whose intake was 560 mg per day (Manton et al., 2003). Similarly, calcium supplementation (1,200 mg/day) in pregnant Mexican women resulted in an 11% reduction in BLL compared with placebo and a 24% average reduction for the most compliant women (Ettinger et al., 2009). When considering baseline BLLs in women who were more compliant in taking calcium supplementation, the reductions were similar for those <5 µg/dL and those ≥5 µg/dL (14% and 17%, respectively). This result is in contrast to a study of women who had blood Pb concentrations <5 µg/dL, wherein calcium supplementation had no effect on

blood Pb concentrations (Gulson et al., 2006). These investigators attributed their results to changes in bone resorption with decoupling of trabecular and cortical bone sites.

Miranda et al. (2010) studied BLL among pregnant women aged 18–44 years old. The older age segments in the study presumably had greater historic Pb exposures and associated stored Pb than the younger age segments. Compared with the BLLs of a reference group in the 25- to 29-year-old age category, pregnant women ≥30 years old had significant odds of having higher BLLs (ages 30–34: OR = 2.39, $p < 0.001$; ages 35–39: OR = 2.98, $p < 0.001$; ages 40–44: OR = 7.69, $p < 0.001$). Similarly, younger women had less chance of having higher BLLs compared with the reference group (ages 18–19: OR = 0.60, $p = 0.179$; ages 20–24: OR = 0.54, $p = 0.015$). These findings indicate maternal BLLs are more likely the result of Pb mobilization of bone stores from historic exposures as opposed to contemporaneous exposures.

BLLs increase during lactation due to alterations in the endogenous bone Pb release rate. After adjusting for patella Pb concentration, an increase in BLLs of 12.7% (95% CI: 6.2, 19.6) was observed in women who practiced partial lactation, and an increase of 18.6% (95% CI: 7.1, 31.4) was observed in women who practiced exclusive lactation compared with those who stopped (Tellez-Rojo et al., 2002). In another Mexico City study (Ettinger et al., 2006; Ettinger et al., 2004b), the authors concluded an interquartile increase in patella Pb was associated with a 14% increase in breast milk Pb, whereas for tibia Pb, the increase was ~5%. Breast milk:maternal blood Pb concentration ratios are generally <0.1, although values of 0.9 have been reported (Koyashiki et al., 2010; Ettinger et al., 2006; Gulson et al., 1998a). Dietary intake of polyunsaturated fatty acids (PUFA) has been shown to weaken the association between Pb levels in patella and breast milk, perhaps indicating decreased transfer of Pb from bone to breast milk with PUFA consumption (Arora et al., 2008). Breast milk as a source of infant Pb exposure was also discussed in Section 4.1.3.3 on dietary Pb exposure.

The Pb content in some bones (i.e., mid femur and pelvic bone) plateaus at middle age and then decreases at older ages (Drasch et al., 1987). This decrease is most pronounced in women and may be due to osteoporosis and release of Pb from resorbed bone to blood (Gulson et al., 2002). Two studies indicate the endogenous release rate in postmenopausal women ranges from 0.13 to 0.14 µg/dL in blood per µg/g bone and is nearly double the rate found in premenopausal women (0.07–0.08 µg/dL per µg/g bone) (Popovic et al., 2005; Garrido Latorre et al., 2003). An analysis of data on blood Pb concentrations and markers of bone formation (serum alkaline phosphatase) and resorption (urinary cross-linked N-telopeptides, NTx) in a sample of U.S. women found that blood Pb concentrations were higher in women (pre- or postmenopausal) who exhibited the highest bone formation or resorption activities (Jackson et al., 2010). Calcium or vitamin D supplementation decreased the blood Pb concentrations in the highest bone formation and resorption tertiles of the population of postmenopausal women. Significant associations between increasing NTx and increasing BLLs (i.e., increased intercept of regression model relating the change in blood Pb per change in bone Pb) have also been observed in elderly men (Nie et al., 2009).

Studies of the effect of hormone replacement therapy on bone Pb mobilization have yielded conflicting results (Popovic et al., 2005; Berkowitz et al., 2004; Garrido Latorre et al., 2003; Korrick et al., 2002; Webber et al., 1995). In women with severe weight loss (28% of body mass index [BMI] in 6 months) sufficient to increase bone turnover, increased BLLs of approximately 2.1 µg/dL (250%) were reported, and these blood Pb increases were associated with biomarkers of increased bone turnover (e.g., urinary pyridinoline cross-links) (Riedt et al., 2009).

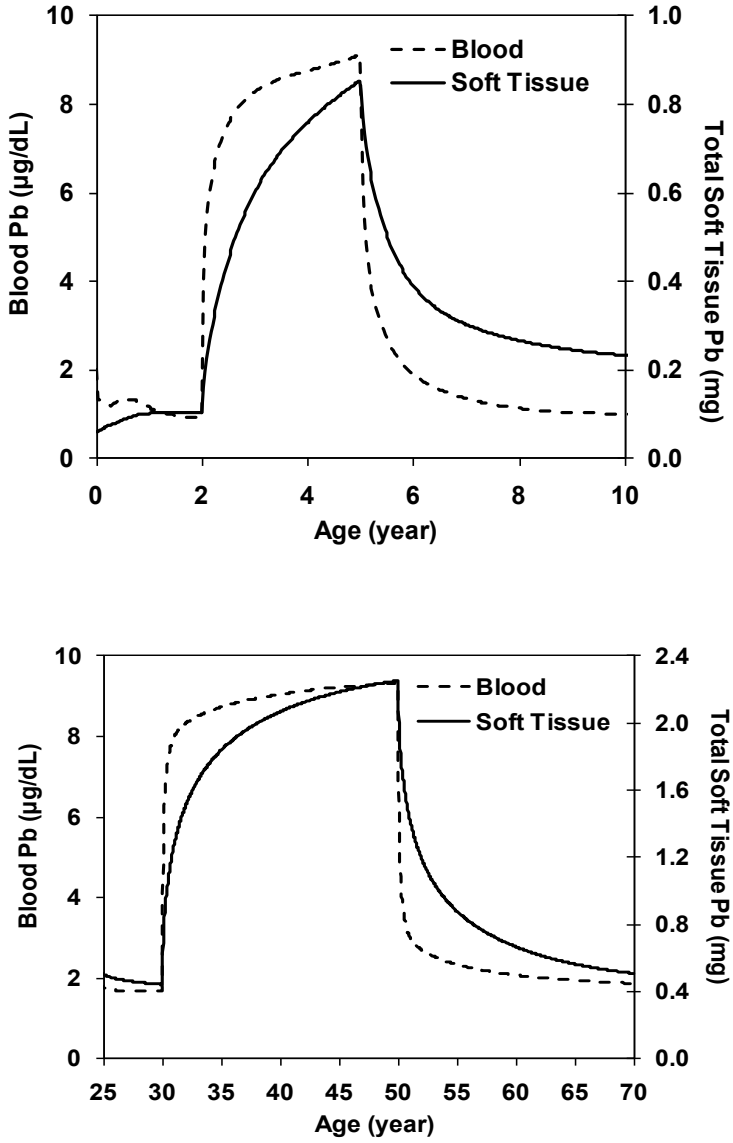
2.3.6 Relationship between Pb in Blood and Pb in Soft Tissues

Figure 2-9 shows simulations of blood and soft tissue Pb (including brain) for the same exposure scenarios previously displayed. Pb uptake and elimination in soft tissues is much faster than in bone. As a result, following cessation of a period of elevated exposure, Pb in soft tissues is more quickly returned to blood. The terminal elimination phase from soft tissue mimics that of blood, and it is similarly influenced by the contribution of bone Pb returned to blood and being redistributed to soft tissue.

Information on Pb levels in human brain is limited to autopsy data. These data indicate brain/blood Pb ratios of approximately 0.5 in infancy, which remain relatively constant over the lifetime (range 0.3 to 1.1) (Barry, 1981; Barry, 1975). The simulation of brain Pb shown in Figure 2-10 reflects general concepts derived from observations made in nonhuman primates, dogs, and rodents. These observations suggest peak Pb levels in the brain are reached 6 months following a bolus exposure, and within 2 months, approximately 80% of steady state brain Pb levels are reached (Leggett, 1993). There is a relatively slow elimination of Pb from brain ($t_{1/2} \approx 2$ years) compared with other soft tissues (Leggett, 1993). This slow elimination rate is reflected in the slower elimination phase kinetics shown in Figure 2-10. Although in this model, brain Pb to blood Pb transfer half-times are assumed to be the same in children and adults, uptake kinetics are assumed to be faster during infancy and childhood, which achieves a higher fraction of the soft tissue burden in brain, consistent with higher brain/body mass relationships. The uptake half-times predicted by Leggett (1993) vary from 0.9 to 3.7 days, depending on age. Brain Pb kinetics represented in the simulations are simple outcomes of modeling assumptions and cannot currently be verified with available observations in humans.

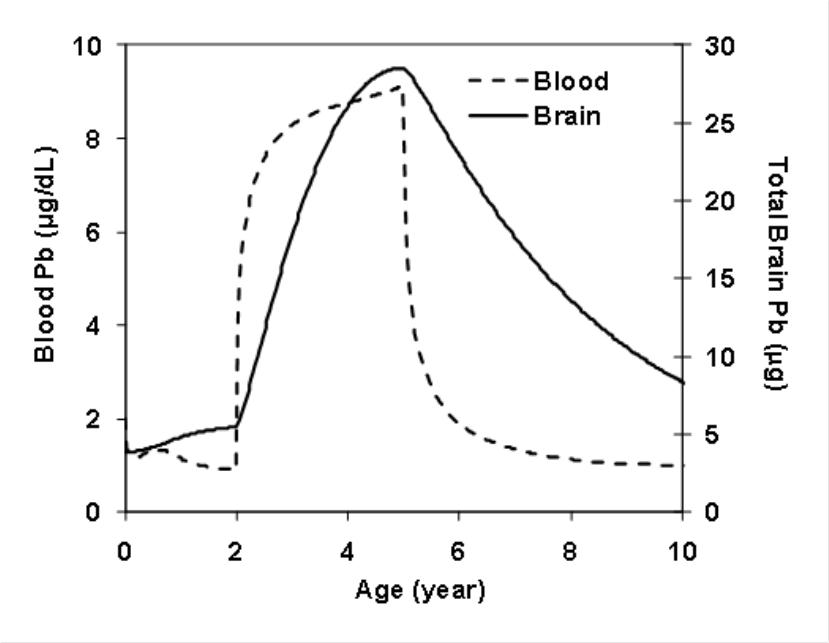
Urinary filtering and excretion of Pb is associated with plasma Pb concentrations. Given the curvilinear relationship between blood Pb and plasma Pb, a secondary expectation is for a curvilinear relationship between blood Pb and urinary Pb excretion that may become evident only at relatively high blood Pb concentrations (e.g., >25 µg/dL). Figure 2-11 shows these relationships predicted from the model. In this case, the exposure scenario shown is for an adult (age 40 years) at a quasi-steady state PbB; the same relationships hold for children (Leggett, 1993). At lower blood Pb concentrations (<25 µg/dL), urinary Pb excretion is predicted to closely parallel plasma Pb concentration for any given BLL (Figure 2-11, top panel). It follows from this that, similar to blood Pb, urinary Pb will respond much more rapidly to an abrupt change in Pb exposure than will bone Pb. One important implication of this relationship is, as

described previously for blood Pb, the relationships between urinary Pb and bone Pb will diverge with increasing exposure duration and age, even if exposure remains constant. Furthermore, following an abrupt cessation of exposure, urine Pb will quickly decrease while bone Pb will remain elevated (Figure 2-11, lower panel).

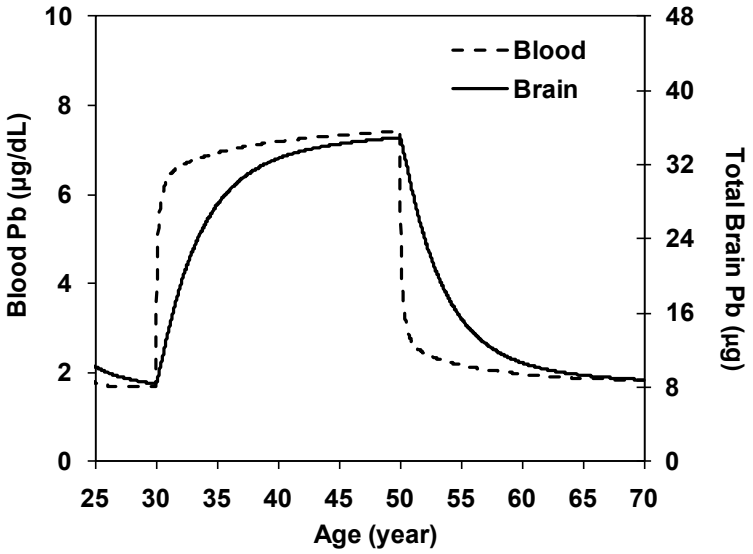


Note: For the child simulation (upper panel), baseline Pb intake is 3.2 µg/day from birth until age 2, followed by a period of increased intake to 38.2 µg/day from age 2 to 5, with a return to baseline intake at age 5. For the adult simulation (lower panel), baseline intake is 20 µg/day from age 0 to 30, followed by a 20-year period of increased intake to 120 µg/day from age 30 to 50, with a return to baseline intake at age 50. Simulation based on ICRP Pb biokinetics model (Leggett, 1993).

Figure 2-9 Simulation of blood and soft tissue (including brain) Pb in children and adults who experience a period of increased Pb intake.



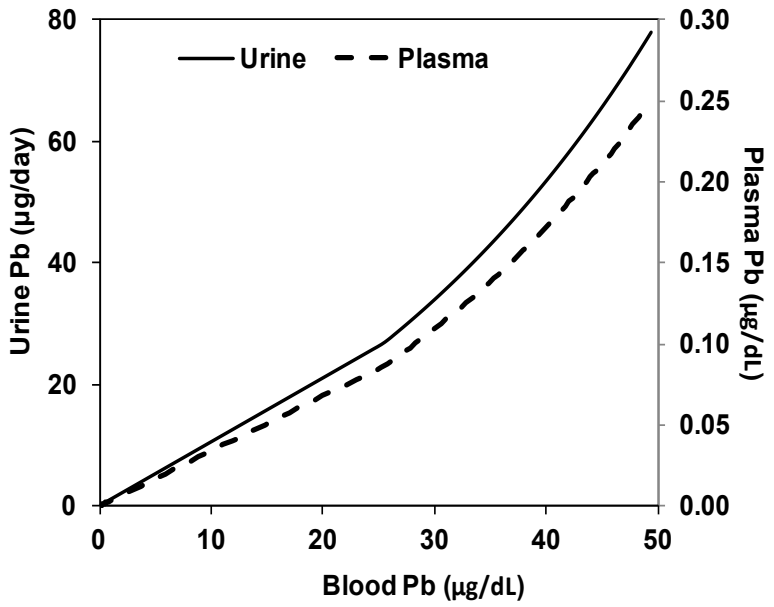
1



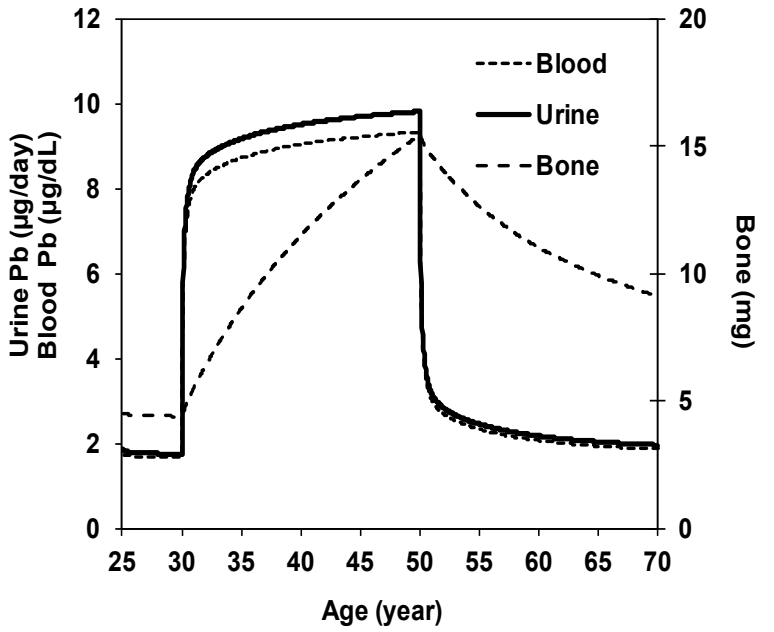
2

Note: For the child simulation (upper panel), baseline Pb intake is 3.2 µg/day from birth until age 2, followed by a period of increased intake to 38.2 µg/day from age 2 to 5, with a return to baseline intake at age 5. For the adult simulation (lower panel), baseline intake is 20 µg/day from age 0 to 30, followed by a 20-year period of increased intake to 120 µg/day from age 30 to 50, with a return to baseline intake at age 50. Simulation based on ICRP Pb biokinetics model (Leggett, 1993).

Figure 2-10 Simulation of blood and brain Pb in children and adults who experience a period of increased Pb intake.



1



2

Note: For the upper panel, model simulations are for a 40-year-old having a constant intake from birth of between 1 and 1,000 µg/day. For the lower panel, the baseline intake is 20 µg/day from age 0 to 30, followed by a 20-year period of increased intake to 120 µg/day from age 30 to 50, with a return to baseline intake at age 50. Simulation based on ICRP Pb biokinetics model (Leggett, 1993).

Figure 2-11 Relationship between Pb in urine, plasma, blood, and bone.

2.4 Studies of Pb Biomarker Levels

This section provides information on studies containing Pb biomarker concentrations, including in blood, bone, urine, teeth, and others. NHANES data show BLLs have continued on a downward trend since 1976. EBLLs have been linked in the literature to air sources (including proximity to airports), soil and dust (including from housing demolition and older homes), dietary sources, and tap water such as in the case of the Flint Water Crisis, among other sources described in 2.1. Continued research since U.S. EPA (2013) has shown there is a seasonality component to BLLs linked to several factors, including higher resuspension rates of soil containing Pb during drier months.

2.4.1 Pb in Blood

As concluded in the 2013 Pb ISA (U.S. EPA, 2013), trends in BLLs have been decreasing for U.S. residents over the past 45 years, as evidenced by NHANES data. Data show a progressive downward trend has occurred during the 1976–2018 period. The 2013 Pb ISA (U.S. EPA, 2013) noted the most dramatic declines occurred coincident with the phase-out of leaded gasoline and reductions in point source Pb emissions. The temporal trend for GM BLLs by age group from the 1999–2018 period is shown below in Figure 2-12. Summary statistics from the National Report on Human Exposure (CDC, 2021b) containing NHANES BLLs from 2011 to 2018 is presented in Table 2-11 below. In agreement with study results presented in Section 2.1.5.4, Figure 2-14 shows the gap in BLLs between non-Hispanic black children and children of different racial/ethnic groups has decreased over time.

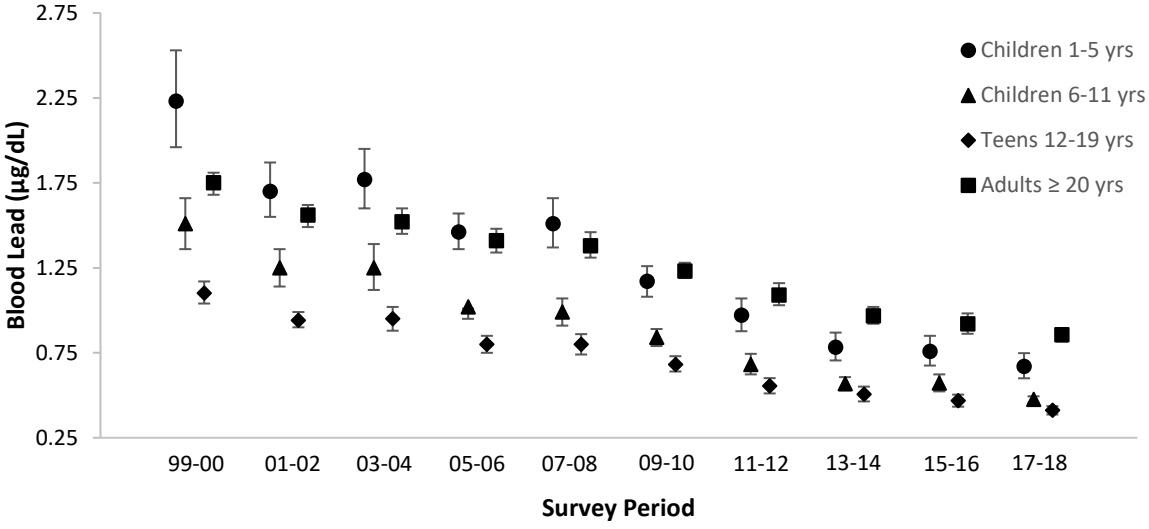
Table 2-11 Blood-Pb concentrations in the U.S. population.

Survey Stratum	Period	Geometric Mean (µg/dL)	95% Confidence Interval	Number of Subjects
All	2011–2012	0.973	0.916, 1.04	7,920
	2013–2014	0.858	0.813, 0.906	5,215
	2015–2016	0.820	0.772, 0.872	4,988
	2017–2018	0.753	0.723, 0.784	7,513
1–5 yr	2011–2012	0.970	0.877, 1.07	713
	2013–2014	0.782	0.705, 0.869	818
	2015–2016	0.758	0.675, 0.850	790
	2017–2018	0.670	0.600, 0.748	629
6–11 yr	2011–2012	0.681	0.623, 0.744	1,048

Survey Stratum	Period	Geometric Mean (µg/dL)	95% Confidence Interval	Number of Subjects
	2013–2014	0.567	0.529, 0.607	1,075
	2015–2016	0.571	0.523, 0.623	1,023
	2017–2018	0.475	0.456, 0.494	833
12–19 yr	2011–2012	0.554	0.511, 0.601	1,129
	2013–2014	0.506	0.464, 0.551	627
	2015–2016	0.467	0.433, 0.504	565
	2017–2018	0.411	0.387, 0.436	1,030
≥20 yr	2011–2012	1.090	1.03, 1.16	5,030
	2013–2014	0.967	0.921, 1.02	2,695
	2015–2016	0.920	0.862, 0.982	2,610
	2017–2018	0.855	0.816, 0.895	5,021
Males	2011–2012	1.130	1.06, 1.21	3,968
	2013–2014	0.994	0.919, 1.08	2,587
	2015–2016	0.921	0.864, 0.981	2,488
	2017–2018	0.860	0.820, 0.902	3,666
Females	2011–2012	0.842	0.796, 0.890	3,952
	2013–2014	0.746	0.715, 0.777	2,628
	2015–2016	0.735	0.679, 0.795	2,500
	2017–2018	0.664	0.632, 0.698	3,847
Mexican Americans	2011–2012	0.838	0.767, 0.916	1,077
	2013–2014	0.746	0.685, 0.813	969
	2015–2016	0.704	0.659, 0.752	994
	2017–2018	0.662	0.610, 0.719	1,134
Non-Hispanic blacks	2011–2012	0.998	0.947, 1.05	2,195
	2013–2014	0.871	0.787, 0.963	1,119
	2015–2016	0.856	0.763, 0.962	1,070
	2017–2018	0.766	0.736, 0.798	1,708
Non-Hispanic whites	2011–2012	0.993	0.914, 1.08	2,493

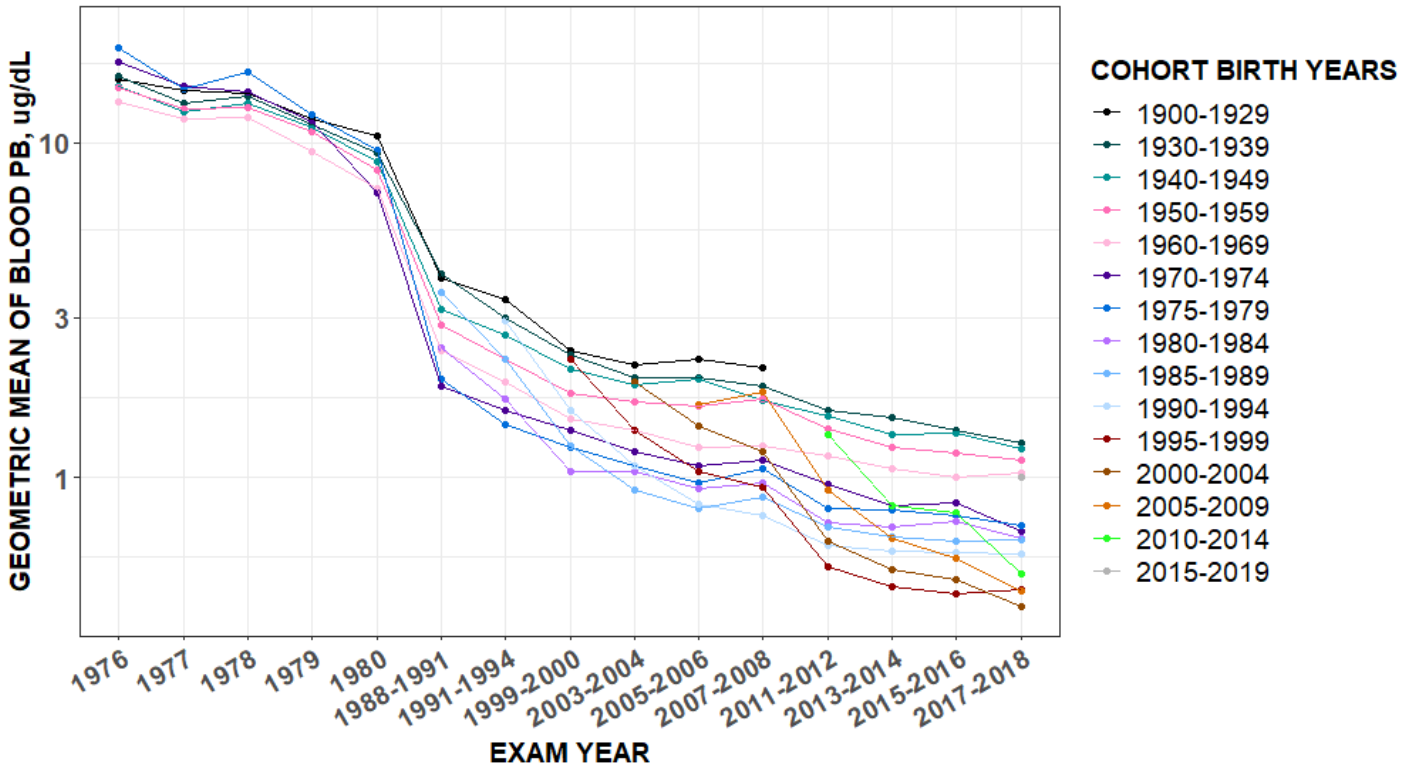
Survey Stratum	Period	Geometric Mean (µg/dL)	95% Confidence Interval	Number of Subjects
	2013–2014	0.882	0.820, 0.950	1,848
	2015–2016	0.835	0.774, 0.900	1,511
	2017–2018	0.772	0.731, 0.816	2,536
All Hispanics	2011–2012	0.855	0.793, 0.922	1,931
	2013–2014	0.742	0.695, 0.793	1,481
	2015–2016	0.703	0.658, 0.750	1,664
	2017–2018	0.629	0.593, 0.667	1,816
Asians	2011–2012	1.150	1.06, 1.24	1,005
	2013–2014	1.010	0.923, 1.11	510
	2015–2016	1.070	0.976, 1.18	479
	2017–2018	1.020	0.909, 1.15	946

yr = years
Limit of detection (LOD) for survey years 11–12, 13–14, 15–16, and 17–18 are 0.25, 0.07, 0.07, and 0.07, respectively.
Source: Data sourced from CDC (2021a).



Note: Shown are geometric means and 95% CIs based on data from NHANES IV CDC (2021a).

Figure 2-12 Temporal trend in blood Pb concentrations.



Note: The means of logged blood Pb were weighted to represent national averages. Data were from the publicly available NHANES II, NHANES III, and continuous NHANES cycles (1999–2000, 2003–2004, 2005–2006, 2007–2008, 2011–2012, 2013–2014, 2015–2016, 2017–2018). 2001–2002 and 2009–2010 were excluded because only 551 blood Pb samples were available for each, respectively.

Figure 2-13 Blood Pb cohort means versus year of exam.

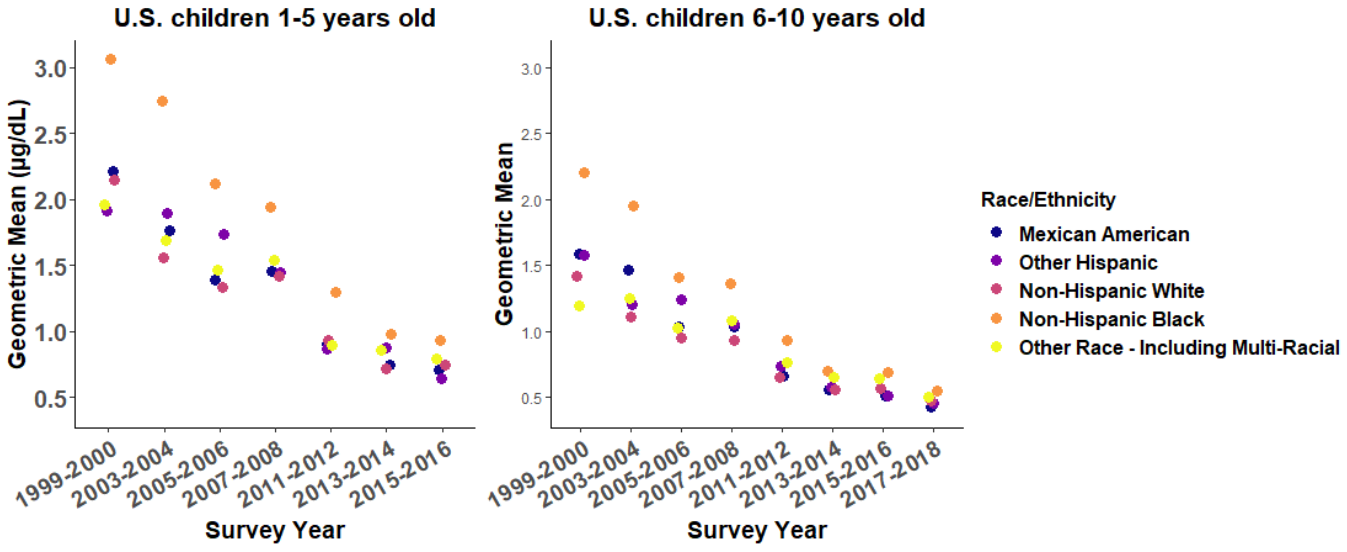


Figure 2-14 Blood Pb geometric means versus year of NHANES exam by race/ethnicity.

Additional analyses have used NHANES data to investigate the decline in BLLs over time. Wang et al. (2021) analyzed NHANES data from 1996 to 2016 that included 68,877 participants (1–85 years; 38-year weighted mean age) and found an annual percentage change of –4.26% ($p < 0.05$) during this time period from a mean BLL of 1.68 µg/dL (95% CI: 1.63, 1.74) to 0.82 µg/dL (95% CI: 0.77, 0.87). Ettinger et al. (2020) analyzed BLLs of women of childbearing age (15–49 years) using 1976–2016 NHANES data (n = 22,408). The authors found the GM of this group dropped over a 40-year period from 10.37 µg/dL (95% CI: 9.95, 10.79) to 0.61 µg/dL (95% CI: 0.59, 0.64) (from 1976–1980 to 2011–2016, respectively). Few women (0.7%) in the 2011–2016 group had BLLs above 5 µg/dL. By comparison, for children aged 1–5 years, the 1976–1980 NHANES showed a blood Pb of 15.2 µg/dL (95% CI: 14.3, 16.1) with nearly all (99.8%) exceeding 5 µg/dL, which declined in 2011–2016 to 0.8 µg/dL (95% CI: 0.8, 0.9) with only 1.3% exceeding 5 µg/dL (Egan et al., 2021).

The 1986 and 2006 Pb AQCDs (U.S. EPA, 2006a, 1986) and the 2013 Pb ISA (U.S. EPA, 2013) contain evidence that BLLs may follow a seasonal pattern in children, with elevated concentrations in the warm season compared with lower levels in the cold season. This is important to understand when studies reporting BLLs are evaluated because seasonal effects may also contribute to findings, especially at low BLLs, wherein contributions from other sources may have a greater impact on BLLs than the source being studied, potentially serving as a confounding variable when the link between BLLs and an exposure pathway is being investigated.

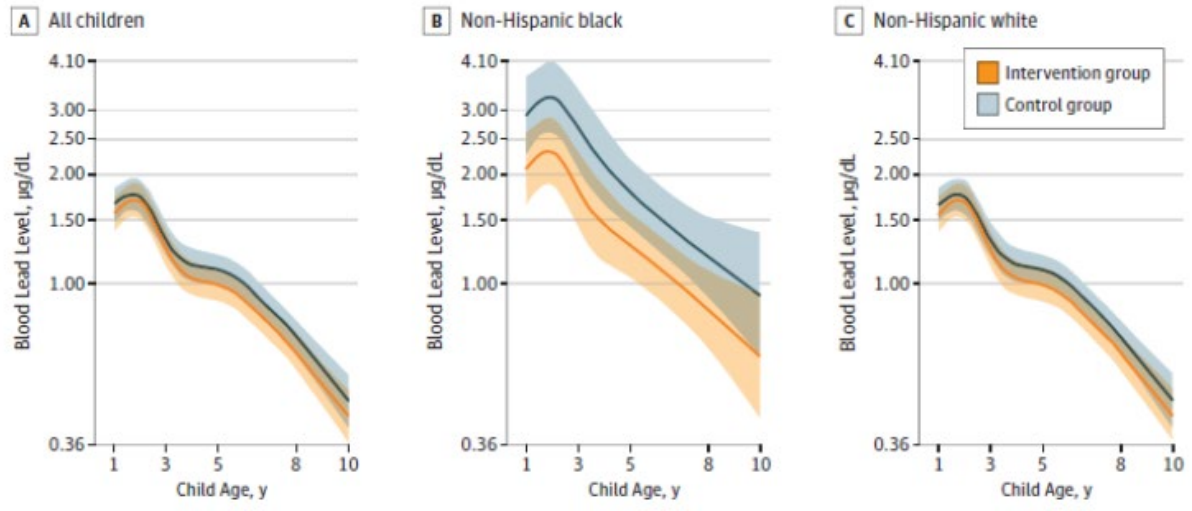
Levin et al. (2020) reviewed literature within the previous Pb ISA and AQCD documents for information on Pb seasonality and supplemented conclusions based on recent research. The authors found seasonality of BLLs could be linked to multiple sources including gasoline usage (prior to 1985), soil and dust, housing renovations, aviation gas, drinking water, diet, consumption of game meat, off-road vehicles, and vitamin D generation. As mentioned in Section 1.2.6 of this document (https://cfpub.epa.gov/ncea/isa/recordisplay.cfm?deid=357282), there is evidence that soil resuspension occurs to the greatest degree during the summer and fall when there are drier soil conditions (Resongles et al., 2021; Mielke et al., 2019b; Laidlaw et al., 2017; Laidlaw et al., 2016; Laidlaw et al., 2014). Laidlaw et al. (2012) concluded soil contributions to atmospheric Pb were highest during the summer and fall in Pittsburgh, PA; Detroit, MI; Chicago, IL; and Birmingham, AL. Laidlaw et al. (2016) investigated seasonality in child BLLs in Flint, MI, finding children's average BLLs consistently peaked in the third quarter of the year between 2010–2015, and concluded there was likely a contribution of soil Pb through resuspension to child BLLs. Zahran et al. (2013a) investigated soil contributions of Pb to atmospheric levels and the effect of this atmospheric Pb on 367,839 BLLs in children in Detroit. Atmospheric soil was derived using a mineral equation based on the elemental composition of soil (Al, Si, Ca, Fe, and Ti), and a regression model was built between atmospheric soil and atmospheric Pb concentrations that included an adjustment using local weather conditions (including humidity, sea level pressure, temperature, visibility,

and wind speed). After controlling for child sex, blood draw type, and year of observation, the authors found an increase of one standard deviation in air Pb (~0.0006 µg/m^3) was associated with an 8.04% (95% CI: 7.1 to 9.0%) increase in BLL for children less than 1 year of age. In addition, it was found that after adjusting for local weather conditions, one of the models showed an air Pb increase of 0.39% (95% CI: 0.28%, 0.50%) for every 1% increase in atmospheric soil (i.e., resuspended soil). Atmospheric soil was found to be a stronger contributor to air Pb than road dust. The study also found that, with the exception of children aged 3, absent soil resuspension, air Pb had little observable effect on child BLLs. This condition was assessed by regressing child BLL on the residual of their model, which represents other unmeasured sources of air Pb present.

Shao et al. (2017) analyzed 83,127 BLL data records of children in Syracuse, NY collected by the Onondaga County Health Department from April 1992 to December 2011. The authors found interventions by the Syracuse Lead Program to remove Pb-based paint in the homes of those children with BLLs over 10 µg/dL resulted in a change of the seasonal peak of BLLs from the summer (June, July, August) to different months, without a consistent pattern by year. This suggested BLL seasonality may have been influenced more by Pb-based paint exposure through opening of windows for natural ventilation in the summer (while being left closed in the winter) than by other factors, such as time outdoors and increased exposure to Pb in soil or dust from soil. Past studies found a regular seasonal peak in summer for BLLs of Syracuse children (Laidlaw et al., 2005; Haley and Talbot, 2004).

The Cochrane Library includes several systematic reviews and meta-analyses of randomized controlled trials (RCTs) and quasi-RCTs (Nussbaumer-Streit et al., 2020; Nussbaumer-Streit et al., 2016; Yeoh et al., 2014; Yeoh et al., 2008). The studies included in these reviews were conducted to evaluate the effectiveness of interventions, including dust control actions like soil excavation and replacement that were intended to reduce children's BLLs. Overall, these reviews found no statistical evidence that these interventions were effective in reducing children's BLL. The authors also noted the evidence specifically pertaining to the effect of soil remediation was limited to two studies (Farrell et al., 1998; Weitzman et al., 1993) reporting contradictory findings.

Braun et al. (2018) conducted an intervention study related to indoor dust Pb in Cincinnati, OH between 2003 and 2006. Pregnant women were randomly assigned to a residential Pb hazard intervention group (n = 174) or a control group (n = 181). The former received interventions such as the covering of bare yard soil areas, repair of deteriorated Pb-based paint areas, and extensive dust control and cleanup, whereas the latter received injury prevention education. Both the control and intervention groups showed reductions in floor, windowsill, and window trough dust Pb loading during the study. The BLLs of children from 1 to 8 years of age were not significantly different between the control and intervention groups, although the geometric mean childhood blood Pb levels were higher in non-Hispanic black children (Figure 2-15). However, the reductions in dust Pb loadings of the control group during the 2-year period following inclusion in the study suggests that the control group may have been influenced by participation in the study so as to undertake measures to reduce dust Pb loadings within their residences.



Note: Age-specific geometric mean blood Pb levels were derived from a mixed model that included the intervention arm, a 5-knot cubic polynomial spline for age and intervention by age interactions. Shading indicates 95% confidence intervals. BLLs are reported in µg/dL. Source: Braun et al. (2018)

Figure 2-15 Geometric mean childhood blood Pb levels assessed between 1 and 8 years old, stratified by race/ethnicity.

Ye et al. (2022) assessed the effect of soil remediation on BLLs of children living in Omaha, NE. Children's BLLs within a 27 mi^2 study area were paired with residential yard soil Pb and remediation status. A 13 mi^2 focus area within the study area delineated where soil Pb concentrations for at least 1 in 20 homes exceeded 400 ppm. Blood Pb data were available for nearly 75,000 children (0–7 years old) living within the study area between 1999 and 2016. Residential soil Pb data were available for 14,000 non-remediated properties and 7,400 properties that received remediation. Before remediation, children's risk of having an EBLL (i.e., >5 µg/dL) was associated with both residential soil Pb [OR = 2.00; 95% confidence interval (CI): 1.83, 2.19; >400–800 versus ≤200 ppm] and neighborhood soil Pb [OR = 1.85 (95% CI: 1.62, 2.11; >400–800 versus ≤200 ppm)]. The odds of having an EBLL was higher before remediation than after [OR = 1.52 (95%CI: 1.34, 1.72)]. This study showed a benefit of soil Pb remediation in reducing the risk of EBLLs in children, but the effects of activities such as community surveillance and health education may have contributed, in part, to this benefit.

As mentioned in Section 1.2 of this document (https://cfpub.epa.gov/ncea/isa/recordisplay.cfm?deid=357282), aviation fuel remains a major source of Pb emissions in ambient air. Miranda et al. (2011) found a monotonically decreasing trend in BLLs of children aged 9 months to 7 years and distance from airports in six counties in North Carolina, although emissions were not included in the model. Children within 500 m, 1,000 m, and 1,500 m had BLLs that were on average 4.4%, 3.8%, and 2.1% higher, respectively, than other children in those counties. Zahran et al. (2017a) analyzed the BLLs of 1,043,391 children, aged 1–5 years, collected from January 2001 through December 2009. Blood samples were collected during doctors' visits with a sampling emphasis on at-risk children in older homes or neighborhoods with EBLLs. BLLs were linked spatially and

temporally to 448 airports in Michigan and emission inventories of Pb-releasing industry sites found in the TRI. 40.2% of measurements were at/below detection levels. The authors found a 3.4% reduction in the odds of surpassing a CDC threshold for EBLL (≥5 and 10 µg/dL) with each km distance of a child's residence from an airport. The authors also found an increased likelihood of exceeding a 5 µg/dL BLL to be associated with increases of 100 piston engine aircraft operations per month; this effect decreased about 1% for every 1-km increase in residence distance from the airport. In another study, BLLs were higher for Republic of Korea Air Force crews working at bases using avgas (4.20 µg/dL) compared with those using jet propellant (3.79 µg/dL), with correlations also observed between BLL and longer working hours on airport runways at the bases using avgas (Park et al., 2013).

Zahran et al. (2023) analyzed 14,000 blood Pb concentration samples for children <5 years of age in neighborhoods surrounding Reid-Hillview Airport, Santa Clara County, CA during a 10-yr observation period from January 2011-December 2020. In addition, three potential indicators of avgas exposure were investigated, including (1) child residential distance from the airport; (2) whether the child's residence was downwind; and (3) volume of piston-engine aircraft traffic from the date of the blood draw. The authors found that the odds of a child's BLL exceeding 4.5 µg/dL increased statistically significantly ($p < 0.05$) with proximity to the airport, for those living east and predominantly downwind, and with increasing volume of piston-engine aircraft traffic. Model results were controlled for the number of EPA TRI facilities ≤ 2 miles of a child's residence, use of Pb-based paint in homes as indicated by the percentage of homes built in the neighborhood before 1960 (i.e. when use of Pb-based paint had declined by more than 90% from peak usage in the 1920s) at the year of blood draw, and SES as indicated by percentage of adults with a college degree, median home prices, and median household incomes.

Hollingsworth and Rudik (2021) analyzed ambient air Pb concentrations and EBLLs in relation to leaded gasoline usage in automotive races. The percentages of BLLs above 10 µg/dL in children under 72 months old for a given county-year were retrieved from CDC State Surveillance data, for which blood Pb sampling was targeted in high-risk areas. Only confirmed cases of EBLLs were used, either a venous blood draw showing a BLL above 10 µg/dL or two capillary draws within two weeks of each other showing a BLL above 10 µg/dL. Using an event study and spatial lag model, the authors estimated that every 100,000 miles driven using leaded gasoline in the previous week resulted in an increase in mean concentrations of ambient Pb within 50 miles of a racetrack equivalent to 10 percent. Data within Figure 4 of the paper shows that the average prevalence of EBLLs for border counties (i.e., counties bordering those where races occurred) and race counties (i.e., counties where races occurred) were one and two percentage points higher than control counties before 2007, respectively, when the National Association for Stock Car Auto Racing (NASCAR) and the Automobile Racing Club of America (ARCA) switched to using unleaded fuel. After 2007, the prevalence of EBLLs was similar to control counties. In addition, the authors developed a regression model linking the prevalence of EBLLs to whether there was a race in a county and whether a county bordered another county where a race occurred. This model also included a set of controls for SES (as indicated by unemployment rate, median income, percent non-white in the county), payroll in the manufacturing sector, and quantity of TRI Pb emissions. They estimated that the

effects of living in a race county on EBLL prevalence were higher by 18 and 13 percent, in 2005 and 2006 respectively, than 2007. This drop from 2005 to 2006 was consistent with the fact that 14 percent of race miles driven in 2006 used unleaded gasoline. These results suggest that leaded gasoline usage in automotive races prior to 2007 led to a greater prevalence of EBLLs in counties that had races as well as bordering counties.

Meng et al. (2014) used 1999–2008 NHANES BLL data and merged it with contemporaneous Pb air concentrations from the EPA AQS at monitors within 4 km of NHANES participants. The authors generally found positive associations between BLLs for all five age groups (from 1–5 years to >60 years) and Pb concentrations at Pb-PM_{10} monitors. This study is described in greater detail in Section 2.5.

Soil and dust have been investigated for contributions to BLLs. As mentioned in Section 2.1.3.2, Mielke et al. and other research teams have published a series of papers (Mielke et al., 2019b; Mielke et al., 2019a, 2017; Rabito et al., 2012; Mielke et al., 2011b; Zahran et al., 2011) demonstrating the importance of soil Pb as a source of children's Pb exposures in New Orleans and other cities. The New Orleans data they developed was especially extensive (>5,000 surface soil samples; >50,000 blood Pb samples) and have included multiple time points demonstrating a now declining pattern of soil Pb concentrations and BLLs. Correlations were found between soil Pb levels and BLLs in children both before and after Hurricane Katrina.

Stewart et al. (2014) used 81 soil samples and bioavailability data to predict BLLs using the IEUBK model in Toledo, OH. EBLLs for the 1–2-year-old age group were predicted in 28.4% of areas sampled. Pavilonis et al. (2022) collected 1,504 soil samples from 43 parks in Brooklyn, NY and EBLL information on children aged 1–5 years made available by the New York City DOHMH. The rate of EBLLs per 1,000 children was highest in the locations within the highest quartile of soil Pb concentrations (≥150 ppm, mean rate: 42.4, median rate: 37.2). The authors did not see a monotonic increase in the rate of EBLL by quartile; however, a multivariable regression model that controlled for race/ethnicity and housing characteristics found a significant positive association between soil Pb concentrations and EBLL rates ($p = 0.004$). Morrison et al. (2013) collected 226 soil samples around neighborhoods in Marion County, IN and year-long tap water filter samples from the interiors of seven homes. The authors analyzed these in relation to 16,232 BLL records of children living within the county. The authors found no statistical association between soil Pb concentrations and BLLs at the census block level; however, children within the urban core of the county were more likely to have EBLLs, likely due to traffic and industrial sources.

Bradham et al. (2017) analyzed the relationship between total Pb soil concentration, bioaccessible Pb soil concentration (38 soil samples), and BLLs of children aged 1 to 7 years (49 children) around Philadelphia residential homes. Regression models developed by the authors found the use of total soil Pb as a predictor of BLL variability accounted for 23% of variability, whereas the use of bioaccessible soil Pb accounted for 26% of variability (R^2 value 0.23 versus 0.26), suggesting bioaccessible soil Pb concentrations may be a better predictor of child BLLs.

To improve preventive methods for Pb exposure from soil and dust Zahran et al. (2013b) performed a study looking at the importance of soil sample locations in predicting child Pb exposure. Soil samples (n = 5,467) were collected across 286 census tracts and compared against geo-referenced blood Pb data of 55,551 children in New Orleans. The authors found the strongest soil type predictor of between-neighborhood variation in BLLs was residential street soils (39.7%), followed by busy street soils (21.97%), open space soils (20.25%), and home foundation soils (18.71%). The authors concluded the turbulent environment created by roadways leads to resuspension of dust in soils, increasing accidental inhalation and ingestion of Pb in those soils.

Several studies have investigated the link between housing, demolitions, and BLLs. Eisenberg et al. (2020) found children younger than 6 years old living in Detroit, MI, in homes previously foreclosed on (which tend to be older and may be less likely to receive Pb remediation actions) were more likely to have EBLLs. Eighty-four percent of the sample population lived in housing built before 1950. Ninety-three percent of children having EBLLs lived in older housing. Thirteen percent of children living in housing near two or more recent demolitions had EBLLs compared with <8% of children who did not live near recent demolitions. Clark et al. (2011) found BLLs declined up to 3 years after housing interventions were enacted to control Pb-based paint standards in low-income, privately owned housing. Chiofalo et al. (2019) compared the BLLs of 4,693 children in New York City and found 2.76% of children in private housing had EBLLs while 0.25% in public housing had EBLLs. Most of the public housing was built before 1960; however, ZIP codes for private housing with the most children who had BLLs at or above 5 µg/dL had a high prevalence of older housing as well. McClure et al. (2016) analyzed 5,266,408 BLLs of children <6 years of age from May 2009 to April 2015 in 36 states. The authors found that living in ZIP codes with ≥51.0% of homes built before 1950 had a significantly larger association with BLLs ≥5.0 µg/dL (OR 5.86, 95% CI: 5.71–6.01) or ≥10 µg/dL (OR 6.34, 95% CI: 5.97–6.74) than living in ZIP codes with <3.6% of homes built before 1950.

Bezold et al. (2020) investigated the association of BLLs in children <6 years of age (n = 54,150 BLL observations) with demolition activities within 400 feet of their homes during an uptick of demolitions within Detroit, MI in 2014–2018. The authors found associations between EBLLs (>5 µg/dL) and housing demolitions for the years between 2014 and 2017 but not 2018 (p = 0.07), which the authors attributed to differences in dust management practices between years, and the fact that homes demolished in 2018 were, on average, newer than those demolished earlier. Spanier et al. (2013) surveyed parents of 276 children in the Rochester area about renovation activities and related it to children's BLLs. It was found that interior housing renovation activities were associated with a 12% increase in children's BLLs. Dignam et al. (2019) performed a study to identify risk factors associated with EBLLs among 104 children in Philadelphia neighborhoods. Higher GM BLLs were significantly associated with door Pb content ≥40 µg/ft^2 (p = 0.0027) and living in a home built before 1980 (p = 0.0017).

As discussed in the 2013 Pb ISA (U.S. EPA, 2013), consumption of Pb-contaminated material, including soil, paint, drinking water, and food, has been linked to increased BLLs. A study of 491

pregnant women in New York City found those who reported engaging in pica had BLLs on average higher than those who did not report pica behavior (29.5 versus 23.8 µg/dL, $p < 0.0001$) and those engaging in pica were 11 times more likely to receive chelation therapy (Thihalolipavan et al., 2013). Keller et al. (2017) investigated factors that contributed to BLLs over 45 µg/dL in 145 children in New York City during the period between 2004 and 2010. The strongest reported risk factor was eating paint (36%), followed by other risk factors such as spending time outside the United States (34%) and having a developmental delay (27%). Children with developmental disorders may behave like younger children, with hand-to-mouth activity that persists longer, leading to greater exposure through ingestion of Pb over time (Shannon and Graef, 1996).

Desai et al. (2021) used 2009–2014 NHANES data for 12- to 36-month-olds to investigate the existence of a link between foods consumed and BLLs. They found that while consumption of the majority of food groups showed little effect on BLLs, cereal and milk consumption was associated with lower BLLs, whereas meat and fruit juice consumption was linked to higher BLLs. Wang et al. (2017a) found higher intakes of processed meat, red meat, refined grains, high-fat dairy products, French fries, butter, and eggs were associated with higher levels of BLLs in middle-aged to elderly men, using data from the VA Normative Aging Study. Savadatti et al. (2019) found that among a sample of licensed anglers and Burmese immigrants in Buffalo, NY, those who were more likely to catch and consume local fish had higher GM BLLs than 2013–2014 reference levels. Davis et al. (2014) examined the associations between 49 foods and biomarkers of Pb, Hg, Cd, and As in NHANES participants. They found diet explained a 2.9% variation in blood Pb in children and a 1.6% variation in adult BLLs. The authors acknowledged dietary data were self-reported, meaning participants may have been subject to misclassification, and their results cannot be generalized to the U.S. population. Colapinto et al. (2016) investigated tea consumption in 1,954 pregnant Canadian women and found increased tea consumption was linked to higher BLLs. However, the GMs of women who consumed the greatest amount of tea were less than 1 µg/dL.

Pb found in drinking water during the Flint Water Crisis has been associated with EBLLs in children. During the period of April 25, 2014 to October 15, 2015, the water source for residents in Flint, MI was switched from Lake Huron to the Flint River (Kennedy et al., 2016). Hanna-Attisha et al. (2016) examined BLLs in children <5 years of age before and during the rise in tap water Pb concentrations ($n = 1,473$; pre = 736; post = 737). They found the incidence of BLLs at or above 5 µg/dL increased from 2.4 to 4.9% from 2013 to mid-2015. Neighborhoods with the highest Pb concentrations in tap water experienced a 6.6% increase in EBLLs. In contrast, for neighborhoods outside the city that did not receive water treated at the Flint facility, there was no statistically significant ($p < 0.05$) change in incidence of EBLLs. Alternative potential Pb exposure sources, such as demolition projects, new Pb-producing factories, changes in Pb remediation programs, or manufacturing that uses Pb, showed no spatial relationship to increased BLLs. Gómez et al. (2018) found that among 15,817 BLLs for children ≤5 years of age, the GM decreased from 2.33 µg/dL in 2006 to 1.15 µg/dL in 2016; however, during that decade, the GM increased twice, once in 2010–2011 (a period before the switch to Flint River water) and again in

2014–2015 (during the Flint Water Crisis). By analyzing BLLs of children <6 years old from April 2013 to March 2016, Kennedy et al. (2016) found that by analyzing BLLs of children less than six years old from April 2013-March 2016 that 3.0% of BLLs were above 5 µg/dL. The percentage of children with EBLLs in the period of April 2014–January 2015, before a water advisory was issued, was 5.0%, significantly higher than before the source water was changed to Flint River water (April 2013–April 2014, a proportion of 3.1%). Multivariate adjusted odds ratios comparing the odds of EBLLs were 1.46 (95% CI: 1.06, 2.01), 1.28 (95% CI: 0.92, 1.76), and 0.75 (95% CI: 0.51, 1.12) for the period after the switch to Flint River water and *before* the water advisory, after the switch to Flint River water and *after* the water advisory, and after the switch back to Lake Huron water, respectively.

Over a longer period of time, BLLs of children in Flint, MI were found to decrease, which is consistent with national trends. Gómez et al. (2019) compared BLLs of children ≤5 years old from the periods of April 2006–October 2007, April 2012–October 2013, and April 2014–October 2015, finding GMs of BLLs decreased from 2.19 ± 0.03 µg/dL to 1.47 ± 0.02 µg/dL and finally to 1.32 ± 0.02 µg/dL, respectively. In addition, Gómez et al. (2019) found that among a population of women 12–50 years of age, GMs decreased from the period of April 2012–October 2013 (0.69 µg/dL; 95% CI 0.63, 0.75) to April 2014–October 2015 (0.65 µg/dL; 95% CI: 0.60, 0.71) to April 2016–October 2017 (0.55 µg/dL; 95% CI 0.54, 0.56).

Research has shown that Pb can be transferred between individuals through blood transfusions. Elabiad and Hook (2013) investigated Pb concentrations in 322 transfusions given to low-birth-weight infants. The average Pb level found in each packed RBC unit was 18.3 ± 1.3 µg/kg, and the average Pb load from each transfusion was 0.21 ± 0.13 µg/kg. Gehrie et al. (2013) found a median Pb concentration of 0.8 µg/dL with a SD of 0.80 µg/dL among 100 packed RBC units.

2.4.2 Pb in Bone

The 2013 Pb ISA (U.S. EPA, 2013) provides a detailed list of studies going back to 1994 that contain bone measurements of Pb. In nonoccupationally exposed individuals, typical group mean tibia bone Pb concentrations ranged from 10 to 30 µg/g. Bone Pb data for occupationally exposed individuals were also generally higher compared with nonoccupationally exposed individuals. The literature search and screening revealed only a few studies related to Pb concentrations in bone for this current document. NHANES does not contain bone Pb concentrations, so this information must be retrieved from studies in the literature.

Wilker et al. (2011) investigated Pb concentration changes over time in the mid-tibia shaft and patella bones for subjects in the VA Normative Aging Study between June 1991 and December 2002. Subjects attended four visits to have bone concentrations measured using KXRF with a drop-off in the number of subjects occurring between visits (n = 554 for 1st tibia measurement, n = 553 for 1st patella measurement versus n = 73 for 4th tibia measurement, n = 72 for 4th patella measurement). Participants

had a mean patella Pb measurement of 31.1 µg/g (SD = 19.9) and a mean tibia Pb measurement of 21.6 µg/g (SD = 13.6) at the 1st visit. Overall, after adjusting for age at baseline, BMI, years of education, pack-years smoked, alcoholic drinks/day, instrument used, and vitamin C intake, tibia Pb concentrations had a decline of 1.4% per year and patella Pb had a decline of 5.1% per year until after 4.6 years when there was no predicted significant change in patella Pb. Older individuals were found to have higher bone Pb concentrations.

McNeill et al. (2018) measured bone Pb levels using in vivo XRF in a Toronto, Ontario, Canada population between 2009 and 2011 and compared them against Hamilton, Ontario, Canada in vivo XRF measurements of bone Pb collected in the early 1990s. Both groups had no record of occupational exposure, and home postal code information revealed there was some overlap between recruitment areas for both studies. The slope of the tibia Pb content versus age was reduced by 36–56% compared with 17 years prior, showing it is likely that over time, there have been reductions in uptake of Pb into the bones, from environmental exposures, among the population within the Ontario region.

2.4.3 Pb in Urine

Urine-Pb concentrations for the U.S. population are monitored in NHANES. Data from the most recent CDC report CDC (2021a) on NHANES data can be found in Table 2-12. NHANES IV data presented in the 2006 AQCD (U.S. EPA, 2006a), 1999-2008 NHANES data presented in the 2013 Pb ISA (U.S. EPA, 2013), and Table 2-12, show urine µg Pb/g creatine GM concentrations have continued to drop over time, similar to BLLs. As an example, the urine GM Pb concentration for subjects ≥20 years of age in the NHANES IV 1999–2000 data was 0.72 (95% CI: 0.68, 0.76), whereas in 2015–2016, it was 0.304 (95% CI: 0.276, 0.315). A discussion of urinary Pb elimination is provided in Section 2.2.3.

Table 2-12 Urine-Pb concentrations in the U.S. population.

Survey Stratum	Period	Geometric Mean (µg Pb/g CR)[a]	95% Confidence Interval	Number of Subjects
All	2011–2012	0.360	0.328, 0.396	2,504
	2013–2014	0.277	0.257, 0.298	2,664
	2015–2016	0.284	0.261, 0.308	3,061
6–11 yr	2011–2012	0.346	0.292, 0.410	399
	2013–2014	0.222	0.192, 0.258	402
	2015–2016	0.257	0.238, 0.276	379

Survey Stratum	Period	Geometric Mean (μg Pb/g CR)[a]	95% Confidence Interval	Number of Subjects
12–19 yr	2011–2012	0.259	0.219, 0.305	390
	2013–2014	0.201	0.166, 0.245	451
	2015–2016	0.196	0.183, 0.211	402
≥20 yr	2011–2012	0.381	0.348, 0.416	1,715
	2013–2014	0.297	0.280, 0.315	1,811
	2015–2016	0.304	0.276, 0.334	1,794
Males	2011–2012	0.414	0.367, 0.466	1,262
	2013–2014	0.315	0.295, 0.337	1,318
	2015–2016	0.313	0.285, 0.343	1,524
Females	2011–2012	0.316	0.282, 0.355	1,242
	2013–2014	0.245	0.222, 0.269	1,346
	2015–2016	0.259	0.233, 0.288	1,537
Mexican Americans	2011–2012	0.372	0.320, 0.431	317
	2013–2014	0.277	0.240, 0.319	453
	2015–2016	0.295	0.260, 0.335	585
Non-Hispanic blacks	2011–2012	0.431	0.385, 0.483	669
	2013–2014	0.371	0.320, 0.429	581
	2015–2016	0.340	0.298, 0.388	671
Non-Hispanic whites	2011–2012	0.346	0.311, 0.385	820
	2013–2014	0.267	0.245, 0.290	985
	2015–2016	0.275	0.247, 0.305	924
All Hispanics	2011–2012	0.372	0.327, 0.423	573
	2013–2014	0.270	0.239, 0.305	701
	2015–2016	0.284	0.258, 0.312	982

Survey Stratum	Period	Geometric Mean (µg Pb/g CR)[a]	95% Confidence Interval	Number of Subjects
Asians	2011–2012	0.383	0.341, 0.429	353
	2013–2014	0.257	0.230, 0.287	292
	2015–2016	0.292	0.264, 0.324	332

yr = years
[a]Values are in µg Pb/g creatine (CR).
Source: Data sourced from CDC (2021a).

2.4.4 Pb in Other Biomarkers

Biomarkers other than blood and bone Pb have been used in various studies to measure Pb body burden, although they are not as well established. Robbins et al. (2010) analyzed tooth enamel samples from 127 individuals born between 1936 and 1993 and found the log-transform of tooth enamel concentration was significantly predicted by the log-transform of Lake Erie sediment core data (i.e., Pb concentrations found in the Lake Erie sediment) obtained by Graney et al. (1995) ($p < 0.00001$) and by the log-transform of U.S. consumption of Pb in gasoline ($p < 0.00001$). Studies performed in Brazil found Pb concentrations in tooth enamel among 4- to 6-year-old kindergarteners in São Paulo to be significantly higher ($p < 0.0001$) for those living near a Pb-acid battery processing plant than those living in other parts of the city (control versus exposed medians: 206 mg/kg versus 786 mg/kg) and Pb in tooth samples to be higher for children 4–12 years of age living near a dam with heavy metal sediments compared with children 4–13 years of age living in a control area (control versus exposed averages: 0.91 mg/kg versus 1.28 mg/kg) (Arruda-Neto et al., 2009; de Almeida et al., 2007). In a study of Pb concentrations in the general population Arruda-Neto et al. (2010) observed 10-year-olds had the highest Pb teeth concentrations, and tooth Pb concentrations stayed constant in adulthood but dropped to just above 30% among 64-year-old subjects, although they did not adjust for confounding factors. Johnston et al. (2019) measured Pb concentrations in 50 deciduous teeth of 43 children living in Los Angeles and modeled soil Pb concentrations in the area using data from the California Department of Toxic Substances Control. The authors found mean prenatal Pb concentrations, reported as $^{208}Pb:^{43}Ca$, were 4.104×10^{-4}, and the mean postnatal level was 4.109×10^{-4}. Soil Pb exposure was a predictor of teeth Pb concentrations.

Jursa et al. (2018) measured Pb concentration levels in the hair of 222 children in the Mid-Ohio Valley region. The median Pb concentration was 0.15 µg/g, with Pb levels higher in males than in females and varying along hair length. Sears et al. (2012) performed a systematic review of Pb secretion in sweat, finding eleven studies. Sweat concentrations were found to vary considerably across studies, with sweat Pb levels up to 283 µg/L in nonoccupationally-exposed subjects. There was mixed evidence as to whether secretion of Pb through the skin could lower PbB.

2.5 Empirical Models of Pb Exposure-Blood Pb Relationships

Multivariate regression models, commonly used in epidemiology, provide estimates of the variability in BLL (or other biomarker) explained by various exposure pathways (e.g., air Pb concentration, surface dust-Pb concentration). Structural equation modeling links several regression models together to estimate the influence of determinants on the internal dose metric. Regression models can provide estimates of the rate of change of blood or bone Pb concentration in response to an incremental change in exposure level (i.e., slope factor). One strength of regression models for this purpose is that they are empirically verified within the domain of observation and have quantitative estimates of uncertainty embedded in the model structure. However, regression models are based on (and require) paired predictor-outcome data and, therefore, the resulting predictions are confined to the domain of observations and are typically not generalizable to other populations. Regression models also frequently exclude numerous parameters that are known to influence human Pb exposures (e.g., soil and dust ingestion rates) and the relationship between human exposure and tissue Pb levels, parameters that are expected to vary spatially and temporally. Thus, extrapolation of regression models to other spatial or temporal contexts can be problematic.

A variety of factors may potentially affect estimates of blood Pb-air Pb slope factors. Simultaneous changes in other (non-air) sources of Pb exposure can affect the relationship indicated for air Pb. For example, remedial programs (e.g., community and home-based dust control and education) may be responsible for partial blood Pb reduction seen in some studies. The effect of remedial programs may lead to an overestimation of declines in blood Pb due to changes in air Pb and a corresponding positive bias in blood Pb-air Pb slopes. However, model adjustment for remedial programs and other factors (e.g., soil Pb concentrations) may also cause a negative bias in blood Pb-air Pb slopes. A tendency over time for children with lower BLLs to not return for follow-up testing has been reported. The follow-up of children with higher BLLs would likely lead to an underestimation of reductions in blood Pb following reductions in air Pb and cause a negative bias in blood Pb-air Pb slopes. Another factor is the extent to which all the air Pb exposure pathways are captured by the data set and its analysis. For example, some pathways (such as exposure through the diet or surface soils) may respond more slowly to changes in air Pb than others (such as inhalation). Additionally, some studies may include adjustments for variables that also reflect an influence from air Pb (e.g., SES or soil Pb). With air Pb concentrations decreasing over time, remaining Pb sources (including contributions of legacy airborne Pb to soil and dust) may be the dominant contributors to current BLLs. Not accounting for Pb exposure from sources other than current air Pb may positively bias estimates of current air Pb concentrations (PbA) on blood Pb. Studies may also vary in the ages of subjects, which given age-related changes in blood Pb can also influence estimates.

Many studies have used TSP measurements of PbA. The sampling efficiency of TSP samplers is affected by particle size distribution, wind speed, and wind direction. For example, especially for larger particles (aerodynamic diameter ≥20 μm), TSP sampling efficiency decreases with increasing wind speed

(see Appendix 1). Such effects on TSP sampling efficiency can, in areas where such large particles are a substantial portion of airborne Pb, lead to uncertainties in the comparability of PbA between samples within a study and across studies. A uniformly low bias in PbA in a study could positively bias estimated blood Pb-air Pb slopes for that study. Moreover, variability in TSP samples is likely to result from temporal variation in wind speed, wind direction, and source strength. Such temporal variability would tend to increase uncertainty and reduce the statistical strength of the relationship between air Pb and blood Pb but may not necessarily affect the slope of this relationship. A number of factors, including those described above, cause uncertainty in the magnitude of estimated blood Pb-air Pb slope factors and may lead to both positive and negative biases in the estimates from individual studies.

2.5.1 Air Pb-Blood Pb Relationships in Children

Within the literature and EPA documents, the relationship between air Pb and blood Pb is commonly characterized in terms a "slope factor" or "air-to-blood ratio." An air-to-blood ratio of 1:5 indicates that for every 1 μg/m^3 of air Pb, there is a 5 μg/dL increase in blood Pb. Synonymously, this is characterized by a slope factor of 5 μg/dL per μg/m^3. The 1986 Pb AQCD (U.S. EPA, 1986) described epidemiologic studies of relationships between air Pb and blood Pb. Drawing from the studies examined, the aggregate blood Pb-air Pb slope factor (when considering both air Pb and Pb in other media derived from air Pb) was estimated to be approximately double the slope estimated from the contribution due to inhaled air alone (U.S. EPA, 1986). Much of the pertinent earlier literature (e.g., prior to 1984, when air Pb was dominated by the use of leaded gasoline in on-road motor vehicles) on children's BLLs was summarized by Brunekreef (1984). The 1986 Pb AQCD also noted ratios derived from occupational studies involving higher blood and air Pb levels are generally smaller than ratios from population studies involving lower blood and air Pb levels [see the 1986 Pb AQCD, Chapter 11, p. 99 (U.S. EPA, 1986)]. Most studies have empirically modeled the air Pb to blood Pb relationship using nonlinear regression (i.e., log-log), which itself gives an increasing slope with decreasing air Pb concentration. In the 2008 final rule for the Pb NAAQS (73 FR 66964), with recognition of uncertainty and variability in the air-to-blood relationship, air-to-blood slopes of 5, 7, and 10 μg/dL per μg/m^3 were used in evaluating air-related IQ loss of children (see Table 4 of that rule). The highest slope of 1:10 μg/dL per μg/m^3 was used to reflect the lower BLLs of children and PbA more recently observed in the United States relative to when most of the studies describing the air-to-blood relationship had been conducted.

At the time of the 2013 Pb ISA (U.S. EPA, 2013), due to the limited evidence, there was uncertainty in projecting the magnitude of the air Pb-blood Pb relationship to ambient PbA below 0.2 μg/m^3. The air Pb-blood Pb relationship in terms of slope factors or ratios was not discussed in the 2006 Pb AQCD (U.S. EPA, 2006a). There are studies since the 2013 Pb ISA that evaluate the air Pb-to-blood Pb relationship that are more reflective of current conditions with central tendency PbA between 0.004 and 0.04 μg/m^3. Table 2-13 summarizes new and old studies from which air-to-blood ratios were derived. With the exception of Ranft et al. (2008), slopes corresponding to a central estimate of the PbA

of each study are provided. Slope factor data as a function of PbA are illustrated in Figure 2-16, which shows slope factors continue to increase with decreasing PbA seen in the newer studies. Although saturable GI absorption and saturation of Pb binding to RBC occur at relatively high rates of Pb intake leading to PbB of 20-30 µg/dL (see Section 2.2), the nonlinear relationship between PbA and PbB cannot be explained by a biokinetic mechanism. With reference to Table 2-13 and Figure 2-16, it is readily apparent that the PbA are considerably higher in older studies (Hilts, 2003; Tripathi et al., 2001; Hayes et al., 1994; Schwartz and Pitcher, 1989; Brunekreef, 1984) than newer studies (Meng et al., 2014; Richmond-Bryant et al., 2014; Richmond-Bryant et al., 2013; Zahran et al., 2013a; Bierkens et al., 2011). An inherent assumption in univariate regression models relating blood Pb to air Pb is that each population has the same relative contribution to blood Pb from other (non-air) pathways or that the non-air contribution is negligible relative to air-related pathways. For the older studies, there may be a greater likelihood of representing the effect of air Pb on blood Pb due to relatively less interference from non-air exposure pathways. However, overarching distinctions between old and new studies should be made with caution given that Pb in other media has also decreased over time (e.g., due to banning the use of Pb solder in food cans and plumbing).

In general, longitudinal studies conducted after phasing out leaded gasoline would best inform the current relationship of PbB change corresponding to PbA fluctuation. Ideally, such studies would compare two populations for which all Pb sources but PbA concentrations are unchanged. Such a nearly ideal study, Hilts (2003) reported the change in PbB from 1996 to 2001 for children under 5 yrs old associated with the emission reduction from a local smelter in Trail, BC, Canada. However, even in this study, the reduction in exposure from pathways other than air cannot be ruled out due to the "comprehensive education and case management programs". Common to all studies, Pb in other media, not just air, were also decreasing, e.g., due to stopping use of Pb solder in food cans and plumbing. An advancement in understanding the PbB-PbA association came from leveraging the USEPA AQS with NHANES surveys. The PbB-PbA associations across different NHANES periods should reflect the change in this association for the U.S. population over time (Richmond-Bryant et al., 2014; Richmond-Bryant et al., 2013) because each NHANES is a representative sample of the U.S. population. However, merging PbB results from multiple NHANES periods with the USEPA AQS could introduce exposure measurement errors as well as uncertainties in terms of population representativeness and availability of covariates. Each single study presented in Table 2-13 deviates from the ideal design in one or more aspects. Collectively, all of these studies contribute to our understanding of how PbA impacts PbB.

For log-log relationships between total blood Pb and PbA, the instantaneous slope factor, d[PbB]/d[PbA], was by Equation 2-2.

$$\frac{d[PbB]}{d[PbA]} = b^{\beta_0} \times \beta_{PbA} \times [PbA]^{(\beta_{PbA}-1)}$$

Equation 2-2

where: b is the logarithm base (either 2.7183 or 10) used in a study, β_0 is the regression intercept, β_{PbA} is the regression slope, and PbA is central estimate of air Pb for the study. The instantaneous slope calculated by Equation 2-2 provides the same estimated slope as derived by evaluating regression equations at ±0.01 μg/m^3 from central estimate of air Pb as done for studies in Table 3-12 of the 2013 Pb ISA (U.S. EPA, 2013). New and old studies vary with regard to the use of single or multivariate regression and, for the latter, with regard to the variables included. Newer studies (Meng et al., 2014; Richmond-Bryant et al., 2014; Richmond-Bryant et al., 2013; Zahran et al., 2013a; Bierkens et al., 2011) that provide estimates for a total blood Pb-air Pb slope factor are described below. The series of studies by Meng et al. and Richmond-Bryant et al. were conducted by EPA to address slope factor-related uncertainties identified while completing the 2013 Pb ISA (U.S. EPA, 2013). Older studies were discussed in detail in Section 3.5.1 of the 2013 Pb ISA (U.S. EPA, 2013).

Table 2-13 Summary of estimated slopes for blood Pb-to-air Pb slope factors in children.

Reference	Study Methods	Model Description	Blood Pb–Air Pb Slope[a]
Child Populations – Air			
Bierkens et al. (2011)	**Location:** European countries **Yr:** 1999–2008 **Subjects:** Children (<6 yr; n = 28) **Analysis:** Univariate regression of blood Pb from literature and air Pb from a European Environment Agency database	**Model:** Log-Log **Blood Pb:** 1.45–4.11 μg/dL (mean range for study groups) **Air Pb:** 0.001–0.056 μg/m^3 (annual mean range for study groups)	12.0 (0.020)[b]
Brunekreef (1984)	**Location:** Various countries **Yr:** 1974–1983 **Subjects**: Children (varying age groups including children from 0 to 18 yr; n > 190,000) **Analysis:** Meta-analysis of 96 child populations from 18 study locations	**Model:** Log-Log **Blood Pb:** 5–76 μg/dL (mean range for study populations) **Air Pb:** 0.1–10.0 μg/m^3 (mean range for study locations, averaging time not typically indicated)	**All children:** 4.6 (1.5)[c] **Children <20 μg/dL:** 4.8 (0.54)[d]
Hayes et al. (1994)	**Location:** Chicago, IL **Yr:** 1974–1988 **Subjects:** 0.5–5 yr (n = 9,604) **Analysis:** Regression of quarterly median blood Pb and quarterly mean air Pb	**Model:** Log-Log **Blood Pb:** 10–28 μg/dL (quarterly median range) **Air Pb:** 0.05–1.2 μg/m^3 (quarterly mean range)	8.2 (0.62)[e]

Reference	Study Methods	Model Description	Blood Pb–Air Pb Slope[a]
Hilts (2003)	**Location:** Trail, BC **Yr:** 1996–2001 **Subjects:** 0.5–5 yr, 1996–2000; 0.5–3 yr, 2001 (Estimated n = 220–460 per yr, based on 292–536 eligible children per yr with 75–85% participation) **Analysis:** Regression of blood Pb screening and community air Pb following upgrading of a local smelter	**Model:** Linear **Blood Pb:** 4.71–1.5 µg/dL (annual GM range) **Air Pb:** 0.13–1.1 µg/m^3 (annual GM range except 2001, which reflects a 9-mo average)	7.0 (0.48)[f]
Meng et al. (2014)	**Location:** United States (contiguous states) **Yr:** 1999–2008 **Subjects**: 1–5 yr (n = 178, TSP; n = 2,150, PM_{10}), 6–11 yr (n = 212, TSP; n = 2,261, PM_{10}) **Analysis**: Age-stratified linear mixed effects models were run to assess the relationship of PbB with PbA without covariates	**Model:** Log-Log **Blood Pb:** 1.7–2.3 µg/dL and 1.4-2.0 µg/dL(range of GMs), respectively, for 1- to 11-yr-old children paired with TSP and PM_{10} data **Air Pb:** 0.0135–0.0151 µg/m^3 and 0.0051–0.0054 µg/m^3 (range of GMs of daily PbA in TSP and PM_{10}, respectively, paired with BLL data for 1- to 11-yr-old children)	**1–5 yr** 9.1 (TSP, 0.0135)[g] 37.7 (PM_{10}, 0.0054) **6–11 yr** 3.0 (TSP, 0.0151) 20.1 (PM_{10}, 0.0051)
Schwartz and Pitcher (1989); U.S. EPA (1986)	**Location:** Chicago, IL **Yr:** 1976–1980 **Subjects**: Black children, 0–5 yr (n = 5,476) **Analysis**: Multivariate regression of blood Pb with mass of Pb in gasoline (derived from gasoline consumption data and Pb concentrations in gasoline for the United States)	**Model:** Linear **Blood Pb:** 18–27 µg/dL (mean range)[h] **Air Pb:** 0.36–1.22 µg/m^3 (annual maximum quarterly mean)[j]	8.6 (0.75)[i]
Tripathi et al. (2001)	**Location:** Mumbai, India (multiple residential locations) **Yr:** 1984–1996 **Subjects**: 6–10 yr (n = 544) **Analysis**: Regression of residential location-specific average blood Pb and air Pb data	**Model:** Linear **Blood Pb:** 8.61–4.4 µg/dL (GM range for residential locations) **Air Pb:** 0.10–1.18 µg/m^3 (GM range of 24-hour samples at residential locations)	3.6 (0.45)[k]
Richmond-Bryant et al. (2014); Richmond-Bryant et al. (2013)	**Location:** United States (contiguous states) **Yr:** 1988–1994, 1999–2008 **Subjects**: 1–5 yr (n = 759), 6–11 yr (n=516) **Analysis**: Age-stratified linear mixed effects models were run to assess the relationship of PbB with PbA, with and without covariates (age, household size, mother's age, poverty-income ratio, and street length)	**Model:** Log-Log **Blood Pb:** 1.7–4.5 µg/dL (range of medians among surveys and ages) **Air Pb:** 0.011–0.037 µg/m^3 (range of median annual averages among surveys and ages)	**1–5 yr** 16.4 (0.037)[l] 15.3 (0.011) **6–11 yr** 15.7 (0.036) 16.5 (0.016)

Reference	Study Methods	Model Description	Blood Pb–Air Pb Slope[a]
Zahran et al. (2013a)	**Location:** Detroit, MI **Yr:** 2001–2009 **Subjects:** 0–<1 yr (n = 19,265), 1–<2 yr (n = 75,070), 2–<3 yr (n = 58,500), 3–<4 yr (n = 66,507), 4–<5 yr (n = 67,061), 5–<6 yr (n = 34,073), 6–<7 yr (n = 18,911), 7–<8 yr (n = 8,649), 8–<11 yr (n = 13,610) **Analysis:** Age-stratified fixed effect regression controlling for confounding variables (Pb facility, capillary blood draw, sex, yr, meteorology)	**Model:** Log-Log **Blood Pb:** <5 µg/dL (67%), ≥5 µg/dL (33%) **Air Pb:** 0.004 ± 0.001 µg/m^3 (monthly mean ± SD)	**0 yr:** 34.0 (0.004)[m] **1 yr:** 57.3 (0.004) **2 yr:** 62.5 (0.004) **3 yr:** 37.2 (0.004) **4 yr:** 30.9 (0.004) **5 yr:** 35.5 (0.004) **6 yr:** 24.8 (0.004) **7 yr:** 21.3 (0.004) **8–10 yr:** 16.7 (0.004)
Child Populations – Air and Soil			
Ranft et al. (2008)	**Location:** Germany **Yr:** 1983–2000 (blood Pb and air Pb), 2000–2001 (soil Pb)[n] **Subjects:** 6–11 yr (n = 843) **Analysis:** Pooled multivariate regression of five cross-sectional studies	**Model:** Log-Linear **Blood Pb:** 2.21–3.6 µg/dL (5th–95th percentile) **Air Pb:** 0.03–0.47 µg/m^3 (5th–95th percentile of annual average)	3.2, 6.4[o]
Mixed Child-Adult Populations			
Schwartz and Pitcher (1989); U.S. EPA (1986)	**Location:** United States **Yr:** 1976–1980 **Subjects**: NHANES II, 0.5–74 yr, whites (n = 9,987) **Analysis:** Multivariate regression of blood Pb with mass of Pb in gasoline (derived from gasoline consumption data and Pb concentrations in gasoline for the United States)	**Model:** Linear **Blood Pb:** 11–18 µg/dL[i] (mean range)[h] **Air Pb:** 0.36–1.22 µg/m^3 (annual maximum quarterly mean)[j]	9.3 (0.75)[p]

Reference	Study Methods	Model Description	Blood Pb–Air Pb Slope[a]

BLL = blood lead level; GM, geometric mean; GSD, geometric standard deviation; mo = month; NHANES = National Health and Nutrition Examination Survey; PbA, air Pb concentration (μg/m^3); PbB, blood Pb concentration (μg/dL); PM = particulate matter; TSP = total suspended particles; yr = years

[a]Slope is predicted change in blood Pb (μg/dL per μg/m^3) at central estimate of air Pb for the study (shown in parentheses), except for Ranft et al. (2008) in which the slope from the paper was used because a regression equation was not available. The central estimate for Brunekreef (1984) and 2014); (Richmond-Bryant et al., 2013) was the median of air Pb concentrations, the central estimate for Meng et al. (2014) was the GM of air Pb concentrations, and for all other studies the mean was used. For multiple regression models, the slope factor was based only on air Pb coefficient and intercept. Depending on the extent to which other variables modeled also represent air Pb, this method may underestimate the slope attributable to air pathways. In single regression models, the extent to which nonmodeled factors, unrelated to air Pb exposures, exert an impact on blood Pb that covaries with air Pb may lead to the slope presented here to overrepresent the role of air Pb.

[b]log(PbB) = log(PbA) × 0.09 + 0.58

[c]ln(PbB) = ln(PbA) × 0.3485 + 2.853

[d]ln(PbB) = ln(PbA) × 0.2159 + 2.620

[e]ln(PbB) = ln(PbA) × 0.24 + 3.17

[f]PbB = PbA × 7.0

[g]1–5 years [TSP, ln(PbB) = ln(Pb A) × 0.056 + 1.024; PM_{10}, ln(PbB) = ln(Pb A) × 0.104 + 1.213]; 6–11 years [TSP, ln(PbB) = ln(Pb A) × 0.028 + 0.596; PM_{10}, ln(PbB) = ln(Pb A) × 0.073 + 0.725]

[h]Observed blood Pb values not provided; data are for regressed adjusted blood Pb.

[i]PbB = PbA × 8.6

[j]Based on air Pb data for United States (1986 Pb AQCD) as a surrogate for Chicago.

[k]PbB = Pb A × 3.6

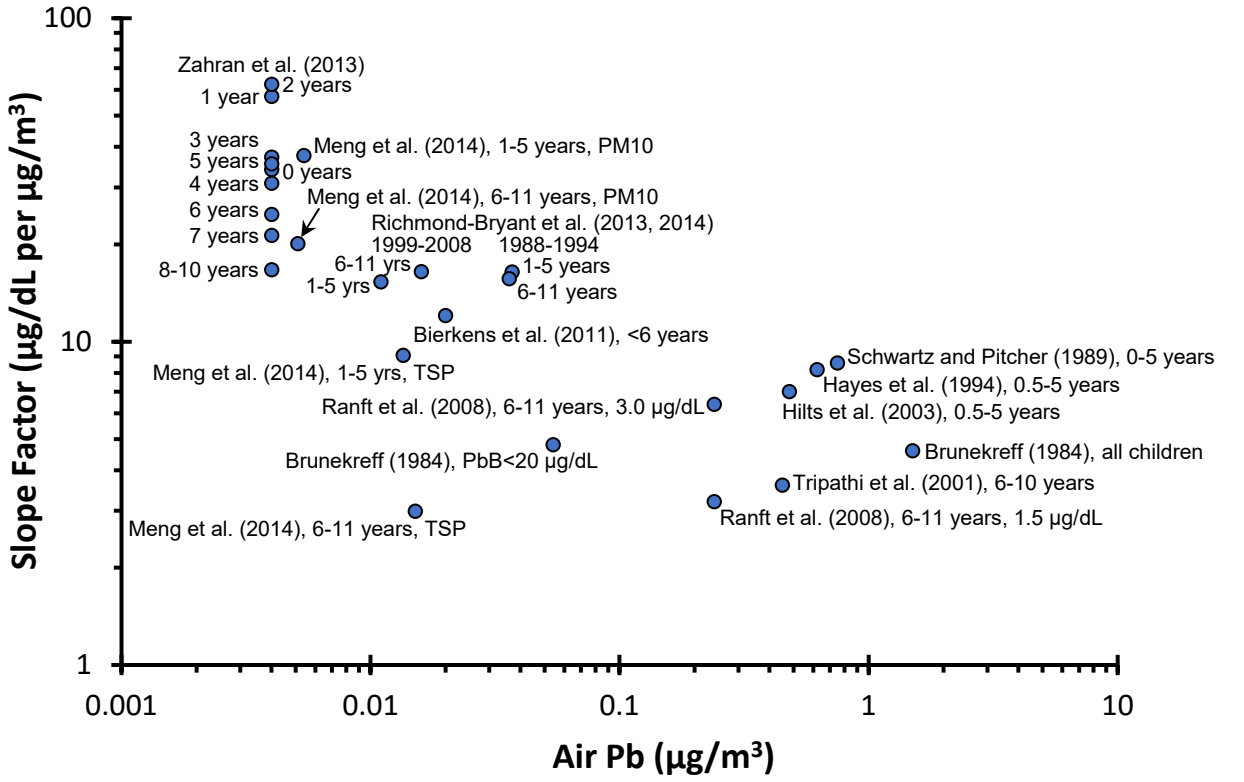
[l]1–5 years [1988–1994, ln(PbB) = ln(Pb A) × 0.1395 + 1.9315; 1999–2008, ln(PbB) = ln(Pb A) × 0.0755 + 1.1419]; 6–11 years [1988–1994, ln(PbB) = ln(Pb A) × 0.1535 + 1.8118; 1999–2008, ln(PbB) = ln(Pb A) × 0.1552 + 1.1709]

[m]0 years [ln(PbB) = ln(Pb A) × 0.080 + 0.973]; 1 years [ln(PbB) = ln(Pb A) × 0.087 + 1.449]; 2 years [ln(PbB) = ln(Pb A) × 0.069 + 1.669]; 3 years [ln(PbB) = ln(Pb A) × 0.040 + 1.535]; 4 years [ln(PbB) = ln(Pb A) × 0.036 + 1.432]; 5 years [ln(PbB) = ln(Pb A) × 0.043 + 1.431]; 6 years [ln(PbB) = ln(Pb A) × 0.031 + 1.333]; 7 years [ln(PbB) = ln(Pb A) × 0.026 + 1.331]; 8–10 years [ln(PbB) = ln(Pb A) × 0.023 + 1.192]; the mean Pb air concentration was provided by authors to EPA as a correction to their paper.

[n]Study that considered air Pb and soil Pb, wherein the air Pb-blood Pb relationship was adjusted for soil Pb.

[o]Slope provided in paper with background blood Pb level of 1.5 and 3 μg/dL, respectively, and a GM blood Pb ratio of 2.55 for ambient air.

[p]PbB = PbA × 9.63



Source: Figure based on Richmond-Bryant et al. (2014) with data from Table 2-13.

Figure 2-16 Slope factors for blood Pb as a function of air Pb.

Bierkens et al. (2011) used published and publicly available blood Pb data and air Pb data from a European Environment Agency database. Data were subdivided into four age groups: adults (+18 y; n = 174; 1999–2008), secondary school children (between 13 and 18 y; n = 4; 2006), primary school children (between 6 and 12 years; n = 123; 1983–1999), and preschool children (<6 years of age; n = 28; 1999–2008). Nonlinear regression of preschool children data showed a statistically significant relationship between blood Pb and air Pb [Log(blood Pb) = 0.58 + 0.09 × Log(Air Pb); $r^2 = 0.1925$; p = 0.0135]. For primary school children, no statistically significant association was observed. Children were located in Belgium (preschool, n = 8), the Czech Republic (primary school, n = 10) Germany (preschool, n = 3; primary school, n = 50), Finland (preschool, n = 3), Netherlands (preschool, n = 5), and Poland (preschool, n = 9; primary school, n = 63).

Richmond-Bryant et al. (2014); Richmond-Bryant et al. (2013) merged participant-level data for PbB from 1988–1994 and 1999–2008 NHANES surveys with PbA data for TSP from the EPA AQS. A 4-km neighborhood scale was used to represent PbA concentrations in urban areas (not near sources) to merge with NHANES data. In Richmond-Bryant et al. (2013), effect of PbA on PbB was estimated using adjusted and unadjusted models for the 1988–1994 and 1999–2008 time periods. In both models, the estimated effect (i.e., the regression slope, β_{PbA}) was higher for the earlier time period. In addition, when

the effect estimates calculated in this study were compared with values reported in older studies (Bierkens et al., 2011; Hayes et al., 1994; Brunekreef, 1984), a declining trend was observed, indicating a decrease in the influence of PbA on PbB over this time. The authors also note that for young children (1–5 years), the effect estimate for 1999–2008 data decreased when models included covariate factors, whereas the effect estimate for the 1988–1994 data was not significantly different between adjusted and unadjusted models. The authors suggested this finding may indicate that estimates of PbA on blood Pb may have a positive bias when not corrected for covariates, and this inflation may be more apparent at lower air PbA concentrations. In Richmond-Bryant et al. (2014), slope factors were estimated by Equation 2-2 and compared with other published data. In Table 2-13 and Figure 2-16, the slope factors were calculated using the median blood Pb of children because they were reported for age grouping (1–5 and 6–11 years) and NHANES survey period (1998–1994 and 1999–2008), whereas mean blood Pb was not reported. The authors concluded their NHANES regression results, compared with those from the literature, show the slope factor increases with decreasing air Pb among children 0–11 years of age.

Meng et al. (2014) merged participant-level data for blood Pb from 1999–2008 NHANES with air Pb data for TSP, PM_{10}, and $PM_{2.5}$ from the EPA AQS. A 4-km neighborhood scale was used to represent PbA concentrations in urban areas (not near sources) to merge with NHANES data. This was the first (and currently only) study comparing the relationship between blood Pb and airborne Pb among multiple size fractionated PM samplers rather than TSP samplers only. The impetus for this research was, in part, due to another EPA study (Cho et al., 2011) showing the mass median diameter of airborne Pb had shifted from <2.5 µm prior to the phase-out of leaded gasoline to somewhere between 2.5 and 10 µm after the phase-out, which might alter exposure pathways and PbA-PbB relationships. They examined the relationship between PbA and PbB by particle size (TSP, PM_{10}, and $PM_{2.5}$) and by age groups included in NHANES sample design (only children <12 years are presented in Table 2-13). PbA in PM_{10} was significantly ($p < 0.01$) related to PbB for all age groups. While PbA in TSP was significantly ($p < 0.05$) related to PbB for the 12–19 and 20–59 age groups, it was not statistically significant for children <12 years of age for Pb-TSP. However, it is provided in Table 2-13 and Figure 2-16 for comparison with other recent studies (Richmond-Bryant et al., 2014; Richmond-Bryant et al., 2013) that used Pb-TSP. The data for $PM_{2.5}$ are not presented in Table 2-13 or Figure 2-16 since there was no significant relationship between blood Pb and air Pb for any age group. The lack of a significant relationship for $PM_{2.5}$ may be attributed to airborne Pb being found associated with particles larger than 2.5 µm (Cho et al., 2011) during the 1999–2008 period. However, the authors also note the data for $PM_{2.5}$ are inherently more uncertain than the other air Pb measurements used because a large portion (~60%) of the $PM_{2.5}$ PbA were below detection limits compared with TSP (25%) and PM_{10} (34%). To derive slope factors at the central tendency for air Pb, it was necessary to solve for β_0 (see Equation 2-2) using data from Tables 2 and 3 of Meng et al. (2014). It was also necessary to use the GM air Pb from Table 1 of Meng et al. (2014) to calculate slope factors as the mean was not available. The GM also showed more variation between age groups than the median and thus was assumed more representative of the central tendency. An important finding from this study was that blood Pb was more consistently and strongly associated with PM_{10} than either TSP or $PM_{2.5}$.

Richmond-Bryant et al. (2015) provided the first study assessing effect modification of age, sex, housing age, and race/ethnicity on the relationship between blood Pb and air Pb. The authors used merged participant-level data for blood Pb from 1999–2008 NHANES with EPA AQS Pb-PM_{10} data because their prior work (Meng et al., 2014) showed Pb-PM_{10} data had the strongest associations with blood Pb. Consistent with their prior studies, the authors merged NHANES data with 4-km neighborhood scale PbA concentrations to represent urban areas not near sources. Effect estimates (i.e., the regression slope, β_{PbA}) were higher for children (1–5, 6–11, and 12–19 years) than for adults or all ages. Living in pre-1950 housing contributed to a higher effect estimate for 1- to 5-year-old children, but not for older ages.

Zahran et al. (2013a) examined the association between children's blood Pb and Pb in air and suspended soil in Detroit, MI using data acquired from January 2001 to December 2009. Estimates for resuspended soil concentrations were derived from measurements of airborne elements known to originate from soil at specific ratios (aluminum, silica, calcium, iron, and titanium). Measurements for airborne Pb and elements used to calculate atmospheric soil concentrations were obtained from four TSP sampling sites in the Detroit metropolitan area. Blood Pb data were obtained from the Michigan Department of Community Health. Concentrations of both Pb and resuspended soil in air were highest in June–September of each year, peaking in August. Air Pb and resuspended soil were 1.45-times and 1.62-times higher, respectively, in August relative to January. Children's blood Pb was also elevated in July–September with peaks in July and August that were 1.13-times (95% CI: 1.12, 1.14) greater than in January. The authors' analyses showed daily variation in air Pb was associated statistically with daily variation in resuspended soil, suggesting resuspended soil is the major source of urban air Pb. However, they note the effect may be more significant in younger children. Their model found a standard deviation rise in atmospheric Pb is associated with a 0.232 µg/dL (95% CI: 0.203 to 0.26 µg/dL) increase in monthly average BLLs of children 0–2 years old compared with a 0.152 µg/dL (95% CI: 0.13 to 0.173 µg/dL) increase in children ≥6 years old. They note this outcome is consistent with prior research and attribute this to higher exposure in younger children through ingestion of fine particles during hand-to-mouth contact. Richmond-Bryant et al. (2014) reported a slope factor of ~60 µg/dL per µg/m^3 for 1- to 2-year-old children in this study, which is the largest illustrated in Figure 2-16.

While the results of the Zahran et al. (2013a) study demonstrated children's BLLs in Detroit varied with season, attributing this variability solely to air Pb does not account for changes to children's BLLs resulting from seasonal changes in Pb in other exposure media. For example, water Pb concentrations in flushed water samples have been observed to be increased in the summer relative to the winter (Ngueta et al., 2014; Deshommes et al., 2013). Although magnitude of water Pb concentrations was considerably greater in homes with Pb-service lines than without, the water Pb concentrations were five to six times greater in July relative to December in both cases, based on Figure 1 of Ngueta et al. (2014). Recent modeling of soil/dust ingestion rates by Özkaynak et al. (2022) found mean daily soil ingestion rates to be approximately doubled (based on Tables S7–S10 of the paper) in the summer relative to the rest of the seasons by increasing from 8 to 15 mg/day in 1- to <2-year-olds, 20 to 47 mg/day in 2- to <3-year-olds, and from 23 to 57 mg/day in 3- to <6-year-olds. Consider the effects on blood Pb from

modest soil Pb (no dust) and water Pb concentrations of 50 ppm (i.e., mg/kg) and 0.9 ppb (i.e., µg/L), respectively. To simulate season effects using IEUBK v2.0 for 1- to <6-year-old children, the default soil ingestion rate can be lowered by 25% for winter (relative to an annual rate), increasing the default soil ingestion rate by 170% to simulate summer (relative to an annual rate), and increasing the water Pb concentration by five times to simulate effects of season (i.e., 0.9 ppm in winter and 4.5 ppm in summer). This IEUBK v2.0 simulation predicts a winter-to-summer increase in the GM BLL of 0.7 µg/dL in 1- to <3-year-olds and 0.6 µg/dL in 3- to <6-year-olds. Figure SI1 of Zahran et al. (2013a) shows median seasonal change in blood Pb of ~0.8 µg/dL across all years of the study. Unaccounted for seasonal effects on water Pb and soil ingestion rates could account for most of the blood Pb changes attributed to air Pb by Zahran et al. (2013a).

2.5.2 Air Pb-Blood Pb Relationships in Adults

2.5.2.1 General Populations

Several of the new publications since the last Pb ISA (U.S. EPA, 2013) provide estimates of slope factors for both children and adults. As the methods of these new publications are discussed above in Section 2.5.1, only the results for adults contrasted with those for children are provided here. Bierkens et al. (2011) analyzed the blood Pb – air Pb relationship in 174 adults (+18 years; 1981–2008; 70 males, 84 females, 20 unspecified). Regression results for women [Log(blood Pb) = 0.79 + 0.34 × Log(Air Pb); $r^2 = 0.3922$; $p \leq 0.001$] and men [Log B-Pb = 0.97 + 0.44 × Log(Air Pb); $r^2 = 0.5158$; $p \leq 0.001$] yielded respective slope factors of 11 and 17 µg/dL per µg/m^3 at the central air Pb of 0.076 µg/m^3. Although the central air Pb was higher for these adults (0.076 µg/m^3) than preschool children (0.020 µg/m^3) in this study, the slope factors were still greater in the adult population. Although Richmond-Bryant et al. (2013) and Richmond-Bryant et al. (2014) assessed the relationship between air Pb and blood Pb in adults (ages 20–59 years and >60 years) for the 1988–1994 and 1999–2008 periods, intercepts were not reported for the calculation of slope factors. However, the effect estimate β_{PbA} was similar in magnitude between children and 20- to 59-year-old adults. For ≥60-year-old adults, the effect estimate β_{PbA} was also similar to children in the 1988–1994 period, whereas β_{PbA} was negative in the later 1999–2008 period. For the 1999–2008 period and air Pb in PM_{10}, Meng et al. (2014) reported BLLs were more sensitive to the changes in PbA in children (1–5 and 6–11 years) and older adults (≥60 years) than teenagers (12–19 years) and adults (20–59 years). Slope factors (µg/dL per µg/m^3) estimated for this study by rank are 38 (1- to 5-year-olds), 30 (≥60 years), 20 (6- to 11-year-olds), 11 (12- to 19-year-olds), and 8 (20- to 59-year-olds). The negative β_{PbA} for older adults (≥60 years) during the 1999–2008 period was also observed by Meng et al. (2014) for TSP but not for PM_{10} data.

2.5.2.2 Occupational Cohorts

At the time of the 1986 Pb AQCD, there was a great deal of information on blood Pb responses to air Pb exposures of workers in Pb-related occupations (U.S. EPA, 1986). Almost all such exposures were at air Pb exposures far in excess of typical nonoccupational exposures and usually did not account for other potential sources of Pb exposure. The air Pb-blood Pb slopes in these studies were generally much less (i.e., 0.03–0.2; 1986 AQCD, p. 11–106) than those observed in children when considering aggregate air Pb contributions (i.e., 3–5; 1986 AQCD, p. 11–106). In addition, the PbA in occupational studies are typically collected at much shorter durations (e.g., over an 8-hour workday) compared with ambient air Pb monitoring (which generally involves 24-hour samples), making it difficult to draw comparisons between occupationally and nonoccupationally-exposed populations. Therefore, only a few occupational studies are presented below to demonstrate that more recent air Pb and BLLs remain much higher in these studies compared with those conducted in the general population.

Rodrigues et al. (2010) examined factors contributing to variability in blood Pb concentration in New England bridge painters, who regularly use electric grinders to prepare surfaces for painting. The study included 84 adults (83 males, 1 female) who were observed during a 2-week period in 1994 or 1995. The GM air Pb concentration obtained from personal PM samplers worn over the workday was 58 $\mu g/m^3$ (GSD 2.8), with a maximum daily value of 210 $\mu g/m^3$. Hand-wipe samples were collected and analyzed for Pb (GM = 793 µg, GSD 3.7). Blood Pb samples were collected at the beginning of the 2-week period (GM = 16.1 µg/dL, GSD 1.7; a level substantially above the general population) and at the end of the period (GM = 18.2 µg/dL, GD = 1.6). Associations between exposure variables and blood Pb concentrations were explored with multivariate regression models. When the model excluded hand-wipe data, the regression coefficient for the relationship between ln[blood Pb concentration (µg/dL)] and ln[air Pb ($\mu g/m^3$)] was 0.11 (SE = 0.05, p = 0.03). This corresponds to a slope of 0.009 µg/dL per $\mu g/m^3$ at the GM air Pb concentration for the study. A second regression model included hand-wipe Pb (n = 54) and yielded a regression coefficient of 0.05 (SE = 0.07, p = 0.45), which corresponds to a slope of 0.02 µg/dL per $\mu g/m^3$ at the GM air Pb concentration for the study.

Two other studies examined the air Pb-blood Pb relationship in occupational settings at higher air Pb concentrations (GM of 82 and 111 $\mu g/m^3$ for Pb battery and crystal workers, respectively) (Pierre et al., 2002; Lai et al., 1997). BLLs for the Pb battery workers averaged 56.9 µg/dL (SD 25.3); for the crystal workers, it averaged 21.9 µg/dL. Both studies employed log-log regression models, resulting in slopes of 0.49 (Pierre et al., 2002) and 0.08 (Lai et al., 1997).

2.5.3 Soil Pb-Blood Pb Relationships

Slope factor models represent the empirically based relationships between BLLs and intake of Pb and/or Pb concentrations in environmental media. Section 3.5.3 of the 2013 Pb ISA (U.S. EPA, 2013)

provides a description of these models and past reviews of environmental Pb-blood Pb data to develop these relationships. The EPA Adult Lead Methodology is a slope factor model that has had extensive use in the EPA Superfund Program. The 2006 AQCD (U.S. EPA, 2006a) and 2013 Pb ISA (U.S. EPA, 2013) also explored the relationship between blood Pb in children and environmental Pb concentrations. Several analyses of epidemiologic data found soil and dust exposures were significant predictors of blood Pb concentrations. Mielke and co-authors have published a series of papers (Mielke et al., 2019b; Zahran et al., 2011; Mielke et al., 2007) demonstrating the importance of soil Pb as a source of children's Pb exposures in New Orleans and other cities. The New Orleans data they developed were especially extensive (>5,000 surface soil samples; >50,000 blood Pb samples) and included multiple time points demonstrating a now declining pattern of soil Pb concentrations and BLLs. The statistical analyses in these papers fitted a nonlinear model between soil Pb level (SLL) and BLL, which becomes increasingly steep for SLLs below 100–200 ppm, as shown in Figure 2-17 that was created using data from the Mielke et al. (2019b) study. The subsequent Figure 2-18 shows the rapid decline in the slope of the soil Pb to blood Pb relationship that is most apparent at soil Pb concentrations <20 mg/kg.

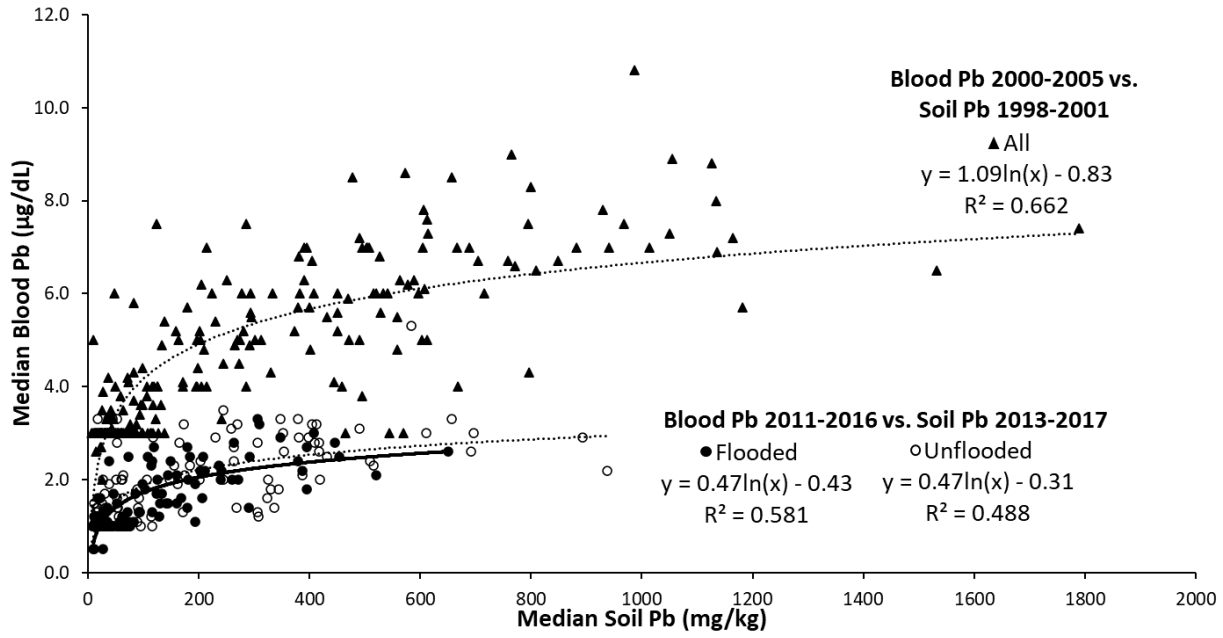


Figure 2-17 Blood Pb versus soil Pb for two New Orleans surveys completed in 2001 and 2017.

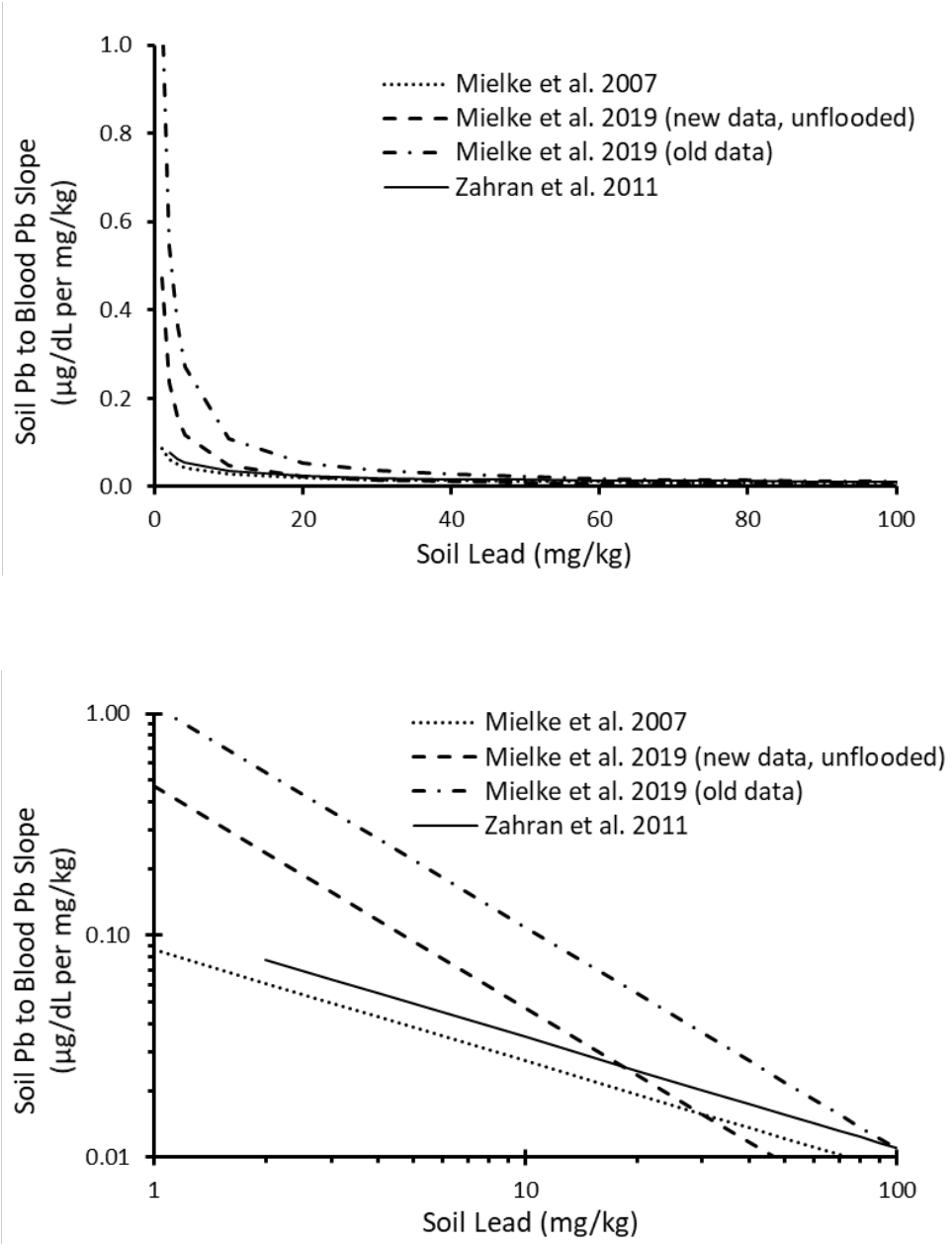


Figure 2-18 Comparison of slope factors in New Orleans data on linear-linear (top) and log-log (bottom) plots.

While this work has been critical in showing the extent to which Pb contamination disproportionally impacts vulnerable populations in the New Orleans community, it does not provide definitive analysis of the relationship between soil Pb concentrations and BLLs at low SLLs (e.g., <100 ppm). There are several uncertainties in the analyses provided in these publications. Venous and capillary data were combined in this analysis; however, capillary tests tend to overestimate BLLs while venous samples, which are more accurate (Wang et al., 2019), are used to confirm EBLLs (i.e., BLLs that

exceed CDC's BLRV or, formerly, the "level of concern") identified using capillary samples. As a result of this BLL screening approach, blood Pb measurements may not be statistically independent because multiple BLLs, including combinations of capillary and venous samples or multiple venous measurements, may be recorded for one child. An additional complexity is that the concentration used to characterize a BLL as elevated (and requiring follow-up with confirmatory venous samples) was lowered from 10 to 5 µg/dL in 2012 and to 3.5 µg/dL in 2021 (Ruckart et al., 2021). As a result of this change, confirmatory venous samples between 5 and 10 µg/dL are likely to be relatively rare before the BLRV was established in 2012. Additionally, the LODs for the analytical methods vary over time, depending on the sample type and laboratory, but may not be recorded in BLL databases that are used for public health screening purposes. In practice, an LOD might be recorded as the measured BLL, making it difficult to distinguish BLLs that are below the LOD from BLLs that are measured at or near the LOD. Notably, BLLs may be measured using analyzers that have LODs as high as 3.3 µg/dL, which is in the range of current health concerns. The median BLLs from Mielke et al. (2019b) show many are reported at levels that are less than or equal to the anticipated LOD of the methods: 3.0 µg/dL and 1.0 µg/dL for the first and second survey, respectively.

Mielke et al. (2007) and Mielke et al. (2019b) did not account for potential individual-level confounding. However, bivariate relationships between BLL, SLL, age of housing, and distance from the post office, which is inversely associated with Pb exposure, were examined in Mielke et al. (2016) and Egendorf et al. (2021a). Egendorf et al. (2021a) analyzed these SLL and BLL data for New Orleans by several variables separately, including distance from the city center, residential racial population, and household income over two time periods, but did not include a multivariate analysis. Table 2 of Egendorf et al. (2021a) provides median values for Pb and demographic variables by city sector and shows sectors closest to the urban core had the highest BLLs, highest SLLs, were primarily black in racial makeup, had higher population density, and lower income. All of these variables may reflect important factors influencing BLLs and that there would be important confounding relationships that would limit the interpretation of univariate modeling of BLLs versus SLLs. In addition, the publications do not provide information on how the authors selected the most appropriate statistical model to capture the relationship between SLL and BLL data. However, it should be noted there is some evidence for nonlinearities at low PbA, as discussed in Section 2.5.1.

2.6 Biokinetic Models of Pb Exposure-Blood Pb Relationships

An alternative to regression models is mechanistic models, which attempt to specify all parameters needed to describe the mechanisms (or processes) of transfer of Pb from the environment to human tissues. Such mechanistic models are more complex than regression models; this added complexity introduces challenges in terms of their mathematical solution and empirical verification. However, by incorporating parameters that can be expected to vary spatially or temporally, or across individuals or populations, mechanistic models can be extrapolated to a wide range of exposure scenarios,

including those that may be outside of the domain of paired predictor-outcome data used to develop the model. Exposure-intake models, a type of mechanistic model, are highly simplified mathematical representations of relationships between levels of Pb in environmental media and human Pb intakes (e.g., µg Pb ingested per day). These models include parameters representing processes of Pb transfer between environmental media (e.g., air to surface dust) and to humans, including rates of human contact with the media and intakes of the media (e.g., g soil ingested per day). Intake-biokinetic models provide the analogous mathematical representation of relationships between Pb intakes and Pb levels in body tissues (e.g., blood Pb concentration). Biokinetic models include parameters that represent processes of Pb transfer (a) from portals of entry into the body and (b) from blood to tissues and excreta. Linked together, exposure-intake and intake-biokinetic models (i.e., integrated exposure-intake-biokinetic models) provide an approach for predicting blood Pb concentrations (or Pb concentrations in other tissues) that corresponds to a specified exposure (medium, concentration, and duration). Detailed information on exposure and internal dose can be obtained from controlled experiments but almost never from epidemiologic observations or from public health monitoring programs. Exposure intake-biokinetic models can provide these predictions in the absence of complete information on the exposure history and blood Pb concentrations for an individual (or population) of interest. Therefore, these models are critical for applying epidemiologic-based information on blood Pb-response relationships to the quantification and characterization of human health risk. These models are also critical for assessing the potential impacts of public health programs directed at mitigating Pb exposure or remediating contaminated sites.

However, these models are not without their limitations. Human exposure-biokinetic models include large numbers of parameters, which are required to describe the many processes that contribute to Pb intake, absorption, distribution, and elimination. The large number of parameters complicates the assessment of confidence in individual parameter values, many of which cannot be directly measured. Statistical procedures can be used to evaluate the degree to which model outputs conform to "real-world" observations, and values of influential parameters can be statistically estimated to achieve good agreement with observations. Still, uncertainty can be expected to remain regarding parameters in complex exposure-biokinetic models. Such uncertainties need to be identified and their impacts on model predictions quantified (i.e., sensitivity analysis or probabilistic methods).

The ICRP Pb biokinetics model (Pounds and Leggett, 1998) consists of a systemic biokinetics model (Leggett, 1993) and absorption factors for inhaled Pb (ICRP, 1995). The Leggett model simulates age-dependent kinetics of tissue distribution and excretion of Pb ingestion and inhalation intakes. This model was originally developed for the purpose of supporting radiation dosimetry predictions, and it has been used to develop cancer risk coefficients for internal radiation exposures to Pb and other alkaline earth elements that have biokinetics similar to those of calcium (ICRP, 1993). Although the ICRP model has not been validated by EPA as a regulatory model for Pb risk assessment, it has been applied in Pb risk assessment (Abrahams et al., 2006; Lorenzana et al., 2005; Khoury and Diamond, 2003), and portions of the model have been incorporated into the AALM.

The IEUBK model was designed to assess changes in blood Pb of children from birth to 7 years of age over periods of no less than a month. Section 4.4.5 of the 2006 AQCD (U.S. EPA, 2006a) provides an introduction to the IEUBK model along with components. EPA has recommended using the IEUBK model at Superfund sites and Resource Conservation and Recovery Act Corrective Action sites to derive a residential Preliminary Remediation Goal for Pb in soil that allows no more than a 5% probability that children exceed a specified target BLL (U.S. EPA, 1994a). The predictive ability of the IEUBK model has been evaluated following established guidelines for use of children's BLLs (measured in the fall to capture peak blood Pb concentrations) paired with measurements of Pb in environmental media. The IEUBK model v0.99 was evaluated with children's blood Pb data paired with measurements of Pb in yard soil of their residences (Hogan et al., 1998). The evaluation assessed the predictive ability of IEUBK to estimate exceedances of a target BLL of 10 µg/dL. The elimination rates of Pb from the body were increased to the upper end of biologically plausible limits to lower IEUBK v0.99 predicted BLLs associated with Pb in soil [see p. 1564 of White et al. (1998) and pp. 32–33 of U.S. EPA (1994b). Thus, the rates of Pb intake from soil are aligned with elimination rates that are hard coded into the IEUBK model. Prior to release of IEUBK v2.0, which lowered the default ingestion rates of children, the predictive ability to estimate exceedances of target blood Pb of 5 µg/dL (GM blood Pb 2.3 µg/dL) was completed using children's blood Pb data paired with concentrations of Pb in yard soil and indoor dust, as well as bioavailability in those media (Brown et al., 2022; U.S. EPA, 2021a). SRC (2020) provides a full description of IEUBK v2.0, including all equations and parameters.

The AALM was created to expand the capability of EPA biokinetic modeling to include adolescents and adults and add the ability to assess the effect of intermittent Pb exposures. The AALM uses modeling concepts taken from Leggett, O'Flaherty, and others to enhance the accuracy of the model (U.S. EPA, 2006a; Maddaloni et al., 2005; O'Flaherty et al., 1998; O'Flaherty, 1998; Pounds and Leggett, 1998; Leggett, 1993; Leggett et al., 1993). Section 4.4.8 of the 2006 AQCD (U.S. EPA, 2006a) provides an introduction to the AALM and its components, including detailed introductions to the Leggett and O'Flaherty models. Since that time, the AALM has gone through significant development. In September 2019, the AALM Version 2.0 was publicly released and subsequently peer reviewed by an EPA Scientific Advisory Board (SAB) panel. Currently, the AALM is under revision to respond to SAB review comments. A detailed technical support document provides details related to all model parameters, equations, and evaluations performed prior to public release of AALM v2.0 (U.S. EPA, 2019b).

As described in Section 2.1.2, Zartarian et al. (2017) used the SHEDS-Multimedia model in combination with an approximation of the IEUBK model to estimate drinking water Pb contributions to blood Pb in U.S. children. In the SHEDS-IEUBK coupled methodology, the SHEDS-Multimedia model takes the place of the exposure and variability components of the IEUBK model by generating a probability distribution of Pb intakes across media. SHEDS-IEUBK relies on an approximation of the IEUBK biokinetics in the form of regression equations relating Pb uptake with BLL at specified months of life. Using these regression equations, the estimated BLL at a specified month of life assumes a constant rate of uptake from birth to the month of interest. Thus, SHEDS-IEUBK is a slope factor model,

not a biokinetic model. When interpreting the results of IEUBK and SHEDS-IEUBK modeling, it is important to recognize that the IEUBK model was developed, calibrated, and evaluated for site-specific risk assessments as described above, whereas the SHEDS-IEUBK methodology uses national databases to estimate exposure distributions for probabilistic, national-scale, population-based aggregate Pb exposure modeling.

2.7 Summary and Conclusions

2.7.1 Exposure

Exposure information discussed in this assessment builds upon conclusions of the 2013 Pb ISA (U.S. EPA, 2013), which built upon conclusions of the 2006 Pb AQCD (U.S. EPA, 2006a). U.S. population exposures have declined over time, as evidenced by the continued reduction in BLLs across the United States. Sources of exposure remain, both related to air sources and other sources and pathways.

Section 2.1 details possible exposure routes for Pb. The air-related pathways for Pb exposure occur through the inhalation of ambient air Pb, inhalation and ingestion of Pb in soil and/or resuspended indoor or outdoor dust, ingestion of drinking water contaminated with Pb deposited from the atmosphere, and Pb in dietary sources such as animals or plants that have taken up Pb that was deposited onto soil with which these organisms interacted. Non-air-related pathways include exposure to corrosion byproducts leaching into drinking water, as in the case of the Flint Water Crisis, occupational exposures to job-related Pb, hand-to-mouth contact with consumer goods, hand-to-mouth contact with paint chips or peeling paint containing Pb, and inhalation of dust related to Pb-containing paint or other materials in homes and demolition of older homes containing Pb. It is difficult to ascertain the original source of Pb involved with different exposure routes. As a result, a wide range of Pb exposures were included in this assessment.

Environmental Pb concentrations used to estimate exposure can be collected from air monitoring, soil Pb samples, dust Pb samples, and dietary sources including water Pb samples and food Pb samples. Biokinetic models, such as the IEUBK and AALM models, simulate human exposure to Pb from multiple sources and through intake routes of inhalation and ingestion. The IEUBK model was designed to assess changes in blood Pb of children from birth to 7 years of age over periods of no less than a month. The predictive ability of the IEUBK model has been evaluated following established guidelines for use of children's BLLs (measured in the fall to capture peak blood Pb concentrations) paired with measurements of Pb in environmental media. The AALM was designed to expand the capability of biokinetic modeling to include adolescents and adults and incorporates modeling concepts from various sources to enhance its accuracy.

There is evidence Pb concentrations in the environment have decreased within the United States over time. As noted in Appendix 1, air Pb concentration in the United States has continued to decline. The AHHS II found the number of homes with Pb-based paint has also decreased. However, environmental Pb concentrations can vary across urban centers as a result of local meteorology, and contributions of point/nonpoint sources of airborne Pb may still lead to exposure. Pb from resuspended dust can also make a contribution to ambient air Pb concentrations. Airborne particles of Pb tend to be small but overall have shifted to larger sizes over the past few decades as a result of the United States phasing out leaded gasoline in automobiles. Pb particles in soil and resuspended dust tend to be coarser. Humans can also be exposed to Pb in soil through hand-to-mouth contact. This is the main pathway of Pb exposure for children, who play closer to the ground and in outdoor areas that may be contaminated with Pb. Finer soil particles (<63 μm in diameter) adhere to human hands more efficiently than larger particles.

Both biological and nonbiological factors can contribute to increased exposure and associated BLLs. EBLLs have been linked to proximity to Pb-emitting sources. Young children have higher risk of exposure due to behaviors close to the ground and EBLLs due to higher bone turnover and lower overall body mass. Seniors may have EBLLs because of higher lifetime Pb exposure due to higher exposures before broad Pb regulation. Factors such as recent immigration, being a member of a racial/ethnic minority, and lower SES have been shown to be linked to increased BLLs. There may also be a variety of co-contaminants present with Pb in the environment, including heavy metals, volatile compounds, and PAHs, depending on the source and environmental pathway.

2.7.2 Toxicokinetics

The major routes of exposure to Pb are ingestion and inhalation. Both particle size and solubility affect systemic absorption of Pb in the respiratory tract. Section 2.2.1.1 summarizes recent research on the bioaccessibility of inhaled Pb in the lung and GI tract as a function of exposure source and particle size. The absorption of Pb in the GI tract is influenced by physiological states of the individual and physiochemical characteristics of the Pb-bearing material ingested. The absence of food in the GI tract increases absorption of water-soluble Pb. Age and nutritional interactions of Pb with dietary elements, most notably Fe, Ca^{2+}, and Zn, may also affect GI absorption of Pb. The RBA of Pb has been tested for different Pb forms and sources, including in swine as summarized in Table 2-10. Research has demonstrated enrichment of Pb in smaller particle sizes (varied among studies, e.g., <50 or <100 μm), which also show greater bioaccessibility than larger particle sizes. As explored in the 2013 Pb ISA (U.S. EPA, 2013), the majority of Pb in the body is found in bone (roughly 90% in adults, 70% in children); only about 1% of Pb is found in blood. Pb in blood is primarily (~99%) bound to RBCs. It has been suggested that the small fraction of Pb in plasma (<1%) may be the more biologically labile and toxicologically active fraction of the circulating Pb. The relationship between Pb in blood and plasma is approximately linear at relatively low daily Pb intakes and at blood Pb concentrations below ~20–30 μg/dL and becomes curvilinear at higher blood Pb concentrations due to saturable binding to RBC

proteins. As BLL increases and the higher affinity binding sites for Pb in RBCs become saturated, a larger fraction of the blood Pb is available in plasma to distribute to brain and other tissues.

The burden of Pb in the body may be viewed as divided between a dominant slow compartment (bone) and smaller fast compartment(s) (soft tissues). Pb uptake and elimination in soft tissues is much faster than in bone. Pb accumulates in bone regions undergoing the most active calcification at the time of exposure. On the basis of Leggett (1993), trabecular bone is expected to receive 56% of Pb depositing from plasma to bone of adults and only 20% of the Pb depositing in 1-year-olds. Cortical bone receives 44% and 80% of Pb deposited from plasma to bone in adults and 1-year-olds, respectively. A high bone formation rate in early childhood results in the rapid uptake of circulating Pb into mineralizing bone; however, in early childhood, bone Pb is also recycled to other tissue compartments or excreted in accordance with a high bone resorption rate (O'Flaherty, 1995). Thus, much of the Pb acquired early in life is not permanently fixed in the bone.

The exchange of Pb from plasma to the bone surface is a relatively rapid process. Pb in bone becomes distributed in trabecular and dense cortical bone. The proportion of cortical to trabecular bone in the human body varies by age but, on average, is about 80% cortical to 20% trabecular. Of the bone types, trabecular bone is more reflective of recent exposures than cortical bone due to the slow turnover rate and lower blood perfusion of cortical bone. Some Pb diffuses to kinetically deeper bone regions, where it is relatively inert, particularly in adults. These bone compartments are much more labile in infants and children than in adults, as reflected by half-times for movement of Pb from bone into to the plasma (e.g., cortical half-time = 0.23 years at birth, 3.7 years at 15 years of age, and 23 years in adults; trabecular half-time = 0.23 years at birth, 2.0 years at 15 years of age, and 3.8 years in adults) (Leggett, 1993).

The dominant elimination phase of Pb kinetics in the blood, exhibited shortly after a change in exposure occurs, has a half-life of ~20–30 days in adults. In children under the age of 3 years, a half-time of only 6.4 days has been observed (Figure 2-7). An abrupt change in Pb uptake gives rise to a relatively rapid change in blood Pb to a new quasi-steady state, achieved in ~75–100 days (i.e., 3–4 times the blood elimination half-life). A slower phase of Pb clearance from the blood may become evident with longer observation periods following a decrease in exposure due to the gradual redistribution of Pb among bone and other compartments.

2.7.3 Pb Biomarkers

Trends in BLLs have been decreasing since 1976. NHANES revealed the GM blood Pb concentration among children 1–5 years of age, based on a sample from 2017–2018, was 0.670 µg/dL (95% CI: 0.600, 0.748), whereas the GM blood Pb concentration among adults ≥20 years of age from samples taken during the same period was 0.855 µg/dL (95% CI: 0.816, 0.895). A GM BLL of 0.753 µg/dL (95% CI: 0.723, 0.784) was representative of the entire U.S. population. Several studies have shown evidence of seasonality of BLLs, with peaks occurring during summer and fall. This is attributed

to several factors, including greater soil resuspension because of drier soil conditions during the warm season.

Because BLLs are, on average, becoming lower as a result of reductions in exposure, methodology has had to improve to measure BLLs at lower levels of detection. At lower BLLs, contamination of equipment can make a proportionally larger contribution to the BLL measured. Pb contamination can occur in laboratory reagents and supplies, as well as during sample collection. Laboratories have had to update equipment to measure at lower limits of detection from flame absorption spectroscopy in the 1970s to newer methods, such as ICP-MS analysis used today. Capillary blood samples are commonly collected due to their ease of collection (i.e., a finger prick) versus venipuncture for venous blood samples. Point-of-care instruments using ASV offer low-cost, "in office" results within minutes. However, capillary samples have been recorded as biased higher and result in more false positives than venous blood samples. CDC recommends a venous sample should be collected if a capillary test results in a value greater than or equal to the BLRV of 3.5 μg/dL. Bone measurements have advanced through the use of portable XRF, providing a less invasive way of measuring bone Pb and spatial measurements of bone Pb to inform how Pb is incorporated into bone.

BLL is the most commonly measured Pb biomarker in literature and has been correlated to air Pb concentrations, soil and dust Pb concentrations, and dietary Pb concentrations including tap water. BLL is influenced by both recent and long-term exposure history, along with contributions from Pb stored in bone. This contribution of bone Pb to blood Pb depends on duration and intensity of exposure, age, and other physiological stressors that affect bone remodeling beyond that which normally and continuously occurs. In children, largely due to faster exchange of Pb to and from bone, blood Pb is both an index of recent exposure and potentially an index of body burden. In adults and children, wherein exposure to Pb has effectively ceased or greatly decreased, a slow decline in blood Pb concentrations over a period of years is most likely due to the gradual release of Pb from bone. Bone Pb is an index of cumulative exposure and body burden. Even bone compartments should be recognized as reflective of differing exposure periods, with Pb in trabecular bone exchanging more rapidly with blood than Pb in cortical bone. This difference in the compartments makes Pb in cortical bone a better marker of cumulative exposure and Pb in trabecular bone more likely to be correlated with blood Pb, even in adults.

The concentration of Pb in urine follows blood Pb concentration in that it mainly reflects the exposure history of the previous few months and, therefore, is likely a relatively poor index of Pb body burden. There is added complexity with Pb in urine because concentration is also dependent upon urine flow rate, which requires timed urine samples that are often not feasible in epidemiologic studies. Hair as a biomarker has methodological issues because of contamination from environmental sources or artificial hair treatments. The neonatal line formed in deciduous teeth during birth can be used to distinguish between prenatal and postnatal dentine and enamel and can be used to discuss exposure history but has not been used extensively. Other biomarkers have been used to a lesser extent (e.g., Pb in saliva).

2.7.4 Air Pb-Blood Pb Relationships

Table 2-13 provides summaries of studies that measured air-to-blood Pb slopes in children. There is variability in study location, population, air and blood Pb concentrations, and analysis used among studies. Studies have described the blood Pb-air Pb slope as either log-log (Meng et al., 2014; Richmond-Bryant et al., 2013; Zahran et al., 2013a; Bierkens et al., 2011; Schnaas et al., 2004; Hayes et al., 1994; Brunekreef, 1984) or linear (Hilts, 2003; Tripathi et al., 2001; Schwartz and Pitcher, 1989). Much of the earlier literature on slope factors was summarized by Brunekreef (1984), who performed a meta-analysis using many of the relevant references in the 1986 AQCD (U.S. EPA, 1986) and found blood Pb versus air Pb slope β was smaller at high blood and air levels.

Newer studies after the time of leaded gasoline usage and not focused on communities near significant air Pb sources show increasing slope factors with decreasing air Pb concentrations. Figure 2-16 shows a range of slope factors as a function of air concentration data sets, including those of recent studies. Richmond-Bryant et al. (2014) compared NHANES regression results with those from the literature and found the slope factor increases with decreasing air Pb among children 0–11 years of age. Using 1999–2008 NHANES BLL data, Meng et al. (2014) found BLL was more consistently and strongly associated with PM_{10} than either TSP or $PM_{2.5}$.

Although slope factors increase with decreasing air Pb concentration, it is possible that contribution from non-air exposure pathways may lead to the high slope factors at low air concentrations. In other words, in older studies in which leaded gasoline or local sources were a major contributor to air Pb, there may be a greater likelihood of discerning the true effect of air Pb on blood Pb due to relatively less contribution from non-air exposure pathways. However, overarching distinctions between old and new studies should be made with caution given that Pb in all media, not just air, has decreased over time.

2.8 References

Aboel Dahab, AA; Elhag, DEA; Ahmed, AB; Al-Obaid, HA. (2016). Determination of elemental toxicity migration limits, bioaccessibility and risk assessment of essential childcare products. Environ Sci Pollut Res Int 23: 3406-3413. http://dx.doi.org/10.1007/s11356-015-5594-0.

Abrahams, PW; Follansbee, MH; Hunt, A; Smith, B; Wragg, J. (2006). Iron nutrition and possible lead toxicity: An appraisal of geophagy undertaken by pregnant women of UK Asian communities. Appl Geochem 21: 98-108. http://dx.doi.org/10.1016/j.apgeochem.2005.09.015.

ACCLPP (Advisory Committee on Childhood Lead Poisoning Prevention). (2013). Guidelines for measuring lead in blood using point of care instruments. Centers for Disease Control and Prevention. https://www.cdc.gov/nceh/lead/acclpp/20131024_pocguidelines_final.pdf.

Adgate, JL; Mongin, SJ; Pratt, GC; Zhang, J; Field, MP; Ramachandran, G; Sexton, K. (2007). Relationships between personal, indoor, and outdoor exposures to trace elements in PM2.5. Sci Total Environ 386: 21-32. http://dx.doi.org/10.1016/j.scitotenv.2007.07.007.

Aelion, CM; Davis, HT. (2019). Blood lead levels in children in urban and rural areas: Using multilevel modeling to investigate impacts of gender, race, poverty, and the environment. Sci Total Environ 694: 133783. http://dx.doi.org/10.1016/j.scitotenv.2019.133783.

Afridi, HI; Talpur, FN; Kazi, TG; Brabazon, D. (2015). Estimation of aluminum, arsenic, lead and nickel status in the samples of different cigarettes and their effect on human health of Irish smoker hypertensive consumers [Abstract]. Clin Lab 61: 1147-1156. http://dx.doi.org/10.7754/Clin.Lab.2015.141120.

Al-Modhefer, AJ; Bradbury, MW; Simons, TJ. (1991). Observations on the chemical nature of lead in human blood serum. Clin Sci (Lond) 81: 823-829. http://dx.doi.org/10.1042/cs0810823.

Alexander, FW; Clayton, BE; Delves, HT. (1974). Mineral and trace-metal balances in children receiving normal and synthetic diets. Q J Med 43: 89-111. http://dx.doi.org/10.1093/oxfordjournals.qjmed.a067380.

Almansour, KS; Arisco, NJ; Woo, MK; Young, AS; Adamkiewicz, G; Hart, JE. (2019). Playground lead levels in rubber, soil, sand, and mulch surfaces in Boston. PLoS ONE 14: e0216156. http://dx.doi.org/10.1371/journal.pone.0216156.

Almerud, P; Zamaratskaia, G; Lindroos, AK; Bjermo, H; Andersson, EM; Lundh, T; Ankarberg, EH; Lignell, S. (2021). Cadmium, total mercury, and lead in blood and associations with diet, sociodemographic factors, and smoking in Swedish adolescents. Environ Res 197: 110991. http://dx.doi.org/10.1016/j.envres.2021.110991.

Amaral, JH; Rezende, VB; Quintana, SM; Gerlach, RF; Barbosa, F, Jr; Tanus-Santos, JE. (2010). The relationship between blood and serum lead levels in peripartum women and their respective umbilical cords. Basic Clin Pharmacol Toxicol 107: 971-975. http://dx.doi.org/10.1111/j.1742-7843.2010.00616.x.

Anderson, MK; Amrich, M; Decker, KL; Mervis, CA. (2007). Using state lead poisoning surveillance system data to assess false positive results of capillary testing. Matern Child Health J 11: 603-610. http://dx.doi.org/10.1007/s10995-007-0196-1.

Apostolou, A; Garcia-Esquinas, E; Fadrowski, JJ; Mclain, P; Weaver, VM; Navas-Acien, A. (2012). Secondhand tobacco smoke: a source of lead exposure in US children and adolescents. Am J Public Health 102: 714-722. http://dx.doi.org/10.2105/AJPH.2011.300161.

Araki, S; Aono, H; Yokoyama, K; Murata, K. (1986). Filterable plasma concentration, glomerular filtration, tubular balance, and renal clearance of heavy metals and organic substances in metal workers. Arch Environ Occup Health 41: 216-221. http://dx.doi.org/10.1080/00039896.1986.9938336.

Araki, S; Sata, F; Murata, K. (1990). Adjustment for urinary flow rate: An improved approach to biological monitoring. Int Arch Occup Environ Health 62: 471-477. http://dx.doi.org/10.1007/BF00379066.

Arora, M; Austin, C; Sarrafpour, B; Hernández-Ávila, M; Hu, H; Wright, RO; Tellez-Rojo, MM. (2014). Determining prenatal, early childhood and cumulative long-term lead exposure using micro-spatial deciduous dentine levels. PLoS ONE 9: e97805. http://dx.doi.org/10.1371/journal.pone.0097805.

Arora, M; Ettinger, AS; Peterson, KE; Schwartz, J; Hu, H; Hernández-Avila, M; Tellez-Rojo, MM; Wright, RO. (2008). Maternal dietary intake of polyunsaturated fatty acids modifies the relationship between lead levels in bone and breast milk. J Nutr 138: 73-79. http://dx.doi.org/10.1093/jn/138.1.73.

Arruda-Neto, JDT; de Oliveira, MCC; Sarkis, JES; Bordini, P; Manso-Guevara, MV; Garcia, F; Prado, GR; Krug, FJ; Mesa, J; Bittencourt-Oliveira, MC; Garcia, C; Rodrigues, TE; Shtejer, K; Genofre, GC. (2009). Study of environmental burden of lead in children using teeth as bioindicator. Environ Int 35: 614-618. http://dx.doi.org/10.1016/j.envint.2008.12.005.

Arruda-Neto, JDT; Geraldo, LP; Prado, GR; Garcia, F; Bittencourt-Oliveira, MC; Sarkis, JES; Martinez-Lusardo, F; Lima-Cazorla, L; Rosa-Medero, D; Rodrigues, TE; Genofre, GC. (2010). Study of metals transfer from environment using teeth as biomonitor. Environ Int 36: 243-246. http://dx.doi.org/10.1016/j.envint.2009.12.003.

Aungst, BJ; Dolce, JA; Fung, HL. (1981). The effect of dose on the disposition of lead in rats after intravenous and oral administration. Toxicol Appl Pharmacol 61: 48-57. http://dx.doi.org/10.1016/0041-008X(81)90006-5.

Aungst, BJ; Fung, HL. (1985). The effects of dietary calcium on lead absorption, distribution, and elimination kinetics in rats. J Toxicol Environ Health 16: 147-159. http://dx.doi.org/10.1080/15287398509530726.

Azar, A; Trochimowicz, HJ; Maxfield, ME. (1973). Review of lead studies in animals carried out at Haskell Laboratory — Two-year feeding study and response to hemorrhage study. In Environmental health aspects of lead: Proceedings of an international symposium (pp. 199-210). Luxembourg: Commission of the European Communities.

Bahéna, ABV; Mendoza, OT; Godínez, MEM; Souto, SAS; Ruiz, J; Beristain, GH. (2017). Source apportionment of lead in the blood of women of reproductive age living near tailings in Taxco, Guerrero, Mexico: An isotopic study. Sci Total Environ 583: 104-114. http://dx.doi.org/10.1016/j.scitotenv.2017.01.030.

Balza, JS; Bikomeye, JC; Beyer, KMM; Rublee, C; Flynn, KE. (2022). Elevated blood lead levels of refugee children in the United States: a systematic review of recent literature (2011-2021) [Review]. Rev Environ Health. http://dx.doi.org/10.1515/reveh-2022-0015.

Bannon, DI; Abounader, R; Lees, PSJ; Bressler, JP. (2003). Effect of DMT1 knockdown on iron, cadmium, and lead uptake in Caco-2 cells. Am J Physiol Cell Physiol 284: C44-C50. http://dx.doi.org/10.1152/ajpcell.00184.2002.

Bannon, DI; Drexler, JW; Fent, GM; Casteel, SW; Hunter, PJ; Brattin, WJ; Major, MA. (2009). Evaluation of small arms range soils for metal contamination and lead bioavailability. Environ Sci Technol 43: 9071-9076. http://dx.doi.org/10.1021/es901834h.

Baranowska-Bosiacka, I; Kosińska, I; Jamioł, D; Gutowska, I; Prokopowicz, A; Rębacz-Maron, E; Goschorska, M; Olszowski, T; Chlubek, D. (2016). Environmental lead (Pb) exposure versus fatty acid content in blood and milk of the mother and in the blood of newborn children. Biol Trace Elem Res 170: 279-287. http://dx.doi.org/10.1007/s12011-015-0482-5.

Barbosa, F, Jr; Ramires, I; Rodrigues, MHC; Saint' Pierre, TD; Curtius, AJ; Buzalaf, MR; Gerlach, RF; Tanus-Santos, JE. (2006a). Contrasting effects of age on the plasma/whole blood lead ratio in men and women with a history of lead exposure. Environ Res 102: 90-95. http://dx.doi.org/10.1016/j.envres.2006.03.007.

Barbosa, F, Jr; Rodrigues, MHC; Buzalaf, MR; Krug, FJ; Gerlach, RF; Tanus-Santos, JE. (2006b). Evaluation of the use of salivary lead levels as a surrogate of blood lead or plasma lead levels in lead exposed subjects. Arch Toxicol 80: 633-637. http://dx.doi.org/10.1007/s00204-006-0096-y.

Barltrop, D; Meek, F. (1979). Effect of particle size on lead absorption from the gut. Arch Environ Health 34: 280-285. http://dx.doi.org/10.1080/00039896.1979.10667414.

Barry, PS. (1975). A comparison of concentrations of lead in human tissues. Occup Environ Med 32: 119-139. http://dx.doi.org/10.1136/oem.32.2.119.

Barry, PSI. (1981). Concentrations of lead in the tissues of children. Br J Ind Med 38: 61-71.

Barry, PSI; Connolly, R. (1981). Lead concentrations in mediaeval bones. Int Arch Occup Environ Health 48: 173-177. http://dx.doi.org/10.1007/BF00378438.

Barton, JC; Conrad, ME; Harrison, L; Nuby, S. (1978a). Effects of calcium on the absorption and retention of lead. J Lab Clin Med 91: 366-376.

Barton, JC; Conrad, ME; Nuby, S; Harrison, L. (1978b). Effects of iron on the absorption and retention of lead. J Lab Clin Med 92: 536-547.

Beamer, PI; Elish, CA; Roe, DJ; Loh, MM; Layton, DW. (2012). Differences in metal concentration by particle size in house dust and soil. J Environ Monit 14: 839-844. http://dx.doi.org/10.1039/c2em10740f.

Becker, F; Marcantonio, F; Datta, S; Wichterich, C; Cizmas, L; Surber, J; Kennedy, K; Bowles, E. (2022). Tracking the source of contaminant lead in children's blood. Environ Res 212: 113307. http://dx.doi.org/10.1016/j.envres.2022.113307.

Benson, NU; Anake, WU; Adedapo, AE; Fred-Ahmadu, OH; Ayejuyo, OO. (2017a). Toxic metals in cigarettes and human health risk assessment associated with inhalation exposure. Environ Monit Assess 189: 619. http://dx.doi.org/10.1007/s10661-017-6348-x.

Benson, SM; Talbott, EO; Brink, LL; Wu, C; Sharma, RK; Marsh, GM. (2017b). Environmental lead and childhood blood lead levels in US children: NHANES, 1999-2006. Arch Environ Occup Health 72: 70-78. http://dx.doi.org/10.1080/19338244.2016.1157454.

Bergdahl, IA; Grubb, A; Schütz, A; Desnick, RJ; Wetmur, JG; Sassa, S; Skerfving, S. (1997a). Lead binding to δ-aminolevulinic acid dehydratase (ALAD) in human erythrocytes. Basic Clin Pharmacol Toxicol 81: 153-158. http://dx.doi.org/10.1111/j.1600-0773.1997.tb02061.x.

Bergdahl, IA; Schütz, A; Gerhardsson, L; Jensen, A; Skerfving, S. (1997b). Lead concentrations in human plasma, urine and whole blood. Scand J Work Environ Health 23: 359-363. http://dx.doi.org/10.5271/sjweh.232.

Bergdahl, IA; Schütz, A; Grubb, A. (1996). Application of liquid chromatography-inductively coupled plasma mass spectrometry to the study of protein-bound lead in human erythrocytes. J Anal At Spectrom 11: 735-738. http://dx.doi.org/10.1039/JA9961100735.

Bergdahl, IA; Sheveleva, M; Schütz, A; Artamonova, VG; Skerfving, S. (1998). Plasma and blood lead in humans: Capacity-limited binding to delta-aminolevulinic acid dehydratase and other lead-binding components. Toxicol Sci 46: 247-253. http://dx.doi.org/10.1093/toxsci/46.2.247.

Bergdahl, IA; Vahter, M; Counter, SA; Schütz, A; Buchanan, LH; Ortega, F; Laurell, G; Skerfving, S. (1999). Lead in plasma and whole blood from lead-exposed children. Environ Res 80: 25-33. http://dx.doi.org/10.1006/enrs.1998.3880.

Berger, OG; Gregg, DJ; Succop, PA. (1990). Using unstimulated urinary lead excretion to assess the need for chelation in the treatment of lead poisoning. J Pediatr 116: 46-51. http://dx.doi.org/10.1016/S0022-3476(05)81643-9.

Bergstrom, C; Shirai, J; Kissel, J. (2011). Particle size distributions, size concentration relationships, and adherence to hands of selected geologic media derived from mining, smelting, and quarrying activities. Sci Total Environ 409: 4247-4256. http://dx.doi.org/10.1016/j.scitotenv.2011.06.005.

Berkowitz, GS; Wolff, MS; Lapinski, RH; Todd, AC. (2004). Prospective study of blood and tibia lead in women undergoing surgical menopause. Environ Health Perspect 112: 1673-1678. http://dx.doi.org/10.1289/ehp.7005.

Bevington, C; Gardner, HD; Cohen, J; Henning, C; Rasmussen, PE. (2021). Relationship between residential dust-lead loading and dust-lead concentration across multiple North American datasets. Build Environ 188: 107359. http://dx.doi.org/10.1016/j.buildenv.2020.107359.

Bezold, C; Bauer, SJ; Buckley, JP; Batterman, G; Haroon, H; Fink, L. (2020). Demolition activity and elevated blood lead levels among children in Detroit, Michigan, 2014-2018. Int J Environ Res Public Health 17: 6018. http://dx.doi.org/10.3390/ijerph17176018.

Bierkens, J; Smolders, R; Van Holderbeke, M; Cornelis, C. (2011). Predicting blood lead levels from current and past environmental data in Europe. Sci Total Environ 409: 5101-5110. http://dx.doi.org/10.1016/j.scitotenv.2011.08.034.

Blake, KCH; Barbezat, GO; Mann, M. (1983). Effect of dietary constituents on the gastrointestinal absorption of 203Pb in man. Environ Res 30: 182-187. http://dx.doi.org/10.1016/0013-9351(83)90178-0.

Blake, KCH; Mann, M. (1983). Effect of calcium and phosphorus on the gastrointestinal absorption of 203Pb in man. Environ Res 30: 188-194. http://dx.doi.org/10.1016/0013-9351(83)90179-2.

Bolanowska, W; Piotrowski, J; Garczynski, H. (1967). Triethyllead in the biological material in cases of acute tetraethyllead poisoning. Arch Toxicol 22: 278-282. http://dx.doi.org/10.1007/BF00577718.

Booker, DV; Chamberlain, AC; Newton, D; Stott, ANB. (1969). Uptake of radioactive lead following inhalation and injection. Br J Radiol 42: 457-466. http://dx.doi.org/10.1259/0007-1285-42-498-457.

Bradham, KD; Nelson, CM; Kelly, J; Pomales, A; Scruton, K; Dignam, T; Misenheimer, JC; Li, K; Obenour, DR; Thomas, DJ. (2017). Relationship between total and bioaccessible lead on children's blood lead levels in urban residential Philadelphia soils. Environ Sci Technol 51: 10005-10011. http://dx.doi.org/10.1021/acs.est.7b02058.

Braun, JM; Hornung, R; Chen, A; Dietrich, KN; Jacobs, DE; Jones, R; Khoury, JC; Liddy-Hicks, S; Morgan, S; Vanderbeek, SB; Xu, Y; Yolton, K; Lanphear, BP. (2018). Effect of residential lead-hazard interventions on childhood blood lead concentrations and neurobehavioral outcomes: A randomized clinical trial. JAMA Pediatr 172: 934-942. http://dx.doi.org/10.1001/jamapediatrics.2018.2382.

Brès, EF; Voegel, JC; Barry, JC; Waddington, WG; Frank, RM. (1986). Feasibility study for the detection of lead substitution sites in the hydroxyapatite crystal structure using high-resolution electron microscopy (HREM) at optimum focus. Journal of Applied Crystallography 19: 168-173. http://dx.doi.org/10.1107/S0021889886089719.

Brink, LA; Talbott, EO; Marsh, GM; Sharma, R; Benson, S; Wu, WC; Duan, C. (2016). Revisiting nonresidential environmental exposures and childhood lead poisoning in the US: Findings from Kansas, 2000-2005. J Environ Public Health 2016: 8791686. http://dx.doi.org/10.1155/2016/8791686.

Brink, LL; Talbott, EO; Sharma, RK; Marsh, GM; Wu, WC; Rager, JR; Strosnider, HM. (2013). Do US ambient air lead levels have a significant impact on childhood blood lead levels: Results of a national study. J Environ Public Health 2013: 278042. http://dx.doi.org/10.1155/2013/278042.

Bronner, F; Pansu, D; Stein, WD. (1986). An analysis of intestinal calcium transport across the rat intestine [Review]. Am J Physiol 250: G561-G569. http://dx.doi.org/10.1152/ajpgi.1986.250.5.G561.

Brown, JS; Spalinger, SM; Weppner, SG; Hicks, KJW; Thorhaug, M; Thayer, WC; Follansbee, MH; Diamond, GL. (2022). Evaluation of the integrated exposure uptake biokinetic (IEUBK) model for lead in children. J Expo Sci Environ Epidemiol 33: 187-197. http://dx.doi.org/10.1038/s41370-022-00473-2.

Brown, MJ; Raymond, J; Homa, D; Kennedy, C; Sinks, T. (2011). Association between children's blood lead levels, lead service lines, and water disinfection, Washington, DC, 1998-2006. Environ Res 111: 67-74. http://dx.doi.org/10.1016/j.envres.2010.10.003.

Brunekreef, B. (1984). The relationship between air lead and blood lead in children: A critical review [Review]. Sci Total Environ 38: 79-123. http://dx.doi.org/10.1016/0048-9697(84)90210-9.

Bugdalski, L; Lemke, LD; McElmurry, SP. (2014). Spatial variation of soil lead in an urban community garden: Implications for risk-based sampling. Risk Anal 34: 17-27. http://dx.doi.org/10.1111/risa.12053.

Butterweck, G; Schuler, C; Vezzù, G; Müller, R; Marsh, JW; Thrift, S; Birchall, A. (2002). Experimental determination of the absorption rate of unattached radon progeny from respiratory tract to blood. Radiat Prot Dosimetry 102: 343- 348. http://dx.doi.org/10.1093/oxfordjournals.rpd.a006103.

Cai, QY; Mo, CH; Wu, QT; Zeng, QY; Katsoyiannis, A. (2007). Concentration and speciation of heavy metals in six different sewage sludge-composts. J Hazard Mater 147: 1063-1072. http://dx.doi.org/10.1016/j.jhazmat.2007.01.142.

Caldwell, KL; Cheng, PY; Jarrett, JM; Makhmudov, A; Vance, K; Ward, CD; Jones, RL; Mortensen, ME. (2017). Measurement challenges at low blood lead levels. Pediatrics 140: e20170272. http://dx.doi.org/10.1542/peds.2017-0272.

Caldwell, KL; Cheng, PY; Vance, KA; Makhmudov, A; Jarrett, JM; Caudill, SP; Ho, DP; Jones, RL. (2019). LAMP: A CDC program to ensure the quality of blood-lead laboratory measurements. J Public Health Manag Pract 25: S23-S30. http://dx.doi.org/10.1097/PHH.0000000000000886.

CalEPA (California Environmental Protection Agency). (2013). Estimating workplace air and worker blood lead concentration using an updated physiologically-based pharmacokinetics (PBPK) model. Sacramento, CA. https://oehha.ca.gov/air/document/estimating-workplace-air-and-worker-blood-lead-concentration-using-updated-pbpk-model.

Campanella, R; Mielke, HW. (2008). Human geography of New Orleans' high-lead geochemical setting. Environ Geochem Health 30: 531-540. http://dx.doi.org/10.1007/s10653-008-9190-9.

Carbone, R; Laforgia, N; Crollo, E; Mautone, A; Iolascon, A. (1998). Maternal and neonatal lead exposure in southern Italy. Neonatology 73: 362-366. http://dx.doi.org/10.1159/000013998.

Cassidy-Bushrow, AE; Sitarik, AR; Havstad, S; Park, SK; Bielak, LF; Austin, C; Johnson, CC; Arora, M. (2017). Burden of higher lead exposure in African-Americans starts in utero and persists into childhood. Environ Int 108: 221-227. http://dx.doi.org/10.1016/j.envint.2017.08.021.

Casteel, SW; Cowart, RP; Weis, CP; Henningsen, GM; Hoffman, E; Brattin, WJ; Guzman, RE; Starost, MF; Payne, JT; Stockham, SL; Becker, SV; Drexler, JW; Turk, JR. (1997). Bioavailability of lead to juvenile swine dosed with soil from the Smuggler Mountain NPL site of Aspen, Colorado. Fundam Appl Toxicol 36: 177-187. http://dx.doi.org/10.1006/faat.1997.2296.

Casteel, SW; Weis, CP; Henningsen, GM; Brattin, WJ. (2006). Estimation of relative bioavailability of lead in soil and soil-like materials using young swine. Environ Health Perspect 114: 1162-1171. http://dx.doi.org/10.1289/ehp.8852.

CDC (Centers for Disease Control and Prevention). (2001). Occupational and take-home lead poisoning associated with restoring chemically stripped furniture--California, 1998. MMWR Morb Mortal Wkly Rep 50: 246-248.

CDC (Centers for Disease Control and Prevention). (2009). Childhood lead poisoning associated with lead dust contamination of family vehicles and child safety seats - Maine, 2008. MMWR Morb Mortal Wkly Rep 58: 890-893.

CDC (Centers for Disease Control and Prevention). (2011). Adult blood lead epidemiology and surveillance: United States, 2008-2009. MMWR Morb Mortal Wkly Rep 60: 841-845.

CDC (Centers for Disease Control and Prevention). (2012). Take-home lead exposure among children with relatives employed at a battery recycling facility — Puerto Rico, 2011. MMWR Morb Mortal Wkly Rep 61: 967-970.

CDC (Centers for Disease Control and Prevention). (2013). Childhood lead exposure associated with the use of kajal, an eye cosmetic from Afghanistan - Albuquerque, New Mexico, 2013. MMWR Morb Mortal Wkly Rep 62: 917-919.

CDC (Centers for Disease Control and Prevention). (2021a). Fourth national report on human exposure to environmental chemicals, Updated tables, March 2021 - Volume Two: NHANES 2011-2016. Washington, DC: U.S. Department of Health & Human Services. https://ecologycenter.org/wp-content/uploads/2021/04/FourthReport_UpdatedTables_Volume2_Mar2021-508.pdf.

CDC (Centers for Disease Control and Prevention). (2021b). Lead (CAS RN: 7439-92-1): NHANES Biomonitoring Data (Blood) [Database]. Atlanta, GA. Retrieved from https://www.cdc.gov/exposurereport/report/pdf/cgroup2_LBXBPB_2011-p.pdf

Ceballosa, DM; Herricka, RF; Dong, Z; Kalweita, A; Miller, M; Quinn, J; Spenglera, JD. (2021). Factors affecting lead dust in construction workers' homes in the Greater Boston Area. Environ Res 195: 110510. http://dx.doi.org/10.1016/j.envres.2020.110510.

Chamberlain, AC. (1983). Effect of airborne lead on blood lead. Atmos Environ 17: 677-692. http://dx.doi.org/10.1016/0004-6981(83)90415-8.

Chamberlain, AC; Clough, WS; Heard, MJ; Newton, D; Stott, ANB; Wells, AC. (1975). Uptake of lead by inhalation of motor exhaust. Proc R Soc Lond B 192: 77-110. http://dx.doi.org/10.1098/rspb.1975.0152.

Chamberlain, AC; Heard, MJ; Little, P; Newton, D; Wells, AC; Wiffin, RD. (1978). Investigations into lead from motor vehicles. (AERE-R9198). Berkshire, England: Transportation and Road Research Laboratory.

Chen, WP; Krage, N; Wu, LS; Page, AL; Chang, AC. (2008). Fertilizer applications and trace elements in vegetable production soils of California. Water Air Soil Pollut 190: 209-219. http://dx.doi.org/10.1007/s11270-007-9594-7.

Cheng, Z; Paltseva, A; Li, I; Morin, T; Huot, H; Egendorf, S; Su, Z; Yolanda, R; Singh, K; Lee, L; Grinshtein, M; Liu, Y; Green, K; Wai, W; Wazed, B; Shaw, R. (2015). Trace metal contamination in New York City garden soils. Soil Sci 180: 167-174. http://dx.doi.org/10.1097/SS.0000000000000126.

Cherkani-Hassani, A; Ghanname, I; Benitez-Rexach, AM; Mouane, N. (2019). Systematic review of the literature of factors affecting the exposure and the levels of lead in human breast milk. In P DeVoogt (Ed.), Reviews of environmental contamination and toxicology (Vol 252) (pp. 97-129). Cham, Switzerland: Springer. http://dx.doi.org/10.1007/398_2019_32.

Chiofalo, JM; Golub, M; Crump, C; Calman, N. (2019). Pediatric blood lead levels within New York City public versus private housing, 2003-2017. Am J Public Health 109: 906-911. http://dx.doi.org/10.2105/AJPH.2019.305021.

Cho, SH; Richmond-Bryant, J; Thornburg, J; Portzer, J; Vanderpool, R; Cavender, K; Rice, J. (2011). A literature review of concentrations and size distributions of ambient airborne Pb-containing particulate matter. Atmos Environ 45: 5005-5015. http://dx.doi.org/10.1016/j.atmosenv.2011.05.009.

Choi, J; Chang, JY; Hong, J; Shin, S; Park, JS; Oh, S. (2017). Low-level toxic metal exposure in healthy weaning-age infants: Association with growth, dietary intake, and iron deficiency. Int J Environ Res Public Health 14: 388. http://dx.doi.org/10.3390/ijerph14040388.

Cimorelli, AJ; Perry, SG; Venkatram, A; Weil, JC; Paine, R; Wilson, RB; Lee, RF; Peters, WD; Brode, RW. (2005). AERMOD: A dispersion model for industrial source applications. Part I: General model formulation and boundary layer characterization. J Appl Meteorol 44: 682-693. http://dx.doi.org/10.1175/JAM2227.1.

Clark, HF; Brabander, DJ; Erdil, RM. (2006). Sources, sinks, and exposure pathways of lead in urban garden soil. J Environ Qual 35: 2066-2074. http://dx.doi.org/10.2134/jeq2005.0464.

Clark, JJ; Knudsen, AC. (2013). Extent, characterization, and sources of soil lead contamination in small-urban residential neighborhoods. J Environ Qual 42: 1498-1506. http://dx.doi.org/10.2134/jeq2013.03.0100.

Clark, S; Galke, W; Succop, P; Grote, J; McLaine, P; Wilson, J; Dixon, S; Menrath, W; Roda, S; Chen, M; Bornschein, R; Jacobs, D. (2011). Effects of HUD-supported lead hazard control interventions in housing on children's blood lead. Environ Res 111: 301-311. http://dx.doi.org/10.1016/j.envres.2010.11.003.

Clayton, CA; Pellizzari, ED; Whitmore, RW; Perritt, RL; Quackenboss, JJ. (1999). National Human Exposure Assessment Survey (NHEXAS): Distributions and associations of lead, arsenic, and volatile organic compounds in EPA Region 5. J Expo Anal Environ Epidemiol 9: 381-392. http://dx.doi.org/10.1038/sj.jea.7500055.

Colapinto, CK; Arbuckle, TE; Dubois, L; Fraser, W. (2016). Is there a relationship between tea intake and maternal whole blood heavy metal concentrations? J Expo Sci Environ Epidemiol 26: 503-509. http://dx.doi.org/10.1038/jes.2015.86.

Cornwell, DA; Brown, RA; Via, SH. (2016). Errata [Erratum]. J Am Water Works Assoc 108: 87. http://dx.doi.org/10.1002/j.1551-8833.2016.tb00079.x.

Cui, XY; Li, SW; Zhang, SJ; Fan, YY; Ma, LQ. (2015). Toxic metals in children's toys and jewelry: Coupling bioaccessibility with risk assessment. Environ Pollut 200: 77-84. http://dx.doi.org/10.1016/j.envpol.2015.01.035.

da Silva, LID; Yokoyama, L; Maia, LB; Monteiro, MIC; Pontes, FVM; Cameiro, MC; Neto, AA. (2015). Evaluation of bioaccessible heavy metal fractions in PM10 from the metropolitan region of Rio de Janeiro city, Brazil, using a simulated lung fluid. Microchem J 118: 266-271. http://dx.doi.org/10.1016/j.microc.2014.08.004.

Dartey, E; Berlinger, B; Thomassen, Y; Ellingsen, DG; Odland, JØ; Nartey, VK; Yeboah, FA; Weinbruch, S. (2014). Bioaccessibility of lead in airborne particulates from car battery repair work. Environ Sci Process Impacts 16: 2782-2788. http://dx.doi.org/10.1039/c4em00455h.

Davis, MA; Gilbert-Diamond, D; Karagas, MR; Li, Z; Moore, JH; Williams, SM; Frost, HR. (2014). A dietary-wide association study (DWAS) of environmental metal exposure in US children and adults. PLoS ONE 9: e104768. http://dx.doi.org/10.1371/journal.pone.0104768.

de Almeida, GRC; Saraiva MDP, C; Barbosa, F, Jr; Krug, FJ; Cury, JA; de Sousa, MDR; Buzalaf, MAR; Gerlach, RF. (2007). Lead contents in the surface enamel of deciduous teeth sampled in vivo from children in uncontaminated and in lead-contaminated areas. Environ Res 104: 337-345. http://dx.doi.org/10.1016/j.envres.2007.03.007.

Dean, JR; Elom, NI; Entwistle, JA. (2017). Use of simulated epithelial lung fluid in assessing the human health risk of Pb in urban street dust. Sci Total Environ 579: 387-395. http://dx.doi.org/10.1016/j.scitotenv.2016.11.085.

Del Río-Celestino, M; Font, R; Moreno-Rojas, R; De Haro-Bailón, A. (2006). Uptake of lead and zinc by wild plants growing on contaminated soils. Ind Crop Prod 24: 230-237. http://dx.doi.org/10.1016/j.indcrop.2006.06.013.

Desai, G; Anzman-Frasca, S; Vernarelli, JA; Ravenscroft, J; Yang, J; Burstein, G; Kordas, K. (2021). Examining links between diet and lead exposure in young children: 2009 to 2014 National Health and Nutrition Examination Survey. Acad Pediatr 21: 471-479. http://dx.doi.org/10.1016/j.acap.2020.06.009.

Deshommes, E; Prévost, M; Levallois, P; Lemieux, F; Nour, S. (2013). Application of lead monitoring results to predict 0-7 year old children's exposure at the tap. Water Res 47: 2409-2420. http://dx.doi.org/10.1016/j.watres.2013.02.010.

deSilva, PE. (1981). Determination of lead in plasma and studies on its relationship to lead in erythrocytes. Br J Ind Med 38: 209-217. http://dx.doi.org/10.1136/oem.38.3.209.

DeSimone, D; Sharafoddinzadeh, D; Salehi, M. (2020). Prediction of children's blood lead levels from exposure to lead in schools' drinking water-A case study in Tennessee, USA. Water 12: 1826. http://dx.doi.org/10.3390/w12061826.

Diamond, GL. (1992). Review of default value for lead plasma-to-urine transfer coefficient (TPLUR) in the U.S. EPA uptake/biokinetic model. (SRC TR-92-135). Syracuse, NY: Syracuse Research Corporation.

Diamond, GL; Thayer, WC; Brown, JS; Burgess, M; Follansbee, MH; Gaines, LGT; Klotzbach, JM. (2019). Estimates of urinary blood lead clearance and its relationship to glomerular filtration rate based on a large population survey. J Toxicol Environ Health A 82: 379-382. http://dx.doi.org/10.1080/15287394.2019.1603280.

Dietrich, M; Shukle, JT; Krekeler, MPS; Wood, LR; Filippelli, GM. (2022). Using community science to better understand lead exposure risks. Geohealth 6: e2021GH000525. http://dx.doi.org/10.1029/2021GH000525.

Dignam, T; Pomales, A; Werner, L; Newbern, EC; Hodge, J; Nielsen, J; Grober, A; Scruton, K; Young, R; Kelly, J; Brown, MJ. (2019). Assessment of child lead exposure in a Philadelphia community, 2014. J Public Health Manag Pract 25: 53-61. http://dx.doi.org/10.1097/PHH.0000000000000711.

DOE (U.S. Department of Energy). (2012). Range design criteria. Washington, DC. https://www.energy.gov/sites/prod/files/2013/05/f1/Range_Design_Criteria.pdf.

Dong, Z; Yan, K; Liu, Y; Naidu, R; Duan, L; Wijayawardena, A; Semple, KT; Rahman, MM. (2016). A meta-analysis to correlate lead bioavailability and bioaccessibility and predict lead bioavailability. Environ Int 92-93: 139-145. http://dx.doi.org/10.1016/j.envint.2016.04.009.

Drasch, GA; Bohm, J; Baur, C. (1987). Lead in human bones. Investigations on an occupationally non-exposed population in southern Bavaria (F.R.G.): I. Adults. Sci Total Environ 64: 303-315. http://dx.doi.org/10.1016/0048-9697(87)90252-X.

Drexler, JW; Brattin, WJ. (2007). An in vitro procedure for estimation of lead relative bioavailability: With validation. Hum Ecol Risk Assess 13: 383-401. http://dx.doi.org/10.1080/10807030701226350.

DuVal, G; Fowler, BA. (1989). Preliminary purification and characterization studies of a low molecular weight, high affinity cytosolic lead-binding protein in rat brain. Biochem Biophys Res Commun 159: 177-184. http://dx.doi.org/10.1016/0006-291X(89)92420-0.

Eaton, DL; Stacey, NH; Wong, KL; Klaassen, CD. (1980). Dose-response effects of various metal ions on rat liver metallothionein, glutathione, heme oxygenase, and cytochrome P-450. Toxicol Appl Pharmacol 55: 393-402. http://dx.doi.org/10.1016/0041-008x(80)90101-5.

Egan, KB; Cornwell, CR; Courtney, JG; Ettinger, AS. (2021). Blood lead levels in U.S. children ages 1-11 years, 1976-2016. Environ Health Perspect 129: 37003. http://dx.doi.org/10.1289/EHP7932.

Egeghy, PP; Quackenboss, JJ; Catlin, S; Ryan, PB. (2005). Determinants of temporal variability in NHEXAS-Maryland environmental concentrations, exposures, and biomarkers. J Expo Anal Environ Epidemiol 15: 388-397. http://dx.doi.org/10.1038/sj.jea.7500415.

Egendorf, SP; Cheng, Z; Deeb, M; Flores, V; Paltseva, A; Walsh, D; Groffman, P; Mielke, HW. (2018). Constructed soils for mitigating lead (Pb) exposure and promoting urban community gardening: The New York City Clean Soil Bank pilot study. Landscape Urban Plan 175: 184-194. http://dx.doi.org/10.1016/j.landurbplan.2018.03.012.

Egendorf, SP; Mielke, HW; Castorena-Gonzalez, JA; Powell, ET; Gonzales, CR. (2021a). Soil lead (Pb) in New Orleans: A spatiotemporal and racial analysis. Int J Environ Res Public Health 18: 1314. http://dx.doi.org/10.3390/ijerph18031314.

Egendorf, SP; Spliethoff, HM; Shayler, HA; Russell-Anelli, J; Cheng, Z; Minsky, AH; King, T; McBride, MB. (2021b). Soil lead (Pb) and urban grown lettuce: Sources, processes, and implications for gardener best management practices. J Environ Manage 286: 112211. http://dx.doi.org/10.1016/j.jenvman.2021.112211.

Eisenberg, A; Seymour, E; Hill, AB; Akers, J. (2020). Toxic structures: Speculation and lead exposure in Detroit's single-family rental market. Health Place 64: 102390. http://dx.doi.org/10.1016/j.healthplace.2020.102390.

Eisenberg, KW; van Wijngaarden, E; Fisher, SG; Korfmacher, KS; Campbell, JR; Fernandez, ID; Cochran, J; Geltman, PL. (2011). Blood lead levels of refugee children resettled in Massachusetts, 2000 to 2007. Am J Public Health 101: 48-54. http://dx.doi.org/10.2105/AJPH.2009.184408.

El Zahran, T; Ralston, A; King, A; Hindman, D; Morgan, BW. (2018). Elevated lead level from a tobacco source requiring chelation in a 12-year-old child. Clin Toxicol 56: 1159-1161. http://dx.doi.org/10.1080/15563650.2018.1458990.

Elabiad, MT; Hook, RE. (2013). Lead content of blood transfusions for extremely low-birth-weight infants. Am J Perinatol 30: 765-770. http://dx.doi.org/10.1055/s-0032-1332803.

Elias, SM; Hashim, Z; Marjan, ZM; Abdullah, AS; Hashim, JH. (2007). Relationship between blood lead concentration and nutritional status among Malay primary school children in Kuala Lumpur, Malaysia. Asia Pac J Public Health 19: 29-37. http://dx.doi.org/10.1177/101053950701900306.

Ettinger, AS; Egan, KB; Homa, DM; Brown, MJ. (2020). Blood lead levels in U.S. women of childbearing age, 1976–2016. Environ Health Perspect 128: 17012. http://dx.doi.org/10.1289/EHP5925.

Ettinger, AS; Lamadrid-Figueroa, H; Téllez-Rojo, MM; Mercado-García, A; Peterson, KE; Schwartz, J; Hu, H; Hernández-Avila, M. (2009). Effect of calcium supplementation on blood lead levels in pregnancy: A randomized placebo-controlled trial. Environ Health Perspect 117: 26-31. http://dx.doi.org/10.1289/ehp.11868.

Ettinger, AS; Roy, A; Amarasiriwardena, CJ; Smith, D; Lupoli, N; Mercado-García, A; Lamadrid-Figueroa, H; Tellez-Rojo, MM; Hu, H; Hernández-Avila, M. (2014). Maternal blood, plasma, and breast milk lead: Lactational transfer and contribution to infant exposure. Environ Health Perspect 122: 87-92. http://dx.doi.org/10.1289/ehp.1307187.

Ettinger, AS; Tellez-Rojo, MM; Amarasiriwardena, C; Bellinger, D; Peterson, K; Schwartz, J; Hu, H; Hernandez-Avila, M. (2004a). Effect of breast milk lead on infant blood lead levels at 1 month of age. Environ Health Perspect 112: 1381-1385. http://dx.doi.org/10.1289/ehp.6616.

Ettinger, AS; Tellez-Rojo, MM; Amarasiriwardena, C; Gonzalez-Cossio, T; Peterson, KE; Aro, A; Hu, H; Hernandez-Avila, M. (2004b). Levels of lead in breast milk and their relation to maternal blood and bone lead levels at one month postpartum. Environ Health Perspect 112: 926-931. http://dx.doi.org/10.1289/ehp.6615.

Ettinger, AS; Tellez-Rojo, MM; Amarasiriwardena, C; Peterson, KE; Schwartz, J; Aro, A; Hu, H; Hernandez-Avila, M. (2006). Influence of maternal bone lead burden and calcium intake on levels of lead in breast milk over the course of lactation. Am J Epidemiol 163: 48-56. http://dx.doi.org/10.1093/aje/kwj010.

Falta, T; Limbeck, A; Koellensperger, G; Hann, S. (2008). Bioaccessibility of selected trace metals in urban PM2.5 and PM10 samples: A model study. Anal Bioanal Chem 390: 1149-1157. http://dx.doi.org/10.1007/s00216-007-1762-5.

Farrell, KP; Brophy, MC; Chisolm, JJ; Rohde, CA; Strauss, WJ. (1998). Soil lead abatement and children's blood lead levels in an urban setting. Am J Public Health 88: 1837-1839. http://dx.doi.org/10.2105/ajph.88.12.1837.

Flannery, BM; Middleton, KB. (2022). Updated interim reference levels for dietary lead to support FDA's Closer to Zero action plan [Review]. Regul Toxicol Pharmacol 133: 105202. http://dx.doi.org/10.1016/j.yrtph.2022.105202.

Fleming, DE; Boulay, D; Richard, NS; Robin, JP; Gordon, CL; Webber, CE; Chettle, DR. (1997). Accumulated body burden and endogenous release of lead in employees of a lead smelter. Environ Health Perspect 105: 224-233. http://dx.doi.org/10.2307/3433246.

Forbes, GB; Reina, JC. (1972). Effect of age on gastrointestinal absorption (Fe, Sr, Pb) in the rat. J Nutr 102: 647-652. http://dx.doi.org/10.1093/jn/102.5.647.

Fowler, BA. (1989). Biological roles of high affinity metal-binding proteins in mediating cell injury. Comments Toxicol 3: 27-46.

Fowler, BA; DuVal, G. (1991). Effects of lead on the kidney: Roles of high-affinity lead-binding proteins. Environ Health Perspect 91: 77-80. http://dx.doi.org/10.1289/ehp.919177.

Frank, JJ; Poulakos, AG; Tornero-Velez, R; Xue, J. (2019). Systematic review and meta-analyses of lead (Pb) concentrations in environmental media (soil, dust, water, food, and air) reported in the United States from 1996 to 2016 [Review]. Sci Total Environ 694: 133489. http://dx.doi.org/10.1016/j.scitotenv.2019.07.295.

Franklin, CA; Inskip, MJ; Baccanale, CL; Edwards, CM; Manton, WI; Edwards, E; O'Flaherty, EJ. (1997). Use of sequentially administered stable lead isotopes to investigate changes in blood lead during pregnancy in a nonhuman primate (Macaca fascicularis). Fundam Appl Toxicol 39: 109-119. http://dx.doi.org/10.1006/faat.1997.2355.

Fullmer, CS; Rosen, JF. (1990). Effect of dietary calcium and lead status on intestinal calcium absorption. Environ Res 51: 91-99. http://dx.doi.org/10.1016/S0013-9351(05)80185-9.

Gaitens, JM; Dixon, SL; Jacobs, DE; Nagaraja, J; Strauss, W; Wilson, JW; Ashley, PJ. (2009). Exposure of US children to residential dust lead, 1999-2004: I. Housing and demographic factors. Environ Health Perspect 117: 461-467. http://dx.doi.org/10.1289/ehp.11917.

Gao, P; Guo, H; Zhang, Z; Ou, C; Hang, J; Fan, Q; He, C; Wu, B; Feng, Y; Xing, B. (2018a). Bioaccessibility and exposure assessment of trace metals from urban airborne particulate matter (PM10 and PM2.5) in simulated digestive fluid. Environ Pollut 242: 1669-1677. http://dx.doi.org/10.1016/j.envpol.2018.07.109.

Gao, P; Lei, T; Jia, L; Yury, B; Zhang, Z; Du, Y; Feng, Y; Xing, B. (2018b). Bioaccessible trace metals in lip cosmetics and their health risks to female consumers. Environ Pollut 238: 554-561. http://dx.doi.org/10.1016/j.envpol.2018.03.072.

Gardener, H; Bowen, J; Callan, SP. (2019). Lead and cadmium contamination in a large sample of United States infant formulas and baby foods. Sci Total Environ 651: 822-827. http://dx.doi.org/10.1016/j.scitotenv.2018.09.026.

Gardner, SL; Geller, RJ; Hannigan, R; Sun, Y; Mangla, A. (2016). Evaluating oral fluid as a screening tool for lead poisoning. J Anal Toxicol 40: 744-748. http://dx.doi.org/10.1093/jat/bkw093.

Garrido Latorre, F; Hernandez-Avila, M; Orozco, JT; Medina, CAA; Aro, A; Palazuelos, E; Hu, H. (2003). Relationship of blood and bone lead to menopause and bone mineral density among middle-age women in Mexico City. Environ Health Perspect 111: 631-636. http://dx.doi.org/10.1289/ehp.111-1241456.

Gavelek, A; Spungen, J; Hoffman-Pennesi, D; Flannery, B; Dolan, L; Dennis, S; Fitzpatrick, S. (2020). Lead exposures in older children (males and females 7-17 years), women of childbearing age (females 16-49 years) and adults (males and females 18+years): FDA total diet study 2014-16. Food Addit Contam Part A Chem Anal Control Expo Risk Assess 37: 104-109. http://dx.doi.org/10.1080/19440049.2019.1681595.

Gehrie, E; Keiser, A; Dawling, S; Travis, J; Strathmann, FG; Booth, GS. (2013). Primary prevention of pediatric lead exposure requires new approaches to transfusion screening. J Pediatr 163: 855-859. http://dx.doi.org/10.1016/j.jpeds.2013.03.003.

Geltman, PL; Smock, L; Cochran, J. (2019). Trends in elevated blood lead levels using 5 and 10 µg/dL levels of concern among refugee children resettled in Massachusetts, 1998-2015. Public Health Rep 134: 608-616. http://dx.doi.org/10.1177/0033354919874078.

Gerhardsson, L; Brune, D; Nordberg, GF; Wester, PO. (1986). Distribution of cadmium, lead and zinc in lung, liver and kidney in long-term exposed smelter workers. Sci Total Environ 50: 65-85. http://dx.doi.org/10.1016/0048-9697(86)90352-9.

Gerhardsson, L; Englyst, V; Lundström, NG; Nordberg, G; Sandberg, S; Steinvall, F. (1995). Lead in tissues of deceased lead smelter worker. J Trace Elem Med Biol 9: 136-143. http://dx.doi.org/10.1016/S0946-672X(11)80037-4.

Ghetu, CC; Rohlman, D; Smith, BW; Scott, RP; Adams, KA; Hoffman, PD; Anderson, KA. (2022). Wildfire impact on indoor and outdoor PAH air quality. Environ Sci Technol 56: 10042-10052. http://dx.doi.org/10.1021/acs.est.2c00619.

Gibson, JM; Fisher, M; Clonch, A; MacDonald, JM; Cook, PJ. (2020). Children drinking private well water have higher blood lead than those with city water. Proc Natl Acad Sci USA 117: 16898-16907. http://dx.doi.org/10.1073/pnas.2002729117.

Gleason, JA; Nanavaty, JV; Fagliano, JA. (2019). Drinking water lead and socioeconomic factors as predictors of blood lead levels in New Jersey's children between two time periods. Environ Res 169: 409-416. http://dx.doi.org/10.1016/j.envres.2018.11.016.

Goix, S; Uzu, G; Oliva, P; Barraza, F; Calas, A; Castet, S; Point, D; Masbou, J; Duprey, JL; Huayta, C; Chincheros, J; Gardon, J. (2016). Metal concentration and bioaccessibility in different particle sizes of dust and aerosols to refine metal exposure assessment. J Hazard Mater 317: 552-562. http://dx.doi.org/10.1016/j.jhazmat.2016.05.083.

Gómez, HF; Borgialli, DA; Sharman, M; Shah, KK; Scolpino, AJ; Oleske, JM; Bogden, JD. (2018). Blood lead levels of children in Flint, Michigan: 2006-2016. J Pediatr 197: 158-164. http://dx.doi.org/10.1016/j.jpeds.2017.12.063.

Gómez, HF; Borgialli, DA; Sharman, M; Weber, AT; Scolpino, AJ; Oleske, JM; Bogden, JD. (2019). Blood lead levels in females of childbearing age in Flint, Michigan, and the water crisis. Obstet Gynecol 134: 628-635. http://dx.doi.org/10.1097/AOG.0000000000003416.

Goyer, RA. (1990). Transplacental transport of lead [Review]. Environ Health Perspect 89: 101-105. http://dx.doi.org/10.2307/3430905.

Graney, JR; Halliday, AN; Keeler, GJ; Nriagu, JO; Robbins, JA; Norton, SA. (1995). Isotopic record of lead pollution in lake sediments from the northeastern United States. Geochim Cosmo Act 59: 1715-1728. http://dx.doi.org/10.1016/0016-7037(95)00077-D.

Gray, PJ; Cunningham, W. (2019). Inductively coupled plasma collision cell quadrupole mass spectrometric determination of extractible arsenic, cadmium, chromium, lead, mercury, and other elements in food using microwave-assisted digestion: Results from an FDA interlaboratory study. J AOAC Int 102: 590-604. http://dx.doi.org/10.5740/jaoacint.18-0129.

Graziano, JH; Popovac, D; Factor-Litvak, P; Shrout, P; Kline, J; Murphy, MJ; Zhao, YH; Mehmeti, A; Ahmedi, X; Rajovic, B; Zvicer, Z; Nenezic, DU; Lolacono, NJ; Stein, Z. (1990). Determinants of elevated blood lead during pregnancy in a population surrounding a lead smelter in Kosovo, Yugoslavia. Environ Health Perspect 89: 95-100. http://dx.doi.org/10.1289/ehp.908995.

Greenberg, N; Frimer, R; Meyer, R; Derazne, E; Chodick, G. (2016). Lead exposure in military outdoor firing ranges. Mil Med 181: 1121-1126. http://dx.doi.org/10.7205/MILMED-D-15-00454.

Griffin, TB; Coulston, F; Wills, H; Russell, JC; Knelson, JH. (1975). Clinical studies on men continuously exposed to airborne particulate lead. In TB Griffin; JH Knelson (Eds.), Lead (pp. 221-240). Stuttgart, Germany: Georg Thieme Verlag.

Griffith, JD. (2020). Electron microscopic characterization of exhaust particles containing lead dibromide beads expelled from aircraft burning leaded gasoline. Atmos Pollut Res 11: 1481-1486. http://dx.doi.org/10.1016/j.apr.2020.05.026.

Gross, SB; Pfitzer, EA; Yeager, DW; Kehoe, RA. (1975). Lead in human tissues. Toxicol Appl Pharmacol 32: 638-651. http://dx.doi.org/10.1016/0041-008X(75)90127-1.

Gulson, B; Jameson, CW; Mahaffey, KR; Mizon, KJ; Patison, N; Law, AJ; Korsch, MJ; Salter, MA. (1998a). Relationships of lead in breast milk to lead in blood, urine, and diet of the infant and mother. Environ Health Perspect 106: 667-674. http://dx.doi.org/10.1289/ehp.98106667.

Gulson, B; Mahaffey, KR; Jameson, CW; Mizon, KJ; Korsch, MJ; Cameron, MA; Eisman, JA. (1998b). Mobilization of lead from the skeleton during the postnatal period is larger than during pregnancy. Transl Res 131: 324-329. http://dx.doi.org/10.1016/S0022-2143(98)90182-2.

Gulson, B; Mahaffey, KR; Mizon, KJ; Korsch, MJ; Cameron, MA; Vimpani, G. (1995). Contribution of tissue lead to blood lead in adult female subjects based on stable lead isotope methods. J Lab Clin Med 125: 703-712.

Gulson, B; Mizon, K; Smith, H; Eisman, J; Palmer, J; Korsch, M; Donnelly, J; Waite, K. (2002). Skeletal lead release during bone resorption: Effect of bisphosphonate treatment in a pilot study. Environ Health Perspect 110: 1017-1023. http://dx.doi.org/10.1289/ehp.021101017.

Gulson, B; Mizon, KJ; Korsch, MJ; Taylor, AJ. (2006). Low blood lead levels do not appear to be further reduced by dietary supplements. Environ Health Perspect 114: 1186-1192. http://dx.doi.org/10.1289/ehp.8605.

Gulson, B; Mizon, KJ; Palmer, JM; Korsch, MJ; Taylor, AJ; Mahaffey, KR. (2004). Blood lead changes during pregnancy and postpartum with calcium supplementation. Environ Health Perspect 112: 1499-1507. http://dx.doi.org/10.1289/ehp.6548.

Gulson, BL; Jameson, CW; Mahaffey, KR; Mizon, KJ; Korsch, MJ; Vimpani, G. (1997). Pregnancy increases mobilization of lead from maternal skeleton. Transl Res 130: 51-62. http://dx.doi.org/10.1016/S0022-2143(97)90058-5.

Gulson, BL; Mahaffey, KR; Jameson, CW; Patison, N; Law, AJ; Mizon, KJ; Korsch, MJ; Pederson, D. (1999). Impact of diet on lead in blood and urine in female adults and relevance to mobilization of lead from bone stores. Environ Health Perspect 107: 257-263. http://dx.doi.org/10.1289/ehp.99107257.

Gulson, BL; Mizon, KJ; Korsch, MJ; Palmer, JM; Donnelly, JB. (2003). Mobilization of lead from human bone tissue during pregnancy and lactation - A summary of long-term research. Sci Total Environ 303: 79-104. http://dx.doi.org/10.1016/S0048-9697(02)00355-8.

Haley, VB; Talbot, TO. (2004). Seasonality and trend in blood lead levels of New York State children. BMC Pediatr 4: 8. http://dx.doi.org/10.1186/1471-2431-4-8.

Hallén, IP; Jorhem, L; Lagerkvist, BJ; Oskarsson, A. (1995). Lead and cadmium levels in human milk and blood. Sci Total Environ 166: 149-155. http://dx.doi.org/10.1016/0048-9697(95)04523-4.

Hanna-Attisha, M; LaChance, J; Sadler, RC; Schnepp, AC. (2016). Elevated blood lead levels in children associated with the flint drinking water crisis: A spatial analysis of risk and public health response. Am J Public Health 106: 283-290. http://dx.doi.org/10.2105/AJPH.2015.303003.

Hansen, S; Nieboer, E; Sandanger, TM; Wilsgaard, T; Thomassen, Y; Veyhe, AS; Odland, JØ. (2011). Changes in maternal blood concentrations of selected essential and toxic elements during and after pregnancy. J Environ Monit 13: 2143-2152. http://dx.doi.org/10.1039/c1em10051c.

Haque, E; Moran, ME; Thorne, PS. (2021). Retrospective blood lead assessment from archived clotted erythrocyte fraction in a cohort of lead-exposed mother-child dyads. Sci Total Environ 754: 142166. http://dx.doi.org/10.1016/j.scitotenv.2020.142166.

Harville, EW; Hertz-Picciotto, I; Schramm, M; Watt-Morse, M; Chantala, K; Osterloh, J; Parsons, PJ; Rogan, W. (2005). Factors influencing the difference between maternal and cord blood lead. Occup Environ Med 62: 263-290. http://dx.doi.org/10.1136/oem.2003.012492.

Hayes, EB; Orbach, HG; Fernandez, AM; Lyne, S; Matte, TD; McElvaine, MD. (1994). Long-term trends in blood lead levels among children in Chicago: Relationship to air lead levels. Pediatrics 93: 195-200. http://dx.doi.org/10.1542/peds.93.2.195.

Hays, MD; Cho, SH; Baldauf, R; JJ, S; Shafer, M. (2011). Particle size distributions of metal and non-metal elements in an urban near-highway environment. Atmos Environ 45: 925-934. http://dx.doi.org/10.1016/j.atmosenv.2010.11.010.

Healy, MA; Harrison, PG; Aslam, M; Davis, SS; Wilson, CG. (1992). Lead sulphide and traditional preparations: Routes for ingestion, and solubility and reactions in gastric fluid. J Clin Hosp Pharm 7: 169-173. http://dx.doi.org/10.1111/j.1365-2710.1982.tb01019.x.

Heard, MJ; Chamberlain, AC. (1982). Effect of minerals and food on uptake of lead from the gastrointestinal tract in humans. Hum Toxicol 1: 411-415. http://dx.doi.org/10.1177/096032718200100407.

Heard, MJ; Wells, AC; Newton, D; Chamberlain, AC. (1979). Human uptake and metabolism of tetra ethyl and tetra methyl lead vapour labelled with 203Pb. In International Conference on Management and Control of Heavy Metals in the Environment, London, England, September. Edinburgh, United Kingdom: CEP Consultants, Ltd.

Hee, SSQ; Peace, B; Clark, CS; Boyle, JR; Bornschein, RL; Hammond, PB. (1985). Evolution of efficient methods to sample lead sources, such as house dust and hand dust, in the homes of children. Environ Res 38: 77-95. http://dx.doi.org/10.1016/0013-9351(85)90074-X.

Hernandez-Avila, M; Gonzalez-Cossio, T; Palazuelos, E; Romieu, I; Aro, A; Fishbein, E; Peterson, KE; Hu, H. (1996). Dietary and environmental determinants of blood and bone lead levels in lactating postpartum women living in Mexico City. Environ Health Perspect 104: 1076-1082. http://dx.doi.org/10.1289/ehp.961041076.

Hernández-Avila, M; Smith, D; Meneses, F; Sanin, LH; Hu, H. (1998). The influence of bone and blood lead on plasma lead levels in environmentally exposed adults. Environ Health Perspect 106: 473-477. http://dx.doi.org/10.1289/ehp.106-1533211.

Hertz-Picciotto, I; Schramm, M; Watt-Morse, M; Chantala, K; Anderson, J; Osterloh, J. (2000). Patterns and determinants of blood lead during pregnancy. Am J Epidemiol 152: 829-837. http://dx.doi.org/10.1093/aje/152.9.829.

Hess, CA; Olmedo, P; Navas-Acien, A; Goessler, W; Cohen, JE; Rule, AM. (2017). E-cigarettes as a source of toxic and potentially carcinogenic metals. Environ Res 152: 221-225. http://dx.doi.org/10.1016/j.envres.2016.09.026.

Hill, DT; Petroni, M; Larsen, DA; Bendinskas, K; Heffernan, K; Atallah-Yunes, N; Parsons, PJ; Palmer, CD; MacKenzie, JA; Collins, MB; Gump, BB. (2021). Linking metal (Pb, Hg, Cd) industrial air pollution risk to blood metal levels and cardiovascular functioning and structure among children in Syracuse, NY. Environ Res 193: 110557. http://dx.doi.org/10.1016/j.envres.2020.110557.

Hilts, SR. (2003). Effect of smelter emission reductions on children's blood lead levels. Sci Total Environ 303: 51-58. http://dx.doi.org/10.1016/S0048-9697(02)00357-1.

Ho, WC; Lin, YS; Caffrey, JL; Faramawi, MF. (2022). Evaluation of lead body burden in US adolescents. Arch Environ Occup Health 77: 219-226. http://dx.doi.org/10.1080/19338244.2020.1864257.

Hodgson, S; Manmee, C; Dirks, W; Shepherd, T; Pless-Mulloli, T. (2015). Determinants of childhood lead exposure in the postleaded petrol era: The Tooth Fairy cohort from Newcastle upon Tyne. J Expo Sci Environ Epidemiol 25: 420-426. http://dx.doi.org/10.1038/jes.2014.79.

Hogan, K; Marcus, A; Smith, R; White, P. (1998). Integrated exposure uptake biokinetic model for lead in children: Empirical comparisons with epidemiologic data. Environ Health Perspect 106 (Suppl. 6): 1557-1567. http://dx.doi.org/10.1289/ehp.98106s61557.

Hollingsworth, A; Rudik, I. (2021). The effect of leaded gasoline on elderly mortality: Evidence from regulatory exemptions. Am Econ J Econ Policy 13: 345-373. http://dx.doi.org/10.1257/pol.20190654.

Hopkins, MR; Ettinger, AS; Hernández-Avila, M; Schwartz, J; Téllez-Rojo, MM; Lamadrid-Figueroa, H; Bellinger, D; Hu, H; Wright, RO. (2008). Variants in iron metabolism genes predict higher blood lead levels in young children. Environ Health Perspect 116: 1261-1266. http://dx.doi.org/10.1289/ehp.11233.

Hore, P; Ahmed, M; Ehrlich, J; Ng, C; Steffen, L; Sedlar, S; Curry-Johnson, P; Graber, N; Nagin, D; Clark, N; Saper, R; Sucosky, MS. (2012). Lead poisoning in pregnant women who used Ayurvedic medications from India--New York City, 2011-2012. MMWR Morb Mortal Wkly Rep 61: 641-646.

Hore, P; Alex-Oni, K; Sedlar, S; Nagin, D. (2019). A spoonful of lead: A 10-year look at spices as a potential source of lead exposure. J Public Health Manag Pract 25(Suppl 1): S63-S70. http://dx.doi.org/10.1097/PHH.0000000000000876.

Hu, H; Aro, A; Payton, M; Korrick, S; Sparrow, D; Weiss, ST; Rotnitzky, A. (1996). The relationship of bone and blood lead to hypertension: The Normative Aging Study. JAMA 275: 1171-1176. http://dx.doi.org/10.1001/jama.1996.03530390037031.

Hu, H; Rabinowitz, M; Smith, D. (1998). Bone lead as a biological marker in epidemiologic studies of chronic toxicity: Conceptual paradigms [Review]. Environ Health Perspect 106: 1-8. http://dx.doi.org/10.1289/ehp.981061.

Huang, CC; Yang, CC; Liu, T; Dai, C; Wang, CL; Chuang, HY. (2020). Use of generalized additive model to detect the threshold of δ-aminolevulinic acid dehydratase activity reduced by lead exposure. Int J Environ Res Public Health 17: 5712. http://dx.doi.org/10.3390/ijerph17165712.

Hubbard, H; Özkaynak, H; Glen, G; Cohen, J; Thomas, K; Phillips, L; Tulve, N. (2022). Model-based predictions of soil and dust ingestion rates for U.S. adults using the stochastic human exposure and dose simulation soil and dust model. Sci Total Environ 846: 157501. http://dx.doi.org/10.1016/j.scitotenv.2022.157501.

Hunt, A. (2016). Relative bioaccessibility of Pb-based paint in soil. Environ Geochem Health 38: 1037-1050. http://dx.doi.org/10.1007/s10653-015-9789-6.

Hursh, JB; Schraub, A; Sattler, EL; Hofmann, HP. (1969). Fate of 212Pb inhaled by human subjects. Health Phys 16: 257-267. http://dx.doi.org/10.1097/00004032-196903000-00001.

Hursh, JB; Suomela, J. (1968). Absorption of 212Pb from the gastrointestinal tract of man. Acta Radiol Ther Phys Biol 7: 108-120. http://dx.doi.org/10.3109/02841866809133184.

ICRP (International Commission on Radiological Protection). (1973). Alkaline earth metabolism in adult man. In Radiological and environmental research division annual report. (ANL-7960). Oxford, England: Pergamon Press. https://www.osti.gov/servlets/purl/4568291#page=38.

ICRP (International Commission on Radiological Protection). (1993). Appendix A: Age-specific biokinetic models for the alkaline earth elements and lead. Ann ICRP 23(3-4): 95-120. http://dx.doi.org/10.1016/0146-6453(93)90031-3.

ICRP (International Commission on Radiological Protection). (1995). Age-dependent doses to members of the public from intake of radionuclides: Part 4: Inhalation dose coefficients. (ICRP Publication 71). Oxford, United Kingdom: Pergamon. http://dx.doi.org/10.1016/S0146-6453(00)80008-1.

ICRP (International Commission on Radiological Protection). (2002a). Basic anatomical and physiological data for use in radiological protection: Reference values. (ICRP Publication 89). New York, NY: Pergamon Press. http://dx.doi.org/10.1016/S0146-6453(03)00002-2.

ICRP (International Commission on Radiological Protection). (2002b). Guide for the practical application of the ICRP Human Respiratory Tract Model. Ann ICRP 32.

ICRP (International Commission on Radiological Protection). (2017). ICRP publication 137: Occupational intakes of radionuclides: Part 3. Ann ICRP 46: 1-486. http://dx.doi.org/10.1177/0146645317734963.

ICRP (International Commission on Radiological Protection). (1996). Basic anatomical & physiological data for use in radiological protection: The skeleton. In H Smith (Ed.). Tarrytown, NY: Elsevier Science Inc.

Inskip, MJ; Franklin, CA; Baccanale, CL; Manton, WI; O'Flaherty, EJ; Edwards, CMH; Blenkinsop, JB; Edwards, EB. (1996). Measurement of the flux of lead from bone to blood in a nonhuman primate (Macaca fascicularis) by sequential administration of stable lead isotopes. Fundam Appl Toxicol 33: 235-245. http://dx.doi.org/10.1006/faat.1996.0161.

Jackson, LW; Cromer, BA; Panneerselvam, A. (2010). Association between bone turnover, micronutrient intake and blood lead levels among pre- and post-menopausal women, NHANES 1999-2002. Environ Health Perspect 118: 1590-1596. http://dx.doi.org/10.1289/ehp.1002158.

Jaeger, RJ; Weiss, AL; Manton, WI. (1998). Isotopic ratio analysis in residential lead-based paint and associated surficial dust. J Toxicol Clin Toxicol691-703.

Jain, RB. (2016). Trends and variability in blood lead concentrations among US adults aged 20-64 years and senior citizens aged ≥65 years. Environ Sci Pollut Res Int 23: 14056-14067. http://dx.doi.org/10.1007/s11356-016-6583-7.

James, HM; Hilburn, ME; Blair, JA. (1985). Effects of meals and meal times on uptake of lead from the gastrointestinal tract of humans. Hum Exp Toxicol 4: 401-407. http://dx.doi.org/10.1177/096032718500400406.

Jin, C; Li, Y; Li, YL; Zou, Y; Zhang, GL; Normura, M; Zhu, GY. (2008). Blood lead: Its effect on trace element levels and iron structure in hemoglobin. Nucl Instrum Methods Phys Res B 266: 3607-3613. http://dx.doi.org/10.1016/j.nimb.2008.05.087.

Johnston, JE; Franklin, M; Roh, H; Austin, C; Arora, M. (2019). Lead and arsenic in shed deciduous teeth of children living near a lead-acid battery smelter. Environ Sci Technol 53: 6000-6006. http://dx.doi.org/10.1021/acs.est.9b00429.

Jones, EA; Wright, JM; Rice, G; Buckley, BT; Magsumbol, MS; Barr, DB; Williams, BL. (2010). Metal exposures in an inner-city neonatal population. Environ Int 36: 649-654. http://dx.doi.org/10.1016/j.envint.2010.04.007.

Jones, RL; Homa, DM; Meyer, PA; Brody, DJ; Caldwell, KL; Pirkle, JL; Brown, MJ. (2009). Trends in blood lead levels and blood lead testing among US children aged 1 to 5 Years, 1988-2004. Pediatrics 123: e376-e385. http://dx.doi.org/10.1542/peds.2007-3608.

Juhasz, AL; Weber, J; Smith, E. (2011). Impact of soil particle size and bioaccessibility on children and adult lead exposure in peri-urban contaminated soil. J Hazard Mater 186: 1870-1879. http://dx.doi.org/10.1016/j.jhazmat.2010.12.095.

Juhasz, AL; Weber, J; Smith, E; Naidu, R; Marschner, B; Rees, M; Rofe, A; Kuchel, T; Sansom, L. (2009). Evaluation of SBRC-gastric and SBRC-intestinal methods for the prediction of in vivo relative lead bioavailability in contaminated soils. Environ Sci Technol 43: 4503-4509. http://dx.doi.org/10.1021/es803238u.

Jursa, T; Stein, CR; Smith, DR. (2018). Determinants of hair manganese, lead, cadmium and arsenic levels in environmentally exposed children. Toxics 6: 19. http://dx.doi.org/10.3390/toxics6020019.

Kang, HG; Jeong, SH; Cho, MR; Cho, JH; Bischoff, K. (2009). Time-dependent changes in lead and δ-aminolevulinic acid after subchronic lead exposure in rats. Hum Exp Toxicol 28: 647-654. http://dx.doi.org/10.1177/0960327109107046.

Kaplowitz, SA; Perlstadt, H; Dziura, JD; Post, LA. (2016). Behavioral and environmental explanations of elevated blood lead levels in immigrant children and children of immigrants. J Immigr Minor Health 18: 979-986. http://dx.doi.org/10.1007/s10903-015-0243-8.

Karna, RR; Noerpel, M; Betts, AR; Scheckel, KG. (2017). Lead and arsenic bioaccessibility and speciation as a function of soil particle size. J Environ Qual 46: 1225-1235. http://dx.doi.org/10.2134/jeq2016.10.0387.

Karwowski, MP; Morman, SA; Plumlee, GS; Law, T; Kellogg, M; Woolf, AD. (2017). Toxicants in folk remedies: Implications of elevated blood lead in an American-born infant due to imported diaper powder. Environ Geochem Health 39: 1133-1143. http://dx.doi.org/10.1007/s10653-016-9881-6.

Kayaaltı, Z; Sert, S; Kaya-Akyüzlü, D; Söylemez, E; Söylemezoğlu, T. (2016). Association between delta-aminolevulinic acid dehydratase polymorphism and placental lead levels. Environ Toxicol Pharmacol 41: 147-151. http://dx.doi.org/10.1016/j.etap.2015.11.017.

Kehoe, RA. (1961a). The Harben Lectures, 1960: The metabolism of lead in man in health and disease. 2(2). The metabolism of lead under abnormal conditions. J R Inst Public Health 24: 129-143.

Kehoe, RA. (1961b). The Harben Lectures, 1960: The metabolism of lead in man in health and disease: Lecture 3: Present hygienic problems relating to the absorption of lead. J R Inst Public Health 24: 177-203.

Kehoe, RA. (1987). Studies of lead administration and elimination in adult volunteers under natural and experimentally induced conditions over extended periods of time. Food Chem Toxicol 25: 425-493.

Keller, B; Faciano, A; Tsega, A; Ehrlich, J. (2017). Epidemiologic characteristics of children with blood lead levels ≥45 µg/dl. J Pediatr 180: 229-234. http://dx.doi.org/10.1016/j.jpeds.2016.09.017.

Kennedy, C; Yard, E; Dignam, T; Buchanan, S; Condon, S; Brown, MJ; Raymond, J; Rogers, HS; Sarisky, J; de Castro, R; Arias, I; Breysse, P. (2016). Blood lead levels among children aged <6 years - Flint, Michigan, 2013-2016. MMWR Morb Mortal Wkly Rep 65: 650-654. http://dx.doi.org/10.15585/mmwr.mm6525e1.

Kessler, M; Durand, PY; Huu, TC; Royer-Morot, MJ; Chanliau, J; Netter, P; Duc, M. (1999). Mobilization of lead from bone in end-stage renal failure patients with secondary hyperparathyroidism. Nephrol Dial Transplant 14: 2731-2733. http://dx.doi.org/10.1093/ndt/14.11.2731.

Khoury, GA; Diamond, GL. (2003). Risks to children from exposure to lead in air during remedial or removal activities at Superfund sites: a case study of the RSR lead smelter superfund site. J Expo Anal Environ Epidemiol 13: 51-65. http://dx.doi.org/10.1038/sj.jea.7500254.

Kim, CS; Wilson, KM; Rytuba, JJ. (2011). Particle-size dependence on metal(loid) distributions in mine wastes: Implications for water contamination and human exposure. Appl Geochem 26: 484-495. http://dx.doi.org/10.1016/j.apgeochem.2011.01.007.

Kim, R; Landrigan, C; Mossmann, P; Sparrow, D; Hu, H. (1997). Age and secular trends in bone lead levels in middle-aged and elderly men: Three-year longitudinal follow-up in the Normative Aging Study. Am J Epidemiol 146: 586-591.

Klemick, H; Mason, H; Sullivan, K. (2020). Superfund cleanups and children's lead exposure. J Environ Econ Manage 100: 102289. http://dx.doi.org/10.1016/j.jeem.2019.102289.

Knobeloch, L; Gorski, P; Christenson, M; Anderson, H. (2013). Private drinking water quality in rural Wisconsin. J Environ Health 75: 16-20.

Kordas, K; Ettinger, AS; Lamadrid-Figueroa, H; Tellez-Rojo, MM; Hérnandez-Avila, M; Hu, H; Wright, RO. (2009). Methylenetetrahydrofolate reductase (MTHFR) C677T, A1298C and G1793A genotypes, and the relationship between maternal folate intake, tibia lead and infant size at birth. Br J Nutr 102: 907-914. http://dx.doi.org/10.1017/s0007114509318280.

Korrick, SA; Schwartz, J; Tsaih, SW; Hunter, DJ; Aro, A; Rosner, B; Speizer, FE; Hu, H. (2002). Correlates of bone and blood lead levels among middle-aged and elderly women. Am J Epidemiol 156: 335-343. http://dx.doi.org/10.1093/aje/kwf042.

Koster, J; Erhardt, A; Stoeppler, M; Mohl, C; Ritz, E. (1989). Mobilizable lead in patients with chronic renal failure. Eur J Clin Invest 19: 228-233. http://dx.doi.org/10.1111/j.1365-2362.1989.tb00222.x.

Kostial, K; Kello, D; Jugo, S; Rabar, I; Maljković, T. (1978). Influence of age on metal metabolism and toxicity. Environ Health Perspect 25: 81-86. http://dx.doi.org/10.1289/ehp.782581.

Kotey, S; Carrico, R; Wiemken, TL; Furmanek, S; Bosson, R; Nyantakyi, F; VanHeiden, S; Mattingly, W; Zierold, KM. (2018). Elevated blood lead levels by length of time from resettlement to health screening in Kentucky refugee children. Am J Public Health 108: 270-276. http://dx.doi.org/10.2105/AJPH.2017.304115.

Koyashiki, GA; Paoliello, MM; Matsuo, T; de Oliveira, MM; Mezzaroba, L; de Fatima Carvalho, M; Momoyo Sakuma, A; Turini, C; Terezinha Oliveira Vannuchi, M; Barbosa, CS. (2010). Lead levels in milk and blood from donors to the breast milk bank in Southern Brazil. Environ Res 110: 265-271. http://dx.doi.org/10.1016/j.envres.2009.12.001.

Kundu, S; Stone, EA. (2014). Composition and sources of fine particulate matter across urban and rural sites in the Midwestern United States. Environ Sci Process Impacts 16: 1360-1370. http://dx.doi.org/10.1039/c3em00719g.

La-Llave-León, O; Mendez-Hernandez, EM; Castellanos-Juarez, FX; Esquivel-Rodríguez, E; Vázquez-Alaniz, F; Sandoval-Carrillo, A; García-Vargas, G; Duarte-Sustaita, J; Candelas-Rangel, JL; Salas-Pacheco, JM. (2017). Association between blood lead levels and delta-aminolevulinic acid dehydratase in pregnant women. Int J Environ Res Public Health 14: 432. http://dx.doi.org/10.3390/ijerph14040432.

Lacey, RF; Moore, MR; Richards, WN. (1985). Lead in water, infant diet and blood: The Glasgow Duplicate Diet Study. Sci Total Environ 41: 235-257.

Lach, K; Steer, B; Gorbunov, B; Mička, V; Muir, RB. (2015). Evaluation of exposure to airborne heavy metals at gun shooting ranges. Ann Occup Hyg 59: 307-323. http://dx.doi.org/10.1093/annhyg/meu097.

Lagerkvist, BJ; Ekesrydh, S; Englyst, V; Nordberg, GF; Soderberg, HA; Wiklund, DE. (1996). Increased blood lead and decreased calcium levels during pregnancy: A prospective study of Swedish women living near a smelter. Am J Public Health 86: 1247-1252. http://dx.doi.org/10.2105/ajph.86.9.1247.

Lai, JS; Wu, TN; Liou, SH; Shen, CY; Guu, CF; Ko, KN; Chi, HY; Chang, PY. (1997). A study of the relationship between ambient lead and blood lead among lead battery workers. Int Arch Occup Environ Health 69: 295-300. http://dx.doi.org/10.1007/s004200050150.

Laidlaw, MAS; Filippelli, GM; Brown, S; Paz-Ferreiro, J; Reichman, SM; Netherway, P; Truskewycz, A; Ball, AS; Mielke, HW. (2017). Case studies and evidence-based approaches to addressing urban soil lead contamination. Appl Geochem 83: 14-30. http://dx.doi.org/10.1016/j.apgeochem.2017.02.015.

Laidlaw, MAS; Filippelli, GM; Sadler, RC; Gonzales, CR; Ball, AS; Mielke, HW. (2016). Children's blood lead seasonality in Flint, Michigan (USA), and soil-sourced lead hazard risks [Review]. Int J Environ Res Public Health 13: 358. http://dx.doi.org/10.3390/ijerph13040358.

Laidlaw, MAS; Mielke, HW; Filippelli, GM; Johnson, DL; Gonzales, CR. (2005). Seasonality and children's blood lead levels: Developing a predictive model using climatic variables and blood lead data from Indianapolis, Indiana, Syracuse, New York, and New Orleans, Louisiana (USA). Environ Health Perspect 113: 793-800. http://dx.doi.org/10.1289/ehp.7759.

Laidlaw, MAS; Zahran, S; Mielke, HW; Taylor, MP; Filippelli, GM. (2012). Re-suspension of lead contaminated urban soil as a dominant source of atmospheric lead in Birmingham, Chicago, Detroit and Pittsburgh, USA. Atmos Environ 49: 302-310. http://dx.doi.org/10.1016/j.atmosenv.2011.11.030.

Laidlaw, MAS; Zahran, S; Pingitore, N; Clague, J; Devlin, G; Taylor, MP. (2014). Identification of lead sources in residential environments: Sydney Australia. Environ Pollut 184: 238-246. http://dx.doi.org/10.1016/j.envpol.2013.09.003.

Lamadrid-Figueroa, H; Téllez-Rojo, MM; Hernández-Cadena, L; Mercado-García, A; Smith, D; Solano-González, M; Hernández-Avila, M; Hu, H. (2006). Biological markers of fetal lead exposure at each stage of pregnancy. J Toxicol Environ Health A 69: 1781-1796. http://dx.doi.org/10.1080/15287390600630195.

Lanphear, BP; Weitzman, M; Winter, NL; Eberly, S; Yakir, B; Tanner, M; Emond, M; Matte, TD. (1996). Lead-contaminated house dust and urban children's blood lead levels. Am J Public Health 86: 1416-1421. http://dx.doi.org/10.2105/AJPH.86.10.1416.

Latimer, JC; Van Halen, D; Speer, J; Krull, S; Weaver, P; Pettit, J; Foxx, H. (2016). Soil lead testing at a high spatial resolution in an urban community garden: A case study in relic lead in Terre Haute, Indiana. J Environ Health 79: 28-35.

Lee, S; Shin, M; Hong, YC; Kim, JH. (2017). Temporal variability of blood lead, mercury, and cadmium levels in elderly panel study (2008–2014). Int J Hyg Environ Health 220: 407-414. http://dx.doi.org/10.1016/j.ijheh.2016.11.014.

Leech, TGJ; Adams, EA; Weathers, TD; Staten, LK; Filippelli, GM. (2016). Inequitable chronic lead exposure: A dual legacy of social and environmental injustice. Fam Community Health 39: 151-159. http://dx.doi.org/10.1097/FCH.0000000000000106.

Leggett, RW. (1993). An age-specific kinetic model of lead metabolism in humans [Review]. Environ Health Perspect 101: 598-616. http://dx.doi.org/10.1289/ehp.93101598.

Leggett, RW; Eckerman, KF; Williams, LR. (1993). An elementary method for implementing complex biokinetic models. Health Phys 64: 260-271. http://dx.doi.org/10.1097/00004032-199303000-00004.

Leibler, JH; Basra, K; Ireland, T; McDonagh, A; Ressijac, C; Heiger-Bernays, W; Vorhees, D; Rosenbaum, M. (2018). Lead exposure to children from consumption of backyard chicken eggs. Environ Res 167: 445-452. http://dx.doi.org/10.1016/j.envres.2018.08.013.

Leroyer, A; Leleu, B; Dehon, B; Frimat, P; Broly, F; Nisse, C. (2013). Influence of delta-aminolevulinic acid dehydratase gene polymorphism on selected lead exposure biomarkers in a cohort of ex-smelter workers. J Toxicol Environ Health A 76: 895-906. http://dx.doi.org/10.1080/15287394.2013.824843.

Levin-Schwartz, Y; Gennings, C; Henn, BC; Coull, BA; Placidi, D; Lucchini, R; Smith, DR; Wright, RO. (2020). Multi-media biomarkers: Integrating information to improve lead exposure assessment. Environ Res 183: 109148. http://dx.doi.org/10.1016/j.envres.2020.109148.

Levin, R; Vieira, CLZ; Mordarski, DC; Rosenbaum, MH. (2020). Lead seasonality in humans, animals, and the natural environment [Review]. Environ Res 180: 108797. http://dx.doi.org/10.1016/j.envres.2019.108797.

Li, F; Wang, Y; Zhang, J; Lu, Y; Zhu, X; Chen, X; Yan, J. (2020). Toxic metals in top selling cigarettes sold in China: Pulmonary bioaccessibility using simulated lung fluids and fuzzy health risk assessment. J Clean Prod 275: 124131. http://dx.doi.org/10.1016/j.jclepro.2020.124131.

Li, J; McDonald-Gillespie, J. (2020). Airborne lead (Pb) from abandoned mine waste in Northeastern Oklahoma, USA. Geohealth 4: e2020GH000273. http://dx.doi.org/10.1029/2020GH000273.

Li, SW; Li, HB; Luo, J; Li, HM; Qian, X; Liu, MM; Bi, J; Cui, XY; Ma, LQ. (2016). Influence of pollution control on lead inhalation bioaccessibility in PM2.5: A case study of 2014 Youth Olympic Games in Nanjing. Environ Int 94: 69-75. http://dx.doi.org/10.1016/j.envint.2016.05.010.

Lima, FS; Do Nascimento, CWA; da Silva, FBV; de Carvalho, VGB; Filho, MRR. (2009). Lead concentration and allocation in vegetable crops grown in a soil contaminated by battery residues. Horticultura Brasileira 27: 362-365. http://dx.doi.org/10.1590/S0102-05362009000300019.

Liu, J; McCauley, L; Compher, C; Yan, C; Shen, X; Needleman, H; Pinto-Martin, JA. (2011). Regular breakfast and blood lead levels among preschool children. Environ Health 10: 28. http://dx.doi.org/10.1186/1476-069X-10-28.

Liu, S; Hammond, SK; Rojas-Cheatham, A. (2013). Concentrations and potential health risks of metals in lip products. Environ Health Perspect 121: 705-710. http://dx.doi.org/10.1289/ehp.1205518.

Ljung, K; Oomen, A; Duits, M; Selinus, O; Berglund, M. (2007). Bioaccessibility of metals in urban playground soils. J Environ Sci Health A Tox Hazard Subst Environ Eng 42: 1241-1250. http://dx.doi.org/10.1080/10934520701435684.

Ljung, K; Selinus, O; Otabbong, E; Berglund, M. (2006). Metal and arsenic distribution in soil particle sizes relevant to soil ingestion by children. Appl Geochem 21: 1613-1624. http://dx.doi.org/10.1016/j.apgeochem.2006.05.005.

Logiewa, A; Miazgowicz, A; Krennhuber, K; Lanzerstorfer, C. (2020). Variation in the concentration of metals in road dust size fractions between 2 µm and 2 mm: Results from three metallurgical centres in Poland. Arch Environ Contam Toxicol 78: 46-59. http://dx.doi.org/10.1007/s00244-019-00686-x.

Long, GJ; Rosen, JF; Pounds, JG. (1990). Cellular lead toxicity and metabolism in primary and clonal osteoblastic bone cells. Toxicol Appl Pharmacol 102: 346-361. http://dx.doi.org/10.1016/0041-008X(90)90032-P.

Lorenzana, RM; Troast, R; Klotzbach, JM; Follansbee, MH; Diamond, GL. (2005). Issues related to time averaging of exposure in modeling risks associated with intermittent exposures to lead. Risk Anal 25: 169-178. http://dx.doi.org/10.1111/j.0272-4332.2005.00576.x.

Lough, GC; Schauer, JJ; Park, JS; Shafer, MM; Deminter, JT; Weinstein, JP. (2005). Emissions of metals associated with motor vehicle roadways. Environ Sci Technol 39: 826-836. http://dx.doi.org/10.1021/es048715f.

Lovestead, TM; Bruno, TJ. (2009). Application of the Advanced Distillation Curve Method to the Aviation Fuel Avgas 100LL. Energy Fuels 23: 2176-2183. http://dx.doi.org/10.1021/ef8011189.

Luo, XS; Yu, S; Li, XD. (2011). Distribution, availability, and sources of trace metals in different particle size fractions of urban soils in Hong Kong: Implications for assessing the risk to human health. Environ Pollut 159: 1317-1326. http://dx.doi.org/10.1016/j.envpol.2011.01.013.

Lupolt, SN; Santo, RE; Kim, BF; Green, C; Codling, E; Rule, AM; Chen, R; Scheckel, KG; Strauss, M; Cocke, A; Little, NG; Rupp, VC; Viqueira, R; Illuminati, J; Schmidt, AE; Nachman, KE. (2021). The safe urban harvests study: A community-driven cross-sectional assessment of metals in soil, irrigation water, and produce from urban farms and gardens in Baltimore, Maryland. Environ Health Perspect 129: 117004. http://dx.doi.org/10.1289/EHP9431.

Lupone, CD; Daniels, D; Lammert, D; Borsuk, R; Hobart, T; Lane, S; Shaw, A. (2020). Lead exposure in newly resettled pediatric refugees in Syracuse, NY. J Immigr Minor Health 22: 34-43. http://dx.doi.org/10.1007/s10903-019-00880-y.

Lynch, EE; Meier, HCS. (2020). The intersectional effect of poverty, home ownership, and racial/ethnic composition on mean childhood blood lead levels in Milwaukee County neighborhoods. PLoS ONE 15: e0234995. http://dx.doi.org/10.1371/journal.pone.0234995.

Machemer, SD. (2004). Characterization of airborne and bulk particulate from iron and steel manufacturing facilities. Environ Sci Technol 38: 381-389. http://dx.doi.org/10.1021/es020897v.

Maddaloni, M; Ballew, M; Diamond, G; Follansbee, M; Gefell, D; Goodrum, P; Johnson, M; Koporec, K; Khoury, G; Luey, J; Odin, M; Troast, R; Van Leeuwen, P; Zaragoza, L. (2005). Assessing lead risks at non-residential hazardous waste sites. Hum Ecol Risk Assess 11: 967-1003. http://dx.doi.org/10.1080/10807030500257838.

Maddaloni, M; Lolacono, N; Manton, W; Blum, C; Drexler, J; Graziano, J. (1998). Bioavailability of soilborne lead in adults, by stable isotope dilution. Environ Health Perspect 106(Suppl. 6): 1589-1594. http://dx.doi.org/10.1289/ehp.98106s61589.

Madrid, F; Biasioli, M; Ajmone-Marsan, F. (2008). Availability and bioaccessibility of metals in fine particles of some urban soils. Arch Environ Contam Toxicol 55: 21-32. http://dx.doi.org/10.1007/s00244-007-9086-1.

Mahaffey, KR; Annest, JL. (1986). Association of erythrocyte protoporphyrin with blood lead level and iron status in the second National Health and Nutrition Examination Survey, 1976-1980. Environ Res 41: 327-338. http://dx.doi.org/10.1016/S0013-9351(86)80194-3.

Mahaffey, KR; Gartside, PS; Glueck, CJ. (1986). Blood lead levels and dietary calcium intake in 1- to 11 year-old children: The second national health and nutrition examination survey, 1976 to 1980. Pediatrics 78: 257-262. http://dx.doi.org/10.1542/peds.78.2.257.

Mani, MS; Kunnathully, V; Rao, C; Kabekkodu, SP; Joshi, MB; D'Souza, HS. (2018). Modifying effects of δ-Aminolevulinate dehydratase polymorphism on blood lead levels and ALAD activity. Toxicol Lett 295: 351-356. http://dx.doi.org/10.1016/j.toxlet.2018.07.014.

Mantha, A; Tang, M; Pieper, KJ; Parks, JL; Edwards, MA. (2020). Tracking reduction of water lead levels in two homes during the Flint Federal Emergency. Water Research: X 7: 100047. http://dx.doi.org/10.1016/j.wroa.2020.100047.

Manton, WI. (1985). Total contribution of airborne lead to blood lead. Occup Environ Med 42: 168-172. http://dx.doi.org/10.1136/oem.42.3.168.

Manton, WI; Angle, CR; Krogstrand, KLS. (2005). Origin of lead in the United States diet. Environ Sci Technol 39: 8995-9000. http://dx.doi.org/10.1021/es051145e.

Manton, WI; Angle, CR; Stanek, KL; Kuntzelman, D; Reese, YR; Kuehnemann, TJ. (2003). Release of lead from bone in pregnancy and lactation. Environ Res 92: 139-151. http://dx.doi.org/10.1016/S0013-9351(03)00020-3.

Manton, WI; Angle, CR; Stanek, KL; Reese, YR; Kuehnemann, TJ. (2000). Acquisition and retention of lead by young children. Environ Res 82: 60-80. http://dx.doi.org/10.1006/enrs.1999.4003.

Manton, WI; Cook, JD. (1984). High accuracy (stable isotope dilution) measurements of lead in serum and cerebrospinal fluid. Br J Ind Med 41: 313-319. http://dx.doi.org/10.1136/oem.41.3.313.

Manton, WI; Malloy, CR. (1983). Distribution of lead in body fluids after ingestion of soft solder. Br J Ind Med 40: 51-57. http://dx.doi.org/10.1136/oem.40.1.51.

Manton, WI; Rothenberg, SJ; Manalo, M. (2001). The lead content of blood serum. Environ Res 86: 263-273. http://dx.doi.org/10.1006/enrs.2001.4271.

Marcus, AH. (1985). Multicompartment kinetic model for lead. III. Lead in blood plasma and erythrocytes. Environ Res 36: 473-489. http://dx.doi.org/10.1016/0013-9351(85)90039-8.

Marcus, AH; Schwartz, J. (1987). Dose–response curves for erythrocyte protoporphyrin vs blood lead: Effects of iron status. Environ Res 44: 221-227. http://dx.doi.org/10.1016/S0013-9351(87)80230-X.

Markowitz, ME; Weinberger, HL. (1990). Immobilization-related lead toxicity in previously lead-poisoned children. Pediatrics 86: 455-457.

Marsh, JW; Birchall, A. (1999). Determination of lung-to-blood absorption rates for lead and bismuth which are appropriate for radon progeny. Radiat Prot Dosimetry 83: 331-337. http://dx.doi.org/10.1093/oxfordjournals.rpd.a032689.

Masten, SJ; Davies, SH; McElmurry, SP. (2016). Flint water crisis: What happened and why? J Am Water Works Assoc 108: 22-34. http://dx.doi.org/10.5942/jawwa.2016.108.0195.

Matt, GE; Quintana, PJE; Hoh, E; Dodder, NG; Mahabee-Gittens, EM; Padilla, S; Markman, L; Watanabe, K. (2021). Tobacco smoke is a likely source of lead and cadmium in settled house dust. J Trace Elem Med Biol 63: 126656. http://dx.doi.org/10.1016/j.jtemb.2020.126656.

McClure, LF; Niles, JK; Kaufman, HW. (2016). Blood lead levels in young children: US, 2009-2015. J Pediatr 175: 173-181. http://dx.doi.org/10.1016/j.jpeds.2016.05.005.

McNeill, FE; Fisher, M; Chettle, DR; Inskip, M; Healey, N; Bray, R; Webber, CE; Manton, WI; Marro, L; Arbuckle, TE. (2018). The decrease in population bone lead levels in Canada between 1993 and 2010 as assessed by in vivo XRF. Physiol Meas 39: 015005. http://dx.doi.org/10.1088/1361-6579/aa904f.

McNeill, FE; Stokes, L; Brito, JAA; Chettle, DR; Kaye, WE. (2000). 109Cd K x-ray fluorescence measurements of tibial lead content in young adults exposed to lead in early childhood. Occup Environ Med 57: 465-471. http://dx.doi.org/10.1136/oem.57.7.465.

Meiman, J; Thiboldeaux, R; Anderson, H. (2015). Lead Poisoning and Anemia Associated with Use of Ayurvedic Medications Purchased on the Internet - Wisconsin, 2015. MMWR Morb Mortal Wkly Rep 64: 883. http://dx.doi.org/10.15585/mmwr.mm6432a6.

Meirer, F; Pemmer, B; Pepponi, G; Zoeger, N; Wobrauschek, P; Sprio, S; Tampieri, A; Goettlicher, J; Steininger, R; Mangold, S; Roschger, P; Berzlanovich, A; Hofstaetter, JG; Streli, C. (2011). Assessment of chemical species of lead accumulated in tidemarks of human articular cartilage by X-ray absorption near-edge structure analysis. J Synchrotron Radiat 18: 238-244. http://dx.doi.org/10.1107/S0909049510052040.

Meltzer, HM; Alexander, J; Brantsæter, AL; Borch-Iohnsen, B; Ellingsen, DG; Thomassen, Y; Holmen, J; Ydersbond, TA. (2016). The impact of iron status and smoking on blood divalent metal concentrations in Norwegian women in the HUNT2 Study. J Trace Elem Med Biol 38: 165-173. http://dx.doi.org/10.1016/j.jtemb.2016.04.008.

Meltzer, HM; Brantsæter, AL; Borch-Iohnsen, B; Ellingsen, DG; Alexander, J; Thomassen, Y; Stigum, H; Ydersbond, TA. (2010). Low iron stores are related to higher blood concentrations of manganese, cobalt and cadmium in non-smoking, Norwegian women in the HUNT 2 study. Environ Res 110: 497-504. http://dx.doi.org/10.1016/j.envres.2010.03.006.

Meng, Q; Richmond-Bryant, J; Davis, JA; Cohen, J; Svendsgaard, D; Brown, JS; Tuttle, L; Hubbard, H; Rice, J; Vinikoor-Imler, L; Sacks, JD; Kirrane, E; Kotchmar, D; Hines, E; Ross, M. (2014). Contribution of particle-size-fractionated airborne lead to blood lead during the National Health and Nutrition Examination Survey, 1999-2008. Environ Sci Technol 48: 1263–1270. http://dx.doi.org/10.1021/es4039825.

Mielke, HW; Covington, TP; Mielke, PW, Jr; Wolman, FJ; Powell, ET; Gonzales, CR. (2011a). Soil intervention as a strategy for lead exposure prevention: The New Orleans lead-safe childcare playground project. Environ Pollut 159: 2071-2077. http://dx.doi.org/10.1016/j.envpol.2010.11.008.

Mielke, HW; Gonzales, C. (2008). Mercury (Hg) and lead (Pb) in interior and exterior New Orleans house paint films. Chemosphere 72: 882-885. http://dx.doi.org/10.1016/j.chemosphere.2008.03.061.

Mielke, HW; Gonzales, C; Powell, E; Mielke, PW, Jr. (2005). Changes of multiple metal accumulation (MMA) in New Orleans soil: Preliminary evaluation of differences between survey I (1992) and survey II (2000). Int J Environ Res Public Health 2: 308-313. http://dx.doi.org/10.3390/ijerph2005020016.

Mielke, HW; Gonzales, CR; Mielke, PW, Jr. (2011b). The continuing impact of lead dust on children's blood lead: Comparison of public and private properties in New Orleans. Environ Res 111: 1164-1172. http://dx.doi.org/10.1016/j.envres.2011.06.010.

Mielke, HW; Gonzales, CR; Powell, E; Jartun, M; Mielke, PW, Jr. (2007). Nonlinear association between soil lead and blood lead of children in metropolitan New Orleans, Louisiana: 2000-2005. Sci Total Environ 388: 43-53. http://dx.doi.org/10.1016/j.scitotenv.2007.08.012.

Mielke, HW; Gonzales, CR; Powell, ET. (2017). Soil lead and children's blood lead disparities in pre- and post-Hurricane Katrina New Orleans (USA). Int J Environ Res Public Health 14: 407. http://dx.doi.org/10.3390/ijerph14040407.

Mielke, HW; Gonzales, CR; Powell, ET. (2019a). Curtailing lead aerosols: Effects of primary prevention on declining soil lead and children's blood lead in metropolitan New Orleans. Int J Environ Res Public Health 16: 2068. http://dx.doi.org/10.3390/ijerph16122068.

Mielke, HW; Gonzales, CR; Powell, ET; Laidlaw, MAS; Berry, KJ; Mielke, PW, Jr; Egendorf, SP. (2019b). The concurrent decline of soil lead and children's blood lead in New Orleans. Proc Natl Acad Sci USA 116: 22058-22064. http://dx.doi.org/10.1073/pnas.1906092116.

Mielke, HW; Gonzales, CR; Powell, ET; Mielke, PW, Jr. (2016). Spatiotemporal dynamic transformations of soil lead and children's blood lead ten years after Hurricane Katrina: New grounds for primary prevention. Environ Int 94: 567-575. http://dx.doi.org/10.1016/j.envint.2016.06.017.

Mielke, HW; Gonzales, CR; Smith, MK; Mielke, PW. (2000). Quantities and associations of lead, zinc, cadmium, manganese, chromium, nickel, vanadium, and copper in fresh Mississippi delta alluvium and New Orleans alluvial soils. Sci Total Environ 246: 249-259. http://dx.doi.org/10.1016/s0048-9697(99)00462-3.

Miranda, ML; Anthopolos, R; Hastings, D. (2011). A geospatial analysis of the effects of aviation gasoline on childhood blood lead levels. Environ Health Perspect 119: 1513-1516. http://dx.doi.org/10.1289/ehp.1003231.

Miranda, ML; Edwards, SE; Swamy, GK; Paul, CJ; Neelon, B. (2010). Blood lead levels among pregnant women: Historical versus contemporaneous exposures. Int J Environ Res Public Health 7: 1508-1519. http://dx.doi.org/10.3390/ijerph7041508.

Miyake, M; Ishigaki, K; Suzuki, T. (1986). Structure refinements of Pb2+ ion-exchanged apatites by x-ray powder pattern-fitting. J Solid State Chem 61: 230-235. http://dx.doi.org/10.1016/0022-4596(86)90026-5.

Molnár, P; Bellander, T; Sällsten, G; Boman, J. (2007). Indoor and outdoor concentrations of PM2.5 trace elements at homes, preschools and schools in Stockholm, Sweden. J Environ Monit 9: 348-357. http://dx.doi.org/10.1039/b616858b.

Momani, KA. (2006). Partitioning of lead in urban street dust based on the particle size distribution and chemical environments. Soil Sediment Contam 15: 131-146. http://dx.doi.org/10.1080/15320380500506289.

Montenegro, MF; Barbosa, F, Jr; Tanus-Santos, JE. (2008). Assessment of how pregnancy modifies plasma lead and plasma/whole blood lead ratio in ALAD 1-1 genotype women. Basic Clin Pharmacol Toxicol 102: 347-351. http://dx.doi.org/10.1111/j.1742-7843.2007.00205.x.

Moody, H; Grady, SC. (2017). Lead emissions and population vulnerability in the Detroit (Michigan, USA) Metropolitan Area, 2006-2013: A spatial and temporal analysis. Int J Environ Res Public Health 14: 1445. http://dx.doi.org/10.3390/ijerph14121445.

Moody, HA; Darden, JT; Pigozzi, BW. (2016). The relationship of neighborhood socioeconomic differences and racial residential segregation to childhood blood lead levels in metropolitan Detroit. J Urban Health 93: 820-839. http://dx.doi.org/10.1007/s11524-016-0071-8.

Morrison, D; Lin, Q; Wiehe, S; Liu, G; Rosenman, M; Fuller, T; Wang, J; Filippelli, G. (2013). Spatial relationships between lead sources and children's blood lead levels in the urban center of Indianapolis (USA). Environ Geochem Health 35: 171-183. http://dx.doi.org/10.1007/s10653-012-9474-y.

Morrison, JN; Quarterman, J. (1987). The relationship between iron status and lead absorption in rats. Biol Trace Elem Res 14: 115-126. http://dx.doi.org/10.1007/BF02795602.

Morrow, PE; Beiter, H; Amato, F; Gibb, FR. (1980). Pulmonary retention of lead: An experimental study in man. Environ Res 21: 373-384. http://dx.doi.org/10.1016/0013-9351(80)90040-7.

Moya, J; Phillips, L. (2014). A review of soil and dust ingestion studies for children [Review]. J Expo Sci Environ Epidemiol 24: 545-554. http://dx.doi.org/10.1038/jes.2014.17.

Mushak, P. (1991). Gastro-intestinal absorption of lead in children and adults: Overview of biological and biophysico-chemical aspects. Chem Speciation Bioavailability 3: 87-104. http://dx.doi.org/10.1080/09542299.1991.11083160.

NASEM (National Academies of Sciences, Engineering, and Medicine). (2020). Review of the Department of Defense biokinetic modeling approach in support of establishing an airborne lead exposure limit. Washington, DC: National Academies Press. http://dx.doi.org/10.17226/25683.

NASEM (National Academies of Sciences, Engineering, and Medicine). (2021). Options for reducing lead emissions from piston-engine aircraft. Washington, DC: National Academies Press. http://dx.doi.org/10.17226/26050.

Newman, N; Jones, C; Page, E; Ceballos, D; Oza, A. (2015). Investigation of childhood lead poisoning from parental take-home exposure from an electronic scrap recycling facility — Ohio, 2012. MMWR Morb Mortal Wkly Rep 64: 743-745.

Ngueta, G; Prévost, M; Deshommes, E; Abdous, B; Gauvin, D; Levallois, P. (2014). Exposure of young children to household water lead in the Montreal area (Canada): The potential influence of winter-to-summer changes in water lead levels on children's blood lead concentration. Environ Int 73: 57-65. http://dx.doi.org/10.1016/j.envint.2014.07.005.

Nie, H; Sánchez, BN; Wilker, E; Weisskopf, MG; Schwartz, J; Sparrow, D; Hu, H. (2009). Bone lead and endogenous exposure in an environmentally exposed elderly population: The Normative Aging Study. J Occup Environ Med 51: 848-857. http://dx.doi.org/10.1097/JOM.0b013e3181aa0106.

Nie, LH; Sanchez, S; Newton, K; Grodzins, L; Cleveland, RO; Weisskopf, MG. (2011). In vivo quantification of lead in bone with a portable x-ray fluorescence system - Methodology and feasibility. Phys Med Biol 56: N39-N51. http://dx.doi.org/10.1088/0031-9155/56/3/N01.

Nielsen, T; Jensen, KA; Grandjean, P. (1978). Organic lead in normal human brains. Nature 274: 602-603. http://dx.doi.org/10.1038/274602a0.

Nilsson, U; Attewell, R; Christoffersson, JO; Schütz, A; Ahlgren, L; Skerfving, S; Mattsson, S. (1991). Kinetics of lead in bone and blood after end of occupational exposure. Basic Clin Pharmacol Toxicol 68: 477-484. http://dx.doi.org/10.1111/j.1600-0773.1991.tb01273.x.

Niu, J; Rasmussen, PE; Hassan, NM; Vincent, R. (2010). Concentration distribution and bioaccessibility of trace elements in nano and fine urban airborne particulate matter: Influence of particle size. Water Air Soil Pollut 213: 211-225. http://dx.doi.org/10.1007/s11270-010-0379-z.

NRC (National Research Council). (2013). Potential health risks to DOD firing-range personnel from recurrent lead exposure. Washington, DC: National Academies Press. http://dx.doi.org/10.17226/18249.

Nriagu, J; Burt, B; Linder, A; Ismail, A; Sohn, W. (2006). Lead levels in blood and saliva in a low-income population of Detroit, Michigan. Int J Hyg Environ Health 209: 109-121. http://dx.doi.org/10.1016/j.ijheh.2005.11.005.

Nriagu, J; Senthamarai-Kannan, R; Jamil, H; Fakhori, M; Korponic, S. (2011). Lead poisoning among Arab American and African American children in the Detroit metropolitan area, Michigan. Bull Environ Contam Toxicol 87: 238-244. http://dx.doi.org/10.1007/s00128-011-0346-4.

Nussbaumer-Streit, B; Mayr, V; Dobrescu, AI; Wagner, G; Chapman, A; Pfadenhauer, LM; Lohner, S; Lhachimi, SK; Busert, LK; Gartlehner, G. (2020). Household interventions for secondary prevention of domestic lead exposure in children. Cochrane Database Syst Rev 10: CD006047. http://dx.doi.org/10.1002/14651858.CD006047.pub6.

Nussbaumer-Streit, B; Yeoh, B; Griebler, U; Pfadenhauer, LM; Busert, LK; Lhachimi, SK; Lohner, S; Gartlehner, G. (2016). Household interventions for preventing domestic lead exposure in children [Review]. Cochrane Database Syst Rev (10): CD006047. http://dx.doi.org/10.1002/14651858.CD006047.pub5.

O'Flaherty, EJ. (1995). Physiologically based models for bone-seeking elements. V. Lead absorption and disposition in childhood [Review]. Toxicol Appl Pharmacol 131: 297-308. http://dx.doi.org/10.1006/taap.1995.1072.

O'Flaherty, EJ. (1998). A physiologically based kinetic model for lead in children and adults [Review]. Environ Health Perspect 106(Suppl. 6): 1495-1503. http://dx.doi.org/10.1289/ehp.98106s61495.

O'Flaherty, EJ; Hammond, PB; Lerner, SI. (1982). Dependence of apparent blood lead half-life on the length of previous lead exposure in humans. Toxicol Sci 2: 49-54. http://dx.doi.org/10.1093/toxsci/2.1.49.

O'Flaherty, EJ; Inskip, MJ; Franklin, CA; Durbin, PW; Manton, WI; Baccanale, CL. (1998). Evaluation and modification of a physiologically based model of lead kinetics using data from a sequential isotope study in cynomolgus monkeys. Toxicol Appl Pharmacol 149: 1-16. http://dx.doi.org/10.1006/taap.1997.8328.

O'Shea, MJ; Krekeler, MPS; Vann, DR; Gieré, R. (2021). Investigation of Pb-contaminated soil and road dust in a polluted area of Philadelphia. Environ Monit Assess 193: 440. http://dx.doi.org/10.1007/s10661-021-09213-9.

Obeng-Gyasi, E; Roostaei, J; Gibson, JM. (2021). Lead distribution in urban soil in a medium-sized city: Household-scale analysis. Environ Sci Technol 55: 3696-3705. http://dx.doi.org/10.1021/acs.est.0c07317.

Odigie, KO; Flegal, AR. (2014). Trace metal inventories and lead isotopic composition chronicle a forest fire's remobilization of industrial contaminants deposited in the Angeles National Forest. PLoS ONE 9: e107835. http://dx.doi.org/10.1371/journal.pone.0107835.

Oldereid, NB; Thomassen, Y; Attramadal, A; Olaisen, B; Purvis, K. (1993). Concentrations of lead, cadmium and zinc in the tissues of reproductive organs of men. J Reprod Fertil 99: 421-425. http://dx.doi.org/10.1530/jrf.0.0990421.

Olmedo, P; Goessler, W; Tanda, S; Grau-Perez, M; Jarmul, S; Aherrera, A; Chen, R; Hilpert, M; Cohen, JE; Navas-Acien, A; Rule, AM. (2018). Metal Concentrations in e-Cigarette Liquid and Aerosol Samples: The Contribution of Metallic Coils. Environ Health Perspect 126: 027010. http://dx.doi.org/10.1289/EHP2175.

Ong, CN; Lee, WR. (1980). Distribution of lead-203 in human peripheral blood in vitro. Br J Ind Med 37: 78-84. http://dx.doi.org/10.1136/oem.37.1.78.

OSHA (Occupational Safety & Health Administration). (2020). 1910.1025 - Lead. Available online at https://www.osha.gov/laws-regs/regulations/standardnumber/1910/1910.1025 (accessed

Özkaynak, H; Glen, G; Cohen, J; Hubbard, H; Thomas, K; Phillips, L; Tulve, N. (2022). Model based prediction of age-specific soil and dust ingestion rates for children. J Expo Sci Environ Epidemiol 32: 472-480. http://dx.doi.org/10.1038/s41370-021-00406-5.

Pakbin, P; Ning, Z; Shafer, MM; Schauer, JJ; Sioutas, C. (2011). Seasonal and spatial coarse particle elemental concentrations in the Los Angeles area. Aerosol Sci Technol 45: 949-963. http://dx.doi.org/10.1080/02786826.2011.571309.

Park, SK; Mukherjee, B; Xia, X; Sparrow, D; Weisskopf, MG; Nie, H; Hu, H. (2009). Bone lead level prediction models and their application to examine the relationship of lead exposure and hypertension in the third National Health and Nutrition Examination Survey. J Occup Environ Med 51: 1422-1436. http://dx.doi.org/10.1097/JOM.0b013e3181bf6c8d.

Park, WJ; Gu, HM; Lee, SH. (2013). Blood lead level and types of aviation fuel in aircraft maintenance crew. Aviat Space Environ Med 84: 1087-1091.

Patel, AB; Prabhu, AS. (2009). Determinants of lead level in umbilical cord blood. Indian Pediatr 46: 791-793.

Pavilonis, B; Cheng, Z; Johnson, G; Maroko, A. (2022). Lead, soils, and children: An ecological analysis of lead contamination in parks and elevated blood lead levels in Brooklyn, New York. Arch Environ Contam Toxicol 82: 1-10. http://dx.doi.org/10.1007/s00244-021-00902-7.

Pavilonis, B; Maroko, A; Cheng, Z. (2020). Lead in New York City's soils: Population growth, land use, and contamination. Int J Hyg Environ Health 229: 113564. http://dx.doi.org/10.1016/j.ijheh.2020.113564.

Pemmer, B; Roschger, A; Wastl, A; Hofstaetter, JG; Wobrauschek, P; Simon, R; Thaler, HW; Roschger, P; Klaushofer, K; Streli, C. (2013). Spatial distribution of the trace elements zinc, strontium and lead in human bone tissue. Bone 57: 184-193. http://dx.doi.org/10.1016/j.bone.2013.07.038.

Perez, AL; Nembhard, M; Monnot, A; Bator, D; Madonick, E; Gaffney, SH. (2017). Child and adult exposure and health risk evaluation following the use of metal- and metalloid-containing costume cosmetics sold in the United States. Regul Toxicol Pharmacol 84: 54-63. http://dx.doi.org/10.1016/j.yrtph.2016.12.005.

Perry, SG; Cimorelli, AJ; Paine, RJ; Brode, RW; Weil, JC; Venkatram, A; Wilson, RB; Lee, RF; Peters, WD. (2005). AERMOD: A dispersion model for industrial source applications. Part II: Model performance against 17 field study databases. J Appl Meteorol 44: 694-708. http://dx.doi.org/10.1175/JAM2228.1.

Pezzi, C; Lee, D; Kennedy, L; Aguirre, J; Titus, M; Ford, R; Cochran, J; Smock, L; Mamo, B; Urban, K; Morillo, J; Hughes, S; Payton, C; Scott, K; Montour, J; Matheson, J; Brown, MJ; Mitchell, T. (2019). Blood lead levels among resettled refugee children in select US states, 2010-2014. Pediatrics 143: e20182591. http://dx.doi.org/10.1542/peds.2018-2591.

Pieper, KJ; Krometis, LA; Gallagher, DL; Benham, BL; Edwards, M. (2015). Incidence of waterborne lead in private drinking water systems in Virginia. J Water Health 13: 897-908. http://dx.doi.org/10.2166/wh.2015.275.

Pieper, KJ; Martin, R; Tang, M; Walters, L; Parks, J; Roy, S; Devine, C; Edwards, MA. (2018). Evaluating water lead levels during the Flint water crisis. Environ Sci Technol 52: 8124-8132. http://dx.doi.org/10.1021/acs.est.8b00791.

Pieper, KJ; Tang, M; Edwards, MA. (2017). Flint Water Crisis Caused By Interrupted Corrosion Control: Investigating "Ground Zero" Home. Environ Sci Technol 51: 2007-2014. http://dx.doi.org/10.1021/acs.est.6b04034.

Pierre, F; Vallayer, C; Baruthio, F; Peltier, A; Pale, S; Rouyer, J; Goutet, P; Aubrège, B; Lecossois, C; Guillemin, C; Elcabache, JM; Verelle, B; Fabriès, JF. (2002). Specific relationship between blood lead and air lead in the crystal industry. Int Arch Occup Environ Health 75: 217-223. http://dx.doi.org/10.1007/s00420-001-0303-3.

Pinto, E; Cruz, M; Ramos, P; Santos, A; Almeida, A. (2017). Metals transfer from tobacco to cigarette smoke: Evidences in smokers' lung tissue. J Hazard Mater 325: 31-35. http://dx.doi.org/10.1016/j.jhazmat.2016.11.069.

Pocock, SJ; Shaper, AG; Walker, M; Wale, CJ; Clayton, B; Delves, T; Lacey, RF; Packham, RF; Powell, P. (1983). Effects of tap water lead, water hardness, alcohol, and cigarettes on blood lead concentrations. J Epidemiol Community Health 37: 1-7. http://dx.doi.org/10.1136/jech.37.1.1.

Popovic, M; Mcneill, FE; Chettle, DR; Webber, CE; Lee, CV; Kaye, WE. (2005). Impact of occupational exposure on lead levels in women. Environ Health Perspect 113: 478-484. http://dx.doi.org/10.1289/ehp.7386.

Pounds, JG; Leggett, RW. (1998). The ICRP age-specific biokinetic model for lead: Validations, empirical comparisons, and explorations [Review]. Environ Health Perspect 106(Suppl. 6): 1505-1511. http://dx.doi.org/10.1289/ehp.98106s61505.

Pounds, JG; Long, GJ; Rosen, JF. (1991). Cellular and molecular toxicity of lead in bone [Review]. Environ Health Perspect 91: 17-32. http://dx.doi.org/10.1289/ehp.919117.

Pounds, JG; Marlar, RJ; Allen, JR. (1978). Metabolism of lead-210 in juvenile and adult rhesus monkeys (Macaca mulatta). Bull Environ Contam Toxicol 19: 684-691. http://dx.doi.org/10.1007/BF01685858.

Pounds, JG; Rosen, JF. (1986). Cellular metabolism of lead: A kinetic analysis in cultured osteoclastic bone cells. Toxicol Appl Pharmacol 83: 531-545. http://dx.doi.org/10.1016/0041-008X(86)90236-X.

Pye, K; Blott, SJ; Croft, DJ; Witton, SJ. (2007). Discrimination between sediment and soil samples for forensic purposes using elemental data: an investigation of particle size effects. Forensic Sci Int 167: 30-42. http://dx.doi.org/10.1016/j.forsciint.2006.06.005.

Rabinowitz, MB; Kopple, JD; Wetherill, GW. (1980). Effect of food intake and fasting on gastrointestinal lead absorption in humans. Am J Clin Nutr 33: 1784-1788. http://dx.doi.org/10.1093/ajcn/33.8.1784.

Rabinowitz, MB; Leviton, A; Bellinger, D. (1993). Relationships between serial blood lead levels and exfoliated tooth dentin lead levels: Models of tooth lead kinetics. Calcif Tissue Int 53: 338-341. http://dx.doi.org/10.1007/BF01351840.

Rabinowitz, MB; Wetherill, GW; Kopple, JD. (1973). Lead metabolism in the normal human: Stable isotope studies. Science 182: 725-727. http://dx.doi.org/10.1126/science.182.4113.725.

Rabinowitz, MB; Wetherill, GW; Kopple, JD. (1976). Kinetic analysis of lead metabolism in healthy humans. J Clin Invest 58: 260-270. http://dx.doi.org/10.1172/JCI108467.

Rabinowitz, MB; Wetherill, GW; Kopple, JD. (1977). Magnitude of lead intake from respiration by normal man. J Lab Clin Med 90: 238-248.

Rabito, FA; Iqbal, S; Perry, S; Arroyave, W; Rice, JC. (2012). Environmental lead after Hurricane Katrina: implications for future populations. Environ Health Perspect 120: 180-184. http://dx.doi.org/10.1289/ehp.1103774.

Ranft, U; Delschen, T; Machtolf, M; Sugiri, D; Wilhelm, M. (2008). Lead concentration in the blood of children and its association with lead in soil and ambient air—Trends between 1983 and 2000 in Duisburg. J Toxicol Environ Health A 71: 710-715. http://dx.doi.org/10.1080/15287390801985117.

Raymond, JS; Kennedy, C; Brown, MJ. (2013). Blood lead level analysis among refugee children resettled in New Hampshire and Rhode Island. Public Health Nursing 30: 70-79. http://dx.doi.org/10.1111/phn.12007.

Rebelo, FM; Caldas, ED. (2016). Arsenic, lead, mercury and cadmium: Toxicity, levels in breast milk and the risks for breastfed infants [Review]. Environ Res 151: 671-688. http://dx.doi.org/10.1016/j.envres.2016.08.027.

Reinard, MS; Adoua, K; Martini, JM; Johnston, MV. (2007). Source characterization and identification by real-time single particle mass spectrometry. Atmos Environ 41: 9397-9409. http://dx.doi.org/10.1016/j.atmosenv.2007.09.001.

Renner, R. (2006). Chloramine's effect on lead in drinking water.[comment] [Letter]. Environ Sci Technol 40: 3129-3130.

Rentschler, G; Broberg, K; Lundh, T; Skerfving, S. (2012). Long-term lead elimination from plasma and whole blood after poisoning. Int Arch Occup Environ Health 85: 311-316. http://dx.doi.org/10.1007/s00420-011-0673-0.

Resongles, E; Dietze, V; Green, DC; Harrison, RM; Ochoa-Gonzalez, R; Tremper, AH; Weiss, DJ. (2021). Strong evidence for the continued contribution of lead deposited during the 20th century to the atmospheric environment in London of today. Proc Natl Acad Sci USA 118: e2102791118. http://dx.doi.org/10.1073/pnas.2102791118.

Riblet, C; Deshommes, E; Laroche, L; Prévost, M. (2019). True exposure to lead at the tap: Insights from proportional sampling, regulated sampling and water use monitoring. Water Res 156: 327-336. http://dx.doi.org/10.1016/j.watres.2019.03.005.

Richmond-Bryant, J; Meng, Q; Cohen, J; Davis, JA; Svendsgaard, D; Brown, JS; Tuttle, L; Hubbard, H; Rice, J; Kirrane, E; Vinikoor-Imler, L; Kotchmar, D; Hines, E; Ross, M. (2015). Effect measure modification of blood lead-air lead slope factors. J Expo Sci Environ Epidemiol 25: 411-416. http://dx.doi.org/10.1038/jes.2014.46.

Richmond-Bryant, J; Meng, Q; Davis, A; Cohen, J; Lu, SE; Svendsgaard, D; Brown, JS; Tuttle, L; Hubbard, H; Rice, J; Kirrane, E; Vinikoor-Imler, LC; Kotchmar, D; Hines, EP; Ross, M. (2014). The influence of declining air lead levels on blood lead–air lead slope factors in children. Environ Health Perspect 122: 754-760. http://dx.doi.org/10.1289/ehp.1307072.

Richmond-Bryant, J; Meng, Q; Davis, JA; Cohen, J; Svendsgaard, D; Brown, JS; Tuttle, L; Hubbard, H; Rice, J; Kirrane, E; Vinikoor-Imler, L; Kotchmar, D; Hines, E; Ross, M. (2013). A multi-level model of blood lead as a function of air lead. Sci Total Environ 461-462: 207-213. http://dx.doi.org/10.1016/j.scitotenv.2013.05.008.

Richter, PA; Bishop, EE; Wang, J; Kaufmann, R. (2013). Trends in tobacco smoke exposure and blood lead levels among youths and adults in the United States: The National Health and Nutrition Examination Survey, 1999-2008. Prev Chronic Dis 10: 130056. http://dx.doi.org/10.5888/pcd10.130056.

Riedt, CS; Buckley, BT; Brolin, RE; Ambia-Sobhan, H; Rhoads, GG; Shapses, SA. (2009). Blood lead levels and bone turnover with weight reduction in women. J Expo Sci Environ Epidemiol 19: 90-96. http://dx.doi.org/10.1038/jes.2008.5.

Rinsky, JL; Higgins, S; Angelon-Gaetz, K; Hogan, D; Lauffer, P; Davies, M; Fleischauer, A; Musolin, K; Gibbins, J; MacFarquhar, J; Moore, Z. (2018). Occupational and take-home lead exposure among lead oxide manufacturing employees, North Carolina, 2016. Public Health Rep 133: 700-706. http://dx.doi.org/10.1177/0033354918795442.

Ritchey, MD; Sucosky, MS; Jefferies, T; McCormick, D; Hesting, A; Blanton, C; Duwve, J; Bruner, R; Daley, WR; Jarrett, J; Brown, MJ. (2011). Lead poisoning among Burmese refugee children - Indiana, 2009. Clin Pediatr (Phila) 50: 648-656. http://dx.doi.org/10.1177/0009922811398958.

Robbins, N; Zhang, ZF; Sun, J; Ketterer, ME; Lalumandier, JA; Shulze, RA. (2010). Childhood lead exposure and uptake in teeth in the Cleveland area during the era of leaded gasoline. Sci Total Environ 408: 4118-4127. http://dx.doi.org/10.1016/j.scitotenv.2010.04.060.

Roberts, JR; Reigart, JR; Ebeling, M; Hulsey, TC. (2001). Time required for blood lead levels to decline in nonchelated children. Clin Toxicol 39: 153-160. http://dx.doi.org/10.1081/CLT-100103831.

Rockway, SW; Weber, CW; Lei, KY; Kemberling, SR. (1984). Lead concentrations of milk, blood, and hair in lactating women. Int Arch Occup Environ Health 53: 181-187. http://dx.doi.org/10.1007/BF00398812.

Rodrigues, EG; Virji, MA; Mcclean, MD; Weinberg, J; Woskie, S; Pepper, LD. (2010). Personal exposure, behavior, and work site conditions as determinants of blood lead among bridge painters. J Occup Environ Hyg 7: 80-87. http://dx.doi.org/10.1080/15459620903418316.

Röllin, HB; Olutola, B; Channa, K; Odland, JØ. (2017). Reduction of in utero lead exposures in South African populations: Positive impact of unleaded petrol. PLoS ONE 12: e0186445. http://dx.doi.org/10.1371/journal.pone.0186445.

Rosen, JF. (1983). The metabolism of lead in isolated bone cell populations: Interactions between lead and calcium. Toxicol Appl Pharmacol 71: 101-112. http://dx.doi.org/10.1016/0041-008X(83)90049-2.

Rothenberg, SJ; Karchmer, S; Schnaas, L; Perroni, E; Zea, F; Alba, JF. (1994). Changes in serial blood lead levels during pregnancy. Environ Health Perspect 102: 876-880. http://dx.doi.org/10.1289/ehp.94102876.

Ruby, MV; Lowney, YW. (2012). Selective soil particle adherence to hands: Implications for understanding oral exposure to soil contaminants. Environ Sci Technol 46: 12759-12771. http://dx.doi.org/10.1021/es302473q.

Ruckart, PZ; Jones, RL; Courtney, JG; Leblanc, TT; Jackson, W; Karwowski, MP; Cheng, PY; Allwood, P; Svendsen, ER; Breysse, PN. (2021). Update of the Blood Lead Reference Value - United States, 2021. MMWR Morb Mortal Wkly Rep 70: 1509-1512. http://dx.doi.org/10.15585/mmwr.mm7043a4.

Ryu, JE; Ziegler, EE; Nelson, SE; Fomon, SJ. (1983). Dietary intake of lead and blood lead concentration in early infancy. Am J Dis Child 137: 886-891. http://dx.doi.org/10.1001/archpedi.1983.02140350060015.

Saikat, S; Barnes, B; Westwood, D. (2007). A review of laboratory results for bioaccessibility values of arsenic, lead and nickel in contaminated UK soils. J Environ Sci Health A Tox Hazard Subst Environ Eng 42: 1213-1221. http://dx.doi.org/10.1080/10934520701435486.

Sakai, T; Yanagihara, S; Kunugi, Y; Ushio, K. (1982). Relationships between distribution of lead in erythrocytes in vivo and in vitro and inhibition of ALA-D. Br J Ind Med 39: 382-387. http://dx.doi.org/10.1136/oem.39.4.382.

Sandell, AMD; Baker, RD; Maccarone, J; Baker, SS. (2017). Health Status and Anthropometric Changes in Resettled Refugee Children. J Pediatr Gastroenterol Nutr 65: 569-573. http://dx.doi.org/10.1097/MPG.0000000000001671.

Sansom, G; Cizmas, L; Aarvig, K; Dixon, B; Kirsch, KR; Katare, A; Sansom, L. (2019). Vulnerable populations exposed to lead-contaminated drinking water within Houston ship channel communities. Int J Environ Res Public Health 16: 2745. http://dx.doi.org/10.3390/ijerph16152745.

Savadatti, SS; Liu, M; Caglayan, C; Reuther, J; Lewis-Michl, EL; Aldous, KM; Parsons, PJ; Kannan, K; Rej, R; Wang, W; Palmer, CD; Steuerwald, AJ; Wattigney, WA; Irvin-Barnwell, E; Hwang, SA. (2019). Biomonitoring of populations in Western New York at risk for exposure to Great Lakes contaminants. Environ Res 179: 108690. http://dx.doi.org/10.1016/j.envres.2019.108690.

Sayyadi, A; Ioannidu, S. (2015). Determination of lead content in the most popular brands of lipsticks in Sulaimani, Iraq. J Indian Chem Soc 92: 1625-1628.

Schauer, JJ; Lough, GC; Shafer, MM; Christensen, WF; Arndt, MF; DeMinter, JT; Park, JS. (2006). Characterization of metals emitted from motor vehicles. (133). Boston, MA: Health Effects Institute. https://www.healtheffects.org/publication/characterization-metals-emitted-motor-vehicles.

Schell, LM; Denham, M; Stark, AD; Ravenscroft, J; Parsons, P; Schulte, E. (2004). Relationship between blood lead concentration and dietary intakes of infants from 3 to 12 months of age. Environ Res 96: 264-273. http://dx.doi.org/10.1016/j.envres.2004.02.008.

Schirmer, J; Havlena, J; Jacobs, DE; Dixon, S; Ikens, R. (2012). Lead exposures from varnished floor refinishing. J Occup Environ Hyg 9: 280-287. http://dx.doi.org/10.1080/15459624.2012.668489.

Schmeltz, MT; Grassman, JA; Cheng, Z. (2020). Assessing soil lead exposure for gardeners in New York City - A pilot study. In V Vasenev; E Dovletyarova; Z Cheng; R Valentini; C Calfapietra (Eds.), Green technologies and infrastructure to enhance urban ecosystem services (pp. 4-11). Cham, Denmark: Springer. http://dx.doi.org/10.1007/978-3-030-16091-3_2.

Schnaas, L; Rothenberg, SJ; Flores, MF; Martinez, S; Hernandez, C; Osorio, E; Perroni, E. (2004). Blood lead secular trend in a cohort of children in Mexico City (1987-2002). Environ Health Perspect 112: 1110-1115. http://dx.doi.org/10.1289/ehp.6636.

Schroeder, HA; Tipton, IH. (1968). The human body burden of lead [Review]. Arch Environ Health 17: 965-978. http://dx.doi.org/10.1080/00039896.1968.10665354.

Schuhmacher, M; Hernandez, M; Domingo, JL; Fernandez-Ballart, JD; Llobet, JM; Corbella, J. (1996). A longitudinal study of lead mobilization during pregnancy: Concentrations in maternal and umbilical cord blood. Trace Elem Electroly 13: 177-181.

Schultz, BD; Morara, M; Buxton, BE; Weintraub, M, ax. (2017). Predicting Blood-Lead Levels Among U.S. Children at the Census Tract Level. Environmental Justice 10: 129. http://dx.doi.org/10.1089/env.2017.0005.

Schütz, A; Bergdahl, IA; Ekholm, A; Skerfving, S. (1996). Measurement by ICP-MS of lead in plasma and whole blood of lead workers and controls. Occup Environ Med 53: 736-740. http://dx.doi.org/10.1136/oem.53.11.736.

Schwartz, J; Pitcher, H. (1989). The relationship between gasoline lead and blood lead in the United States. J Offic Stat 5: 421-431.

Seagle, EE; Montour, J; Lee, D; Phares, C; Jentes, ES. (2020). Health screening results of Cubans settling in Texas, USA, 2010-2015: A cross-sectional analysis. PLoS Med 17: e1003233. http://dx.doi.org/10.1371/journal.pmed.1003233.

Sears, ME; Kerr, KJ; Bray, RI. (2012). Arsenic, cadmium, lead, and mercury in sweat: A systematic review [Review]. J Environ Public Health 2012: 184745. http://dx.doi.org/10.1155/2012/184745.

Seifu, S; Tanabe, K; Hauck, FR. (2020). The Prevalence of Elevated Blood Lead Levels in Foreign-Born Refugee Children Upon Arrival to the U.S. and the Adequacy of Follow-up Treatment. J Immigr Minor Health. http://dx.doi.org/10.1007/s10903-019-00878-6.

Sesli, E; Tuzen, M; Soylak, M. (2008). Evaluation of trace metal contents of some wild edible mushrooms from Black Sea region, Turkey. J Hazard Mater 160: 462-467. http://dx.doi.org/10.1016/j.jhazmat.2008.03.020.

Shah, MP; Shendell, DG; Strickland, PO; Bogden, JD; Kemp, FW; Halperin, W. (2017). Lead content of sindoor, a Hindu religious powder and cosmetic: New Jersey and India, 2014-2015. Am J Public Health 107: 1630-1632. http://dx.doi.org/10.2105/AJPH.2017.303931.

Shakya, S; Bhatta, MP. (2019). Elevated blood lead levels among resettled refugee children in Ohio, 2009-2016. Am J Public Health 109: 912-920. http://dx.doi.org/10.2105/AJPH.2019.305022.

Shannon, M; Graef, JW. (1996). Lead intoxication in children with pervasive developmental disorders. Clin Toxicol 34: 177-181. http://dx.doi.org/10.3109/15563659609013767.

Shao, LY; Zhang, LJ; Zhen, Z. (2017). Interrupted time series analysis of children's blood lead levels: A case study of lead hazard control program in Syracuse, New York. PLoS ONE 12: e0171778. http://dx.doi.org/10.1371/journal.pone.0171778.

Shawahna, R. (2021). Breast milk to blood lead ratios among women from the West Bank of Palestine: A cross-sectional study of associated factors. Int Breastfeed J 16: 61. http://dx.doi.org/10.1186/s13006-021-00410-3.

Shepherd, TJ; Dirks, W; Manmee, C; Hodgson, S; Banks, DA; Averley, P; Pless-Mulloli, T. (2012). Reconstructing the life-time lead exposure in children using dentine in deciduous teeth. Sci Total Environ 425: 214-222. http://dx.doi.org/10.1016/j.scitotenv.2012.03.022.

Shepherd, TJ; Dirks, W; Roberts, NMW; Patel, JG; Hodgson, S; Pless-Mulloli, T; Walton, P; Parrish, RR. (2016). Tracing fetal and childhood exposure to lead using isotope analysis of deciduous teeth. Environ Res 146: 145-153. http://dx.doi.org/10.1016/j.envres.2015.12.017.

Sherlock, J; Smart, G; Forbes, GI; Moore, MR; Patterson, WJ; Richards, WN; Wilson, TS. (1982). Assessment of lead intakes and dose-response for a population in Ayr exposed to a plumbosolvent water supply. Hum Exp Toxicol 1: 115-122. http://dx.doi.org/10.1177/096032718200100203.

Sherlock, JC; Ashby, D; Delves, HT; Forbes, GI; Moore, MR; Patterson, WJ; Pocock, SJ; Quinn, MJ; Richards, WN; Wilson, TS. (1984). Reduction in exposure to lead from drinking water and its effect on blood lead concentrations. Hum Toxicol 3: 383-392. http://dx.doi.org/10.1177/096032718400300503.

Sherlock, JC; Quinn, MJ. (1986). Relationship between blood and lead concentrations and dietary lead intake in infants: The Glasgow Duplicate Diet Study 1979-1980. Food Addit Contam 3: 167-176. http://dx.doi.org/10.1080/02652038609373579.

Shih, RA; Hu, H; Weisskopf, MG; Schwartz, BS. (2007). Cumulative lead dose and cognitive function in adults: A review of studies that measured both blood lead and bone lead [Review]. Environ Health Perspect 115: 483-492. http://dx.doi.org/10.1289/ehp.9786.

Shim, YK; Lewin, MD; Ruiz, P; Eichner, JE; Mumtaz, MM. (2017). Prevalence and associated demographic characteristics of exposure to multiple metals and their species in human populations: The United States NHANES, 2007-2012. J Toxicol Environ Health A 80: 502-512. http://dx.doi.org/10.1080/15287394.2017.1330581.

Siciliano, SD; James, K; Zhang, GY; Schafer, AN; Peak, JD. (2009). Adhesion and Enrichment of Metals on Human Hands from Contaminated Soil at an Arctic Urban Brownfield. Environ Sci Technol 43: 6385-6390. http://dx.doi.org/10.1021/es901090w.

Silbergeld, EK. (1991). Lead in bone: Implications for toxicology during pregnancy and lactation [Review]. Environ Health Perspect 91: 63-70. http://dx.doi.org/10.2307/3430984.

Silbergeld, EK; Schwartz, J; Mahaffey, K. (1988). Lead and osteoporosis: Mobilization of lead from bone in postmenopausal women. Environ Res 47: 79-94. http://dx.doi.org/10.1016/S0013-9351(88)80023-9.

Simon, DL; Maynard, EJ; Thomas, KD. (2007). Living in a sea of lead — Changes in blood- and hand-lead of infants living near a smelter. J Expo Sci Environ Epidemiol 17: 248-259. http://dx.doi.org/10.1038/sj.jes.7500512.

Skröder, H; Kippler, M; Nermell, B; Tofail, F; Levi, M; Rahman, SM; Raqib, R; Vahter, M. (2017). Major limitations in using element concentrations in hair as biomarkers of exposure to toxic and essential trace elements in children. Environ Health Perspect 125: 067021. http://dx.doi.org/10.1289/EHP1239.

Smith, D; Hernandez-Avila, M; Téllez-Rojo, MM; Mercado, A; Hu, H. (2002). The relationship between lead in plasma and whole blood in women. Environ Health Perspect 110: 263-268. http://dx.doi.org/10.1289/ehp.02110263.

Smith, DB; Cannon, WF; Woodruff, LG; Solano, F; Kilburn, JE; Fey, DL. (2013). Geochemical and mineralogical data for soils of the conterminous United States. (Data Series 801). Reston, VA: U.S. Department of the Interior, U.S. Geological Survey. http://pubs.usgs.gov/ds/801/.

Smith, DM; Mielke, HW; Heneghan, JB. (2008). Subchronic lead feeding study in male rats. Arch Environ Contam Toxicol 55: 518-528. http://dx.doi.org/10.1007/s00244-008-9138-1.

Smith, DM; Mielke, HW; Heneghan, JB. (2009). Subchronic lead feeding study in male rats and micropigs. Environ Toxicol 24: 453-461. http://dx.doi.org/10.1002/tox.20448.

Smith, DR; Kahng, MW; Quintanilla-Vega, B; Fowler, BA. (1998). High-affinity renal lead-binding proteins in environmentally-exposed humans. Chem Biol Interact 115: 39-52. http://dx.doi.org/10.1016/S0009-2797(98)00060-X.

Smith, DR; Osterloh, JD; Flegal, AR. (1996). Use of endogenous, stable lead isotopes to determine release of lead from the skeleton. Environ Health Perspect 104: 60-66. http://dx.doi.org/10.1289/ehp.9610460.

Smith, E; Weber, J; Naidu, R; McLaren, RG; Juhasz, AL. (2011). Assessment of lead bioaccessibility in peri-urban contaminated soil. J Hazard Mater 186: 300-305. http://dx.doi.org/10.1016/j.jhazmat.2010.10.111.

Sobin, C; Parisi, N; Schaub, T; Gutierrez, M; Ortega, AX. (2011). δ-Aminolevulinic acid dehydratase single nucleotide polymorphism 2 and peptide transporter 2*2 haplotype may differentially mediate lead exposure in male children. Arch Environ Contam Toxicol 61: 521-529. http://dx.doi.org/10.1007/s00244-011-9645-3.

Sowers, MR; Scholl, TO; Hall, G; Jannausch, ML; Kemp, FW; Li, XH; Bogden, JD. (2002). Lead in breast milk and maternal bone turnover. Am J Obstet Gynecol 187: 770-776. http://dx.doi.org/10.1067/mob.2002.125736.

Sowers, TD; Nelson, CM; Diamond, GL; Blackmon, MD; Jerden, ML; Kirby, AM; Noerpel, MR; Scheckel, KG; Thomas, DJ; Bradham, KD. (2021). High lead bioavailability of indoor dust contaminated with paint lead species. Environ Sci Technol 55: 402-411. http://dx.doi.org/10.1021/acs.est.0c06908.

Spalinger, SM; von Braun, MC; Petrosyan, V; von Lindern, IH. (2007). Northern Idaho house dust and soil lead levels compared to the Bunker Hill superfund site. Environ Monit Assess 130: 57-72. http://dx.doi.org/10.1007/s10661-006-9450-z.

Spanier, AJ; Wilson, S; Ho, M; Hornung, R; Lanphear, BP. (2013). The contribution of housing renovation to children's blood lead levels: A cohort study. Environ Health 12: 72. http://dx.doi.org/10.1186/1476-069X-12-72.

Specht, AJ; Dickerson, AS; Weisskopf, MG. (2019a). Comparison of bone lead measured via portable x-ray fluorescence across and within bones. Environ Res 172: 273-278. http://dx.doi.org/10.1016/j.envres.2019.02.031.

Specht, AJ; Lin, Y; Weisskopf, M; Yan, C; Hu, H; Xu, J; Nie, LH. (2016). XRF-measured bone lead (Pb) as a biomarker for Pb exposure and toxicity among children diagnosed with Pb poisoning. Biomarkers 21: 347-352. http://dx.doi.org/10.3109/1354750X.2016.1139183.

Specht, AJ; Weisskopf, M; Nie, LH. (2019b). Childhood lead biokinetics and associations with age among a group of lead-poisoned children in China. J Expo Sci Environ Epidemiol 29: 416-423. http://dx.doi.org/10.1038/s41370-018-0036-y.

Spliethoff, HM; Mitchell, RG; Ribaudo, LN; Taylor, O; Shayler, HA; Greene, V; Oglesby, D. (2014). Lead in New York City community garden chicken eggs: Influential factors and health implications. Environ Geochem Health 36: 633-649. http://dx.doi.org/10.1007/s10653-013-9586-z.

Spliethoff, HM; Mitchell, RG; Shayler, H; Marquez-Bravo, LG; Russell-Anelli, J; Ferenz, G; McBride, M. (2016). Estimated lead (Pb) exposures for a population of urban community gardeners. Environ Geochem Health 38: 955-971. http://dx.doi.org/10.1007/s10653-016-9790-8.

Spungen, JH. (2019). Children's exposures to lead and cadmium: FDA total diet study 2014-16. Food Addit Contam Part A Chem Anal Control Expo Risk Assess 36: 893-903. http://dx.doi.org/10.1080/19440049.2019.1595170.

SRC (Syracuse Research Corporation). (2020). System requirements and design for the integrated exposure uptake biokinetic model for lead in children (IEUBK) version 2.0. Washington, DC: U.S. Environmental Protection Agency. https://semspub.epa.gov/work/HQ/400709.pdf.

Staff, JF; Harding, AH; Morton, J; Jones, K; Guice, EA; McCormick, T. (2014). Investigation of saliva as an alternative matrix to blood for the biological monitoring of inorganic lead. Toxicol Lett 231: 270-276. http://dx.doi.org/10.1016/j.toxlet.2014.09.018.

Stalcup, D. (2016). [Recommendations for sieving soil and dust samples at lead sites for assessment of incidental ingestion]. Available online at http://semspub.epa.gov/src/document/HQ/100000133 (accessed

Stanek, LW; Xue, J; Lay, CR; Helm, EC; Schock, M; Lytle, DA; Speth, TF; Zartarian, VG. (2020). Modeled impacts of drinking water Pb reduction scenarios on children's exposures and blood lead levels. Environ Sci Technol 54: 9474-9482. http://dx.doi.org/10.1021/acs.est.0c00479.

Stevens, C; Williams, R; Jones, P. (2014). Progress on understanding spatial and temporal variability of PM(2.5) and its components in the Detroit Exposure and Aerosol Research Study (DEARS). Environ Sci Process Impacts 16: 94-105. http://dx.doi.org/10.1039/c3em00364g.

Stewart, LR; Farver, JR; Gorsevski, PV; Miner, JG. (2014). Spatial prediction of blood lead levels in children in Toledo, OH using fuzzy sets and the site-specific IEUBK model. Appl Geochem 45: 120-129. http://dx.doi.org/10.1016/j.apgeochem.2014.03.012.

Stillo, F; MacDonald Gibson, J. (2018). Racial disparities in access to municipal water supplies in the American South: Impacts on children's health. International Public Health Journal 10: 309-323.

Sweeney, LM. (2021). Probabilistic pharmacokinetic modeling of airborne lead corresponding to toxicologically relevant blood lead levels in workers. Regul Toxicol Pharmacol 122: 104894. http://dx.doi.org/10.1016/j.yrtph.2021.104894.

Tawinteung, N; Parkpian, P; DeLaune, RD; Jugsujinda, A. (2005). Evaluation of extraction procedures for removing lead from contaminated soil. J Environ Sci Health A Tox Hazard Subst Environ Eng 40: 385-407. http://dx.doi.org/10.1081/ESE-200045631.

Tellez-Rojo, MM; Hernandez-Avila, M; Gonzalez-Cossio, T; Romieu, I; Aro, A; Palazuelos, E; Schwartz, J; Hu, H. (2002). Impact of breastfeeding on the mobilization of lead from bone. Am J Epidemiol 155: 420-428. http://dx.doi.org/10.1093/aje/155.5.420.

Teye, SO; Yanosky, JD; Cuffee, Y; Weng, X; Luquis, R; Farace, E; Wang, L. (2021). Exploring persistent racial/ethnic disparities in lead exposure among American children aged 1-5 years: Results from NHANES 1999-2016. Int Arch Occup Environ Health 94: 723-730. http://dx.doi.org/10.1007/s00420-020-01616-4.

Theppeang, K; Glass, TA; Bandeen-Roche, K; Todd, AC; Rohde, CA; Schwartz, BS. (2008). Gender and race/ethnicity differences in lead dose biomarkers. Am J Public Health 98: 1248-1255. http://dx.doi.org/10.2105/ajph.2007.118505.

Thihalolipavan, S; Candalla, BM; Ehrlich, J. (2013). Examining pica in NYC pregnant women with elevated blood lead levels [Review]. Matern Child Health J 17: 49-55. http://dx.doi.org/10.1007/s10995-012-0947-5.

Trampel, DW; Imerman, PM; Carson, TL; Kinker, JA; Ensley, SM. (2003). Lead contamination of chicken eggs and tissues from a small farm flock. J Vet Diagn Invest 15: 418-422. http://dx.doi.org/10.1177/104063870301500503.

Treble, RG; Thompson, TS. (1997). Preliminary results of a survey of lead levels in human liver tissue. Bull Environ Contam Toxicol 59: 688-695. http://dx.doi.org/10.1007/s001289900535.

Triantafyllidou, S; Burkhardt, J; Tully, J; Cahalan, K; DeSantis, M; Lytle, D; Schock, M. (2021). Variability and sampling of lead (Pb) in drinking water: Assessing potential human exposure depends on the sampling protocol [Review]. Environ Int 146: 106259. http://dx.doi.org/10.1016/j.envint.2020.106259.

Tripathi, RM; Raghunath, R; Kumar, AV; Sastry, VN; Sadasivan, S. (2001). Atmospheric and children's blood lead as indicators of vehicular traffic and other emission sources in Mumbai, India. Sci Total Environ 267: 101-108. http://dx.doi.org/10.1016/S0048-9697(00)00770-1.

Trueman, BF; Camara, E; Gagnon, GA. (2016). Evaluating the Effects of Full and Partial Lead Service Line Replacement on Lead Levels in Drinking Water. Environ Sci Technol 50: 7389-7396. http://dx.doi.org/10.1021/acs.est.6b01912.

Tu, JW; Fuller, W; Feldpausch, AM; Van Landingham, C; Schoof, RA. (2020). Objective ranges of soil-to-dust transfer coefficients for lead-impacted sites. Environ Res 184: 109349. http://dx.doi.org/10.1016/j.envres.2020.109349.

Turgut, ET; Açıkel, G; Gaga, EO; Çalişir, D; Odabasi, M; Ari, A; Artun, G; İlhan, SÖ; Savaci, U; Can, E; Turan, S. (2020). A comprehensive characterization of particulate matter, trace elements, and gaseous emissions of piston-engine aircraft. Environ Sci Technol 54: 7818-7835. http://dx.doi.org/10.1021/acs.est.0c00815.

Turlakiewicz, Z; Chmielnicka, J. (1985). Diethyllead as a specific indicator of occupational exposure to tetraethyllead. Br J Ind Med 42: 682-685. http://dx.doi.org/10.1136/oem.42.10.682.

U.S. APHC (U.S. Army Public Health Command). (2014). Provisional blood lead guidelines for occupational monitoring of lead exposure in the DoD. (AD1169209). Washington, DC: Office of the Deputy Under Secretary of Defense, Installations and Environment. https://apps.dtic.mil/sti/pdfs/AD1169209.pdf.

U.S. EPA (U.S. Environmental Protection Agency). (1986). Air quality criteria for lead [EPA Report]. (EPA/600/8-83/028aF-dF). Research Triangle Park, NC. http://cfpub.epa.gov/ncea/cfm/recordisplay.cfm?deid=32647.

U.S. EPA (U.S. Environmental Protection Agency). (1990). Field evaluation of a high volume surface sampler for pesticides in floor dust [EPA Report]. (EPA/600/S3-90/030). Research Triangle Park.

U.S. EPA (U.S. Environmental Protection Agency). (1994a). Revised interim soil lead guidance for CERCLA sites and RCRA corrective action facilities [EPA Report]. (OSWER Directive #9355.4-12; EPA/540/F-94/043). Washington, DC: U.S. Environmental Protection Agency, Office of Solid Waste and Emergency Response. https://nepis.epa.gov/Exe/ZyPURL.cgi?Dockey=P100A72S.txt.

U.S. EPA (U.S. Environmental Protection Agency). (1994b). Technical support document: Parameters and equations used in integrated exposure uptake biokinetic model for lead in children (v 0.99d) [EPA Report]. (EPA/540/R-94/040). Washington, DC. https://ntrl.ntis.gov/NTRL/dashboard/searchResults/titleDetail/PB94963505.xhtml.

U.S. EPA (U.S. Environmental Protection Agency). (2003a). Evaluation of the ICRP lead biokinetics model: Empirical comparisons with observations of plasma-blood lead concentration relationships in humans [draft final]. (SRC No. FA332). Washington, DC.

U.S. EPA (U.S. Environmental Protection Agency). (2003b). Revised guidance manual for selecting lead and copper control strategies. (EPA-816-R-03-001). Washington, DC. https://nepis.epa.gov/Exe/ZyPURL.cgi?Dockey=P100999U.txt.

U.S. EPA (U.S. Environmental Protection Agency). (2006a). Air quality criteria for lead (Final report, 2006): Volume I of II [EPA Report]. (EPA/600/R-05/144aF). Washington, DC. http://cfpub.epa.gov/ncea/CFM/recordisplay.cfm?deid=158823.

U.S. EPA (U.S. Environmental Protection Agency). (2006b). Air quality criteria for lead (Final report, 2006): Volume II of II [EPA Report]. (EPA/600/R-05/144bF). Washington, DC. https://cfpub.epa.gov/ncea/risk/recordisplay.cfm?deid=158823.

U.S. EPA (U.S. Environmental Protection Agency). (2007a). Estimation of relative bioavailability of lead in soil and soil-like materials using in vivo and in vitro methods [EPA Report]. (OSWER 9285.7-77). Washington, DC. https://nepis.epa.gov/Exe/ZyPURL.cgi?Dockey=93001C2U.txt.

U.S. EPA (U.S. Environmental Protection Agency). (2007b). Guidance for evaluating the oral bioavailability of metals in soils for use in human health risk assessment. (OSWER 9285.7-80). Washington, DC. https://semspub.epa.gov/work/HQ/175333.pdf.

U.S. EPA (U.S. Environmental Protection Agency). (2011). Exposure factors handbook: 2011 edition [EPA Report]. (EPA/600/R-090/052F). Washington, DC: U.S. Environmental Protection Agency, Office of Research and Development, National Center for Environmental Assessment. https://nepis.epa.gov/Exe/ZyPURL.cgi?Dockey=P100F2OS.txt.

U.S. EPA (U.S. Environmental Protection Agency). (2013). Integrated science assessment for lead [EPA Report]. (EPA/600/R-10/075F). Washington, DC. https://nepis.epa.gov/Exe/ZyPURL.cgi?Dockey=P100K82L.txt.

U.S. EPA (U.S. Environmental Protection Agency). (2014). Technical review workgroup recommendations regarding gardening and reducing exposure to lead-contaminated soils. (OSWER 9200.2-142). Washington, DC. https://semspub.epa.gov/work/HQ/174577.pdf.

U.S. EPA (U.S. Environmental Protection Agency). (2015). Guidance for sample collection for in vitro bioaccessibility assay for arsenic and lead in soil and applications of relative bioavailability data in human health risk assessment. Washington, DC: U.S. Environmental Protection Agency, Office of Solid Waste and Emergency Response. https://semspub.epa.gov/work/HQ/100002711.pdf.

U.S. EPA (U.S. Environmental Protection Agency). (2017). Update for Chapter 5 of the Exposure Factors Handbook: Soil and dust ingestion [EPA Report]. (EPA/600R-17/384F). Washington, DC: National Center for Environmental Assessment, Office of Research and Development. https://nepis.epa.gov/Exe/ZyPURL.cgi?Dockey=P100TTX4.txt.

U.S. EPA (U.S. Environmental Protection Agency). (2019a). Air Quality System (AQS) [database]: CASRNs 106-99-0, 75-34-3, 78-87-5, 106-93-4, 50-00-0, 106-46-7, and 79-00-5. Washington, DC: Environmental Protection Agency. Retrieved from https://aqs.epa.gov/aqsweb/airdata/download_files.html#Annual

U.S. EPA (U.S. Environmental Protection Agency). (2019b). All-Ages Lead Model (AALM), version 2.0 (external review draft, 2019). Washington, DC. https://cfpub.epa.gov/ncea/risk/recordisplay.cfm?deid=343670.

U.S. EPA (U.S. Environmental Protection Agency). (2019c). Integrated Science Assessment (ISA) for particulate matter (final report, Dec 2019) [EPA Report]. (EPA/600/R-19/188). Washington, DC. https://cfpub.epa.gov/ncea/isa/recordisplay.cfm?deid=347534.

U.S. EPA (U.S. Environmental Protection Agency). (2019d). Technical support document for residential dust-lead hazard standards rulemaking. Title Page. (EPA TSD LDHS).

U.S. EPA (U.S. Environmental Protection Agency). (2020). Review of dust-lead post-abatement clearance levels. Fed Reg 85(122): 37810-37819.

U.S. EPA (U.S. Environmental Protection Agency). (2021a). Advancing Pb exposure and biokinetic modeling for U.S. EPA regulatory decisions and site assessments using Bunker Hill Mining and Metallurgical Complex Superfund Site data [EPA Report]. (EPA/600/R-21/017F). Washington, DC: U.S. Environmental Protection Agency, Office of Research and Development. https://cfpub.epa.gov/ncea/risk/recordisplay.cfm?deid=351563.

U.S. EPA (U.S. Environmental Protection Agency). (2021b). Estimation of lead bioavailability in soil and dust: Evaluation of the default value for the integrated exposure uptake biokinetic model for lead in U.S. children. https://semspub.epa.gov/work/HQ/400701.pdf.

U.S. EPA (U.S. Environmental Protection Agency). (2022). EPA's Risk-Screening Environmental Indicators (RSEI) methodology: RSEI version 2.3.10. Washington, DC: U.S Environmental Protection Agency. https://www.epa.gov/system/files/documents/2022-06/RSEI%20Methodology%20V2.3.10.pdf.

Uzu, G; Sobanska, S; Sarret, G; Munoz, M; Dumat, C. (2010). Foliar lead uptake by lettuce exposed to atmospheric fallouts. Environ Sci Technol 44: 1036-1042. http://dx.doi.org/10.1021/es902190u.

Van de Wiele, TR; Oomen, AG; Wragg, J; Cave, M; Minekus, M; Hack, A; Cornelis, C; Rompelberg, CJM; De Zwart, LL; Klinck, B; Van Wijnen, J; Verstraete, W; Sips, AJA, M. (2007). Comparison of five in vitro digestion models to in vivo experimental results: Lead bioaccessibility in the human gastrointestinal tract. J Environ Sci Health A Tox Hazard Subst Environ Eng 42: 1203-1211. http://dx.doi.org/10.1080/10934520701434919.

Van Overmeire, I; Pussemier, L; Waegeneers, N; Hanot, V; Windal, I; Boxus, L; Covaci, A; Eppe, G; Scippo, ML; Sioen, I; Bilau, M; Gellynck, X; De Steur, H; Tangni, EK; Goeyens, L. (2009). Assessment of the chemical contamination in home-produced eggs in Belgium: General overview of the CONTEGG study. Sci Total Environ 407: 4403-4410. http://dx.doi.org/10.1016/j.scitotenv.2008.10.066.

Vandenhove, H; Olyslaegers, G; Sanzharova, N; Shubina, O; Reed, E; Shang, Z; Velasco, H. (2009). Proposal for new best estimates of the soil-to-plant transfer factor of U, Th, Ra, Pb and Po. J Environ Radioact 100: 721-732. http://dx.doi.org/10.1016/j.jenvrad.2008.10.014.

Vander, AJ; Taylor, DL; Kalitis, K; Mouw, DR; Victery, W. (1977). Renal handling of lead in dogs: Clearance studies. Am J Physiol 233: F532-F538. http://dx.doi.org/10.1152/ajprenal.1977.233.6.F532.

Vasquez, FA; Heaviside, R; Tang, Z; Taylor, JS. (2006). Effect of free chlorine and chloramines on lead release in a distribution system. J Am Water Works Assoc 98: 144-154.

Vearrier, D; Greenberg, MI. (2012). Blood lead levels in the United States "oldest-old" population. Clin Toxicol 50: 838-840. http://dx.doi.org/10.3109/15563650.2012.727094.

Verbeeck, RMH; Lassuyt, CJ; Heijligers, HJM; Driessens, FCM; Vrolijk, JWG, A. (1981). Lattice parameters and cation distribution of solid solutions of calcium and lead hydroxyapatite. Calcif Tissue Int 33: 243-247. http://dx.doi.org/10.1007/BF02409444.

Victery, W; Vander, AJ; Mouw, DR. (1979). Effect of acid-base status on renal excretion and accumulation of lead in dogs and rats. Am J Physiol 237: F398-F407. http://dx.doi.org/10.1152/ajprenal.1979.237.5.F398.

von Lindern, I; Spalinger, S; Stifelman, ML; Stanek, LW; Bartrem, C. (2016). Estimating children's soil/dust ingestion rates through retrospective analyses of blood lead biomonitoring from the Bunker Hill Superfund Site in Idaho. Environ Health Perspect 124: 1462-1470. http://dx.doi.org/10.1289/ehp.1510144.

Vural, N; Duydu, Y. (1995). Biological monitoring of lead in workers exposed to tetraethyllead. Sci Total Environ 171: 183-187. http://dx.doi.org/10.1016/0048-9697(95)04676-6.

Waalkes, MP; Klaassen, CD. (1985). Concentration of metallothionein in major organs of rats after administration of various metals. Fundam Appl Toxicol 5: 473-477. http://dx.doi.org/10.1016/0272-0590(85)90094-6.

Walsh, D; Glass, K; Morris, S; Zhang, H; McRae, I; Anderson, N; Alfieri, A; Egendorf, SP; Holberton, S; Owrang, S; Cheng, Z. (2018). Sediment exchange to mitigate pollutant exposure in urban soil. J Environ Manage 214: 354-361. http://dx.doi.org/10.1016/j.jenvman.2018.03.013.

Wang, A; Rezania, Z; Haugen, KMB; Baertlein, L; Yendell, SJ. (2019). Screening for elevated blood lead levels: False-positive rates of tests on capillary samples, Minnesota, 2011-2017. J Public Health Manag Pract 25(Suppl 1): S44-S50. http://dx.doi.org/10.1097/PHH.0000000000000879.

Wang, T; Zhou, YP; Sun, Y; Zheng, YX. (2021). Trends in blood lead levels in the U.S. from 1999 to 2016. Am J Prev Med 60: e179-e187. http://dx.doi.org/10.1016/j.amepre.2020.10.024.

Wang, X; Ding, N; Tucker, KL; Weisskopf, MG; Sparrow, D; Hu, H; Park, SK. (2017a). A western diet pattern is associated with higher concentrations of blood and bone lead among middle-aged and elderly men. J Nutr 147: 1374-1383. http://dx.doi.org/10.3945/jn.117.249060.

Wang, Y; Specht, A; Liu, Y; Finney, L; Maxey, E; Vogt, S; Zheng, W; Weisskopf, M; Nie, LH. (2017b). Microdistribution of lead in human teeth using microbeam synchrotron radiation X-ray fluorescence (μ-SRXRF). X Ray Spectrom 46: 19-26. http://dx.doi.org/10.1002/xrs.2720.

Wang, Z; Wade, AM; Richter, DD; Stapleton, HM; Kaste, JM; Vengosh, A. (2022). Legacy of anthropogenic lead in urban soils: Co-occurrence with metal(loids) and fallout radionuclides, isotopic fingerprinting, and in vitro bioaccessibility. Sci Total Environ 806: 151276. http://dx.doi.org/10.1016/j.scitotenv.2021.151276.

Warrington, NM; Zhu, G; Dy, V; Heath, AC; Madden, PAF; Hemani, G; Kemp, JP; Mcmahon, G; St Pourcain, B; Timpson, NJ; Taylor, CM; Golding, J; Lawlor, DA; Steer, C; Montgomery, GW; Martin, NG; Smith, GD; Evans, DM; Whitfield, JB. (2015). Genome-wide association study of blood lead shows multiple associations near ALAD. Hum Mol Genet 24: 3871-3879. http://dx.doi.org/10.1093/hmg/ddv112.

Watson, WS; Morrison, J; Bethel, MIF; Baldwin, NM; Lyon, DTB; Dobson, H; Moore, MR; Hume, R. (1986). Food iron and lead absorption in humans. Am J Clin Nutr 44: 248-256. http://dx.doi.org/10.1093/ajcn/44.2.248.

Webber, CE; Chettle, DR; Bowins, RJ; Beaumont, LF; Gordon, CL; Song, X; Blake, JM; Mcnutt, RH. (1995). Hormone replacement therapy may reduce the return of endogenous lead from bone to the circulation. Environ Health Perspect 103: 1150-1153. http://dx.doi.org/10.2307/3432612.

Weber, AK; Bannon, DI; Abraham, JH; Seymour, RB; Passman, PH; Lilley, PH; Parks, KK; Braybrooke, G; Cook, ND; Belden, AL. (2020). Reduction in lead exposures with lead-free ammunition in an advanced urban assault course. J Occup Environ Hyg 17: 598-610. http://dx.doi.org/10.1080/15459624.2020.1836375.

Weiss, AL; Caravanos, J; Blaise, MJ; Jaeger, RJ. (2006). Distribution of lead in urban roadway grit and its association with elevated steel structures. Chemosphere 65: 1762-1771. http://dx.doi.org/10.1016/j.chemosphere.2006.04.079.

Weiss, D; Baertlein, LA; Yendell, SJ; Christensen, KY; Tomasallo, CD; Creswell, PD; Camponeschi, JL; Meiman, J; Anderson, HA. (2018). Lead exposure among workers at a shipyard—Wisconsin, 2015 to 2016. J Occup Environ Med 60: 928-935. http://dx.doi.org/10.1097/JOM.0000000000001370.

Weitzman, M; Aschengrau, A; Bellinger, D; Jones, R; Hamlin, JS. (1993). Lead-contaminated soil abatement and urban children's blood lead levels. JAMA 269: 1647-1654.

Wennberg, M; Lundh, T; Sommar, JN; Bergdahl, IA. (2017). Time trends and exposure determinants of lead and cadmium in the adult population of northern Sweden 1990-2014. Environ Res 159: 111-117. http://dx.doi.org/10.1016/j.envres.2017.07.029.

Wharton, SE; Shayler, HA; Spliethoff, HM; Marquez-Bravo, LG; Ribaudo, L; McBride, MB. (2012). A comparison of screening tests for soil Pb. Soil Sci 177: 650-654. http://dx.doi.org/10.1097/SS.0b013e318277718b.

Wheeler, DC; Boyle, J; Nelson, EJ. (2022). Modeling annual elevated blood lead levels among children in Maryland in relation to neighborhood deprivation. Sci Total Environ 805: 150333. http://dx.doi.org/10.1016/j.scitotenv.2021.150333.

Wheeler, DC; Jones, RM; Schootman, M; Nelson, EJ. (2019a). Explaining variation in elevated blood lead levels among children in Minnesota using neighborhood socioeconomic variables. Sci Total Environ 650: 970-977. http://dx.doi.org/10.1016/j.scitotenv.2018.09.088.

Wheeler, DC; Raman, S; Jones, RM; Schootman, M; Nelson, EJ. (2019b). Bayesian deprivation index models for explaining variation in elevated blood lead levels among children in Maryland. Spat Spatio-temporal Epidemiol 30: 100286. http://dx.doi.org/10.1016/j.sste.2019.100286.

White, PD; Van Leeuwan, P; Davis, BD; Maddaloni, M; Hogan, KA; Marcus, AH; Elias, RW. (1998). The conceptual structure of the integrated exposure uptake biokinetic model for lead in children [Review]. Environ Health Perspect 106(Suppl. 6): 1513-1530. http://dx.doi.org/10.1289/ehp.98106s61513.

Wilker, E; Korrick, S; Nie, LH; Sparrow, D; Vokonas, P; Coull, B; Wright, RO; Schwartz, J; Hu, H. (2011). Longitudinal changes in bone lead levels: The VA Normative Aging Study. J Occup Environ Med 53: 850-855. http://dx.doi.org/10.1097/JOM.0b013e31822589a9.

Williams, E; Vanderslice, R; Feliz, CB. (2012). Analysis of blood lead screening data (2008-2011) for refugee children in Rhode Island. Med Health R I 95: 129-130.

Williams, R; Rea, A; Vette, A; Croghan, C; Whitaker, D; Stevens, C; Mcdow, S; Fortmann, R; Sheldon, L; Wilson, H; Thornburg, J; Phillips, M; Lawless, P; Rodes, C; Daughtrey, H. (2009). The design and field implementation of the Detroit exposure and aerosol research study. J Expo Sci Environ Epidemiol 19: 643-659. http://dx.doi.org/10.1038/jes.2008.61.

Williamson, K; Das, S; Ferro, AR; Chellam, S. (2021). Elemental composition of indoor and outdoor coarse particulate matter at an inner-city high school. Atmos Environ 261: 118559. http://dx.doi.org/10.1016/j.atmosenv.2021.118559.

Wilson, J; Dixon, S; Galke, W; Mclaine, P. (2007). An investigation of dust lead sampling locations and children's blood lead levels. J Expo Sci Environ Epidemiol 17: 2-12. http://dx.doi.org/10.1038/sj.jes.7500514.

Wilson, J; Dixon, SL; Jacobs, DE; Akoto, J; Korfmacher, KS; Breysse, J. (2015). An investigation into porch dust lead levels. Environ Res 137: 129-135. http://dx.doi.org/10.1016/j.envres.2014.11.013.

Wiseman, CLS; Zereini, F. (2014). Characterizing metal(loid) solubility in airborne PM10, PM2.5 and PM1 in Frankfurt, Germany using simulated lung fluids. Atmos Environ 89: 282-289. http://dx.doi.org/10.1016/j.atmosenv.2014.02.055.

Wright, RO; Silverman, EK; Schwartz, J; Tsaih, SW; Senter, J; Sparrow, D; Weiss, ST; Aro, A; Hu, H. (2004). Association between hemochromatosis genotype and lead exposure among elderly men: The Normative Aging Study. Environ Health Perspect 112: 746-750. http://dx.doi.org/10.1289/ehp.6581.

Xie, Y; Chiba, M; Shinohara, A; Watanabe, H; Inaba, Y. (1998). Studies on lead-binding protein and interaction between lead and selenium in the human erythrocytes. Ind Health 36: 234-239. http://dx.doi.org/10.2486/indhealth.36.234.

Xing, W; Yang, H; Ippolito, JA; Zhao, Q; Zhang, Y; Scheckel, KG; Li, L. (2020). Atmospheric deposition of arsenic, cadmium, copper, lead, and zinc near an operating and an abandoned lead smelter. J Environ Qual 49: 1667-1678. http://dx.doi.org/10.1002/jeq2.20151.

Xue, J; Zartarian, V; Tornero-Velez, R; Stanek, LW; Poulakos, A; Walts, A; Triantafillou, K; Suero, M; Grokhowsky, N. (2022). A generalizable evaluated approach, applying advanced geospatial statistical methods, to identify high lead exposure locations at census tract scale: Michigan case study. Environ Health Perspect 130: 77004. http://dx.doi.org/10.1289/EHP9705.

Yadav, V; Turner, J. (2014). Gauging intraurban variability of ambient particulate matter arsenic and other air toxic metals from a network of monitoring sites. Atmos Environ 89: 318-328. http://dx.doi.org/10.1016/j.atmosenv.2014.02.030.

Yamamoto, N; Takahashi, Y; Yoshinaga, J; Tanaka, A; Shibata, Y. (2006). Size distributions of soil particles adhered to children's hands. Arch Environ Contam Toxicol 51: 157-163. http://dx.doi.org/10.1007/s00244-005-7012-y.

Ye, D; Brown, JS; Umbach, DM; Adams, J; Thayer, W; Follansbee, MH; Kirrane, EF. (2022). Estimating the effects of soil remediation on children's blood lead near a former lead smelter in Omaha, Nebraska, USA. Environ Health Perspect 130: 37008. http://dx.doi.org/10.1289/EHP8657.

Yeoh, B; Woolfenden, S; Lanphear, B; Ridley, GF; Livingstone, N; Jorgensen, E. (2014). Household interventions for preventing domestic lead exposure in children [Review]. Cochrane Database Syst Rev (12): CD006047. http://dx.doi.org/10.1002/14651858.CD006047.pub4.

Yeoh, B; Woolfenden, S; Wheeler, DM; Alperstein, G; Lanphear, B. (2008). Household interventions for prevention of domestic lead exposure in children [Review]. Cochrane Database Syst Rev (2): CD006047. http://dx.doi.org/10.1002/14651858.CD006047.pub2.

Yu, CH; Yiin, LM; Lioy, PJ. (2006). The bioaccessibility of lead (Pb) from vacuumed house dust on carpets in urban residences. Risk Anal 26: 125-134. http://dx.doi.org/10.1111/j.1539-6924.2006.00710.x.

Yu, M; Teitelbaum, SL; Dolios, G; Dang, LHT; Tu, P; Wolff, MS; Petrick, LM. (2022). Molecular gatekeeper discovery: Workflow for linking multiple exposure biomarkers to metabolomics. Environ Sci Technol 56: 6162-6171. http://dx.doi.org/10.1021/acs.est.1c04039.

Yun, K; Matheson, J; Payton, C; Scott, KC; Stone, BL; Song, L; Stauffer, WM; Urban, K; Young, J; Mamo, B. (2016). Health Profiles of Newly Arrived Refugee Children in the United States, 2006-2012. Am J Public Health 106: 128-135. http://dx.doi.org/10.2105/AJPH.2015.302873.

Zahran, S; Iverson, T; McElmurry, SP; Weiler, S. (2017a). The effect of leaded aviation gasoline on blood lead in children. J Assoc Environ Resour Econ 4: 575-610. http://dx.doi.org/10.1086/691686.

Zahran, S; Keyes, C; Lanphear, B. (2023). Leaded aviation gasoline exposure risk and child blood lead levels. PNAS Nexus 2: pgac285. http://dx.doi.org/10.1093/pnasnexus/pgac285.

Zahran, S; Laidlaw, MAS; McElmurry, SP; Filippelli, GM; Taylor, M. (2013a). Linking source and effect: Resuspended soil lead, air lead, and children's blood lead levels in Detroit, Michigan. Environ Sci Technol 47: 2839-2845. http://dx.doi.org/10.1021/es303854c.

Zahran, S; McElmurry, SP; Sadler, RC. (2017b). Four phases of the Flint Water Crisis: Evidence from blood lead levels in children. Environ Res 157: 160-172. http://dx.doi.org/10.1016/j.envres.2017.05.028.

Zahran, S; Mielke, HW; Gonzales, CR; Powell, ET; Weiler, S. (2010). New Orleans before and after hurricanes Katrina/Rita: A quasi-experiment of the association between soil lead and children's blood lead. Environ Sci Technol 44: 4433-4440. http://dx.doi.org/10.1021/es100572s.

Zahran, S; Mielke, HW; McElmurry, SP; Filippelli, GM; Laidlaw, MAS; Taylor, MP. (2013b). Determining the relative importance of soil sample locations to predict risk of child lead exposure. Environ Int 60: 7-14. http://dx.doi.org/10.1016/j.envint.2013.07.004.

Zahran, S; Mielke, HW; Weiler, S; Gonzales, CR. (2011). Nonlinear associations between blood lead in children, age of child, and quantity of soil lead in metropolitan New Orleans. Sci Total Environ 409: 1211-1218. http://dx.doi.org/10.1016/j.scitotenv.2010.11.036.

Zartarian, V; Poulakos, A; Garrison, VH; Spalt, N; Tornero-Velez, R; Xue, J; Egan, K; Courtney, J. (2022). Lead Data Mapping to Prioritize US Locations for Whole-of-Government Exposure Prevention Efforts: State of the Science, Federal Collaborations, and Remaining Challenges [Review]. Am J Public Health 112: S658-S669. http://dx.doi.org/10.2105/AJPH.2022.307051.

Zartarian, V; Xue, J; Tornero-Velez, R; Brown, J. (2017). Children's lead exposure: A multimedia modeling analysis to guide public health decision-making. Environ Health Perspect 125: 097009. http://dx.doi.org/10.1289/EHP1605.

Zervas, E; Matsouki, N; Kyriakopoulos, G; Poulopoulos, S; Ioannides, T; Katsaounou, P. (2020). Transfer of metals in the liquids of electronic cigarettes. Inhal Toxicol 32: 240-248. http://dx.doi.org/10.1080/08958378.2020.1776801.

Zhang, W; Zhang, GG; He, HZ; Bolt, HM. (1994). Early health effects and biological monitoring in persons occupationally exposed to tetraethyl lead. Int Arch Occup Environ Health 65: 395-399. http://dx.doi.org/10.1007/BF00383250.

Zhang, X; Specht, AJ; Wells, E; Weisskopf, MG; Weuve, J; Nie, LH. (2021). Evaluation of a portable XRF device for in vivo quantification of lead in bone among a US population. Sci Total Environ 753: 142351. http://dx.doi.org/10.1016/j.scitotenv.2020.142351.

Ziegler, EE; Edwards, BB; Jensen, RL; Mahaffey, KR; Fomon, SJ. (1978). Absorption and retention of lead by infants. Pediatr Res 12: 29-34. http://dx.doi.org/10.1203/00006450-197801000-00008.

Zota, AR; Schaider, LA; Ettinger, AS; Wright, RO; Shine, JP; Spengler, JD. (2011). Metal sources and exposures in the homes of young children living near a mining-impacted Superfund site. J Expo Sci Environ Epidemiol 21: 495-505. http://dx.doi.org/10.1038/jes.2011.21.