Distribution Agreement

Prevalence and Risk Factors of Elevated Blood Lead in Children in Mining and Non-Mining Communities, Zamfara, Nigeria, 2012

By

John A. Kaufman
Master of Public Health

Global Environmental Health

Matthew Strickland
Committee Chair

Paige Tolbert
Committee Member

Prevalence and Risk Factors of Elevated Blood Lead in Children in Mining and Non-Mining Communities, Zamfara, Nigeria, 2012

By

John A. Kaufman

Bachelor of Arts, Public Health
University of California, Berkeley
2011

Thesis Committee Chair: Matthew Strickland, PhD

An abstract of
A thesis submitted to the Faculty of the
Rollins School of Public Health of Emory University
in partial fulfillment of the requirements for the degree of
Master of Public Health
in Global Environmental Health
2014

Abstract

Prevalence and Risk Factors of Elevated Blood Lead in Children in Mining and Non-Mining Communities, Zamfara, Nigeria, 2012

By John A. Kaufman

Background: In March 2010, Medecins San Frontieres detected an outbreak of acute lead poisoning linked to low-technology gold mining in Zamfara State, northwestern Nigeria. The outbreak has killed over 400 children <5 years of age and left over 2,000 more children with permanent disabilities.

Objectives: The aims of this study were to estimate the statewide prevalence of children <5 with elevated blood lead levels (BLLs) in mining and non-mining communities and to identify factors contributing to increased BLL in children.

Methods: We took a representative, population-based sample of mining and non-mining villages throughout Zamfara. Blood samples from children, outdoor soil samples, indoor dust samples, and survey data on mining activities and other potential lead exposures were collected from 383 children <5 years of age in 383 compounds in 54 villages.

Results: 17% of compounds reported ore processing in the preceding 12 months. The prevalence of BLLs $\geq$10 μg/dL in children <5 was 26% in ore-processing compounds and 22% in non-ore-processing compounds. Ore-processing activities were associated with higher lead concentrations in soil, dust, and blood samples. Other factors associated with BLL were child's age and sex, breastfeeding, drinking water from a piped tap, and exposure to eye cosmetics.

Conclusion: Childhood lead poisoning is widespread in Zamfara State. Though most children's BLLs were below the recommended level for chelation therapy, environmental remediation is needed to prevent further exposures.

Implications: Childhood lead exposure is a preventable disease with largely irreversible and untreatable health effects. An understanding of the prevalence and impacts of gold mining on childhood lead exposure can help guide future environmental and public health protection efforts in mining communities.

Key words: environmental contamination, lead poisoning, mining

Prevalence and Risk Factors of Elevated Blood Lead in Children in Mining and Non-Mining Communities, Zamfara, Nigeria, 2012

By

John A. Kaufman

Bachelor of Arts, Public Health
University of California, Berkeley
2011

Thesis Committee Chair: Matthew Strickland, PhD

A thesis submitted to the Faculty of the
Rollins School of Public Health of Emory University
in partial fulfillment of the requirements for the degree of
Master of Public Health
in Global Environmental Health
2014

Prevalence and Risk Factors of Elevated Blood Lead in Children in Mining and Non-Mining Communities, Zamfara, Nigeria, 2012

Master of Public Health Thesis
April 2014

Prepared by John Kaufman, Rollins School of Public Health, Emory University

Table of Contents

Abstract

Background: In March 2010, Medecins San Frontieres detected an outbreak of acute lead poisoning linked to low-technology gold mining in Zamfara State, northwestern Nigeria. The outbreak has killed over 400 children <5 years of age and left over 2,000 more children with permanent disabilities.

Objectives: The aims of this study were to estimate the statewide prevalence of children <5 with elevated blood lead levels (BLLs) in mining and non-mining communities and to identify factors contributing to increased BLL in children.

Methods**:** We took a representative, population-based sample of mining and non-mining villages throughout Zamfara. Blood samples from children, outdoor soil samples, indoor dust samples, and survey data on mining activities and other potential lead exposures were collected from 383 children <5 years of age in 383 compounds in 54 villages.

Results**:** 17% of compounds reported ore processing in the preceding 12 months. The prevalence of BLLs ≥10 μg/dL in children <5 was 26% in ore-processing compounds and 22% in non-ore-processing compounds. Ore-processing activities were associated with higher lead concentrations in soil, dust, and blood samples. Other factors associated with BLL were child's age and sex, breastfeeding, drinking water from a piped tap, and exposure to eye cosmetics.

Conclusion**:** Childhood lead poisoning is widespread in Zamfara State. Though most children's BLLs were below the recommended level for chelation therapy, environmental remediation is needed to prevent further exposures.

Implications**:** Childhood lead exposure is a preventable disease with largely irreversible and untreatable health effects. An understanding of the prevalence and impacts of gold mining on childhood lead exposure can help guide future environmental and public health protection efforts in mining communities.

Key words: environmental contamination, lead poisoning, mining

Introduction

Zamfara Lead Poisoning Outbreak

In March 2010, an outbreak of acute lead poisoning was detected in Zamfara State of northwestern Nigeria that resulted in severe neurological morbidity and death in several hundred children. The source of the outbreak was found to be lead-contaminated gold ore, processed with low technology or "artisanal" methods in rural villages (Dooyema et al., 2012). Gold ore processing became increasingly common in Zamfara in response to the dramatic rise in the price of gold during the global economic recession (Plumlee et al., 2013). Lack of environmental or occupational health controls during ore processing caused extensive contamination of villages and fatal amounts of lead being inhaled and ingested by children. Since 2010, lead poisoning associated with gold mining has killed over 400 children and permanently disabled over 2,000 children in Zamfara (I. H. von Lindern, von Braun. M.C., Tirima, S., Bartrem, C., 2011). An initial investigation found two mining villages where 118 of 463 children <5 years old (25%) had died in the previous 12 months (Dooyema et al., 2012). Of these children, 82% experienced convulsions prior to death, a symptom of acute lead poisoning. Of surviving children, 97% had blood lead levels (BLLs) >45 μg/dL, the level recommended by CDC for initiating chelation therapy. Children were found with BLLs up to 370 μg/dL, over 70 times higher than the level for public health action currently set by the World Health Organization (WHO) and US Centers for Disease Control. Lead concentrations in soil exceeded the 400 ppm limit set by the US Environmental Protection Agency in 85% of samples, ranging upward of 100,000 ppm. A follow-up investigation reported that the odds of lead poisoning or lead contamination were 3.5 times higher in ore-processing villages than in villages that did not process ore (Lo et al., 2012). Previous investigations focused on identifying the worst contaminated villages for priority environmental and medical interventions. This study is the first to estimate the statewide prevalence of lead poisoning. As United Nations-supported remediation efforts continue in Zamfara, the agencies involved must understand the extent of the problem to comprehensively address it.

Health Effects of Lead

Childhood lead poisoning is an entirely preventable disease with effects that are largely irreversible and untreatable by modern medicine (WHO, 2010). Lead is highly toxic and can affect virtually every organ system in the human body (Sanders, Liu, Buchner, & Tchounwou, 2009). Children are especially vulnerable to lead toxicity because of the physiology of their developing bodies, and are exposed primarily through their hand-to-mouth behaviors (Lidsky & Schneider, 2003). Lead exposure in children is associated with impaired neurodevelopment and cognitive function, lower IQ, impaired hearing, and reduced stature (Canfield et al., 2003). Symptoms of acute lead poisoning include convulsions, coma, and death (Needleman, 2004). Toxicological studies have not identified a safe BLL threshold below which health effects are not seen (Jusko et al., 2008). The US Centers for Disease Control and Prevention currently uses a BLL in children of ≥5 µg/dL as the level for initiating public health actions to reduce exposures, and recommends chelation therapy to remove lead from the blood of children with BLLs ≥45 µg/dL (CDC 2013). Blood lead levels (BLLs) below 10 µg/dL in infants and children are associated with an array of developmental problems (Canfield et al., 2003). In a pooled analysis of data from several cohort studies, the decrease in IQ associated with increasing blood lead levels below 10 µg/dL was more pronounced than the decrease observed at levels above 10 µg/dL (Lanphear et al., 2005).

Lead Exposures Worldwide

Lead enters the biosphere from the earth's crust through its many uses by humans (NRC, 1992). The use of lead in gasoline, which began in the 1920s, has by far been the largest contributor to global lead contamination (Landrigan, 2002). Other major sources of lead exposure vary depending on the national and local context, but include leaded paint, industry such as smelting and mining, electronic waste, food cans with leaded solder, ceramic glazes, and drinking water with lead pipes and solder (WHO, 2010). Artisanal gold mining such as in Zamfara is estimated to account for 20-30% of global gold production and represents an important source of lead contamination for rural, low-income communities (Swenson, Carter, Domec, & Delgado, 2011; van Geen, 2012). In parts of Asia, the Middle East, and Africa with large Muslim populations, such as in Zamfara, children are frequently exposed to eye cosmetics made of galena, or lead sulfate, (al-Hazzaa & Krahn, 1995) which can be >80% lead in composition (Nasidi, 2012). In addition to lead exposures, some important biological interactions that increase lead absorption and toxicity are more prevalent in low-income countries. One salient example is iron deficiency anemia, which synergistically increases lead absorption and toxicity (Khan, Ansari, & Khan, 2011)and is estimated to affect 30% of the world's population and 65% of children <5 years old in Africa (Miller, 2013).

Global Burden of Lead Poisoning

International efforts have successfully reduced lead exposures in many parts of the world. In 2006, for example, leaded gasoline was banned in all sub-Saharan African nations (UNEP, 2008). Still, lead poisoning accounts for an estimated 0.6% of the total global burden of disease, and about 9 million disability-adjusted life years (WHO, 2010). WHO estimates that at least 16% of children worldwide have BLLs >10 μg/dL, and that 90% of these children live in low-income countries (WHO, 2009). Others have estimated that 97% of children with

BLLs >5 µg/dL and 99% of children with BLLs >10 µg/dL live in low-income countries (Fewtrell, Pruss-Ustun, Landrigan, & Ayuso-Mateos, 2004). In high-income countries, lead exposure disproportionately affects low-income adults and children (Cureton, 2011; Hicken et al., 2012; Lanphear, Weitzman, & Eberly, 1996). The effects of aggregate intelligence loss in societies with widespread lead exposures can be substantial due to the burden of lead-induced mild mental retardation, cardiovascular outcomes, and lost economic productivity (Landrigan, Schechter, Lipton, Fahs, & Schwartz, 2002).

The goals of this study were to estimate the statewide prevalence of elevated BLLs in children <5 in mining and non-mining communities and to identify factors associated with increased BLL. Using a population-based representative sampling design, we collected survey data and soil, dust, and blood samples from a total of 383 children <5 years old during June and July of 2012.

Methods

Study location*:* Zamfara State, located in northwestern Nigeria, has an estimated population of 3.8 million, of which 20% are estimated to be children <5 years old. Zamfara has 14 local government areas, similar to counties in the US. The population is predominantly Muslim, and the traditional religious leadership system, chaired by local Emirs, has strong political and social influence. Farming is the major livelihood, with >80% of the population participating in agriculture. The 2008 Nigeria Demographic and Health Survey showed that in Zamfara State, 19% of households had access to electricity, 28% had access to an improved source of water, and 27% had improved sanitation facilities (DHS, 2009).

Sampling frame*:* The target population of this study included children aged <5 years residing in Zamfara. A child was defined as being a resident of Zamfara if he/she lived there for at least 10 months of the previous year. Children <5 years were the focus of the study because they are the age group that is most vulnerable to health damage from lead, and no current child blood lead surveillance system currently exists in Nigeria. A 110cm stick was used for subject selection to represent the average height of a 5 year old, per MSF recommendations. While the level of lead contamination varies by village, discussions with colleagues at MSF, TerraGraphics Environmental Engineering, and the Zamfara State Ministry of Health (SMoH) informed the data collection team that gold ore appears to be distributed in villages state-wide. Therefore, all villages in all LGAs were included in the sampling frame, so as to be representative of the entire state.

Sampling approach*:* While simple random sampling would have been the ideal approach, it is logistically difficult and expensive in a large geographic area and dispersed population like Zamfara. In addition, it would have required a listing of every member of the population, which does not exist. Zamfara State is divided into 14 local government areas (LGAs), for which census data are incomplete. A 2008 census only provided data down to the LGA level, not the village level. Therefore, population estimates were obtained using LandScan imagery data (Oak Ridge National Laboratory, Oak Ridge, TN, USA) which uses satellite data to provide 1km^2 resolution population estimates. A sum of the one km^2 grids in each LGA yielded population estimates comparable to the 2008 census. To obtain a representative sample of this region, at least two villages were randomly selected from each LGA. Each LGA was divided into five-by-five square kilometer grids, and villages were randomly selected from these grids, with the probability of selection relative to the LandScan population estimates. Seven compounds were randomly sampled within each selected village. Using an estimated average of 2.5 children <5 years old per compound, one child was selected for each compound with parental consent.

Sample size: Sample size calculations for estimating prevalence of elevated BLL in mining and non-mining villages were based on the previous investigations of lead poisoning in Zamfara. In October-November of 2010, Lo et al (2012) found a prevalence of BLL ≥ 10 μg/dL in children of 46% in 54 mining villages and 15% in 16 non-mining villages. While these villages were not a representative sample of all Zamfara villages, they were the best available data at the time. The sample size was calculated to provide for a large enough sample so that the margin of error around the prevalence estimate would be ±10%, assuming a 95% confidence interval, accounting for the design effect, and inflating the sample size by 15% to account potential for non-response. The original sample size target was 46 villages, with seven children sampled per village, for a total of 322 children. During data collection, representatives from eight additional villages requested that their villages also be studied for contamination, so a total of 54 villages were included. Two of the sampled villages were much larger than anticipated, so 14 children were selected from these villages instead of seven, for a total of 392 children included in the study. Blood samples were not collected from nine of these children, leaving 383 observations available for analysis.

Ethical Clearance and Informed Consent: The study protocol was granted approval by US CDC. Two weeks prior to conducting research in villages, informed consent was obtained in Hausa (the language of choice) from LGA emirs and civil authority chairmen to conduct research in their respective LGAs. LGA leaders were read a standard prompt to inform them of the study objectives and activities. Leaders of all LGAs granted approval. For villages randomly selected for inclusion, informed consent was obtained in Hausa from village chiefs. For compounds randomly selected for inclusion, informed consent was obtained in Hausa from compound heads. Compound and village heads were read a standard prompt to inform them of the study objectives and activities, and of their role in the study.

Interviews and Visual Assessments*:* After obtaining informed consent from randomly selected compounds as described above, field teams asked four screening questions to determine the compound's eligibility. One child <5 living in the compound was randomly selected for inclusion in the study. The survey questionnaire was then administered to the head of the compound to gather data about demographics and risk factors for compound lead contamination and lead exposure, described below. To complement survey responses, field teams conducted rapid visual assessments for evidence of current or historic ore processing activities, including piles or bags of ore, grinding machines, grinding wheels, tailings, drying piles, and sluicing locations.

Blood Sample Collection and Analysis*:* After parental informed consent was obtained and the risk-factor questionnaire was completed, two venous blood samples (minimum 1.5mL in a 5mL Vacutainer designed to normally collect 3mL blood) were drawn by a trained phlebotomist from the randomly selected eligible child. If the child was not at the compound, the parent was asked when it would be most convenient for the team to return. If the selected child was not at the compound at any time during the team's visit to that village, the study team proceeded to the next randomly selected compound. One venous blood sample per child was taken to a central processing laboratory where samples were tested on a LeadCare II (LCII) portable blood lead analyzer by trained members of study team within 24 hours of collection. The other blood sample was sent unopened to the CDC Division of Laboratory Sciences (DLS) for quality assurance/quality control using an Inductively Coupled Plasma Mass Spectrometer. In addition to testing BLL and other blood metal concentrations, CDC tested blood samples for sickle cell status. Blood spots were also collected and dried on Guthrie cards. The LCII analyzer, when used according to the CLIAapproved instructions, has a reportable blood lead range of 3.3 μg/dL to 65 μg/dL, reporting only "HI" for blood lead results >65 μg/dL. To identify children with extremely high lead exposures for priority medical treatment, a dilution procedure recommended by the LeadCare II manufacturer was implemented to estimate blood concentrations >65 μg/dL, which has previously been found to provide useful approximations of extremely high BLLs in the field. All supplies used to collect blood were verified lead free by the CDC DLS. All results from the LCII and Guthrie card were shared with the MSF physicians accompanying field teams, Zamfara SMoH, and the Nigerian CDC. The Zamfara SMoH was responsible for notifying parents regarding their children's results. All study team members were trained in counseling parents on their child's blood lead status. At the time samples were collected, an informational sheet was given to the heads of compounds to inform parents who to contact if they have questions, concerns or problems.

Dust and Soil Sampling and Analysis*:* Environmental sampling was performed to identify villages that engaged in gold ore processing by measuring lead in soil and dust. After administering the compound survey, field teams collected indoor dust samples obtained from piles created by sweeping or scooping loose floor dust from a $1m^2$ area from the area where the child sleeps as identified by the child's mother. A minimum of 1 cubic inch ($16\ cm^3$) dust was collected from each child's household using small, dedicated lead-free brushes, and placed in a plastic bag. An outdoor soil sample was collected from the compound in a location identified as an area where the child plays. Dust and soil samples were labelled with study identification numbers to match those on the corresponding child's blood sample. Dust and soil samples were split similarly to blood samples, with one sample analyzed in Nigeria with an x-ray fluorescence (XRF) reader and the other sample sent to CDC in Atlanta for QA/QC analysis. Samples sent to CDC were analyzed by the Department of Geosciences at Georgia State University in Atlanta, Georgia, USA. Samples were sieved at 2.0μm with a nylon sieve, and ground using ceramic mills and handled in a HEPA-filtered hood. Powders were digested using a combination of hydrofluoric, perchloric, hydrochloric, and nitric acids, in open Teflon beakers. All constituents were analyzed on a Varian VISTA AX CCD Simultaneous Inductively Coupled Plasma Atomic Emission Spectrometer, low level Pb values (e. g. <50 mg/kg) were confirmed using a Vista AA 220 Atomic Absorption Spectrophotometer.

Water Sample Collection and Analysis*:* A common source of drinking water was identified for each village. Generally speaking, there were two types of wells in the study villages: 1) an open well, which is at greater risk of surface contamination, and 2) a closed well (bore-hole and pump), which is a proxy for aquifer contamination. The field team collected a sample from one of each type of well when possible. All villages had at least one type of well, but not all had both. Water samples were sent to laboratories at the University of Wisconsin for lead analysis.

Outcome, Exposure, and Effect Modifying Variables*:* The primary outcome of interest was BLL, as measured by CDC laboratory analysis in Atlanta, GA. Due to a highly right-skewed distribution, the natural log of BLL was used for statistical tests requiring a normal distribution of observations. Some tests treated lead concentrations in the soil and dust samples as the outcome variable; these were likewise natural log-transformed to account for highly right-skewed distributions. Gold ore processing in Zamfara has been described as a series of six activities (Dooyema et al., 2012). These activities are 1) breaking ore rocks into gravel-sized pieces ("breaking"), 2) grinding these smaller pieces into a powder with a gas-powered crop grinder or mortar and pestle ("grinding"), 3) washing the powder with water to separate gold particles ("washing"), 4) drying the powdered ore after washing ("drying"), 5) mixing the ore powder with liquid mercury to separate gold from other particles and to amalgamate the gold particles ("separating"), and 6) heating the gold mixture to evaporate the mercury and amalgamate the gold particles ("melting"). The household survey used in this study asked participating compounds about their participation in each of the six activities. Compounds reported participation in from zero to all six activities, with different combinations of activities being reported from different compounds. Binary variables were used to indicate whether a compound processed ore, and if so, which activities they performed. Binary variables were also created to indicate whether members of the child's compound participated in galena-based eyeliner manufacture, smelting, auto repair, activities on a firing range, painting, ceramics production, pottery, electrical work, and battery recycling; whether the child's family used ceramic plates or cups at home; whether or not the child had been exposed to galena-based eyeliner, other cosmetics, or home remedies in the past 30 days; whether the child's home was cleaned daily; and whether the child had been breastfed in the past 30 days. 18 binary dummy variables were created for categorical variables to indicate the child's primary and alternative drinking water sources (borehole, open well inside the compound, open well outside the compound, pond, stream, or piped tap) and the child's sickle cell status, as tested by the CDC in Atlanta, GA (typical, sickle cell carrier, sickle cell disease, hemoglobin C, hemoglobin C disease, and non-detect). Variables for the child's sex and child's age in months were also included. Water samples were excluded from the analyses presented here, as we explain in the discussion.

Statistical Analysis*:* We analyzed the data in SAS version 9.3 (SAS Institute Inc., Cary, NC, USA). Children were the unit of analysis, since compound level data pertained to each individual child from which a blood sample was collected. When appropriate, we applied sampling weights to account for the unequal probabilities of selection into the study due to the sampling design. Some epidemiologists have argued that while analyses to estimate prevalence should always maintain representativeness, analyses to investigate causal associations need not necessarily do this (Rothman, Gallacher, & Hatch, 2013). This distinction is between maintaining the abilities to make statistical inferences about prevalence and scientific inferences about causality (Elwood, 2013). Thus, we performed analyses for prevalence estimates using only the 322 children from the 46 randomly sampled villages and included the sampling weights. For analyses aimed at answering questions about potential causal factors linked to BLL, we included all 383 children from all 54 villages and did not include the sampling weights. The weights represent the inverse of each child's probability of selection at each stage in the sampling approach. We performed multiple imputation in SAS using the expectation-maximization method to account for missing values for 19 sleep area dust samples (5.0% of all observations) and 18 play area soil samples (4.7% of all observations). The missing values were assumed to be missing at random. The method used creates five estimates for each missing value, runs the statistical test requested, then takes the mean of the results from the five separate tests.

Results

Characteristics of Study Population

We collected data from 392 compounds, but because blood samples were available for 383 children, we only analyzed data from these children and their respective compounds. 328 compounds were located in 46 randomly selected villages, while an additional 55 compounds were located in eight villages that requested inclusion in the study. Age in months for all 383 children was approximately normally distributed, with a mean of 35.2 (2.9 years), median of 36.0 (3.0 years) and standard deviation of 16.2. There were 200 boys (52.2%) and 183 girls (47.8%) in the full sample of 383 compounds, with 171 boys (52.1%) and 157 girls (47.9%) in the random sample of 328 compounds. Of the nine occupations asked about in the survey to control for potential take-home lead exposures, all were reported by fewer than six percent of the 383 compounds except for auto repair, reported by 12.8% of compounds. Of all 383 children, 28.9% (111) had been breastfed in the previous 12 months, 94.5% (362) lived in homes cleaned daily, and 87.0% (333) had been exposed to galena-based eyeliner in the previous 30 days.

Prevalence of ore processing and elevated BLL

To estimate the prevalence of mining activities and the prevalence of elevated BLLs, we performed weighted analyses on the 328 randomly-selected compounds to maintain statistical generalizability at the state-wide level. Of the 328 randomly sampled compounds, 55 reported ore processing in the previous 12 months and 273 reported that they had not processed ore in the previous 12 months. The prevalence of any ore processing among the randomly compounds was 17.2%. The prevalence of each of the six ore-processing activities is reported in Table 1.

Table 1: Estimate prevalence of ore processing activities among the 328 randomly sampled compounds:

Ore-processing activity	Prevalence (n)	95% Confidence Interval	Standard error
Any activity	17.23% (55)	9.74, 24.72	3.68
Breaking	12.83 (43)	7.08, 18.58	2.82
Grinding	7.62% (31)	2.87, 12.37	2.33
Washing	16.27% (50)	9.32, 23.21	3.41
Drying	13.12% (45)	6.70, 19.54	3.15
Separating	7.32% (30)	2.28, 12.36	2.47
Melting	4.89% (18)	0.54, 9.24	2.14

Though CDC in 2012 lowered the BLL reference level for intervention from 10 μg/dL to 5 μg/dL, we present prevalence estimates for both levels (Table 2). Previous studies in Zamfara have used the 10 μg/dL level as a benchmark, and providing both estimates gives further insight into how widespread elevated BLLs are in children in Zamfara. The prevalence of BLL ≥10 μg/dL was 19% higher among children living in ore-processing compounds than among children in non-processing compounds (25.9% compared to 21.8%). The prevalence of BLL ≥5 μg/dL was 11% higher among children living in ore-processing compounds than among children in non-processing compounds (73.4% compared to 66.4%). We also estimated prevalence of BLLs over 40 μg/dL to compare to the results of previous studies, which reported alarmingly high rates of children with BLLs above this level. The prevalence of BLL ≥40 μg/dL was 3.0% for children living in ore-processing compounds and 0.2% for children in non-ore-processing compounds.

Table 2: Estimated prevalence of BLLs in ore-processing and non-ore-processing compounds:

BLL	Ore-processing compounds (n=55)			Non-ore-processing compounds (n=273)		
	N	Prevalence	95% Confidence interval	n	Prevalence	95% Confidence interval
BLL ≥5 μg/dL	45	73.35%	54.75, 91.94	188	66.40%	53.96, 78.83
BLL ≥10 μg/dL	21	25.88%	14.93, 36.83	34	21.78%	14.43, 29.17
BLL ≥20 μg/dL	11	7.56%	0.00, 15.15	5	1.64%	0.00, 3.28
BLL ≥30 μg/dL	7	5.12%	0.00, 11.33	3	0.79%	0.00, 1.67
BLL ≥40 μg/dL	4	3.00%	0.00, 6.66	1	0.16%	0.00, 0.48

The percentage of all 383 children with BLLs >30 μg/dL was ten times higher in ore-processing compounds than in non-ore-processing compounds (13% compared to 1.3%). Table 3 shows the differences in BLL distribution among children living in ore-processing and non-ore-processing compounds. The percentages shown are for all 383 children and are unweighted.

Table 3: Comparison of BLL distribution in mining and non-mining compounds

	Percentage of children with BLLs in the specified range (n)	
BLL range (μg/dL)	Ore-processing compounds (69)	Non-processing compounds (314)
<5	18.8 (13)	33.1 (104)
5 to 9.9	43.5 (30)	47.5 (149)
10 to 29.9	24.6 (17)	18.2 (57)
30 to 61	13.0 (9)	1.3 (4)

Environmental Contamination and BLL

In contrast to previous investigations which studied the most contaminated mining villages in Zamfara, this investigation sought a representative sample to measure lead concentrations in soil, dust, and children's blood. Table 4 shows the median and range for lead concentrations for gold ore-processing and non-processing compounds. Medians are reported because each of these variables had a highly right-skewed distribution. Mean children's BLL was 13.12 μg/dL in ore-processing compounds and 7.53 μg/dL in non-ore-processing compounds. While medians for each variable were higher in ore-processing compounds, the highest concentrations of lead in dust and soil were not found in compounds that reported ore processing in the previous 12 months.

Table 4: Median and range for lead concentrations in blood, soil, and dust samples:

	Ore-processing compounds		Non-ore-processing compounds	
	Median	Range	Median	Range
BLL (µg/dL)	8.3	2.6 – 61.3	6.4	1.6 – 44.7
Pb in sleep area dust (mg/kg)	34.0	14.0 – 710.0	28.0	6.8 – 20,000.0
Pb in play area soil (mg/kg)	35.0	11.0 – 560.0	23.5	5.3 – 1,100.0

To assess whether increasing lead concentrations in soil and dust were associated with increasing BLL, we ran correlation analyses for all children for which we had both measurements (n=364 for dust and n=365 for soil). Pearson correlation analyses revealed statistically significant (p-value < 0.05) positive linear relationships between lead concentrations in soil and blood, dust and blood, and between soil and dust (Table 5). There was a weak but statistically significant negative relationship between child's age and BLL. BLL, dust Pb, and soil Pb concentrations were natural log-transformed to satisfy the assumption of normal distribution.

Table 5: Pearson correlation tests for linear associations between continuous variables*:

Independent variable	Dependent variable	R	p-value
Dust Pb	BLL	0.329	<0.0001
Soil Pb	BLL	0.304	<0.0001
Soil Pb	Dust Pb	0.575	<0.0001
Child's age	BLL	-0.120	0.0184

*BLL, dust, and soil Pb concentrations were natural-log-transformed to produce normal distributions

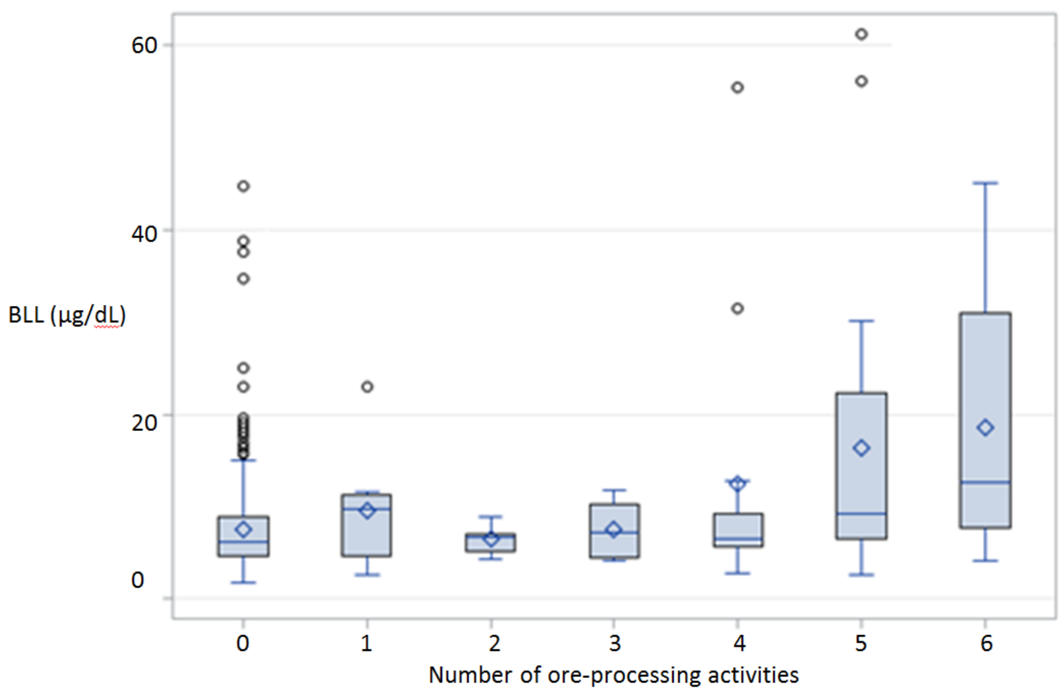
We performed two-sample t-tests for differences in mean lead concentrations in blood, soil, and dust samples between ore-processing and non-processing compounds. T-tests were performed with natural-log-transformed values for BLL, soil lead, and dust lead concentrations. There were statistically significant (p-value < 0.05) differences in mean lead concentrations for all three media between ore-processing and non-ore-processing compounds, both for participation in any activity as well as for each of the six processing activities (results not shown).

To assess whether children living in compounds reporting a higher number of processing activities had higher BLLs, we ran ANOVA tests using natural-log-transformed BLL. Compounds were grouped by the number of different mining activities compound members had performed in the past 12 months (zero to six). Using Scheffe's method, we found statistically significant differences in mean natural-log-transformed BLL between compounds engaged in six activities and five activities compared to compounds engaged in zero activities at the 0.05 level (results not shown). Comparing descriptive statistics for BLL by number of processing activities, compounds engaged in all six activities had higher mean and median BLLs than compounds engaged in fewer activities (Table 6 and Figure 1).

Table 6: Mean BLL in children <5 by number of ore-processing activities performed by the child's compound

Number of ore-processing activities	Number of compounds	Mean BLL	Standard deviation	Median BLL
0	314	7.53	5.17	6.13
1	11	9.49	5.38	9.65
2	5	6.41	1.74	6.74
3	8	7.44	3.23	7.12
4	13	12.42	14.81	6.50
5	20	16.27	16.43	9.17
6	12	18.53	14.33	12.60

Figure 1: Distribution of children's BLL by number of ore-processing activities performed by the child's compound*



*Means, standard deviations, and medians for each group are displayed in table 6 above.

Linear Regression

To estimate the effect of ore processing and other potential risk factors on BLL, we performed linear regression using natural-log-transformed BLL as the outcome. We initially included all binary variables in the independent variable selection process. Soil and dust data were excluded from linear regression because we were testing the association between mining activities on BLL, with the assumption that the dust and soil concentrations are the intermediate media for Pb from ore to children's blood as suggested by previous studies (Plumlee et al., 2013). Before reducing the model, the full model had an adjusted R^2 of 0.25. Using forward selection with a p-value entry criteria of <0.10, the variables that were positively associated with increasing BLL were being a child of male sex, living in a compound that had ground, separated, or melted ore in the past 12 months, using a piped tap as the primary drinking water source for the past 12 months, being breastfed in the past 12 months, and being exposed to galena-based eyeliner in the past 30 days. The variables that were negatively associated with increasing BLL were child's age, reporting an alternative water source of "other", having a family member working on a firing range, having a family member who makes pottery, and having a blood test positive for sickle cell disease.

A second linear regression analysis was done, dropping out sickle cell status, firing range, pottery, and alternative water source of "other". Sickle cell status was dropped due to the fact that the observed effect was only based on two observations, and that the protective effect observed in these two observations is inconsistent with current scientific understandings of the interaction between sickle cell disease and lead toxicity (Erenberg, Rinsler, & Fish, 1974; Issaivanan, Ahmed, Shekher, Esernio-Jenssen, & Manwani, 2009). Firing range, pottery, and alternative water source of "other" were dropped because these factors only occurred for a small number of children, and did not need to be controlled for since they are not related to mining. Again using a forward selection method with a p-value entry criteria of <0.10, the final model included child's age, male sex, living in a compound in which family members participated in ore grinding, separating, and melting in the last 12 months, using a piped tap as the primary drinking water source, being breastfed in the past 12 months, and being exposed to galena-based eyeliner in the past 30 days. All factors were positively associated with BLL except for child's age, in which case being older had a protective effect. The final model without environmental measurements had an adjusted R^2 of 0.18.

Table 7: Linear regression coefficients for natural-log-transformed BLL in all 383 sampled children. Adjusted R^2 = 0.18

Parameter	Beta coefficient*	95% Confidence Interval	Standard Error	P-value
Child's age	-0.004	-0.008, -0.0004	0.002	0.033
Male sex	0.12	0.008, 0.232	0.06	0.036
Compound ground ore in past 12 months	0.30	0.060, 0.548	0.12	0.015
Compound separated ore with Hg in past 12 months	0.16	-0.200, 0.513	0.18	0.389**
Compound melted Hg off of ore in past 12 months	0.45	0.103, 0.805	0.18	0.012
Compound's main drinking H_2O was a piped tap	0.63	0.326, 0.927	0.15	<.0001
Child was breastfed in past 12 months	0.14	0.002, 0.281	0.07	0.047
Child was exposed to eyeliner in past 30 days	0.15	-0.018, 0.314	0.08	0.081**

* Beta coefficients refer to the parameter's effect on natural-log-transformed BLL
** Upon entry into the model, all parameters had a p-value less than 0.10 when controlling for all other covariates

Discussion

The goals of this study were to quantify the prevalence of children <5 with elevated BLLs in mining and non-mining communities in Zamfara and to identify factors associated with elevated BLL. The results of this investigation suggest that elevated BLLs in children are widespread across Zamfara, but are significantly higher among children living in ore-processing compounds. As seen in previous studies in Zamfara, ore processing is associated with elevated BLLs (Lo et al., 2012), functioning through exposure to environmental contamination of soil and household dust (Plumlee et al., 2013). In addition to living in a compound that processes gold ore, other factors which appear to contribute to children's

BLLs in Zamfara include age, sex, breastfeeding, drinking water from a piped tap, and galena-based eyeliner exposure.

Prevalence of Elevated BLL

Previous investigations in Zamfara reported alarmingly high rates of elevated BLLs from highly contaminated villages. Lo et al investigated 314 children in 70 villages in three LGAs in 2010, and found that the proportion of children with a BLL >10 μg/dL was 68% in ore-processing villages and 50% in non-ore-processing villages (results at the compound level were not reported). In our study in 2012, the weighted proportion of children in randomly sampled villages with a BLL >10 μg/dL was 26% in ore-processing compounds and 22% in non-ore-processing compounds – a difference of 19%. In striking contrast with our results, Dooyema et al's 2010 investigation of two heavily contaminated mining villages reported that 97% of all 204 children <5 years old had BLLs ≥45 μg/dL. Our study was conducted in part to estimate the statewide prevalence of elevated BLLs, rather than focusing only on highly contaminated mining villages. Thus, we expected to find a smaller proportion of children with BLLs >10 μg/dL. How our estimates compare to other areas of rural Nigeria is difficult to say, as few studies have attempted to estimate the range of background BLLs in rural Nigeria. We found that ore-processing communities had a wider range in children's BLL, with ten times the percentage of children with BLLs over 30 than among children in non-ore-processing compounds. While children in ore-processing compounds had BLLs significantly higher than children in non-ore-processing compounds, 22% of children in non-ore-processing compounds still had BLLs over 10 μg/dL. Most studies in Nigeria to date have focused on urban areas, and the age range for children included varied between studies. A 2008 study (J. Nriagu et al., 2008) found mean BLLs of 9.9 μg/dL (n=400), 8.3 μg/dL (n=183), and 4.7 μg/dL (n=69), in children aged 2-9 years in the cities of Ibadan, Nnewi, and Port Harcourt. In the northern city of Jos, Pfiztner and colleagues found a mean of 15.2 μg/dL (n=218) in children aged 6-35 months (Pfitzner, 2000), while Wright and colleagues found a mean of 11.2 μg/dL (n=64) in children aged 0-5 years (Wright, Thacher, Pfitzner, Fischer, & Pettifor, 2005). Pfiztner reported that 70% of children studied had BLLs >10 μg/dL. Several of the risk factors identified in these urban studies are less practically relevant as risk factors for children in a rural area such as Zamfara, including living near a battery smelter, living near a road with heavy car traffic, and length of time the child plays outside. Children in Zamfara who have not been exposed to contaminated mine tailings likely have exposures lower than urban children due to fewer lead sources such as automobiles, heavy industry such as battery smelters, and leaded paint on buildings. Many of the children in this study who live in non-ore-processing compounds were still likely exposed to mine tailings if other compounds in their village processed ore. Thus it could be difficult to estimate a true background risk for lead exposure in Zamfara, where artisanal gold mining was widespread – reported in 11 of Zamfara's 14 LGAs in this study. Our estimates for the mean (7.53 μg/dL) and median (6.4 μg/dL) BLL in children in non-ore-processing compounds are within the range estimated for Nigerian children living in urban environments. Higher-than-expected BLLs in non-ore-processing compounds may be explained by a family moving into an area with contaminated soil, using contaminated building materials for their home, or processing prior to the 12 month period in question.

Gold Ore Processing

Gold ore processing was widespread in the areas surveyed in 2012. We sampled villages in all 14 of Zamfara's LGAs, and found ore processing compounds in 11 of them. The weighted prevalence of ore processing in the 328 randomly sampled compounds was 17%. However, these compounds were located in 44% (20/46) of randomly sampled villages, which is close to the estimate from previous investigations that approximately 50% of villages in Zamfara participated in gold ore processing (Lo et al., 2012; I. H. von Lindern, von Braun. M.C., Tirima, S., Bartrem, C., 2011) The ore processing activities most strongly associated with higher BLL were grinding, separating, and melting. These activities were also the least prevalent of the six ore-processing activities, with grinding reported by 7.6%, separating by 7.3%, and melting by 4.9% of compounds. Our finding that breaking, washing, and drying were the most common activities is consistent with the findings of Lo et al in 2010. Prior to the investigation, it was suspected that grinding ore would be most associated with elevated BLL due to the large amount of dust generated by passing ore through crop grinders. However, we found that ore grinding was the activity second most strongly associated with BLL. Of the six activities, melting was the most strongly associated in terms of both statistical significance and effect on BLL. This could be related to the fact that this is the final step in the gold extraction process, so these compounds may be more likely to have discarded tailings close by. All compounds engaged in the final steps of ore processing reported discarding the tailings in the bush or, less commonly, in a stream. Thus, it is reasonable to hypothesize that compounds engaged in melting would have more environmental contamination, and that children in these compounds would have worse lead exposures. Our finding that compounds engaged in five or six processing activities have the highest average BLLs can be explained by multiple hypotheses. It is likely that lead contamination of soil, dust, and water occurs at multiple steps in the refining process, so compounds engaging in more steps allow more lead to enter their compound. It may also be true that compounds that engaged in more steps in the gold refining process handled more ore overall than compounds engaged in fewer steps in the process.

Environmental Contamination

Most compounds had levels of environmental contamination below the US EPA's recommended limits for child's play area soil and indoor sleep area dust. EPA's recommended limit for play area soil is 400 ppm (EPA, 2001), which was exceeded by four of the 364 compounds for which soil data were available. Indoor dust samples in 10 villages exceeded this level (for indoor dust, EPA uses units of mg/m^2 of surface, but we measured concentrations in mg/kg). Previous investigations in Zamfara found soil contamination in children's play areas ranging over 100,000 ppm. 85% of compounds sampled by Dooyema et al in 2010 had soil concentrations >400 ppm (Dooyema et al., 2012). Lo et al found that 37% of the 20 ore-processing villages they sampled had soil samples >1,200 ppm, the level they set for priority environmental remediation (Lo et al., 2012). While medians for each variable were higher in ore-processing compounds in our study, the highest concentrations of lead in dust and soil were not found in compounds that reported ore processing in the previous 12 months. These highly contaminated compounds may have processed ore prior to June 2011, which was the beginning of the period that compounds were asked about. It is also possible that the families sampled had not processed ore, but moved into a previously contaminated area within the past few years where prior occupants processed ore. Compounds that do not process ore may have also used building materials such as soil, mud, or water which were contaminated from processing elsewhere in the village.

Risk Factors for Elevated BLL

The factors associated with increased BLL in our analyses are consistent with current understandings of lead exposure. Living in a compound that had processed ore in the previous 12 months, particularly in a compound that participated in grinding, melting, or separating, was associated with increased BLL. Grinding is associated due to dust generation. As suggested above, melting may be associated with increased BLL because it is the last step in the refining process and these compounds may have more discarded waste. Of the other factors associated with increased BLL for all 383 children in this study, male sex and younger age are well-documented in the scientific literature as risk factors for increased BLL. Boys are frequently found to be more vulnerable to lead toxicity than girls

(Llop, Lopez-Espinosa, Rebagliato, & Ballester, 2013), and are frequently found to have higher BLLs than girls (Xie et al., 2013). This is likely a function of both biological and behavioral differences (Llop et al., 2013). Behavioral differences may lead boys to ingest more soil, which is the primary lead exposure pathway for children (Plumlee et al., 2013; I. H. von Lindern, Spalinger, Bero, Petrosyan, & von Braun, 2003). Younger children are more vulnerable to increased BLL due to their physiology and hand-to-mouth behaviors. Exposure to galena-based eyeliner was also found to be associated with increased BLL. Children exposed to galena-based eyeliners can ingest lead via eyelid-hand-mouth behaviors or via dermal absorption (Behbod, 2012). Previous studies of Nigerian children have found eye cosmetics to be associated with elevated BLLs (Pfitzner, 2000; Wright et al., 2005). Breastfeeding has also been found to be a pathway for exposure (Marques, Bernardi, Dorea, de Fatima, & Malm, 2014), though it is unclear in our study whether exposure occurs through the mother's milk itself, or through the child's ingestion of dust on the mother's skin . The final significant factor we found to be associated with increased BLL was reporting a piped tap as the primary drinking water source for the previous 12 months. It is reasonable to hypothesize that this is due to the use of lead pipes. Analyses of the effect of water contamination levels on BLL are not presented here, as discussed below. The water samples collected were from wells, not taps, so concentrations in lead pipes were not available for analysis.

Strengths and Limitations

This study was the first to estimate statewide prevalence of lead poisoning in Zamfara. The strengths of this study include a large sample size of ore-processing and non-ore-processing compounds, and a large body of data including household surveys and blood, soil, and dust samples. The samples were all analyzed at the limit of detection in state-of-the-art laboratories to provide precise estimates. Additionally, these data are likely free from effects of seasonal variation in lead exposures that could confound the associations between BLL and potential risk factors, as all field work was performed during June and July of 2012. This was the beginning of the rainy season in Zamfara, when mine tailings are less likely to be spread by dry, windy conditions occurring at other times of the year (J. O. Nriagu, 1992).

Ideally, we would have been able to present lead concentrations in drinking water, as this is a likely route for lead ingestion that may vary depending on the processing activities performed by compounds. Though water samples were collected from at least one well per village, linking these village-level samples to compound-level outcomes greatly diminishes the observed association. While the sampled wells represent primary drinking water sources for many village residents, in reality most families use multiple seasonal water sources throughout the year. For example, compound respondents in our study may have lived in a village for which open (uncovered) and closed (i.e. covered borehole) well samples were obtained, but responded that their primary and alternative drinking water sources were a pond, stream, piped tap, or water of unknown origin sold by a vendor. Additionally, nearly all compounds responded that they used rainwater when available. Future analyses with this data set will use the water data for a village-level analysis.

Another factor limiting our understanding of statewide contamination in Zamfara is that this study was a cross-sectional design, which does not capture changes that may have occurred in mining practices since 2010. After the initial detection and investigation of the lead poisoning outbreak in 2010, emergency efforts were made to remediate badly contaminated villages and to educate mining communities of the dangers of processing ore in close proximity to their compounds (UNEP/OCHA, 2010). Though no remediated villages were included in this study, it is possible that spillover of safe practices encouraged ore processors to move operations further from their villages. Remediation efforts have continued since these data were collected in 2012. Nevertheless, our results demonstrate a difference in lead poisoning prevalence between processing and non-processing compounds. Additionally, the blood samples measured in our study represent recent exposures to existing environmental contamination, and do not capture the lifetime lead exposures of these children. Blood serves as the initial repository for absorbed lead as well as the medium for transport to other parts of the body, but most of the body burden of lead is eventually stored in the bones and teeth (ATSDR, 2007). The half-life of lead in blood is approximately 28 to 36 days, with elimination occurring through the urine and feces. Approximately 74% of the total lead body burden in children and 94% in adults is stored in the bones and teeth, where the half-life is about 27 years. Despite the relatively short half-life of lead in blood, BLLs can remain elevated for longer periods in individuals experiencing bone growth, bone injuries, or pregnancy, due to the release of lead stored in bone (Lidsky & Schneider, 2003). Though the data collected in this cross-sectional study do not tell us how exposures have changed in these villages, we do know that elevated BLLs are widespread, though most are under levels necessitating medical intervention.

Though correlation and regression analyses linking environmental media to BLLs showed significant positive relationships, survey responses were subject to potential recall bias. It is possible that compound respondents whose children had died or fallen ill due to suspected lead poisoning remembered potential exposures better. However, this is unlikely given that the survey only asked questions about activities that occurred up to 12 months prior. Though field teams looked for visual signs of ore processing in sampled compounds to confirm respondents' answers to survey questions, it is possible that mismeasurement of exposure to ore-processing activities occurred if compounds which had processed ore responded that they had not. This would have biased our results towards the null.

Implications

The results of this study demonstrate that lead poisoning (BLL >10 μg/dL) is widespread in Zamfara, though the proportion of children with BLLs ≥ 45 μg/dL (CDC's level for initiating chelation therapy) appears lower at the statewide level than previously reported for highly contaminated villages. While not usually resulting in acute mortality, the effects of childhood lead poisoning at BLLs between 10 and 45 μg/dL are nevertheless a burden to the families and villages of Zamfara. Many of these children, and the children who continue to be exposed, will likely have compromised health for the rest of their lives, taking the form of learning and behavioral disorders, anemia, reduced stature, hearing loss, reproductive problems, peripheral neuropathy, renal effects, and hypertension. Childhood lead poisoning is entirely preventable. It will require thorough remediation, education, and policy enforcement efforts to prevent the continued exposure of children to lead in Zamfara. The results of this study can be used to further such efforts, and in the process to strengthen the capacities of local and federal Nigerian agencies to protect public health and the environment.

References

al-Hazzaa, S. A., & Krahn, P. M. (1995). Kohl: a hazardous eyeliner. *Int Ophthalmol, 19*(2), 83-88.

ATSDR. (2007). *Lead Toxicity*. Atlanta, GA.

Behbod, B., Nasisi, A. (2012). Infant lead poisoning associated with use of tiro, an eye cosmetic from Nigeria--Boston, Massachusetts, 2011. *MMWR Morb Mortal Wkly Rep, 61*(30), 574-576.

Canfield, R. L., Henderson, C. R., Jr., Cory-Slechta, D. A., Cox, C., Jusko, T. A., & Lanphear, B. P. (2003). Intellectual impairment in children with blood lead concentrations below 10 microg per deciliter. *N Engl J Med, 348*(16), 1517-1526. doi: 10.1056/NEJMoa022848

Cureton, S. (2011). Environmental victims: environmental injustice issues that threaten the health of children living in poverty. *Rev Environ Health, 26*(3), 141-147.

DHS. (2009). Nigeria Demographic and Health Survey, 2008. Abuja, Nigeria: ICF International.

Dooyema, C. A., Neri, A., Lo, Y. C., Durant, J., Dargan, P. I., Swarthout, T., . . . Brown, M. J. (2012). Outbreak of fatal childhood lead poisoning related to artisanal gold mining in northwestern Nigeria, 2010. *Environ Health Perspect, 120*(4), 601-607. doi: 10.1289/ehp.1103965

Elwood, J. M. (2013). Commentary: On representativeness. *Int J Epidemiol, 42*(4), 1014-1015. doi: 10.1093/ije/dyt101

EPA. (2001). Identification of Dangerous Levels of Lead, Final Rule. In E. P. Agency (Ed.). Washington, DC: Environmental Protection Agency.

Erenberg, G., Rinsler, S. S., & Fish, B. G. (1974). Lead neuropathy and sickle cell disease. *Pediatrics, 54*(4), 438-441.

Fewtrell, L. J., Pruss-Ustun, A., Landrigan, P., & Ayuso-Mateos, J. L. (2004). Estimating the global burden of disease of mild mental retardation and cardiovascular diseases from environmental lead exposure. *Environ Res, 94*(2), 120-133.

Hicken, M. T., Gee, G. C., Morenoff, J., Connell, C. M., Snow, R. C., & Hu, H. (2012). A novel look at racial health disparities: the interaction between social disadvantage and environmental health. *Am J Public Health, 102*(12), 2344-2351. doi: 10.2105/ajph.2012.300774

Issaivanan, M., Ahmed, R., Shekher, M., Esernio-Jenssen, D., & Manwani, D. (2009). Sickle cell disease and plumbism in children. *Pediatr Blood Cancer, 52*(5), 653-656. doi: 10.1002/pbc.21919

Jusko, T. A., Henderson, C. R., Lanphear, B. P., Cory-Slechta, D. A., Parsons, P. J., & Canfield, R. L. (2008). Blood lead concentrations < 10 microg/dL and child intelligence at 6 years of age. *Environ Health Perspect, 116*(2), 243-248. doi: 10.1289/ehp.10424

Khan, D. A., Ansari, W. M., & Khan, F. A. (2011). Synergistic effects of iron deficiency and lead exposure on blood lead levels in children. *World J Pediatr, 7*(2), 150-154. doi: 10.1007/s12519-011-0257-9

Landrigan, P. J. (2002). The worldwide problem of lead in petrol. *Bull World Health Organ, 80*(10), 768.

Landrigan, P. J., Schechter, C. B., Lipton, J. M., Fahs, M. C., & Schwartz, J. (2002). Environmental pollutants and disease in American children: estimates of morbidity, mortality, and costs for lead poisoning, asthma, cancer, and developmental disabilities. *Environ Health Perspect, 110*(7), 721-728.

Lanphear, B. P., Hornung, R., Khoury, J., Yolton, K., Baghurst, P., Bellinger, D. C., . . . Roberts, R. (2005). Low-level environmental lead exposure and children's intellectual function: an international pooled analysis. *Environ Health Perspect, 113*(7), 894-899.

Lanphear, B. P., Weitzman, M., & Eberly, S. (1996). Racial differences in Urban children's environmental exposures to lead. *Am J Public Health, 86*(10), 1460-1463.

Lidsky, T. I., & Schneider, J. S. (2003). Lead neurotoxicity in children: basic mechanisms and clinical correlates. *Brain, 126*(Pt 1), 5-19.

Llop, S., Lopez-Espinosa, M. J., Rebagliato, M., & Ballester, F. (2013). Gender differences in the neurotoxicity of metals in children. *Toxicology, 311*(1-2), 3-12. doi: 10.1016/j.tox.2013.04.015

Lo, Y. C., Dooyema, C. A., Neri, A., Durant, J., Jefferies, T., Medina-Marino, A., . . . Brown, M. J. (2012). Childhood lead poisoning associated with gold ore processing: a village-level investigation-Zamfara State, Nigeria, October-November 2010. *Environ Health Perspect, 120*(10), 1450-1455. doi: 10.1289/ehp.1104793

Marques, R. C., Bernardi, J. V., Dorea, J. G., de Fatima, R. M. M., & Malm, O. (2014). Perinatal multiple exposure to neurotoxic (lead, methylmercury, ethylmercury, and aluminum) substances and neurodevelopment at six and 24 months of age. *Environ Pollut, 187*, 130-135. doi: 10.1016/j.envpol.2014.01.004

Miller, J. L. (2013). Iron deficiency anemia: a common and curable disease. *Cold Spring Harb Perspect Med, 3*(7). doi: 10.1101/cshperspect.a011866

Nasidi, A. e. a. (2012). Infant lead poisoning associated with use of tiro, an eye cosmetic from Nigeria--Boston, Massachusetts, 2011. *MMWR Morb Mortal Wkly Rep, 61*(30), 574-576.

Needleman, H. (2004). Lead poisoning. *Annu Rev Med, 55*, 209-222. doi: 10.1146/annurev.med.55.091902.103653

NRC. (1992). *Environmental Neurotoxicology*. Washington, DC: National Academy Press.

Nriagu, J., Afeiche, M., Linder, A., Arowolo, T., Ana, G., Sridhar, M. K., . . . Adesina, A. (2008). Lead poisoning associated with malaria in children of urban areas of Nigeria. *Int J Hyg Environ Health, 211*(5-6), 591-605. doi: 10.1016/j.ijheh.2008.05.001

Nriagu, J. O. (1992). Toxic metal pollution in Africa. *Sci Total Environ, 121*, 1-37.

Pfitzner, M. A. (2000). Prevalence of Elevated Blood Lead Levels in Nigerian Children. *Ambulatory Child Health*(6), 115-123.

Plumlee, G. S., Durant, J. T., Morman, S. A., Neri, A., Wolf, R. E., Dooyema, C. A., . . . Brown, M. J. (2013). Linking geological and health sciences to assess childhood lead poisoning from artisanal gold mining in Nigeria. *Environ Health Perspect, 121*(6), 744-750. doi: 10.1289/ehp.1206051

Rothman, K. J., Gallacher, J. E., & Hatch, E. E. (2013). Why representativeness should be avoided. *Int J Epidemiol, 42*(4), 1012-1014. doi: 10.1093/ije/dys223

Sanders, T., Liu, Y., Buchner, V., & Tchounwou, P. B. (2009). Neurotoxic effects and biomarkers of lead exposure: a review. *Rev Environ Health, 24*(1), 15-45.

Swenson, J. J., Carter, C. E., Domec, J. C., & Delgado, C. I. (2011). Gold mining in the Peruvian Amazon: global prices, deforestation, and mercury imports. *PLoS One, 6*(4), e18875. doi: 10.1371/journal.pone.0018875

UNEP. (2008). Leaded Gasoline. Nairobi, Kenya: United Nations Environment Programme

UNEP/OCHA. (2010). Lead Pollution and Poisoning Crisis: Environmental Emergency Response Mission. Geneva, Switzerland: Joint UNEP/OCHA Environment Unit.

van Geen, A., Bravo, C., Gil, V., Sherpa, S., & Jack, D. (2012). Lead exposure from soil in Peruvian mining towns. *Bull World Health Organ*(90), 878-886.

von Lindern, I. H., Spalinger, S. M., Bero, B. N., Petrosyan, V., & von Braun, M. C. (2003). The influence of soil remediation on lead in house dust. *Sci Total Environ, 303*(1-2), 59-78.

von Lindern, I. H., von Braun. M.C., Tirima, S., Bartrem, C. (2011). Zamfara, Nigeria Lead Poisoning Epidemic Emergency Response, March 2010 - March 2011, Final Report to the United Nations Childrens Fund (UNICEF): Terragraphics Environmental Engineering

WHO. (2009). *Global health risks: mortality and burden of disease attributable to selected major risks*. Geneva, Switzerland: WHO Press.

WHO. (2010). *Childhood Lead Poisoning*. Geneva, Switzerland: WHO Press.

Wright, N. J., Thacher, T. D., Pfitzner, M. A., Fischer, P. R., & Pettifor, J. M. (2005). Causes of lead toxicity in a Nigerian city. *Arch Dis Child, 90*(3), 262-266. doi: 10.1136/adc.2003.043562

Xie, X. H., Tan, Z. W., Jia, N., Fan, Z. Y., Zhang, S. M., Lu, Y. Y., . . . Dai, Y. H. (2013). Blood lead levels among children aged 0 to 6 years in 16 cities of China, 2004-2008. *Chin Med J (Engl), 126*(12), 2291-2295.