Childhood Blood Lead Levels and Environmental Risk Factors in Madagascar

Wyatt M. Champion (championw@usf.edu)
University of South Florida https://orcid.org/0000-0003-3968-1811

Adaline M. Buerck
University of South Florida

Christopher Nenninger
University of South Florida

Korede Yusuf
Adelphi University

Luke J.P. Barrett
ONG Ranontsika

Lova Rakototarisoa
ONG Ranontsika

Rinah Rakotondrazaka
ONG Ranontsika

Katherine Alfredo
University of South Florida

Jeffrey Cunningham
University of South Florida

Mahmooda Khaliq
University of South Florida

James R. Mihelcic
University of South Florida

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Abstract

One-third of children globally have blood lead levels (BLLs) exceeding the US CDC reference value of 5 μg/dL; this value may be as high as one-half for children in low- and middle-income countries (LMICs). Lead exposure occurs through a variety of routes (e.g., water, dust, air), and in LMICs specifically, informal economies (e.g., battery recycling) can drive lead exposures due in part to absent regulation. Previous work by our team identified a ubiquitous source of lead (Pb), in the form of Pb-containing components used in manually-operated pumps, in Toamasina, Madagascar. Characterization of BLLs of children exposed to this drinking water, and identification of additional exposure routes were needed. BLLs were measured for 362 children (aged 6 mo to 6 yr) in parallel with surveying to assess 14 risk factors related to demographics/socioeconomics, diet, use of pitcher pumps, and parental occupations. BLL data were also compared against a recent meta-review of BLLs for LMICs. Median childhood BLL (7.1 μg/dL) was consistent with those of other Sub-Saharan African LMICs (6.8 μg/dL) and generally higher than LMICs in other continents. Risk factors significantly associated ($p<0.05$, univariate logistic regression) with elevated BLL (at ≥5 μg/dL) included male gender, living near a railway or major roadway (owing potentially to legacy lead pollution), having lower-cost flooring, daily consumption of foods (beans, vegetables, rice) commonly cooked in recycled aluminum pots (a previously identified lead source for this community), and a maternal occupation (laundry-person) associated with lower socioeconomic status. Findings were similar at the ≥10 μg/dL BLL status. Our methods and findings may be appropriate in identifying and reducing lead exposures for children in other urbanizing cities, particularly in Sub-Saharan Africa, where lead exposure routes are complex and varied owing to informal economics and substantial legacy pollution.

Introduction

An estimated 815 million children globally have blood lead levels (BLLs) exceeding the U.S. Centers for Disease Control and Prevention (CDC) reference value of 5 μg/dL (UNICEF and Pure Earth, 2020, U.S. Centers for Disease Control and Prevention, 2020a). Elevated BLLs place children at risk of long-term effects including damage to the brain and nervous system, slowed development, and learning and behavior problems (U.S. Centers for Disease Control and Prevention, 2020b, World Health Organization, 2019). The majority of children globally with elevated BLLs reside in low- and middle-income countries (LMICs). A recent literature review of BLL data in LMICs determined 'background' (i.e., non-exposed in terms of occupation or nearby point sources) country-level mean childhood BLLs to range between 1.7 and 9.3 μg/dL globally, and that 49% of children in these countries have BLLs exceeding 5 μg/dL (Ericson et al., 2021).

Typical routes for lead exposure include leaded paint, plumbing, food, and medicine (Agency for Toxic Substances and Disease Registry, 2020). The youngest populations are considered to be both the most vulnerable and susceptible to lead poisoning given their behavior and developing neurological system (World Health Organization, 2010). Additional exposure routes specific to children in LMICs include the more recent phasing-out of leaded gasoline (resulting in higher dust and soil lead concentrations) and poorly regulated, highly-emitting informal industries (Buerck et al., 2021, Street et al., 2020). Communities are thus often exposed, simultaneously, to multiple lead sources. Malnutrition (Mahaffey, 1995, Kordas, 2017), limited awareness of the deleterious effects of lead (Williams et al., 2021), and reduced access to health screening and treatment (Wagner et al., 2011) further compound the issue.

Madagascar, located off the coast of East Africa, is one of the world's least developed countries, ranking 222 of 232 in terms of gross domestic product purchasing power parity (World Bank, 2021a) and with more than 80% of its population living in extreme poverty (UNICEF, 2017). Pollution of air, water, and soil are leading health risk factors in Madagascar, resulting in an estimated US$117-166 million in lost productivity annually (Global Alliance on Health and Pollution, 2018). In coastal Madagascar, centrally treated or piped 'utility' water is out of reach for many, and the use of locally-manufactured tube wells and hand pumps ('pitcher pumps') is common (MacCarthy et al., 2013). These pumps employ two valves using components typically manufactured with lead sourced from used lead-acid batteries (ULABs). Our previous work determined the self-supply market for pitcher pumps here to be a robust model for supply of water (MacCarthy et al., 2013), but that levels of lead in the pumped water exceed WHO drinking water guidelines in many circumstances (Akers et al., 2015, Akers et al., 2019).

The characterization of BLLs in this community in relation to an on-going pump lead-remediation intervention was the impetus for the present study. The objectives of the present study are to i) characterize BLLs in Toamasina, Madagascar, ii) identify potential environmental risk factors, iii) relate the measured BLL data to existing LMIC datasets, and iv) provide guidance for similar urbanizing areas with disperse lead sources. This study is unique in that it characterizes childhood BLLs in a 'typical' community as opposed to a higher risk population (e.g., mining communities, neighborhoods next to battery recycling facilities) (Haefliger et al., 2009, Dooyema et al., 2012, Amin Chowdhury et al., 2021). Additionally, the location is a rapidly urbanizing city in Sub-Saharan Africa, representative of the urbanization occurring throughout other LMICs, especially within the African continent.

Methods

The location of this study is Toamasina (Tamatave), the chief seaport of Madagascar. The city has undergone rapid urbanization in the past few decades, and faces issues common among other rapidly urbanizing areas including lack of reliable and affordable drinking water supply (MacCarthy et al., 2013) and informal/unregulated industries that can drive dispersed pollution that results in high exposures (Buerck et al., 2021).

Sample size calculation

The estimated sample size for the study (n=367) was based on the 2009 population of Toamasina (the most recent available from the national statistics bureau) (N≈233,000) (INSTAT, 2009), a confidence interval of 95%, and a hypothesized prevalence of BLL >5 μg/dL of 34.4% in the region, based on previous BLL modeling efforts (National Institute of Standards and Technology, 2012, Kadam and Bhalerao, 2010).

Study recruitment

Study participants were recruited from nine local health clinics (consisting of public and private clinics and a biomedical center, and accounting for all health facilities in the target community) dispersed throughout the five city districts (or *arrondissements*) following a cluster sampling approach. Most families in Toamasina utilize these clinics, and recruitment was intended to capture a representative sample of the city population. While visiting a clinic, potential adult participants were referred to a trained team member if their child was between the age of 6 months and 6 years. Following a description of the research and signed consent, the participant and their child were enrolled in the study. Recruitment aimed to represent the population from each of the five districts.

Collection and determination of blood lead levels

Blood samples were collected and measured for lead level by local Malagasy public health officials using the LeadCare II instrument (Meridian Bioscience, Cincinnati, OH) at the local health clinics. Health officials were trained by the study team in the use of the instrument and followed manufacturer quality assurance/control (QA/QC) guidelines. In brief, the child's finger was carefully cleaned with soap and water, wiped with alcohol, and lanced. The first drop of blood was wiped away, and 50 μL of blood were collected into a capillary tube. The blood was added to the reagent tube, and a sensor from the appropriate lot number (corresponding to a specific QA/QC batch) was inserted into the machine. Finally, a dropper was used to place the lysed blood from the treatment/reagent tube onto the sensor and the BLL reading recorded.

The operating range of the LeadCare II is 3.3-65 μg/dL. Values below the detection limit (DL) were imputed as the lower $DL/\sqrt{2}$ (i.e., 2.33 μg/dL), consistent with previous studies (Desai et al., 2020), while those above were assumed to be the upper DL itself (65 μg/dL). Sixteen percent of our BLL data were at or below detection and imputed, while only one data point (0.3%) required imputation for exceedance of the instrument's upper DL. The LeadCare II instrument can be sensitive to operating temperature and relative humidity (Magellan Diagnostics, 2021), with high temperatures (exceeding 27°C) potentially resulting in readings biased high due to sample evaporation (Neri et al., 2014), and high relative humidity (exceeding 80%) resulting in lower (i.e., more conservative) readings (Personal communication, February 11, 2021); it is unclear the relative effect of these conditions in relation to one another. Using historic daily weather data (Weather Underground, 2021), 4.4% and 20% of sampling days respectively had average temperature and relative humidity readings with levels exceeding the manufacturer's recommendations; a Wilcoxon test found no significant difference in BLLs ($p=0.88$) between the "normal" and "high" relative humidity groups.

Environmental scan survey

An environmental scan survey was administered in the local language (Malagasy) by local health officials and project personnel to the consenting adult present with the child (typically a mother) in combination with the aforementioned BLL testing. The English version of this survey is presented in the

Appendix Section A1 and was based on past efforts to relate risk factors to childhood BLLs (Sun et al., 2018) but modified for the local context. The survey included 14 questions pertaining to demographics, socioeconomic status (SES), diet, habits, and potential exposure routes. Environmental scan data were collected at the clinic, transported to the local project partner's office, and then inputted into an online application for review.

Geospatial analyses

Geospatial analyses were conducted to relate pump location (as a proxy for home location) to railways and major roadways using ArcMap (v10.8.1). A total of 197 BLL readings were associated to 175 pump locations; these pumps are located nearby the home. Railroads were identified using default base maps provided in the ArcMap database. Major roadways were identified by our study team living in Toamasina (in addition to national roads typically mapped). Based on previous studies of lead in air and soil (Smith, 1976, Maxwell and Nelson, 1978, Jian-Hua et al., 2009, Stojic et al., 2017), buffer zones of 400 m and 200 m were defined for railways and major roadways, respectively.

Data processing and statistics

Blood lead level and environmental scan data were entered and verified in Microsoft Excel. Survey data were post-processed and coded in R (R Core Team, 2020). BLL data were lognormally distributed (i.e., natural log transformations yielded normal distributions) (Shapiro-Wilks test, $p<0.001$). Descriptive statistics were calculated for BLL data and included geometric mean and standard deviation (both considered to be more appropriate than their arithmetic counterparts for these lognormal data). Additionally, Wilcoxon ranksum tests were conducted between response groups (e.g., 'Child usually eats beans on daily basis' *vs.* counterfactual) to determine significant differences, here defined as $p<0.05$. The Wilcoxon ranksum test was employed here for two reasons: 1) non-normal distribution of BLL data, and 2) many survey questions were open-ended, allowing for multiple responses (e.g., numerous foods consumed daily, multiple maternal/paternal occupations owing to nature of informal economy), thereby making the 'yes' *vs.* 'no' comparison more appropriate (compared to, for example, a reference group/level). Note that survey questions have been grouped by the nature of their response (i.e., single *vs.* open-ended response).

Numerous comparisons of BLL distributions were made against a recent meta-analysis of BLLs in LMICs (Ericson et al., 2021). This analysis compiled study-wise "pooled" means and standard deviations. Here, these pooled means and standard deviations were aggregated first by study (to reduce weighting by multiple subgroups reported in a single study) and then by country (to reduce weighting by multiple studies reported in a single country) to determine "pooled" country-wise means and standard deviations. Countries were parsed into 'Sub-Saharan Africa LMICs' and 'global LMICs' based on World Bank regional classifications (World Bank, 2021b), with the latter excluding the former. Countries were also parsed into their respective World Bank income classifications; low, lower-middle, and upper-middle income countries are defined by 2019 per capita gross national incomes of ≤\$1,035, \$1,036-\$4,045, and \$4,046-12,535, respectively. These countries, their regional and income classifications, and their country-wise pooled data are tabulated in the Appendix Table A1.

Univariate logistic regression was employed with a dichotomous outcome defined as elevated BLL status, here using the current CDC reference value (i.e., <5 *vs.* ≥5 ug/dL), similar to previous assessments of childhood BLLs in LMICs (Carpenter et al., 2019). Comparisons were also made at the former CDC "level of concern" (i.e., <10 *vs.* ≥10 ug/dL) (Albalak et al., 2003, Kaiser et al., 2001, Carpenter et al., 2019), with these results summarized in the Appendix and briefly discussed in the main text. Therefore, the focus of this manuscript is those children with elevated BLL as defined using the current CDC reference value (≥5 ug/dL). Crude odds ratios (ORs) were determined by calculating the exponential of the slope coefficient (β_i) (i.e., logit transformation).

Finally, adjusted ORs were determined using a multiple logistic regression model (eq. 1) that included significant factors (i.e., those with significant crude ORs, defined as $p<0.05$, using univariate logistic regression). Note that categories of variables with fewer than 5 observations (i.e., at or below ~1% of study population size) were excluded from discussions on statistical significance, including tabulation and reporting of odds ratios. Single-response questions/factors included all factor levels in the calculation of adjusted ORs, while multiple-response questions (i.e., those without a 'reference' level) included only the significant levels as model terms.

$$ln\left(\frac{\hat{p}}{(1-\hat{p})}\right) = b_0 + b_1X_1 + b_2X_2 + b_3X_3 + b_4X_4 + b_5X_5 + b_6X_6 + b_7X_7 + b_8X_8 + b_9X_9 \text{ (eq. 1)}$$

Where:

$\hat{p}$: expected probability that outcome is present (i.e., elevated BLL status at 5 μg/dL)

b_0: model intercept

b_1 through b_9: estimated regression coefficients for model terms defined below

X_1 through X_9: predictor variables (i.e., model terms), in order: (1) gender, (2) living within 400m of a railway, (3) living within 200m of a major roadway, (4) home flooring type, daily diet term of (5) beans, (6) vegetables, (7) rice, or (8) baby food, and (9) maternal occupation of laundry-person.

IRB Approval

The study was approved by the Ministry of Public Health General Secretariat of the Medicines Agency of Madagascar (#051-MSANP/SG/AGMED/CERBM) and the University of South Florida Institutional Review Board (IRB #000143) prior to field sampling.

Results

Study demographics

A total of 362 children aged 6 mo to 6 yr took part in the study. Mean (SD) age was 2.6 (1.7) yr; 50.3% were male and 49.7% female. Regarding household flooring, 68% of children lived in homes with cement, 21% wood, 9.1% tile, and 5.0% bamboo. For household fuel, 90% used charcoal, 17% used wood, 3.0% used induction (i.e., electric and requiring specialized cooking pot), and 1.9% used bottled propane (or liquified petroleum gas, LPG). Every home in this study used an aluminum pot to cook. There has been a ban on export of aluminum pots from Madagascar to Réunion Island since 2019 due to high lead content (ranging between 3-4,600 times the guideline) from the recycled metals used in production and repair of the pots (Imax Press Réunion, 2019); recycled aluminum pots are an established lead exposure route in the global south (Weidenhamer et al., 2017). Only one child (0.3%) lived in a home also using glazed ceramics to cook. Tables 1 and 2 present descriptive statistics and results of the Wilcoxon test for those risk factors identified by the survey (for single and open-ended responses, respectively).

Table 1
Descriptive statistics of environmental risk factors identified by survey (single response). Bold values are those identified as significant ($p<0.05$) by the Wilcoxon ranksum test.

Exposure Variable	*Category*	*n*[a]	*Geomean (µg/dL)*	*Geo SD (µg/dL)*	*p-value Wilcoxon*
Gender	Male	182	7.3	2.0	0.12
	Female	180	6.6	2.0	
BMI	>=85th percentile	53	6.1	2.2	0.16
	<85th percentile	296	7.2	2.0	
Does child have the habit of washing hands?	Yes	11	6.9	1.7	0.96
	No	350	6.9	2.0	
Do you live near the railway?	Within 400m	33	8.1	1.7	0.13
	Not Within 400m	164	6.7	2.0	
Do you live near a major road?	**Within 200m**	**29**	**8.7**	**1.8**	**0.05**
	Not Within 200m	**168**	**6.6**	**2.0**	
Are you breastfeeding?	Yes	152	6.6	2.1	0.36
	No	210	7.2	1.9	
Do you use the pitcher pump for drinking/cooking?	Water Only	10	8.1	2.2	0.70
	Neither	89	7.1	2.0	0.88
	Water and Food	211	7.0	1.9	0.46
	Food Only	44	6.2	2.3	0.27
What type of floor does your house have?	Wood	74	7.4	1.9	0.25
	Cement	237	7.1	2.0	0.52
	Bamboo	18	6.9	1.7	0.85
	Tile	**33**	**5.3**	**2.0**	**0.01**

[a]Note that sums of responses for a given factor may not equal the study sample size (n=362) due to either missing survey data, or for the geospatial analyses, lack of associated pump (and therefore location) information.

Table 2
Descriptive statistics of environmental risk factors identified by survey (open-ended response). Bold values are those identified as significant (p<0.05) by the Wilcoxon ranksum test.

Exposure Variable	*Category*	*n*	*Geomean (μg/dL)*	*Geo SD (μg/dL)*	*p-value Wilcoxon*
Where does the child spend most of their time?	Shop	7	10.8	2.4	0.09
	Family	**129**	**7.6**	**1.9**	**0.02**
	Outside	269	7.0	2.0	0.55
	School	128	7.0	2.0	0.93
	House	347	6.9	2.0	0.82
What does your child usually eat on a daily basis?	**Beans**	**40**	**9.3**	**1.7**	**0.00**
	Fruit	**104**	**7.8**	**2.1**	**0.01**
	Pasta	27	7.8	1.9	0.28
	Vegetables	**186**	**7.7**	**2.0**	**0.00**
	Meat/Fish	124	7.5	2.0	0.08
	Rice	**297**	**7.3**	**2.0**	**0.00**
	Bread	67	7.0	2.2	0.98
	Soup	17	6.4	2.4	0.38
	Dairy/Eggs	59	6.1	1.9	0.14
	Baby Food	**22**	**5.3**	**2.0**	**0.01**
What does your child usually drink on a daily basis?	Tap Water	108	7.4	2.2	0.41
	Tea	220	7.1	1.9	0.19
	Bottled Water	14	7.1	1.9	0.97
	Milk	9	6.4	2.2	0.64
	Pitcher Pump	11	6.0	1.9	0.29
	Boiled Water	19	5.7	2.4	0.23
Household fuel?	Charcoal	325	7.0	2.0	0.94
	Wood	63	6.1	1.9	0.20
	Induction	11	5.9	1.4	0.41
	Natural Gas	7	5.1	1.9	0.25
Have there been	Furniture/Sawmill	23	7.5	1.8	0.69

infrastructural changes in your home surroundings within last 6 months?	Smelter/Welding/Aluminum Pot	16	7.5	1.9	0.57
	Car/Posy/Moto/Bicycle Repair	21	5.8	2.1	0.28
	House Built	10	4.9	1.8	0.15
Father's occupation?	**Metal Seeker/Worker**	**8**	**15.5**	**2.1**	**0.00**
	Plumber/Pump Technician	**6**	**12.7**	**2.5**	**0.03**
	Gardener/Fertilizer/Farmer	7	10.0	2.3	0.28
	Gas Pump Attendant	5	7.3	2.0	0.88
	Tour Guide/Driver	56	7.2	2.0	0.68
	Port Worker/Fisherman	18	7.2	2.2	0.66
	Manager/Secretary/Accountant/Office	15	6.8	2.6	0.74
	Mechanic	13	6.8	2.3	0.67
	Police	42	6.8	2.1	0.77
	Painter	5	6.8	1.2	0.87
	Builder/Mason	32	6.5	2.0	0.62
	Seller	38	6.4	1.9	0.71
	Welder	11	6.4	1.8	0.65
	Teacher/Student	11	4.8	1.5	0.05
Father's job/hobby exposure routes	Valves/Fittings	23	8.6	2.1	0.13
	Furniture	43	8.3	2.2	0.09
	Welding/Smelting	51	7.1	1.9	0.93
	Fishing	15	7.0	2.0	0.88
	Electrical	42	6.5	2.1	0.55
	Building Houses	54	6.1	2.0	0.17
	Painting	56	6.0	2.0	0.06
	Radiators	19	5.9	1.8	0.21
	Mechanic	35	5.8	1.7	0.07
	Battery/Lead Recycling	**38**	**5.6**	**1.8**	**0.03**
	Chemicals	14	5.1	1.7	0.06
	Pipeline	**17**	**4.9**	**1.9**	**0.03**

Mother's occupation	**Laundry-person**	**21**	**9.8**	**1.7**	**0.01**
	Businessperson/Manager	79	7.3	2.0	0.46
	Housekeeper	191	6.7	2.1	0.31
	Dress/Matting Maker	6	6.6	1.4	0.77
	Chef/Baker	6	6.4	1.8	0.87
	Teacher/Student/University Worker	17	6.2	2.1	0.40
	Health Worker/Midwife/Caregiver	12	5.8	1.7	0.33
	Agent/Real Estate	6	3.8	2.1	0.06
Do you take herbal remedies?	Fruit	5	8.6	1.8	0.40
	Leaves	38	7.7	1.8	0.14
	Roots	105	6.9	1.9	0.64
	Bark	11	6.7	2.3	0.95
	Other	13	5.3	2.0	0.19

Blood lead levels in a global context

The geometric mean BLL (geo-SD) in our study was 6.9 (2.0) µg/dL. The median BLL was 7.1 µg/dL, exceeding that of both Sub-Saharan Africa LMICs (6.8 µg/dL, n=6 countries) and global LMICs (5.5 µg/dL, n=10 countries) for the same age range (≤6 yr; Table A1). Specific to Sub-Saharan LMICs, median and geomean values for the present study exceeded “pooled” mean values (i.e., those estimated to be representative of each country’s population, and typically approximating a geomean) for half of the countries with available data (i.e., 3 of 6, or the 50th percentile), and was lower than Cameroon (8.7 µg/dL), Democratic Republic of Congo (8.2 µg/dL), and Nigeria (7.7 µg/dL).

Compared to global LMICs, our data ranked higher than most, but lower than Pakistan (11.4 µg/dL) and Palestine (10.4 µg/dL). Median country-wise pooled means for other World Bank-defined regions were 10.4 (n=2) (Middle East & North Africa), 6.6 (n=4) (South Asia), 4.9 (n=2) (East Asia & Pacific), 3.3 (n=2) (Latin America & Caribbean), and 2.3 µg/dL (n=2) (Europe & Central Asia). Regarding income groups, low-income countries had the highest median BLL at the 0-6 yr age range (7.1 µg/dL, n=2), matching that of the present study for the same age group (7.1 µg/dL). Lower-middle and upper-middle income countries had lower median BLLs of 6.7 (n=7) and 3.6 µg/dL (n=7), respectively.

Environmental risk factors and elevated BLL status

Tables 3 and 4 report crude odds ratios using the dichotomous BLL status at ≥5 µg/dL. Responses with statistically significant ($p<0.05$) crude ORs related to elevated BLL status at ≥5 µg/dL were: male gender (OR: 1.57), living within 400m of a railway (OR: 2.80), living within 200m of a major roadway (OR: 3.25), having bamboo flooring (OR: 4.71), daily consumption of beans (OR: 6.58), vegetables (OR: 1.59), and rice (OR: 2.14), and maternal occupation of laundry-person (OR: 4.71). The only protective response identified (i.e., significant crude OR < 1.0) at the BLL status of ≥5 μg/dL was daily consumption of baby food (here, a fortified porridge distributed by a local NGO) (OR: 0.24).

Tables A2 and A3 of the Appendix report crude odds ratios using the dichotomous BLL status at 10 μg/dL. Responses with statistically significant ($p<0.05$) crude ORs related to elevated BLL status at ≥10 μg/dL included: living within 200m of a major roadway (OR: 2.30), daily consumption of fruit (OR: 1.64), meat/fish (OR: 1.63), or rice (OR: 2.71), paternal occupation of metal worker/seeker (OR: 8.42), and maternal occupation of laundry-person (OR: 3.16). Therefore, living within 200m of a major roadway, daily consumption of rice, and maternal occupation of laundry-person were the factors significantly associated with elevated BLL status at both ≥5 and ≥10 μg/dL. Differences in risk factors identified between the two BLL statuses occur due to variation in BLL distributions at said statuses.

Table 3
Summary of crude odds ratios (single response) at ≥5 μg/dL status. Bold values are those identified as significant (p<0.05) using univariate logistic regression.

Exposure Variable	*Category*	*≥ 5 μg/dL*	
		Crude OR (95% CI)	*p-value*
Gender	**Male**	**1.57 (1.01 - 2.46)**	**0.05**
	Female	1.00 (ref)	na
BMI	>=85th percentile	0.57 (0.31 - 1.05)	0.07
	<85th percentile	1.00 (ref)	na
Does child have the habit of washing hands?	Yes	0.47 (0.07 - 1.85)	0.33
	No	1.00 (ref)	na
Do you live near the railway?	**Within 400m**	**2.80 (1.11 - 8.58)**	**0.04**
	Not Within 400m	1.00 (ref)	na
Do you live near a major road?	**Within 200m**	**3.25 (1.20 - 11.4)**	**0.04**
	Not Within 200m	1.00 (ref)	na
Are you breastfeeding?	Yes	0.71 (0.45 - 1.10)	0.13
	No	1.00 (ref)	na
Do you use the pitcher pump for drinking/cooking?	Water Only	0.45 (0.12 - 1.72)	0.23
	Food Only	0.87 (0.41 - 1.87)	0.71
	Water and Food	1.01 (0.59 - 1.68)	0.98
	Neither	1.00 (ref)	na
What type of floor does your house have?	**Bamboo**	**4.71 (1.26 - 23.15)**	**0.03**
	Cement	2.06 (0.98 - 4.32)	0.05
	Wood	2.27 (0.97 - 5.32)	0.06
	Tile	1.00 (ref)	na

Table 4
Summary of crude odds ratios (open-ended response) at ≥5 μg/dL status. Bold values are those identified as significant ($p<0.05$) using univariate logistic regression.

Exposure Variable	*Category*	*≥ 5 μg/dL*	
		Crude OR (95% CI)	*p-value*
Where does the child spend most of their time?	Shop	2.84 (0.48 - 53.93)	0.34
	Family	1.33 (0.83 - 2.14)	0.24
	Outside	1.18 (0.71 - 1.93)	0.53
	School	1.04 (0.65 - 1.66)	0.88
	House	0.52 (0.12 - 1.69)	0.33
What does your child usually eat on a daily basis?	**Beans**	**6.58 (2.31 - 27.67)**	**0.00**
	Fruit	1.58 (0.96 - 2.67)	0.08
	Pasta	1.69 (0.70 - 4.71)	0.27
	Vegetables	**1.59 (1.02 - 2.50)**	**0.04**
	Meat/Fish	1.45 (0.90 - 2.36)	0.13
	Rice	**2.14 (1.23 - 3.70)**	**0.01**
	Bread	0.87 (0.50 - 1.54)	0.62

	Soup	0.65 (0.24 - 1.84)	0.40
	Dairy/Eggs	0.63 (0.35 - 1.12)	0.11
	Baby Food	**0.24 (0.09 - 0.58)**	**0.00**
What does your child usually drink on a daily basis?	Tap Water	1.23 (0.76 - 2.03)	0.41
	Tea	1.17 (0.74 - 1.83)	0.50
	Bottled Water	1.74 (0.53 - 7.80)	0.40
	Milk	0.57 (0.15 - 2.35)	0.41
	Pitcher Pump	0.55 (0.16 - 1.94)	0.33
	Boiled Water	0.50 (0.19 - 1.28)	0.14
Household fuel?	Charcoal	0.66 (0.29 - 1.41)	0.31
	Wood	1.10 (0.61 - 2.01)	0.76
	Induction	2.14 (0.54 - 14.16)	0.34
	Natural Gas	0.61 (0.13 - 3.16)	0.53
Have there been infrastructural changes in your home surroundings within last 6 months?	Furniture/Sawmill	1.34 (0.54 - 3.81)	0.55
	Smelter/Welding/Aluminum Pot	2.07 (0.65 - 9.18)	0.26

	Car/Posy/Moto/Bicycle Repair	0.74 (0.30 - 1.93)	0.52
	House Built	0.45 (0.12 - 1.66)	0.22
Father's occupation?	Metal Seeker/Worker	3.32 (0.58 - 62.53)	0.26
	Plumber/Pump Technician	2.36 (0.37 - 45.40)	0.44
	Gardener/Fertilizer/Farmer	2.84 (0.48 - 53.93)	0.34
	Gas Pump Attendant	0.69 (0.11 - 5.33)	0.69
	Tour Guide/Driver	0.98 (0.54 - 1.84)	0.95
	Port Worker/Fisherman	0.93 (0.35 - 2.72)	0.88
	Manager/Secretary/Accountant/Office	0.39 (0.13 - 1.11)	0.08
	Mechanic	0.53 (0.17 - 1.68)	0.26
	Police	0.92 (0.47 - 1.87)	0.82
	Painter	1.88 (0.27 - 36.93)	0.58
	Builder/Mason	1.03 (0.48 - 2.34)	0.95
	Seller	1.34 (0.65 – 3.00)	0.45
	Welder	0.55 (0.16 -	0.33

		1.94)	
	Teacher/Student	0.55 (0.16 - 1.94)	0.33
Father's job/hobby exposure routes	Valves/Fittings	1.34 (0.54 - 3.81)	0.55
	Furniture	1.41 (0.70 - 3.02)	0.36
	Welding/Smelting	0.68 (0.37 - 1.27)	0.22
	Fishing	0.93 (0.32 - 3.04)	0.89
	Electrical	0.82 (0.42 - 1.64)	0.56
	Building Houses	0.76 (0.42 - 1.40)	0.37
	Painting	0.74 (0.41 - 1.35)	0.32
	Radiators	0.50 (0.19 - 1.28)	0.14
	Mechanic	0.52 (0.25 - 1.06)	0.07
	Battery/Lead Recycling	0.54 (0.27 - 1.07)	0.07
	Chemicals	0.45 (0.15 - 1.34)	0.14
	Pipeline	0.39 (0.14 - 1.06)	0.06
Mother's occupation	**Laundry-person**	**4.71 (1.34 - 29.88)**	**0.04**
	Businessperson/Manager	1.17	0.57

		(0.69 - 2.05)	
	Housekeeper	0.72 (0.46 - 1.13)	0.15
	Dress/Matting Maker	2.36 (0.37 - 45.40)	0.44
	Chef/Baker	2.36 (0.37 - 45.40)	0.44
	Teacher/Student/University/Worker	0.65 (0.24 - 1.84)	0.40
	Health Worker/Midwife/Caregiver	0.64 (0.20 - 2.21)	0.46
	Agent/Real Estate	0.23 (0.03 - 1.18)	0.09
Do you take herbal remedies?	Fruit	0.64 (0.10 - 5.02)	0.64
	Leaves	2.30 (0.98 - 6.08)	0.07
	Roots	0.75 (0.35 - 1.54)	0.44
	Bark	0.75 (0.21 - 2.97)	0.66
	Other	0.67 (0.21 - 2.34)	0.51

Table 5
Summary of adjusted odds ratios for exposure variables (factors) included in model with elevated BLL status at ≥5 μg/dL.

Exposure Variable	*Category*	*≥ 5 μg/dL*	
		Adjusted OR (95% CI)	*p-value*
Gender	Male	1.26 (0.66 - 2.44)	0.48
	Female	1.00 (ref)	na
Do you live near the railway?	Yes	1.98 (0.75 - 5.82)	0.19
	No	1.00 (ref)	na
Do you live near a major road?	Yes	1.74 (0.63 - 5.27)	0.30
	No	1.00 (ref)	na
What type of floor does your house have?	Bamboo	6.66 (0.76 - 152.51)	0.13
	Cement	1.60 (0.60 - 4.27)	0.34
	Wood	1.76 (0.49 - 6.51)	0.39
	Tile	1.00 (ref)	na
What does your child usually eat on a daily basis?	Beans	4.62 (0.76 - 90.06)	0.17
	Vegetables	**2.66 (1.41 - 5.13)**	**0.00**
	Rice	1.59 (0.70 - 3.63)	0.27
	Baby Food	0.41 (0.07 - 2.12)	0.29
Mother's occupation	Laundry-person	[a]	0.99

[a]Calculation of odds ratio not possible due to low sample size and high variability in data.

Table 5 summarizes adjusted ORs as estimated by the multiple logistic regression analysis, controlling for gender, living near either the railway or a major roadway, home flooring type, daily diet terms, and maternal occupation. The only factor identified as having a significant adjusted OR at the ≥5 μg/dL threshold was daily consumption of vegetables (OR: 2.66). Table A4 reports adjusted ORs at the ≥10 μg/dL threshold and using the model described by eq. A1 (section A3 of the Appendix). Four factors were identified as having significant adjusted ORs at the ≥10 μg/dL status: living near a major roadway (OR: 4.06), daily consumption of meat/fish (OR: 2.25), paternal occupation of metal seeker/worker (OR: 24.74) and maternal occupation of laundry-person (OR: 11.39). Note that the relatively high adjusted ORs as related to occupational terms were also associated with large confidence intervals about the point estimates, owing in part to limited sample size and high variability of BLL data associated with those factors.

Discussion

Observed BLLs in the present study are slightly higher than those of other 'non-exposed' children in Sub-Saharan LMICs, and generally higher than global LMICs and LMICs in other regions. Our BLL data agree closely with literature data for similar non-exposed/background childhood (0-6 yr) populations in low-income countries, and are higher than those groups in more wealthy nations. Therefore, the population studied here may be considered to be representative of that in other urbanizing, low-income areas, especially in Sub-Saharan Africa (e.g., median and geomean data from the present study lie in the 50th percentile of pooled mean data for Sub-Saharan Africa as compiled by Ericson et al. 2021).

Several risk factors were identified by the survey and significantly related to elevated BLL status using crude ORs (here with discussion focusing on ≥5 μg/dL unless otherwise noted). Male gender (OR: 1.57) was associated with elevated BLLs as previously observed (Filigrana and Mendez, 2012, Morales et al., 2005), owing potentially to distinct behavior patterns that increase exposure (e.g., playing outside more often, pica/geophagy). Living near a railway (OR: 2.80) or major roadway (OR: 3.25) was significantly associated with risk of elevated BLL status; proximity to major roadway was also significantly associated at the 10 μg/dL threshold (OR: 2.30). Despite a country-wide phaseout of leaded gasoline beginning around 2005, it is plausible that stocks of leaded fuel may still be in use, or that marine-grade fuels contribute to this potential exposure source (Lin and Lin, 2006). Also, this more recent phase-out of leaded fuel, and an estimated ~15 year half-life of lead in soil (Mielke et al., 2019), suggests that lead contamination of soil is a likely on-going source of exposure as observed in other LMICs (Pan et al., 2018, Shabanda et al., 2019). Additionally, the use of low-grade, so-called "Africa-quality" fuels in poorly-maintained vehicles and machinery, often lacking pollution control devices, is common in Madagascar (Global Alliance on Health and Pollution, 2018). Children are especially prone to lead exposure from contaminated soil given their propensity for hand-to-mouth activities. Presence of bamboo flooring (OR: 4.71), as opposed to tile, a metric previously used to identify homes with higher SES (Arias and De Vos, 1996), was identified as a significant factor for elevated BLL status. Less expensive flooring (e.g., bamboo here) has been previously related to higher BLLs in Indonesian children (Albalak et al., 2003).

Daily consumption of beans was significantly associated with elevated BLL (OR: 6.58), owing potentially to the ubiquitous use of aluminum pots in this community. The extended cooking time required for this staple compared to foods requiring different preparation (e.g., grilled foods) may result in leaching of lead into solution, especially in acidic solution (e.g., with vinegar) (Weidenhamer et al., 2017); fresh beans (*vs.* dried) require reduced cooking times, but are more expensive, and so lower SES may in part drive exposure through this route. Rice was significantly associated with elevated BLL (OR: 2.14), potentially for this same reason; rice was also significantly associated at the ≥10 μg/dL threshold (OR: 2.71). Lead sorbs to starches such as rice (Sharma et al., 2021), and as the concentration of lead in water increases, the contribution of overall lead exposure owing to consumption of starches increases (Akers et al., 2019). Anecdotally, it is common for there to be a grey/silver residue observed on top of the cooked rice, potentially from the cooking vessel, or from hardness of the water. Export of these cooking pots have been banned from Madagascar to Réunion Island owing to analyses confirming high lead content.

Consumption of vegetables was also significantly associated with elevated BLL status (OR: 1.59). Unwashed vegetables may serve as an ingestion source for lead, especially if sold near highly-trafficked areas where lead-contaminated soil and dust may serve as exposure routes, as previously observed in Tanzania (Magoha et al., 2008); vendors in this community typically reside near major roadways. Legacy lead contamination of soil here is plausible as the half-life of lead in soil is on the order of ~15 years (Mielke et al., 2019). Additionally, vegetables may be cooked in a similar manner to beans and rice, therefore likely resulting in lead leaching into the cooked product. Additional diet terms identified as significant at the ≥10 μg/dL threshold included fruit (OR: 1.64) and meat/fish (OR: 1.63). If unwashed, fruit may serve as a similar exposure route as vegetables. Aforementioned results of the geospatial analyses (e.g., distances from railways and major roadways) support the importance of legacy soil contamination from leaded fuel use. Interestingly, consumption of baby food was a protective factor against elevated BLL status (OR: 0.24). Baby food (here, a fortified porridge) is used to supplement breastfeeding for malnourished infants in this community. Additionally, breastfeeding can be a key lead exposure route for infants in LMICs (Lozoff et al., 2009) due to mobilization of bone-stored lead in nursing mothers (Téllez-Rojo et al., 2002); however our survey data included a question specific to breastfeeding, and found no relationship to elevated BLLs.

Regarding potential occupational or 'take-home' exposures (i.e., those associated with occupational exposures but affecting a home environment, an important contributor to lead exposures in LMICs) (Williams et al., 2021), the maternal occupation of laundry-person was significantly related to elevated BLL status (OR: 4.71); the same association was observed at the ≥10 μg/dL threshold as well. This finding may be related to the typically lower SES of this occupation, or potentially to exposures owing to use of local river water for washing; these rivers (e.g., the Pangalan) may contain mining tailing from nearby cobalt-nickel operations. Additionally, the paternal occupation of metal/seeker (i.e., either someone who finds scrap metal at disposal/construction sites, or who works with metal soldering) was significantly related to elevated BLL status at ≥10 μg/dL (OR: 8.42), owing potentially to exposures to co-produced/recycled materials/metals containing lead (Obeng-Gyasi, 2019, UNICEF and Pure Earth, 2020).

In terms of adjusted ORs (Table 5), only the diet consumption of vegetables (OR: 2.66) was associated with elevated BLL at the ≥5 μg/dL threshold. This finding further supports the hypotheses of cooking vessels (i.e., aluminum pots in this community), and contamination of foods sold by roadside vendors owing to legacy soil contamination by leaded fuel use. At the ≥10 μg/dL threshold (Table A4), living near a major roadway (OR: 4.06), daily consumption of meat/fish (OR: 2.25), paternal occupation of metal seeker/worker (OR: 24.74), and maternal occupation of laundry-person (OR: 11.39) were associated with elevated BLL. The risk associated with living near a major roadway aligns with legacy soil contamination. The relationship between elevated BLL and the diet term associated with meat/fish is unclear, though previous work has associated higher BLLs with frequent consumption of fish (Birgisdottir et al., 2013). Finally, the occupational terms of metal seeker/worker and laundry-person may be related to direct exposures and overall lower SES, respectively.

Strengths of the present study include novel measurement of BLLs in Madagascar, one of the world's least developed nations, as well as use of established statistical approached to relate BLL data to results of an environmental risk factor survey. Additionally, comparison against recently compiled and published global BLL data allowed for an understanding of BLLs in the target community in the context of other Sub-Saharan African and low-income nations. Limitations of the study included relatively limited sample size, and use of a point-of-care *vs.* reference-grade instrument. Future work with larger sample sizes may also explore interaction terms (e.g., in terms of daily diet combinations).

In summary, more than two-thirds (68%) of the children in our study were at or above the CDC threshold of 5 μg/dL, higher than the 49% estimated by Ericson and colleagues for children in LMICs with published BLL data. More than one-quarter (27%) were above 10 μg/dL, compared to 32% as estimated by Ericson and colleagues. In addition to the lead-containing hand pumps in the community, there likely exist multiple exposure routes including air, soil, food, and those associated with parental occupations and infrastructure near the home. Air quality data are limited in the country, but sampling in Antananarivo in 2007-2008 (the capital city, located 350 km west of Toamasina) determined lead concentrations in $PM_{2.5}$ to be well below the WHO guideline (0.5 $\mu g/m^3$) following the phase-out of leaded gasoline (Rasoazanany et al., 2012); therefore exposures to lead in the air may be minimal unless there is a source not accounted for in Toamasina (a port-city, and location of a mine tailing storage site).

However, legacy use of leaded fuel in the country likely results in continuous daily exposures via contaminated dust and soil (with relatively long lead contamination half-life), as confirmed by our geospatial analyses. The practice of pica and geophagy observed in some Sub-Saharan African communities, and especially among children (girls in particular), may contribute to elevated lead exposures in these younger populations (Msoffe et al., 2019, Nchito et al., 2004). Regarding ingestion however, the use of recycled aluminum pots for cooking is a likely contributor to lead exposure in this community, where staple foods requiring extended cooking times (e.g., rice) are common (82% of respondents consume rice daily); previous modeling efforts by our team have highlighted the importance of rice consumption in Madagascar as a potential lead exposure route (especially at elevated pump water lead levels) (Akers et al., 2019), and additional work should be conducted to assess contributions of the dietary exposure route in this community.

Finally, nearly half (47%) of Madagascar's children suffer from chronic malnutrition (US AID, 2018), and more than one-third of adults are anemic. Iron deficiency has been extensively linked to elevated BLLs (Kwong et al., 2004), owing to similar biological pathways of iron and lead. Therefore, nutritional interventions may serve as secondary prevention in this community. However, sources of lead linked to exposed children must be the priority of any intervention here. Proposed lead exposure interventions must occur over extended time periods and involve multiple sectors/approaches (e.g., regulatory, environmental, educational) (Pfadenhauer et al., 2014).

Declarations

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Competing Interests

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

Author Contributions (CRediT)

Wyatt M. Champion: Writing – Original Draft, Writing – Review & Editing, Data Curation, Formal Analysis, Validation, Software, Methodology **Adaline M. Buerck:** Writing – Review & Editing, Project Administration, Validation **Christopher Nenninger:** Writing – Review & Editing, Formal Analysis, Methodology **Korede Yusuf:** Writing – Original Draft, Writing – Review & Editing, Supervision, Data Curation, Formal Analysis, Validation, Methodology, Conceptualization **Luke J.P. Barrett:** Funding Acquisition, Project Administration, Supervision, Data Curation, Resources, Investigation, Validation, Conceptualization **Lova Rakototarisoa:** Funding Acquisition, Project Administration, Supervision, Data Curation, Investigation, Validation **Rinah Rakotondrazaka:** Project Administration, Data Curation, Investigation, Validation **Katherine Alfredo:** Writing – Review & Editing, Conceptualization **Jeffrey Cunningham:** Funding Acquisition, Writing – Review & Editing, Conceptualization **Mahmooda Khaliq:** Writing – Original Draft, Writing – Review & Editing, Funding Acquisition, Project Administration, Supervision, Methodology, Conceptualization **James R. Mihelcic:** Writing – Original Draft, Writing – Review & Editing, Funding Acquisition, Project Administration, Supervision, Methodology, Conceptualization

Ethical Approval

The study was approved by the Ministry of Public Health General Secretariat of the Medicines Agency of Madagascar (#051-MSANP/SG/AGMED/CERBM) and the University of South Florida Institutional Review Board (IRB #000143) prior to field sampling.

Consent to Participate

Informed consent was obtained from all individual participants included in the study.

Consent to Publish

Not applicable.

Availability of Data and Materials

The datasets generated during and/or analysed during the current study are available from the corresponding author on reasonable request.

References

1. AGENCY FOR TOXIC SUBSTANCES AND DISEASE REGISTRY (2020)Toxicological Profile for Lead
2. AKERS DB, BUERCK A, MACCARTHY MF, MIHELCIC JR (2019) Estimates of Blood Lead Levels (BLLs) for Children in Coastal Madagascar: Accounting for Dietary Uptake of Lead (Pb). Exposure and Health 12:501–511
3. AKERS DB, MACCARTHY MF, ANNIS CUNNINGHAMJA, MIHELCIC JR (2015) Lead (Pb) contamination of self-supply groundwater systems in coastal Madagascar and predictions of blood lead levels in exposed children. Environ Sci Technol 49:2685–2693
4. ALBALAK R, NOONAN G, BUCHANAN S, FLANDERS WD, GOTWAY-CRAWFORD C, KIM D, SULAIMAN JONESRL, BLUMENTHAL R, TAN R (2003) Blood lead levels and risk factors for lead poisoning among children in Jakarta, Indonesia. Sci Total Environ 301:75–85
5. AMIN CHOWDHURY KI, KABIR NURUNNAHARS, ISLAM ML, BAKER MT, ISLAM M, SIKDER MSRAHMANMHASANMA, NASH AKWONGLHBINKHORSTGK, MCCARTOR EKEITHJ, FORSYTH JE (2021) Child lead exposure near abandoned lead acid battery recycling sites in a residential community in Bangladesh: risk factors and the impact of soil remediation on blood lead levels.*Environ Res*,110689
6. ARIAS E, DE VOS S (1996) Using housing items to indicate socioeconomic status - Latin America.*Social Indicators Research*,38
7. BIRGISDOTTIR BE, KNUTSEN HK, HAUGEN M, GJELSTAD IM, JENSSEN MT, THOMASSEN ELLINGSENDG, MELTZER YALEXANDERJ, BRANTSAETER AL (2013) Essential and toxic element concentrations in blood and urine and their associations with diet: results from a Norwegian population study including high-consumers of seafood and game. Sci Total Environ 463–464:836–844
8. BUERCK AM, USOWICZ M, KHALIQ CUNNINGHAMJA, BARRETT M, ROAKOTOARISOA LJP, ROKOTONDRAZAKA L, SOMMARIVA R, MIHELCIC JR (2021) Health and Economic Consequences of Lead Exposure Associated with Products and Services Provided by the Informal Economy. Environ Sci Technol 55:8362–8370
9. CARPENTER C, POTTS B, BONNELL VONOETTINGENJ, SAINVIL R, JEAN-BAPTISTE MLORGEATVMASCARYMCSHEX, PALFREY J 2019. Elevated Blood Lead Levels in Infants and Children in Haiti, 2015.*Public Health Rep*, 134,47–56
10. DESAI G, ANZMAN-FRASCA S, RAVENSCROFT VERNARELLIJA, YANG J, BURSTEIN J, KORDAS K (2020) Examining Links Between Diet and Lead Exposure in Young Children: 2009 to 2014 National Health and Nutrition Examination Survey. *Acad Pediatr*

11. DOOYEMA CA, LO NERIA, DURANT YC, DARGAN J, SWARTHOUT PI, HALADU TBIYAOGIDADOSO, SANI-GWARZO S, AKPAN NNGUKUPM, BROWN MJ (2012) Outbreak of fatal childhood lead poisoning related to artisanal gold mining in northwestern Nigeria, 2010. Environ Health Perspect 120:601–607
12. ERICSON B, NASH HUH, FERRARO E, SINITSKY G, TAYLOR MP (2021) Blood lead levels in low-income and middle-income countries: a systematic review. The Lancet Planetary Health 5:e145–e153
13. FILIGRANA PA, MENDEZ F (2012) Blood lead levels in schoolchildren living near an industrial zone in Cali, Colombia: the role of socioeconomic condition. Biol Trace Elem Res 149:299–306
14. GLOBAL ALLIANCE ON HEALTH AND POLLUTION (2018)Madagascar Health and Pollution Action Plan
15. HAEFLIGER P, MATHIEU-NOLF M, NDIAYE LOCICIROS, COLY C, SOW MDIOUFAFAYEAL, PRONCZUK ATEMPOWSKIJ, FILIPE J, JUNIOR AP, NEIRA M (2009) Mass lead intoxication from informal used lead-acid battery recycling in dakar, senegal. Environ Health Perspect 117:1535–1540
16. IMAX PRESS RÉUNION (2019) *Les marmites malgaches interdites à La Réunion* [Online]. Réunion. Available: https://www.ipreunion.com/actualites-reunion/reportage/2019/09/25/des-tau-de-plomb-tres-eleves-les-ustensiles-de-cuisine-en-aluminium-malgaches-interdits-a-la-reunion,108396.html [Accessed]
17. INSTAT (2009) Pyramide Tamatave. Institut National de la Statistique, Tananarive, Madagascar
18. JIAN-HUA M, CHUN-JIE C, JIAN L, BO S (2009) Heavy metal pollution in soils on railroad side of Zhengzhou-Putian section of Longxi-Haizhou railroad, China. Pedosphere 19:121–128
19. KADAM P, BHALERAO S (2010) Sample size calculation. International journal of Ayurveda research 1:55
20. KAISER R, DALEY HENDERSONAK, NAUGHTON WR, RAHMAN MKHANMH, RUBIN CH (2001) Blood lead levels of primary school children in Dhaka, Bangladesh. *Environmental Health Perspectives*, 109, 563-566
21. KORDAS K (2017) The "Lead Diet": Can Dietary Approaches Prevent or Treat Lead Exposure? J Pediatr 185:224–231e1
22. KWONG WT, FRIELLO P, SEMBA RD (2004) Interactions between iron deficiency and lead poisoning: epidemiology and pathogenesis. Sci Total Environ 330:21–37
23. LIN B, LIN C-Y (2006) Compliance with international emission regulations: Reducing the air pollution from merchant vessels. Marine Policy 30:220–225
24. LOZOFF B, JIMENEZ E, ANGELILLI WOLFAW, KACIROTI MLZATAKIAJJACOBSONSW, TAO NCLARKKM, WALTER MCASTILLOM, PINO P (2009) Higher Infant Blood Lead Levels with Longer Duration of Breastfeeding.*The Journal of Pediatrics*, 155
25. MACCARTHY MF, MIHELCIC JR (2013) Unsubsidised Self-Supply in Eastern Madagascar. Water Alternatives 6:424–438

26. MAGELLAN DIAGNOSTICS 2021. Lead Care II Test Kit Insert
27. MAGOHA HS, MAKOKHA AO, NAKAJUGO MGHWENOLR, WEKESA JM (2008) Lead pollution in the environment and contamination in food around Mwanza, Tanzania. Journal of Applied Biosciences 9:396–402
28. MAHAFFEY KR (1995) Nutrition and Lead: Strategies for Public Health. Environmental Health Perspectives
29. MAXWELL CM, NELSON DW (1978) A Lead Emission Factor for Reentrained Dust from a Paved Roadway. Environmental Protection Agency, Office of Air and Waste Management, Office …
30. MIELKE HW, GONZALES CR, LAIDLAW POWELLET, BERRY MAS (2019) K. J., MIELKE, P. W., JR. & EGENDORF, S. P. The concurrent decline of soil lead and children's blood lead in New Orleans. *Proc Natl Acad Sci U S A*, 116, 22058-22064
31. MORALES LS, GUTIERREZ P, ESCARCE JJ (2005) Demographic and Socioeconomic Factors Associated with Blood Lead Levels Among Mexican-American Children and Adolescents in the United States.*Public Health Reports*,120
32. MSOFFE CU, JAHANPOUR NYANZAECTHOMASDSK, DEWEY D (2019) The sources and chemical content of edible soil sticks sold in markets in Tanzania: a cross-sectional analytical study. Environ Geochem Health 41:893–906
33. NATIONAL INSTITUTE OF STANDARDS AND TECHNOLOGY (2012) *NIST/SEMATECH e-Handbook of Statistical Methods, 3.3.3.3 Selecting Sample Sizes* [Online]. Available: https://www.itl.nist.gov/div898/handbook/ppc/section3/ppc333.htm [Accessed]
34. NCHITO M, WENZEL GEISSLER P, MUBILA L, FRIIS H, OLSEN A (2004) Effects of iron and multimicronutrient supplementation on geophagy: a two-by-two factorial study among Zambian schoolchildren in Lusaka. Trans R Soc Trop Med Hyg 98:218–227
35. NERI AJ, PAN ROYJJARRETTJ, DOOYEMA Y, UMAR-TSAFE CCALDWELLK, OLUBIYO NT, BROWN MJ (2014) Analysis of a novel field dilution method for testing samples that exceed the analytic range of point-of-care blood lead analyzers. Int J Environ Health Res 24:418–428
36. OBENG-GYASI E (2019) Sources of lead exposure in various countries. Rev Environ Health 34:25–34
37. PAN L, WANG Y, MA J, SU HUY, WANG BFANGG, XIANG B (2018) A review of heavy metal pollution levels and health risk assessment of urban soils in Chinese cities. Environ Sci Pollut Res Int 25:1055–1069
38. PFADENHAUER LM, ROHWER BURNSJ, REHFUESS EA (2014) A protocol for a systematic review of the effectiveness of interventions to reduce exposure to lead through consumer products and drinking water. Syst Rev 3:36
39. R CORE TEAM 2020. R: A Language and Environment for Statistical Computing.R Foundation for Statistical Computing
40. RASOAZANANY EO, ANDRIAMBOLOLONA ANDRIAMAHENINANNRAVOSONHN, RAMAHERISON RRANDRIAMANIVOLV, AHMED H, HARINOELY M (2012) Air pollution studies in terms of PM2.5,

PM2.5-10, PM10, lead and black carbon in urban areas of Antananarivo - Madagascar. *arXiv preprint*, 1204.1498

41. SHABANDA IS, KOKI IB, ZAIN LOWKH, KHOR SM, ABU BAKAR, N. K (2019) Daily exposure to toxic metals through urban road dust from industrial, commercial, heavy traffic, and residential areas in Petaling Jaya, Malaysia: a health risk assessment. Environ Sci Pollut Res Int 26:37193–37211
42. SHARMA S, KAUR I, NAGPAL AK (2021) Contamination of rice crop with potentially toxic elements and associated human health risks-a review. Environ Sci Pollut Res Int 28:12282–12299
43. SMITH WH (1976) Lead contamination of the roadside ecosystem. Journal of the Air Pollution Control Association 26:753–766
44. STOJIC N, STOJIC G (2017) Railway transportation as a source of soil pollution. Transportation Research Part D: Transport and Environment 57:124–129
45. STREET RA, NAIDOO GOESSLERW, SHEZI S, REDDY BCELENRIEGERJETTINGERK, MATHEE A (2020) Exposure to lead and other toxic metals from informal foundries producing cookware from scrap metal. Environ Res 191:109860
46. SUN X, LI X, LIU D, YANG T, ZHAO Y, WU T, CAI Y, ZHANG AIY, YANG XWANGJ, YU R, MIELKE HW (2018) Use of a Survey to Assess the Environmental Exposure and Family Perception to Lead in Children (<6 Years) in Four Valley Cities, Northwestern China.*Int J Environ Res Public Health*, 15
47. TÉLLEZ-ROJO MM, HERNÁNDEZ-AVILA M, GONZÁLEZ-COSSÍO T, ARO ROMIEUI, PALAZUELOS A, SCHWARTZ E, HU H (2002) Impact of Breastfeeding on the Mobilization of Lead from Bone. Am J Epidemiol 155:420–428
48. U.S, CENTERS FOR DISEASE CONTROL, AND PREVENTION (2020a). *Childhood Lead Poisoning Prevention: Blood Lead Reference Value* [Online]. Available: https://www.cdc.gov/nceh/lead/data/blood-lead-reference-value.htm [Accessed March 16 2021]
49. U.S, CENTERS FOR DISEASE CONTROL, AND PREVENTION (2020b). *Health Effects of Lead Exposure* [Online]. Available: https://www.cdc.gov/nceh/lead/prevention/health-effects.htm [Accessed]
50. UNICEF (2017) Madagascar Nutrition Investment Case
51. UNICEF & PURE EARTH (2020) The Toxic Truth: Children’s Exposure to Lead Pollution Undermines a Generation of Future Potential. 2nd ed. New York, NY
52. US AID (2018) Madagascar Nutrition Profile
53. WAGNER AK, LECATES GRAVESAJREISSSK, ZHANG R, ROSS-DEGNAN D (2011) Access to care and medicines, burden of health care expenditures, and risk protection: results from the World Health Survey. Health Policy 100:151–158
54. WEATHER UNDERGROUND (2021) *Toamasina, Atsinanana, Madagascar Weather History* [Online]. Available: https://www.wunderground.com/history/monthly/mg/toamasina/FMMT [Accessed May 19 2021]
55. WEIDENHAMER JD, FITZPATRICK MP, BIRO AM, HUDSON KOBUNSKIPA, GOTTESFELD P (2017) Metal exposures from aluminum cookware: An unrecognized public health risk in developing

countries. Sci Total Environ 579:805–813

56. WILLIAMS PRD, STACKELBERG VON, GUERRA K, LOPEZ MG, SANCHEZ-TRIANA E (2021) Risk Analysis Approaches to Evaluating Health Impacts from Land-Based Pollution in Low- and Middle-Income Countries. *Risk Analysis*
57. WORLD BANK (2021a) *GDP, PPP (current international $)* [Online]. Available: https://data.worldbank.org/indicator/NY.GDP.MKTP.PP.CD [Accessed 3/22 2021]
58. WORLD BANK (2021b) *World Bank Country and Lending Groups* [Online]. Available: https://datahelpdesk.worldbank.org/knowledgebase/articles/906519-world-bank-country-and-lending-groups [Accessed]
59. WORLD HEALTH ORGANIZATION (2010)Childhood lead poisoning
60. WORLD HEALTH ORGANIZATION (2019) *Lead poisoning and health* [Online]. Available: https://www.who.int/news-room/fact-sheets/detail/lead-poisoning-and-health [Accessed]

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- MadagascarBLLAppendix.pdf