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1 **Current Trends of Blood Lead Levels, Distribution Patterns and Exposure Variations among**
2 **Household Members in Kabwe, Zambia**

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26

27 **Abstract**

28 Childhood lead (Pb) poisoning has devastating effects on neurodevelopment and can cause overt
29 clinical signs including convulsions and coma. Health effects including hypertension and various
30 reproductive problems have been reported in adults. Historical Pb mining in Zambia's Kabwe town
31 left a legacy of environmental pollution and childhood Pb poisoning. However, the previous
32 knowledge on Pb poisoning in Kabwe is limited to the close neighbourhood of the mine and
33 exposure patterns among household members are not known. The current study aimed at establishing
34 the extent of Pb poisoning and exposure differences among family members in Kabwe as well as
35 determining populations at risk and identify children eligible for chelation therapy. Blood samples
36 were collected in July and August 2017 from 1,190 household members and Pb was measured using
37 a portable LeadCare© II analyser. Participants included 291 younger children (3 months to 3 years
38 old), 271 older children (4 - 9 years old), 412 mothers and 216 fathers from 13 townships with
39 diverse levels of Pb contamination. The Blood Lead Levels (BLL) ranged from 1.65 to 162 µg/dL,
40 with residents from Kasanda Township (mean BLL of 45.7 µg/dL) recording the highest BLL while
41 Hamududu residents recorded the lowest (mean BLL of 3.3 µg/dL). Of the total number of children
42 sampled (n = 562), 23 % exceeded the 45 µg/dL, the threshold required for chelation therapy. A few
43 children (total of 5) exceeded the 100 µg/dL whereas none of the parents exceeded the 100 µg/dL
44 value. Children had higher BLL than parents, with peak BLL recorded at the age of 2 years old. Lead
45 exposure differences in Kabwe were attributed to distance and direction from the mine, with younger
46 children at highest risk. Exposure levels in parents were equally alarming. For prompt diagnosis and
47 treatment, a portable point-of-care device such as a LeadCare II analyser would be preferable in
48 Kabwe.

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50 **KEY WORDS:** Childhood lead poisoning; LeadCare II analyser; Pb exposure differences, Kabwe

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61 **1. Introduction**

62 Lead (Pb) poisoning accounts for about 0.6 % of the global burden of disease (WHO 2010),
63 posing a serious public health concern worldwide. While acute toxicity is related to occupational
64 exposure and is quite uncommon, low level chronic toxicity due to environmental pollution is much
65 more common (ATSDR, 2017). Lead poisoning has devastating effects on neurodevelopment such as
66 mental retardation and lowering of intelligence quotient (IQ) in children, which may further result in
67 poor school performance, lower tertiary education attainment, behavioural disorders and poor
68 lifetime earnings (WHO, 2018; Dapul and Laraque, 2014; Miranda et al., 2007; Canfield et al., 2003;
69 Lidsky and Schneider, 2003;). If not treated, Pb poisoning is characterized by persistent vomiting,
70 anaemia, encephalopathy, lethargy, delirium, convulsions, coma and death (WHO, 2018; Flora et al.,
71 2012; Pearce, 2007). The Institute for Health Metrics and Evaluation (IHME, 2017) estimated that in
72 2016 Pb exposure accounted for 540,000 deaths worldwide. In chronically exposed adults,
73 significant health effects including renal dysfunction, hypertension and various reproductive
74 problems have been shown even at low Pb exposures (Kumar 2018; Wani et al., 2015). Cases of
75 reduced fertility following chronic exposure have been reported in males (Benoff et al., 2003;
76 Telisman et al., 2000; Benoff et al. 2000) as well as miscarriages in pregnant women (Wani et al.,
77 2015). Moreover, childhood Pb exposure poses significant economic losses in affected countries,
78 especially in low- and middle-income countries (Attina and Trasande, 2013).

79 Clinical presentations of Pb poisoning vary widely depending upon the age, the amount and the
80 duration of exposure, with some individuals seeming well at a blood lead levels (BLLs) that in others
81 results in overt clinical signs (Bellinger 2004). Given that detrimental effects of chronic Pb exposure
82 are usually subclinical (Yabe et al., 2015; Yabe et al., 2018), it may result in a delay in the
83 appropriate diagnosis and chelation therapy, which has been recommended to be initiated at levels \geq
84 45 $\mu\text{g/dL}$ (CDC 2002; Needleman 2004). Early diagnosis and chelation therapy are crucial as it has

85 been reported that high BLLs exceeding 100 µg/dL in children can cause encephalopathy,
86 convulsions, coma and death (CDC 2002). Therefore, measurement of BLLs plays a pivotal role in
87 the diagnosis and management of patients (Lowry, 2010), as described in Pb poisoned children in
88 Nigeria (Thurtle et al., 2014). Traditionally, BLLs have been measured using atomic absorption
89 spectrophotometer (AAS), inductively coupled plasma mass spectrometry (ICP-MS), etc. Although
90 highly sensitive to Pb measurement, these equipment are laboratory-based and require trained
91 laboratory technologists. Moreover, they are expensive and would be time-consuming to ship
92 samples to appropriate laboratories.

93 In a set-up like Kabwe town in Zambia, where historical Pb mining has resulted in alarming Pb
94 poisoning, especially in children from townships in the vicinity of the closed mine and its tailing
95 wastes (Yabe et al., 2018; Bose-O'Reilly et al., 2018; Yabe et al., 2015), prompt diagnosis and
96 immediate chelation therapy would be required. Therefore, a portable point-of-care device such as a
97 LeadCare II analyser, which can be used on-site in remote medical facilities like Kabwe would be
98 appropriate and preferable. Given that BLL results are read within 3 minutes, Pb poisoning would be
99 diagnosed and chelation therapy initiated promptly. Therefore, the current study investigated trends
100 of BLL using a LeadCare II Analyser in Kabwe to identify children that required medical
101 management to minimize the toxic effects of Pb. In addition, factors influencing Pb exposure in
102 Kabwe were analysed and exposure patterns among household members including fathers, mothers
103 and children were evaluated.

104

105 2. Materials and methods

106 2.1 Sampling sites

107 Kabwe town, with a population of about 230, 000 inhabitants and area size of 1, 547 km², is the
108 fourth largest town in Zambia. It is the provincial capital of Zambia's Central Province and is located

109 at about 28°26'E and 14°27'S. Kabwe has a long history of open-pit Pb-Zn mining, from 1902 to
110 1994. As observed by the Blacksmith Institute (2013), despite closure of the mine, scavenging of
111 metal scraps from the abandoned tailings and wastes stored on the mine has continued to serve as a
112 source of metal pollution, especially dusts emanating from the mine dumps (Fig. 1).



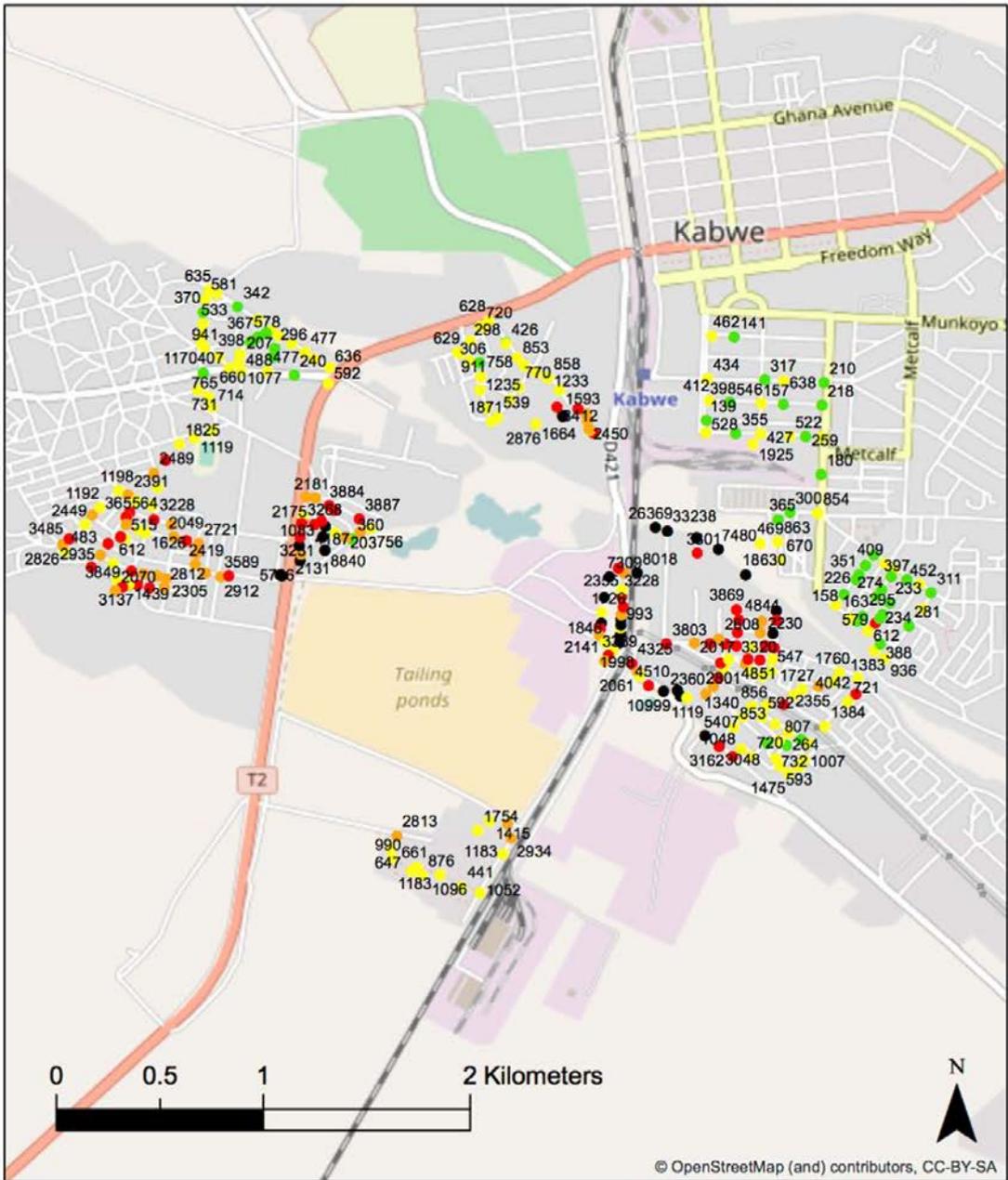
113

114 Fig. 1.

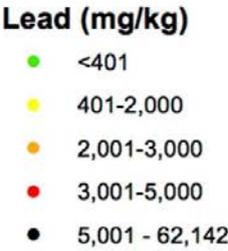
115 Figure showing men scavenging for scrape metals at the Kabwe Pb-Zn mine tailings (left) and
116 houses located within 500 m to the tailings (right).

117

118 Moreover, some households were within 500 m of the tailings. As shown in Fig. 2, soils in
119 townships in the vicinity of the mine and homes downwind from the tailings were highly polluted
120 with Pb exceeding acceptable levels for residential areas (Bose-O'Reilly et al., 2018). In the current
121 study, blood samples were collected from family members including fathers, mothers and children at
122 health centres around the town of Kabwe, in July and August of 2017. More details about the study
123 site and descriptions of townships that are within the vicinity of the mine can be obtained from the
124 previous study (Yabe et al., 2015).



Lead (Pb) in Surface Soil (mg/kg)
 Kabwe, Zambia
 August 2014



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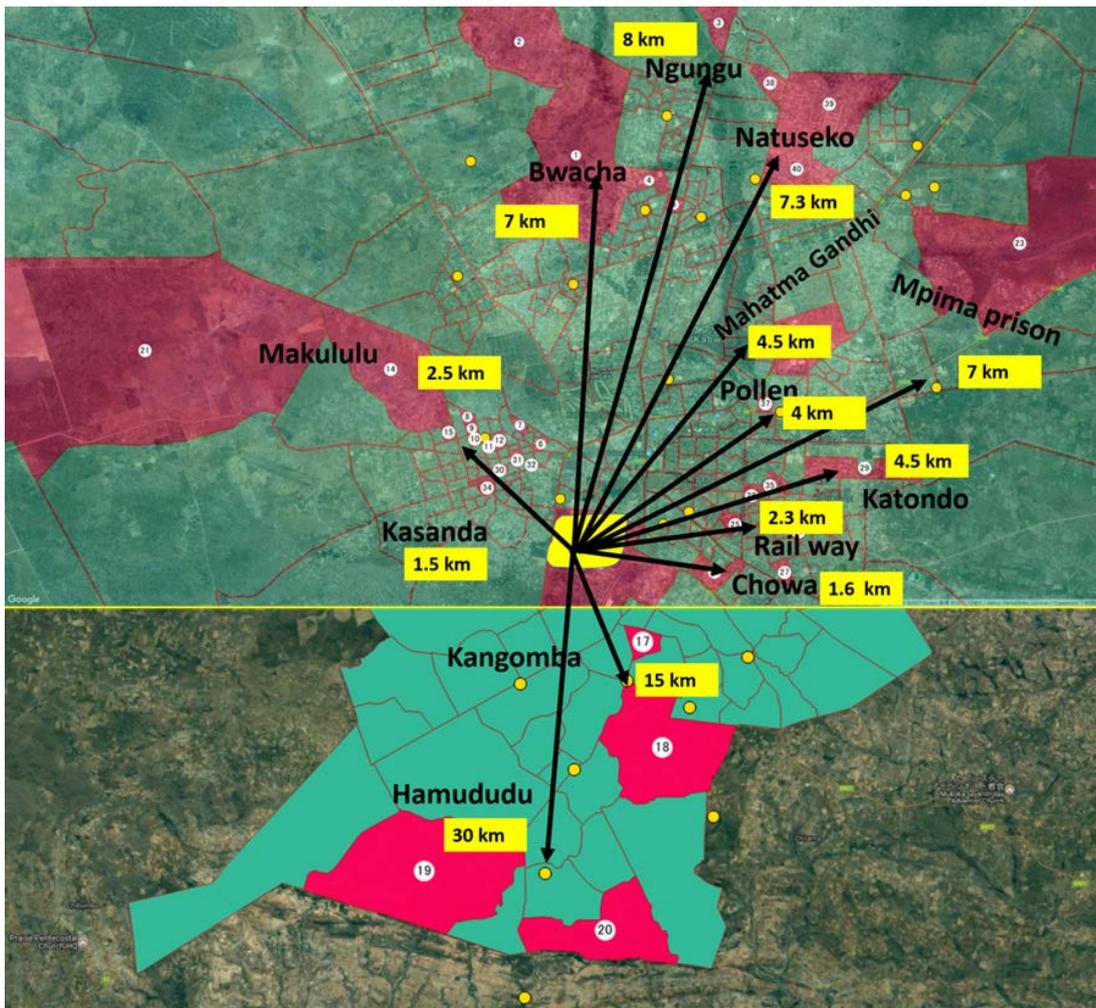
126 Fig. 2.

127 Map of Kabwe showing distribution of Pb (mg/kg) in township soils around the Pb-Zn mining
 128 complex (Bose-O'Reilly et al., 2018).

129

130 2.2 *Sample collection*

131 The study was approved by the University of Zambia Research Ethics Committee (UNZAREC;
132 REF. No. 012-04-16). Further approvals were granted by the Ministry of Health through the Zambia
133 National Health Research Ethics Board and the Kabwe District Medical Office. The study targeted
134 households from areas diverse in the levels of Pb contamination based on the sample design in a
135 parallel socioeconomic survey under the KAMPAI project (Hiwatari et al., 2018). 1,000 target
136 households were randomly chosen in two steps. In the first step, following the sampling frame of
137 Central Statistical Office (CSO), which conducts official census in Zambia and has divided Kabwe
138 town into 384 Standard Enumeration Areas (SEAs). Forty SEAs falling within the catchment area of
139 health facilities were randomly selected (Fig. 3) while 25 households from each SEA were randomly
140 selected in the second stage.



141

142 Fig. 3.

143 Map of Kabwe showing the 40 selected SEAs (numbers 1 - 40 in white circles) widely distributed
 144 across the whole Kabwe town and the 13 health centres (yellow blocks) that were included in the
 145 study.

146

147 To conduct blood sampling, up to four household members (father, mother, and two children)
 148 were invited to local health centres. Younger non-school-going children up to 3 years old and older
 149 school-aged children older than 4 years were selected in the study. The age criterion was according
 150 to Yabe et al. (2015) who found significant differences BLL in children of the two age groups.

151 Thirteen health centres with catchments areas covering the 40 SEAs were included. These included
152 Kasanda, Chowa, Makululu, Katondo, Railway, Pollen, Mahatma Ghandi, Bwacha, Ngungu,
153 Natuseko, Mpima Prison, Kang'omba and Hamududu with distances between the mine and the
154 health centres ranging from 1.5 - 30 km (Fig. 3). After informed and written consent were obtained
155 from household heads, blood samples were collected as described earlier by Yabe et al. (2015). For
156 each of the four family members included in the study, data on the age and sex were recorded.
157 Sample collection and questionnaire administration were done by certified local nurses. In
158 accordance with ethical requirements, confidentiality was upheld in the study.

159 To avoid sample contamination, all sample collection supplies were kept in plastic ziploc
160 storage bags before sample collection. Moreover, the blood collection site on the arm was thoroughly
161 cleaned and wiped with alcohol swabs before needle pricking to minimize contamination from dust.
162 For infants, blood was collected by fingerstick after cleaning the finger with an alcohol swab. A new
163 sterile lancet was used for each infant to penetrate a fingertip. The first drop of blood was wiped off
164 with a clean and dry swab and 50 μ L blood sample was collected with a pre-supplied LeadCare II
165 capillary tube and transferred into the LeadCare II reagent vial. After collection, blood samples were
166 immediately analysed for Pb using a LeadCare[©] II analyser. The remaining samples were
167 immediately stored at -20 °C at the health centres before being transported in cooler boxes on dry ice
168 to the laboratory of the Kabwe District Health Offices where they were again stored at - 20 °C.

169

170 2.3 *Blood Pb analysis*

171 Lead metal analysis in whole blood samples was done on-site immediately after blood sample
172 collection using a point-of-care blood Pb testing analyser, LeadCare[©] II (Magellan Diagnostics,
173 USA) according to the manufacturer's instructions. The analyser uses an electrochemical technique
174 called Anodic Stripping Voltammetry (ASV) to determine the amount of Pb in a blood sample

175 (Magellan Industries Inc., 2013). The analyser has been evaluated by several researchers including
176 (Stanton and Fritsch, 2007; Sobin et al., 2011; Neria et al., 2014). Briefly, individual heparinized
177 venous blood samples were drawn using the manufacturer-supplied LeadCare II capillary tubes
178 (approximately 50 μ L) and dispensed into labeled vials containing LeadCare II treatment reagent
179 (250 μ L of 0.1 % of HCl). These were thoroughly mixed by tipping the bottle ten times to enhance
180 red blood cell lysis, which released the bound Pb. About 50 μ L of the blood/reagent mixture was
181 then transferred to a sensor using the provided transfer dropper and analyzed for blood Pb
182 concentration. Single analyses were performed with results reflected within 3 minutes in μ g/dL on
183 the analyzer's screen. For quality assurance, the instrument was calibrated using a probe before each
184 new lot of test supplies (every 48 tests). Standard controls, one high and one low blood-based
185 controls supplied by the manufacturer were analyzed to assess accuracy, these fell within the
186 manufacturer-specified acceptability limits of 6.9 - 13.7 μ g/dL for the low control and 21.8 - 32.6
187 μ g/dL for the high control. Since limits of quantitation were 3.3 to 65 μ g/dL as the LeadCare II
188 Analyzer can only detect BLL above 3.3 μ g/dL. The precise values of BLLs below the 3.3 μ g/dL
189 detection limit could not be determined. These BLLs below instrument detection limit were therefore
190 treated as 1.65 μ g/dL, the mean of 0 and 3.3 as suggested in other environmental studies (Wood et al.,
191 2011; Ogden, 2010).

192 For samples above 65 μ g/dL, a 3 times dilution was done using 0.1 % HCl. Briefly, 50 μ L of
193 collected blood was added into 100 μ L of 0.1 % HCl. Then 50 μ L of diluted blood was pipetted into
194 the LeadCare II reagent. This was mixed thoroughly and analyzed in the same way as for undiluted
195 blood. The blood specimens and blood/reagent mixtures were maintained at room temperature
196 throughout the analytical process.

197

198

199 2.4 *Statistical analysis*

200 All data were combined into a single electronic database and checked for accuracy and outliers.
201 Statistical analysis was performed using JMP version 10 (SAS Institute, USA). The data are
202 presented as mean, geometric mean (GM), median and minimum-maximum values in $\mu\text{g/dL}$. Tukey
203 Kramer test was used to analyze BLL differences among family members (younger child, older child,
204 father and mother) as well as area difference. Different letters indicated significant difference.
205 Principal component analysis (PCA) was used to evaluate the relatedness between BLL with age,
206 wind direction and distance from the mine. The data of BLLs ($\mu\text{g/dL}$) were log-transformed before
207 PCA analysis to stabilize variances.

208
209 **3. Results**

210 3.1 *Subjects and BLL*

211 The current study focused on blood samples that were collected from a total number of 1,190
212 household members including 291 younger children (3 months to 3 years old) with an average age of
213 1.9 years; 271 older children (4 - 9 years old) with an average age of 6.5 years; 412 mothers with an
214 average age of 39 years and 216 fathers with an average age of 46 years. Participants were drawn
215 from 13 health centres servicing Kasanda, Chowa, Makululu, Katondo, Railway, Pollen, Mahatma
216 Ghandi, Bwacha, Ngungu, Natuseko, Mpima Prison, Kang'omba and Hamududu townships. The
217 recorded BLL ranged from 1.65 to 162 $\mu\text{g/dL}$ (Table 1).

218
219 **Table 1.**

220
221 BLL ($\mu\text{g/dL}$) exposure characteristics among household members in Kabwe, Zambia

Category	All <i>n</i> = 1190	Younger child <i>n</i> = 291	Older child <i>n</i> = 271	Mother <i>n</i> = 412	Father <i>n</i> = 216
Mean	20.8	29.9	24.3	14.8	15.7
Geo. Mean	11.1	17.0	14.2	8.2	8.1

Standard Error	0.62	1.59	1.32	0.74	1.20
Median	13.0	22.0	17.3	10.8	8.6
Standard Deviation	21.4	27.1	21.7	15.0	17.7
Minimum	1.65	1.65	1.65	1.65	1.65
Maximum	162	162	103	86.7	88.2

222

223

224 3.2 Critical BLL values among household members

225 As shown in Table 2, of the 1, 190 participants, 30 % had BLL below 5 µg/dL, which is the
 226 level of concern. These comprised 57 younger children, 59 older children, 151 mothers and 85
 227 fathers. Of the total number of children sampled ($n = 562$), a total of 130 (23 %) exceeded the 45
 228 µg/dL, the threshold required for chelation therapy. A few children (total of 5) exceeded the 100
 229 µg/dL whereas none of the parents exceeded the 100 µg/dL value.

230

231 **Table 2.**

232

233 BLL (µg/dL) exposure characteristics among household members in Kabwe, Zambia

234

Category	All	Young child	Child	Mother	Father
BLL ranges	Number (%)	Number (%)	Number (%)	Number (%)	Number (%)
BLL < 5 µg/dL	352 (30)	57 (20)	59 (22)	151 (37)	85 (39)
BLL 5 - 44 µg/dL	666 (56)	154 (53)	162 (60)	239 (58)	111 (51)
BLL 45-99 µg/dL	167 (14)	76 (26)	49(18)	22 (5.3)	20 (9.3)
BLL > 100 µg/dL	5 (0.4)	4 (1.4)	1 (0.4)	0 (0.0)	0 (0.0)

235

236 3.3 *Pb exposure patterns among household members*

237 Tukey test was performed to analyse age differences in BLL accumulation among family
238 members. Children had significantly higher BLL than parents. However, there was no accumulation
239 difference in BLL between younger children between the ages of 3 months to 3 years and older
240 children aged 4 - 9 years. Moreover, BLL between fathers and mothers were not different. Similarly,
241 there was no sex difference in blood Pb concentrations as the BLL between boys and girls were not
242 different (data not shown). A positive correlation was seen in the BLL of mothers and their infants
243 (data not shown).

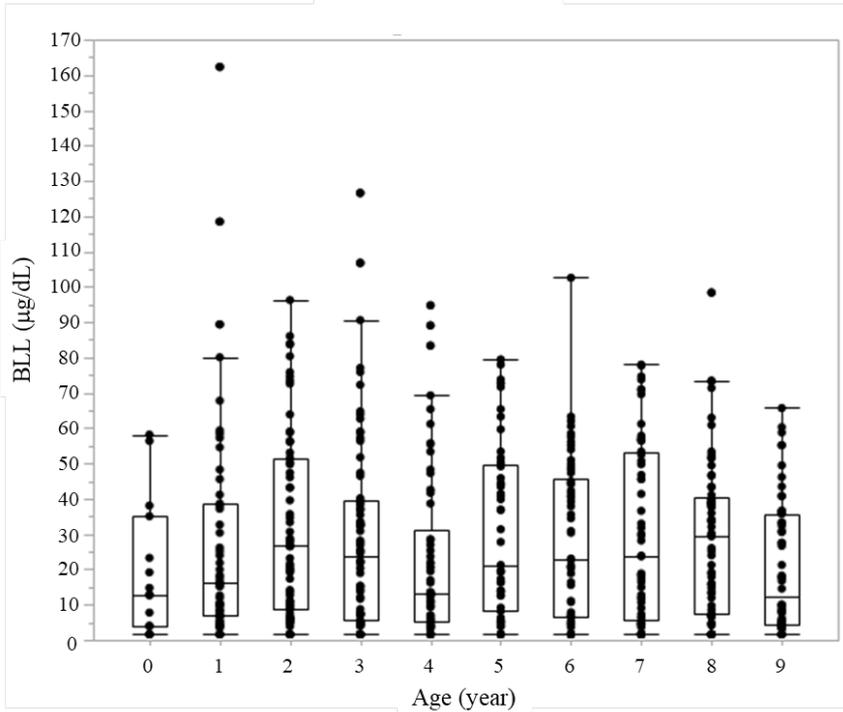
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245

246 3.4 *Relationship between BLL and age*

247 A combined dot plot and box-whisker plot was performed to evaluate the relationship between
248 BLL and age (Fig. 4). In terms of the median BLL, a general trend indicated a high peak in children
249 around the age of 2 years and lower BLL in older children, albeit with fluctuations. Very high BLLs
250 are also more frequently observed among young children although BLL above 45 µg/dL is observed
251 in any age group.

252



253

254 Fig. 4.

255 Figure of combined dot plot and box-whisker plot showing relationship between BLL and age, with
 256 peak BLL recorded at 2 years old.

257

258

259 3.5 *Pb exposure differences among townships*

260 In order to fully understand the Pb exposure patterns in Kabwe, differences in blood Pb
 261 accumulations in residents from the 13 townships were compared. Descriptive statistics of the BLL
 262 in residents enrolled at the 13 health centres are shown in Table 3.

263 **Table 3.**

264

265 Area differences in BLL ($\mu\text{g/dL}$) among Kabwe residents from 13 health centres

266

	Kasanda	Makululu	Chowa	Railway	Natuseko	Bwacha	Ngungu	Pollen	Mahatma Ghandi	Mpima Prison	Katondo	Kang'omba	Hamududu
Mean	45.7	29.3	16.5	11.4	8.58	6.78	5.38	4.70	4.51	5.41	6.51	8.48	3.31
St'd Error	1.64	1.01	1.02	1.97	0.98	1.10	0.59	0.98	0.63	0.59	1.09	1.01	0.41
Median	44.9	24.3	16.6	10.5	6.95	3.90	4.80	1.65	4.60	4.90	3.80	5.40	1.65
Standard Deviation	23.5	19.0	10.5	6.81	6.92	11.1	3.50	4.69	2.36	4.13	7.17	9.94	4.08
Minimum	1.65	1.65	1.65	3.30	1.65	1.65	1.65	1.65	1.65	1.65	1.65	1.65	1.65
Maximum	162	119	48.3	26.2	34.3	94.8	14.2	16.8	9.00	23.3	38.7	63.5	35.6
Count	204	355	105	12	50	103	35	23	14	49	43	96	101

267

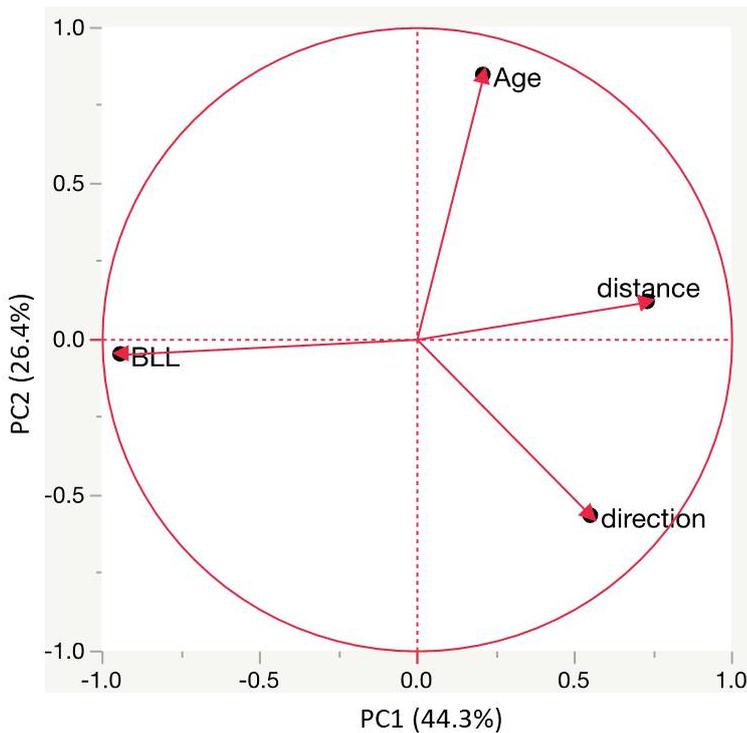
268 Residents in Kasanda Township, with mean BLL of 45.7 $\mu\text{g/dL}$ accumulated higher BLL than
269 residents in the other 12 locations. Makululu Township had second highest mean BLL (29.3 $\mu\text{g/dL}$)
270 followed by Chowa and Railway townships. Similar but lower BLL were recorded in residents from
271 Natuseko, Kang'omba, Ngungu, Mpima Prison, Katondo and Mahatma Ghandi followed by Bwacha
272 and Pollen townships. Residents in Hamududu community had the lowest BLL, with a mean value of
273 3.3 $\mu\text{g/dL}$.

274

275 *3.6 Factors contributing to Pb exposure patterns in Kabwe*

276 Principle component analysis (PCA) was performed on log-transformed data to evaluate the
277 relationships among BLL, age, direction and distance from the mine to the township health centres.
278 As shown in Fig. 5, the results of PCA accounted for 44.3% of the variation by the first principal
279 component (PC1) and 26.4% by the second principal component (PC2). Whereas PC1 was positively
280 determined by distance as well as a slight positive influence by age and direction, it was negatively
281 influenced by BLL. On the other hand, PC2 had a strongly positive relationship with age, but rarely
282 with distance and BLL. It was indicated that distance from the mine had a strong and bigger negative
283 relationship with BLL while direction and age had lower negative relationship with BLL.

284



285

286

287 Fig. 5.

288

289 Principal component analysis on log transformed data showing the influence of age, distance and
 290 wind direction on BLL among Kabwe residents.

291

292 **4. Discussion**

293 A portable LeadCare© II analyzer was used and proved to be an effective point of care blood Pb
 294 analyzer in Kabwe, where alarming childhood Pb poisoning was previously reported (Yabe et al.,
 295 2015). Moreover, the LeadCare II analyser is less invasive and suitable for infants as it requires a
 296 smaller finger stick blood sample. In an environment like Kabwe where non-specific clinical
 297 symptoms of cumulative Pb poisoning can easily be confused with other diseases like malaria, a
 298 rapid and appropriate diagnosis of Pb poisoning cannot be overemphasized. The current study
 299 analyzed Pb exposure patterns among family members in Kabwe, where household members shared
 300 similar risk factors such as area, direction and living conditions. The study revealed that not only
 301 children were at risk of the toxic effects of Pb in Kabwe town but women and men as well. Young

302 age was a significant risk factor given that BLL were highest in children, with peak levels recorded
303 at the age of two, in agreement with similar trends in earlier studies (Yabe et al., 2015; Koller et al.,
304 2004). This trend could be attributed to the hand-to-mouth or object-to-mouth (pica) behavior of
305 children as they explore their environment after their onset of independent ambulation. In addition to
306 increased exposure, children absorb a greater proportion of ingested Pb from the gastrointestinal tract
307 than adults (Wani et al., 2015). Acute Pb poisoning exceeding 100 µg/dL can be fatal as seen in the
308 Pb poisoning disaster in Nigeria, where more than 400 children died leaving numerous others with
309 long-term neurological impairment (Dooyema et al., 2012; Lo et al., 2012). To minimize the
310 pernicious effects of Pb toxicity in children, chelation therapy is recommended at levels ≥ 45 µg/dL
311 as clinical symptoms such as abdominal pain, encephalopathy, convulsions, coma and death have
312 been observed in BLLs > 60 (CDC, 2002; Needleman, 2004). The current study revealed that of the
313 556 children, 29 % had BLL that exceeded 45 µg/dL and were recommended for chelation therapy.
314 Moreover, the children were followed up for further assessment including neurodevelopmental
315 impairment assessment (data not provided).

316 For the first time, the current study revealed high BLL in women in some areas in Kabwe, with
317 concentrations up to 86 µg/dL. These findings were similar to BLLs reported in women of
318 child-bearing age in Sub-Saharan Africa where the overall weighted mean BLLs of 24.73 µg/dl was
319 recorded, with the highest mean of 99 µg/dl being recorded in women from Nigeria (Bede-Ojimadu
320 et al., 2018). Most of the mothers that participated in current the study (58 %) had BLL ranging
321 between 5 - 44 µg/dL, a few (5 %) were above 45 µg/dL with none exceeded 100 µg/dL. Exposure to
322 Pb in the women could be attributed to multiple sources including dust inhalation, ingestion via diet
323 or soil (pica), a habit that is common among pregnant women in Zambia, including Kabwe. Although
324 most studies are focused on childhood Pb exposure, the findings in the current study should be
325 considered carefully as increased BLLs in women of child-bearing age in Sub-Saharan Africa were
326 associated with incidences of preeclampsia and hypertension (Bede-Ojimadu et al., 2018). Delayed

327 puberty due to Pb exposure has also been observed in girls (Schoeters et al., 2008). With a half-life
328 of many years to decades in adults, endogenous exposure to Pb due to increased bone resorption as
329 seen in women during pregnancy and lactation (Rothenberg et al., 2000; Tellez-Rojo et al., 2002;
330 Gulson et al., 2003; Manton et al., 2003) could also not be ruled out in the exposed mothers in
331 Kabwe. When pregnant, blood Pb accumulation in women could pose a threat to the developing fetus
332 given that maternal-fetal transfer is a major source of early life exposure to Pb (Chen et al., 2006;
333 Gardella, 2001; Li et al., 2000; Lin et al., 1998). Additional Pb exposure to the infant can occur via
334 breast milk as breastfeeding is a recognized source of postnatal Pb exposure (Counter et al., 2014).
335 These exposure pathways could explain the alarmingly high BLL in infants in the current study, even
336 before their ambulatory stage. This is critical as pediatric Pb poisoning during a vulnerable period of
337 development can lead to negative neurodevelopmental impacts such as low IQ and cognitive
338 impairments (ATSDR, 2007; Lanphear et al., 2005).

339 Similarly, increased Pb exposure in men from some Kabwe townships was recorded in the
340 current study, with median BLLs of 8.60 $\mu\text{g}/\text{dL}$ and maximum levels of 88.2 $\mu\text{g}/\text{dL}$. This is also the
341 first time that Pb exposure is being investigated in men in Kabwe and the sources of exposure could
342 be similar to those of women, with the exception of pica, a practice common especially among
343 expectant mothers. Findings in the current study were similar to reports in Iran where mean BLL of
344 41.41 $\mu\text{g}/\text{dl}$ were reported in male workers at a battery manufacturing plant (Sadeghniat haghghi et
345 al., 2013). Given that chronic low level Pb exposure has been associated with health complications
346 including reduced sperm quality (Wu et al., 2012; Apostoli et al., 1998), the findings of the current
347 study highlight the reproductive health risks that men in Kabwe could be exposed to through chronic
348 Pb exposure. Moreover, Pb exposure has an interactive relationship with socioeconomic factors.
349 While socioeconomic conditions have been established as important predictors of exposure to Pb
350 (Elias et al., 2007; Sargent et al., 1995), health effects of Pb exposure can be the sources of economic
351 losses that can impact families negatively (UMRSC and MNCEH, 2014; Attina and Trasande, 2013;

352 Gould, 2009; Ogunseitan and Smith, 2007). While many studies may place emphasis only on health
353 effects of Pb exposure, the impact of Pb exposure and poisoning in Kabwe could be broad and
354 include healthcare, social, and behavioral costs.

355 Area differences in BLL exposure patterns among Kabwe residents were established in the
356 current study, where residents from Kasanda Mine Township had the highest BLL followed by
357 Makululu and Chowa Townships. BLLs in Railway, Natuseko, Katondo, Pollen, Mahatma Ghandi,
358 Bwacha, Ngungu, Mpima Prison, Kang'omba were similar, with residents from Hamududu
359 recording the lowest. These results reveal that severity to Pb poisoning risks among residents of
360 Kabwe was different depending on area of residence. These differences could be attributed to
361 distance from the mine and direction, with distance from the mine exerting the majority influence as
362 seen on PCA analysis. It was shown that townships closest to the mine and lying in the western
363 direction of the mine were affected the most, especially Kasanda, followed by Makululu. Since the
364 wind direction is from east to west in Kabwe, more Pb contaminated dusts emanating from the mine
365 tailings are likely to settle in Kasanda and Makululu than the other townships. Of interest was
366 Natuseko Township, which is located in similar direction with similar distance from the mine as
367 Bwacha and Ngungu Townships but recorded slightly higher BLLs than these two townships.
368 Although not established, this could be attributed to transportation and piling of contaminated soils
369 and stones from the mine in Natuseko Township many years ago (verbal communication from
370 community members).

371

372 **5. Conclusions**

373 This is the first study that has revealed the true extent of Pb exposure in the whole Kabwe town,
374 which poses a serious public hazard and should be given urgent attention. Exposure to Pb does not
375 only affect children but their parents as well. Factors contributing to Pb exposure included age,
376 distance and direction, with distance playing the major role. Therefore, younger children in

377 townships closer to the mine and lying on the western side of the mine were the most vulnerable. To
378 avert overt Pb toxicity, children with BLL exceeding 45 µg/dL would require chelation therapy.
379 These children were referred to the office of the District Medical Director. Regular BLL monitoring
380 using a portable analyser such as the LeadCare II should be considered for prompt diagnosis and
381 initiation of treatment to avoid the irreversible Pb-induced neurological dysfunction in children. A
382 thorough clinical evaluation of Pb poisoning among the affected children, including
383 neurodevelopmental and cognitive impairments, would reveal the true extend of Pb poisoning in
384 Kabwe. Measuring blood Pb in pregnant women and breast milk will be significant to clarify the
385 exposure pathway from mother to child and recommend appropriate medical management and advice
386 for the mother. Socio-economic factors contributing to Pb exposure and socio-economic impacts of
387 Pb exposure also need to be thoroughly investigated to fully understand the Pb exposure-effect cycle.
388 Moreover, urgent environmental remediation is required to reduce Pb exposure in Kabwe.

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405

406 **Conflict of interest**

407 The authors declare no conflicts of interest

408

409 **References**

- 410
411 Agency for Toxic Substances and Disease Registry (ATSDR). 2007. Toxicological profile for lead.
412 Available: <https://www.atsdr.cdc.gov/toxprofiles/tp13.pdf> [accessed 16 December 2018].
- 413 Agency for Toxic Substances and Disease Registry (ATSDR). 2017. Lead Toxicity. What are
414 possible health effects from lead exposure? Available:
415 https://www.atsdr.cdc.gov/csem/lead/docs/csem-lead_toxicity_508.pdf [accessed 21 January
416 2019].
- 417 Apostoli P, Kiss P, Porru S, Bonde JP, Vanhoorne M., 1998. Male reproductive toxicity of lead in
418 animals and humans. *Occup. Environ. Med.* 55, 364-374.
- 419 Attina TM, Trasande L., 2013. Economic costs of childhood Pb exposure in low- and middle-income
420 countries. *Environ. Health Perspect.* 121, 1097-1102.
- 421 **Bede-Ojimadu O, Amadi CN, Orisakwe OE., 2018. Blood Lead Levels in Women of Child-Bearing**
422 **Age in Sub-Saharan Africa: A Systematic Review. *Front. Public Health.* 6, 367.**
- 423 Benoff S, Centola GM, Millan C, Napolitano B, Marmar JL, Hurley IR., 2003. Increased seminal
424 plasma lead levels adversely affect the fertility potential of sperm in IVF. *Hum. Reprod.* 18,
425 374-383.
- 426 Benoff S, Jacob A, Hurley IR., 2000. Male infertility and environmental exposure to lead and
427 cadmium. *Hum. Reprod. Update* 6, 107-21.
- 428 **Blacksmith Institute (PureEarth). 2013. The world's worst 2013: the top ten toxic threats. Available:**
429 **<https://www.worstpolluted.org> [accessed 29 October 2019].**
- 430 Bose-O'Reilly S, Yabe J, Makumba J, Schutzmeier P, Ericson B, Caravanos J., 2018. Lead
431 intoxicated children in Kabwe, Zambia. *Environ. Res.* 168, 420-424.
- 432 Canfield RL, Henderson Jr CR, Cory-Slechta DA, Cox C, Jusko TA, Lanphear BP., 2003.
433 Intellectual impairment in children with blood lead concentrations below 10 µg per deciliter.
434 *N. Engl. J. Med.* 348, 1517-1526.
- 435 Centers for Disease Control and Prevention (CDC). 2012. Low level lead exposure harms children: a
436 renewed call for primary prevention. Report of the Advisory Committee on Childhood Lead
437 Poisoning Prevention of the Centers for Disease Control and Prevention. Atlanta, Ga. [online].
438 Available at URL: www.cdc.gov/nceh/lead/acclpp/final_document_030712.pdf [accessed 16
439 December 2018].

- 440 Centers for Disease Control and Prevention (CDC). 2002. Managing elevated blood lead levels
441 among young children: recommendations from the Advisory Committee on Childhood Lead
442 Poisoning Prevention. Available: <https://stacks.cdc.gov/view/cdc/26980> [accessed 29
443 December 2018].
- 444 Chen PC, Pan IJ, Wang JD., 2006. Parental exposure to lead and small for gestational age births. *Am.*
445 *J. Ind. Med.* 49, 417-422.
- 446 Counter SA, Buchanan LH, Ortega F, Chiriboga R, Correa R, Collaguaso MA., 2014. Lead levels in
447 the breast milk of nursing Andean mothers living in a lead-contaminated environment. *J.*
448 *Toxicol. Environ. Health A.* 77, 993-1003.
- 449 Dapul H, Laraque D., 2014. Lead Poisoning in Children. *Adv. Pediatr.*, 61, 313-333.
- 450 Dooyema CA, Neri A, Lo YC, Durant J, Dargan PI, Swarthout T, Biya O, Gidado SO, Haladu S,
451 Sani-Gwarzo N, Nguku PM, Akpan H, Idris S, Bashir AM, Brown MJ., 2012. Outbreak of
452 fatal childhood lead poisoning related to artisanal gold mining in northwestern Nigeria, 2010.
453 *Environ. Health Perspect.* 120, 601-607.
- 454 Elias SM, Hashim Z, Marjan ZM, Abdullah AS, Hashim JH., 2007. Relationship between blood Pb
455 concentration and nutritional status among Malay primary school children in Kuala Lumpur,
456 Malaysia. *Asia. Pac. J. Public Health* 19, 29-37.
- 457 Flora G, Gupta D, Tiwari A., 2012. Toxicity of lead: a review with recent updates. *Interdiscip.*
458 *Toxicol.* 5, 47-58.
- 459 Gardella C., 2001. Lead exposure in pregnancy: a review of the literature and argument for routine
460 prenatal screening. *Obstet. Gynecol. Surv.* 56, 231-238.
- 461 Gould E., 2009. Childhood lead poisoning: conservative estimates of the social and economic
462 benefits of lead hazard control. *Environ. Health Perspect.* 117, 1162-1167.
- 463 Gulson BL, Mizon KJ, Korsch MJ, Palmer JM, Donnelly JB., 2003. Mobilization of lead from
464 human bone tissue during pregnancy and lactation - a summary of long-term research. *Sci.*
465 *Total Environ.* 303, 79-104.
- 466 Hiwatari M, Yamada D, Hangoma P, Narita D, Mphuka C, Chitah B., 2018. Kabwe Household
467 Socioeconomic Survey (KHSS) 2017 Report. Kabwe Mine Pollution Amelioration Initiative

468 (KAMPAI). pp 1-91 (ISBN978-4-909032-02-7), available at
469 <http://satreps-kampai.vetmed.hokudai.ac.jp/publications/>

470 Institute for Health Metrics and Evaluation (IHME). 2017. Global Burden of Disease (GBD)
471 Compare. Seattle, WA: IHME, University of Washington. Available:
472 <https://vizhub.healthdata.org/gbd-compare/> [accessed 10 February 2019].
473

474 Koller K, Brown T, Spurgeon A, Levy L., 2004. Recent developments in low-level lead exposure
475 and intellectual impairment in children. *Environ. Health Perspect.* 112, 987-994.

476 Kumar S., 2018. Occupational and Environmental Exposure to Lead and Reproductive Health
477 Impairment: An Overview. *Indian J. Occup. Environ. Med.* 22, 128-137.

478 Lanphear BP, Hornung R, Khoury J, Yolton K, Baghurst P, Bellinger DC, Canfield RL, Dietrich KN,
479 Bornschein R, Greene T, Rothenberg SJ, Needleman HL, Schnaas L, Wasserman G, Graziano
480 J, Roberts R., 2005. Low-level environmental lead exposure and children's intellectual
481 function: an international pooled analysis. *Environ. Health Perspect.* 113, 894-899.

482 Li PJ, Sheng YZ, Wang QY, Gu LY, Wang YL., 2000. Transfer of lead via placenta and breast milk
483 in human. *Biomed. Environ. Sci.* 13, 85-89.

484 Lidsky TL, Schneider JS., 2003. Lead neurotoxicity in children: basic mechanisms and clinical
485 correlates. *Brain* 126, 5-19.

486 Lin S, Hwang SA, Marshall EG, Marion D., 1998. Does paternal occupational lead exposure increase
487 the risks of low birth weight or prematurity? *Am. J. Epidemiol.* 148, 173-181.

488 Lo YC, Dooyema CA, Neri A, Durant J, Jefferies T, Medina-Marino A, de Ravello L, Thoroughman
489 D, Davis L, Dankoli RS, Samson MY, Ibrahim LM, Okechukwu O, Umar-Tsafe NT, Dama
490 AH, Brown MJ., 2012. Childhood lead poisoning associated with gold ore processing: a
491 village-level investigation-Zamfara State, Nigeria, October-November 2010. *Environ. Health
492 Perspect.* 120, 1450-1455.

493 Manton WI, Angle CR, Stanek KL, Kuntzelman D, Reese YR, Kuehnemann TJ., 2003. Release of
494 lead from bone in pregnancy and lactation. *Environ. Res.* 92, 139-151.

- 495 Magellan Industries Inc. 2013. LeadCare II Blood Lead Analyzer User's Guide (v 1.09, Rev 04),
496 Magellan Industries Inc, North Billerica, Mass, USA,
497 <http://www.leadcare2.com/Product-Support/Product-Literature-Downloads> [accessed 20
498 February 2019].
- 499 Miranda ML, Kim D, Galeano MA, Paul CJ, Hull AP, Morgan SP., 2007. The relationship between
500 early childhood blood lead levels and performance on end-of-grade tests. *Environ. Health*
501 *Perspect.* 115, 1242-1247.
- 502 Nakayama SMM, Ikenaka Y, Hamada K, Muzandu K, Choongo K, Teraoka H, Mizuno N, Ishizuka
503 M., 2011. Metal and metalloid contamination in roadside soil and wild rats around a Pb-Zn
504 mine in Kabwe, Zambia. *Environ. Pollut.* 159, 175-181.
- 505 Needleman H., 2004. Lead poisoning. *Annu. Rev. Med.* 55, 209-222.
- 506 Neria AJ, Royb J, Jarrettc J, Panc Y., Dooyemaa C, Caldwellc K, Umar-Tsafed NT, Olubiyoe R,
507 Brownf MJ., 2014. Analysis of a novel field dilution method for testing samples that exceed
508 the analytic range of point-of-care blood lead analyzers. *Int. J. Environ. Health Res.* 24,
509 418-428.
- 510 Ogden TL., 2010. Handling results below the level of detection. *Ann. Occup. Hyg.* 54, 255-256.
- 511 Ogunseitani OA, Smith TR., 2007. The Cost of environmental lead (Pb) poisoning in Nigeria. *Afr. J.*
512 *Environ. Sci. Technol.* 1, 27-36.
- 513 Pearce JM., 2007. Burton's line in lead poisoning. *Eur. Neurol.* 57, 118-119.
- 514 Rothenberg SJ, Khan F, Manalo M, Jiang J, Cuellar R, Reyes S, Acosta S, Jauregui M, Diaz M,
515 Sanchez M, Todd AC, Johnson C., 200. Maternal bone lead contribution to blood lead during
516 and after pregnancy. *Environ. Res.* 82, 81-90.
- 517
- 518 **Sadeghniat haghghi K, Aminian O, Chavoshi F, Sadat BL, Soltani S, Rahmati NF., 2013.**
519 **Relationship between blood lead level and male reproductive hormones in male lead exposed**
520 **workers of a battery factory: A cross-sectional study. *Iran J. Reprod. Med.* 11, 673-676.**

521

522 Sargent JD, Brown MJ, Freeman JL, Bailey A, Goodman D, Freeman Jr DH., 1995. Childhood Pb
523 Poisoning in Massachusetts Communities: it's association with sociodemographic and housing
524 characteristics. *Am. J. Public Health* 85, 528-534.

525 Schoeters G, Den Hond E, Dhooge W, van Larebeke N, Leijs M., 2008. Endocrine disruptors and
526 abnormalities of pubertal development. *Basic Clin. Pharmacol. Toxicol.* 102, 168-75.

527 Sobin C, Parisi N, Schaub T, de la Riva E., 2011. A Bland-Altman comparison of the lead Care®
528 System and Inductively Coupled Plasma Mass Spectrometry for detecting low-level lead in
529 child whole blood samples. *J. Med. Toxicol.* 7, 24-32.

530 Stanton NV, Fritsch TBS., 2007. Evaluation of a second-generation portable blood lead analyzer in
531 an occupational setting. *Am. J. Ind. Med.* 50, 1018-1024.

532 Téllez-Rojo MM, Hernández-Avila M, González-Cossío T, Romieu I, Aro A, Palazuelos E,
533 Schwartz J, Hu H., 2002. Impact of breast-feeding on the mobilization of lead from bone. *Am.*
534 *J. Epidemiol.* 155, 420-428.

535 Telisman S, Cvitkovic P, Juraasovic J, Pizent A, Gavella M, Rocic B., 2000. Semen quality and
536 reproductive endocrine function in relation to biomarkers of lead, cadmium, zinc and copper
537 in men. *Environ. Health Perspect.* 108, 45-53.

538 University of Michigan Risk Science Center (UMRSC) and Michigan Network for Children's
539 Environmental Health (MNCEH). 2014. Economic Impacts of Lead Exposure and
540 Remediation in Michigan. Available at:
541 [http://www.mnceh.org/sites/www.mnceh.org/files/mnceh/press-releases/Lead_Cost_Report_](http://www.mnceh.org/sites/www.mnceh.org/files/mnceh/press-releases/Lead_Cost_Report_MI_2014_smaller.pdf)
542 [MI_2014_smaller.pdf](http://www.mnceh.org/sites/www.mnceh.org/files/mnceh/press-releases/Lead_Cost_Report_MI_2014_smaller.pdf) [accessed 11 April 2019].

543 Wani AL, Ara A, Usmani JAH., 2015. Lead toxicity: a review. *Interdiscip. Toxicol.* 8, 55-64.

544 Wood MD, Beresford NA, Copplestone D., 2011. Limit of detection values in data analysis: Do they
545 matter? *Radioprotection* 46, S85-S90.

546 World Health Organization. 2010. Childhood lead poisoning. WHO Press. Available:
547 <http://www.who.int/ceh/publications/leadguidance.pdf> [accessed 12 February 2019].

- 548 World Health Organization. 2018. Lead poisoning and health. Available:
549 <https://www.who.int/news-room/fact-sheets/detail/lead-poisoning-and-health> [accessed 12
550 February 2019].
- 551 Wu HM, Lin-Tan DT, Wang ML, Huang HY, Lee CL, Wang HS, Soong YK, Lin JL., 2012. Lead
552 level in seminal plasma may affect semen quality for men without occupational exposure to
553 lead. *Reprod. Biol. Endocrinol.* 10, 91.
- 554 Yabe J, Ishizuka M, Umemura T., 2010. Current levels of heavy metal pollution in Africa. *J. Vet.*
555 *Med. Sci.*72, 1257-1263.
- 556 Yabe J, Nakayama SMM, Ikenaka Y, Yohannes YB, Bortey-Sam N, Oroszlany B, Muzandu K,
557 Choongo K, Kabalo AN, Ntapisha J, Mweene A, Umemura T, Ishizuka M., 2015. Lead
558 poisoning in children from townships in the vicinity of a lead-zinc mine in Kabwe, Zambia.
559 *Chemosphere* 119, 941-947.
- 560 Yabe J, Nakayama SMM, Ikenaka Y, Yohannes YB, Bortey-Sam Kabalo A.N, Ntapisha J,
561 Mizukawa H, Umemura T, Ishizuka M., 2018. Lead and cadmium excretion in feces and urine
562 of children from polluted townships near a lead-zinc mine in Kabwe, Zambia. *Chemosphere*
563 202, 48-55.