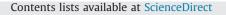
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## The pediatric burden of disease from lead exposure at toxic waste sites in low and middle income countries



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## ABSTRACT

*Background:* The impact of lead from toxic waste sites on children in low and middle income countries has not been calculated due to a lack of exposure data. We sought to calculate this impact in Disability Adjusted Life Years (DALYs).

*Materials and methods:* Using an Integrated Exposure Uptake Biokinetic (IEUBK) model, we converted soil and drinking water lead levels from sites in the Blacksmith Institute's Toxic Sites Identification Program (TSIP) into mean blood lead levels (BLLs). We then calculated the incidence of mild mental retardation (MMR) and DALYs resulting from these BLLs.

*Results:* The TSIP included 200 sites in 31 countries with soil (n=132) or drinking water (n=68) lead levels, representing 779,989 children younger than 4 years of age potentially exposed to lead. Environmental lead levels produced a range of BLLs from 1.56 to 104.71 µg/dL. These BLLs equated to an estimated loss of 5.41–8.23 IQ points, resulting in an incidence of MMR of 6.03 per 1000 population and 76.1 DALYs per 1000 population.

*Discussion:* Soil and water lead levels at toxic waste sites predict BLLs that lower the intelligence quotient (IQ), with the resulting MMR potentially limiting individual- and country-level development. The preventable burden of disease produced by these sites highlights the need for toxic waste sites to be systematically identified, evaluated, and remediated.

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### 1. Introduction

Since lead has long-term health consequences, including the potential to impair cognitive development in children, the potential sources of lead in a community should be identified and addressed. With the decreasing use of leaded gasoline in the past decade in low and middle income countries (LMICs), lead from toxic waste sites and environmental "hotspots" may contribute relatively more to overall lead exposure in certain communities. While high income countries such as the United States (U.S.) have made progress in identifying,

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mapping, and evaluating these sites, LMICs have made less progress (Yáñez et al., 2002). Exposures to toxic waste sites in LMICs may be greater than in high income countries given the higher population densities around these sites; the lack of environmental controls to contain toxicant release; and the barriers to proper identification and tracking of toxic waste and industrial byproducts (Dutta et al., 2006; Misra and Pandey, 2005).

Lead-induced mild mental retardation (MMR) and cardiovascular disease account for 0.6% of the global burden of disease quantified by disability adjusted life years (DALYs) (World Health Organization, 2009). Due to a paucity of exposure data and biomonitoring around toxic waste sites and environmental "hotspots," the exact contribution of these sites to the global burden of disease from lead is unclear. In this analysis we characterize environmental exposures at these sites in LMICs, estimate the resulting blood lead levels (BLLs), and calculate the burden of disease resulting from lead-induced MMR.

*Abbreviations:* BLL, Blood lead level; DALYs, Disability adjusted life years; EPA, Environmental protection agency; IEUBK, Integrated exposure uptake biokinetic; LMICs, Low and middle income countries; MMR, Mild mental retardation; TSIP), Toxic sites identification program; U.S., United States; WHO, World Health Organization; YLD, Years lived with disability; YLL, Years of life lost

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#### 2. Materials and methods

#### 2.1. Site identification

We used sites from the Blacksmith Institute's Toxic Sites Identification Program (TSIP), an effort to identify, evaluate, and remediate toxic waste sites in low and middle income countries. The TSIP focuses on point-source, legacy sites, which were formerly active sites, as well as artisanal "hotspots" (e.g., informal lead battery recycling, small-scale gold mining). As part of each site evaluation, the Blacksmith Institute identifies the dominant chemical pollutant, the contaminated environmental medium, and the population at risk of exposure. The key pollutant is determined through prior environmental testing or the historical use of the property (e.g., lead for a battery recycling operation and hexavalent chromium for a tannery). If sampling results are not available from a government agency or academic partner, then up to five convenience samples are obtained. The highest value is selected for analysis to model a worst-case scenario.

We previously outlined the TSIP methodology, which is a modified version of the Hazard Ranking System used in the U.S. Environmental Protection Agency's (EPA) Superfund program, and characterized the findings from 2095 sites cataloged in the TSIP (Ericson et al., 2013). In brief, the Blacksmith TSIP estimates the population at risk of exposure to the key pollutant through the specific environmental medium using local census projections, aerial photographs, and government interviews. Since the TSIP estimates the total exposed population, we calculated the child population by applying U.S. Census Bureau country-specific age distributions for each site (United States Census Bureau, International Data Base, 2012). For this analysis, we defined the key pollutant as lead, the environmental medium as soil or drinking water, and the population at risk as children between 6 and 48 months of age. We categorized countries in the TSIP data base into low income; lower-middle income; and upper-middle income (World Bank, 2012). The majority of site evaluations were conducted in 2010, so we selected 2010 as the year for the analysis.

#### 2.2. Calculation of BLLs

To calculate BLLs, we used the U.S. EPA's Integrated Exposure Uptake Biokinetic (IEUBK) Model for Lead in Children (IEUBKwin v1.1 build 11), which has been used in the U.S. EPA's Superfund program. The IEUBK Model is a validated tool that estimates the geometric mean of BLL from exposure to multiple sources of lead. We entered drinking water or soil lead levels for each site into the model and calculated mean BLLs for each site. In the IEUBK Model sites with soil lead levels greater than 38,550 mg/kg defaulted to 38,550 mg/kg, and sites with drinking water lead levels greater than  $6000 \,\mu\text{g/L}$  defaulted to  $6000 \,\mu\text{g/L}$ . We kept the default values for other inputs, including air lead concentrations, dietary intake of lead, water consumption rates, maternal BLL, alternate sources of lead, and bioavailability of lead. For example, the default values for dietary intake of lead are 5.53  $\mu g/day,$  5.78  $\mu g/day,$  6.49  $\mu g/day,$  and 6.24  $\mu g/day$  for children aged 0–11 months, 12-23 months, 24-35 months, and 36-47 months, respectively (White et al., 1998). Using the IEUBK Model we calculated a single mean BLL for each toxic waste site overall and BLLs for each of the following age groups: 6-12 months, 12-24 months, 24-36 months, and 36-48 months. We then calculated the median BLL for each age group across all the sites.

#### 2.3. Calculating impact on IQ and DALYs

We calculated the loss of intelligence quotient (IQ) points resulting from the estimated BLLs and the DALYs resulting from incident cases of MMR. We entered each site's mean BLL from the IEUBK model into equations derived from the Schwartz 1994 meta-analysis and the 2005 pooled analysis by Lanphear et al. (2005). Both of these projects analyzed multiple studies of lead's impact on neurodevelopment, specifically IQ. Since Schwartz documented a loss of 2.57 IQ points with an increase in BLL from 10 to 20  $\mu$ g/dL, we estimated the loss of IQ points by multiplying 0.257 by the BLL. Lanphear et al. (2005) documented a loss of IQ points equal to  $-2.70 \times ln$  (concurrent BLL). By entering a BLL into these equations, we produced two different estimates of IQ points potentially lost from lead exposure for each site. For all the sites combined, we then calculated two another estimated using the Lanphear formula.

Using the mean BLL for each site from the IEUBK model, we also calculated the incidence of lead-induced MMR and the resulting DALYs with World Health Organization (WHO) spreadsheets (Fewtrell et al., 2003). By entering a mean BLL into the first spreadsheet, we obtained the incidence of MMR. The spreadsheet calculates the number of children just above the MMR threshold of 70 IQ points who would drop into the MMR range due to lead-induced loss of IQ points and presents the rate of lead-induced MMR per 1000 population. This spreadsheet incorporates a regional adjustment ratio for MMR since the incidence of non-congenital causes of MMR, such as anemia and meningitis, varies in different geographic regions. In addition, the spreadsheet calculates the population and

mean BLL from the population. By entering the incidence of MMR from the first WHO spreadsheet and population at risk of exposure into the second WHO spreadsheet, we calculated the resulting DALYs and DALYs per 1000 children.

DALYs are a combination of Years Lived with Disability (YLD) and Years of Life Lost (YLL) from a disease or health state. To calculate YLD, which represents the morbidity from a disease, the duration of the disease in years is multiplied by a disability weight. The disability weight is a value from zero to one that estimates the severity of the disease. For example, periodontal disease has a disability weight of 0.001. MMR due to lead has a disability weight of 0.361, and a first-time stroke has a disability weight of 0.920 (World Health Organization, 2008). There is no disability weight associated with loss of IQ points that does not result in MMR (Fewtrell et al., 2003). For example, if an individual's IQ decreased from 85 to 81 due to lead, then this change would not be captured in DALYs. DALY calculations typically incorporate only the lead-induced loss of IQ points resulting in MMR (Fewtrell et al., 2003). A child who develops MMR from lead at the age of 2 years and has a life expectancy of 80 years accumulates 28.2 YLD (78 years  $\times$  0.361). While the calculation of DALYs from lead typically involves calculating YLL, which represents the premature mortality from a disease, from increase in blood pressure and the resulting cardiovascular disease, we did not include this component since the analysis is limited to children younger than 4 years of age. Therefore, our DALY calculations represent solely the morbidity associated with lead exposure at these sites and do not incorporate the premature mortality associated with lead exposure.

#### 2.4. Sensitivity analysis

We performed a sensitivity analysis by calculating DALYs using different discount rates and age weights. Calculation of DALYs typically incorporates a 3% discount rate due to the societal preference of a healthy year of life now versus in the future, and non-uniform age weights due to the relative societal value of certain ages (Mathers et al., 2006). The notation DALYs<sub>(*K*,*K*)</sub> signifies where discount rate (*r*) and age weight (*K*) are used. We present our primary results in DALYs<sub>(3,1)</sub> including both the 3% discount rate and the full age weight. We also present DALYs<sub>(3,0)</sub> with only the 3% discount rate and DALYs<sub>(0,0)</sub> without any weighting. Since Hogan et al., 1998 recommend caution in relying on the IEUBK model when calculated BLLs exceed 30 µg/dL, we capped the maximum BLL from each site at 30 µg/dL and report the subsequent change in DALYs<sub>(3,1)</sub>.

#### 3. Results

As of August 2012, the TSIP database contained 200 sites in 31 countries with soil (n=132) or drinking water (n=68) lead levels. India (n=32), the Philippines (n=27), Indonesia (n=26), China (n=19), and the United Republic of Tanzania (n=17) had the most sites (Table 1). The total population of children between 6 and 48 months of age at risk of exposure to lead at these sites was 779,989, with a median population of 579 children per site. 409,748 (52.5%) of these children lived in low income countries; 303,872 (39.0%) lived in lower-middle income countries. Low income countries contained 39 sites with a median of 8520 children per site; lower-middle income countries contained 39 sites with a median of 266 children per site (Table 2).

Soil lead levels ranged from 55 to 543,809 mg/kg, with a median of 2016 mg/kg. Drinking water lead levels ranged from 5 to 124,800 µg/L, with a median of 500 µg/L. Based on input of these environmental lead levels into the IEUBK model, we estimated geometric mean BLLs from 1.56 to 104.71 µg/dL, with a median of 21.04 µg/dL (1st quartile=8.28, 3rd quartile=45.03). Table 3 presents the median BLL for each of the 4 age groups. 86% of children at these sites had BLLs greater than 5 µg/dL, with 75 sites predicted to have 100% of the BLLs greater than 5 µg/dL.

By entering each site-specific BLL into the formulas from Schwartz (1994) and Lanphear et al. (2005), the median loss of IQ points was 5.41 IQ points (1st quartile=2.12, 3rd quartile=11.59) and 8.23 IQ points (1st quartile=5.7, 3rd quartile=10.28), respectively. These reductions in IQ lead to an incidence of MMR of 6.03 per 1000 children (1st quartile=2.46 per 1000, 3rd quartile=8.05 per 1000), resulting in a total of 51,614 DALYs<sub>(3,1)</sub> and 76.1 DALYs<sub>(3,1)</sub> per 1000

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