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Blood Lead Levels of Children in Flint, Michigan: 2006-2016

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Objective We evaluated the increases in blood lead levels (BLLs) observed in young children in Flint, Michigan, during their exposure to corrosive Flint River water during the years 2014 and 2015 and compared their BLLs to those of Flint children measured during the years 2006-2013 and 2016.

Study design This was a retrospective study design using BLLs extracted from databases from 2006 to 2016. We analyzed a population sample of 15 817 BLLs from children aged ≤5 years with potential exposure to contaminated Flint River water. Percentages of BLLs ≥5.0 µg/dL and geometric mean (GM) BLLs were analyzed over time.

Results A significant decline in the percentages of BLLs ≥5.0 µg/dL from 11.8% in 2006 to 3.2% in 2016 was observed ($P < .001$). GM ± SE BLLs decreased from 2.33 ± 0.04 µg/dL in 2006 to 1.15 ± 0.02 µg/dL in 2016 ($P < .001$). GM BLLs increased twice: from 1.75 ± 0.03 µg/dL to 1.87 ± 0.03 µg/dL (2010-2011) and from 1.19 ± 0.02 µg/dL to 1.30 ± 0.02 µg/dL (2014-2015). Overall, from 2006 to 2016, there was a 72.9% decrease in the percentage of children with BLLs ≥5.0 µg/dL and a 50.6% decrease in GM BLLs.

Conclusion These findings suggest that the 11 year trend of annual decreases in BLLs in children in Flint, Michigan, reversed to a degree consistent with random variation from 2010 to 2011, and again during the exposure to Flint River water in 2014-2015. Historically, public health efforts to reduce BLLs of young children in Flint have been effective over the 11-year period studied. *(J Pediatr 2018;■■:■■-■■).*

See editorial, p •••

The exposure of young children to lead has been and continues to be widespread in the US.[1-4] Lead is a potent neurotoxin, and elevated blood lead levels (BLLs) are associated with decreased IQ scores, academic failure, and aggressive behaviors in children.[5-9] Mean lifetime BLLs as low as 1.0-10.0 µg/dL are inversely associated with childhood IQ scores; greater blood lead concentrations can cause other toxic effects, including anemia, encephalopathy, and kidney damage.[2,5,6]

Flint is a "rust-belt" community with a high percentage of Medicaid recipients matching the socioeconomic profile of a city with children at greater risk for lead exposure from multiple sources. The well-publicized water source switch of April 25, 2014, to October 15, 2015, resulted in a much greater percentage of households having tap water that exceeded the maximum lead water concentration of 15 parts per billion allowable by the 1991 Lead and Copper Rule.[10,11] Previous studies of children from Flint, Michigan, observed an increase in the percentage of BLLs greater than the current Centers for Disease Control and Prevention (CDC) reference value of 5.0 µg/dL during 2014-2015.[10,11] Given that there is no safe established BLL, we set out to analyze annual BLL changes in children in Flint, Michigan, over the last decade, including the months of exposure to Flint River water, and place their BLLs in historical context. Previously published studies have only contained percentages of BLLs of children in Flint, Michigan, greater than or equal to the threshold concentrations of 5.0 µg/dL and/or 10.0 µg/dL. This study reports mean BLLs of children from Flint, Michigan, before 2013 and the percentages of BLLs ≥5.0 µg/dL in children from Flint, Michigan, before 2013 and thus, provides a complete assessment of their lead exposure. In addition, this study includes blood lead concentrations of children from Flint, Michigan, for a prolonged time period that includes years before, during, and after their exposure to Flint River drinking water.

Methods

We conducted a retrospective study of BLLs from a population sample of children aged ≤5 years residing in Flint, Michigan, over an 11-year period from 2006

BBL	Blood lead level
CDC	Centers for Disease Control and Prevention
DWA	Detroit Water Authority
GM	Geometric mean
HMC	Hurley Medical Center

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to 2016. Hurley Medical Center (HMC) contains the regional children's hospital and is the major single source that analyzes pediatric BLLs in Flint. In the medical center databases, 2006 is the earliest year available for analysis and allows for a decade-long examination of BLLs. The first full year following cessation of exposure to the Flint River water is 2016. All blood samples were collected at the medical center or sent to the institution from participating medical practices. Primary care doctors affiliated with this institution provide primary care clinical services for the majority of Medicaid-enrolled children in the region. BLLs associated with home addresses were obtained through the Epic EMR (Epic Systems Corporation, Verona, Wisconsin) for 2012-2016. Other databases were used to access BLLs at the medical center before 2012.

We verified that all samples in the database had a subject with a matching home address within Flint boundaries for all years tested. If a subject had more than 1 BLL obtained during any 1 year studied, only the single greatest value was retained for analysis to avoid having >1 BLL per child for that year and to match previously used methodology using HMC data.[10] All data were reviewed, cleaned, and manually de-duplicated, and each tested child was assigned a unique identifier based on individual demographics including sex, date of birth, and home address. All BLLs were analyzed in Warde Medical Laboratory, Ann Arbor, Michigan, by using atomic absorption spectrophotometry; electrothermal atomizer methodology (Zeeman Atomic Absorption Spectrophotometer, Model AA280Z; Agilent Technologies, Santa Clara, California), which was coupled with the graphite tube atomizer (Model GTA120). The detection limit of the method used was 0.5 µg/dL. Therefore, we conservatively assigned a value of 0.4 µg/dL to the BLL of any child with an undetectable BLL. The study was approved by the institutional review board of the medical center (HMC) where the data were obtained.

Outcome Measures

Changes in the percentage of BLLs ≥5.0 µg/dL and in geometric mean (GM) BLLs in children were analyzed. We opted to use GM BLLs to evaluate BLLs instead of arithmetic means because the CDC uses GM data to analyze population exposure to environmental toxins in blood.[12] GMs are used specifically to provide a better estimate of central tendency for data that are distributed with a long tail at the upper end of the distribution.[13] The CDC used national estimates of GMs based on data from the National Health and Nutrition Examination Survey to determine the current CDC reference value of 5.0 µg/dL for BLLs.[14]

We evaluated BLLs in children aged ≤5 years from January 1, 2006, through December 31, 2016. Geocoded addresses were used to determine trends over time in BLLs inside the boundaries of Flint, Michigan. The switch to Flint River water exposure occurred on April 25, 2014, and the switch back to the Detroit Water Authority (DWA) occurred on October 15, 2015. Our results include data obtained over a full year (2016) after the switch back to the DWA and controlled for seasonal variability of BLLs.[15]

Statistical Analyses

We first computed estimates of BLL percentages greater than the CDC reference level of 5.0 µg/dL based on the data for each of the years between 2006 and 2016. Differences in the percentages between years were assessed by performing pairwise comparisons. This analysis accounted for the possibility that some children might have had multiple BLL tests over the 11 years studied. The SEs of the differences in the percentages arising from these pairwise comparisons allowed for the possibility that blood samples of a given child may have been measured multiple times, introducing non-zero covariances among observations in the data. Essentially, a child with the same medical record number was treated as a cluster of related observations when estimating the SEs of the differences in the percentages.

The percentages of elevated BLLs from different years were compared formally by computing an estimate of their difference, along with a delta method[16] estimate of the SE of the difference (once again allowing for clustering of repeated measures on the same child across any 2 years); forming a test statistic defined by the estimated difference divided by its standard error; and forming a 95% CI for the difference. The null hypothesis that the difference in percentages for any 2 given years was zero was tested formally by comparing the test statistic with a standard normal distribution to compute a 2-tailed *P* value. Comparisons of the aforementioned percentages and the GM BLLs between 2006 and all succeeding years through 2016 were performed to globally understand the magnitude of the BLL changes over this time frame. Percentages of elevated BLLs and GM BLLs in 2012, 2013, 2014, and 2015 were compared with those in the succeeding year. Percentages and GM BLLs in 2013 (last prewater switch year) also were compared with those in 2015 (first postwater switch year).

A modified Bonferroni[17-19] adjustment, which is known to be less conservative than a full Bonferroni adjustment, was applied to all *P* values from these comparative analyses to account for the multiple year or period comparisons performed. The Bonferroni adjustment is an adjustment made to *P* values when multiple pairwise comparison tests are being performed simultaneously on a single data set and reduces the chances of making a Type I error when performing the multiple comparisons. We sought to perform a large number of pairwise comparisons of the percentages of BLLs ≥5.0 µg/dL and GM BLLs of interest (14 comparisons for each statistic). Applying a standard Bonferroni adjustment for these multiple pairwise comparisons would require a given comparison to produce a *P* value of .05/14 = 0.003571 for a difference to be deemed significant, using the standard .05 level of significance. This approach was deemed to be extremely conservative and would have limited our statistical power to detect differences that may have been important in magnitude. All analyses were performed with commands in the Stata software (Version 14.2; StataCorp LLC, College Station, Texas).

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Table. Demographic summary for 2012-2016

Flint study demographics	2012	2013	2014	2015	2016
Number of children	1379	1151	1182	1316	2421
Race/ethnicity, %					
African American	71	72	73	70	71
Caucasian or other	29	28	27	30	29
Mean age, y	2.3	2.3	2.3	2.3	2.5
Male, %	53	51	51	49	52
Medicaid insurance, %	NA	94	91	87	88

NA, not available.
Details from HMC legacy databases other than age, n, and sex are not available before 2012. The authors suspect the extensive media coverage of the Flint River water switch may have resulted in the larger n in 2016.

Results

Between 2006 and 2016, 15 817 BLLs of children in Flint, Michigan, were available for analysis, with the number per year ranging from 1151 in 2013 to 2421 in 2016. The population studied had a mean age of 2.4 years, and 52% of the samples were from male children (Table). Information regarding race, ethnicity, or Medicaid status was not available before the introduction of the Epic EMR in 2012. Medicaid insurance status collection through Epic EMR began in 2013. From 2013 to 2016, 88% of children were insured through Medicaid (Table). Children insured by Medicaid, a government-funded health coverage program for low-income individuals and families, are typically at greater risk of lead poisoning.[20] Federal regulations mandate that Medicaid-enrolled children be tested for lead at the age of 1 and 2 years or at 3 through 5 years of age if not previously tested.[20]

Percentages and GM BLLs Over Time

BLL percentages equal to and greater than the CDC reference level of 5.0 μg/dL for 2006 through 2016 are shown in Figure 1. From 2006 to 2016, there was a 72.9% decrease in the percentage of BLLs ≥5.0 μg/dL in children from Flint, Michigan. A steady decline in the percentage of children above the reference level was observed from 2006 (11.8%) through 2016 (3.2%) (95% CI 6.7-10.4; $P < .001$). Focusing on the years immediately proximate to the Flint River water switch, a percentile decrease occurred from 2012 (4.1%) to 2013 (2.2%) (95% CI 0.6-3.2; $P = .006$), before the Flint River water switch. The well-publicized increase noted from 2013 (2.2%), before the Flint River water switch to 2015 (3.7%) during the Flint River water exposure, although significant at the .05 level when not accounting for the multiple pairwise comparisons performed, did not reach significance after we applied the post hoc modified Bonferroni adjustment (95% CI −2.8 to −0.3; $P = .019$). All other changes between adjacent years from 2012 to 2016 did not reach statistical significance in this study.

GM BLLs of children aged ≤5 years residing within Flint, Michigan, boundaries from 2006 through 2016 are shown in Figure 2. There was a 50.6% decrease in GM mean BLLs from

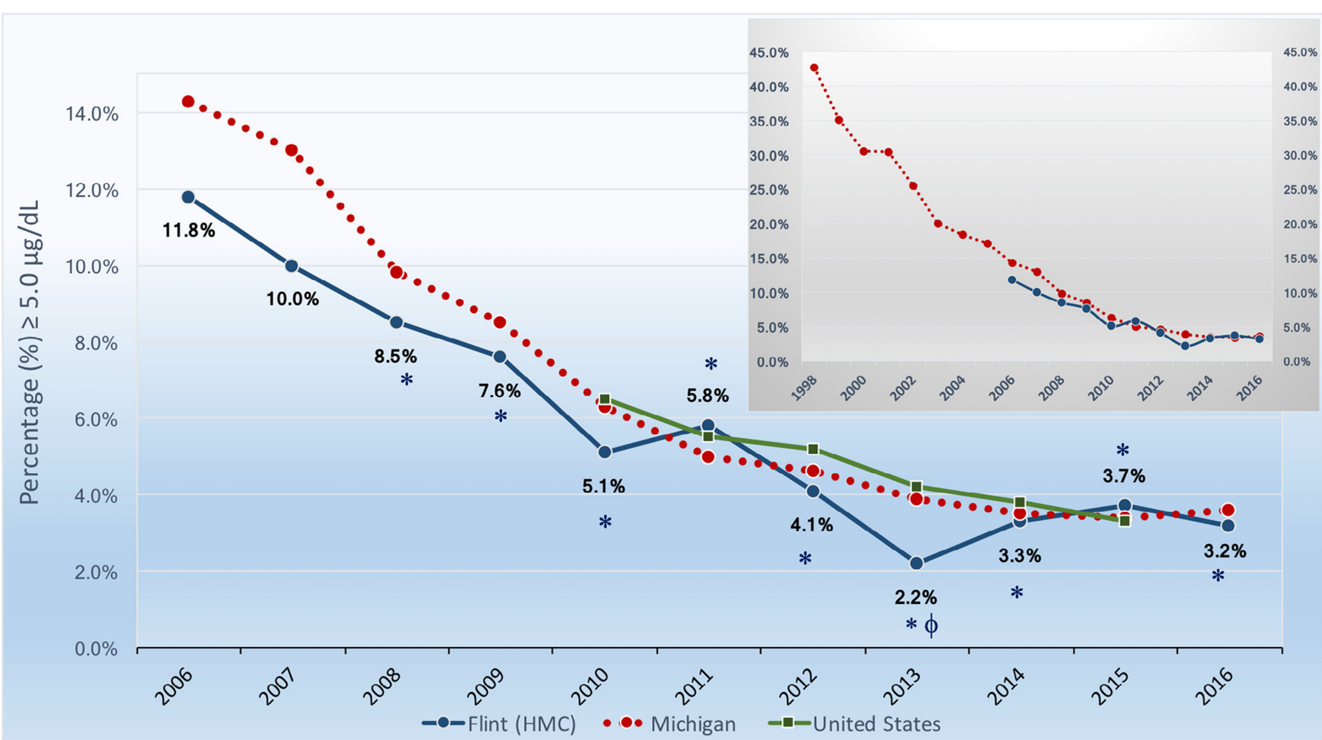

Figure 1. BLL percentages in children ≤5 years of age greater than the CDC reference level (≥5.0 μg/dL) for 2006-2016 (Flint), 2006-2016 (Michigan),[21,22] and 2010-2015 (US).[23] Inserted graph shows Michigan percentages to 1998.[21,22] *Bonferroni-adjusted significance vs 2006. ϕ = Bonferroni-adjusted significance vs 2012.

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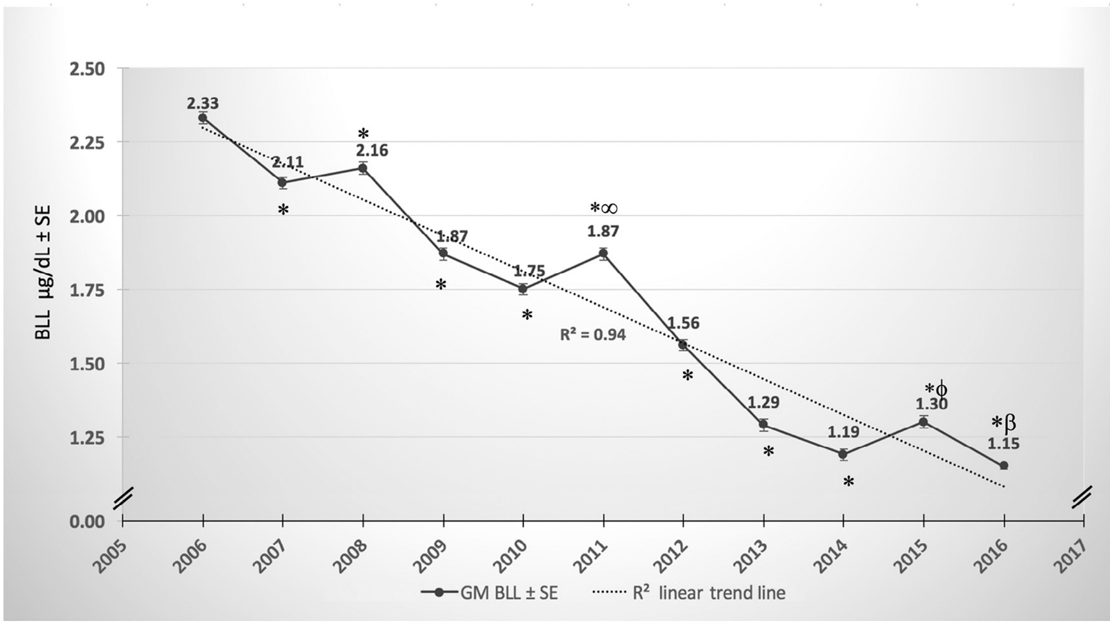

Figure 2. GM BLL (µg/dL ± SE) of children ≤5 years residing within Flint boundaries, 2006-2016. *Bonferroni-adjusted significance vs 2006. ∞Bonferroni-adjusted significance vs 2010. ϕ = Bonferroni-adjusted significance vs 2014. β = Bonferroni-adjusted significance vs 2015.

2.33 ± 0.04 µg/dL in 2006 to 1.15 ± 0.02 µg/dL in 2016 (95% CI 1.08-1.26; $P < .001$). An increase in GM BLLs was observed from 2010 (1.75 ± 0.03 µg/dL) to 2011 (1.87 ± 0.03 µg/dL) (95% CI 0.05-0.20; $P < .001$) 4 years before the water supply switch. An increase also was observed from 2014 (1.19 ± 0.02 µg/dL) to 2015 (1.30 ± 0.02 µg/dL) (95% CI 0.05-0.19; $P < .001$) during the Flint River water switch. GM BLLs then decreased to 1.15 ± 0.02 in 2016 (95% CI 0.10-0.20; $P < .001$).

In Figure 2 we included the fit of a simple linear regression model (with year predicting the GM), along with an R-squared value (0.94) quantifying the fit of this simple model. Figure 3 further shows the changes during the "critical years" before, during, and after Flint River water exposure. The distribution of BLLs in clearly defined intervals is shown, with the inclusion of years just before the water switch (2012, 2013), the years of the Flint River water exposure (2014, 2015), and the first full year after the switch back to the Detroit Water Authority (2016). We note that a combination of annual changes in lower BLLs (≤2.0 µg/dL) combined with a modest number of elevated BLLs ≥5 µg/dL contributed to the GM BLL differences observed between the years 2012 and 2016.

Discussion

This investigation demonstrates a substantial decline in both the percentage of BLLs ≥5.0 µg/dL (Figure 1) and GM BLLs (Figure 2) in children in Flint, Michigan, from 2006 through 2016. The pairwise percentage increases noted in Figure 1 in years 2010-2011, 2013-2014, and 2013 vs 2015 were not statistically significant. However, there was a significant pairwise decrease from 2012 (4.1%) to 2013 (2.2%), the year immediately before the Flint River water switch of 2014.

There was a significant interruption in the declining GM BLL trend in 2 years: an increase of 0.12 µg/dL during 2010-2011 that clearly predates the Flint River water switch with another transient increase of 0.11 µg/dL during the Flint River water years of 2014-2015. The observed R-squared value of 0.94 in a simple linear regression model predicting the GM with year suggests that there is a very strong linear association between the variable "year" studied and GM BLL, with year explaining 94% of the variation in the observed GM BLLs over time. We observe small deviations (in both directions) around this fitted trend line in each year, suggesting that the overall historical trend is very close to linear and characterized by what is essentially random variation in the GM BLL for each year.

The random variability of the data suggests that, whereas no child should have been unnecessarily exposed to drinking water with elevated lead concentrations, changes in GM BLLs in young children in Flint, Michigan, during the Flint River water exposure did not meet the level of an environmental emergency. We note that not a single BLL from a child ≤5 years of age attained a BLL of 45 µg/dL (or greater), the minimum level for which the current CDC guidelines suggest initiation of chelation therapy during the switch to the Flint River water source. In addition, no child was hospitalized in the area for acute or chronic lead toxicity during this time frame.

Historically, the overall decline of BLLs in Flint, and the State of Michigan, during the 11-year study period (Figure 1) is the result of more than a half century of successful major public health initiatives to reduce lead exposure in the US.[24,25] During

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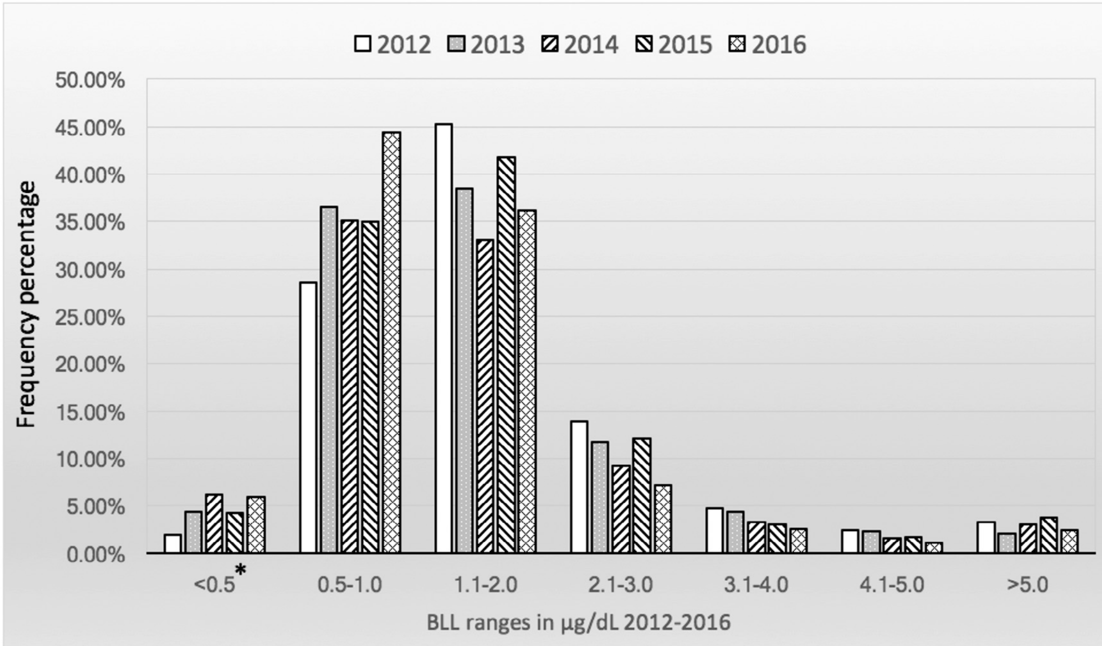

Figure 3. Frequency percentages of BLLs in defined intervals; years 2012-2016. *Undetectable BLL by atomic absorption spectrophotometry.

the 1970s and 1980s, a series of legislation was enacted to phase out lead in consumer products, including the Lead-based Poisoning Prevention Act (1971), phase out of leaded gasoline (1973), and ban of lead in plumbing (1986).[24,25] Additionally, lead-abatement measures have led to reduced dust lead loadings on windows and floors.[26] In 1991, the Environmental Protection Agency released the Lead and Copper Rule to provide guidance for monitoring these metals in drinking water at consumer taps.[27]

The CDC has responded to the accumulated evidence of adverse effects associated with environmental lead exposure by lowering the BLL reference concentration periodically over the last 60 years. Between 1960 and 1990, the BLL reference concentration was gradually lowered from 60 µg/dL to 25 µg/dL.[24,25] In 1991, the CDC lowered the reference concentration to 10 µg/dL and in 2012 to the current value of 5 µg/dL.[24,25] This reference concentration, originally intended by the CDC as a tool to identify children at greater risk, has been frequently misinterpreted as a definitive threshold of lead toxicity or poisoning.[24,25] These and other measures sharply reduced the prevalence of BLLs ≥10 µg/dL in US children aged 1-5 years from nearly 90% in 1976 to 0.8% of children ≥10 µg/dL in 2010.[28,29] Despite these public health measures, the current percentage of children with BLLs ≥ 5.0 µg/dL varies considerably by city and state.[4]

Our analysis of BLLs in children in Flint, Michigan, beginning with 2006, shows an overall decline in BLLs in Flint largely due to the state and federal public health efforts described previously. Overall, there was a 72.9% decrease in the percentage of children with BLLs above the current CDC reference value of ≥5.0 µg/dL from 2006 to 2016. The percentage of BLLs ≥ 5.0 µg/dL declined from 11.8% in 2006 to a statistically significant nadir of 2.2% in 2013, before the Flint River water switch. Data before 2006 were not available for study from our medical center databases; however, in the State of Michigan, using publicly available data, we found the percentage of BLLs ≥5 µg/dL decreased from 42.7% in 1998 to 3.5% in 2014, 3.4% in 2015, and 3.6% in 2016 (**Figure 1**).[21,22] This investigation shows that in Flint, during the Lead and Copper Rule violation, the downward trend of declining BLL transiently regressed to levels noted in the year 2012, when the percentage ≥5.0 µg/dL was 4.1% (**Figure 1**).

Media coverage of Flint has increased national awareness of the important public health issue of lead exposure of young children.[30] Other areas in Michigan have not fared as well as Flint. The following Michigan counties had greater percentages of BLLs ≥5.0 µg/dL than Flint during the 2015 Flint River water switch year: Jackson 5.1%, Lenawee 10.0%, Mason 6.5%, Menominee 5.1%, Kent 6.6%, as well as the City of Detroit 7.5%.[31] Kent County includes Grand Rapids, the second largest city in Michigan.

On October 16, 2015, the Flint water source was switched back to the DWA, which obtains its water from one of the Great Lakes (Lake Huron). Residents were instructed to use filtered tap water for cooking, and increased consumption of bottled water was encouraged.[11] Data from the Environmental Protective Agency and Virginia Tech have shown significant progress with water lead levels in Flint substantially decreased since

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the implementation of corrective measures.[31] The steady decline in GM BLLs of children in Flint, Michigan, from 2.33 μg/dL in 2006 to 1.15 μg/dL in 2016 is a 50.6% decrease of 1.18 μg/dL. GM BLLs increased in 2 time frames in this study; from 1.75 μg/dL in 2010 to 1.87 μg/dL in 2011, and from 1.19 μg/dL in 2014 to 1.30 μg/dL in 2015. These are differences of 0.12 μg/dL and 0.11 μg/dL, respectively. One increase occurred several years before the water switch and the other coincided with the switch to Flint River water. The neurologic impact of a GM BLL elevation of 0.12 or 0.11 μg/dL over a period as brief as 12 months has never been studied and the hypothesized effects of very low lead levels on IQs in young children was questioned in a recent analysis.[32] From a historical context, the larger and prolonged GM BLL decline of 1.18 μg/dL from 2006 to 2016 is of a magnitude and duration that may have benefited young children in Flint.[5,6] We suspect that if mean BLLs in Flint followed the trend noted in the rest of the state of Michigan, the public health benefit of the decline in mean BLLs likely extends to years before 2006 (**Figure 1**). Effects of mitigation efforts before and during 2016, the first full year studied after the water switch back to the DWA, resulted in the lowest GM BLL for young children in the history of Flint (1.15 μg/dL).

For a community struck with hardship and the recipient of negative news over 3 years regarding lead-contaminated drinking water, this investigation reveals that, whereas the GM BLL increased during the Flint River water switch, the increase was no greater than the random increase noted from 2010 to 2011, and GM BLLs in Flint have since returned to historical lows. These findings suggest that, while taking into account the elevation of BLLs in children in Flint, Michigan, during the exposure to Flint River water, public health efforts to reduce BLLs of children in Flint, Michigan, have been largely effective over the 11-year period studied.

Lead exposure comes from many sources, such as older housing containing lead-contaminated paint, water, dust, or soil. We did not have any method to determine the extent to which various lead sources may have contributed to changes in BLLs from 2006 to 2016. There was a small elevation of GM BLLs of children from 2010 to 2011 and during the Flint River water switch, although our study was not designed to prove a causal relationship to exposure from specific lead sources, nor was it intended to evaluate socioeconomic factors for lead exposure such as race, ethnicity, poverty, and age of housing. Although HMC-affiliated clinics and physicians are the primary source of care of high-risk children in Flint, Michigan, who are exposed to lead, our data do not account for every BLL of every child in Flint. Based on CDC data, we estimate that our investigation accounts for approximately 50% of BLLs in children in Flint, Michigan, during 2006-2016.[11] Few children aged <1 year were tested, and no child tested was young enough to be formula dependent. Therefore, changes in BLLs in the very young from water used in formula preparation during 2014-2015 Flint River water switch cannot be determined.

The use of Flint River water from April 25, 2014, to October 15, 2015, in Flint coincided with an increase in BLLs of young children in Flint, Michigan. This investigation reveals that BLLs during the Flint River water exposure did not exceed values found before 2013. Over the 11-year period of 2006-2016, there was a 72.9% decrease in the percentage of children with BLLs ≥5.0 μg/dL and a 50.6% decrease in GM BLLs. A random and quantitatively similar increase in BLLs occurred in 2010-2011, which was 4 years before the Flint River water switch. These findings suggest that public health efforts to reduce BLLs of young children in Flint have been effective over the 11-year period studied. Nevertheless, public health officials, legislators, and clinicians should continue efforts and allocate appropriate resources to continue reducing environmental lead exposure of children in all communities at risk. ■

Formal statistical analysis of the data was performed by staff of the Consulting for Statistics, Computing & Analytics Research (CSCAR) team of the University of Michigan.

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