The effect of the Environmental Protection Agency maximum contaminant level on arsenic exposure in the USA from 2003 to 2014: an analysis of the National Health and Nutrition Examination Survey (NHANES)

Anne E Nigra, Tiffany R Sanchez, Keeve E Nachman, David E Harvey, Steven N Chillrud, Joseph H Graziano, Ana Navas-Acien

Summary

Background In 2006, the current US Environmental Protection Agency (EPA) maximum contaminant level for arsenic in public water systems (10 µg/L) took effect. We aimed to assess national trends in water arsenic exposure in the USA, hypothesising that urinary arsenic concentrations would decrease over time in individuals using public water systems but not in those using well water (which is not federally regulated). We further estimated the expected number of avoided skin or lung and bladder cancer cases.

Methods In this analysis of the 2003–14 cycles of the National Health and Nutrition Examination Survey (NHANES), we used data for dimethylarsinate (DMA), the main metabolite of inorganic arsenic in human beings, and total urine arsenic to reflect water arsenic exposure in survey participants. To isolate exposure to water arsenic, we expanded a residual-based method to remove tobacco and dietary sources of urinary DMA and total arsenic. We also applied EPA risk-assessment approaches to estimate the expected annual number of avoided skin or lung and bladder cancer cases comparing arsenic exposure in 2013–14 with 2003–04.

Findings We obtained data from 14 127 individuals who participated in the NHANES between 2003 and 2014. Among public water users, fully adjusted geometric means of DMA decreased from 3·01 µg/L in 2003–04 to 2·49 µg/L in 2013–14 (17% reduction; 95% CI 10–24; p-trend=0·001); no change was observed in well water users (p-trend=0·35). Assuming these estimated exposure reductions will remain similar across a lifetime, we estimated a reduction of 200–900 lung and bladder cancer cases or 50 cases of skin cancer per year depending on the approach used.

Interpretation The decrease in urinary arsenic observed in public water but not private well users in NHANES 2003–14 suggests that the implementation of the current maximum contaminant level regulation is associated with reduced arsenic exposure in the US population. Our study suggests that well water users are inadequately protected against drinking water arsenic, and supports the crucial role of federal drinking water regulations in reducing toxic exposures and protecting human health.

Funding The National Institute of Environmental Health Sciences.

Introduction

Arsenic is an established carcinogen naturally occurring in drinking water across the USA. Inorganic arsenic is associated with numerous adverse health outcomes, including lung, skin, and bladder cancers, skin lesions and cardiovascular disease. Drinking water and diet are the main sources of chronic low-level arsenic exposure in the US population. For decades, the US Environmental Protection Agency (EPA) set the maximum contaminant level for arsenic in public water systems at 50 µg/L. In January 2006, the current arsenic maximum contaminant level (10 µg/L) took effect. The compliance determination process allowed additional time to test and address non-compliance for public water systems with mean annual arsenic concentrations exceeding 10 µg/L based on quarterly samples. However, private wells, the main source of drinking water for roughly 45·5 million Americans, are not enforced under the arsenic maximum contaminant level. In 2000, EPA estimated that the excess population risk of lung and bladder cancer at water arsenic concentrations of 50 µg/L were between 1 in 100 and 1 in 300. The effect of the 2006 maximum contaminant level change on individual arsenic exposure in the USA is unknown.

Using data from a national population survey (National Health and Nutrition Examination Survey [NHANES]), we aimed to assess national trends in water arsenic exposure from 2003 through 2014. We hypothesised that urinary arsenic concentrations would decrease over time in participants who relied on public water systems but not in those who used well water. The public NHANES database does not allow public access to geographical information of the participants; however, Mexican-Americans in the USA are more likely to live in the...
Articles

Research in context

Evidence before this study
We searched for articles published in English in PubMed, MEDLINE, and Embase up to July 27, 2017, using the following search terms: “arsenic” AND “EPA” or “Environmental Protection Agency” AND “MCL” or “Maximum Contaminant Level”. We found no studies that assessed the effect of the implementation of the 2006 maximum contaminant level regulation on reducing arsenic exposure at the individual level or by using biomarker data. One study identified through hand search did not assess individual exposure, but found that arsenic maximum contaminant level violations decreased in California after 2010, suggesting that arsenic concentrations in drinking water decreased in California several years after implementation of the current regulation in 2006.

Added value of this study
These novel nationally representative estimates derived from urinary arsenic support that the implementation of the current maximum contaminant level Environmental Protection Agency (EPA) regulation has decreased drinking water arsenic exposure in residents reliant on public water but not in private well users. Well water users remain inadequately protected against drinking water arsenic, especially residents of lower socioeconomic status who are less likely to test for arsenic and maintain treatment systems. Our risk analysis estimates the expected number of avoided skin or lung and bladder cancer cases based on arsenic exposure reductions measured in NHANES.

Implications of all the available evidence
Subsequent research should assess changes in arsenic exposure geographically, by population subgroups, and evaluate the economic and health impact of arsenic exposure reduction.

southwest. In the southwest, many cities’ public water supplies come from water sources with naturally occurring arsenic above the maximum contaminant level (eg, Los Angeles, Albuquerque, Scottsdale, and Tucson) and the enactment of the current maximum contaminant level regulation has resulted in infrastructure investments to ensure water arsenic is lower than 10 µg/L. We therefore hypothesised that the decrease in urinary arsenic concentrations would be more pronounced in Mexican-American NHANES participants.

Methods

Data source and population
In this survey analysis, we analysed data from the 2003–14 cycles of NHANES, a nationally-representative sample of the general non-institutionalised US population. NHANES is conducted by the National Center for Health Statistics which is part of the Centers for Disease Control and Prevention. NHANES employs a multi-stage, cluster-sampling design in 2-year cycles to ensure nationally-representative samples and the evaluation of trends over time. Participants complete an in-person interview, dietary recall, and physical examination. All NHANES protocols were approved by the NCHS institutional review board, and all participants gave written informed consent. Our study was exempt from institutional review board approval because we used de-identified, publicly available data.

Although the change in the maximum contaminant level regulation from 50 to 10 µg/L was initiated in 2006, the compliance determination process under the drinking water arsenic rule allowed time to test and address a level exceedance. Therefore, we studied the effect of the maximum contaminant level on drinking water arsenic concentrations and subsequent exposures by comparing urinary arsenic measurements from NHANES participants in the 2003–04 cycle (ie, before the implementation of the maximum contaminant level change) with those from the 2013–14 cycle, assuming full compliance with the new maximum contaminant level at that point in time.

Additionally, we estimated the expected number of avoidable skin or lung and bladder cancer cases assuming exposure reductions persisted across the lifetime.

Urine arsenic measurements
In the survey, arsenic was measured in spot urine samples in a one-third random subsample of participants aged 6 years and older (n=16 332). Total urinary arsenic concentrations were measured via inductively coupled plasma-mass spectrometry with dynamic reaction cell (ICP-DRC-MS), and speciated arsenic concentrations were established via high-performance liquid chromatography (HPLC) coupled to ICP-MS; these analyses have been described elsewhere in detail.

We used dimethylarsinate (DMA), the main metabolite of inorganic arsenic in human beings, and total urine arsenic to reflect water arsenic exposure. Inter-assay coefficients of variation varied from 2.2% to 6.0% for DMA and from 1.0 to 19.4% for total arsenic. The limit of detection varied from 1.70 to 1.91 μg/L for DMA and from 0.26 to 0.74 μg/L for total arsenic. The percentage of samples below the limit of detection was 17.2% for DMA and 0% for total arsenic. Undetectable DMA was replaced by the limit of detection divided by the square root of two. Arsenite, arsenate, and monomethylarsonate were not studied as their limits of detection were too high and the concentrations for these substances were mostly undetectable. Participants missing DMA, arsenobetaine, total arsenic, BMI, education, urinary creatinine,
dietary recall, or who were pregnant were excluded for a final sample size of 14127.

**Exposure assessment analysis**

Urinary arsenic integrates multiple exposure sources, including water, diet, and tobacco, which are contaminated with arsenic of anthropogenic or natural origins. Seafood contributes high concentrations of arsenobetaine and other largely non-toxic organic arsenicals to urine arsenic.\(^\text{10}\) To isolate exposure to water arsenic, we expanded a residual-based method previously validated to remove the contribution of seafood, to also remove tobacco and other dietary sources of urinary DMA and total arsenic.\(^\text{15}\) Estimated urinary DMA and total arsenic concentrations reflecting water arsenic were obtained by first regressing their original log-transformed concentrations (μg/L) on log-transformed arsenobetaine (μg/L), smoking status (never, former, or current), and past 24-h intake of rice, cereals, juice, wine, chicken, and turkey (log-transformed g/kg bodyweight). The conditional means of urinary DMA and total arsenic among non-smoking participants with undetectable arsenobetaine and no arsenic dietary sources were then added back to model residuals to estimate the amount of urinary DMA and total arsenic that probably represents water arsenic exposure in the US population.

Food intake was derived from past 24-h dietary recalls using recipe codes from the Food Commodity Index Database, averaging commodity weights across all recipe modification codes.\(^\text{21}\) Cereal intake was derived using United States Department of Agriculture food codes only because no Food Commodity Index Database codes exist for cereal. Urinary cotinine is not yet available in the NHANES public database for the 2013–14 cycle, preventing us from using cotinine in addition to self-reported smoking in our correction. The appendix (p 1) shows the distributions of estimated urinary total arsenic and DMA likely due to drinking water.

Geometric means and geometric mean ratios of urinary DMA and total arsenic comparing each subsequent 2-year cycle from NHANES 2003–04 were estimated separately for participants reporting a primary tap water source of “well or rain cistern” (categorised as well water users as rain cisterns are rare) and “community supply” (categorised as public water users) during the interview. Participants who reported not drinking tap water were excluded from this analysis. Geometric means and geometric mean ratios were adjusted for sex, age, race and ethnic origin, BMI, and education. We conducted sensitivity analyses further adjusting for urinary creatinine with similar results (data not shown). All analyses were done with R (version 3.1.2) using the survey package to account for NHANES complex sampling design and weights.\(^\text{15, 14}\)

**Risk analyses**

Although the change in the maximum contaminant level regulation from 50 to 10 μg/L was initiated in 2006, the compliance determination process under the drinking water arsenic rule allowed time to test and address a level exceedance. Therefore, we studied the effect of the maximum contaminant level on drinking water arsenic concentrations and subsequent exposures by comparing urinary arsenic measurements from NHANES participants in the 2003–04 cycle (ie, before the implementation of the maximum contaminant level change) with those from the 2013–14 cycle, assuming full compliance with the new maximum contaminant level at that point in time.

Water arsenic exposure was estimated from both urinary DMA and total arsenic measurements. For total arsenic, we assumed that water arsenic was present solely in the inorganic form and that the ratio of urinary arsenic to ingested water arsenic was 1:1 μg/L, based on earlier work in Taiwan and the USA.\(^\text{15, 16}\) In the study population, the mean proportion of DMA in urinary total arsenic was 74%. We thus estimated water inorganic arsenic concentrations by multiplying urinary DMA concentrations by 1.36, assuming that water arsenic exposure is entirely inorganic arsenic.\(^\text{1}\)

Bodyweight-adjusted lifetime average daily inorganic arsenic dose was estimated by multiplying the drinking water arsenic concentration by the mean drinking water consumption rate for individuals aged 21 years and older (only in those who reported consuming tap water) and dividing by the mean adult bodyweight (80 kg).\(^\text{17}\) We estimated cancer risks by multiplying the resulting lifetime average daily inorganic arsenic dose by the EPA Integrated Risk Information System inorganic arsenic cancer slope factor.\(^\text{18}\) Risks were calculated separately using the current slope factor of 1.5 per μg (kg bodyweight-day)\(^-1\), corresponding to skin cancer,\(^\text{19}\) and the 2010 proposed slope factor of 25.7 per μg (kg bodyweight-day)\(^{-1}\) for combined lung and bladder cancers.\(^\text{20}\)

Expected 70-year cancer burdens were calculated by multiplying the estimated risks by the size of the population at risk. Burdens were calculated for the portion of the US population served by public water systems and separately for Mexican-Americans served by public water systems. The size of the US population served by public water systems was calculated by multiplying the 2014 US Census Bureau population estimate (318,563,456 people) by the fraction of the overall NHANES sample served by public water systems (70.3%). The size of the US population served by public water systems was calculated by multiplying the 2014 US Census Bureau population estimate (318,563,456 people) by the fraction of the overall NHANES sample served by public water systems (70.3%). The size of the Mexican-American population was calculated by multiplying the 2014 US Census Bureau population estimate by the Mexican-American fraction (9.4%), and then by the fraction of Mexican-Americans served by public water systems (61.5%). 70-year cancer burdens were divided by 70 to give an annual number of expected cancer cases due to the consumption of arsenic in drinking water. The number of cancer cases avoided as a result of the maximum contaminant level was calculated by subtracting the expected post-maximum contaminant level change 2013–2014 cancer burden from the pre-maximum contaminant level change cancer burden.

See Online for appendix
Table 1: Participant characteristics by NHANES survey cycle

<table>
<thead>
<tr>
<th>Overall (N=14,127)</th>
<th>2003–04 (n=2279)</th>
<th>2005–06 (n=2285)</th>
<th>2007–08 (n=2355)</th>
<th>2009–10 (n=2679)</th>
<th>2011–12 (n=2214)</th>
<th>2013–14 (n=2315)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>39.9 (0.3)</td>
<td>39.3 (0.6)</td>
<td>39.6 (0.9)</td>
<td>40.0 (0.6)</td>
<td>40.1 (0.8)</td>
<td>40.1 (1.0)</td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Female</td>
<td>50.6% (0.01)</td>
<td>51.1% (1.3)</td>
<td>50.2% (1.6)</td>
<td>50.7% (1.3)</td>
<td>50.9% (0.9)</td>
<td>50.8% (0.9)</td>
</tr>
<tr>
<td>Male</td>
<td>49.4% (0.01)</td>
<td>48.9% (1.3)</td>
<td>49.8% (1.6)</td>
<td>49.3% (1.3)</td>
<td>49.1% (0.9)</td>
<td>49.2% (0.9)</td>
</tr>
<tr>
<td>Race or ethnic origin</td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Non-Hispanic white</td>
<td>67.4% (0.1)</td>
<td>71.3% (4.2)</td>
<td>70.7% (3.1)</td>
<td>68.3% (3.6)</td>
<td>65.3% (3.3)</td>
<td>65.1% (3.8)</td>
</tr>
<tr>
<td>Non-Hispanic black</td>
<td>11.8% (0.01)</td>
<td>11.7% (2.2)</td>
<td>11.7% (1.9)</td>
<td>12.3% (2.0)</td>
<td>12.0% (1.0)</td>
<td>12.1% (2.4)</td>
</tr>
<tr>
<td>Mexican-American</td>
<td>9.4% (0.01)</td>
<td>8.6% (2.4)</td>
<td>8.8% (1.2)</td>
<td>9.1% (1.9)</td>
<td>10.0% (2.1)</td>
<td>9.1% (2.1)</td>
</tr>
<tr>
<td>Other, including multiple</td>
<td>11.4% (0.01)</td>
<td>8.4% (1.4)</td>
<td>8.8% (1.5)</td>
<td>10.3% (1.8)</td>
<td>12.7% (1.9)</td>
<td>13.7% (1.4)</td>
</tr>
<tr>
<td>Education</td>
<td></td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>&lt;High school</td>
<td>18.0% (0.1)</td>
<td>18.0% (1.7)</td>
<td>17.9% (1.6)</td>
<td>20.7% (2.1)</td>
<td>18.8% (1.1)</td>
<td>17.8% (2.1)</td>
</tr>
<tr>
<td>High school or equivalent</td>
<td>23.9% (0.1)</td>
<td>28.7% (1.2)</td>
<td>24.9% (1.3)</td>
<td>25.1% (1.5)</td>
<td>23.0% (1.3)</td>
<td>20.1% (2.0)</td>
</tr>
<tr>
<td>&gt;High school</td>
<td>58.1% (0.01)</td>
<td>53.8% (1.8)</td>
<td>57.2% (2.1)</td>
<td>54.3% (2.4)</td>
<td>58.2% (2.3)</td>
<td>62.1% (3.3)</td>
</tr>
<tr>
<td>Smoking</td>
<td></td>
<td></td>
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<tr>
<td>Never</td>
<td>58.2% (0.01)</td>
<td>53.8% (1.8)</td>
<td>56.0% (1.5)</td>
<td>56.7% (1.8)</td>
<td>58.8% (2.0)</td>
<td>59.9% (1.3)</td>
</tr>
<tr>
<td>Former</td>
<td>19.2% (0.01)</td>
<td>19.0% (0.9)</td>
<td>19.4% (1.4)</td>
<td>19.3% (1.1)</td>
<td>18.1% (1.3)</td>
<td>18.7% (1.0)</td>
</tr>
<tr>
<td>Current</td>
<td>22.6% (0.01)</td>
<td>27.3% (1.9)</td>
<td>24.6% (1.3)</td>
<td>24.0% (1.5)</td>
<td>23.2% (1.2)</td>
<td>23.1% (1.3)</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>27.2% (0.1)</td>
<td>27.0% (0.2)</td>
<td>27.0% (0.3)</td>
<td>26.8% (0.2)</td>
<td>27.2% (0.2)</td>
<td>27.3% (0.3)</td>
</tr>
<tr>
<td>Consumption in past 24 h of arsenic-containing foods</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Poultry*</td>
<td>40.5% (0.01)</td>
<td>43.4% (2.1)</td>
<td>44.1% (1.5)</td>
<td>39.8% (1.5)</td>
<td>39.5% (1.3)</td>
<td>39.4% (2.6)</td>
</tr>
<tr>
<td>Rice*</td>
<td>19.9% (0.01)</td>
<td>22.0% (1.8)</td>
<td>22.6% (1.4)</td>
<td>21.7% (1.7)</td>
<td>24.4% (1.5)</td>
<td>15.2% (1.2)</td>
</tr>
<tr>
<td>Juice*</td>
<td>12.3% (0.01)</td>
<td>12.8% (1.4)</td>
<td>13.0% (1.0)</td>
<td>13.1% (0.8)</td>
<td>12.8% (0.6)</td>
<td>13.2% (0.8)</td>
</tr>
<tr>
<td>Wine*</td>
<td>6.9% (0.01)</td>
<td>5.6% (0.9)</td>
<td>7.3% (0.9)</td>
<td>6.3% (1.1)</td>
<td>6.3% (0.8)</td>
<td>8.2% (1.5)</td>
</tr>
<tr>
<td>Cereal*</td>
<td>25.3% (0.01)</td>
<td>22.6% (1.3)</td>
<td>27.3% (1.2)</td>
<td>26.6% (1.5)</td>
<td>27.1% (1.5)</td>
<td>24.8% (1.3)</td>
</tr>
<tr>
<td>Urine arsenobetaine (µg/L)</td>
<td>0.84 (0.04)</td>
<td>1.02 (0.30–5.10)</td>
<td>1.54 (0.28–6.79)</td>
<td>0.70 (0.28–8.18)</td>
<td>0.94 (0.28–6.18)</td>
<td>0.84 (0.04–4.39)</td>
</tr>
<tr>
<td>Public water†</td>
<td>70.3 (0.01)</td>
<td>83.5 (0.04)</td>
<td>64.5 (0.04)</td>
<td>69.6 (0.02)</td>
<td>68.2 (0.04)</td>
<td>68.3 (0.03)</td>
</tr>
<tr>
<td>Well water†</td>
<td>12.7 (0.01)</td>
<td>12.8 (0.03)</td>
<td>17.6 (0.04)</td>
<td>12.3 (0.02)</td>
<td>12.0 (0.03)</td>
<td>12.1 (0.02)</td>
</tr>
<tr>
<td>Urine DMA (µg/L)§</td>
<td>2.63 (1.56–4.22)</td>
<td>2.77 (1.69–4.28)</td>
<td>2.83 (1.82–4.44)</td>
<td>2.88 (1.71–4.49)</td>
<td>2.61 (1.52–4.46)</td>
<td>2.44 (1.39–3.19)</td>
</tr>
<tr>
<td>Urine total arsenic (µg/L)§</td>
<td>4.07 (2.69–6.12)</td>
<td>4.51 (2.99–6.56)</td>
<td>4.39 (2.99–7.67)</td>
<td>4.67 (2.79–7.19)</td>
<td>4.64 (2.97–13.2)</td>
<td>3.32 (1.97–4.66)</td>
</tr>
</tbody>
</table>

For purposes of comparison, risks and burdens were also estimated using the dose-response method and metrics employed in the benefit-cost analysis supporting the establishment of the 10 µg/L maximum contaminant level.13 Adhering to the methods used by EPA, we calculated sex-specific unit cancer risk factors (R cunt) for bladder and lung cancers by dividing 0·01 by the excess doses associated with 1% risk of bladder and lung cancers (ED cunt) and the lower bounds on those doses (LED cunt) from Model 1 as presented by Morales and colleagues.1 This model employs an exponential linear dose effect with a quadratic age effect and does not use a reference population. Using this approach, risk was estimated by multiplying gender-weighted, lung-specific and bladder-specific R cunt (in cases per person per µg/L) by drinking water arsenic concentrations (estimated as described above). Lung and bladder cancer burdens and cases avoided were calculated from risk and population at risk estimates as described above. The appendix (p 3) provides an example derivation for estimating the number of avoided lung and bladder cancer cases using total arsenic estimations.

Role of the funding source The funding source had no role in study design, collection, analysis, or interpretation of the data, writing of the report, or raw data collection. The corresponding author had full access to all of the data and the final responsibility to submit for publication.

Results We analysed data from 14127 participants from the 2003–14 NHANES. Over the 10-year study period, the population in each of the 2-year NHANES cycles became older, more racially and ethnically diverse, and the prevalence of never-smoking and wine intake increased (table I). The percentage of the population served by public water and private well systems remained similar.
Median DMA concentrations for the entire study population were higher before versus after removing dietary and tobacco sources of arsenic (3.46 µg/L [IQR 2.00–5.82] vs 2.63 µg/L [1.56–4.22]); a similar change was observed for total arsenic (7.15 µg/L [3.68–14.99] vs 4.07 µg/L [2.69–6.12]; table 1).

Figure 1 shows the distribution of urinary DMA and total arsenic for both public water and private well users stratified by NHANES survey cycle. After adjustment, the estimated geometric mean of urinary DMA for public water users likely related to drinking water remained similar between NHANES 2003–04 and 2009–10 (3.01 µg/L vs 2.93 µg/L, respectively) but decreased in NHANES 2011–12 (2.64 µg/L) and NHANES 2013–14 (2.49 µg/L) on both the absolute and relative scales (p-trend <0.001; figure 2). For private well users, the estimated geometric mean of total arsenic was lower in 2011–12 than in 2003–04 (2.82 µg/L vs 4.24 µg/L), but it was higher again in 2013–14 (3.23 µg/L; figure 2).

Among Mexican-Americans using public water, between 2003 and 2014, geometric means of DMA decreased (4.06 µg/L to 2.58 µg/L; 36% reduction; 95% CI 25–46; p-trend <0.001) as did total arsenic (6.05 µg/L to 3.18 µg/L; 47% reduction; 95% CI 40–54; p-trend <0.001; table 2).

Based on our estimates of arsenic exposure reduction in the US population served by public water systems, we estimated the actual number of cancer cases avoided by lowering the arsenic maximum contaminant level to 10 µg/L using exposure measurements from NHANES combined with the current and proposed cancer slope factors from the Integrated Risk Information System programme, as well as with drinking water unit cancer.
risk factors employed by the EPA in its benefit-cost analysis in the year 2000 (table 3). We report results to one significant figure to acknowledge the uncertainty in the appropriate cancer dose-response metric used. The appendix provides these results to three significant figures. When using changes in urinary DMA to approximate reductions in drinking water arsenic exposure, the annual reduction in lung and bladder cancer was 200 cases avoided based on the 2000 EPA benefit-cost analysis approach[20] versus 900 cases avoided using the 2010 EPA slope factor.[21] Using the current EPA slope factor,[21] the estimated annual reduction in cases of skin cancer was 50 (table 3). Table 3 provides estimates derived using changes in urinary total arsenic.

Discussion

The decrease in urinary arsenic in public water users in NHANES 2003–14 supports the hypothesis that the implementation of the current arsenic maximum contaminant level regulation has reduced arsenic exposure in the general US population. The decrease was only observed after the 2009–10 cycle, consistent with the reported violations in the state of California and the compliance determination process of the drinking water arsenic rule, which required time for testing and time to address a maximum contaminant level exceedance (eg, change source or install water treatment).[20,21] Exceedance of the maximum contaminant level for the drinking water arsenic rule is based on a running annual average of quarterly samples. Public water systems were allowed up to 1 year of additional sampling time since the 2000 drinking water arsenic rule was based on a running annual average of quarterly samples. Public water systems were allowed up to 1 year of additional sampling time since the 2000 drinking water arsenic rule was based on a running annual average of quarterly samples. Public water systems were allowed up to 1 year of additional sampling time since the 2000 drinking water arsenic rule was based on a running annual average of quarterly samples.

<table>
<thead>
<tr>
<th>Year</th>
<th>N</th>
<th>DMA</th>
<th>Total arsenic</th>
<th>p value for trend</th>
</tr>
</thead>
<tbody>
<tr>
<td>2003-04</td>
<td>257</td>
<td>4.06 (3.93–4.19)</td>
<td>6.05 (5.86–6.24)</td>
<td>p=0.001</td>
</tr>
<tr>
<td>2005-06</td>
<td>300</td>
<td>3.37 (3.27–3.49)</td>
<td>5.23 (5.07–5.40)</td>
<td>0.87 (0.75–1.00)</td>
</tr>
<tr>
<td>2007-08</td>
<td>263</td>
<td>3.67 (3.55–3.79)</td>
<td>5.79 (5.61–5.98)</td>
<td>0.96 (0.82–1.12)</td>
</tr>
<tr>
<td>2009-10</td>
<td>327</td>
<td>3.23 (3.12–3.33)</td>
<td>5.38 (5.25–5.57)</td>
<td>0.89 (0.78–1.01)</td>
</tr>
<tr>
<td>2011-12</td>
<td>160</td>
<td>2.69 (2.60–2.78)</td>
<td>3.54 (3.43–3.65)</td>
<td>0.79 (0.52–0.66)</td>
</tr>
<tr>
<td>2013-14</td>
<td>262</td>
<td>2.58 (2.50–2.67)</td>
<td>3.18 (3.08–3.28)</td>
<td>0.53 (0.46–0.60)</td>
</tr>
</tbody>
</table>

Data are mean (95% CI) unless otherwise stated. Recalibrated urine DMA and total arsenic were obtained from residuals regressing each log-transformed arsenic variable (DMA and total arsenic) on smoking status (never, ever, current), natural log-transformed arsenobetaine, and natural log-transformed intake of rice, cereals, juices, wine, chicken, and turkey in g/kg bodyweight per day. Geometric means were further adjusted for age, education, and BMI. P for trend was estimated by entering each NHANES 2-year cycle in the model as an ordinal variable. NHANES=National Health and Nutrition Examination Survey. DMA=dimethylarsinate.

Figure 2: Geometric means and geometric mean ratios of urine DMA and total arsenic recalibrated to reflect non-dietary and non-smoking sources of arsenic in public water versus well water users stratified by NHANES cycle

Squares and lines represent geometric mean ratio estimates and 95% CIs. Recalibrated urine DMA and total arsenic were obtained from residuals regressing each log-transformed arsenic variable (DMA and total arsenic) on smoking status (never, ever, current), natural log-transformed arsenobetaine, and natural log-transformed intake of rice, cereals, juices, wine, chicken, and turkey in g/kg bodyweight per day. Geometric means were further adjusted for age, race or ethnic origin, education, and BMI. P for trend was estimated by entering each NHANES 2 year cycle in the model as an ordinal variable. DHHS=Public Health Service.
December, 2006, for surface water systems and by December, 2007, for groundwater systems) before a compliance determination was made. This time lag can be observed in California’s public water supply arsenic violation data, which suggest that it took several years for the California public water supply systems to first identify and then comply with the arsenic rule, with violations gradually decreasing after 2008. In view of the built-in time delay of full enforcement of the 10 µg/L maximum contaminant level, the similarity in geometric means for urinary DMA and total arsenic concentrations between 2003–04 and 2007–08 among public water users provides an indication of the amount of natural variability in water arsenic exposure over time, enhancing our confidence in the changes recorded in the later years.

For public water users, we estimated a reduction in water arsenic exposure of 17% from 2003 to 2014, which represents a substantial exposure reduction when applied at the population level. It is unknown whether these positive changes in arsenic prevention have occurred across all US geographic and geological regions because this spatial analysis is not possible with the NHANES public database. However, the decrease was markedly stronger in Mexican-Americans than in the overall population. These findings support that the recent infrastructure investments in many cities in the southwest that focused on ensuring water arsenic was lower than 10 µg/L is associated with reduced arsenic exposure in the population.6

The National Cancer Institute’s Surveillance, Epidemiology, and End Results (SEER) programme estimated 301 530 new combined lung and bladder cancer cases for 2017.24 In its benefit-cost analysis in support of revising the arsenic in drinking water rule, EPA estimated an annual reduction of 37·4–55·7 combined lung and bladder cancer cases at a maximum contaminant level of 10 µg/L.25 The EPA did not quantify the reduction in number of skin cancer cases at the time. Using the same unit cancer risk factor employed in the 2000 EPA benefit-cost analysis for the arsenic maximum contaminant level, we estimated an avoidance of 200 lung and bladder cancer cases using our measured exposure reductions from NHANES, as compared with EPA’s original estimate of 37·4–55·7 avoided cases per year. One explanation for this difference might lie in EPA’s assumptions regarding exposure reduction; in its benefit-cost analysis, EPA assumed that for water systems with arsenic concentrations in excess of 10 µg/L before the implementation of the new maximum contaminant level, post-implementation concentrations would be 8 µg/L.26 In reality, investments made across US public water systems might have been more effective than EPA originally assumed, possibly resulting in reductions in arsenic in water much lower than 8 µg/L.

Table 3: Estimated annual number of cancer cases avoided by lowering the arsenic maximum contaminant level from 50 to 10 µg/L based on estimated arsenic exposure reduction (using DMA or total arsenic) in the US population served by public water systems comparing NHANES 2013-14 with NHANES 2003-04

<table>
<thead>
<tr>
<th>Overall population</th>
<th>Mexican-Americans</th>
</tr>
</thead>
<tbody>
<tr>
<td>Skin cancer</td>
<td>Lung and bladder cancer</td>
</tr>
<tr>
<td><strong>Based on measured urine DMA reduction</strong></td>
<td></td>
</tr>
<tr>
<td>EPA 2000 benefit-cost analysis*</td>
<td>–</td>
</tr>
<tr>
<td>EPA current cancer slope factor†</td>
<td>50</td>
</tr>
<tr>
<td>EPA 2010 proposed cancer slope factor‡</td>
<td>–</td>
</tr>
<tr>
<td><strong>Based on measured urine total arsenic reduction</strong></td>
<td></td>
</tr>
<tr>
<td>EPA 2000 benefit-cost analysis*</td>
<td>–</td>
</tr>
<tr>
<td>EPA current cancer slope factor†</td>
<td>100</td>
</tr>
<tr>
<td>EPA 2010 proposed cancer slope factor‡</td>
<td>–</td>
</tr>
</tbody>
</table>

The original 2000 EPA analysis had estimated 37·4–55·7 annual cases of lung and bladder cancer avoided in the overall US population.25 The number of annual skin cancer cases avoided was not estimated in the original 2000 EPA analysis. *The 2000 EPA benefit-cost analysis used the unit cancer risk factor (also called drinking water unit risk) to estimate the number of cases avoided per year instead of a cancer slope factor. †The current EPA cancer slope factor was established in 1995 for skin cancer only; and it is the only cancer slope factor that has been finalised in the Integrated Risk Information System. ‡The EPA proposed cancer slope factor was proposed by the EPA for combined lung and bladder cancer in 2010 but it has never been finalised. NHANES=National Health and Nutrition Examination Survey.

In view of the lack of consensus (and associated uncertainty) regarding the appropriate cancer dose-response metric, it is probably better to interpret estimations with just one significant figure; the difference between these estimations depends largely on the dose-response metric used. Although the 2010 EPA proposed slope factor has been controversial, it assumes a linear-dose response, which is consistent with the approach used by EPA for most carcinogens, and is supported by the findings of recent studies of arsenic and lung and bladder cancer at low-to-moderate arsenic exposure concentrations in US populations.25,26 Although arsenic is toxic for multiple organs and systems, we did not consider additional non-cancer endpoints, which EPA considered qualitatively. Additionally, EPA’s risk assessment approach does not address the synergistic effects of tobacco smoking status and inorganic arsenic exposure on cancer risk. Given that the proportion of never smokers increased in the US population throughout the study period, it is possible that the current approach overestimates the effect of arsenic reduction on cancer risk. A more sophisticated risk assessment approach could assess slope factors separately for smokers and non-smokers and could consider changes in the population smoking status over time.

Additional analyses are needed to fully assess the potential economic benefits associated with the implementation of the current maximum contaminant level. In 2007, SEER estimated that lung and bladder cancer together result in 2 523 000 years of life lost and a loss of productivity cost of US$40 billion for the US population.27 It is likely that the indirect economic benefit of avoiding 200–900 excess cancer cases per year over several generations experiencing reduced exposure could outweigh the initial capital costs and continuing operation and maintenance costs of implementing arsenic-reduction initiatives for public water systems.
We noted no consistent changes in urinary arsenic concentrations in private well users between 2003 and 2014. However, the results for well-water users should be interpreted cautiously in view of the small sample size within each survey cycle and the possibility that well-water users sampled in NHANES are not geographically representative of the underlying population of well users in the USA because NHANES did not intentionally oversample for this population subgroup, which is markedly smaller in size as compared with the public-water users. While estimated concentrations of urinary total arsenic for well users decreased in the 2011–12 cycle compared with the 2003–04 cycle, these results were not consistent for urinary DMA, the primary metabolite of inorganic arsenic. Although the EPA maximum contaminant level does not apply to private wells, testing and treatment for arsenic in drinking water among US residents relying on private well water differs widely by state and by socioeconomic status. In NHANES, urinary DMA and total arsenic concentrations were lower in well-water users compared with public-water users. No previous study has compared arsenic exposure concentrations in populations served by public water systems or private wells in the USA. The geographic clustering of high-arsenic wells throughout the USA and the challenges to adequately sample the vast US rural areas in NHANES could explain higher inter-survey variability and wider confidence intervals in urine arsenic concentrations in the population served by private wells compared with the population served by community water systems. It has been estimated that 1.7 million Americans are at risk of exposure to arsenic concentrations higher than 10 µg/L and 3.8 million to arsenic concentrations higher than 5 µg/L in household well water. Efforts are needed to protect affected private well water users from arsenic exposure. In New Jersey, for instance, all wells need to be tested for water contaminants (including arsenic in northern counties) as part of any real estate transaction via the Private Well Testing Act, but only about one quarter of private wells in the northern parts of New Jersey have been tested for arsenic through this act. For affected wells, families can receive a no-interest loan to pay for the purchase and installation of a water treatment system. Although the Private Well Testing Act has resulted in the installation of more arsenic treatment systems in northern New Jersey, no state government requires homeowners to install treatment systems to reduce arsenic if test results for arsenic exceed the maximum contaminant level. Moreover, many private well owners who test for arsenic continue to experience drinking water arsenic concentrations greater than the maximum contaminant level due to incorrect or improperly maintained treatment systems. Additional state and federal initiatives are needed to help families sample, test, and address arsenic exposure from unregulated private wells. Nationally representative studies of private well water users are needed to assess whether testing and treatment behaviours have changed over time for the US population.

Additional limitations of this study include the lack of directly measured water arsenic in the study participants and the possibility that our water arsenic estimation method might have incompletely removed other sources of arsenic (eg, airborne arsenic, which is likely minimal). In estimating water arsenic via our residual-based method, we accounted for the contribution of past 24 h intake of arsenic-containing foods (eg, rice, poultry, juices, wine, and cereals) to both DMA and total arsenic. Urinary arsenic concentrations reflect exposure from the previous 1–3 days. In addition to dietary recall bias, it is possible that the 24-h dietary recall method did not fully remove the contribution of arsenic from these dietary sources. Also, because NHANES does not provide public information on the counties selected for sampling in each cycle, we cannot assess whether counties with lower overall arsenic exposure in public water systems were more likely to be recruited in later compared with earlier years.

In conclusion, following the implementation of the 2006 EPA maximum contaminant level regulation, arsenic exposure decreased in public-water users but not in private-well users. Our study supports that residents who rely on public water systems have experienced reductions in drinking water arsenic exposure and confirms the crucial role of federal drinking water regulations in reducing toxic exposures and protecting human health.

**Contributors**
AEN, KEN, SNC, JHG, and AN-A designed the study, AEN, TRS, KEN, and AN-A analysed data. AEN, TRS, KEN, DEH, SNC, JHG, and AN-A contributed to data interpretation and manuscript writing.

**Declaration of interests**
We declare no competing interests. The views and opinions of authors expressed in this article do not necessarily state or reflect those of the US Government.

**Acknowledgments**
This work was supported by the National Institute of Environmental Health Sciences (1R01ES025216, R01ES021367, 5P30ES009089, and P42ES010349). AEN was supported by ST32ES007322.

**References**


The power of environmental protection: arsenic in drinking water

2017 has not been a good year for environmental protection in the USA. President Trump administration is attempting to roll back more than 400 rules and regulations that protect the environment and human health. In addition to announcing their intention to withdraw from the Paris Climate Accord, the administration is undoing the Clean Power Plan, the Clean Water Rule, new source performance standards for oil and gas drilling, and a proposal to ban the neurotoxic organophosphate insecticide, chlorpyrifos. These rollbacks are based on political and economic arguments that focus on the costs of regulation. They echo the long-held position of the Republican Party that environmental protections are unduly burdensome, stifle innovation, and hold back economic growth.

However, it is important to put these arguments into perspective and to consider not only the costs of environmental protections, but also their benefits—the diseases and deaths averted, and the health-care and other costs saved by cleaning up the environment. Calculating the benefits of environmental protection is not easy, because the diseases and deaths prevented by environmental interventions are spread across large populations over many years and the costs of these diseases are buried in health-care budgets, while the costs of regulation are concrete, tangible, and readily counted. Nonetheless such calculations are worth doing because data quantifying the benefits of environmental protection can provide a powerful counterpoint to one-sided arguments that focus solely on the costs of pollution control.

An analysis of the 2003–14 cycles of the National Health and Nutrition Examination Survey (NHANES) reported in The Lancet Public Health by Anne Nigra and colleagues assesses the health benefits of a legally mandated intervention to reduce arsenic concentrations in drinking water in the USA. Arsenic is a major public health problem, and apart from exposures in the workplace, drinking water is the main source of exposure worldwide. The WHO estimates that more than 200 million people worldwide are chronically exposed to unsafe levels of arsenic in drinking water. Especially severe exposures are reported in southeast Asia, notably in Bangladesh, as well as in Taiwan, Chile, Argentina, and in areas of the USA in northern New England and the southwest. Arsenic is a human carcinogen and has been shown to cause dose-related increases in lung, bladder, and skin cancer, and is also associated with cancer of the kidney, liver, and prostate. Arsenic is also linked to diabetes and cardiovascular disease. Prenatal exposure is associated with neurodevelopmental impairment. In 2006, in response to these data, the US Environmental Protection Agency reduced the legally permitted maximum contaminant level for arsenic in drinking water from 50 μg/L to 10 μg/L. However, this intervention applied only to public water supplies, and private wells were exempted.

To take advantage of this unplanned regulatory experiment, Nigra and colleagues undertook a longitudinal analysis of arsenic exposure in the USA comparing changes in exposure levels between consumers of water from public and private supply systems. They obtained data for urinary arsenic concentrations from 14 127 participants from NHANES 2003–04 (before the reduction in the maximum contaminant level) to 2013–14 (ie, analysing six consecutive NHANES cycles). The main finding was that the geometric mean level of dimethylarsinate (DMA), the main metabolite of inorganic arsenic, fell by 17% among consumers of water from public supply systems over the 10-year period (from 3.01 µg/L in 2003–04 to 2.49 µg/L in 2013–14 [95% CI 10–24; p-trend<0.001]). By contrast, no reduction in arsenic exposure was recorded in consumers of water from private wells. The researchers estimate that this intervention could prevent between 200 and 900 cases of lung and bladder cancer in the USA each year.

This is a model analysis of the health benefits that can result from a carefully designed, evidence-based environmental intervention. The findings are consistent with data from previous studies of the health benefits of reducing arsenic concentrations in drinking water. They are also concordant with analyses of the benefits of interventions against air pollution, which have been shown produced major gains both for human health and the economy. Legally mandated improvements
in air quality in the USA since the passage of the Clean Air Act in 1970 have reduced concentrations of six common air pollutants by 70%, and yielded an estimated economic benefit of US$30 (IQR 4–88) for every dollar invested, an aggregate benefit of $1.5 trillion against a total investment of $65 billion since 1970. Moreover these health and environmental improvements occurred during a time when the US GDP grew by nearly 250%.

Government leaders who might be tempted by the siren call of deregulation, blinded by its promised short-term economic benefits, and pressured by powerful vested interests opposed to any form of environmental control, need to pay attention to these findings. Environmental pollution is now recognised to be a major cause of disease, death, and environmental degradation. It was responsible in 2015 for an estimated 9 million deaths, 16% of total global mortality, as well as for 268 million disability-adjusted lifeyears. However, it is far from being an insoluble problem. Interventions to control pollution have been shown to be technically and economically feasible. They include targeted reductions in emissions of pollutants; transitions to non-polluting, renewable sources of energy; the adoption of non-polluting technologies for production and transportation; and the development of efficient, accessible, and affordable public transportation systems. Interventions to control pollution provide an extraordinary opportunity to improve public health and also to slow the pace of global climate change. Pollution prevention is a winnable battle.12

I declare no competing interests.

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