

Estimated burden of disease from arsenic in drinking water supplied by domestic wells in the United States

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ABSTRACT

Well water around the world can be contaminated with arsenic, a naturally occurring geological element that has been associated with myriad adverse health effects. Persons obtaining their drinking water from private wells are often responsible for well testing and water treatment. High levels of arsenic have been reported in well water-supplied areas of the United States. We quantified – in cases and dollars – the potential burden of disease associated with the ingestion of arsenic through private well drinking water supplies in the United States. To estimate cancer and cardiovascular disease burden, we developed a Monte Carlo model integrating three input streams: (1) regional concentrations of arsenic in drinking water wells across the United States; (2) dose–response relationships in the form of cancer slope factors and hazard ratios; and (3) economic cost estimates developed for morbidity endpoints using ‘cost-of-illness’ methods and for mortality using ‘value per statistical life’ estimates. Exposure to arsenic in drinking water from U.S. domestic wells is modeled to contribute 500 annual premature deaths from ischemic heart disease and 1,000 annual cancer cases (half of them fatal), monetized at \$10.9 billion (2017 USD) annually. These considerable public health burden estimates can be compared with the burdens of other priority public health issues to assist in decision-making.

Key words | arsenic, burden of disease, cancer, cardiovascular disease, economic analysis, human health risk assessment

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INTRODUCTION

Arsenic is a naturally occurring element commonly present in the Earth’s crust and was used as a pesticide in the United States prior to 1960. Exposure to arsenic is associated with a wide range of adverse human health effects, including cancers of the skin, lung, liver, bladder, and kidney (NRC 2013). Other effects include skin lesions, inflammation, neurologic impairment in children, hypertension, cardiovascular disease, and diabetes (Naujokas *et al.* 2013). While people can be exposed to arsenic by inhaling contaminated air at certain workplaces or eating certain foods, drinking contaminated water remains a primary route of exposure (Oberoi *et al.* 2014).

Exposure to arsenic via groundwater is a concern in many countries around the world, including Bangladesh, Taiwan, and some areas of Canada and the United States (Naujokas *et al.* 2013). The World Health Organization (WHO) provisional guideline value for arsenic is 10 µg/L (WHO 2011), lowered from 50 µg/L, which is still a challenge to meet in some countries. Drinking water limits are only enforceable by jurisdictions that supply water to communities (Chappells *et al.* 2014). Unfortunately, this standard does not apply to private wells. For example, in 2001, the United States Environmental Protection Agency

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(U.S. EPA) set a maximum contaminant level for arsenic of 10 µg/L that applies to community water systems (i.e., a system serving at least 15 locations or 25 residents year-round) and noncommunity water systems (e.g., schools, residential facilities, and factories), but not domestic wells (U.S. EPA 2001). Domestic wells are the primary source of drinking water for approximately 40 million people or about 13% of households in the United States (NGWA 2017). Nearly 7% of sampled domestic wells in the United States had arsenic concentrations exceeding 10 µg/L (DeSimone *et al.* 2009), with some individual domestic wells in Maine having arsenic concentrations 50 times higher than the limit, exceeding 500 µg/L (Nielsen *et al.* 2010). Treatment systems such as reverse osmosis, activated alumina filtration, and ion exchange can remove arsenic from water at either the point of well water entry to the home or the point of use (i.e., at the tap). However, these systems can be expensive and costs are borne by the well owners who face challenges in implementing such systems (Schmidt 2014). In addition, household arsenic treatment is not completely effective in eliminating arsenic exposure, particularly when the source water concentration is high (Smith *et al.* 2016). An evaluation of arsenic remediation approaches in North America concluded that a key priority was to 'ensure that such cost evaluations fully consider the averted costs to the health care and social welfare system of well water interventions to reduce arsenic and other drinking water contaminants' (Chappells *et al.* 2014). The authors further lamented that no such data were available.

Previous efforts exist to estimate the burden of disease for arsenic. The Global Burden of Disease (GBD) Study examined occupational exposure to arsenic, which is predominantly through the inhalation route of exposure rather than the ingestion route pertinent to private wells (Gakidou *et al.* 2017). A WHO study noted that arsenic, among other exposures, contributed to neonatal effects and cancer, but their assessment was based on an expert survey and not linked to exposure (Prüss-Üstün *et al.* 2016). The authors also noted the role of arsenic in relation to ischemic heart disease (cardiovascular disease primarily due to atherosclerosis or narrowing of the arteries), but did not attempt to quantify this burden. Lokuge *et al.* (2004) did quantify ischemic heart disease, as well as diabetes and skin, bladder, lung, and kidney cancer in terms of deaths

and disability-adjusted life years (DALYs) for high arsenic exposure levels encountered in Bangladesh to evaluate mitigation interventions for arsenic-related and infectious disease. (DALYs combine mortality and morbidity and are often used for comparison across countries, notably in the GBD study.) Similarly, Howard *et al.* (2007) developed a tool to estimate the disease burden (in DALYs) to support decision-making for arsenic mitigation options (e.g., shallow or deep tube well).

In terms of previous studies conducted on private wells in the United States, Kumar *et al.* (2010) modeled arsenic concentrations in domestic wells across seven regions of the country based on data collected during 1976–1996 to estimate cancer risk. They reported an excess lifetime risk of lung and bladder cancer mortality combined of 66 cases per million population or 33 annual deaths for a domestic well population of 40 million and averaged across an 80-year lifetime. The authors did not monetize this public health burden.

In this assessment, we combined expertise across multiple disciplines – environmental science, exposure assessment, toxicology, epidemiology, and economics – to estimate the burden of exposure to arsenic in private wells in the United States. Arsenic exposure in wells was modeled using more refined geographic resolution (12 regions across the United States) and more recent data (1992–2004) than previous estimates. We evaluated cancer endpoints as well as, for the first time for a North American population, ischemic heart disease mortality. The quantified public health burden associated with arsenic in domestic wells – in terms of cases as well as the economic value of avoiding these cases – can help communicate the public health burden of arsenic in domestic wells to decision-makers and inform comparisons with other priority public health issues and mitigation costs.

METHODS

We modeled the public health burden from exposure to arsenic in domestic wells by synthesizing information on (1) arsenic concentrations in domestic well water, (2) health effects due to arsenic exposure, and (3) monetized values of these health effects. We examined mortality

and morbidity endpoints. Our simulation considered the spatial variability in arsenic concentrations and in age- and sex-specific baseline ischemic heart death rates, as well as uncertainty surrounding arsenic concentration distributions and the ‘value per statistical life’ (VSL) distribution. We generated a distribution of burden estimates (in cases and dollars) for 12 regions across the United States, which are summarized using central tendency, lower-bound and upper-bound estimates of the distribution (mean, 5th and 95th percentiles, respectively). Additional modeling details are available with the online version of this paper, in Supplementary Materials Section 1.

Exposure estimation

We obtained estimates of the population that uses domestic wells as a source of drinking water from the U.S. Geological Survey (USGS) National Water Information System data for 2005, which was the most recent year available USGS (2005). This population constituted roughly 13% of

the total 2010 population in the contiguous United States, or 41 million persons. The information was available at the county level; a county is an administrative subdivision of a U.S. State containing, on average, 100,000 persons (U.S. Census Bureau 2010). To characterize arsenic levels in drinking water for this population, we relied on domestic well arsenic sampling data collected during 1991–2004 from the USGS National Water-Quality Assessment Program (DeSimone *et al.* 2009). There were insufficient samples to perform the analysis at the county or state level, so we modeled arsenic concentrations for 12 USGS Ground Water Atlas regions located in the contiguous United States (Miller 1999). The estimates of the domestic well-supplied population by each of the 12 regions are shown in Table 1.

We estimated region-specific distributions of arsenic concentrations using a hierarchical Bayesian model, whose specification closely parallels other Bayesian drinking water contaminant modeling work in the literature (e.g., Lockwood *et al.* 2001; Qian *et al.* 2004). We also generated

Table 1 | Estimated domestic well-supplied population, arsenic concentrations, and monetized burden results in 2017 USD, by the USGS Ground Water Atlas Region

Ground Water Atlas Region definition ^a	Population (thousands) ^b	Estimated distribution of arsenic concentrations ^c				Mean economic burden for all endpoints (millions) ^f
		Median (µg/L)	95th percentile (µg/L)	Percent above 1 µg/L ^d	Percent above 10 µg/L ^e	
Region B: CA, NV	2,889	2.9	17	83	13	\$1,080
Region C: AZ, CO, NM, UT	962	1.9	24	66	14	\$369
Region D: KS, MO, NE	1,312	2.6	17	79	12	\$508
Region E: OK, TX	1,644	0.94	12	48	6.5	\$389
Region F: AR, LA, MS	1,306	0.32	4.9	25	1.9	\$137
Region G: AL, FL, GA, SC	5,188	0.18	2.8	15	0.8	\$271
Region H: ID, OR, WA	2,035	1.2	9.1	57	4.2	\$350
Region I: MT, ND, SD, WY	600	0.48	9.5	34	4.7	\$100
Region J: IA, MI, MN, WI	6,216	0.25	8.2	26	4.1	\$991
Region K: IL, IN, KY, OH, TN	5,947	0.37	37	36	12	\$3,640
Region L: DE, MD, NJ, NC, PA, WV	8,904	0.19	6.8	22	3.4	\$1,220
Region M: CT, ME, MA, NH, NY, RI, VT	4,635	0.23	22	30	8.7	\$1,860
Total for contiguous United States	41,638	0.62	14	35	6.3	\$10,900

^aRegions are defined by states that comprise them. Each state is identified by the two-letter code used by the United States Postal Service. There is no Region A.

^bPopulation size data for 2005 from the USGS National Water Information System were used to estimate the domestic well-supplied population (USGS 2005).

^cAuthors' estimates based on domestic well arsenic sampling data for 1992–2004 from the USGS National Water-Quality Assessment Program (DeSimone *et al.* 2009).

^d1 µg/L is the minimum reporting level in the National Water-Quality Assessment dataset. This is the smallest concentration that can be reliably measured.

^e10 µg/L is the U.S. Environmental Protection Agency's current maximum contaminant level for arsenic in public water systems (U.S. EPA 2001).

^fThe ‘all endpoint’ damage total differs from the sum of the cancer and noncancer totals in Table 3, because it is the mean of the overall damage distribution. Rounded to three significant figures.

estimates of the uncertainty surrounding the central concentration estimates. Details on the concentration modeling, including the region-specific estimates, are provided in Supplementary Materials Section 2 (available online). Table 1 shows select characteristics of the estimated arsenic concentration distributions by the region.

To obtain arsenic exposure distributions for a representative person in each region, we made three assumptions. First, each domestic well serves the same number of persons, so that the distribution of arsenic concentrations over domestic wells is the same as the distribution of arsenic concentrations over the domestic well-supplied population in a given region. Second, each person in the domestic well-supplied population consumes untreated drinking water from the home tap, following age-specific estimates of daily drinking water intake (U.S. EPA 2004). Third, a person is exposed to the same domestic well arsenic concentration over their lifetime.

Our core estimates reflect the public health burden for all nonzero exposures. This is in line with the assumptions made by WHO (2011) for genotoxic carcinogens. In sensitivity analyses, we also estimated the public health burden above a common analytical minimum reporting level of 1 µg/L and above the internationally recognized limit in drinking water of 10 µg/L.

Health effect estimation

We evaluated the weight of evidence linking arsenic exposure (ingestion) with adverse health effects and selected endpoints from those that were deemed to have evidence of a causal association by the U.S. National Research Council (2013). Based on our evaluation, we selected the following health endpoints for inclusion in the burden estimation: skin cancer, bladder cancer, lung cancer, and ischemic heart disease mortality. It should be noted that exposure to arsenic is linked with more adverse health endpoints than the ones we examined, so this should be considered an illustrative analysis and an underestimate of the true burden.

Following convention, we used separate approaches for cancer and noncancer risk assessment, even though there are recommendations to harmonize these approaches (NRC 2009). For cancer risk assessment, we used standard U.S. EPA approaches and assumptions (U.S. EPA 2005).

For noncancer risk assessment, we used an attributable fraction approach (e.g., GBD Study 2016 as described in Gakidou *et al.* (2017)).

In modeling health endpoints, we reflected the sex- and age-related variability in the baseline health conditions. We assumed that the age and sex distribution of the county's domestic well-supplied population in a region paralleled that of the general population at the national level based on U.S. census data (U.S. Census Bureau 2000). We also assumed that there is no time lag between the elimination of arsenic exposure from wells and cessation of health risk.

Lung, bladder, and skin cancer (cancer endpoints)

Exposure to arsenic has been associated with many cancer types, but the strongest and most consistent evidence is for nonmelanoma skin cancers (basal cell carcinoma and squamous cell carcinoma), bladder cancer (transitional cell carcinoma), and lung cancer (non-small cell). Furthermore, skin, bladder, and lung cancers are the three cancer types comprising the top tier of the U.S. National Research Council's hierarchy of health concerns linked with arsenic exposure (NRC 2013).

The U.S. EPA developed estimates of carcinogenic risk from oral exposure to arsenic, the oral slope factor, based on studies conducted in Taiwan comparing the risk of skin cancer in persons exposed to arsenic in drinking water to unexposed controls (U.S. EPA IRIS 1995). For lung and bladder cancer, we calculated the central (rather than upper-bound) oral slope factors from estimates of the effective dose for 1% risk in health effect in a U.S. EPA draft report (U.S. EPA 2010). We converted the central oral slope factors for skin cancer to lifetime drinking water unit risks using standard ingestion and lifetime assumptions (see Table 2). Conceptually, the lifetime excess cancers are the product of the drinking water unit risk, the drinking water arsenic level, and the population. Finally, life expectancy was used to convert lifetime excess cancer cases to annual cancer cases.

We assumed that all cases of nonmelanoma skin cancer were nonfatal since these cases are usually cured before they spread (ACS 2013). To determine the share of fatal cases for lung and bladder cancer, we analyzed data on the distribution of cases at each cancer stage and survival rates by

Table 2 | Summary of dose–response and valuation estimates for arsenic health effects

Health effect ^a	Central estimate of annual risk per 1 µg/L as exposure	Type of statistical case (percent)	Value per statistical case, in 2017 US dollars
Bladder cancer	Females: 2.92×10^{-6b} Males: 3.41×10^{-6b}	Fatal (17) Nonfatal, invasive (8) Nonfatal, noninvasive (75)	10.7 million ^e 37,500 ^f /2,500 ^g 13,700 ^f /900 ^g
Lung cancer	Females: 4.69×10^{-6b} Males: 1.98×10^{-6b}	Fatal (81) Nonfatal, Stage II (2) Nonfatal, Stage I (17)	10.7 million ^e 72,300 ^f /900 ^g 39,300 ^f /900 ^g
Skin cancer	Females: 3.52×10^{-7c} Males: 7.49×10^{-7c}	Nonfatal, squamous cell invasive (63) Nonfatal, squamous cell noninvasive (21) Nonfatal, basal cell (16)	3,200 ^f /400 ^g 1,600 ^f /300 ^g 1,300 ^f /300 ^g
Ischemic heart disease mortality	Ages 0–59: 5.97×10^{-7d} Ages 60+ : 1.84×10^{-5d}	Fatal (100)	10.7 million ^e

^aBladder cancer (transitional cell carcinoma), lung cancer (non-small cell), nonmelanoma skin cancers (basal cell carcinoma and squamous cell carcinoma), and cardiovascular disease (ischemic heart disease and other forms of heart disease mortality as defined by ID-10 I20-25 and I30-52).

^bAnnual drinking water risk per µg/L is lifetime drinking water risk divided by life expectancy (81.1 years for females; 76.3 years for males). Lifetime drinking water risk is computed from the central oral slope factor using an ingestion rate of 2 L/day and a bodyweight of 70 kg. The central oral slope factors are 13.3 (female) and 5.3 (male) for lung cancer; 8.3 (female) and 9.1 (male) for bladder cancer; all units are risk per mg/kg-day. The oral slope factors are calculated from 1% effective dose (ED01) estimates in Table 5-3 of U.S. EPA (2010) as 0.01/ED01.

^cAnnual drinking water risk per µg/L is lifetime drinking water risk divided by life expectancy (81.1 years for females; 76.3 years for males). Lifetime drinking water risk is computed from the central oral slope factor using an ingestion rate of 2 L/day and a bodyweight of 70 kg. The central oral slope factors are 1 (females) and 2 (males); all units are risk per mg/kg-day. The U.S. EPA IRIS entry reports an oral slope factor of 1.5 per mg/kg-day and lifetime drinking water unit risk of 5E-5 per µg/L.

^dAnnual drinking water risk per µg/L is the baseline cardiovascular disease death rate multiplied by $1 - \exp(-\beta\Delta C)$. The value of β of 2.21×10^{-3} is derived from the cardiovascular disease (ICD-10 I20-25, I30-52) mortality HR of 1.29 per 115 µg/L increase in well water arsenic (Chen *et al.* 2011). Baseline ischemic disease death rate per 100,000 is 27.7 for ages 0–59 and 832 for ages 60+ (CDC WONDER National Average for 2010).

^eThe U.S. EPA-estimated VSL of \$4.8 million (in 1990 USD) (U.S. EPA 1999) was adjusted for inflation and real growth between 1990 and 2017.

^fAuthors' cost-of-illness estimate in the year of diagnosis. See Supplementary Materials Section 3 for more information.

^gAuthors' annual cost-of-illness estimate in subsequent years. See Supplementary Materials Section 3 for more information.

cancer stage. All cases of cancer in stages with a low 5-year survival rate (<15%) were assumed to be fatal in the long term. For other cancer stages, the share of fatal cases was one minus the 5-year survival rate (see Supplementary Materials Section 3 for additional details, available online).

Ischemic heart disease (noncancer endpoint)

The top noncancer health endpoints listed in the U.S. National Research Council's hierarchy of effects of arsenic exposure are ischemic heart disease and skin lesions (NRC 2013). As we did not expect skin lesions to figure prominently in the economic valuation of arsenic public health burden, we focused on cardiovascular disease. NRC (2013) further suggested that ischemic heart disease dose–response analysis is possible at low-to-moderate levels of exposure. We selected a study relating arsenic and ischemic heart disease mortality based on the strength of the study design (e.g., prospective cohort, wide range of exposures, validated outcome ascertainment, and specificity of outcome) and additional

guidelines on study selection from Hertz-Picciotto (1995) and Vlaanderen *et al.* (2008). The study by Chen *et al.* (2011) was a prospective cohort study of over 11,000 participants examining cardiovascular disease mortality in Bangladesh. The authors estimated the relationship between arsenic water concentrations and 'ischemic and other forms of heart disease mortality' using Cox proportional hazards models, controlling for sex, age, body mass index, smoking status, educational attainment, and urinary creatinine. For the International Classification of Disease (ICD) codes I20-I25 and I30-I52, Chen *et al.* (2011) reported a hazard ratio (HR) of 1.29 (95% CI: 1.10–1.52) per 115 µg/L change in arsenic well water concentration (see Table 2).

The functional relationship between the HR and the risk coefficient, β , which reflects the impact of the arsenic exposure change, ΔC , on the baseline death hazard, is $HR = e^{\beta\Delta C}$. A value of β , or $\ln(HR)/\Delta C$, corresponding to the Chen *et al.* (2011) results listed above is 2.21×10^{-3} per µg/L. We estimated the number of ischemic heart deaths attributable to arsenic exposure via drinking water as a

product of (1) the attributable fraction, assuming 100% population exposure, $(HR - 1)/HR$ or $1 - e^{(-\beta\Delta C)}$, (2) the baseline ischemic heart disease mortality rate, and (3) the size of the affected population. While the same β was applied to the entire population, the ΔC was based on our Bayesian model which varied across and within the 12 regions. The region-specific ischemic heart disease death rate estimated using 2010 U.S. county-level ischemic heart disease death rates from CDC WONDER (Centers for Disease Control & Prevention 2016) and other demographic data as described in Supplementary Materials Section 4 (available online).

Economic valuation

We followed standard environmental economic methods to value the public health burden, treating fatal (mortality) and nonfatal (morbidity) cases with separate approaches (e.g., U.S. EPA OPEI 2010). We adjusted all nominal monetary values for inflation between the dollar year of the estimate and 2017 dollar year. When applicable, we applied a discount rate of 3%. Table 2 summarizes the mortality (VSL) and morbidity (cost-of-illness) estimates we developed, with additional details below. Additional details on the economic valuation are provided in Supplementary Materials Section 3.

Mortality valuation

To value mortality risk reductions, we used the U.S. EPA's estimate of VSL: the amount that a population is collectively willing to pay to avoid one statistical case of premature death from adverse health conditions related to the environmental pollution. We updated the U.S. EPA's (1999) VSL estimate of \$4.8 million (in 1990 USD) for inflation and growth in real income between 1990 and 2017. The mean VSL estimate for 2017 used in this analysis is \$10.7 million (in 2017 USD). Our modeling also reflects uncertainty in the VSL estimate. For example, the 95% confidence interval is \$0.9 million to \$28.2 million (further described in Supplementary Materials Section 3.1).

Morbidity valuation

'Willingness to pay' is the theoretically preferred valuation approach for morbidity risk reductions, but there were no

available estimates for the nonfatal cancers of interest. Therefore, we used a 'cost-of-illness' approach, which estimates a reduction in the economic burden of a disease per avoided statistical case of this disease. A disease-specific cost-of-illness estimate comprises medical costs and 'opportunity costs' of time lost to treating the disease, based on typical treatment profiles for each disease and recent health services and labor market data. Notably, the cost-of-illness valuation method cannot value the pain and suffering associated with the disease, which is likely a considerable omission for cancers.

For each cancer type and stage, we estimated (1) medical and opportunity costs in the year of diagnosis and (2) annual medical and opportunity costs in subsequent years. Per-incident costs of skin cancers are the lowest since these are readily treatable, whereas per-incident costs of lung cancer are the highest because lung cancer requires more intensive treatment and often leads to the inability to work. For nonfatal cancer cases, we estimated the present discounted value of medical and opportunity costs based on life expectancy and using a discount rate of 3%.

RESULTS

The public health burden of exposure to arsenic via domestic wells across the United States is estimated as approximately 500 ischemic heart deaths and 1,070 cases of cancer (510 non-small cell lung, 480 bladder, and 80 nonmelanoma skin cancer cases). About half of the cancer cases were fatal. Using standard health economic valuation assumptions, the mean burden corresponded to \$10.9 billion (2017 USD). See Table 3 for the point and range (5th and 95th percentiles) burden estimates.

The range for the case burden reflects uncertainty in the arsenic exposure, while the range for the economic burden reflects uncertainty in the arsenic exposure and VSL estimates. It can be noted (e.g., by comparing the 95th percentile to the 5th percentile) that the range for the monetized health burden is much wider than the range for cases, due to the considerable uncertainty in the VSL estimate used to monetize fatal cases. For example, the 95th to 5th percentile burden estimates ratio for ischemic heart

Table 3 | Estimated number of cases (cardiovascular disease mortality; bladder, lung, and skin cancer) and economic costs (2017 US dollars) due to exposure to arsenic in domestic well drinking water

Health endpoint categories ^a	Number of cases ^b		Economic costs (2017\$, millions) ^c	
	Point estimate	Range estimate (P5–P95) ^d	Point estimate	Range estimate (P5–P95) ^d
<i>Ischemic heart disease mortality</i>	500	(395–576)	\$4,730	(\$663–\$10,200)
<i>Lung cancer</i>				
Fatal	414	(323–486)	\$3,910	(\$544–\$9,030)
Nonfatal: Stage 1	86	(67–101)	\$4.06	(\$3.17–\$4.76)
Nonfatal: Stage 2	11	(8–12)	\$0.84	(\$0.658–\$0.990)
Total	511	(398–599)	\$3,920	(\$548–\$9,040)
<i>Bladder cancer</i>				
Fatal	82	(64–96)	\$774	(\$108–\$1,790)
Nonfatal: invasive	39	(30–45)	\$2.29	(\$1.79–\$2.69)
Nonfatal: noninvasive	359	(280–422)	\$7.81	(\$6.09–\$9.16)
Total	480	(374–563)	\$784	(\$115–\$1,800)
<i>Skin cancer</i>				
Nonfatal: basal cell	14	(11–16)	\$0.05	(\$0.0422–\$0.0635)
Nonfatal: squamous cell invasive	52	(41–61)	\$0.35	(\$0.269 – \$0.405)
Nonfatal: squamous cell noninvasive	17	(13–20)	\$0.07	(\$0.0526–\$0.0792)
Total	83	(65–97)	\$0.47	(\$0.364–\$0.548)

^aIschemic heart disease (defined by ICD-10 I20-25 and I30-52), lung cancer (non-small cell), bladder cancer (transitional cell carcinoma), and nonmelanoma skin cancers (basal cell carcinoma and squamous cell carcinoma).

^bCase values were rounded to the nearest whole number.

^cValuations were rounded to three significant figures.

^d5th–95th percentile range (P5–P95) reflects uncertainty in arsenic exposure for nonfatal health endpoints and uncertainty in exposure and the VSL for fatal health endpoints.

disease is approximately 1.5 for cases but 15 for the monetized burden.

The main estimates presented here reflect all nonzero arsenic well exposures. We also conducted our analysis considering only exposures above 1 µg/L (the reporting level in the USGS arsenic concentration dataset) and above 10 µg/L (the drinking water standard adopted by the U.S. EPA and the provisional guideline proposed by the WHO). With those assumptions, the monetized public health burden was reduced from \$10.9 billion to \$9.9 billion and \$6.6 billion, respectively. (All estimates are presented in 2017 USD.)

The mean economic costs across the four health endpoints considered are summarized in the last column of Table 1, by the geographic region and for the United States. The monetized public health burden was dominated by mortality, because fatal cases were monetized using a much larger value (i.e., the VSL) than nonfatal cases (i.e., the disease-specific cost-of-illness estimates). The annual

fatal cases of 1,000 were nearly equally split between cancer deaths and ischemic heart disease deaths. For these reasons, nearly half of the monetized public health burden came from ischemic heart disease mortality. While the number of lung cancer cases was nearly the same as the number of bladder cancer cases, lung cancer's higher 5-year fatality rate (81% versus 17%) resulted in a larger share of monetized public health burden from this cancer type. The monetized public health burden from nonmelanoma skin cancer (\$0.466 million) was by far the lowest of the health endpoints considered, mainly because this type of cancer is usually nonfatal and the cost-of-illness estimates applied to nonfatal cases are so much less than the VSL estimate applied to fatal cases.

Overall, the regional distribution of the public health burden from domestic well arsenic reflects the regional patterns in domestic well population size, arsenic levels, and baseline ischemic heart disease mortality. However,

the overall public health burden from arsenic in domestic wells appears to be driven by 'hotspots', i.e., a few locations with very high arsenic concentrations, rather than by a relatively uniform exposure to arsenic. For example, despite having a relatively low median level of arsenic in domestic well samples, region K (Illinois, Indiana, Kentucky, Ohio, and Tennessee) has the highest public health burden because this region had a very high 95th percentile arsenic concentration (37 µg/L).

DISCUSSION

We estimated a considerable potential public health burden from exposure to arsenic in U.S. domestic wells using conventional risk assessment, attributable fraction, and environmental economic assumptions and approaches. The mean burden estimates – over 1,000 cases of cancer and 500 deaths from ischemic heart disease, with a corresponding dollar figure of \$10.9 billion (2017 USD) – can be compared to remediation costs or to the burden of other well contaminants and priority public health issues.

For context, our economic estimates fall within the range of others reported for priority public health issues in the United States. Namely, the annual costs from five waterborne pathogens were estimated at \$0.97 billion (Collier *et al.* 2012), and those for mercury and lead were \$5 billion and \$51 billion, respectively (Trasande & Liu 2011). Furthermore, we note that cancer and ischemic heart disease are common diseases with high underlying incidence rates. Our estimates of excess skin, bladder, and lung cancer cases resulting from exposure to arsenic in domestic wells represent, respectively, 0.03%, 2%, and 6% of total cancer cases expected in the 2010 domestic well population in the United States (Rogers *et al.* 2010; National Cancer Institute 2014). Similarly, our estimate of ischemic heart disease deaths corresponds to 0.7% of ischemic heart disease deaths expected for the well water-supplied population.

This work makes several important contributions to the literature. While others (e.g., Lokuge *et al.* 2004) have estimated the burden of arsenic in wells in terms of deaths and DALYs, this is – to our knowledge – the first effort to assess the economic value of avoiding the adverse health impacts of arsenic in domestic well drinking water across

the United States. The lack of data to inform cost-benefit analysis of arsenic mitigation options in North America has been pointed out by other researchers (Chappells *et al.* 2014), and this study helps fill that gap.

This is also the first study to consider the endpoint of ischemic heart disease mortality at the low-to-moderate levels of arsenic exposure that are observed in North America and other regions of the world. (Among other health endpoints, Lokuge *et al.* (2004) considered ischemic heart disease to estimate the burden of arsenic in wells for high arsenic exposure levels encountered in Bangladesh). Evidence for the contributing role of metals in cardiovascular disease morbidity and mortality is rapidly progressing (Moon *et al.* 2017; Chowdhury *et al.* 2018), and neglecting it in our burden analysis would have missed half of the dollar figure. This work also provides more geographically resolved estimates than previous efforts to estimate the burden of cancer in private wells for the United States (Kumar *et al.* 2010).

As with all burden simulation studies, there are a number of limitations associated with this analysis. First, we did not account for all of the potential adverse health effects associated with arsenic exposure (e.g., kidney cancer, diabetes, and hypertension) as the evidence relating these effects to low-level arsenic exposures is still evolving (Zierold *et al.* 2004; Navas-Acien *et al.* 2008; Sung *et al.* 2015). Second, our estimates also do not include potential arsenic exposures from food, which is expected to increase the total burden in this population. According to NRC (2013), when drinking water exposures are less than 50 µg/L, most of total exposure comes from food. In our analysis, only 0.8% of the well population was exposed to arsenic levels above 50 µg/L, indicating the importance of exposure from food for those drinking water from private wells.

Third, the association between chronic arsenic exposure and ischemic heart disease at high doses has been well established and the evidence at low-to-moderate doses is growing (Moon *et al.* 2012, 2017; Chowdhury *et al.* 2018). Fourth, we had to assume the male/female and under/over 60-year-old splits using national-level census data as the age and sex distribution of the domestic well-supplied population is not available. While these assumptions are unlikely to match the domestic well mix perfectly, they are unlikely to invalidate our conclusions. Fifth, the USGS

data on arsenic concentration in domestic wells were collected to be representative of average arsenic concentrations in domestic wells nationwide, therefore likely missed many 'hot-spots'. Incorporation of additional information on high-end arsenic concentrations would likely increase the magnitude of public health burden estimates.

Sixth, in converting the oral slope factor estimates to drinking water unit risks, we assumed a fixed consumption of private well water of 2 L/day, which is the default assumption in many human health risk assessments and in the calculations in WHO's (2011) drinking water guidelines, though others have used 1 L/day (Kumar *et al.* 2010). Using the lower consumption rate would have reduced the burden for the cancer endpoints. Furthermore, it is likely that many private well owners did not consume untreated well water. Shaw *et al.* (2006) reported that in a community with known arsenic issues (two-thirds of household wells had arsenic levels above commonly used drinking water limit of 10 µg/L), 18% used a system that was effective at removing arsenic and a similar percentage (16%) consumed only bottled water. Finally, while our simulation reflected all sources of variability and uncertainty we were able to characterize, there remain sources of uncertainty in some modeling inputs that we have no information about (e.g., extrapolating dose–response relationships from one study population to another).

On the subject of the cost-of-illness estimates for non-fatal cancer cases, which were much smaller than the VSL estimates, it should be noted that the cost-of-illness estimates do not capture all components of the burden associated with disease, such as pain and suffering. There are also several uncertainties in the cost-of-illness estimates, such as basing medical costs on typical disease profiles and treatments and using average costs per procedure. Actual medical costs would vary across individuals. Similarly, since opportunity costs cannot be measured directly, we assigned values to time away from normal activities due to the disease and its treatment.

While we presented the results of a modeling analysis using two approaches – human health risk assessment (for cancer health endpoints) and attributable fraction (for noncancer health endpoints), the NRC (2009) has recommended to harmonize cancer and noncancer approaches. Evidence is evolving to do just that. For

example, Baris *et al.* (2016) reported an odds ratio linking well arsenic exposure to bladder cancer in New England. Such a metric would be amenable to an attributable fraction approach, rather than the human health risk assessment approach we used in the present study, and this should be investigated in the future.

Reducing the public health burden from arsenic in domestic wells at the low-to-moderate levels of contamination observed in many regions of the world will be challenging. For example, in the United States, the current location of domestic wells is tracked by individual states with varying resources available to even identify the location of these wells (Backer & Tosta 2011). Furthermore, many domestic well owners in Canada and the United States do not regularly test their wells for contaminants, much less install expensive arsenic removal systems. Further complicating the problem, even in households that have arsenic treatment systems in place, the use of untreated water to make beverages or in cooking could contribute significantly to the total arsenic dose (Smith *et al.* 2016). It is essential that any interventions reflect the uniqueness of a region, as others have demonstrated that there is no 'one-size-fits-all' solution for all regions (Morris *et al.* 2016).

CONCLUSIONS

This simulation indicates a considerable burden from potential exposure to arsenic in private wells in the United States. To be clear, the potential arsenic exposure is primarily at low-to-moderate levels. Specifically, the highest median concentration for the regions we examined was just under 3 µg/L, while a median level previously examined was over 50 µg/L (Lokuge *et al.* 2004).

These burden simulation results help to define the public health burden of arsenic related to domestic well drinking water, providing an indication of the plausible range of the burden. This study can serve as a framework for other jurisdictions who wish to conduct a burden of disease analysis for arsenic in well water. The results can also be used to garner financial and community support for initiatives aimed at reducing arsenic exposure from domestic wells. Moreover, the attributable cases and costs of certain cancers and ischemic heart disease can serve as

inputs in cost–benefit analyses of interventions intended to reduce arsenic exposure, whether the proposed intervention is installing a point-of-use reverse osmosis treatment system, digging a new well, or connecting to an existing community water system.

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