An estimation of the global burden of disease due to skin lesions caused by arsenic in drinking water

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ABSTRACT

The global burden of disease due to skin lesions caused by arsenic in drinking water was estimated by combining country-based exposure data with selected exposure–response relationships derived from the literature. Populations were considered to be exposed to elevated arsenic levels if their drinking water contained arsenic concentrations of 50 $\mu g\ l^{-1}$ or greater. Elevated arsenic concentrations in drinking water result in a significant global burden of disease, even when confining the health outcome to skin lesions. The burden of disease was particularly marked in the World Health Organization (WHO) comparative risk assessment (CRA) 'Sear D' region, which includes Bangladesh, India and Nepal. Unsurprisingly, Bangladesh was the worst affected country with 143 disability adjusted life years (DALYs) per 1,000 population. Although this initial estimate is subject to a large degree of uncertainty, it does represent an important first step in allowing the comparison of the problem relating to elevated arsenic in drinking water to other environmental health outcomes.

Key words | arsenic, DALYs, disease burden, drinking water, exposure estimates, skin lesions

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INTRODUCTION

Arsenic is a metalloid element well known for both its acute and chronic toxicity. Many of the chronic health effects were identified as a result of its medicinal use and occupational exposure (IPCS 2001). The most obvious effects from the long-term ingestion of arsenic are skin lesions (pigmentation and keratosis). Arsenic is also classified as a carcinogen (IARC 2002).

Arsenic-related health effects have been seen following a number of environmental exposures, including mining and smelting activities, burning of arsenic-rich coal and ingestion of drinking water containing elevated levels of arsenic.

In 1993, the World Health Organization specified a provisional drinking-water guideline value for arsenic of 10 $\mu g l^{-1}$ (WHO 1993); this has been retained in the third edition of the drinking water guidelines (WHO 2004). Many national standards, however, still use a value of 50 $\mu g l^{-1}$, at least as an interim measure, and numerous drinking water supplies around the world still have arsenic concentrations in excess of 50 $\mu g l^{-1}$, which is clearly a health concern (NRC 1999; Smith *et al.* 2000; WHO 2004).

Global disease burden estimates can be used for:

- assessing the performance of a country or region in terms of interventions to improve health;
- mapping out geographical or population-specific differences;
- monitoring trends;
- identifying, quantifying and ranking health priorities; and, thus
- informing policy decisions (Prüss & Havelaar 2001).

An accepted metric in disease burden quantification is the disability adjusted life year (DALY), which is a summary measure of population health that combines mortality and morbidity into a single unit (Murray & Lopez 1996). Traditionally, public health policy has concentrated on mortality, with the severity of disease being expressed in death rates or number of years lost due to certain causes.

However, not all diseases lead to premature mortality, but they may still represent a major burden of ill health. DALYs allow comparisons between widely differing outcomes.

This is an initial attempt to examine the adequacy of existing data to underpin quantification of the global burden of disease resulting from elevated arsenic in drinking water.

METHODOLOGY

Arsenic ingestion has been implicated in a number of negative health outcomes. These health outcomes have been extensively reviewed and it has been concluded that exposure to elevated levels of arsenic via drinking water is causally related to skin lesions, peripheral vascular disease and cancer of the lungs, kidney, bladder and skin (IPCS 2001).

Exposure

Data on populations exposed to elevated levels of drinking water arsenic were accessed through a search of the literature using database searches (including Medline and Poltox), bibliographic lists collected from references, the Internet and personal communication. A number of countries retain the $50\,\mu g\,l^{-1}$ arsenic in drinking water standard and most data available within the literature relate to concentrations greater than $50\,\mu g\,l^{-1}$ (Smedley & Kinniburgh 2002). For this reason, levels in excess of $50\,\mu g\,l^{-1}$ were defined as elevated. Arsenic in natural waters reflects local geology and environmental conditions (Smedley & Kinniburgh 2002), while in a small number of cases anthropogenic sources, such as mining wastes, have contributed. The elevated arsenic concentrations, particularly in groundwaters, will vary greatly and will not necessarily affect a whole country. The numbers of people estimated to be exposed in each area were split into age groups assuming the same age distribution as the country population as a whole.

Exposure–response relationship

A literature review was conducted to identify studies on arsenic-related health effects and arsenic concentration in drinking water in order to establish possible exposure–response relationships. A similar literature search technique was used to the one outlined above.

Disease burden

The populations assumed to be exposed to drinking water arsenic concentrations greater than $50\,\mu g\,l^{-1}$ were used in the exposure–response relationships in order to calculate the number of people suffering from arsenic-related health effects. These figures were then used to calculate the number of DALYs attributable to elevated drinking water arsenic, using an adapted DALY calculation template that has been made available by WHO.[1] Country data were combined on a regional basis to derive regional and global estimates.

RESULTS

Exposure

A total of 18 different countries from eight regions[2] were found to have elevated arsenic in their drinking water supplies. These are summarised in Table 1. There were inadequate data to determine the number of people exposed to differing arsenic concentrations greater than $50\,\mu g\,l^{-1}$. Further analysis was, therefore, based on the single country figure shown in Table 1. Where a population at risk estimate is a range, only the highest estimate was used for the disease burden calculation.

Exposure–response relationship

As with most environmental exposures, there are few data on which to base exposure–response relationships. This is further complicated, in the example of arsenic, by having only crude exposure figures. Although a number of studies reporting exposure–response relationships were identified, only those documenting skin lesions in Bangladesh, Inner Mongolia and West Bengal, India (Luo *et al.* 1997; Guha Mazumder *et al.* 1998; Tondel *et al.* 1999), were useful in terms of attempting to estimate disease burden.

[1] www3.who.int/whosis/menu.cfm?path = whosis,burden,burden_manual,burden_manual_other&language = english.

[2] For the purposes of the WHO comparative risk assessment, 14 regions have been identified (Afr D; Afr E; Amr A; Amr B; Amr D; Emr B; Emr D; Eur A; Eur B; Eur C; Sear B; Sear D; Wpr A; Wpr B) based on geographical location and the level of infant and adult mortality.

Table 1 | Principal populations exposed to elevated drinking water arsenic concentrations (adapted from WHO (in production))

Location	Region	Estimated population at risk (i.e. exposed to $>50\,\mu g\,l^{-1}$ arsenic)	Maximum reported arsenic conc ($\mu g\,l^{-1}$)	Comments
Canada	Amr A	Unknown	5,000	Elevated levels linked to mining activity
USA	Amr A	Unknown		
Argentina	Amr B	2,000,000	11,500	
Chile	Amr B	500,000	21,000	$<1{,}000\,\mu g\,l^{-1}$ more typical
Mexico	Amr B	400,000	3,980	
Bolivia	Amr D	20,000	12,600	
Peru	Amr D	250,000	500	
Pakistan	Emr D	Small	>50	
Romania	Eur B	14,000	>50	
Hungary	Eur C	10,000–15,000	330	
Thailand	Sear B	2,000	5,000	Elevated levels linked to mining activity
Bangladesh	Sear D	28,100,100–35,000,000	3,200	
India	Sear D	4,500,000–6,000,000	3,700	
Myanmar	Sear D	13,000 households	>50	
Nepal	Sear D	500,000	2,620	
Cambodia	Wpr B	Unknown	504	Exposure since late 1990s
China	Wpr B	5,600,000	1,860	
Vietnam	Wpr B	>1,000,000	3,050	Exposure started mid-1990s

Tondel *et al.* (1999) report age-adjusted prevalence rates for skin lesions in Bangladesh by arsenic levels for both males and females (Table 2). A total of 1,481 subjects were interviewed and examined from four villages that were known to be dependent on wells with elevated arsenic concentrations for drinking water. Luo *et al.* (1997) report skin lesions in Inner Mongolia in people exposed to levels up to $950\,\mu g\,l^{-1}$. Prevalence was shown to increase with increasing arsenic concentration and also age, as shown in Table 3. Although these figures were based on only 70 cases, the DALY calculation was done in order to provide a comparison age-prevalence and arsenic concentration-prevalenc data.

Guha Mazumder *et al.* (1998) also report the prevalence of keratosis and hyperpigmentation separately. Their data derive from a study population of 7,683 in West Bengal and is outlined in Table 4.

Disease burden

It was necessary to make a number of assumptions before the disease burden could be estimated. These are outlined below.

Table 2 | Age-adjusted prevalence rate per 100 population of skin lesions by drinking water arsenic concentrations (adapted from Tondel *et al.* 1999)

	Arsenic concentrations ($\mu g l^{-1}$)					
	≤150	151–350	351–550	551–1000	>1000	Total
Males						
Age adj. PR	18.6	21.9	32.9	36.8	37.0	30.1
CI	11.8–25.4	15.3–28.5	26.0–39.7	29.3–44.4	27.8–46.1	26.7–33.5
Females						
Age adj. PR	17.9	20.5	32.1	34.0	24.9	26.5
CI	3.1–32.6	9.7–31.3	19.6–44.6	25.4–42.6	16.0–33.8	21.9–31.2
Average	18.3	21.2	32.5	35.4	30.9	28.3

Age adj. PR: age adjusted prevalence rate per 100 population.
CI: confidence interval.

- The age of onset, assuming exposure from shortly after birth is 10 years. Estimates of the latency period for skin lesions vary and cases have been reported in children under the age of 10. It is not possible, however, to account for individual variability in estimates such as this, so a single onset age was assumed.
- Where a population has not been exposed to elevated drinking water arsenic levels for 10 years or more, no health effects were calculated (e.g. Cambodia and Vietnam).
- Where two population estimates have been given (in Table 1) the highest has been used to estimate disease burden (e.g. India and Bangladesh).

Table 3 | Skin lesions by age in people exposed to arsenic-rich drinking water in Inner Mongolia (Luo *et al.* 1997)

Age	Prevalence (%)
5–19	11
20–39	24
40–59	32
60 +	39

- The prevalence of skin lesions clearly increases with increasing arsenic concentration. Exposure figures, however, are only available for levels of arsenic $>50\,\mu g l^{-1}$, although maximum recorded arsenic levels are often well in excess of $1{,}000\,\mu g l^{-1}$ (Table 1). For this reason, it was necessary to choose a prevalence relating to a defined exposure. The figures from Tondel *et al.* (1999) show that above $350\,\mu g l^{-1}$ the prevalence rises sharply. This, coupled with data from India, which notes that, of the population exposed to drinking water arsenic concentrations greater than $50\,\mu g l^{-1}$, only 35% are exposed to levels greater than $300\,\mu g l^{-1}$ (Chakraborti *et al.* 2003), suggests that using the $350\,\mu g l^{-1}$ prevalence figures provides a conservative but realistic estimate.
- The prevalence figures relating to arsenic exposure up to $350\,\mu g l^{-1}$ was averaged between males and females (in the case of the Tondel *et al.* 1999 study) or averaged between skin effects (in the case of the Guha Mazumder *et al.* 1998 study).
- An upper estimate was determined by using the overall prevalence figure of 28.3 from Tondel *et al.* (1999).
- The prevalence data provided by Luo *et al.* 1997 were used to provide a comparison between age-related and arsenic concentration prevalence data.

Table 4 | Age-adjusted prevalence per 100 population of keratosis and hyperpigmentation by drinking water arsenic concentration (adapted from Guha Mazumder *et al.* 1998)

	Arsenic concentration ($\mu g l^{-1}$)						
	50–99	100–149	150–199	200–349	350–499	500–799	≥ 800
Keratosis	0.95	1.4	3.5	3.2	5.9	6.0	9.5
Hyperpigmentation	2.0	8.4	6.5	9.8	12.6	9.6	17.1
Average	1.5	4.9	5.0	6.7	9.3	7.8	13.3

- The severity of skin lesions increases with age (from 0.10 up to 0.20). There are no official WHO severity weights for arsenic-related skin lesions; however, the severity weights chosen here have been set according to disability classes and indicator diseases outlined by Murray (1996) and information of similar disease outcomes (Murray & Lopez 1996). The severity of skin lesions increases with length of exposure, to the point where they affect movement. Age is used as a surrogate measure for the length of exposure and therefore severity increases with age.
- Skin lesions are not reversible after onset.
- Skin lesions are not fatal (while they may progress to skin cancer this is not accounted for in this estimate) and therefore the DALY calculation is based on YLD (years lived with disability) only.
- Life expectancy is 80 years.

Figure 1 shows the number of DALYs per 1,000 population using the Tondel *et al.* (1999) prevalence data (up to 350 $\mu g l^{-1}$ arsenic) on a country-by-country basis. It can be seen from this figure that Bangladesh is the most heavily affected country, with almost five times the number of DALYs per 1,000 population in comparison with Argentina, which is the next most affected country.

The DALYs per 1,000 population estimated from the exposure–response relationships of Luo *et al.* (1997) and Tondel *et al.* (1999) are very similar (as shown in Figure 2). The DALYs per 1,000 population estimated from Guha Mazumder *et al.* (1998) data and the overall prevalence rate from Tondel *et al.* (1999) can be considered to be lower and upper bounding estimates. These are shown on a regional basis in Figure 2.

DISCUSSION

Elevated arsenic concentrations in drinking water result in a significant burden of disease at the global level (1.5–6.7 DALYs per 1,000 population). Sear D (South East Asia) is the worst affected region; the majority of DALYs per 1,000 population seen in the region are attributable to Bangladesh. The DALY estimates for this region range from 6.2 per 1,000 population to 26.5 per 1,000 population, depending upon which prevalence data are used.

There are a number of possible reasons for the wide range in these estimates:

- The dose of arsenic ingested depends on the drinking water arsenic concentration and the amount of water consumed. This is likely to vary on a regional, if not a country, basis. This is not explicitly allowed for in the exposure–response relationships used for the burden of disease estimate.

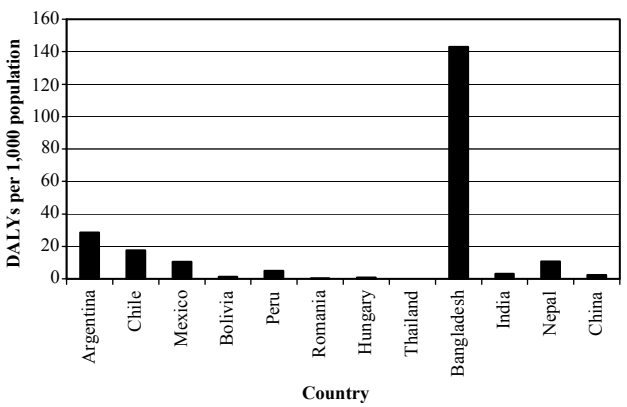

Figure 1 | DALYs per 1,000 population caused by skin lesions due to elevated drinking water arsenic concentrations (prevalence based on data from Tondel *et al.* 1999).

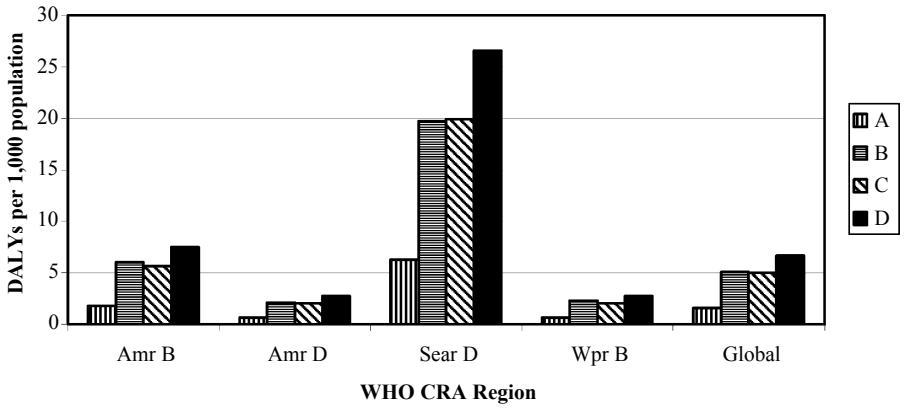

Figure 2 | Regional DALYs per 1,000 population. A, lower estimate based on prevalence data (up to 350 $\mu g l^{-1}$ arsenic) from Guha Mazumder *et al.* 1998; B, age prevalence data from Luo *et al.* 1997; C, estimate based on prevalence data (up to 350 $\mu g l^{-1}$ arsenic) from Tondel *et al.* 1999; D, upper estimate based on overall prevalence figure from Tondel *et al.* 1999.

- In the study by Guha Mazumder *et al.* (1998) the prevalence of keratosis was found to be greater among individuals with a body weight in the lowest quintile. It is likely, therefore, that the nutritional status of the population may affect symptom prevalence.
- Past research into arsenic-related health outcomes has not used a standard case definition of the clinical effects of chronic arsenic exposure (Guha Mazumder 2002). This hampers direct comparison of different studies and may account for some of the variability in apparent prevalence rates reported in the literature (Caussy 2002). Other factors reducing study comparability include differences in population susceptibility (related to dietary or genetic factors) and differences in the ratio between As^{3+} and As^{5+} to which people are exposed.

Thus, the global burden of disease estimate outlined above is based on limited exposure–response data, which may not be globally applicable. Arsenic toxicity is seen to increase with both increasing length of exposure and the greater concentration of arsenic to which people are exposed. The method outlined in this paper provides initial estimates based on likely age-related prevalence and presumed prevalence in those exposed to arsenic concentrations greater than 50 $\mu g l^{-1}$. At this stage, it has not been able to account for more severe, cancer-related health outcomes.

CONCLUSIONS

Elevated arsenic concentrations in drinking water result in a significant burden of disease at the global level (ranging from 1.5 to 6.7 DALYs per 1,000 population) and, most especially, regional level, with Sear D (comprising Bangladesh, India and Nepal) being particularly badly affected. The estimate derived in this paper relies on limited exposure–response data and relatively crude exposure data and is, thus, subject to a large degree of uncertainty. It does, however, represent an important initial attempt to quantify this problem.

The provision of guidance for assessing burden of disease due to arsenic in drinking water at national level (Fewtrell and Fuge, in preparation) and the results from a large scale prospective epidemiological study currently under way in Bangladesh (Ahsan *et al.* 2002) should help to provide data to refine this estimate.

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