



## Review

# Epidemiology of chronic disease related to arsenic in Argentina: A systematic review



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## HIGHLIGHTS

- Arsenic content in Argentina was associated with increased risk of chronic diseases.
- The median arsenicosis prevalence was 2.6% in exposed areas.
- The relative risk of mortality by skin cancer was 2.5 to 5.2 in affected areas.
- The median percentage of water samples above the cut-off point value was 87% in BA.
- We found important gaps in literature regarding the impact of arsenic on health.

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## ABSTRACT

Four million people in Argentina are exposed to arsenic contamination from drinking waters of several center-northern provinces. A systematic review to examine the geographical distribution of arsenic-related diseases in Argentina was conducted, searching electronic databases and gray literature up to November 2013. Key informants were also contacted. Of the 430 references identified, 47 (mostly cross-sectional and ecological designs) referred to arsenic concentration in water and its relationship with the incidence and mortality of cancer, dermatological diseases and genetic disorders. A high percentage of the water samples had arsenic concentrations above the WHO threshold value of 10 µg/L, especially in the province of Buenos Aires. The median prevalence of arsenicosis was 2.6% in exposed areas. The proportion of skin cancer in patients with arsenicosis reached 88% in case-series from the Buenos Aires province. We found higher incidence rate ratios per 100 µg/L increment in inorganic arsenic concentration for colorectal, lung, breast, prostate and skin cancer, for both genders. Liver and skin cancer mortality risk ratios were higher in regions with medium/high concentrations than in those with low concentrations. The relative risk of mortality by skin cancer associated to arsenic exposure in the province of Buenos Aires ranged from 2.5 to 5.2. In the north of this province, high levels of arsenic in drinking water were reported; however, removal interventions were scarcely documented. Arsenic contamination in Argentina is associated with an increased risk of serious chronic diseases, including cancer, showing the need for adequate and timely actions.

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## 1. Introduction

Arsenic (As) is the 20th most common element in the Earth's crust (IARC, 2012). It is a metalloid and can be easily solubilized in groundwaters depending on pH, redox conditions, temperature, and solution composition (Nordstrom, 2002). Human exposure occurs from ingestion of water and food contaminated with As coming from natural and anthropogenic sources (IARC, 2012). Water pollution by As is a worldwide problem with high impact in the poorest regions of the world (Litter, 2010), with over 226 million persons exposed (Murcott, 2012; McCarty et al., 2011; Smedley and Kinnirugh, 2013). The highest concentrations and, consequently, the most important health problems are localized in Argentina, Bangladesh, Nepal, Chile, China, Hungary, India, Mexico, Rumania, Taiwan, Vietnam and the USA (Bundschuh et al., 2008). In Latin America, the problem affects at least 14 countries (Argentina, Bolivia, Brazil, Chile, Colombia, Cuba, Ecuador, El Salvador, Guatemala, Honduras, Mexico, Nicaragua, Peru and Uruguay), and the number of exposed people is about 14 million. The most critical areas are in Argentina, Chile and Mexico (Figueiredo et al., 2010). It is currently estimated that the population living in areas with As contaminated water in Argentina rises to about 4,000,000 people (International Society of Groundwater for Sustainable Development, 2014). The anthropogenic activities in mining areas that enhance the mobilization of As and other copollutants makes the environmental problem more dramatic (Bundschuh et al., 2012). Additionally, the use of arsenic-contaminated groundwater for irrigation purposes in crop fields elevates the arsenic contamination (Rosas-Castor et al., 2014). Both pathways were observed in a recent review from Colombia that revealed that As is present in soil sediments, water and in the food chain, exceeding the national and international limits, particularly in mining and agricultural areas (Alonso et al., 2014).

The US Environmental Protection Agency (USEPA) classifies As as carcinogenic in group "A" (US Environmental Protection Agency) and the International Agency on Research on Cancer (IARC) includes it in group "I" (IARC, 2004). In 1993, the World Health Organization (WHO) updated the recommendations on the limits in drinking water, decreasing the guideline value from 50 to 10 µg/L (WHO, 2011). At present, in Argentina, the threshold is still under discussion. In 2007, a joint resolution (No. 68 and 196/2007) modified the 982 and 983 articles of the Argentine Food Code (CAA, Código Alimentario Argentino), decreasing the normative in drinking water from 50 to 10 µg/L, and a 5-year period to reach it. In 2012, this normative was modified again, indicating that the adopted value would be determined after the end of an epidemiological study undertaken by governmental institutions (ANMAT, 2012).

Chronic exposure to As has been associated with a variety of health problems including several types of cancer (skin, lung, bladder, kidney),

neurological disease, cardiovascular disease, perinatal conditions and other benign diseases (Smith et al., 1998; Chen et al., 1992; Hopenhayn-Rich et al., 1996; Brouwer et al., 1992; Rahman et al., 1999; Bates et al., 2004). Palmoplantar thickening and hyperkeratosis, increase of skin pigmentation and development of skin, lung and larynx cancers are the health problems most frequently reported in the literature (Hopenhayn-Rich et al., 1996; Besuschio et al., 1980). In Argentina, since the beginning of the 20th century, the set of symptoms and signs associated with the consumption of water or food contaminated with As has been denominated chronic endemic regional hydroarsenicism (HACRE from its Spanish acronym) (Litter, 2010; Ayerza, 1917a, 1917b, 1918; Gerstenfeld et al., 2012). A clinical definition of the condition can be found in Supplementary material 1. It has been documented that up to 30% of patients with HACRE in Argentina will die of skin, liver, lung, bladder, stomach and pancreas cancer (Padial, 2004). Lower-limb vascular pathologies, diabetes mellitus, hypertension and reproductive conditions are also common conditions among exposed subjects (United Nations Synthesis Report on Arsenic in Drinking Water, 2009; Mazumder et al., 2000; Biagini, 1996).

In 2006, a comprehensive study was conducted in Argentina where levels of As in water were reported for each Argentine province with the available information up to 2005 (National Commission of Health Research Programs, 2006). In many provinces such as Santiago del Estero and Santa Fe, elevated levels of As in water and food as well as elevated excretion of As in urine of the population have been reported (Carballo et al., 2006; Swiecky et al., 2006). Furthermore, several neoplasms were reported to be at increased frequency in relation to the high concentrations detected in the province of Chaco (Hopenhayn-Rich et al., 1996; Besuschio et al., 1980).

Therefore, it is important to have updated information on As levels in Argentine waters nationwide and, in particular, in the Buenos Aires province, where more than one third of the country population lives. It is also crucial to identify the arsenic abatement techniques available for future implementation of cost-effective programs for safe water supply in the exposed areas.

The overall objective of this systematic review (SR) was to examine the evidence of As concentrations in surface and drinking water aquifers, and its relation to the geographical distribution of disease caused by arsenic in terms of morbidity, mortality and population risk in Argentina, especially for the province of Buenos Aires.

## 2. Methods

A systematic review of the published and gray literature has been performed. A meta-analysis was not possible due to significant heterogeneity of populations, study designs and methods. However, by protocol, we followed the Meta-Analysis of Observational Studies in Epidemiology

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