VoR DOI: https://doi.org/10.1016/j.envres.2019.109076

Manuscript Number:

Title: Arsenic: Geochemical distribution and age-related health risk in Italy

Article Type: Research paper

Section/Category: Environmental Chemistry & Modeling

Keywords: arsenic; water; soil; stochastic; human health risk; Italy.

Corresponding Author: Dr. Daniela Zuzolo, Ph.D.

Corresponding Author's Institution: University of Sannio

First Author: Daniela Zuzolo, Ph.D.

Order of Authors: Daniela Zuzolo, Ph.D.; Domenico Cicchella, Ph.D.; Alecos Demetriades; Manfred Birke; Stefano Albanese, PhD; Enrico Dinelli; Annamaria Lima; Paolo Valera, PhD; Benedetto De Vivo

Abstract: This study represents the first work at a national scale for Italy about As occurrence, distribution and health impact. The As geochemical distribution in different environmental matrices throughout Italy has been assessed both for carcinogenic and non-carcinogenic risks with respect to different exposure routes and age groups. Risks were analysed by both deterministic and probabilistic methods. Geochemical mapping provided a useful tool to spatially analyse and represent As geochemical variation and to highlight the most critical areas in terms of As population exposure at the national scale. The results show that in Italy As is present in significant concentrations in both tap water (up to 27.2 mg/l) and soil (up to 70 mg/kg). Its presence is mainly governed by geological processes and locally reflects the industrial history of the country. The population of central Italy, where high levels of As occur, due to the presence of alkaline volcanic materials, is likely to be exposed to a health risk. Based on the results of this work, tap water for human consumption is the most effective route for daily As exposure, and plays an important role in potential cancer and non-cancer risks for the considered population. An interesting observation is that the Incremental Life Cancer Risk through tap water ingestion shows that almost 80% of data fall above the internationally accepted benchmark value of 1 x 10-5. The application of the probabilistic method of risk assessment demonstrated to be preferable than the deterministic method, as it accounted for variability and uncertainty. The results of this study may be a good starting point to support urgently needed policy actions to prevent and reduce human health risk to As exposure.

Cover Letter

Dear Editor,

We would like to submit the enclosed manuscript to *Environmental Research*.

The manuscript is entitled “Arsenic: Geochemical distribution and age-related health risk in Italy” is co-authored by Daniela Zuzolo, Domenico Cicchella, Alecos Demetriades, Manfred Birke, Stefano Albanese, Enrico Dinelli, Annamaria Lima, Paolo Valera and Benedetto De Vivo.

In our opinion the paper would be interesting to the audience of *Environmental Research* because it deals with risk assessment and public health. There is a pressing need to increase the focus on the public health implications of exposure to low arsenic levels, since low-dose arsenic exposure has been recognised as a human health threat. In our research a national scale study for Italy about As occurrence in different environmental matrices, distribution and health impact was conducted.

This study does not involved human subject. It has not been published elsewhere and that it has not been submitted simultaneously for publication elsewhere.

All of the authors have read and approved the paper and it has not been published previously nor is it being considered by any other peer-reviewed journal.

Thank you very much for your consideration.

Yours Sincerely,

PhD Daniela Zuzolo

Department of Science and Technology,

University of Sannio, 82100 Benevento, Italy

Highlights

1. *First cancer risk exposure assessment of As at national scale in Italy.*
2. *As concentrations exceed WHO and Italian standard limits in both water and soil.*
3. *Population is exposed to carcinogenic and non-carcinogenic risks posed by As.*
4. *One of the most important pathways for exposure to As is drinking water ingestion.*
5. *Infants and children are at higher risk relative to adults.*

Arsenic: Geochemical distribution and age-related health risk in Italy

Daniela Zuzolo[1*], Domenico Cicchella[1], Alecos Demetriades[2], Manfred Birke[3], Stefano Albanese[4], Enrico Dinelli[5], Annamaria Lima[4], Paolo Valera[6], Benedetto De Vivo[7,8]

[1] Department of Science and Technology, University of Sannio, 82100 Benevento, Italy
[2] Institute of Geology and Mineral Exploration (retired), 1 Spirou Louis St., Olympic Village, 136 77 Acharnae, Athens, Hellas
[3] Federal Institute for Geosciences and Natural Resources, Stilleweg 2, 30655 Hannover, Germany
[4] Department of Earth Sciences, Environment and Resources, University of Napoli “Federico II”, 80125 Napoli, Italy
[5] Department of Biological, Geological and Environmental Sciences, University of Bologna, 40100 Bologna, Italy
[6] Department of Civil-Environmental Engineering and Architecture, University of Cagliari, 09123 Cagliari, Italy
[7] Norwest Italia Srl, 80138 Napoli, Italy
[8] Pegaso University, 80132 Napoli, Italy

*Corresponding author: Daniela Zuzolo (dzuzolo@unisannio.it)

Declaration of interests: none

Abstract

This study represents the first work at a national scale for Italy about As occurrence, distribution and health impact. The As geochemical distribution in different environmental matrices throughout Italy has been assessed both for carcinogenic and non-carcinogenic risks with respect to different exposure routes and age groups. Risks were analysed by both deterministic and probabilistic methods. Geochemical mapping provided a useful tool to spatially analyse and represent As geochemical variation and to highlight the most critical areas in terms of As population exposure at the national scale. The results show that in Italy As is present in significant concentrations in both tap water (up to 27.2 mg/l) and soil (up to 70 mg/kg). Its presence is mainly governed by geological processes and locally reflects the industrial history of the country. The population of central Italy, where high levels of As occur, due to the presence of alkaline volcanic materials, is likely to be exposed to a health risk. Based on the results of this work, tap water for human consumption is the most effective route for daily As exposure, and plays an important role in potential cancer and non-cancer risks for the considered population. An interesting observation is that the Incremental Life Cancer Risk through tap water ingestion shows that almost 80% of data fall above the internationally accepted benchmark value of 1 x 10^{-5}. The application of the probabilistic method of risk assessment demonstrated to be preferable than the deterministic method, as it accounted for variability and uncertainty. The results of this study may be a good starting point to support urgently needed policy actions to prevent and reduce human health risk to As exposure.

Keywords: arsenic, water, soil, stochastic, human health risk, Italy

1. Introduction

Arsenic (As) toxicity is a global health hazard affecting hundreds of millions of people worldwide (Carlin et al., 2016). The International Agency for Research on Cancer (IARC) classifies As in the Group I elements, which are known human carcinogens that induce other non-cancer effects (ATSDR 2007; IARC, 2012).

Arsenic is one of the most toxic metals in the natural environment (Chappell et al., 1999; Appelo and Heederik, 2008; Panagiotaras and Nikolopoulos, 2015). Both organic and inorganic As species are toxic in nature but the latter are considered the most toxic (WHO, 2001). Arsenic exposure occurs from inhalation, absorption through the skin and ingestion of contaminated drinking water, food, soil and dust. Although dietary As exposure assessment continues to be investigated (EFSA, 2014), drinking water remains of major concern (Naujokas et al., 2013; Roh et al., 2017; Saint-Jacques et al., 2018; Zhang et al., 2017). Contamination of drinking water is mainly due to natural geological sources and processes; it may also occur from anthropogenic sources like mining, smelting, and agricultural activities (pesticide or fertiliser application). Worldwide chronic As toxicity has been recognised as a human health threat for almost half a century (Matisoff et al., 1982; Chen et al., 1994; Morton and Dunette 1994), since the World Health Organisation (WHO) took a public position on As in drinking water in 1958 (WHO, 1958).

There are several well-documented cases of large-scale drinking-water As contamination in many countries, e.g., Bangladesh (Argos et al., 2010), Chile (Smith et al., 1998), Europe (Selinus et al., 2010; Tarvainen et al., 2013, 2014), Ghana (Smedley et al., 1996), India (Dissanayake et al., 2010); United States of America (Matisoff et al., 1982; James et al., 2014), Taiwan (Chen et al., 2010), and Pakistan (Rasool et al., 2016). Arsenic contamination is a long-standing health-related hazard also in Italy, since As levels in its volcanic areas are quite elevated, exceeding the European and Italian regulatory limits for both drinking water (Cicchella et al., 2010; Dinelli et al., 2012; Pompili et al., 2017) and soil (Cicchella et al., 2015). In 2014, the European Commission opened infringement proceedings against Italy for its failure to ensure that water intended for human consumption meets European standards. D'Ippoliti et al. (2015) assessed chronic exposure to low-medium As levels via drinking water using a large sample of 165,609 residents in 17 municipalities of central-Italy from 1990-2010. In this study, a correlation between As exposure and several diseases was found, suggesting that even concentrations below the European regulatory limit of 10 μg/l for drinking water (EC, 1998) carry a mortality risk.

On the basis of the above information, about human health risks with respect to As exposure, it was decided to use available national scale data for Italy on As occurrence and distribution in different environmental matrices and to explore the potential human health impact. The main objectives of this study were: (1) to investigate the As levels and spatial distribution in Italy in different sample types; (2) to assess human exposure to As by estimating daily intake via different exposure routes; (3) to define the potential health risk on the Italian population, and (4) to delineate critical areas for which it is necessary to intervene because of low-dose chronic As exposure, and to recommend the carrying out of follow-up studies and to propose remediation measures where it is deemed necessary.

2. Source and occurrence of As in the environment

Arsenic is a metalloid trace element widely distributed throughout the natural environment, air, water and soil. It is the 40th most abundant element in the Earth's upper continental crust (Hu and Gao, 2008), and is one of the most hazardous toxic elements for the environment and human health (Chappell et al., 1999; Reimann et al., 2009). The mobilisation of As in the environment is due to a sequence of natural processes such as geo-biochemical weathering reactions, volcanic emissions, as well as anthropogenic activities. The principal factors influencing the concentration of As in soil are, firstly, the geochemistry of parent rock and human activities; secondly, factors such as climate, organic and inorganic components and redox potential status in soil have their role in the distribution of As in the environment (Kabata-Pendias and Pendias, 2001; Kabata-Pendias and Mukherjee, 2007; Panagiotaras and Nikolopoulos, 2015). Natural low-temperature processes such biomethylation and microbial reduction also produce As in aerobic and anaerobic conditions. Arsenic has a strong chalcophile character, so it is often associated with sulphides and sulphosalts, such as arsenopyrite, pyrite, orpiment, realgar, enargite and tennantite, which are typically related to sulphide deposits. Despite the large number of As minerals (more than 200 minerals; Table 1), the most common arseniferous mineral in crustal rocks is pyrite. It can be formed under reducing conditions in low-temperature sedimentary environments and it is often present, in its authigenic form, in rivers, lakes, oceans and aquifers sediments.

Arsenic, in As^{3+} and As^{5+} oxidation states, can substitute for P^{5+}, Si^{4+}, Al^{3+}, Fe^{3+}, and Ti^{4+} in various mineral structures and it is, therefore, present in different concentrations, in many rock-forming minerals. It tends to sorb strongly to secondary Fe, clay and organic matter, so its mobility in soil and sediments is limited in comparison to its solubility.

Arsenic concentration is ordinarily lower in sandstone, about 0.5-1.2 mg/kg, it is higher in granitoid rocks, 1-2.5 mg/kg, up to 24 mg/kg in coal and 13 mg/kg in shale (Kabata-Pendias and Mukherjee, 2007). Arsenic is associated with magmatic and hydrothermal processes and it is used as a 'pathfinder' for metallic ore deposits, e.g., Au, Sn, Cu and W (Boyle, 1974; Bowell et al., 2014).

Arsenic dispersion and mobilisation in water is possible at pH values typically found in ground water (pH 6.5-8.5) and in both oxidising and reducing conditions. Biological activity in surface water can produce organic As compounds that are predominant in biological tissues. Arsenic concentration in water can be related also to volcanic and geothermal and anthropogenic input, especially mining-influenced water (Smedley and Kinniburgh, 2002; Webster and Nordstrom, 2003).

Table 1. *Typical ranges of As concentrations (mg/kg) in common rock-forming minerals (from Smedley and Kinniburgh, 2002).*

Sulphide minerals		**Silicate minerals**	
Pyrite	100 – 77,000	Quartz	0.4 – 1.3
Pyrrhotite	5 – 100	Feldspar	<0.1 – 2.1
Marcasite	20 – 126,000	Biotite	1.4
Galena	5 – 10,000	Amphibole	1.1 – 2.3
Sphalerite	5 – 17,000	Olivine	0.08 – 0.17
Chalcopyrite	10 – 5,000	Pyroxene	0.05 – 0.8
Oxide minerals		**Carbonate minerals**	
Haematite	up to 160	Calcite	1 – 8
Fe(III) oxyhydroxide	up to 76,000	Dolomite	<3
Magnetite	2.7 – 41	Siderite	< 3
Ilmenite	<1	–	–
Sulphate minerals		**Other minerals**	
Gypsum/anhydrite	<1 – 6	Apatite	<1 – 1,000
Baryte	<1 – 12	Halite	<3 – 30
Jarosite	34 – 1,000	Fluorspar	<2

Natural concentrations of As in aquifers can reach 50 μg/l. Such conditions are found in Bangladesh, West Bengal, Chile, Argentina, China, Mexico, Vietnam, and parts of Canada and the U.S.A. (Bowell et al., 2014). Abnormal As levels are related to bedrock type, hydrogeological history, and geochemical environment. Arsenic is released to ground water by reduction of Fe hydroxides and arseniferous minerals, as a sorbed species, sulphide oxidation and competitive sorption with other oxyanions.

Human activities contribute to the enrichment and mobilisation of As via mining, mineral processing, and combustion of fossil fuels. In addition, As has also historically been used in a variety of commercial applications. The principal As uses are as a component of wood preservatives and in the production of agricultural chemicals, such as insecticides, herbicides, algaecides, and growth stimulants. Smaller amounts are used in the production of glass, nonferrous alloys, in the electronics industry and in medicine.

3. Arsenic and health implications

Arsenic is ubiquitous in the environment and is a human carcinogen (IARC, 2012). Dietary intake from food, beverages, and drinking water are the primary sources of As exposure in humans (Roseet al., 2007; Jorhem et al., 2008; Heitkemper et al., 2009; Liang et al., 2010; Chung et al., 2014). The adverse health effects of As depend strongly on the dose and frequency of exposure, as well as on biological factors of the exposed population. The effects of acute and chronic exposure to

As are well documented in the scientific literature (Table 2). Most cases of acute As poisoning occur from accidental ingestion of insecticides or pesticides; it causes problems in the gastrointestinal system like nausea, vomiting, colicky abdominal pain and diarrhoea. Other clinical symptoms are acute psychosis, a diffuse skin rash, toxic cardiomyopathy and seizures. The fatal dose of ingested As in humans is difficult to determine from case reports, and it depends upon many factors (e.g., solubility, valence state, etc.). Long-term As toxicity leads to multisystem diseases and the most serious consequence is cancer; these effects may take many years to become clinically apparent. Chronic As toxicity in humans has been documented in many countries worldwide, particularly in south and south-east Asia. There are also areas in Europe (e.g., the Pannonian Basin) that are affected. Significant As chronic exposure mostly occurs via drinking As-contaminated water. A larger number of scientific papers has been published on chronic As exposure and its associated health effects (e.g., Kapaj et al., 2006; Brinkel et al., 2009; Saha et al., 2010) and the clinical evidence of As toxicity is manifold (Ratnaike, 2003; Dangleben et al., 2013; Jain et al., 2018).

Table 2. *Effects of As oral exposure adapted from ATSDR (2007).*

System	Exposure duration	Exposure level (As mg/kg/day)	Effects	Source
HIGH DOSE EXPOSURE				
Death	1 week	2	death	Armstrong et al. (1984)
Death	once	22	death	Levin-Scherz et al. (1987)
Gastrointestinal	1 week	0.2	vomiting, diarrhoea, abdominal pain	Armstrong et al. (1984)
Haematological	2 weeks	0.2	pancytopenia, leukopenia	Armstrong et al. (1984)
Hepatic	once	2	slight increase in serum bilirubin	Hantson et al. (1996)
Ocular	once	13	constricted vision	Kamijo et al. (1998)
Cardiovascular	once pregnancy - week 30	6	hypotension, rapid pulse	Lugo et al. (1969)
Gastrointestinal	once pregnancy - week 30	6	abdominal pain, vomiting	Lugo et al. (1969)
Haematological	once pregnancy - week 30	6	high leukocyte count, low haematocrit	Lugo et al. (1969)
Renal	once pregnancy - week 30	6	acute renal failure	Lugo et al. (1969)
LOW-DOSE				

EXPOSURE				
Respiratory	2-3 weeks	0.05	sore throat, rhinorrhoea, cough, sputum	Mizuta et al. (1956)
Dermal	>8 years	0.0012	increased risk of premalignant skin lesions	Ahsan et al. (2006)
Cardiovascular	>10 years	0.022	increased risk of ischemic heart disease mortality	Chen et al. (1996)
Haematological	lifetime	0.002	anaemia during pregnancy	Hopenhayn et al. (2006)
Hepatic	55 years	0.03	portal fibrosis and hypertension, bleeding from oesophageal varices	Szuler et al. (1979)
Neurological	lifetime	0.005	reduced performance in neuro behavioural tests	Wasserman et al. (2004)
Reproductive	lifetime	0.006	increased incidence of spontaneous abortion	Milton et al. (2005)
Developmental	continuous	0.002	reduced birth weight	Hopenhayn et al. (2003)
Cancer	NS*	0.003	bladder cancer	Chiou et al. (2001)
Cancer	NS*	0.0011	lung cancer	Ferreccio et al. (1998)
Cancer	NS*	0.0049	squamous cell carcinoma of the skin	Guo et al. 2001
Cancer	>1 year	0.0075	basal or squamous skin carcinoma	Haupert et al. (1996)
Cancer	5 years	0.033	lung, urinary tract cancer	Tsuda et al. (1995)

*Not specified

The main dermatological symptoms observed in As-affected people are melanosis (change of pigmentation) and keratosis (dry, rough, papular skin lesions) (Guo et al., 2001; Ramasamy et al., 2015). Chronic As exposure may also cause reproductive, neurological, cardiovascular (Ramasamy and Lee, 2015; Mendez et al., 2016), respiratory and pulmonary (Mazumder et al., 2000; Islam et al., 2007; Ramasamy and Lee, 2015), gastrointestinal, hepatic, haematological, and diabetic effects in humans (Chiu et al., 2004; Ramasamy and Lee, 2015). Problems to development and reproductive systems have also been recognised (Hopenhayn et al., 2003; Milton et al., 2005). Moreover, intake of inorganic As was recognised as a cause of skin, bladder, kidney, and lung cancer (IARC, 2004).

4. Guidelines for As

WHO since 1958 expressed its public position on As in drinking water with the publication of the first International Standards for Drinking-Water (WHO, 1958); a maximum allowable concentration of 0.2 mg/l for As, based on health concerns was recommended. In the 1963 version of WHO International Standards for Drinking-Water, this value was lowered to 0.05 mg/l (WHO, 1963). An update in 1971 kept As in the toxic substances category and reaffirmed the guideline value of 0.05 mg/l (WHO, 1971). This value was also retained in the first edition of the Guidelines for Drinking-Water Quality (WHO, 1984). The fourth edition of WHO Guidelines for Drinking-Water Quality established 10 µg/l as a provisional guideline value for As in drinking water (WHO, 2011). The fact that inorganic As compounds are classified by IARC in Group 1 (carcinogenic to humans; IARC, 2004) was taken into consideration in this study.

At present, in most of the As-affected Asian countries and Russia, the permissible limit of As in drinking water is 50 µg/l (Table 3). In Europe, the maximum permissible limit of As in drinking water varies from 5 to 50 µg/l (refer to Appendix A in Reimann and Birke, 2010). Italian threshold value for As in drinking water is set at 10 µg/l in accordance with the WHO (2011) guidelines.

Widely divergent guidelines and clean-up targets for As in soil have been established by many regulatory organisations in the past decades, worldwide. The Japanese soil quality guidelines for As state a limit of 0.01 mg/l in a sample solution and 15 mg/kg in soil for agricultural land (paddy fields only) (MEJ, 2019). In Italy, the As limit value for recreational/residential land use is set at 20 mg/kg (D.L. 152/2006). The target of 20 mg/kg As is also reported in U.S.A (Henke, 2009) and Australian (National Environment Protection Council, 1999) environmental legislation. Significantly higher As limits are set for soil in residential (50 mg/kg) and recreational (125 mg/kg) areas in the German Federal Soil Protection Act (BBodSchG, 1998), while the lowest As soil limit of 2 mg/kg is used in Russia (Vodjanickij, 2009). A summary of guideline limits for As in different countries is shown in Table 3.

Table 3. *Currently accepted national maximum permissible guideline limit in different countries for As in drinking water and soil.*

Sample type	Maximum permissible limit	Country	References
drinking water (µg/l)	10	European Union Japan New Zealand U.S.A. Canada	European Union (1998) MEJ (2008) Ministry of Health (2005) CFR (2006) CDWG (2007)

	50	Bangladesh	BRAC (2000)
		China	Guo and Wang (2005)
		India	Indian Bureau of Standards (1991)
		Chile	Caceres et al. (2005)
		Nepal	Shrestha et al. (2003)
		Pakistan	NSDWQ (2008)
		Vietnam	Berg et al. (2001)
soil (mg/kg)	12[a]	Vietnam	Trang Hoang and Hahn (2015)
	15[a]	Japan	MEJ (2008)
	20	Italy[b]	D.L. 152/2006
		Canada[c]	CCME (2001)
		Norway	Hansen and Danielsberg (2009)
		Australia	Henke (2009)
		U.S.A. (New Jersey)	Henke (2009)
	50[d]	Germany	BBodSchG (1998)

[a] Soil for agricultural land (paddy fields only); [b] Recreational/residential soil; [c] Agricultural; [d] Agricultural, partially reducing conditions.

6. Material and methods

6.1. Data sets

The As concentration data in the various environmental samples, which are used in this study, come from several projects carried out in Europe and to which the authors of this work have actively participated.

Specifically, tap and bottled mineral water has been studied within the '*European Groundwater Geochemistry Project' (EGG;* Reimann and Birke, 2010*)* in which 157 tap and 186 bottled mineral water samples were collected in 2007-2008 throughout Italy. Tap water was analysed at the German Geological Survey (BGR) in Hannover for more than 70 determinands. Sample preparation and analytical methods can be found in Birke et al. (2010), Dinelli et al. (2012), Banks et al. (2015) and Flem et al. (2015). Soil data are from the *Geochemical mapping of agricultural and grazing land soil of Europe (GEMAS)* project (Reimann et al., 2014). In total, 118 agricultural (0-20 cm) and 118 grazing land (0-10 cm) topsoil samples were collected between 2008 and early 2009 according to the Field Manual of the GEMAS project (EGS, 2008). Sampling methods, sample preparation, analytical methods and other technical and operative information can be found in Birke et al. (2014), Reimann et al. (2014) and Cicchella et al. (2015). Stream sediment (n=51 samples), stream water (n=48) and floodplain sediment (n=50) data are from the FOREGS (Forum of European Geological Surveys) *Geochemical Atlas of Europe* project (Salminen et al., 2005), where all the relevant information for sampling, sample preparation and analytical methods can be found.

6.2. Data treatment and map plotting

Univariate statistical analysis was conducted to show the single-element statistical distribution. Geochemical maps displaying the spatial As distribution in the different types of samples were generated using the Multifractal Inverse Distance Weighted (MIDW) interpolation method with the GeoDAS™ software; for more details on this methodology refer to Cheng et al. (1999). It has been demonstrated in previous studies at regional and local scales (Lima et al., 2003) that this algorithm preserves high frequency information (anomalies) by considering both spatial associations and local singularities in the geochemical data. The concentration intervals of the interpolated surfaces were set by the concentration–area (C–A) fractal method (Cicchella et al., 2005) in order to better visualise the different geochemical distribution patterns.

6.3. Exposure and human health risk assessment

The definition of risk given by the US Environmental Protection Agency (US EPA, 1989) was considered, which assumes a linear relation between exposure (as daily intake) and risk for both carcinogenic and non-carcinogenic (toxic) substances. Initially, the deterministic risk assessment was used, based on the obtained results, and subsequently the study was extended to a stochastic approach.

First, the daily intake and related human health risk was assessed by identifying potential key exposure points for soil and water. Two routes of exposure were examined, ingestion and dermal contact. Regarding water, chronic daily intake (CDI_w) was assessed, based on the residential use of tap water for drinking and bathing and showering. This section describes the methodology for calculating chemical-specific intake for the population and exposure pathways selected for quantitative evaluation. It is important to underline that intake is not equivalent to absorbed dose, which is the amount of a chemical absorbed into the blood stream.

The chronic daily intake $\mathrm{CDI}_{\mathrm{w(ing)}}$ via ingestion of water and the absorbed dermal dose by contact with water $\mathrm{CDI}_{\mathrm{w(derm)}}$ were calculated according to Equations 1 and 2 (US EPA, 1989, 2004):

Equation 1: $$\mathrm{CDI_{w(ing)}} = \frac{\mathrm{CW*IR*EF*ED}}{\mathrm{BW*AT}}$$

Equation 2: $$\mathrm{CDI_{w(derm)}} = \frac{\mathrm{CW*SA*PC*ET*EF*ED*CF}}{\mathrm{BW*AT}}$$

where CW is the chemical concentration in water (mg/l); IR is the ingestion rate (litres/day); ET is the exposure time (hours/day); EF is the exposure frequency (days/year); ED is the exposure duration (years); SA is the skin surface area available for contact (cm^2/event); PC is the chemical-specific dermal permeability constant (cm/hr); CF is the volumetric conversion factor for water (1 litre/1000 cm^3); BW is the body weight (kg), and AT is the average time period over which exposure is averaged (days).

The average daily intake $\mathrm{CDI_{s(ing)}}$ via accidental ingestion of soil and the absorbed dermal dose through soil contact $\mathrm{CDI_{s(derm)}}$were calculated according to Equations 3 and 4 (US EPA, 1989, 2004):

Equation 3: $$\mathrm{CDI_{s(ing)}} = \frac{\mathrm{CS*}IR_{soil}\mathrm{*CF*ET*EF*ED}}{\mathrm{BW*16*AT}}$$

Equation 4: $$\mathrm{CDI_{s(derm)}} = \frac{\mathrm{CS*CF*SA*AF*ABS*EF*ED}}{\mathrm{BW*AT}}$$

where CS is the chemical concentration in soil (mg/kg), IR_{soil} is the ingestion rate (mg/day); ET is the exposure time (0 – 16 hours/day, where 16 is the maximum assumed awake hours per day); EF is the exposure frequency (days/year); ED is the exposure duration (years); CF is the conversion factor (10^{-6} kg/mg); SA is the skin surface area available for contact (cm^2/event); AF is the soil to skin adherence factor (mg/cm^2); ABS is the absorption factor for the skin (unitless – 0.03 for As as stated by Health Canada (2007a); BW is the body weight (kg), and AT is the average time period over which exposure is averaged (days).

The internationally adopted equations for $\mathrm{CDI_{(s(ing))}}$ calculation generally offer an overestimation of exposure, since they do not account for exposure time per day. The above was verified for the Italian data sets by including the hours of exposure in order to have a more realistic model.

The values and description of all the parameters, used for deterministic and probabilistic approaches (water ingestion scenario), are summarised in Table S1 in the Supplementary Material. Tables S2, S3 and S4 in the Supplementary Material, show the age related parameters used for water dermal contact, soil ingestion and soil dermal contact scenarios, respectively.

Exposure was calculated for different age groups with similar contact rates, i.e., children of 1 to 8, teenagers of 9 to 16, and adults of 16 to 70 years old, as well as lifetime exposure. The body weight used in the intake calculation for each age group is the average body weight for that particular age group. So, lifetime exposure was calculated by taking the time-weighted average of exposure estimates over all age groups. For pathways, where contact rate to body weight ratios are fairly constant over a lifetime (e.g., drinking water ingestion), a body weight of 70 kg was used.

Once exposure assessment was evaluated, the risk was estimated. In this study, both non-cancer Hazard Quotient (HQ) and carcinogenic risk (calculated as Incremental Lifetime Cancer Risk - ILCR) levels were assessed.

The HQ (Equation 5), used to describe the potential for non-carcinogenic toxicity, assumes that there is a level of exposure (i.e., TDI) below which it is unlikely for even sensitive population groups to experience adverse health effects:

Equation 5:
$$\mathrm{HQ} = \frac{\mathrm{CDI}}{\mathrm{TDI}}$$

where CDI is the chronic daily intake (mg/kg/day) and TDI is the Tolerable Daily Intake for As for assessing non-cancer health effects (0.0003 mg/kg/day as stated by Health Canada, 2007b). The health risk generally occurs when the HQ values are >1 (Khan et al., 2008). If the exposure level (CDI) exceeds this threshold (i.e., if CDI/TDI exceeds unity), there may be concern for potential non-cancer effects (US EPA, 1998).

ILCR (Equation 6) is the incremental probability of an individual developing cancer over a lifetime as a result of exposure to a potential carcinogen. The estimated exposure (CDI) is multiplied by the appropriate Cancer Slope Factor (CSF) to derive an estimate of the potential Incremental Lifetime Cancer Risk (ILCR) associated with that particular exposure (Health Canada, 2004). The US EPA's Office of Water (US EPA, 2018) advises consideration of conservative cancer risk levels (10^{-5}, 10^{-6}). The Italian legislation (D.L. 152/2006) sets as a maximum acceptable cancer risk level at 1×10^{-6} for a single substance (i.e., 1 case of cancer in 1,000,000 exposed people).

Equation 6:
$$\mathrm{ILCR} = \mathrm{CDI} * \mathrm{CFS}$$

where CDI is the chronic daily intake (mg/kg/day) and CSF is the cancer slope factor (mg/kg/day). According to Health Canada (2007b) database, the cancer slope factor (CSF) for As is 1.8 mg/kg/day, for both ingestion and dermal absorption.

7. Results and discussion

7.1. As concentration levels in different environmental samples

Table 4 summarises the descriptive statistics of As concentration in different environmental samples.

Table 4. *Main statistical parameters of As content in different sample types collected throughout Italy.*

Sample type	n	Unit	Min	Q25	Mean	Median	Q75	Q95	Max	SD
Agricultural soil	118	mg/kg	0.79	5.04	10.0	7.56	11.4	28.18	62.2	9.07
Grazing land soil	118	mg/kg	0.97	4.72	9.76	8.08	11.9	22.9	54.3	7.53
Stream sediment	51	mg/kg	2.5	2.5	7.2	6.0	9.5	15.5	38	6.23
Floodplain sediment	50	mg/kg	2.5	2.5	8.86	7	9	26.5	51	9.77
Bottled Mineral water	186	µg/l	0.01	0.13	0.89	0.25	0.67	5.08	8.91	1.54
Stream water	48	µg/l	0.08	0.27	1.79	0.47	1.71	9.94	13	3.21
Tap water	157	µg/l	0.02	0.11	0.94	0.25	0.73	4.39	27.2	2.51

The large standard deviation (SD) for almost all data sets (Table 4) indicates a significant spatial variability. A wider concentration range characterises floodplain sediment and soil samples (both agricultural and grazing land). The agricultural soil samples show the largest variability with As concentration varying from 0.79 mg/kg to 62.2 mg/kg, with a median of 7.56 mg/kg. The As content in grazing land soil samples ranges from 0.97 mg/kg to 54.3 mg/kg, with a median value of 8.08 mg/kg. Stream and floodplain sediment samples are characterised by maximum As values of 38 and 51 mg/kg, respectively. All these types of samples show values above the intervention limit of 20 mg/kg according to Italian legislation (D.L. 152/2006) for soil intended for residential/recreational use. Regarding stream water, As concentration ranges from 0.8 to 13 µg/l, with a median of 0.47 mg/kg. Arsenic content in Italian bottled mineral water varies from 0.01 to 8.91 µg/l, with a median of 0.25 µg/l. A wider concentration range is reported for tap water, i.e., 0.02-27.2 µg/l, with a median of 0.25 µg/l, which is the same as that for bottled mineral water.

7.2. Environmental occurrence and geochemical distribution of As in Italy

The spatial distribution of As concentration in different environmental samples is shown in Fig. 1.

In Italy, the intervention limit for As in drinking water is 10 µg/l, while in soil is 20 mg/kg for residential and recreational land use, as defined by D.L.152/2006.

Arsenic is widely distributed throughout Italy in both water and soil (Table 4; Fig. 1). The As spatial variation reflects well the lithological differences, geological processes and industrial history of the country.

7.2.1. As anomalies in soil

Arsenic anomalies in soil (>20 mg/kg) represent local and regional geological conditions (Figs. 1A, B). The major As enrichment in soil is related to metamorphic rocks of the Alpine chain, alluvial sediments of the Po River plain, pyroclastic deposits of the Magmatic Roman Neapolitan Province, Calabrian coastal metamorphic rocks and mineralised areas of Sardinia.

Subdividing the Alpine arch in geographical sectors, the North-West sector, between Milano and Aosta, is characterised by As enrichment that could be due to metamorphic rocks such as biotitic gneiss, and amphibolitic norite and to a former gold mining site along the Toce River. The North-Central sector of the Alps has high As levels in soil, which are probably due to the presence of metamorphic rocks such as two-mica gneiss and orthogneiss. In the North-East sector of the Alps, the enrichment in As could be due to moraine deposits, which have transported material from the upper group of Atesine volcanites, comprising ignimbrite, lava and tuff. In the Po River plain, between Milan and Venice, the high As levels in soil are probably related to alluvial deposits, and local environmental conditions. Silty and clayey soil rich in organic material, when under reducing conditions, induced by organic matter, it can be enriched in As due to adsorption onto Fe-hydroxides (Tarvainen et al., 2013). The Magmatic Roman Neapolitan Province is characterised by Quaternary pedogenic pyroclastic deposits from Plinian type eruptions (discontinuous pozzolan and tuff) and have high As levels in soil. Along the Tyrrhenian Calabrian margin, As anomalies in soil are correlated to metamorphic rocks, such as shale, phyllite, quartzite, marl and ophiolite, indicating the complex geodynamic processes that occurred in this area. Subduction induces upwelling of magmatic fluids and thus hydrothermal processes are present. Sardinia's As anomalies could be connected to the occurrence of sulphide mineralisation, the subsequent exposure of the deposits to weathering (Villaputzu, Baccu Locci), and to mining.

7.2.2. As anomalies in sediment

The main As anomalies in stream sediment are found in the Roman Neapolitan Magmatic Province, Sardinia (presence of sulphide mineralisation and mining activities), and Calabrian coastal metamorphic rocks (Fig. 1C). In the Brenta River plain, the high As levels can be related to stream sediment derived from the Trentino Alps and the Alpine foothills, where two of the most important intrusive Alpine masses are located (the Màsino-Bregaglia valley pluton and the Adamello pluton near Trentino). Metal mining and overbank sedimentation, which is considered to represent longer-term storage (Matys Grygar et al., 2016) may have influenced As enrichment in floodplain sediment of the Swiss Alpine sector and southern Sardinia, where concentrations over 20 mg/kg were found (Fig. 1D). Moderate As levels were also found in the Roman Magmatic Province and Apulia region (S.E. Italy).

7.2.3. As anomalies in water

Arsenic concentrations in water, as has already been discussed, are very important for human health, because it can be easily adsorbed by the human body. High As concentrations in bottled mineral and stream water are located in the central sector of the Alps, along the Magmatic Roman Neapolitan Province and in northern Sardinia. Stream water in the Magmatic Roman Neapolitan Province and northern Sardinia has As concentrations up to 13 µg/l (Fig. 2D). High As level in the Baccu Locci stream, which were found by Ardau et al. (2013), are not fully captured due to the wide-spaced sampling design at approximately 1 site/4800 km^2 of the FOREGS Geochemical Atlas of Europe project (Salminen et al., 2005).

Elevated As concentrations in water in the Central Alps could be related to the occurrence of arseniferous mineralisation, and their wider dispersion to moraine deposits transported by glacial processes. The area surrounding Alpe Stabiello-Sondalo is a former native As mining area. The Magmatic Roman Neapolitan Province, particularly the northern area of Lazio, has high As values in water, probably due to the geological peculiarity of the Province (pyroclastic rocks). The Cimino-Vico volcanic system, near Viterbo city, has a continuous basal aquifer flow within Pliocene-Pleistocene sedimentary rocks with very high As concentrations due to an active hydrothermal system. According to previous studies (e.g., Baiocchi et al., 2007) this volcanic aquifer discharges mainly into adjoining springs and streams. Northern Sardinia has As anomalies in stream and bottled mineral water (Fig. 2), ascribed to a hydrogeological complex of volcanites affected by widespread hydrothermal events. In southern Sardinia, the extraction of Pb and As from arsenopyrite veins was carried out without observance of environmental law; processing wastes were discharged, for about 15 years, directly into the Baccu Locci stream (Frau et al., 2003). Arsenic ferrihydrites at Baccu Locci are from precipitation of metal rich mine slurry from the flotation plant. The As content in tap water (0.02-27.2 μg/l-is higher than in bottled mineral water (0.01-8.91 μg/l), but the origin of tap water is not related to the distribution source, because it comes from several possible sources, so it is not representative of local geological conditions.

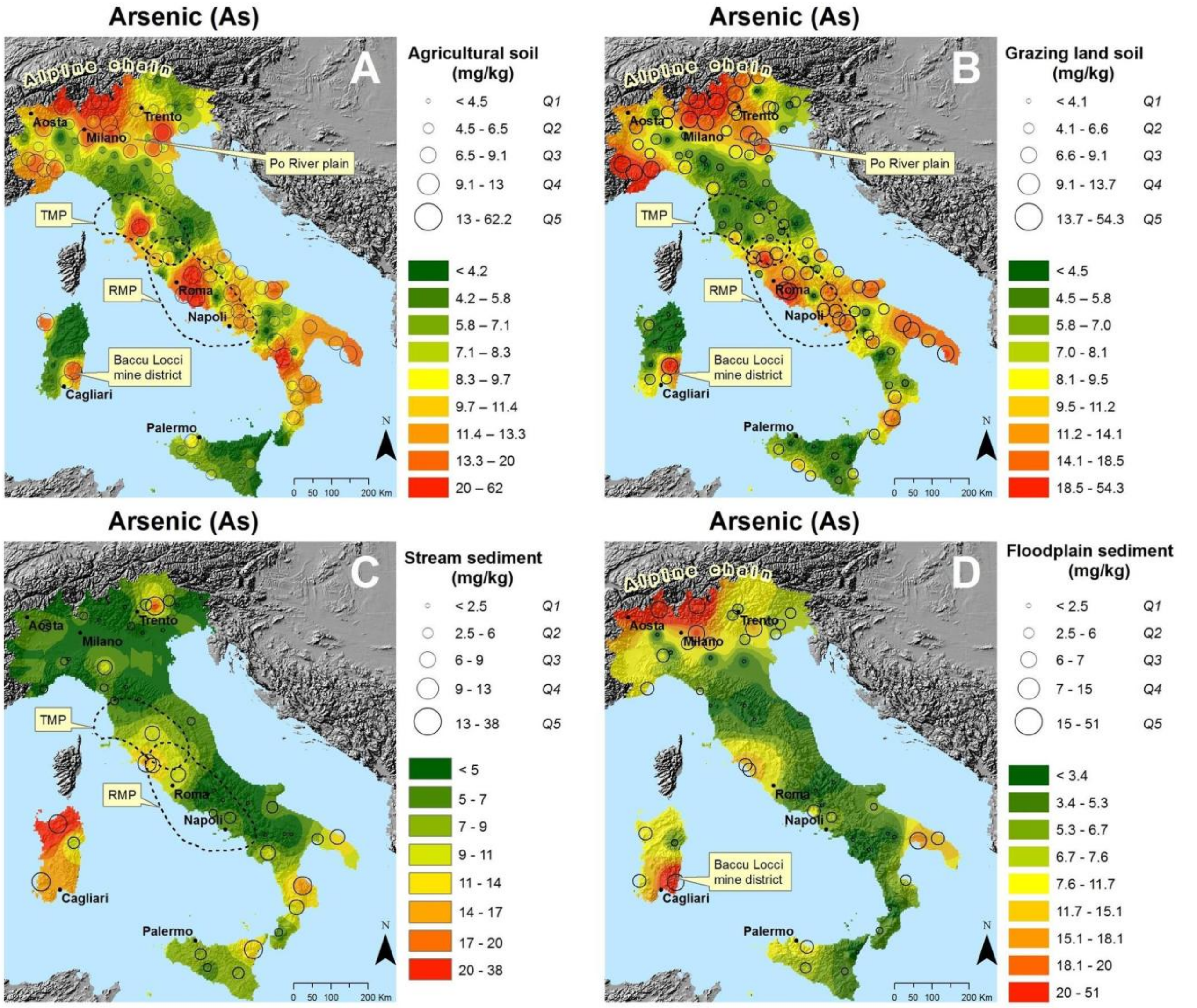


Fig. 1. *Deterministic As geochemical maps showing the distribution in (A) agricultural soil, (B) grazing land soil, (C) stream sediment, and (D) floodplain sediment. TMP = Tuscany Magmatic Province; RMP = Roman Neapolitan Magmatic Province. Arsenic intervention limit for soil is 20 mg/kg.*

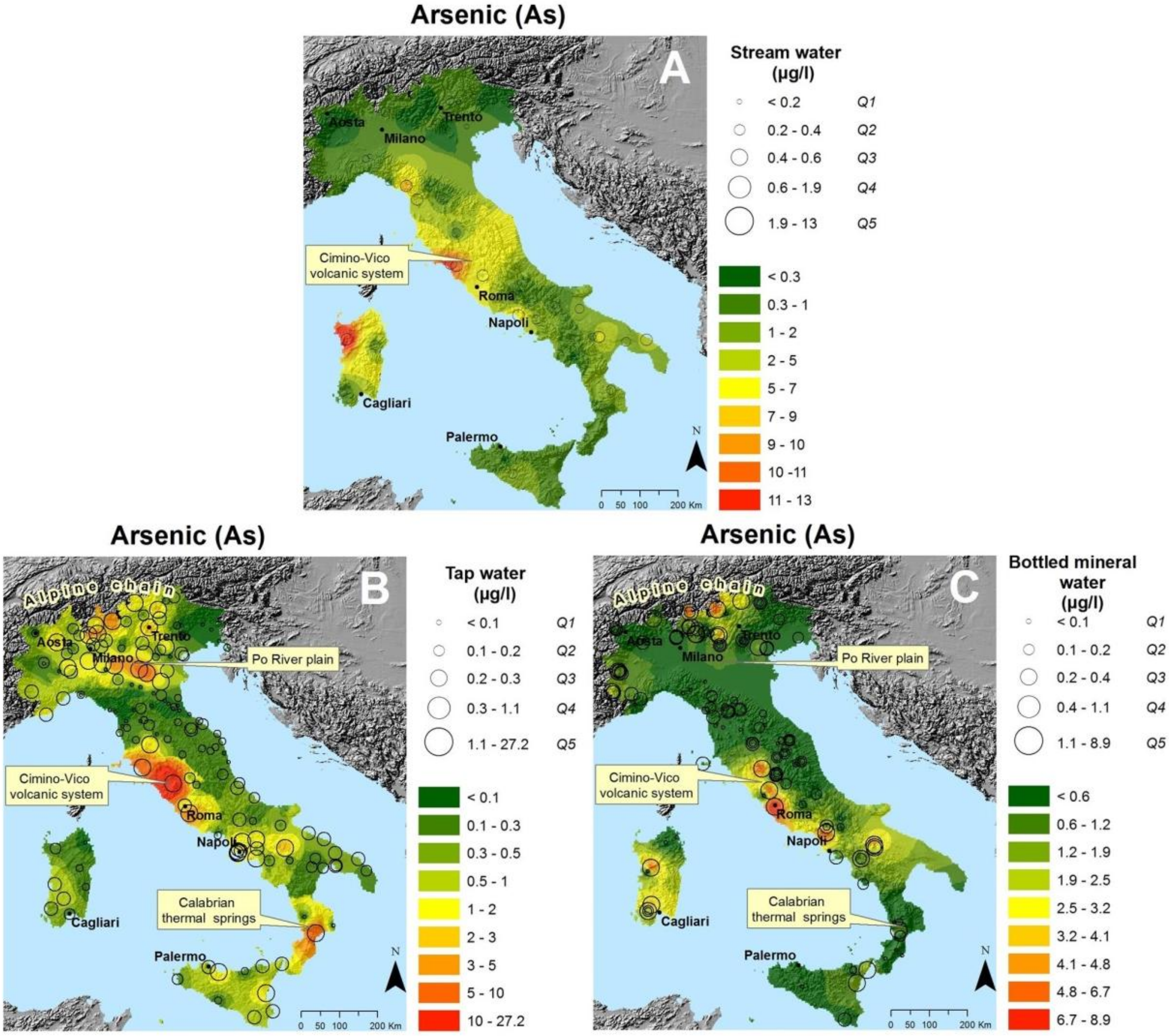


Fig. 2. *Deterministic As geochemical maps showing the distribution in (A) stream water, (B) tap water, and (C) bottled mineral water. TMP = Tuscany Magmatic Province; RMP = Roman Neapolitan Magmatic Province. Arsenic intervention limit for water is 10 μg/l.*

7.3. Estimation of risk for the Italian population

The daily intake of As via different exposure pathways for both carcinogenic (ILCR) and non-carcinogenic (HQ) risks for different age groups (children, teenagers, adults) was estimated to highlight the relevance of the analysed source of exposure and age related risk. Further, the lifetime risk was modelled by taking into consideration the duration of exposure to As from birth to an average age of 70 years. The ILCR and HQ risk indices, derived for each pathway, are summarised in Tables 5 and 6, respectively.

***Table 5**. Data of Incremental Life Cancer Risk (ILCR) calculated for different age groups, with respect to tap water and soil for two exposure pathways, ingestion and dermal contact.*

Sample type	Exposure pathway		Age group			
			Children	Teenagers	Adults	Lifetime
Tap water	ingestion	Range of ILCR	2.2 x 10^{-7} – 3.9 x 10^{-4}	1.9 x 10^{-7} – 3.2 x 10^{-4}	5.5 x 10^{-7} – 9.4 x 10^{-4}	9.6 x 10^{-7} – 1.7 x 10^{-3}
	dermal contact		1.2 x 10^{-9} – 2.1 x 10^{-6}	1.1 x 10^{-9} – 1.8 x 10^{-6}	4.7 x 10^{-9} - 8.1 x 10^{-6}	6.9 x 10^{-9} - 1.2 x 10^{-5}
Soil	ingestion		1.2 x 10^{-8} – 9.4 x 10^{-7}	5.5 x 10^{-9} – 4.3 x 10^{-7}	1.7 x 10^{-8} – 1.3 x 10^{-6}	3.4 x 10^{-8}- 2.7 x 10^{-6}
	dermal contact		1.2 x 10^{-10} – 9.8 x 10^{-9}	9.6 x 10^{-11} -7.5 x 10^{-9}	4.7 x 10^{-10} - 3.7 x 10^{-8}	6.9 x 10^{-10} - 5.4 x 10^{-8}
Pseudo-total risk		Mean	1.4 x 10^{-5}	1.2 x 10^{-5}	3.4 x 10^{-5}	5.8 x 10^{-5}

Overall, the average pseudo-total incremental lifetime cancer risk, posed by exposure to As (calculated as the sum of the different exposure pathway mean values), was in the order of adults>children>teenagers. The multi-pathway risk from now on will be indicated as ‘total’. For children, the mean total risk is 1.4 x 10^{-5} (i.e., almost 14 additional cases of cancer in a million). For adults, the mean total risk is 3.4 x 10^{-5}, which is slightly higher than that of children (i.e., almost 34 additional cases of cancer in one million exposed individuals). The mean total risk for teenagers is 1.2 x 10^{-5}, which is less than that for adults and children. The average total lifetime mean risk, modelled from birth to 70 years old, is 5.8 x 10^{-5} (i.e., almost 58 additional cases of cancer in a million).

***Table 6**. Range of Hazard Quotient (HQ) calculated for different age groups, with respect to tap water and soil for two exposure pathways, ingestion and dermal contact.*

Sample type	Exposure pathway		Age group			
			Children	Teenagers	Adults	Lifetime
Tap water	ingestion	Range of HQ	3.6 x 10^{-3} - 6.25	3.8 x 10^{-3} – 6.6	1.5 x 10^{-3} - 2.6	2.3 x 10^{-2} – 3.9 x 10^{1}
	dermal contact		3.2 x 10^{-5} – 5.5 x 10^{-2}	1.7 x 10^{-5} – 2.8 x 10^{-2}	1.3 x 10^{-5} - 1.8 x 10^{-2}	6.2 x 10^{-5} – 1 x 10^{-1}
Soil	ingestion		2.2 x 10^{-5} -1.7 x 10^{-3}	1 x 10^{-5} – 8.1 x 10^{-4}	3.2 x 10^{-5} – 2.4 x 10^{-3}	6.4 x 10^{-5}- 4.9 x 10^{-3}

	dermal contact		3.3 x 10^{-6} – 2.5 x 10^{-4}	1.5 x 10^{-6} -1.2 x 10^{-4}	1.4 x 10^{-6} -1.1 x 10^{-4}	6.1 x 10^{-6} - 4.6 x 10^{-4}

There are no absolute criteria for acceptable number of additional cancers over a lifetime. In most jurisdictions, the value of one additional case of cancer in one-million (1 x 10^{-6}), proposed by the US EPA (US EPA, 2004) is frequently used as a management goal for risks posed by environmental contamination. This value is also included in the Italian law (D.L. 4/2008). However, in the context of drinking water guidelines, Health Canada (2004) has defined as “essentially negligible” ILCR ranges from one new cancer above background per 100,000 people to one new cancer above background per 1 million people (i.e., 10^{-5} to 10^{-6}) over a lifetime. The probability plot (Fig. 3) shows that the exposure route, which involves a higher incremental cancer risk, is the oral ingestion. For soil ingestion, it was found that probabilities of risk through lifetime exceeding 1 x 10^{-6} is 6.8%.

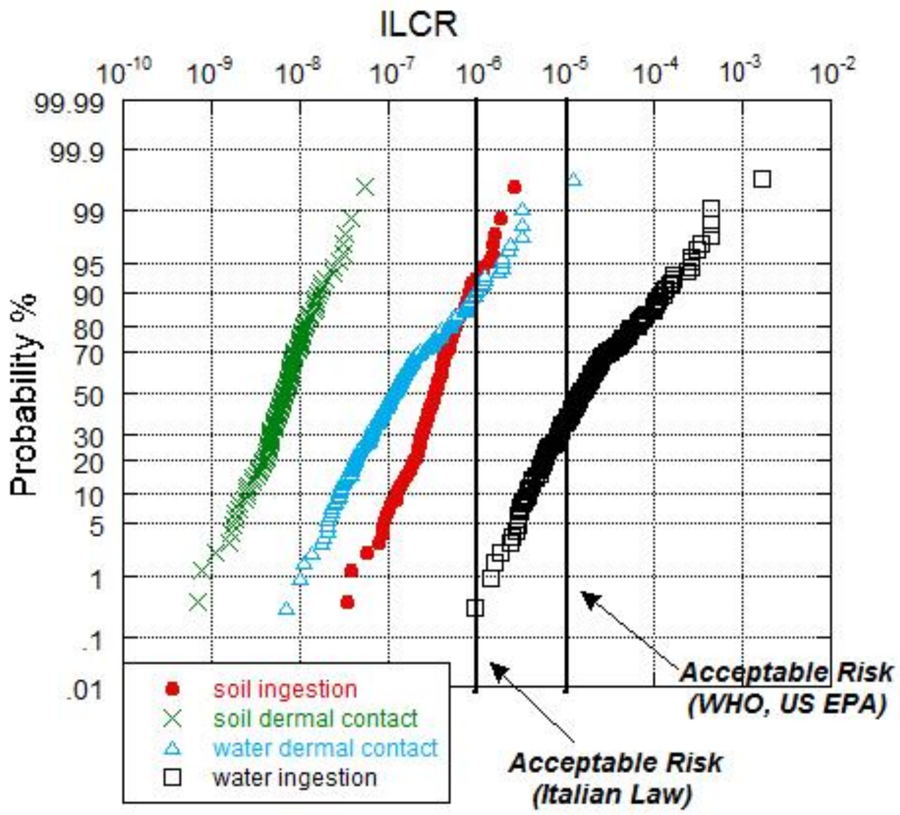


Fig. 3. *Probability plot of Incremental Life Cancer Risk (ILCR) posed by different expousure routes for Italian population, i.e., soil ingestion, soil dermal contact, water dermal contact and water ingestion.*

Regarding water ingestion, it is clear that this is the most serious exposure route with an elevated impact on human health. The incremental life cancer risk due to drinking water for the Italian population provides interesting information about the variation from children to adults. The ILCR through lifetime ranges from 9.6 x 10^{-7} to 1.7 x 10^{-3}; there are, of course, several orders of magnitude between lower and upper percentiles (Fig. 4). Duration of exposure seems to play a decisive role in risk estimation.

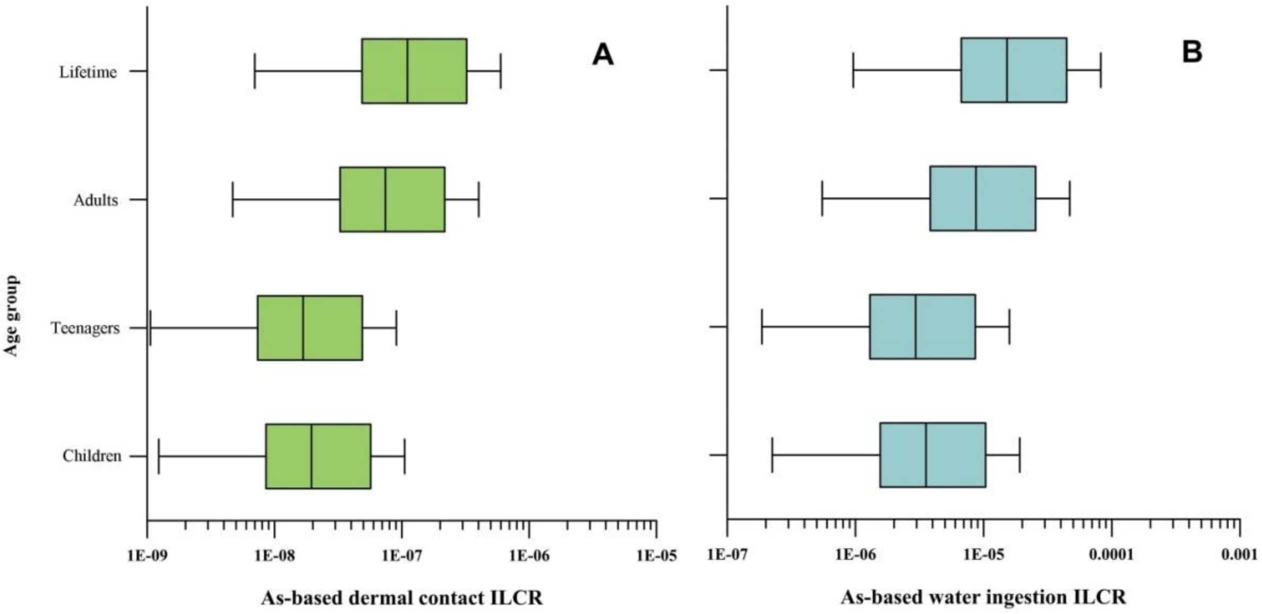


Fig. 4. *Multiple boxplot comparing ILCR values estimated for different age groups (children 1-8; teenagers 9-16; adults 16-70 years old; lifetime) and different water exposure routes (A = water dermal contact; B = water ingestion).*

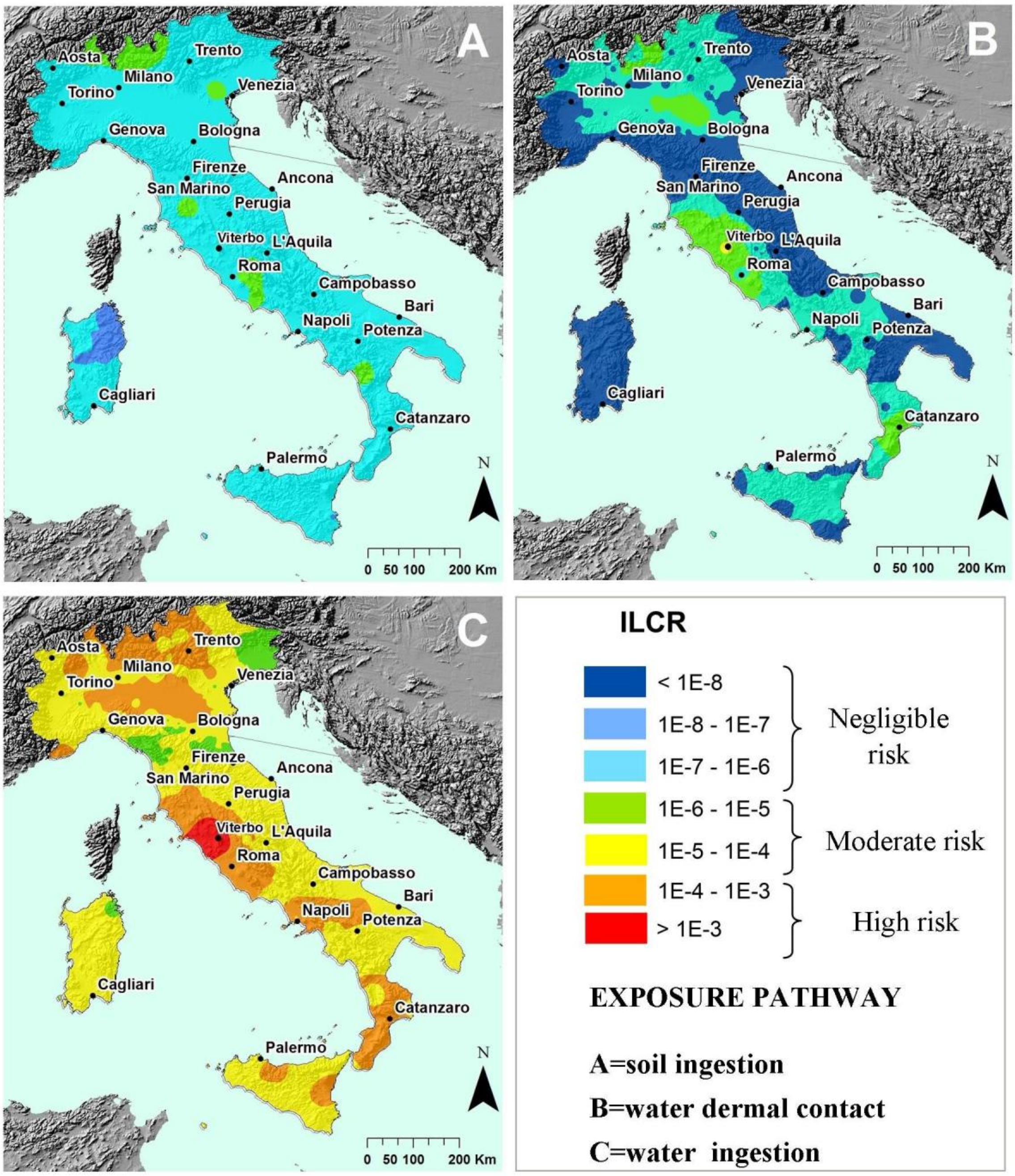


Fig. 5. *Spatial distribution of carcinogenic risk due to As exposure, calculated as Incremental Life Cancer Risk. The exposure scenario used here is based on a continuous lifetime daily exposure for (A) soil ingestion, (B) water dermal contact and (C) water ingestion*.

Regarding the dermal absorption route (both through water and soil dermal contact), it contributed little to the total risk and could be considered negligible for all three age groups.

Almost 20% of analysed tap water samples are responsible for an increased probability of 1 x 10^{-4} developing cancer, which means that there is a potential carcinogenic risk to local residents. Based on the geographical distribution of ILCR zones obtained from the IDW approach, the hazardous ILCR zones are mostly located in the central area of Italy including the township of Viterbo (Fig.

5). The incremental probability developing cancer over a lifetime in Viterbo province is almost 350 cases of cancer in 322,000 exposed people.

The determined values of non-carcinogenic effects expressed by the hazard quotient (HQ) are shown in Table 6. They indicate that As soil concentrations do not cause an increase in non-carcinogenic incidences to the inhabitants.

Soil ingestion is usually an accidental route of exposure for children (which can unintentionally ingest soil when playing outdoors) and people employed in the agricultural sector. The results of this study indicate that a significant potential health risk, associated with chronic exposure to As, occurs only from water ingestion.

The most susceptible age groups are children and teenagers, with more than 5.7% of data above the threshold of 1. There may be concern for potential non-cancer effects for 12.7% of the population during a lifetime exposure (from birth to an average age of 70 years).

Based on the geographical distribution of HQ zones, there are medium to high risk HQ zones (derived from water ingestion exposure scenario) in the western coastal areas of central Italy (including Rome), the Po River plain and the central Alps (Fig. 6).

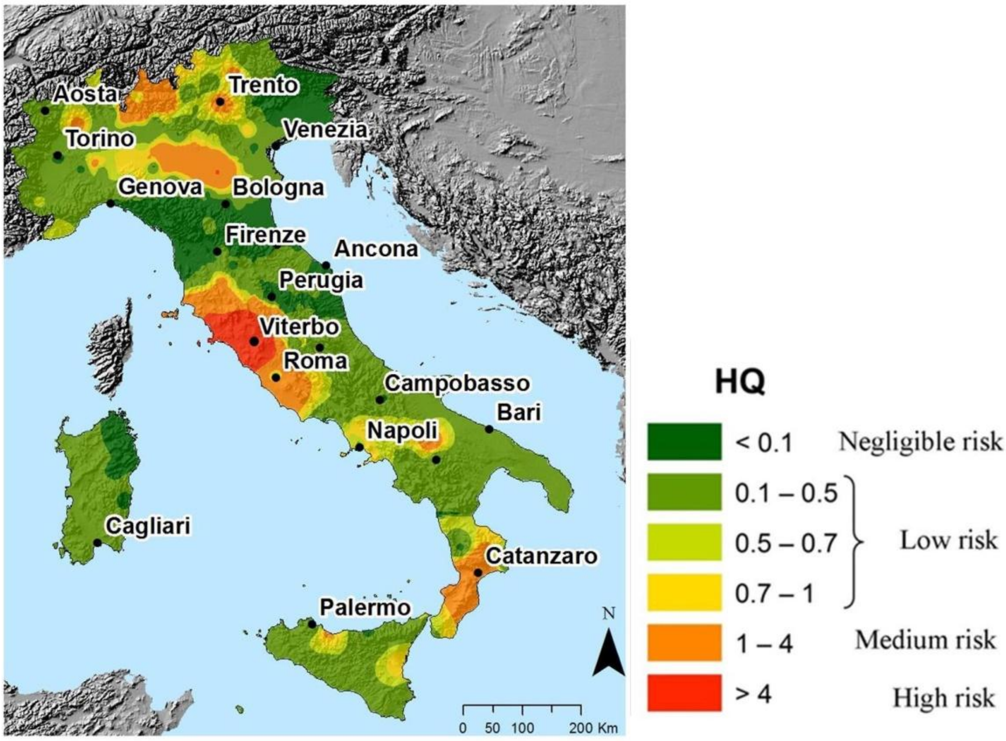


Fig. 6. *Spatial distribution of non-carcinogenic risk, calculated as Hazard Quotient occurring during a lifetime exposure to As. The exposure scenario is based on water ingestion continuous lifetime daily exposure. Risk classes for HQ are based on Chowdhury and Maiti (2016).*

7.4. Stochastic simulation of risk

As an extension to the deterministic approach, a probabilistic analysis of risk was performed. It accounted for uncertainty and variability of the drinking water scenario, which provided the worst health risk threat. Integration of uncertainty and variability can lead to a more realistic understanding of risk, as it is known that a wide variety of features and habits occur in any given population. To capture this variability, the Monte-Carlo simulation technique was run with Oracle Crystal ball software (version 11.1.1.1.00, Oracle, Inc., USA). Monte-Carlo simulation used all available information about the variability and uncertainty inherent in the assessment of risk, and provided a more meaningful estimate of the probable range of exposures (Wu et al., 2016) than point estimates. The statistical distribution of random variables was defined and are tabulated in Table S1 in the Supplementary Material. To verify the log-normality of As concentration values, the R package routine fitdistrplus (Delignette-Muller et al., 2014) was used. It must be stated that geochemical data do not belong to the classical Euclidean space and should be considered in their own Euclidean geometry on the simplex (Aitchison, 1986; Filzmoser et al., 2009, 2010, 2014; Egozcue and Pawlowsky-Glahn, 2011; Reimann et al., 2012). However, the selected stochastic simulation risk procedures use parametric statistics and is, therefore, necessary to estimate some classical statistical parameters.

Anthropometric and water consumption data were extrapolated from the Italian National Food Consumption Survey INRAN-SCAI 2005-06 (Leclercq et al., 2009). This survey was conducted on a representative sample of households randomly selected and stratified into the four main geographical areas of Italy (North-West, North-East, Centre, South and Islands) between October 2005 and December 2006. Sensitivity analysis was also performed to evaluate the impact of variables on the outcome of the risk assessment.

After 500, 1000, 1500, 2000, 3000, 5000 and 10000 iterations, the results showed that 2000 trials are sufficient to ensure the stability of the results. The results of Monte Carlo simulation for the incremental lifetime cancer risks posed by exposure to As in drinking water are presented in Fig. 7. Overall, the ILCR magnitude was in the order of adults > children > teenagers, as already has been shown by the deterministic approach. The results indicate that the 50% probability ILCRs for children exposed to As in drinking water have orders of magnitude above the acceptable cancer risk threshold of 1×10^{-6}. For adults there is a greater than 70% chance the ILCR will exceed the above mentioned limit, indicating a high potential health risk. In addition, there is roughly a 33% chance for teenagers to exceed the 1×10^{-6} threshold. The results of this study also showed that lifetime exposure ILCR have a 97% probability of exceeding the above mentioned threshold (Fig. 8A). Probabilistic exposure estimates return quite similar results to the deterministic point estimates.

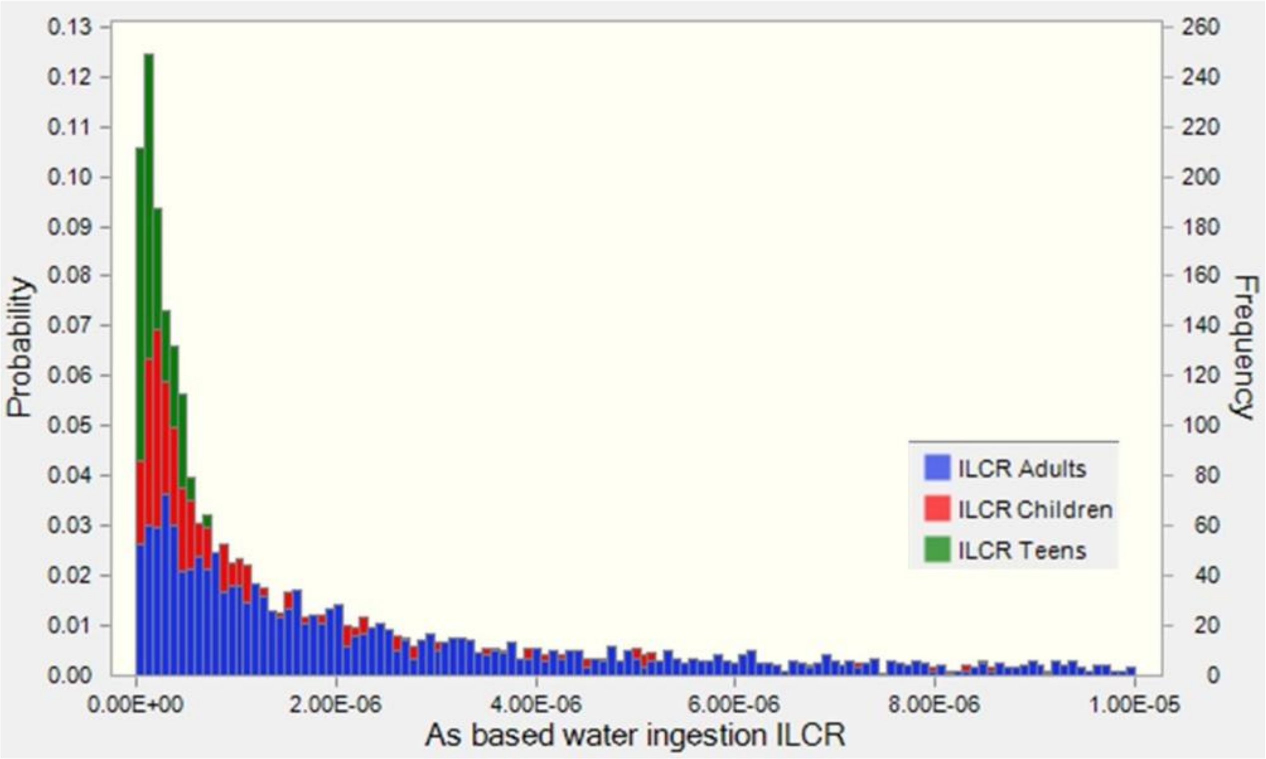


***Fig. 7**. Predicted probability density functions of As-based ingestion ILCR for three age groups in Italy (adults, children and teenagers).*

Sensitivity analysis was performed to rank the parameters contributing most significantly to the cancer risk. Sensitivity analysis results, which are portrayed in the form of tornado plot (Fig. 8B), showed that contaminant concentration in drinking water (Cw) has the greatest impact on the outcome of risk assessment (for all age groups), followed by exposure duration (ED) and volume of water ingested (ingestion rate – IR). Body weight (BW) showed a slightly negative coefficient, thus, indicating that an increase of BW might be associated with a decrease risk. This seems, however, unrealistic from a biological point of view, as several studies highlighted that environmentally-related cancer risks may be markedly increased in people with elevated body mass index (BMI), especially in those with an elevated BMI in early-life (Steinmaus et al., 2015). Unfortunately, the accepted models take into account body weight rather than BMI, and this represents a limitation. Indeed, an implementation of the last variable should be supported.

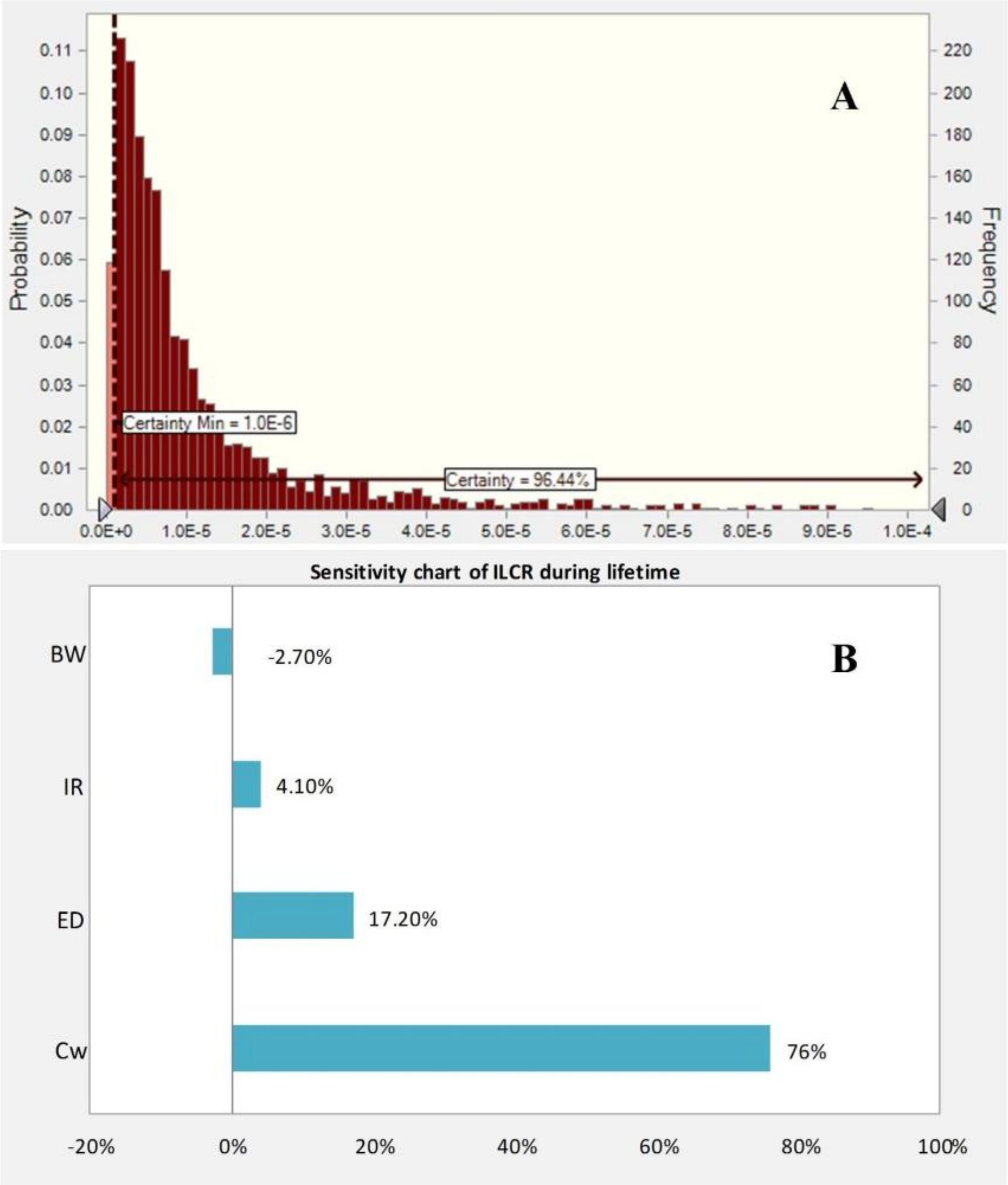


Fig. 8. *(A) Predicted probability density functions of As-based ingestion ILCR over a lifetime; (B) tornado plot displaying sensitivity analysis data of As-based ingestion ILCR over a lifetime.*

8. Conclusions

This study represents the first work at the national scale for Italy about the occurrence and spatial distribution of As in different environmental media. Further, the risk for human health due to As exposure through different pathways was determined (using both deterministic and stochastic approaches).

High As levels in different environmental media are apparently responsible for an elevated health impact, as recognised by the international community, and is characterised by important geochemical anomalies in different environmental media in this study.

Arsenic is widely distributed throughout Italy both in water and soil, a feature reflecting geological processes, lithology and industrial history. The Risk Assessment for both carcinogenic and non-carcinogenic impacts, yielded interesting results. Based on these results, it is clear that tap water ingestion plays an important role in governing potential cancer and non-cancer risk of human exposure to As. The comparison of deterministic and probabilistic risk values (the latter refers to a probability density function of risk), indicates that for the latter the integration of uncertainty and variability leads to a more realistic understanding of human health risk.

Indeed, it is of interest that the Incremental Life Cancer Risk through water ingestion shows that almost 100% of analysed drinking water is responsible for an increment of cancer risk above the limit of 1×10^{-6}, stated by international agencies (e.g., US EPA, 2004) and Italian legislation (D.L. 4/2008). It must be emphasised that the results obtained by the probabilistic approach are always comparable with the deterministic ones.

This work confirms adulthood is the most susceptible group to As exposure, due to the long-term exposure. The population of central Italy is the most endangered, where high As contents in the analysed samples is due to the presence of alkaline volcanic material,.

Although mathematical models are useful tools in risk assessment, they are oversimplifications of complex natural systems, which are influenced to a variable extent by human activities. Probabilistic simulation of risk has been developed by considering the inherent variability of modelled parameters. It is noted that quantitative risk estimates may give an impression of certainty which, in fact, they do not have. In general, when discussing risk index values, these should be considered only as ‘order of magnitude’ estimates.

This study could be considered as a critical example of challenging the current international and Italian As regulatory levels. More than 80% of the analysed water samples are responsible for an excess cancer risk, which are higher than the benchmark value of 1×10^{-5}. Most of these As concentrations are lower than the current As statutory level for drinking water (10 μg/l). Further, Tchounwou et al. (2004) report that cancer risks of 10^{-5}, 10^{-6} and 10^{-7} have been estimated for drinking water containing 0.022, 0.0022, and 0.00022 μg/l As, respectively. While the debate about low-dose exposure is ongoing, D'Ippoliti et al. (2015) provide new evidence that even As concentrations below the EU limit of 10 μg/l can raise mortality risks.

What could the above discussion mean? Should the As standard level for drinking water be reviewed? Could the assumption of As to be a non-threshold contaminant (non-threshold acting contaminants exhibit effects at virtually all levels of exposure, so any exposure results in some level of risk) lead to a risk overestimation? Of course, this is a toxicological issue, which should be researched by taking into consideration the natural occurrence of As to begin with.

Although specific regulatory levels might be debatable, all would agree that minimising As exposure is the best solution, especially in early life. However, it should not be forgotten that As is a global health hazard affecting millions of people worldwide, and it is fundamental to anticipate that any changes to regulatory limits may cause a future alarm for the population.

Therefore, determination of As concentrations in drinking water is particularly important, given its well-known carcinogenic and non-carcinogenic effects. Strategies to reduce the As intake (public water treatment or residential correction systems) and changes in vulnerable population habits, may be a good starting point to reduce the health risk for the Italian population. The return on the investment can be substantial, as reduced incidence of chronic disease and lower rates of cancer, should result in the reduction of hospital treatment costs.

It is, therefore, concluded that further research should be directed to specific human exposure, and a geomedical based approach could be helpful to understand the link between low-dose As exposure and induced human disease in several areas of Italy.

Acknowledgments

The authors wish to thank Reijo Salminen and Clemens Reimann for active cooperation and all the members of the FOREGS and EuroGeoSurveys Geochemistry Expert Group that made this study possible. Many thanks to colleagues who enthusiastically helped in the sample collection in Italy. The manuscript presents the opinions of the authors and do not represent the position of EuroGeoSurveys.

References

Note: All web links checked on 02nd May 2019.

Ahsan H, Chen Y, Parvez F, Argos M, Hussain I, Momotaj H, Levy D, van Geen A, Howe G, Graziano J., 2006. Health Effects of Arsenic Longitudinal Study (HEALS): Description of a multidisciplinary epidemiologic investigation. J. Exposure Science and Environmental Epidemiology16(2), 191-205.

Aitchison, J., 1986. The statistical analysis of compositional data. Chapman & Hall, London, 416 pp.

Appelo, T., Heederik, J.P., 2008. Arsenic in groundwater – A World problem. Seminar proceedings, Utrecht 9 November 2006. Netherlands National Committee of the IAH, 136 pp.

Ardau, C., Podda, F., Da Pelo, S., Frau, F., 2013. Stream water chemistry in the arsenic-contaminated Baccu Locci mine watershed (Sardinia, Italy) after remediation. Environ Sci Pollut Res Int. 20(11):7550-9. doi: 10.1007/s11356-013-1790-y.

Argos M, Kalra T, Rathouz PJ, Chen Y, Pierce B, Parvez F, Islam T, Ahmed A, Rakibuz-Zaman, Hasan R, Sarwar G, Slavkovich V, van Geen A, Graziano, J, Ahsan H, 2010. Arsenic exposure from drinking water, and all-cause and chronic-disease mortalities in Bangladesh (HEALS): a prospective cohort study. Lancet 376(9737), 252–258.

Armstrong, C.W., Stroube, R.B., Rubio, T., Siudyla, E.A., Miller, G.B. Jr., 1984. Outbreak of fatal arsenic poisoning caused by contaminated drinking water. Arch Environ Health 39(4), 276-279

ATSDR (Agency for Toxic Substances and Disease Registry) 2007. Arsenic Toxicological Profile. Atlanta, GA:ATSDR. http://www.atsdr.cdc.gov/ToxProfiles/tp.asp?id=22&tid=3

Baiocchi, A., Lotti, F., Piscopo, V., Chiocchini, U., Madonna, S., Manna, F., 2007. Hydraulic interactions between aquifers in Viterbo area (Central Italy). In: Howard, K.W.F. (Ed.), *Urban Groundwater -Meeting the Challenge*. *Volume 8*. Taylor & Francis Group, London. IAH Selected Papers 8, 223-238.

Banks, D., Birke, M., Flem, B. & Reimann, C., 2015. Inorganic chemical quality of European tap-water: 1. Distribution of parameters and regulatory compliance. Applied Geochemistry 59, 200-210.

BBodSchG, 1998. Federal soil protection act (Bodenschutzgesetz, BBodSchG) – Excerpts) - Act on Protection against Harmful Changes to Soil and on Rehabilitation of Contaminated Sites. Federal Law Gazette, 502 pp.

Berg, M., Tran, H.C., Nguyen, T.C., Pham, H.V., Schertenleib, R., Giger, W., 2001. Arsenic contamination of groundwater and drinking water in Vietnam: A human health threat. Environmental Science and Technology, 35(13), 2621–26.

Birke, M., Reimann, C., Demetriades, A., Rauch, U., Lorenz, H., Harazim, B., Glatte, W., 2010. Determination of main and trace elements in European bottled mineral water — analytical methods. . In: M. Birke, A. Demetriades, B. De Vivo (Guest Editors), Mineral Waters of Europe. Special Issue, J. Geochem. Explor. 107(3), 217–226.

Birke, M., Reimann, C., Fabian, K., 2014a. Analytical methods used in the GEMAS project. Chapter 5 In: Reimann, C., Birke, M., Demetriades, A., Filzmoser, P., O'Connor, P.(Eds.), Chemistry of Europe's Agricultural Soils. Part A: Methodology and Interpretation of the GEMAS Data Set. Schweizerbart Science Publishers, Stuttgart, 41-46.

Boyle, R.W., 1974. Elemental associations in mineral deposits and indicator elements of interest in geochemical prospecting. Energy, Mines and Resources Canada, Geological Survey Paper 74-45, 40 pp.; https://doi.org/10.4095/102553.

Bowell, R.J., Alpers, C.N., Jamieson, H.E., Nordstrom, D.K., Majzlan, J., 2014. The environmental geochemistry of arsenic—an overview. Rev. Mineral. Geochem. 79(1), 1–16.

BRAC (Bangladesh Rural Advancement Committee), 2000. Combating a Deadly Menace: Early Experiences with a Community-Based Arsenic Mitigation Project in Bangladesh, Research Monograph Series No. 16, BRAC, Dhaka.

Brinkel, J., Khan, M.H., Kraemer, A., 2009. A Systematic review of arsenic exposure and its social and mental health effects with special reference to Bangladesh. International Journal Environmental Research and Public Health 6(5), 1609–1619; https://doi.org/10.3390/ijerph6051609.

Caceres, D.D., Pino, P., Montesinos, N., Atalah, E., Amigo, H., Loomis, D., 2005. Exposure to inorganic arsenic in drinking water and total urinary arsenic concentration in a Chilean population. Environmental Research, 98(2), 151–59.

Carlin DJ, Naujokas MF, Bradham KD, Cowden J, Heacock M, Henry HF, Lee JS, Thomas DJ, Thompson C, Tokar EJ, Waalkes MP, Birnbaum LS, Suk WA, 2016. Arsenic and environmental health: state of the science and future research opportunities. Environ Health Persp 124, 890–899

CCME, 2001. Canadian Council of Ministers of Environment (CCME) Water Quality Guidelines for Arsenic (2001 update)

CDWG (Federal-Provincial-Territorial Committee on Drinking Water of the Federal-Provincial-Territorial Committee on Health and the Environment), 2007. Guidelines for Canadian Drinking Water Quality: Summary Table, Health Canada.

CFR (Code of Federal Regulations), 2006. US Government Printing Office, Superintendent of Documents, Washington, DC.

Chappell, W.R., Abernathy, C.O., Calderon, R.L., 1999. Arsenic exposure and health effects. Elsevier, Amsterdam, 416 pp.

Chen, S-L., Dzeng, S.R., Yang, M-H., Chiu, K-H., Shieh, G-M., Wai, C.M., 1994. Arsenic species in groundwater of the Blackfoot disease area, Taiwan. Environmental Science Technology 28, 877-881.

Chen, C.J., Chiou, H.Y., Chiang, M.H., Lin, L.J., Tai, T.Y., 1996. Dose-response relationship between ischemic heart disease mortality and long-term arsenic exposure. Arterioscler Thromb Vasc Biol 16(4), 504-510.

Chen CL, Chiou HY, Hsu LI, Hsueh YM, Wu MM, Chen CJ., 2010. Ingested arsenic, characteristics of well water consumption and risk of different histological types of lung cancer in northeastern Taiwan. Environ Res 110(5):455–462.

Cheng, Q., 1999. Multifractality and spatial statistics. Computer & Geosciences 25 (10), 946–961.

Chiou, H.Y., Chiou, S.T., Hsu, Y.H., et al., 2001. Incidence of transitional cell carcinoma and arsenic in drinking water: A follow-up study of 8,102 residents in an arseniasis-endemic area in northeastern Taiwan. Am J Epidemiol 153(5):411-418.

Chiu HF, Ho SC, Wang LY, Wu TN, Yang CY., 2004. Does arsenic exposure increase the risk for liver cancer? J. Toxicol. Environ. Health A. 67, 1491–1500.

Chowdhury, A., Maiti, S.K., 2016. Assessing the ecological health risk in a conserved mangrove ecosystem due to heavy metal pollution: A case study from Sundarbans Biosphere Reserve, India. Hum Ecol Risk Assess 20(3), 257–269

Cicchella, D., De Vivo, B., Lima, A., 2005. Background and baseline concentration values of elements harmful to human health in the volcanic soils of the metropolitan and provincial areas of Napoli (Italy). Geochemistry: Exploration, Environment, Analysis 5, 29–40.

Cicchella D., Albanese, S., De Vivo, B., Dinelli, E., Giaccio, L., Lima, A., Valera, P., 2010. Trace elements and ions in Italian bottled mineral waters: identification of anomalous values and human health related effects. *Journal of Geochemical Exploration*107(3), 336-349.

Cicchella, D., Giaccio, L., Dinelli, E., Albanese, S., Lima, A., Zuzolo, D., Valera, P., De Vivo, B., 2015. GEMAS: Spatial distribution of chemical elements in agricultural and grazing land soil of Italy. In: A. Demetriades, M. Birke, S. Albanese, I. Schoeters & B. De Vivo (Guest Editors), Continental, Regional and Local scale Geochemical Mapping, Special Issue, J. Geochem. Explor. 154, 129– 42.

Chung, J. Y., Yu, S.D., Hong, Y.S. 2014. Environmental source of arsenic exposure. J. Prev. Med. Public Health, 47, 253–257.

Dangleben, N.L., Skibola, C.F., Smith, M.T., 2013. Arsenic immunotoxicity: a review. Environmental Health 12, 73; https://doi.org/10.1186/1476-069X-12-73.

Delignette-Muller, M., Pouillot, R., Denis, J., and Dutang, C., 2014. fitdistrplus: Help to Fit of a Parametric Distribution to Non-Censored or Censored Data. R package version 1.0-2.

Dinelli E., Lima A., Albanese S., Birke M., Cicchella D., Giaccio L., Valera P., De Vivo B., 2012. Major and trace elements in tap water from Italy. *Journal of Geochemical Exploration* 112, 54-75.

D'Ippoliti D., Santelli E., De Sario M., Scortichini M., Davoli M., Michelozzi P., 2015. Arsenic in Drinking Water and Mortality for Cancer and Chronic Diseases in Central Italy, 1990-2010. PLoS One 18;10(9):e0138182. https://doi.org/10.1371/journal.pone.0138182.

Dissanayake, C.B., Rao, C.R.M., Chandrajith, R., 2010. Some aspects of the medical geology of the Indian subcontinent and neighbouring regions. In: Selinus, O., Finkelman, R.B., Centeno, J.A. (Eds.), Medical Geology. Springer Science+Business Media B.V., 175-198.

D.L. 152/2006 (Legislative Decree 2006 n.152) “Norme in materia ambientale”. Gazzetta Ufficiale n. 88 14-4-2006, Suppl Ord n. 96; http://www.camera.it/parlam/leggi/deleghe/06152dl.htm. Accessed 04 April 2019

D.L. 4/2008 (Legislative Decree 2008 n.4), Ulteriori disposizioni correttive ed integrative del D.L. 152/2006, (GU Serie Generale n.24 del 29-01-2008 - Suppl. Ordinario n. 24); http://www.gazzettaufficiale.it/atto/serie_generale/caricaDettaglioAtto/originario?atto.dataPubblicazioneGazzetta=2008-01-29&atto.codiceRedazionale=008G0020&elenco30giorni=false

EC, 1998. Council Directive 98/83/EC of November 1998 on the quality of water intended for human consumption. Official Journal of the European Communities, L330, 32-54; https://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:31998L0083&from=EN.

EFSA (European Food Safety Authority), 2004. Dietary exposure to inorganic arsenic in the European population. EFSA Journal 12(3):3597, 68 pp.; https://doi.org/10.2903/j.efsa.2014.3597.

EGS, 2008. EuroGeoSurveys Geochemistry Working Group. EuroGeoSurveys Geochemical Mapping of Agricultural and Grazing Land in Europe (GEMAS) — Field manual. Norges Geologiske Undersokelse Report, 2008.038, 46 pp.; http://www.ngu.no/upload/Publikasjoner/Rapporter/2008/2008_038.pdf).

European Union, 1998. Council directive 98/83/EC on the quality of water intended for human consumption. Official Journal of the European Communities, L 330/32, 32–54.

Ferreccio, C., Gonzalez Psych, C., Milosavjlevic Stat, V., Gredis, M.G., Sancha, A.M., 1998. Lung cancer and arsenic exposure in drinking water: A case-control study in northern Chile. Cad Saude Publica 14(Suppl 3),193-198.

Filzmoser, P., Hron, K., Reimann, C., 2009. Univariate statistical analysis of environmental (compositional) data — problems and possibilities. Sci. Total Environ. 407, 6100-6108.

Filzmoser, P., Hron, K., Reimann, C., 2010. The bivariate statistical analysis of environmental (compositional) data. Sci. Total Environ. 408, 4230-4238.

Filzmoser, P., Reimann, C., Birke, M., 2014. Univariate Data Analysis and Mapping. Chapter 8 In: C. Reimann, M. Birke, A. Demetriades, P. Filzmoser, P. O’Connor (Editors), Chemistry of Europe's agricultural soils - Part A: Methodology and interpretation of the GEMAS data set. Geologisches Jahrbuch (Reihe B102), Schweizerbarth, Hannover, 67-81.

Flem, B., Reimann, C., Birke, M., Banks, D., Filzmoser, P., Frengstad, B., 2015. Inorganic chemical quality of European tap-water: 2. Geographical distribution. Applied Geochemistry 59, 211-224.

Frau, F. Ardau, C., 2003. Geochemical controls on arsenic distribution in the Baccu Locci stream catchment (Sardinia, Italy) affected by past mining. Applied Geochemistry 18(9),1373-1386; https://doi.org/10.1016/S0883-2927(03)00057-X

Guo, H.R., Yu, H.S., Hu, H., Monson, R.R., 2001. Arsenic in drinking water and skin cancers: Cell-type specificity (Taiwan, R.O.C.). Cancer Causes Control 12(10), 909-916.

Guo, H., Wang, Y., 2005. Geochemical characteristics of shallow groundwater in Datong Basin, northwestern China. Journal of Geochemical Exploration, 87(3), 109–20.

Hansen, H.J., Danielsberg, A., 2009. Condition Classes for Contaminated Sites. The Environment Agency, Report TA-2533 (in Norwegian).

Hantson, P., Verellen-Dumoulin, C., Libouton, J.M., Leonard, A., Leonard, E.D., Mahieu, P., 1996. Sister chromatid exchanges in human peripheral blood lymphocytes after ingestion of high doses of arsenicals. Int Arch Occup Environ Health 68, 342-344.

Haupert, T.A., Wiersma, J.H., Goldring, J.M., 1996. Health effects of ingesting arsenic-contaminated groundwater. Wis Med J 95(2), 100-104.

Health Canada, 2004. Federal Contaminated Site Risk Assessment in Canada Part I: Guidance on human health Preliminary Quantitative Risk Assessment (PQRA), Cat. H46-2/04-367E; http://www.hc-sc.gc.ca/ewh-semt/contamsite/risk-risque-eng.php.

Health Canada. 2007a. Federal Contaminated Site Risk Assessment in Canada. Part I: Guidance on Human Health Preliminary Quantitative Risk Assessment. Version 2.0.

Health Canada. 2007b. Federal Contaminated Site Risk Assessment in Canada. Part II: Health Canada Toxicological Reference Values (TRVs). Cat. H46-2/04-368E.

Heitkemper, D.T., Kubachka, K.M., Halpin, P.R., Allen, M.N., Shockey, N.V., 2009. Survey of total arsenic and arsenic speciation in US-produced rice as a reference point for evaluating change and future trends. Food Addit. Contam. B2, 112–120; https://doi.org/10.1080/02652030903148298.

Henke, J., 2009. Arsenic: Environmental Chemistry, Health Threats and Waste Treatment. John Wiley & Sons, Ltd. ISBN: 978-0-470-02758-5

Hopenhayn, C., Ferreccio, C., Browning, S.R., Huang, B., Peralta, C., Gibb, H., Hertz-Picciotto, I., 2003. Arsenic exposure from drinking water and birth weight. Epidemiology 14(5), 593-602.

Hopenhayn, C., Bush, H.M., Bingcang, A., Hertz-Picciotto I., 2006. Association between arsenic exposure from drinking water and anemia during pregnancy. J Occup Environ Hyg 48(6), 635-643.

Hu, Z., Gao, S., 2008. Upper crustal abundances of trace elements: A revision and update. Chem Geol 253, 205- 221.

Huy, T.B., Tuyet-Hanh, T.T., Johnston, R., Nguyen-Viet, H., 2014. Assessing health risk due to exposure to arsenic in drinking water in Hanam Province, Vietnam. Int. J. Environ. Res. Public Health., 11:7575–7591. doi: 10.3390/ijerph110807575.

IARC (International Agency for Research on Cancer), 2004. Some Drinking Water Disinfectants and Contaminants, including Arsenic. Vol. 84. Lyon: IARC Press. Monographs on evaluation of carcinogenic risk to humans; pp. 269–477.

IARC (International Agency for Research on Cancer) 2012. A Review of Human Carcinogens: Arsenic, Metals, Fibres, and Dusts. Lyon: World Health Organization

Indian Bureau of Standards, 1991. Specifications for Drinking Water, IS 10500, New Delhi.

Islam LN, Nabi AH, Rahman MM, Zahid, MS, 2007. Association of respiratory complications and elevated serum immunoglobulins with drinking water arsenic toxicity in human. J Environ Sci Health A Tox Hazard Subst Environ Eng 42(12), 1807–1814.

Jain, N., Chandramani, S., 2018. Arsenic poisoning – An overview. Indian Journal of Medical Specialities 9(3), 143-145; https://doi.org/10.1016/j.injms.2018.04.006.

James KA, Meliker JR, Buttenfield BE, Byers T, Zerbe GO, Hokanson JE, Marshall JA, 2014. Predicting arsenic concentrations in groundwater of San Luis Valley, Colorado: implications for individual-level lifetime exposure assessment. Environ Geochem Health 36(4), 773–782.

Jorhem, L., Åstrand, C., Sundström, B., Baxter, M., Stokes, P., Lewis, J., Grawé, K.P., 2008. Elements in rice from the Swedish market: 1. Cadmium, lead and arsenic (total and inorganic). Food Addit. Contam. Part A 25, 284–292.

Kabata-Pendias, A., Pendias, H., 2001. Trace elements in soils and plants. CRC Press, Inc., Boca Raton, Florida, 413 pp.

Kabata-Pendias, A., Mukherjee, A.B., 2007. Trace elements from Soil to Human. Springer-Verlag, Berlin 550 pp.

Kapaj, S., Peterson, H., Liber, K., Bhattacharya, P., 2006. Human health effects from chronic arsenic poisoning – A review. Journal of Environmental Science and Health Part A 41, 2399–2428; https://doi.org/10.1080/10934520600873571.

Kamijo, Y., Soma, K., Asari, Y., Ohwada, T., 1998. Survival after massive arsenic poisoning self-treated by high fluid intake. Clin Toxicol 36(1-2):27-29.

Khan, S., Q.Y.Z. Cao, Y.Z. Huang and Y.G. Zhu, 2008. Health risks of heavy metals in contaminated soils and food crops irrigated with wastewater in Beijing, China. Environ. Poll., 125(3): 686-692.

Leclercq, C., Arcella, D., Piccinelli, R., Sette, S., Le Donne, C., Turrini, A., 2009. The Italian National Food Consumption Survey INRAN-SCAI 2005-06: main results in terms of food consumption. Public Health Nutr. 12(12):2504-32. doi: 10.1017/S1368980009005035.

Levin-Scherz JK, Patrick JD, Weber FH, Garabedian C Jr., 1987. Acute arsenic ingestion. Ann Emerg Med 16(6), 702-704.

Liang, F., Li, Y., Zhang, G., Tan, M., Lin, J., Liu, W., Li, Y., Lu, W., 2010. Total and speciated arsenic levels in rice from China. Food Addit. Contam. 27, 810-816.

Lima, A., De Vivo, B., Cicchella, D., Cortini, M., Albanese, S., 2003. Multifractal IDW interpolation and fractal filtering method in environmental studies: an application on regional stream sediments of Campania Region (Italy). Appl. Geochem. 18, 1853–1865.

Lugo, G., Cassady, G., Palmisano, P., 1969. Acute maternal arsenic intoxication with neonatal death. Am J Dis Child 117, 328-330.

Matisoff, G., Khourey, C.J., Hall, J.F., Varnes, A.W., Strain, W.H., 1982. The nature and source of arsenic in northeastern Ohio groundwater. Groundwater 20, 446-456.

Matys Grygar, T., Elznicová, J., Tůmová, Š., Faměra, M., Balogh, M., Kiss, T., 2016. Floodplain architecture of an actively meandering river (the Ploučnice River, the Czech Republic) as revealed by the distribution of pollution and electrical resistivity tomography. Geomorphology, 254, 41–56.

Mazumder, D.N., Haque, R., Ghosh, N., De, B.K., Santra, A., Chakraborti, D., Smith, A.H., 2000. Arsenic in drinking water and the prevalence of respiratory effects in West Bengal, India. Int J Epidemiol. 29(6), 1047-1052.

MEJ (Ministry of the Environment, Japan), 2008. http://www.env.go.jp/en/standards/. Last accessed on March 14, 2019.

MEJ (Ministry of Environment, Japan), 2019. Environmental quality standards for soil pollution. Ministry of Environment, Government of Japan; http://www.env.go.jp/en/water/soil/sp.html. Last accessed on March 14, 2019

Mendez, M.A.,González-Horta, C.,Sánchez-Ramírez, B., Ballinas-Casarrubias, L., Cerón, R.H., Morales, D.V., Baeza Terrazas, F.A., Ishida, M.C., Gutiérrez-Torres, D.S., Saunders, R.J., Drobná, Z., Fry, R.C., Buse, J.B., Loomis, D., García-Vargas, G.G., Del Razo, L.M., Stýblo, M., 2016. Chronic exposure to arsenic and markers of cardiometabolic risk: A cross-sectional study in Chihuahua, Mexico. Environmental Health Perspectives 124(1), 104-111

Milton, A.H., Smith, W., Rahman, B., Hasan, Z., Kulsum, U., Dear, K., Rakibuddin, M., Ali, A., 2005. Chronic arsenic exposure and adverse pregnancy outcomes in Bangladesh. Epidemiology 16(1), 82-86

Ministry of Health, 2005: Drinking-water Standards for New Zealand 2005. Wellington: Ministry of Health.

Mizuta, N., Mizuta, M., Ito, F., Ito, T., Uchita, H., Watanabe, Y., Akama, H., Murakami, T., Hayashi, F., Nakamura, K., Yamaguchi, T., Mizuta, W., Oishi, S., Matsumura, H., 1956. An outbreak of acute arsenic poisoning caused by arsenic contaminated soy-sauce (shoyu): A clinical report of 220 cases. Bull Yamaguchi Med Sch 4(2-3), 131 149.

Morton, W.E., Dunnette, D.A., 1994. Health effects of environmental arsenic. In: Nriagu, J.O. (Ed.), Arsenic in the Environment, Part II: Human Health and Ecosystem Effects. Wiley, New York, 159-172.

Naujokas, M. F., Anderson, B., Ahsan, H., Aposhian, H. V., Graziano, J. H., Thompson, C., Sulk, W.A., 2013. The broad scope of health effects from chronic arsenic exposure: update on a worldwide public health problem. Environ. Health Perspect. 121, 295–302. https://doi.org/10.1289/ehp.1205875

NSDWQ, 2008. Pakistan Environmental Protection Agency, Ministry of Environment, Government of Pakistan. National Standards for Drinking Water Quality.

Panagiotaras, D., Nikolopoulos, D., 2015. Arsenic occurrence and fate in the environment; A geochemical perspective. Journal of Earth Science & Climate 6(4), 9 p.; DOI: 10.4172/2157-7617.1000269.

Pompili M., Vichi M., Dinelli E., Erbuto D., Pycha R., Serafini G., Giordano G., Valera P., Albanese S., Lima A., De Vivo B., Cicchella D., Rihmer Z., Fiorillo A., Amore M., Girardi P., Ross Baldessarini J., 2017. Arsenic: Association of regional concentrations in drinking water with suicide and natural causes of death in Italy. Psychiatry Research 249, 311-317.

Ramasamy, S., Lee, J.S., 2015. Arsenic Risk Assessment. Handbook of Arsenic Toxicology, 95-120.

Rasool A., Farooqi A., Masood S., Hussain K., 2016. Arsenic in groundwater and its health risk assessment in drinking water of Mailsi, Punjab, Pakistan Hum. Ecol. Risk Assess. 22, 187–202.

Ratnaike, R., 2003. Acute and chronic arsenic toxicity. Postgraduate Medical Journal 79(933), 391–396; https://doi.org/10.1136/pmj.79.933.391.

Reimann, C., Matschullat, J., Birke, M., Salminen, R., 2009. Arsenic distribution in the environment: The effects of scale. Applied Geochemistry 24, 1147–1167.

Reimann, C. and Birke, M. (Editors), 2010. Geochemistry of European Bottled Water. Borntraeger Science Publishers, Stuttgart, 268 pp.; http://www.schweizerbart.de/publications/detail/artno/001201002#.

Reimann, C., Filzmoser, P., Fabian, K., Hron, K., Birke, M., Demetriades, A., Dinelli, E., Ladenberger, A., The GEMAS Project Team, 2012. The concept of compositional data analysis in practice — Total major element concentrations in agricultural and grazing land soils of Europe. Sci. Total Environ. 426, 196-210; http://dx.doi.org/10.1016/j.scitotenv.2012.02.032.

Reimann, C., Birke, M., Demetriades, A., Filzmoser, P., O'Connor, P. (Eds.), 2014. Chemistry of Europe's agricultural soils — Part A: Methodology and interpretation of the GEMAS data set. Geologisches Jahrbuch (Reihe B 102).Schweizerbarth, Hannover, 528 pp.; http://www.schweizerbart.de/publications/detail/isbn/9783510968466.

Roh T., Lynch C.F., Weyer P.,Wang K., Kelly K.M., Ludewig G., 2017. Low-level arsenic exposure from drinking water is associated with prostate cancer in Iowa. Environ. Res.159, 338-343.

Rose, M., Lewis, J., Langford, N., Baxter, M., Origgi, S., Barber, M., MacBainb, H., Thomas, K., 2007. Arsenic in seaweed—forms, concentration and dietary exposure. Food Chem Toxicol., 45(7):1263–1267.

Saha, J.C., Dikshit, A.K., Banyopadhyay, M., Saha, K.C., 2010. A review of arsenic poisoning and its effects on human health. Critical Reviews in Environmental Science and Technology 29(3), 281-313; https://doi.org/10.1080/10643389991259227.

Saha, N., Rahman, M.S,; Ahmed, M.B., Zhou, J.L., Ngo, H.H., Guo, W., 2017. Industrial metal pollution in water and probabilistic assessment of human health risk. J. Environ. Manag., 185, 70–78. https://doi.org/10.1016/j.jenvman.2016.10.023.Saint-Jacques N., Brown P., Nauta L., Boxall J., Parker L., Dummer T.J.B., 2018. Estimating the risk of bladder and kidney cancer from exposure to low-levels of arsenic in drinking water, Nova Scotia, Canada. Environ. Int. 110, 95-104.

Salminen, R. (Chief Ed.), Batista, M.J., Bidovec, M., Demetriades, A., De Vivo, B., De Vos, W., Duris, M., Gilucis, A., Gregorauskiene, V., Halamic, J., Heitzmann, P., Lima, A., Jordan, G., Klaver, G., Klein, P., Lis, J., Locutura, J., Marsina, K., Mazreku, A., O'Connor, P.J., Olsson, S.Å., Ottesen, R.T., Petersell, V., Plant, J.A., Reeder, S., Salpeteur, I., Sandström, H., Siewers, U., Steenfelt, A., Tarvainen, T., 2005. Geochemical Atlas of Europe, Part 1 — Background Information, Methodology and Maps. Geological Survey of Finland, Espoo, 526 pp.; http://www.gtk.fi/publ/foregsatlas.

Selinus, O., Cave, M., Kousa, A., Steinnes, E., Varet, J., Silva, E.F. da, 2019. Medical Geology in Europe. . In: Selinus, O., Finkelman, R.B., Centeno, J.A. (Eds.), Medical Geology. Springer Science+Business Media B.V., 259--301.

Shrestha, R.R., Shrestha, M.P., Upadhyay, N.P, Pradhan, R., Khadka, R., Maskey, A., Maharjan, M., Tuladhar, S., Dahal, B.M., Shrestha, K., 2003. Groundwater arsenic contamination, its health impact and mitigation program in Nepal. Journal of Environmental Science and Health - Part A Toxic/Hazardous Substances and Environmental Engineering, 38(1), 185–200.

Smedley, P.L., Edmunds, W.M., Pelig-Ba, K.B., 1996. Mobility of arsenic in groundwater in the Obuasi gold-mining area of Ghana: some implications for human health. In: Appleton, J.D., Fuge, R., McCall, G.J.H. (Eds.), Environmental Geochemistry and Health. Geological Society Special Publication No. 113, 163-181.

Smedley PL, Kinniburgh DG, 2002. A review of the source, behaviour and distribution of arsenic in natural waters. Appl Geochem 17, 517–568

Smith AH, Goycolea M, Haque R, Biggs ML., 1998. Marked increase in bladder and lung cancer mortality in a region of Northern Chile due to arsenic in drinking water. Am J Epidemiol 147(7), 660–669.

Szuler, I.M., Williams, C.N., Hindmarsh, J.T., Park-Dincsoy, H., 1979. Massive variceal hemorrhage secondary to presinusoidal portal hypertension due to arsenic poisoning. Can Med Assoc J 120(2), 168-171.

Steinmaus, C., Castriota, F., Ferreccio, C., Smith, A.H., Yuan, Y., Liaw, J., Acevedo, J., Perez, L., Meza, R., Calcagno, S., Uauy, R., Smith, M.T., 2015. Obesity and excess weight in early adulthood and high risks of arsenic-related cancer in later life. Environ Res. 142, 594–601; doi: 10.1016/j.envres.2015.07.021.

Tarvainen, T., Albanese, S., Birke, M., Ponavic, M., Reimann, The GEMAS Project Team, 2013. Arsenic in agricultural and grazing land soils of Europe. Appl. Geochem. 28, 2–10.

Tarvainen, T., Birke, M., Reimann, C., Ponavic, M., Albanese, S., 2014. Arsenic anomalies in European agricultural and grazing land soil. In: Reimann, C., Birke, M., Demetriades, A., Filzmoser, P., O'Connor, P. (Eds.), Chemistry of Europe's Agricultural Soils. Part B: General Background Information and Further Analysis of the GEMAS Data Set. Geologisches Jahrbuch (Reihe B103), Schweizerbarth, Hannover, 81-88.

Tchounwou PB, Patlolla AK, Centeno JA., 2003. Carcinogenic and systemic health effects associated with arsenic exposure—a critical review. Toxicol Pathol. 31(6), 575–588.

Trang Hoang, T.Q. and Hahn, C., 2015. Arsenic Fractionation in Agricultural Soil in Vietnam using the Sequential Extraction Procedure. 4th International Conference on Informatics, Environment, Energy and Applications Volume 82 of IPCBEE (2015) DOI: 10.7763/IPCBEE. 2015.V82.24

Tsuda T, Babazono A, Yamamoto E, Kurumatani N, Mino Y, Ogawa T, Kishi Y, Aoyama H., 1995. Ingested arsenic and internal cancer: a historical cohort study followed for 33 years. Am J Epidemiol. 141, 198–209.

US EPA, 1989. Risk Assessment Guidance for Superfund Volume I Human Health Evaluation Manual (Part A). EPA/540/1-89/002, Office of Emergency and Remedial Response U.S. Environmental Protection Agency, Washington, D.C.; http://www.epa.gov/oswer/riskassessment/ragsa/pdf/rags_a.pdf.

US EPA, 1996. Quantitative Uncertainty Analysis of Superfund Residential Risk Pathway Models for Soil and Groundwater: White Paper, US Environmental Protection Agency, USA.

US EPA, 1997. Exposure factors handbook (final report) 1997. Washington, DC: USEPA.US EPA, 1998. Arsenic, Inorganic. United States Environmental Protection Agency, Integrated Risk Information System (IRIS), (CASRN 7440-38-2). Available online at https://cfpub.epa.gov/ncea/risk/recordisplay.cfm?deid=12464

US EPA, 1998. Arsenic, Inorganic. United States Environmental Protection Agency, Integrated Risk Information System (IRIS), (CASRN 7440-38-2); http://www.epa.gov/iris/subst/0278.htm.

US EPA, 2004. Risk Assessment Guidance for Superfund Volume I: Human Health Evaluation Manual (Part E, Supplemental Guidance for Dermal Risk Assessment). EPA/540/R/99/005, Office of Superfund

Remediation and Technology Innovation U.S. Environmental Protection Agency, Washington, DC. Available online at: http://www.epa.gov/oswer/riskassessment/ragse/.

US EPA, 2018. 2018 Edition of the Drinking Water Standards and Health Advisories. EPA 822-F-18-001, Office of Water U.S. Environmental Protection Agency, Washington, DC. Available online at: https://www.epa.gov/dwstandardsregulations/2018-drinking-water-standards-and-advisory-tables.

Wasserman, G.A., Liu, X., Parvez, F., Ahsan, H., Factor-Litvak, P., van Geen, A., Slavkovich, V., Lolacono, N.J., Cheng, Z., Hussain, I., Momotaj, H., Graziano, J.H., 2004. Water arsenic exposure and children's intellectual function in Araihazar, Bangladesh. Environ Health Perspect. 112(13), 1329-1333.

Webster, J.G., Nordstrom, D.K., 2003. Geothermal Arsenic. In: Welch AH, Stollenwerk KG (eds), Arsenic in Ground Water: Geochemistry and Occurrence. Kluwer Academic Publishers, Boston, 101-126.

WHO. 1958. International standards for drinking-water. World Health Organization, Geneva, 152 pp.; https://apps.who.int/iris/bitstream/handle/10665/43845/a91160.pdf?sequence=1.

WHO, 1963. International standards for drinking-water. World Health Organization, Geneva, 206 pp.; https://apps.who.int/iris/bitstream/handle/10665/205104/205104_eng.pdf?sequence=2.

WHO, 1971. International standards for drinking-water. World Health Organization, Geneva, 72 pp.; https://apps.who.int/iris/bitstream/handle/10665/39989/9241540249_eng.pdf?sequence=1.

WHO, 1984. Guidelines for Drinking-water Quality: Volume 2. – Health criteria and other supporting information. World Health Organization, Geneva, 352 pp.; https://apps.who.int/iris/bitstream/handle/10665/252073/9241541695-eng.pdf?sequence=1.

WHO, 2001. Arsenic and arsenic compounds. Environmental health criteria 224. World Health Organization, Geneva, 512 pp.; https://www.who.int/water_sanitation_health/dwq/chemicals/arsenic.pdf?ua=1.

WHO, 2011. Guidelines for drinking-water quality. World Health Organization, Geneva, 564 pp.; https://apps.who.int/iris/bitstream/handle/10665/44584/9789241548151_eng.pdf?sequence=1.

Wu, H., Liao, Q., Chillrud, S.N., Yang, Q., Huang, L., Bi, J., Yan' B., 2016. Environmental Exposure to Cadmium: Health Risk Assessment and its Associations with Hypertension and Impaired Kidney Function. *Sci. Rep.*,**6**:29989; doi: 10.1038/srep29989.

Zhang H., Zhou X., Wang K., Wang W.D., 2017. Health risk assessment of arsenic from blended water in distribution systems. Journal of Environmental Science and Health, Part A, 52 (14), 1322-1329.

Table 1

Table 1. *Typical ranges of As concentrations (mg/kg) in common rock-forming minerals (from Smedley and Kinniburgh, 2002).*

Sulphide minerals		**Silicate minerals**	
Pyrite	100 – 77,000	Quartz	0.4 – 1.3
Pyrrhotite	5 – 100	Feldspar	<0.1 – 2.1
Marcasite	20 – 126,000	Biotite	1.4
Galena	5 – 10,000	Amphibole	1.1 – 2.3
Sphalerite	5 – 17,000	Olivine	0.08 – 0.17
Chalcopyrite	10 – 5,000	Pyroxene	0.05 – 0.8
Oxide minerals		**Carbonate minerals**	
Haematite	up to 160	Calcite	1 – 8
Fe(III) oxyhydroxide	up to 76,000	Dolomite	<3
Magnetite	2.7 – 41	Siderite	< 3
Ilmenite	<1	–	–
Sulphate minerals		**Other minerals**	
Gypsum/anhydrite	<1 – 6	Apatite	<1 – 1,000
Baryte	<1 – 12	Halite	<3 – 30
Jarosite	34 – 1,000	Fluorspar	<2

Table 2. *Effects of As oral exposure adapted from ATSDR (2007).*

System	Exposure duration	Exposure level (As mg/kg/day)	Effects	Source
HIGH DOSE EXPOSURE				
Death	1 week	2	death	Armstrong et al. (1984)
Death	once	22	death	Levin-Scherz et al. (1987)
Gastrointestinal	1 week	0.2	vomiting, diarrhoea, abdominal pain	Armstrong et al. (1984)
Haematological	2 weeks	0.2	pancytopenia, leukopenia	Armstrong et al. (1984)
Hepatic	once	2	slight increase in serum bilirubin	Hantson et al. (1996)
Ocular	once	13	constricted vision	Kamijo et al. (1998)
Cardiovascular	once pregnancy - week 30	6	hypotension, rapid pulse	Lugo et al. (1969)
Gastrointestinal	once pregnancy - week 30	6	abdominal pain, vomiting	Lugo et al. (1969)
Haematological	once pregnancy - week 30	6	high leukocyte count, low haematocrit	Lugo et al. (1969)
Renal	once pregnancy - week 30	6	acute renal failure	Lugo et al. (1969)
LOW-DOSE EXPOSURE				
Respiratory	2-3 weeks	0.05	sore throat, rhinorrhoea, cough, sputum	Mizuta et al. (1956)
Dermal	>8 years	0.0012	increased risk of premalignant skin lesions	Ahsan et al. (2006)
Cardiovascular	>10 years	0.022	increased risk of ischemic heart disease mortality	Chen et al. (1996)
Haematological	lifetime	0.002	anaemia during pregnancy	Hopenhayn et al. (2006)
Hepatic	55 years	0.03	portal fibrosis and hypertension, bleeding from oesophageal varices	Szuler et al. (1979)
Neurological	lifetime	0.005	reduced performance in neuro behavioural tests	Wasserman et al. (2004)
Reproductive	lifetime	0.006	increased incidence of spontaneous abortion	Milton et al. (2005)
Developmental	continuous	0.002	reduced birth weight	Hopenhayn et al. (2003)
Cancer	NS*	0.003	bladder cancer	Chiou et al. (2001)
Cancer	NS*	0.0011	lung cancer	Ferreccio et al. (1998)
Cancer	NS*	0.0049	squamous cell carcinoma of the skin	Guo et al. 2001
Cancer	>1 year	0.0075	basal or squamous skin carcinoma	Haupert et al. (1996)
Cancer	5 years	0.033	lung, urinary tract cancer	Tsuda et al. (1995)

Table 3. *Currently accepted national maximum permissible guideline limit in different countries for As in drinking water and soil.*

Sample type	Maximum permissible limit	Country	References
drinking water (μg/l)	10	European Union Japan New Zealand U.S.A. Canada	European Union (1998) MEJ (2008) Ministry of Health (2005) CFR (2006) CDWG (2007)
	50	Bangladesh China India Chile Nepal Pakistan Vietnam	BRAC (2000) Guo and Wang (2005) Indian Bureau of Standards (1991) Caceres et al. (2005) Shrestha et al. (2003) NSDWQ (2008) Berg et al. (2001)
soil (mg/kg)	12[a]	Vietnam	Trang Hoang and Hahn (2015)
	15[a]	Japan	MEJ (2008)
	20	Italy[b] Canada[c] Norway Australia U.S.A. (New Jersey)	D.L. 152/2006 CCME (2001) Hansen and Danielsberg (2009) Henke (2009) Henke (2009)
	50[d]	Germany	BBodSchG (1998)

Table 4

Table 4. *Main statistical parameters of As content in different sample types collected throughout Italy.*

Sample type	n	Unit	Min	Q25	Mean	Median	Q75	Q95	Max	SD
Agricultural soil	118	mg/kg	0.79	5.04	10.0	7.56	11.4	28.18	62.2	9.07
Grazing land soil	118	mg/kg	0.97	4.72	9.76	8.08	11.9	22.9	54.3	7.53
Stream sediment	51	mg/kg	2.5	2.5	7.2	6.0	9.5	15.5	38	6.23
Floodplain sediment	50	mg/kg	2.5	2.5	8.86	7	9	26.5	51	9.77
Bottled Mineral water	186	µg/l	0.01	0.13	0.89	0.25	0.67	5.08	8.91	1.54
Stream water	48	µg/l	0.08	0.27	1.79	0.47	1.71	9.94	13	3.21
Tap water	157	µg/l	0.02	0.11	0.94	0.25	0.73	4.39	27.2	2.51

Table 5

***Table 5**. Data of Incremental Life Cancer Risk (ILCR) calculated for different age groups, with respect to tap water and soil for two exposure pathways, ingestion and dermal contact.*

Sample type	Exposure pathway		Age group			
			Children	Teenagers	Adults	Lifetime
Tap water	ingestion	Range of ILCR	2.2 x 10^{-7} – 3.9 x 10^{-4}	1.9 x 10^{-7} – 3.2 x 10^{-4}	5.5 x 10^{-7} – 9.4 x 10^{-4}	9.6 x 10^{-7} – 1.7 x 10^{-3}
	dermal contact		1.2 x 10^{-9} – 2.1 x 10^{-6}	1.1 x 10^{-9} – 1.8 x 10^{-6}	4.7 x 10^{-9} - 8.1 x 10^{-6}	6.9 x 10^{-9} - 1.2 x 10^{-5}
Soil	ingestion		1.2 x 10^{-8} – 9.4 x 10^{-7}	5.5 x 10^{-9} – 4.3 x 10^{-7}	1.7 x 10^{-8} – 1.3 x 10^{-6}	3.4 x 10^{-8}- 2.7 x 10^{-6}
	dermal contact		1.2 x 10^{-10} – 9.8 x 10^{-9}	9.6 x 10^{-11} -7.5 x 10^{-9}	4.7 x 10^{-10} - 3.7 x 10^{-8}	6.9 x 10^{-10} - 5.4 x 10^{-8}
Pseudo-total risk		Mean	1.4 x 10^{-5}	1.2 x 10^{-5}	3.4 x 10^{-5}	5.8 x 10^{-5}

Table 6

***Table 6**. Range of Hazard Quotient (HQ) calculated for different age groups, with respect to tap water and soil for two exposure pathways, ingestion and dermal contact.*

Sample type	Exposure pathway		Age group			
			Children	Teenagers	Adults	Lifetime
Tap water	ingestion	Range of HQ	3.6 x 10^{-3} - 6.25	3.8 x 10^{-3} – 6.6	1.5 x 10^{-3} - 2.6	2.3 x 10^{-2} – 3.9 x 10^{1}
	dermal contact		3.2 x 10^{-5} – 5.5 x 10^{-2}	1.7 x 10^{-5} – 2.8 x 10^{-2}	1.3 x 10^{-5} - 1.8 x 10^{-2}	6.2 x 10^{-5} – 1 x 10^{-1}
Soil	ingestion		2.2 x 10^{-5} -1.7 x 10^{-3}	1 x 10^{-5} – 8.1 x 10^{-4}	3.2 x 10^{-5} – 2.4 x 10^{-3}	6.4 x 10^{-5}- 4.9 x 10^{-3}
	dermal contact		3.3 x 10^{-6} – 2.5 x 10^{-4}	1.5 x 10^{-6} -1.2 x 10^{-4}	1.4 x 10^{-6} -1.1 x 10^{-4}	6.1 x 10^{-6} - 4.6 x 10^{-4}

Figure 1

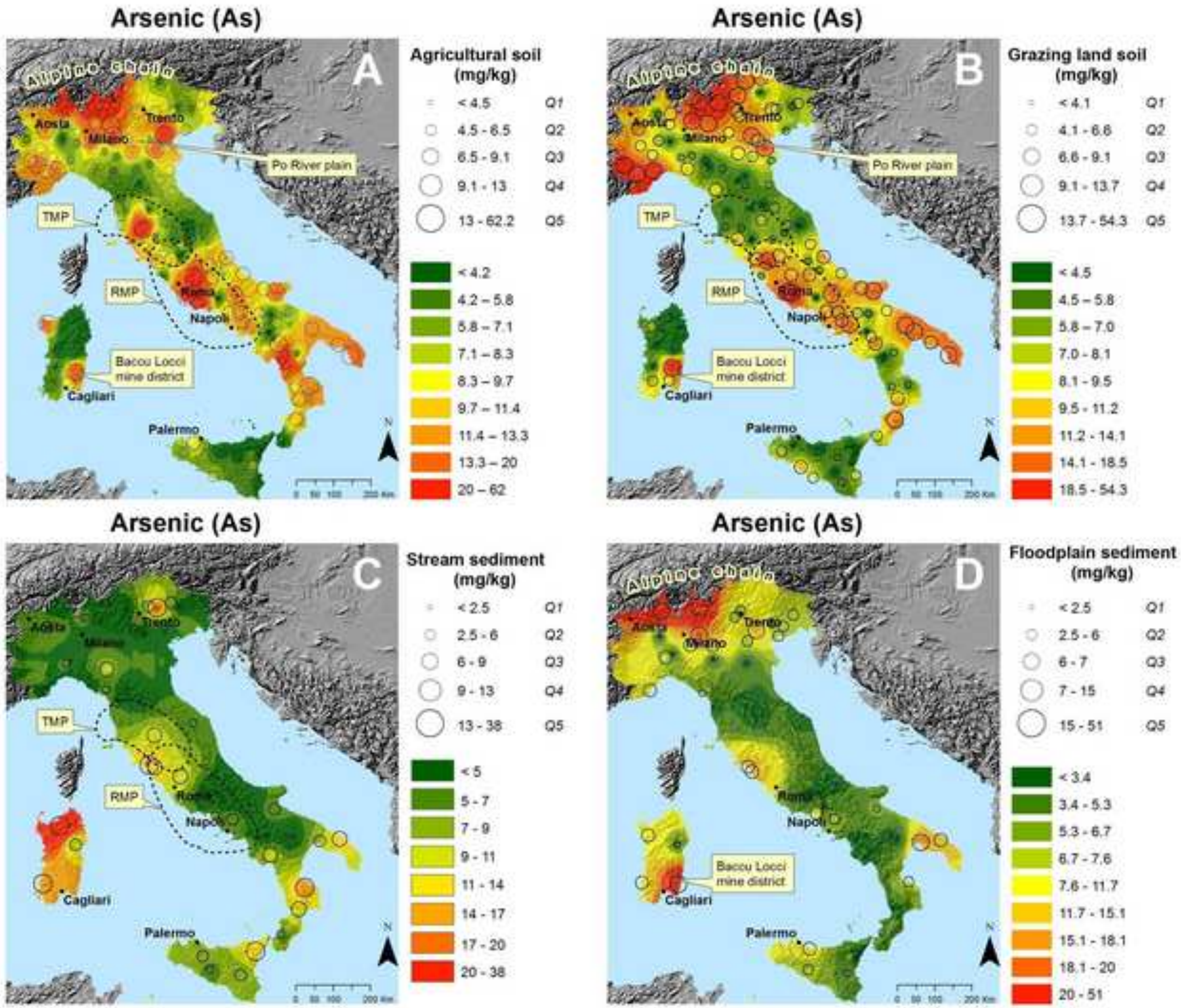

Arsenic (As)
A
Alpine chain
Aosta
Milano
Trento
Po River plain
TMP
RMP
Roma
Napoli
Bacou Locci mine district
Cagliari
Palermo
N
0 50 100 200 Km
Agricultural soil (mg/kg)
< 4.5 Q1
4.5 - 6.5 Q2
6.5 - 9.1 Q3
9.1 - 13 Q4
13 - 62.2 Q5
< 4.2
4.2 – 5.8
5.8 – 7.1
7.1 – 8.3
8.3 – 9.7
9.7 – 11.4
11.4 – 13.3
13.3 – 20
20 – 62
Arsenic (As)
B
Grazing land soil (mg/kg)
< 4.1 Q1
4.1 - 6.6 Q2
6.6 - 9.1 Q3
9.1 - 13.7 Q4
13.7 - 54.3 Q5
< 4.5
4.5 – 5.8
5.8 – 7.0
7.0 - 8.1
8.1 - 9.5
9.5 - 11.2
11.2 - 14.1
14.1 - 18.5
18.5 - 54.3
Arsenic (As)
C
Stream sediment (mg/kg)
< 2.5 Q1
2.5 - 6 Q2
6 - 9 Q3
9 - 13 Q4
13 - 38 Q5
< 5
5 - 7
7 - 9
9 - 11
11 - 14
14 - 17
17 - 20
20 - 38
Arsenic (As)
D
Floodplain sediment (mg/kg)
< 2.5 Q1
2.5 - 6 Q2
6 - 7 Q3
7 - 15 Q4
15 - 51 Q5
< 3.4
3.4 - 5.3
5.3 - 6.7
6.7 - 7.6
7.6 - 11.7
11.7 - 15.1
15.1 - 18.1
18.1 - 20
20 - 51

Figure 2

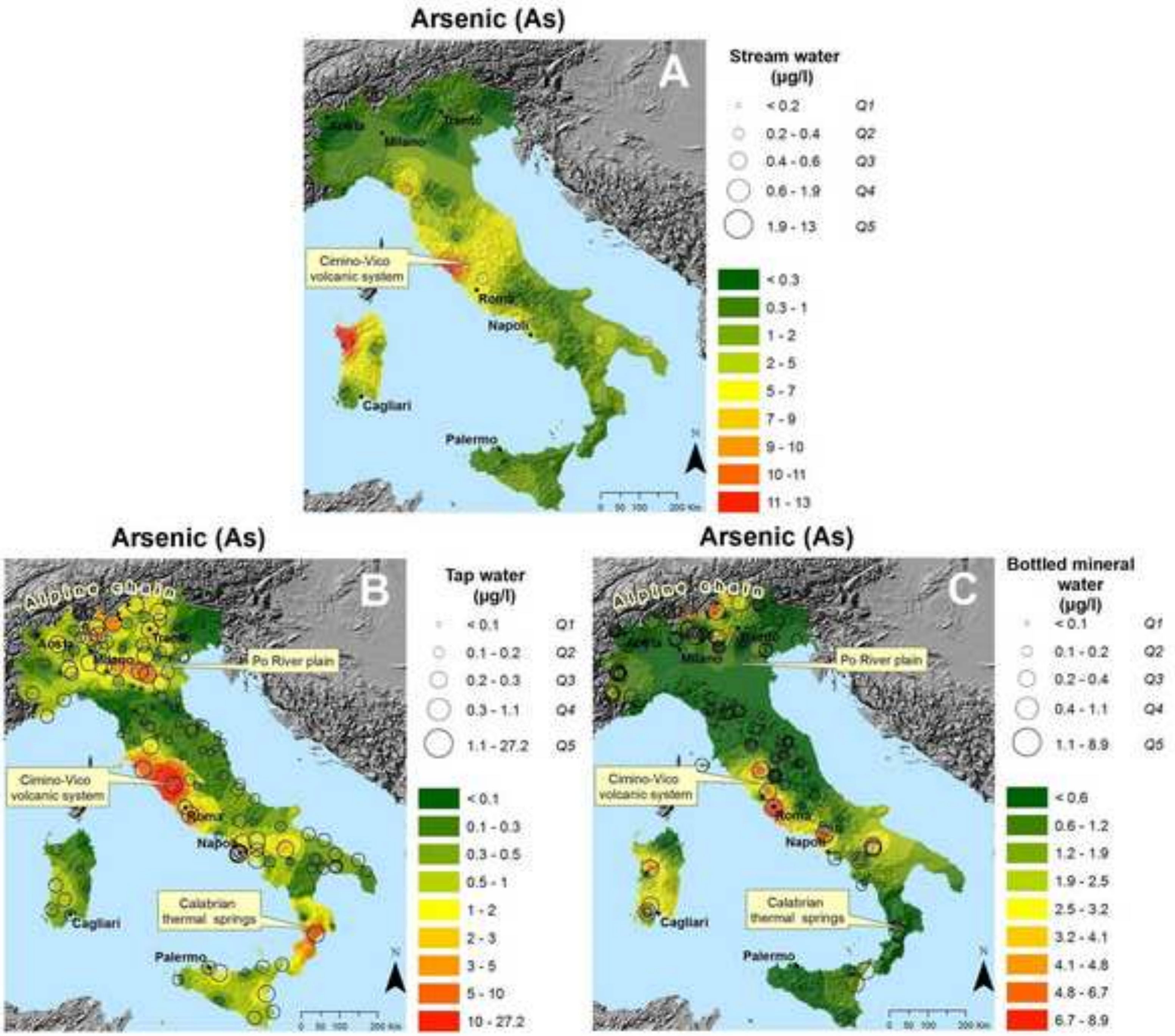

Arsenic (As)
A
Stream water (µg/l)
< 0.2 Q1
0.2 - 0.4 Q2
0.4 - 0.6 Q3
0.6 - 1.9 Q4
1.9 - 13 Q5
< 0.3
0.3 - 1
1 - 2
2 - 5
5 - 7
7 - 9
9 - 10
10 - 11
11 - 13
Cimino-Vico volcanic system
Aosta
Milano
Trento
Roma
Napoli
Cagliari
Palermo
N
0 50 100 200 Km
Arsenic (As)
B
Alpine chain
Po River plain
Cimino-Vico volcanic system
Calabrian thermal springs
Tap water (µg/l)
< 0.1 Q1
0.1 - 0.2 Q2
0.2 - 0.3 Q3
0.3 - 1.1 Q4
1.1 - 27.2 Q5
< 0.1
0.1 - 0.3
0.3 - 0.5
0.5 - 1
1 - 2
2 - 3
3 - 5
5 - 10
10 - 27.2
Arsenic (As)
C
Alpine chain
Po River plain
Cimino-Vico volcanic system
Calabrian thermal springs
Bottled mineral water (µg/l)
< 0.1 Q1
0.1 - 0.2 Q2
0.2 - 0.4 Q3
0.4 - 1.1 Q4
1.1 - 8.9 Q5
< 0.6
0.6 - 1.2
1.2 - 1.9
1.9 - 2.5
2.5 - 3.2
3.2 - 4.1
4.1 - 4.8
4.8 - 6.7
6.7 - 8.9

Figure 3

Click here to download high resolution image

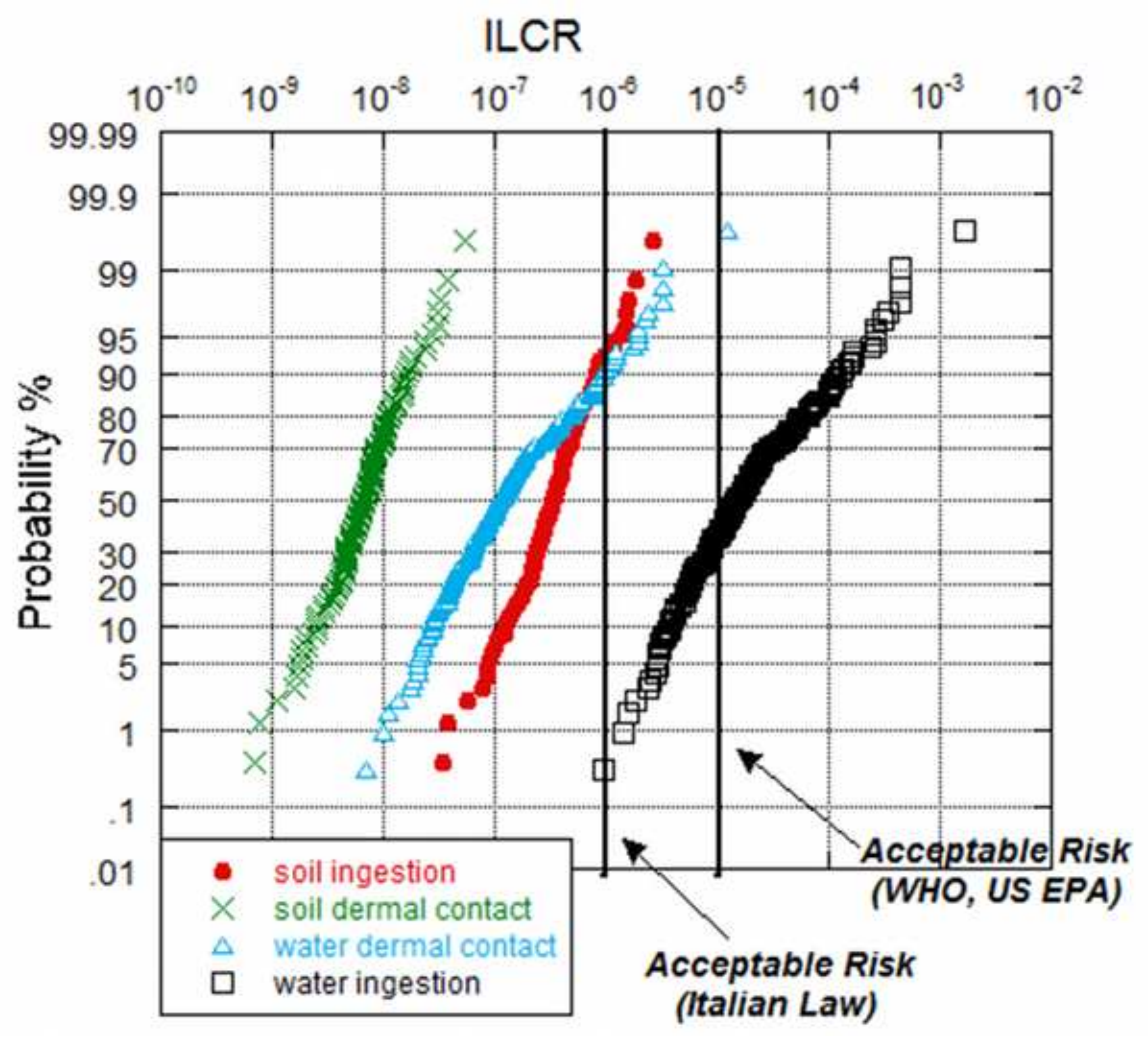


Figure 4

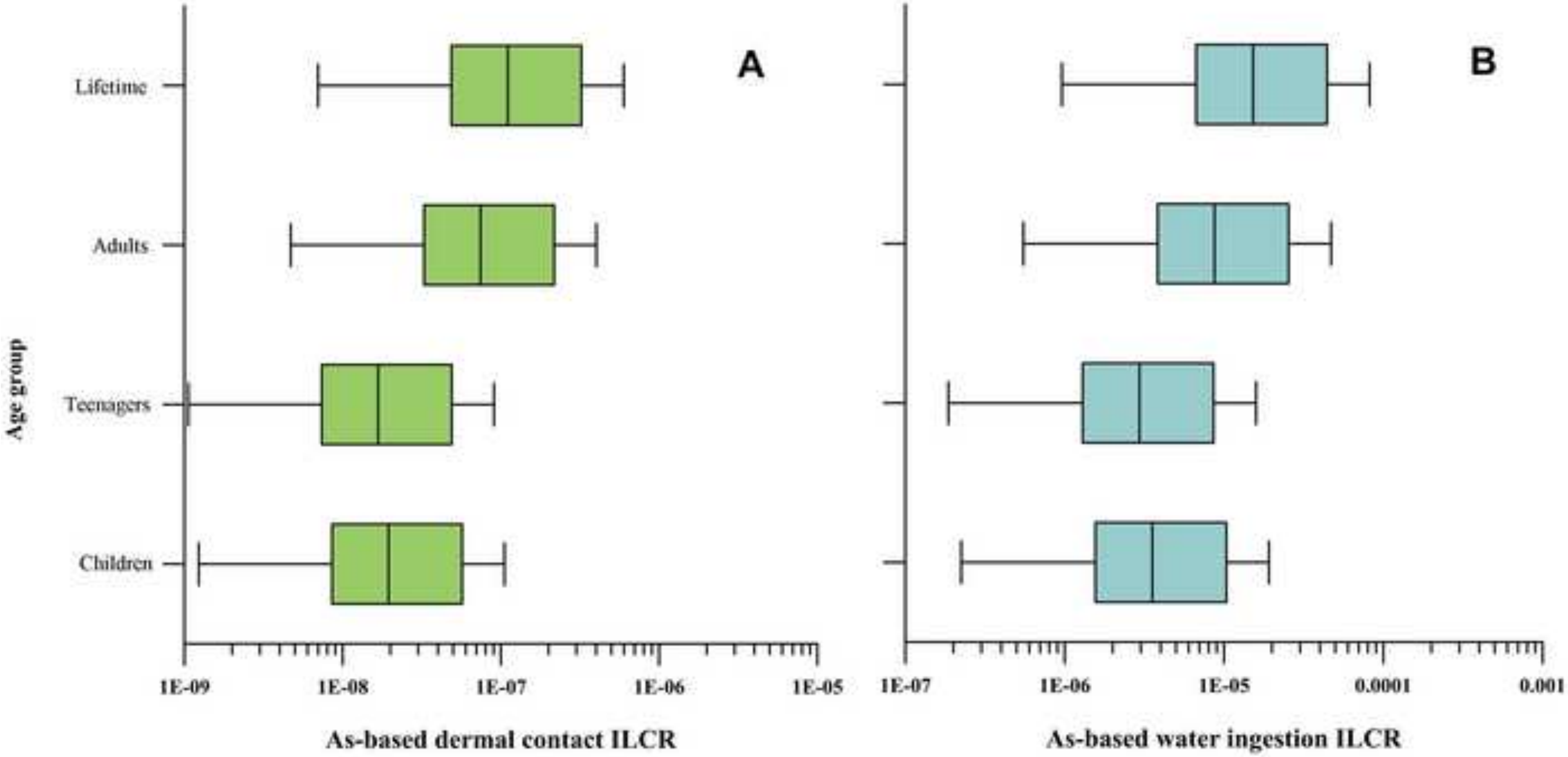

A
B
Age group
Lifetime
Adults
Teenagers
Children
1E-09
1E-08
1E-07
1E-06
1E-05
As-based dermal contact ILCR
1E-07
1E-06
1E-05
0.0001
0.001
As-based water ingestion ILCR

Figure 5

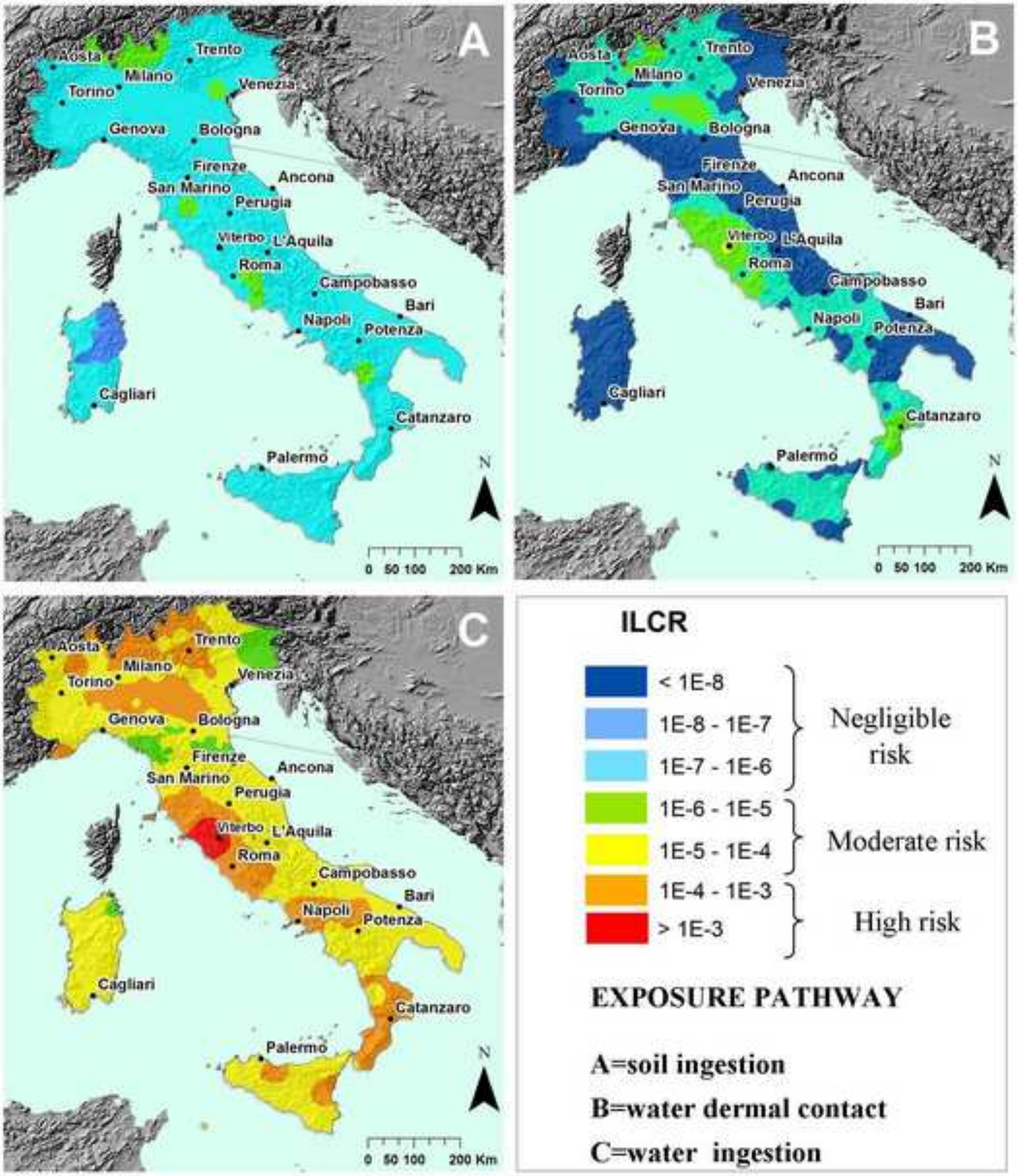

A
B
C
Aosta
Trento
Milano
Torino
Venezia
Genova
Bologna
Firenze
San Marino
Ancona
Perugia
Viterbo
L'Aquila
Roma
Campobasso
Bari
Napoli
Potenza
Cagliari
Catanzaro
Palermo
N
0 50 100 200 Km
ILCR
< 1E-8
1E-8 - 1E-7
1E-7 - 1E-6
Negligible risk
1E-6 - 1E-5
1E-5 - 1E-4
Moderate risk
1E-4 - 1E-3
> 1E-3
High risk
EXPOSURE PATHWAY
A=soil ingestion
B=water dermal contact
C=water ingestion

Figure 6

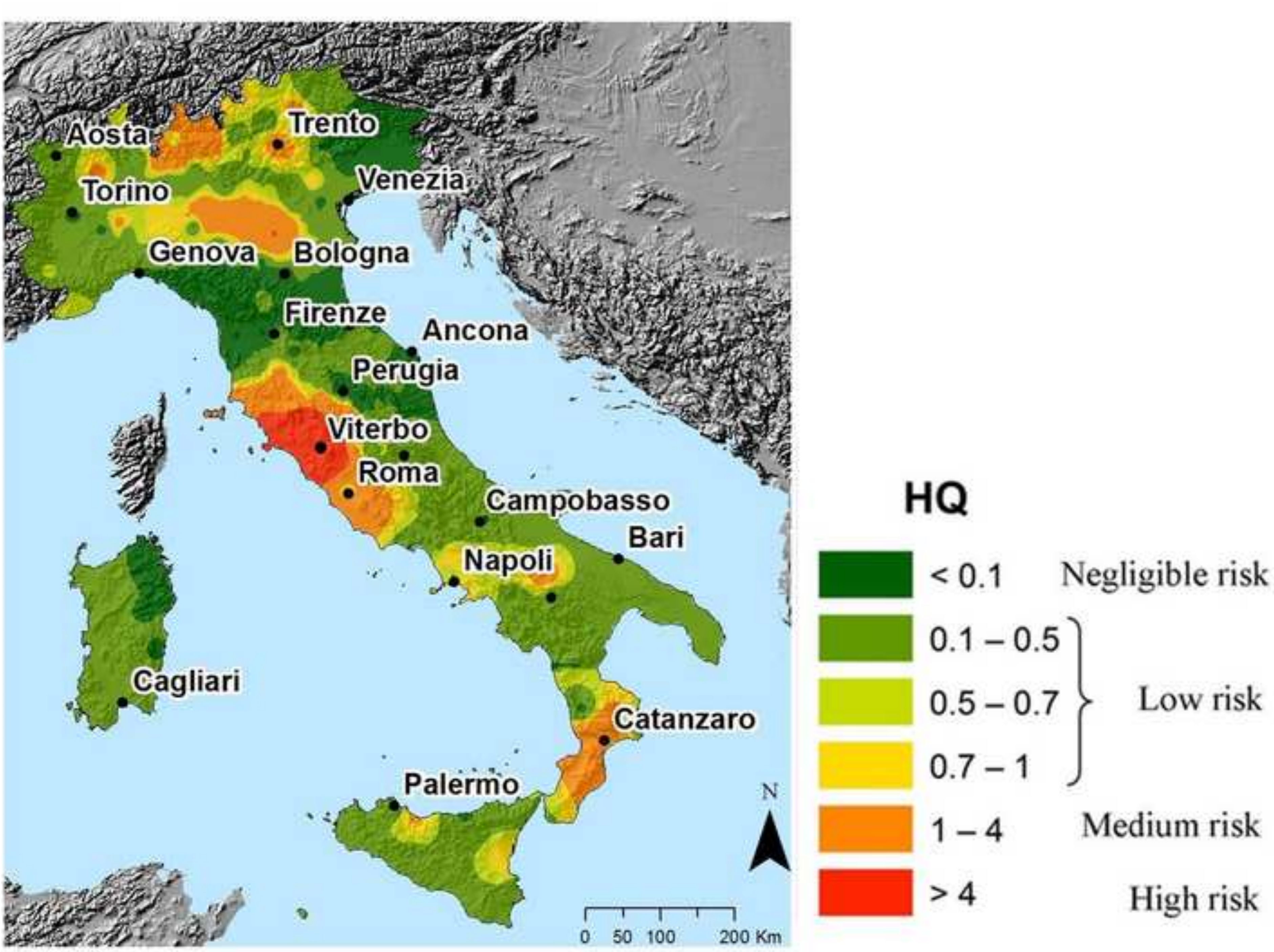

Aosta
Trento
Torino
Venezia
Genova
Bologna
Firenze
Ancona
Perugia
Viterbo
Roma
Campobasso
Bari
Napoli
Cagliari
Catanzaro
Palermo
N
0
50
100
200 Km
HQ
< 0.1
Negligible risk
0.1 – 0.5
0.5 – 0.7
0.7 – 1
Low risk
1 – 4
Medium risk
> 4
High risk

Figure 7

Click here to download high resolution image

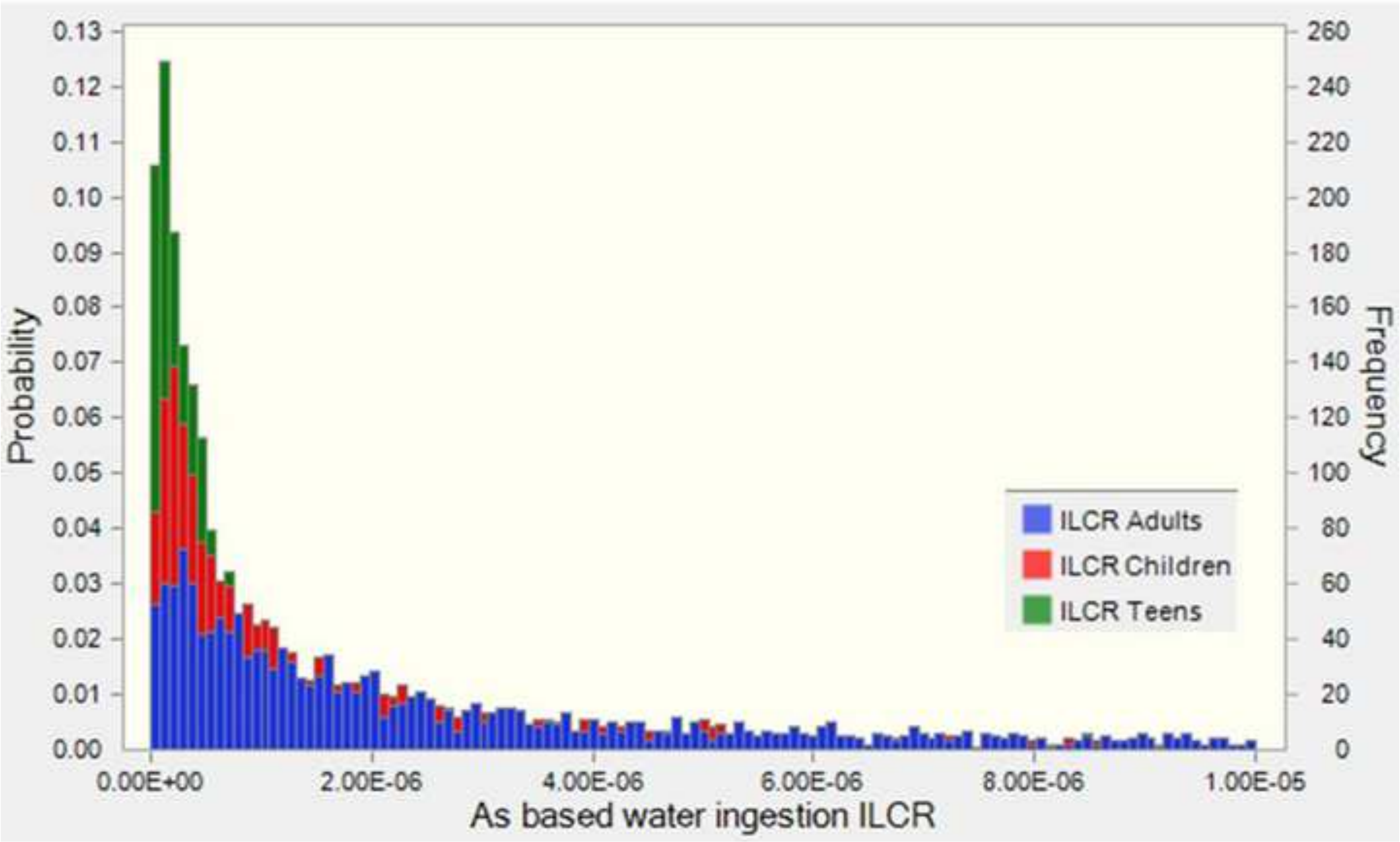
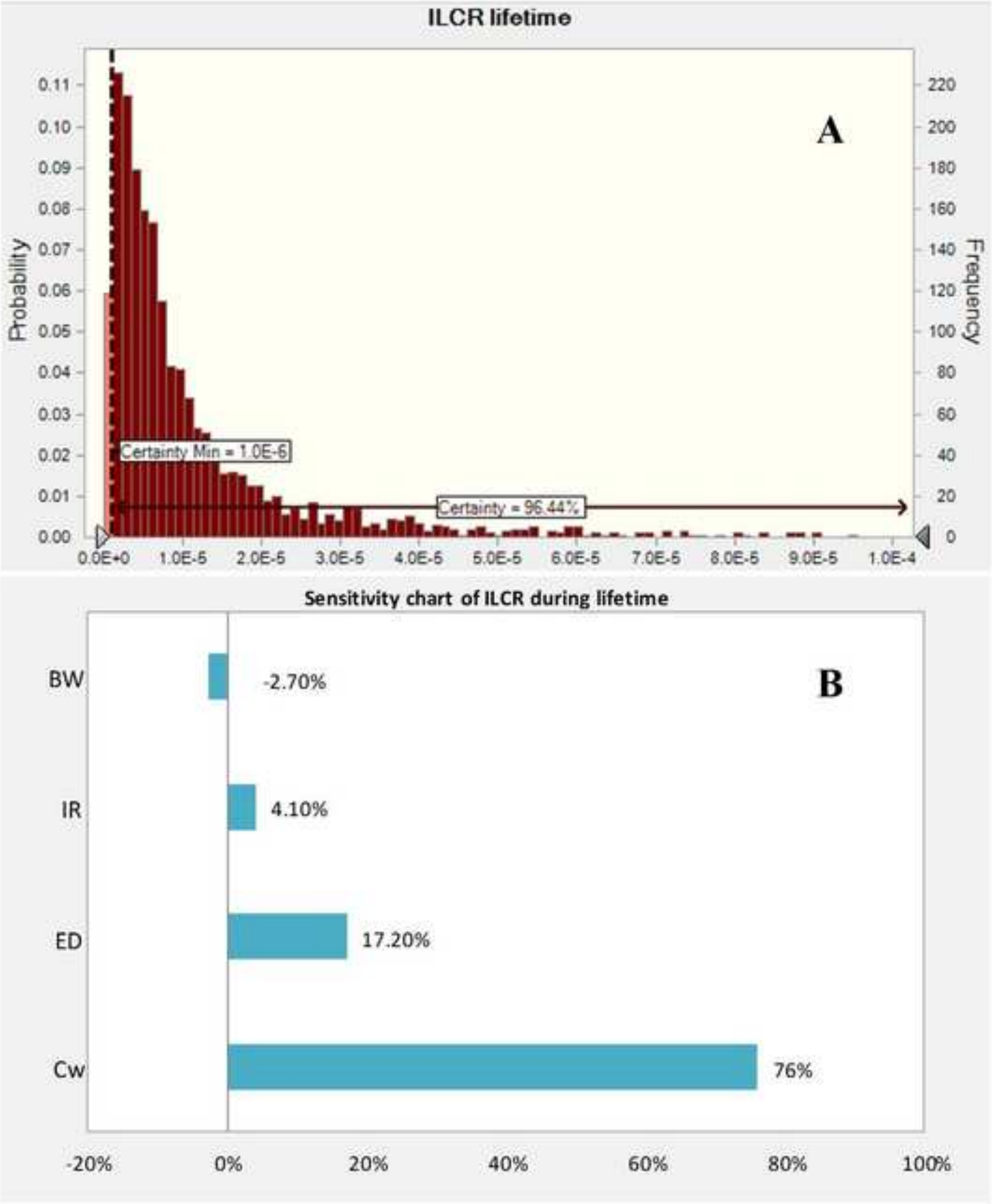
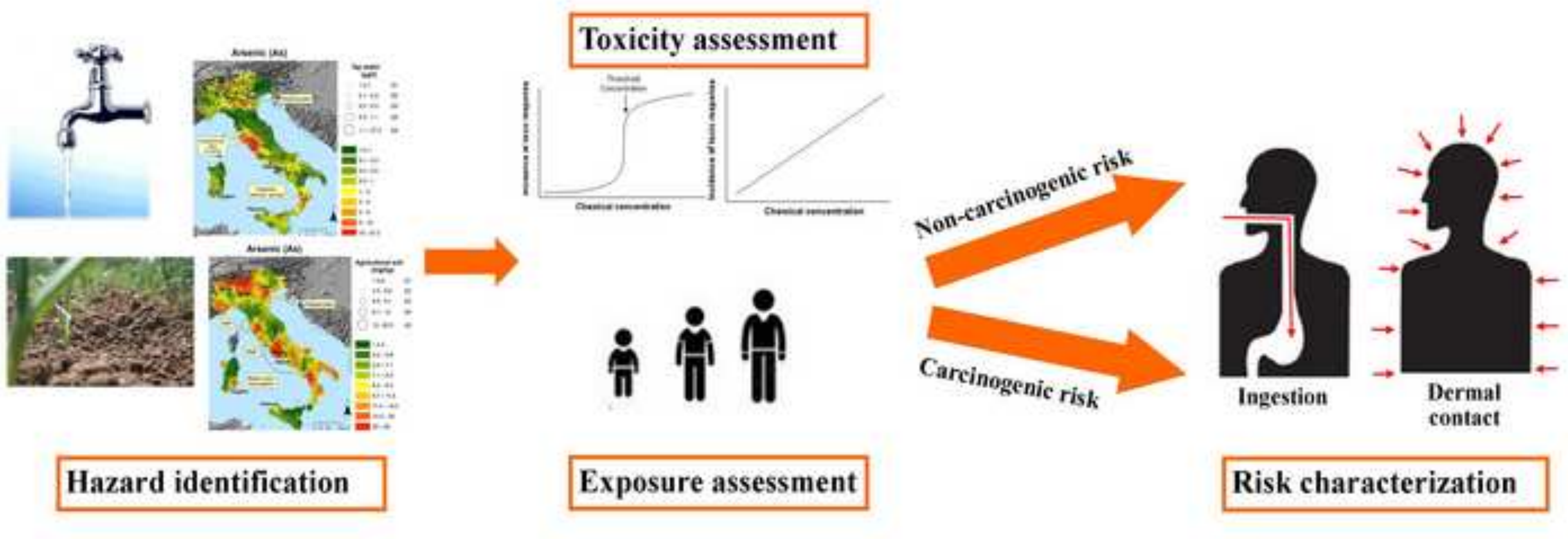


Figure 8

Click here to download high resolution image




Arsenic (As)
Arsenic (As)
Hazard identification
Toxicity assessment
Threshold concentration
Incidence of toxic response
Chemical concentration
Incidence of toxic response
Chemical concentration
Exposure assessment
Non-carcinogenic risk
Carcinogenic risk
Ingestion
Dermal contact
Risk characterization

Credit Author Statement

Ethical statements

“Arsenic: Geochemical distribution and age-related health risk in Italy” co-authored by Daniela Zuzolo, Domenico Cicchella, Alecos Demetriades, Manfred Birke, Stefano Albanese, Enrico Dinelli, Annamaria Lima, Paolo Valera, Benedetto De Vivo.

On behalf of the authors of this paper, as corresponding author I hereby certify that:

- there are no known conflicts of interest associated with this publication and there has been no significant financial support for this work that could have influenced its outcome. The authors’ freedom to design, conduct, interpret, and publish research is not compromised by any controlling sponsor as a condition of review and publication.
- The manuscript has not been submitted to more than one journal for simultaneous consideration.
- The manuscript has not been published previously (partly or in full).
- The present study has not been splitted up into several parts to increase the quantity of submissions and submitted to various journals or to one journal over time.
- No data have been fabricated or manipulated (including images) to support our conclusions.
- We confirm that the manuscript has been read and approved by all named authors and that there are no other persons who satisfied the criteria for authorship but are not listed. We further confirm that the order of authors listed in the manuscript has been approved by all of us.
- Authors whose names appear on the submission have contributed sufficiently to the scientific work and therefore share collective responsibility and accountability for the results.

Signature	*Date*
	02/05/2019
Print Name	*Affiliation*
Daniela Zuzolo	University of Sannio