Drinking-Water and Human Health Challenges in the 21st Century

Konstantinos C. Makris, PhD

Water and Health Laboratory, Cyprus International Institute for Environmental and Public Health, Cyprus University of Technology, Limassol, Cyprus

[*] **Corresponding author.** Associate Professor of Environmental Health, Cyprus International Institute for Environmental and Public Health, Cyprus University of Technology. Irinis 95, Limassol 3041, Cyprus

Telephone: +357-25002398

Fax: +357-25002676

Email: konstantinos.makris@cut.ac.cy

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FOCUS: The focus of this chapter is on drinking-water pressures of current and emerging nature that exert adverse health effects on humanity.

Keywords: scales, biofilms, drinking water, exposure, environmental health, pollution.

ABSTRACT

Water and human health issues are intertwined within a changing urban setting. There is a momentum of societal demand to act on the aging drinking-water pipe infrastructure to protect human health and at the same time to devise control options that will promote further the well-being and quality of urban life in the developed world. The main objective of this work was to critically review the main challenges, opportunities and risks associated with drinking-water's current and emerging pressures as exerted on human health in urban centers of middle-, and high-income countries. Discussion about drinking-water distribution systems did not focus on their portion extending from the water meter to the home tap, i.e., the premise plumbing system characteristics. One city does not hold a single water quality metric that remains constant, because it changes in the urban space and time. Bigger urban centers will be differentially more complex to address water and health risks, because of their numerous neighborhoods (district-metered areas, DMA) being spread apart geographically in large distances. The water and health issues are multi-disciplinary in nature and demand the close cooperation among health scientists, engineers, environmental scientists, social scientists, economists and local policy makers to address each city's unique challenges and risks.

Environmental Burden of Disease: Water and Health

The Lancet Commission report on pollution and health (2017) estimated that 16% of all deaths worldwide were attributed to pollution, being the largest environmental cause of disease and premature death in the world today. The global burden of disease due to pollution risk factors based on the Global Burden of Disease (GBD) study in 2015 and on World Health Organization (WHO) data in 2012 using the Disability-Adjusted Life Year (DALY) method [the sum of the Years of Life Lost (YLL) and Years Lost due to living with Disability (YLD)] showed that a quarter of all annual deaths were attributed to preventable environmental disease risks [1]. These health costs may be hidden in population health expenditures, hospital budgets, productivity reports but policy makers have not yet clearly attributed these costs to environmental pollution. The WHO and GBD teams estimated the costs associated with pollution-based premature deaths but there was inadequate or missing data of pollution-related morbidity and mortality in numerous countries. Global costs of premature deaths due to pollution are 6.2% of world global gross domestic product (GDP), an appreciably high estimate. Therefore, more research is needed on pollution and health outcome associations.

Human exposures to polluted water, air and soil kill more people than a high-sodium diet, obesity, alcohol, road accidents, or child and maternal malnutrition; environmental pollution was also responsible for 3x as many deaths as those attributed to AIDS, tuberculosis and malaria altogether combined [1]. Various forms of pollution can affect health in numerous ways. Water pollution, i.e. unsafe water, sanitation and hygiene is linked to gastrointestinal diseases and infections. Water pollutants may be simultaneously present also in other environmental compartments such as food; organophosphate pesticides detected in both water and diet are notorious developmental neurotoxicants and exposure to these chemicals during early development is associated with behavioural disorders and learning disabilities that translate to reduced work performance later in life. Productivity losses in low income countries were mainly attributed to unsafe water and lack of sanitation and hygiene (1.3-1.9% of GDP) followed by exposures to air pollution (0.49-0.68% of GDP). Water pollution was less influential than ambient air pollution in causing most of the economic losses in high and middle-income countries due to pollution-related diseases, being at 3.5% of total health expenditures. The total health costs of environmental chemical exposures likely exceeded 10% of the global GDP, hence, environmental chemicals need to be prioritized in public health policies and related interventions [2]; for example, the estimated costs of cognitive impairment associated with known childhood lead exposure, represented about 1.83% of the global GDP in 2010, which was > 4-fold greater than the corresponding DALYs estimate (0.45%).

At the regional policy level, a joint effort by United Nations Economic Commission for Europe (UNECE) and the WHO Regional Office for Europe was backed up by 36 countries signing the protocol on Water and Health, which is primarily aimed at preventing, controlling, and reducing water-related disease [3]. At the highest political level, the goals of Parma Declaration commitments on Environment and Children Health, as adapted at the 5th ministerial conference on Environment and Health were designed to protect children from chemical hazards, including those hazards associated with water [4]. Most recently, the Ostrava 6th Ministerial Conference on Environment and Health reinforced the need for prompt action by the EU policy makers on coherent actions to decrease the burden of diseases caused by environmental factors, including water contamination and emphasized the need to promote synergies along with the health and well-being objectives of the United Nations 2030 Agenda for sustainable development [5].

The health risks associated with water pollution, particularly for middle-, and high-income countries have not been at the core of environmental health studies. This trend could be partially explained by the fact that the developed world has for quite a while rested on the success of post Second World War intervention practices, such as the water chlorination treatment and the wide spread of centralized water treatment facilities, essentially eradicating the waterborne and microbially-originating burden of disease. As such, during the past 30 years, water and health issues in the developed world have not been prioritized; as such, an instrumental effort compiling technical features of EU-based pregnancy–birth cohorts (PBC) showed that out of 37 registered EU PBC, only 13 cohorts included exposures to water contaminants in their design and analyses [6].

Water and health issues are inter-connected within a changing urban setting. There is a growing momentum of societal demand to act on the aging water pipe infrastructure to protect human health and at the same time to devise control options that will promote further the well-being and quality of life in the developed world. The main objective of this work was to critically review the main challenges, opportunities and risks associated with drinking-water's current and emerging pressures as exerted on human health in urban centers of middle-, and high-income countries. Discussion about drinking-water distribution systems did not focus on their portion extending from the water meter to the home tap, i.e., the premise plumbing system characteristics, because of the unique properties and peculiarities of the premise plumbing system. Also, point of use solutions (e.g., water filters, or UV lamps, etc.) to address water and health risks have not been considered in this work.

Setting the scene--Challenges and pressures on water cycle and public health implications

Currently, major reform in the regulatory and health policy aspects of water and health is in place in the EU and the USA, being aligned with the observed increase in the environmental burden of disease, including water contamination. What has changed during the last 2-3 decades in the societies of the middle-, and high-income countries?

Water quality surveillance data collected during the past couple of decades within urban drinking-water distribution systems (UDWDS) call for re-evaluation of water and health issues. According to a report by the U.S. Government Accountability Office, the number of annual waterborne outbreaks (both of chemical and microbiological origins) may be exceeding current estimates, highlighting the alarming number of health-related breaches in drinking-water going unreported [7]. For example, an increasing number of USA-based water-borne outbreaks have been ascribed to chemicals/toxins (27%), or to *Legionella spp*. (27%) or other bacteria (17%) [8]. The EU drinking-water directive (98/83/EC) is also under scrutiny by scientific experts and stakeholders on whether extensive revision is necessary. The UDWDS around the globe have been charged with increasing incidents of waterborne illnesses, revisiting the notion that pathogens and contaminants behave conservatively between the point of entry (after conventional or reverse osmosis-desalination water treatment) and the point of use. The EU drinking water directive (DWD) (98/83/EC) is currently under scrutiny by scientific experts and stakeholders on whether extensive revision would be warranted [9]. The DWD re-evaluation was conducted part of the European Commission's (EC) Regulatory Fitness and Performance programme (REFIT) and it was based on five criteria: effectiveness, efficiency, coherence, relevance, and EU added value [10]. Except for relevance, the rest of the evaluation criteria were met by the current DWD. With regards to relevance, the analysis found that the drinking-water quality standards may not be appropriate anymore to protect human health from the adverse effects of any contamination of drinking water [10]. Home tap water quality integrity continues to be compromised by issues arising between the point of entry and the point of use [11]. The lead and copper rule of the USA is undergoing revisions and modifications after the recent tragedy at Flint city, Michigan, USA with the mass lead pollution case [12].

The impact of global stressors acting horizontally on water supply and demand, such as, increasing number of mega cities around the globe coupled with booming urbanization rates observed primarily in developing countries [13] pose tremendous pressure to stakeholders and regulatory bodies in securing safe access to clean water for urban dwellers. Global stressors like (micro) climate manifestations and changing demographics towards larger urban-based populations, put pressure to regulators towards achieving sustainable urban drinking-water management practices [13]. Cities are rapidly growing and they now accommodate >50% of the world's population [14].-Gradually-changing or acute shocks associated with technological threats and deficiencies in potable water quality are encountered or anticipated in the near future, particularly in aging UDWDS pressured by increasing water demand by urban dwellers given world's population growing. Evolving socio-economic disparities among neighborhoods within the same city and health inequalities [15], are expected to also modify the magnitude and variability of waterborne contaminant exposures and their health effects. The size of urban community served by a single UDWDS has been increasing, necessitating shifts in performance and reliability of safe water provision by water authorities. Concomitant challenges exist to maintain finished water quality in the context of increased urban agglomeration trends, and higher potable water demand at distant neighborhoods within the same city. Pipe networks that reliably convey water to EU households are aged, vulnerable to corrosion and to pipe scale/biofilm development, suffering from frequent pipe leak incidences.

Despite improvements in sanitation and hygiene via access to centralized water treatment facilities and advances in water treatment technologies, i.e., reverse osmosis, it is widely accepted that human exposure to water-borne pathogens and episodic events of chemicals release in water systems of the developed world, e.g., lead, still continue to occur [16]. It was reported that ~50% of the waterborne outbreaks in community water systems in the USA during 1995-2002 were ascribed to compromises in water quality integrity within UDWDS [17]. The problem may be exacerbated in cases where only lead and copper out of numerous contaminants that might be present in UDWDS are required to be monitored at the home tap [18]. The tip of the iceberg was the recent Flint case where an otherwise innocent change in water source for the city of Flint in Michigan USA, from Detroit's Lake Huron to the Flint river led to unprecedented population health consequences [12].

Current and emerging water and health risks in urban settings

We identified several water and health risk scenaria that are becoming more frequent in occurrence in urban centers located in both sides of the Atlantic Ocean, carrying substantial human health risk:

[1] *Sporadic deterioration of finished water quality in drinking-water distribution pipe network*: The classical notion of finished water quality conservation between the point of entry (water treatment plants) and point of use (households) in aging UDWDS (pipes in place for several decades) has been scrutinized during the last decade [19, 20]. Pipe networks that reliably convey water to urban households are aged, vulnerable to corrosion, and they suffer from frequent pipe leak incidences. As UDWDS age, inner-pipe surfaces comprised of historically-accumulating chemical scales and/or biofilms could act as release sources for pipe-anchored contaminants into finished water under certain episodic release events, and thus, related human exposures will often go undetected with current water quality surveillance schemes [21]. For example, episodic release of arsenic into finished water from pipe scales occurred in eight different USA-based utilities, despite water arsenic concentrations being routinely $<10\ \mu g\ L^{-1}$ [22]. The wide spatial variability of residual chlorine and formed disinfection byproducts (DBP) concentrations observed among areas of the same city's UDWDS underpinned differences in pipe network characteristics at the neighborhood level, calling for spatially resolved urban water management approaches.

Multiple water sources for multiple consumption purposes and relevant routes of exposure: The plethora of available potable water sources in urban settings present us with difficulties in capturing detailed water consumption patterns that will help researchers in accurately estimating daily intakes for a suite of water contaminants. In water-stressed areas, tap water composition may be the blended product after properly treating two or more water sources, e.g. blend of desalinated and dam surface waters or treating a multitude of different groundwater-based sources. This presents an unintended introduction of water contaminants from blending and/or precursors for formation of newer classes of disinfection byproducts (DBP) contaminants or transformation products with unknown health effects (bisphenol A, BPA); BPA's high reactivity with chlorine could lead to the formation of more toxic chlorinated BPA congeners, our unpublished data). In addition to conventionally-treated tap water, new sources emerge in the market, such as reverse osmosis-treated potable water packaged in plastic contact materials, raw untreated water, or packaged water from mountainous or pristine-perceived areas sold in kiosks; reverse osmosis treated water could be implicated with water quality deficiencies in essential minerals, like calcium/magnesium and iodine appearing during temporary storage, transportation and storage at point of use. In several parts of the globe, there is an increasing use of desalinated tap water where only mineral calcium addition may be post-treatment applied, being the only mineral supplementation practiced. The absence of certain essential minerals from potable water, such as magnesium and iodine has been discussed in the context of health implications to chronic disease such as cardiovascular disease [23] and thyroid gland abnormalities [24]. Therefore, the health status of pregnant and lactating mothers and children consuming potable water previously treated with reverse-osmosis membranes either centralized or at each point of use could be undermined, because it is often deprived by essential minerals, like calcium/magnesium and iodine known to regulate human growth homeostasis and thyroid hormonal production, respectively.

It is often the case that consumers in several developed countries use a combination of bottled waters (packed in polyethylene terephthalate-PET and polycarbonate-PC bottles) for consumption in forms other than plain water (e.g. preparing cold and hot beverages), or even consume raw water from underground springs (new marketing trend in the USA). Water consumption in other forms raised the per capita water consumption from 2.20 L day^{-1} person^{-1} for plain water to 3.44 L day^{-1} person^{-1} for water used to prepare beverages [20, 25], increasing water contaminant daily intake for leached plasticizers, such as bisphenol A and nonylphenol from PC bottles [20] and antimony and phthalates from PET bottles [25]. A recent global report focused on the presence of microplastics in bottled water; the team tested 259 individual bottles from 27 different lots across 11 brands showing microplastics levels being nearly double than those in tap water [26]. No human studies currently exist on the exposure assessment or health risks associated with microplastics, while being ubiquitous in water supplies and foodstuffs.

Oral ingestion is not the sole route of exposure to water contaminants: In addition to oral ingestion, inhalation and dermal uptake are important routes of exposure to water contaminants via a suite of common water use activities (i.e. cooking, swimming, showering, etc.). For example, the four trihalomethanes [trichloromethane-chloroform (TCM) and the brominated compounds: bromodichloromethane (BDCM), dibromochloromethane (DBCM) and tribromomethane (TBM)] are common DBP, routinely found in disinfected potable water. Humans come in contact with the THM through all routes of exposure, such as, ingestion, inhalation and dermal uptake, because they may be generated as the result of various daily activities such as showering, swimming, mopping, dishwashing etc.–The totality of exposures to harmful agents occurring in more than one environmental compartment, such as in water, air, or food and their possible health risks, ranging from simple irritation, to infections, or even cancer and endocrine disruption bring forward the significance of assessing personal exposures through all routes within the context of population health studies.–The parallel consideration of water contaminants that may be concurrently present in other linked environmental compartments (air, diet, personal care products, etc.) is warranted to further improve the exposure assessment of water contaminants in health studies.

Changes in water source or treatment parameters: Austerity measures and budgetary cuts have also been implemented in water-related, city hall, regional or national budgets. As such, economic savings-driven changes in water source or water treatment practices have unintentionally instigated a series of adverse consequences to water quality and health impacts for water consumers that may or may not become obvious to water scientists. The tip of the iceberg was the recent Flint case where an otherwise innocent change in water source for the city of Flint in Michigan USA from Detroit's Lake Huron to the Flint river led to unprecedented population health consequences. As a water source change, the Flint river water was more corrosive than that previously used for decades, resulting in excessive lead leaching from water pipes into tap water supply, leaving Flint's residents complaining about water's color, taste and odor. A retrospective study on Flint, MI children (younger than 5 years old) was conducted with available blood lead test results that were stratified by those tests obtained before (pre) or after (post) the water source switch [27]; a statistically significant increase in the proportion of Flint children with elevated blood lead levels obtained after the water source change when compared with the reference period (before water source change), which led to unprecedented population health consequences [27, 28]. In addition to lead, excess Legionella spp. and disinfection by-products were detected in Flint tap water.

A similar drinking-water related public health emergency erupted in Washington, D.C. in 2003 [29] and in Greenville in North Carolina in 2006. In both cases, widespread contamination of water supplies with leached lead from UDWDS occurred, affecting thousands of residents due to changes in water treatment and particularly after substituting the disinfectant type from chlorine to chloramine [30]. Use of chloramine was devastating under these conditions, resulting in mass lead leaching from inner pipe/fixtures/solder surfaces into finished water [31, 32].

Growth of pipe scales and biofilm conglomerates as a source of water contamination: Accumulation of contaminants and/or microorganisms onto pipe scales and biofilm conglomerates (SBC) within UDWDS has been increasingly recognized as an underestimated source of chemicals and pathogens in finished water [33]. Scales, corrosion products, and associated contaminants on the inner surface of the pipe material and their release into drinking water in the distribution systems have gained a heightened interest in recent years [33]. Internal pipe surfaces (covered or not by pipe scales) support growth and establishment of microbial colonies in drinking water distribution systems [34, 35]. The structures formed by microorganisms adhered to and growing up on surfaces are called biofilms Vast differences exist in the extent of predominant pipe materials used in European UDWDS where lead pipes comprise 50% of the pipe network in UK, Ireland, and France, asbestos/cement pipes comprise approximately 70% of the pipe network in Greece, Cyprus, Bulgaria, and the rest of the EU countries are characterized by a high Fe type of pipe (either cast or galvanized) [36], whereas lead and asbestos/cement dominate the pipe material types used in the USA-based UDWDS.

Swimming and disinfection: Year-round swimming in indoor/outdoor pools is a common lifestyle trend in both the EU and USA, particularly in central and northern European countries. Swimming is considered as an important recreational activity for hundreds of millions of people worldwide and has been associated with significant positive health benefits. Hygiene and swimming water quality issues exist, especially risks associated with ear/lung/skin infections caused by feces-associated microbes and protozoa. Chemical disinfection of swimming pool water has been also scrutinized with respect to chemical exposures present in water. Swimming pool water chemistry deals with the composition of the source water, the transformation of this water (e.g. disinfection processes) and the actions in the swimming pool (disinfection, swimmers, etc.) [37]. Swimmers introduce undesirable biological matter (e.g. skin, sweat, urine or fecal matter) possibly containing pathogens (*Legionella spp. or Cryptosporidium spp*.). In most swimming pools, microbiological control is performed by disinfection with the addition of chlorine (as a gas or bleach). The disinfection properties of free chlorine are linked to its oxidant capacity. It is well-known that chlorination of drinking or swimming pool water leads to the formation of disinfection by-products (DBPs) including chloramines (referred as combined chlorine) or trihalomethanes (THMs) [38]. Some of these chemical compounds have been associated with health effects. The hypothesis of a link between the presence of eye and skin irritation syndromes in swimmers and contact with swimming pool water treated with chlorine was initially proposed by Mood in 1953. This author developed a theory that the main causal agent of eye irritation was not chlorine but a combination of chlorine and ammonia [39]. Other than some remaining microbiological risks such as the microbiological quality of swimming pool water is now very good, with little risk to swimmers [40]. Consequently, the potential health risks from chemical exposures linked to swimming pools now seems to be a priority. Many recent papers have described the health consequences linked to these by-products [40, 41].

Industrially-contaminated sites: A worrisome environmental health scenario is that ascribed to an increasing number of such industrial sites appearing nearby residential areas affecting thousands of residents through water or other environmental media. Unintentional exposures to chemical(s) and their mixtures for the general population residing around industrial activities in urban areas is an upcoming environmental health issue for the European Commission [42]. The chemical-based health risks for the general population living near industrial activities have not yet been quantified, primarily due to lack of such epidemiological datasets.

PFAS water contamination (C6 case): The mid-Ohio River Valley residents were systematically exposed to per- and polyfluoroalkyl substances (PFAS), especially the perfluorooctanoic acid (PFOA), through contaminated drinking water from the Ohio River or Ohio River Aquifer. PFAS exposure levels for the residents were above National Health and Nutrition Examination Survey (NHANES) medians as reported in the C-8 Health Project cohort in Parkersburg, WV for serum PFOA concentrations, and in two Cincinnati cohorts, the Breast Cancer and the Environment Research Project (BCERP) Puberty Study, and the Health Outcomes and Measures of the Environment (HOME) study [43]. Serum PFOA concentrations were significantly associated with water utility or Ohio River Aquifer use. The Ohio River Aquifer in the C-8 study area was contaminated by industrial PFOA discharges to the Ohio River, where downstream Ohio River PFOA concentrations were 9.2–19.1 ng/L; historical PFOA concentrations were typically higher [43].

Volatile organic contamination in water for US Marines: Operations in the United States Marine Corps (USMC) Base at Camp Lejeune, North Carolina started during the early 1940s. During the USMC base's water-quality testing and sampling program in 1980-85, volatile organic compounds (VOCs) were detected in few supply wells that provided drinking water for some of the barracks, family housing, and other buildings on base. The VOCs included trichloroethylene (TCE), tetrachloroethylene (PCE), vinyl chloride, and benzene. The Agency for Toxic Substances and Disease Registry (ATSDR) determined that contamination began in the 1950s and continued until the most highly contaminated wells were removed from service in February 1985 [37]. Maximum measured concentrations of selected contaminants in drinking water were 215 parts per billion (ppb) of PCE in the Tarawa Terrace distribution system in February 1985 and 1,400 ppb of TCE in the Hadnot Point distribution system in May 1982. PCE was also present in the Hadnot Point system (maximum measured concentration was 100 ppb in February 1985), and vinyl chloride and trans-1,2- dichloroethylene (DCE) were present in the distribution system due to degradation of TCE. Benzene was also present in the Hadnot Point system. The sources of contamination were attributed to a privately-owned dry cleaning business adjacent to Camp Lejeune for Tarawa Terrace and base activities such as leaking underground storage tanks, industrial area spills, and waste disposal sites releasing fuel and chlorinated solvents for Hadnot Point. Previous mortality studies conducted of Marines and Navy personnel and civilian employees at Camp Lejeune by ATSDR found elevated mortality risk of the lung, kidney, prostate, rectum, leukemia and multiple myeloma [37].

Additionally, risk for deaths from cancers of the esophagus, liver, pancreas, cervix, and soft tissue were elevated in Marines and Navy personnel, and risk for deaths from cancers of the female breast and oral cavity were elevated in civilian employees. Drinking water studies conducted in other populations found associations between TCE and leukemia and non-Hodgkin lymphoma (NHL); PCE and NHL; and PCE and lung cancer, bladder cancer, leukemia, rectal cancer, and female breast cancer [37].

Hexavalent chromium contamination: In 1996, the PG&E electricity company paid a U.S. $333 million settlement to residents of Hinkley, CA after Erin Brockovich investigation on the chromium-contaminated groundwater and associated increased cancer mortality rates. A more recent case of hexavalent chromium (VI) contamination is the infamous Asopos case in Greece. Asopos river basin in Central Greece was at the center of heavy industrial development for more than 30 years, allowing for the establishment of textile/tanneries/dyes, metallurgical works and plastics industries. A retrospective cohort mortality study in this industrial area of Greece showed the water consumed by the population was contaminated with hexavalent chromium (41 - 156 μg/L in 2007-2009, exposures consistent for at least 20 years). Results of a retrospective mortality study in the CrVI-contaminated area in Greece showed significantly elevated cancer mortality (SMR), adding lines of evidence on the carcinogenicity of hexavalent chromium via the oral ingestion pathway of exposure [44]. To the best of our knowledge, this is the largest human case of environmental exposures to Cr(VI) in a European member country's drinking water supplies (groundwater). By the end of 2000, a total of ~300 industrial units had been operating in the Asopos basin. The Top 3 types of industry in the area, in order of greatest frequency, were textiles/dyes/tanneries > metallurgic works > plastics and food production/manufacturing discharging toxic wastewater into the Asopos river and its tributaries, polluting the surface and ground-water reservoirs with hexavalent chromium (CrVI) and xenobiotics [45].

Arsenic Case study: A drinking-water arsenic (As) case in Cyprus emerged due to environmental and public health concerns associated with the elevated arsenic concentrations in the Mammari area of Cyprus. This peculiarity lies in the fact that measured As concentrations in groundwater (~ 18 ppb) was above the maximum contaminant level (MCL) (10 ppb), representing a low-level contamination scenario.

Arsenic is a known carcinogen that exerts both cancerous and non-cancerous health effects. The As MCL at 10 ppb has been used as a precautionary measure to maintain the lung and bladder cancer risks to the exposed population within the typical target risk range for drinking water contaminants of $1x10^{-6}$ to $1x10^{-4}$, or below. This probability range is historically considered as protective of public health. Hyperpigmentation and keratosis (on human parts not exposed to sun) are the main noncancerous effects of As exposure in such epidemiologic studies. Not much is known regarding As health effects at low-level environmental As concentrations, but in the past 5 years new data come out that show increased risk for cancerous and noncancerous diseases, such as diabetes [46]. Until the late 1980s, skin cancer was the cancer classically associated with As in drinking water. The weight of evidence for ingested arsenic as a causal factor of carcinogenicity is much greater now than a decade ago, and the types of cancer occurring as a result of ingesting inorganic arsenic have even greater health implications than the occurrence of skin cancer alone. The As MCL standard (10 ppb) is based on consideration of all of the risk management factors (e.g., risk, costs, benefits, treatment technology and analytical method capabilities, small systems affordability, etc.).

In the case of epidemiologic studies focusing on cancerous effects of As, significantly increased risks of death from bladder, lung and kidney cancer have been reported [47, 48]. In a population of approximately 400,000 in northern Chile, Smith et al. (1998) [49] found significantly increased risks of bladder and lung cancer mortality due to As in drinking-water. Kurttio et al. (1999) conducted a case-cohort design study of 61 bladder and 49 kidney cancer cases and 275 controls to evaluate the risk of these diseases with respect to arsenic drinking water concentrations. In this study the median exposure was 0.1 ppb and the maximum reported was 64 ppb; authors reported that very low concentrations of arsenic in drinking water were significantly associated with bladder cancer when exposure occurred two to nine years prior to diagnosis [50].

It is not uncommon that historic As exposures may be unknown, as in the case of Cyprus-affected area. Correspondingly, the duration of exposure was unknown and possible health effects were highly uncertain. The relative contribution of dietary items to the overall As daily dose was largely unknown. Food items cooked in As-contaminated water absorb As at the cooking temperature and, thus, enter the food chain. Interestingly, for water As concentrations > 50 ppb, drinking water was the dominant route of exposure to humans, whereas at As concentrations in drinking water < 50ppb, the dominant route of exposure was diet (food cooked with As-contaminated water, or crops irrigated with contaminated water) [51, 52].

Thirdly, biomarkers, such as, toenails seem to be the best available matrix to measure cumulative As exposures. A strong positive correlation existed between toenail As and drinking-water/food As concentrations [53, 54]. A positive highly significant ($p<0.001$) correlation between toenail As concentrations and low As concentrations (<50 ppb) was observed for drinking water. Even greater correlation was observed between low water As concentrations and daily As dose measured in exposed individuals when water and food As intake were both incorporated in the dose-response models [51, 52], suggesting that toenail biomarkers were appropriate in tracking As exposures.

Disinfectants and disinfection byproducts (DBPs): Trihalomethanes (THM) represent the highest in magnitude and frequently occurring class of DBP. The THM are short-lived halogenated compounds that are formed in water and other environmental compartments (air, foodstuff, etc.) when disinfectants come in contact with natural organic matter [55]. The four THM species may come in contact with humans via all routes of exposure, such as, ingestion, inhalation and dermal uptake, because they may be generated as the result of various daily activities such as showering, swimming, mopping, dishwashing etc. [56, 57]. The range of health outcomes associated with disinfectants and DBP exposures is explained by the suite of existing DBP (>600 in number) in the environment (primarily in tap water) and their varying toxicological potencies. Emerging DBP (EDBP) have been also considered, such as, the haloacetic acids (HAA) and haloacetonitriles (HAN) that exhibit relatively high frequency and magnitude of occurrence in finished water of UDWDS and at the same time they exhibit higher

(100-300x) genotoxicity and cytotoxicity values compared with those of THM [58], and they are not (yet) included in any EU Water Directive; however, HAA have already been included in the USA water directive.

Exposure variability may substantially complicate the issue of DBP health effects expressed by: i) multitude of routes of exposure (inhalation, dermal and ingestion), ii) sources (tap water, swimming pools, domestic cleaning, occupational use of disinfectants), iii) disinfectant types (UV, chlorine, ozone, chlorine dioxide, chloramine), iv) different initial water qualities to be treated and v) varying conditions of water pipe network (old age of pipes, pipe material, neighborhood distance from chlorination tank, climatic conditions).

Raw water source, disinfectant type and dosage, types and concentrations of natural organic matter, water pH, soluble bromide/iodide levels, temperature, and duration of disinfectant contact with water have been considered as major factors influencing the magnitude of formation of THM in finished water [59]. It is only during the last couple of decades that the structural integrity and characteristics of piped UDWDS are studied along with the formation of THM in tap water, including, the size of UDWDS [60] and the duration of water stagnation [61]. Most of field studies collected water samples along the UDWDS [62-64], while a few of them sampled directly at the points of use in households with a limited number of sampling points (17 households, [65]; 6 houses [66]). Other pertinent field studies considered a limited number of sampled points (>3) along a UDWDS [67], the effect of water residence time on water DBP levels [68], the selection of sampling points based on distances from the water treatment plants [69], and the influence of hydraulic parameters [67].

The water boards of major EU cities divide their UDWDS into district metered areas (DMA), which are smaller autonomous sub-networks with distinct geographical boundaries that are easier to manage. Improved assessment of environmental exposures at various urban scales, particularly those at the small-area level could greatly facilitate the assessment of health disparities in urban settings. Small-area health disparities are considered to be primarily driven by differences in individual exposure to small-area resources and stressors [70]. It is often the case that health disparities among neighborhoods within the same city are larger than reported health inequalities between cities [15, 71].

Significant differences between two urban areas (areas 1 and 2) in creatinine-adjusted urinary total trihalomethanes (TTHM) and trichloromethane (TCM) levels were observed even after adjusting for age, sex and season, corroborating the older pipe network characteristics of area 1 than that of area 2 [72]. This was corroborated by finished tap water measurements where during summer in this study, TBM levels increased followed by a concomitant decrease in TCM levels presumably due to enhanced water TCM volatility losses [57]. Such TCM losses from water during elevated air temperatures render ingestion-based THM exposures inactive, while non-ingestion routes, such as inhalation of volatile TCM dominated daily THM intake estimates [73].

It was shown that deterioration of water quality was more likely in a water-district with reported high risks of distribution pipe integrity as partially expressed with a higher pipe leaking incidence rate per unit pipe length (HRA) versus that of a lower risk (LRA) (Figure 1). These reports support our findings on the presence of significantly higher THM in water from households (76 μg L^{-1}) in aged pipe network when compared to those households (56 μg L^{-1}) (*$p < 0.001$*) in a newly established neighborhood of the same city. It was further observed that the household distance from the chlorination tank was positively correlated with trihalomethane levels (*$p < 0.001$*).

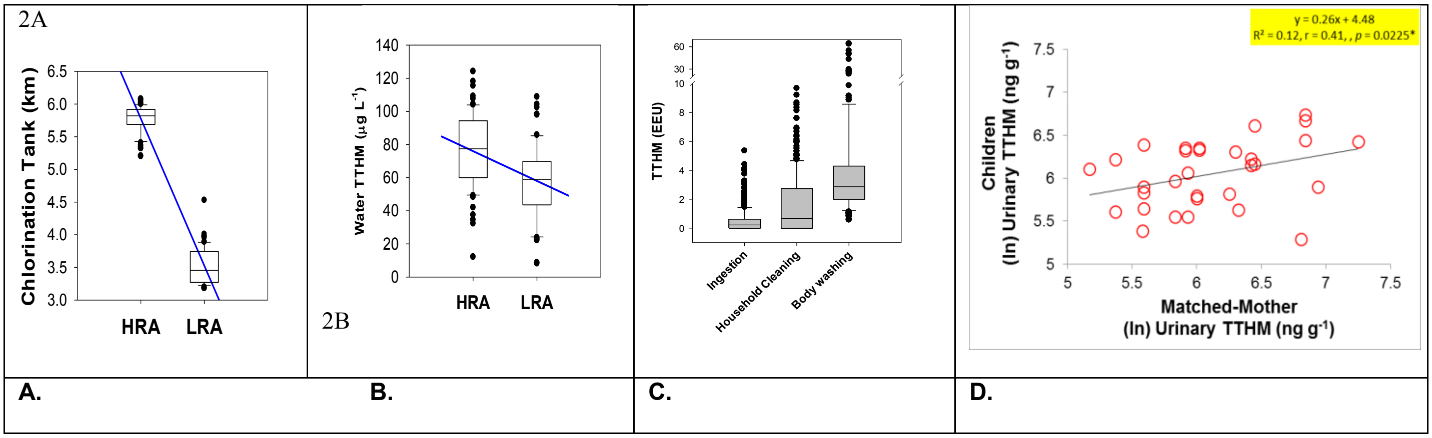

Figure 1. Indicative schematics of within the city differentiation of drinking-water quality, depending on the condition of the pipe network system. A. Household distances from the chlorination tank were significantly greater in the high risk (HRA) compared to those in a low risk water-district (LRA); B. Corresponding significantly higher mean water trihalomethanes was recorded for HRA versus LRA; C. Trihalomethane levels exposure equivalency units based on exposure type; and D. Relationship between log-transformed creatinine-adjusted total trihalomethane urinary concentrations (ng g^{-1}) for the study children with matched-pair mother samples.

Aging of water pipe networks: Gradually-changing or acute shocks associated with technological threats and deficiencies in potable water quality are either already encountered or anticipated in the near future, particularly in aging UDWDS pressured by increasing water demand by urban dwellers. Compromised structural features of UDWDS promote corrosion and biofilm spread (for a review, see Makris et al., 2013 [25]), while the presence of corrosion and biofilm affects chlorine demand and residual chlorine levels [74]. The prohibiting cost of replacing the majority of the existing aged UDWDS network calls for intervention measures that extend pipe durability, longevity and functionality. Buildup of corrosion products and pipe scales result in pipe fouling that diminishes pipe effective diameter available for water flow, exacerbating energy requirements for water carrying capacity. It is warranted that aging of UDWDS in the EU and USA in combination with enhanced vulnerability at the physical, hydraulic and water quality level imposes economic and health adverse consequences. Economic burden of the aged UDWDS has been primarily calculated on the basis of corrosive effects at a rate of US$36 billion year^{-1} in the USA alone [75]. Recent epidemiologic data on the burden of disease associated with the presence of pathogens/contaminants in UDWDS raise the additional total social cost to tenths of US$ billions year^{-1} [76, 77]. Similarly, 3-4% GDP goes into corrosion costs in other countries, such as, Australia, Great Britain, and Japan [78]. Anticipated upgrade in the existing corroded public water distribution system in the USA was valued between 77-325 US$ billion [33]. At the small community, and home owner level, corrosion-related cost in drinking-water distribution systems is about 10-20 times greater than that documented for UDWDS [79].

Seasonal Effects and Climate Change Considerations

The manifestations of climate change are anticipated taking a toll on public health and well-being of populations located in both sides of the Atlantic Ocean, being perhaps particularly aggressive in climate sensitive parts of the globe (e.g. Mediterranean area, Southwest USA). Season-altered concentration profiles for certain (semi)volatile contaminants may be documented, such as higher urinary chloroform and trihalomethanes were detected in summer were observed for two urban areas [72]. Similar seasonal patterns in blood trihalomethanes have been previously reported where summer blood trihalomethane levels were higher than those in winter for a population of postpartum women [80]. Pipe repairs due to deterioration/failure show a peak in frequency during end of spring and summer [81]. Similarly, the international literature suggests summer peaks for disinfection by=products in drinking-water of UDWDS [82]. Customer complaints mostly related to unpleasant odours (geosmin, MIB, chlorine, etc.) peak in summer when authorities increase disinfectant dose as safety precaution against fears of waterborne diseases. The DBP concentrations increase with residence time in UDWDS, while free residual chlorine levels may concomitantly decrease [83].

The impact of increased rainfall or drought events on water quality, part of the aggressive manifestations of climate change will have to be thoroughly characterized. Heavy downpour could increase runoff events carrying downstream heavy metals and microbes that could end up loading the water bodies with contaminants. Also, in the case of droughts, little is known about the impact of continued droughts on water quality as this could alter biogeochemical cycles of several elements. The impact of climate change on water cycle, water quality in urban settings will have to be thoroughly investigated in the near future, because of the lack of relevant data, so far.

Synthesis

Reliability and availability of drinking-water, including safety and health aspects will continue being a highly sensitive topic for the society. Moving forward into the 21st century, urban centers dominate the production of the global GDP (>70%) and by 2050 more than half of the global population will be living in urban centers; according to World Bank projections, half of the area that will be urbanized by 2050 has not yet been constructed [111]. Thus, cities are anticipated to face vast challenges with respect to the drinking-water quality, reliability and availability parameters as they strive to satisfy consumers' potable needs.

The water utilities and local or national authorities will have to continuously strive for measures that will safeguard tap water quality, such as, (i) coping with uncertainty of continuous supply of raw water source(s), (ii) optimizing the 'mix and manage' protocols for the diverse, yet limited water sources, (iii) conserving the water quality threshold from the point of entry (water treatment plant) to point of use (household) in an aging water distribution infrastructure (typical scenario for the majority of district-metered areas in urban settings), and (iv) understanding the influence of water treatment types and disinfectant type used as a means to explain fluctuations in tap water quality within a UDWDS. The wide spatial variability of residual disinfectant (chlorine, chlorine dioxide, etc.) and formed disinfection by-products (DBP) concentrations along with variable concentrations of contaminants (microbial or chemical) that might episodically occur in the pipe network observed across district-metered areas (DMA) of the same city's UDWDS underpins the complexity in pipe network characteristics at the neighborhood level (Figure 2).

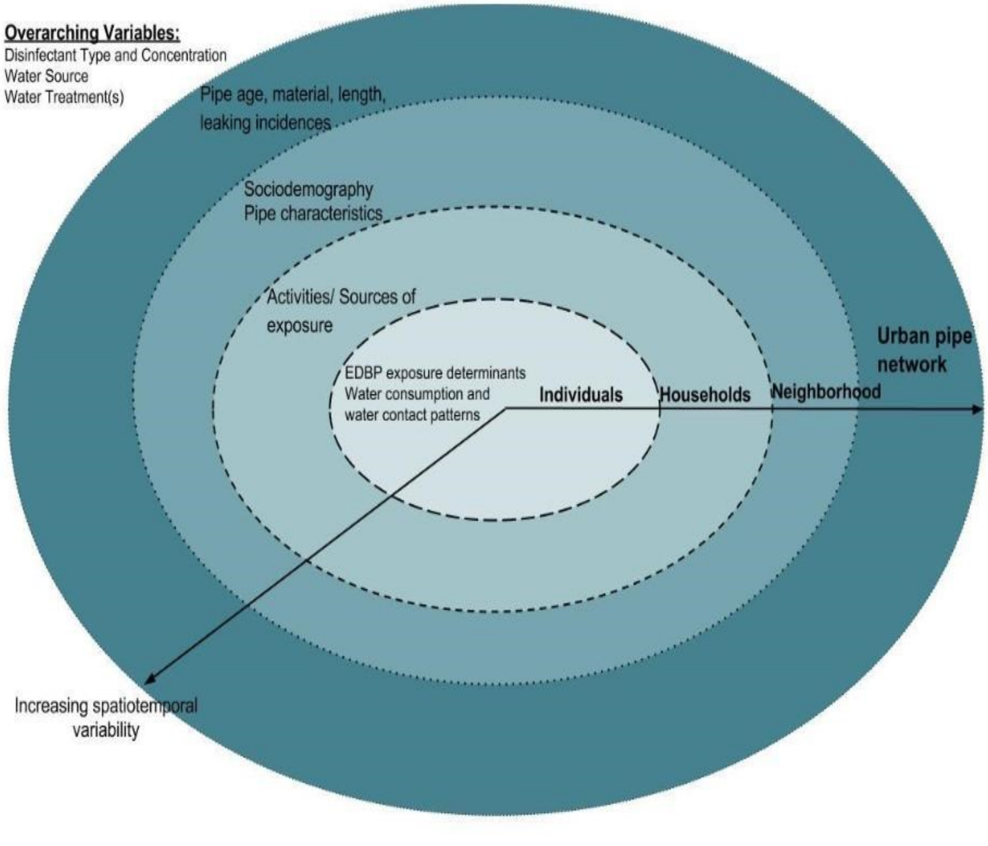

Figure 2. Concentric circle-based model incorporating all dimensions and networks associated with holistically addressing drinking-water and health risks in the urban setting of the 21st century.

Currently, major reform in the regulatory and health policy aspects of water and health in both sides of the Atlantic Ocean is in place. The classical notion that water quality remains intact from the exit of the water treatment plant to the consumer tap is challenged by well-known case studies of drinking water contamination, such as the Flint case in Michigan, USA. Compromised structural features of UDWDS promote corrosion and biofilm spread, while the presence of corrosion products and biofilms affects chlorine demand and residual chlorine levels. *The process of balancing the risk of human exposures to either microbial or chemical contaminants in potable water via optimization of disinfectant dosing and water treatment options often proves a Herculean task in aging and deteriorated UDWDS, particularly those in cities with few human and economic resources.* It is also of utmost importance in accounting for the multitude of routes of exposure for water contaminants, where both ingestion and non-ingestion routes may prevail; in addition to tap water consumption, water contact activities of showering, bathing, dishwashing or household hygiene activities (mopping, toilet cleaning, bathroom cleaning, surfaces cleaning) may be collectively exposing humans to the same contaminant in tap water. Water contamination has been consistently the least assessed environmental/lifestyle risk factor in 76 pregnancy–birth cohorts around the EU, since only 12 of them have incorporated water contamination into their study designs [33]. This underpins the so far, little attention paid to water and health issues by the public health practitioners and researchers.

There is a particular need for addressing research questions of water and health foci that center around the following themes of water resilience and surveillance: (i) long-term vision on monitoring and interpreting the data for water contaminant(s) exposures over a person's lifetime, (ii) climate change manifestations and their impact on water cycle and concomitant human health risks for the general population and its vulnerable subpopulation groups, (iii) life-course toxicity assessment of both current and emerging water contaminants to identify windows of susceptibility, and (iv) novel (chemical mixtures effect) (wells, surface water) for both ingestion and non-ingestion purposes.

Water and health issues are intertwined within a changing urban setting. There is an ongoing momentum of societal demand to act on drinking-water quality associated with aging water pipe infrastructures to protect human health and to devise measures and interventions that will promote further the well-being and quality of life. *One city does not hold a single water quality metric that is often perceived remaining unchanged, because* *drinking-water quality in a city changes in space and time*. Bigger urban centers will be differentially more complex to address water and health risks, because their neighborhoods (DMA) are spread apart geographically in large distances. The water and health issues are multi-disciplinary in nature and demand the close cooperation of health scientists with engineers, environmental scientists, social scientists, economists and local policy makers to address each city's unique challenges and risks. Thus, every city is unique with respect to its water quality; And within each city, each DMA is unique. World Bank projections refer to the typical 21st century's urban setting being bigger in size due to urban population size increase where climate change impacts on water availability and quality within urban water pipe networks will have to be tackled. Addressing water challenges in such reformed urban settings will be of paramount importance in meeting United Nations's sustainable development goals.

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Table 1. Indicative examples of drinking water-based health risks associated with either chemical or microbiological parameters in finished tap water.

	Contaminant	Pipe material	Country	Exposure and Epidemiology	Health Concern	Drinking-Water Regulatory Limit	References
				Pipe scales			
	Copper	Copper	USA	Elevated drinking water copper levels in newly constructed and remodeled homes in Wisconsin, USA.	Copper in drinking water above 3 mg/L induced nausea, vomiting, diarrhea and stomach cramps, and off-flavored water affecting the aesthetics	USEPA standard: 1.3 mg/L	[84-86]
	Copper	Copper	Germany, Holland, and Canada	Tap water consumption	Gastrointestinal problems at acute levels as high as >30 mg/L, and possible death above >1 g/L	WHO standard: 2 mg/L, European Union: 2 mg/L	[17, 87-91]
	Lead	PVC, polypropylene, and galvanized iron	Egypt	Tap water show Pb levels greater than WHO recommendation	Range of symptoms form anemia to nervous system degeneration	WHO standard for Pb in drinking water is 10µg/L; Maximum allowable lead extraction level from PVC pipes is 5µg/L	[92-96]
	Lead	Lead	Germany	Tap water	6.5% of the study drinking water samples have > 10 µg/L (WHO limit) and 2.8% had >25 µg/L (Germany's current limit) (25 µg/L)	WHO standard: 10µg/L, Germany standard: 25µg/L	[92, 97-99]
	Lead	Lead	USA	Tap water	Water lead levels are proportional to children blood lead levels in the	WHO standard: 10µg/L	[16, 92]

					Washington DC area, USA		
	Aluminum	Cement pipes	USA	Drinking water	Al levels were as high as 700 mg/L. Resulted in death of 9 dialysis patients in Curaco	MCL: 0.05-0.2 mg/L	[100, 101]
	Vinyl chloride	PVC	USA	Drinking water	8.9 mg/L when tested. The leaching went up to 280-410 mg/L at temperatures above 50°F	MCL: 0.002 mg/L	[102, 103]
	Organotin	PVC	Canada	Drinking water	Organotin levels increased with time and distance traveled in the distribution pipe systems. Also organotin was reported to accumulate in blood and liver of human beings	USEPA placed organotin on the drinking water contaminant candidate list (CCL)	[104, 105]
Pipe biofilms							
	Acanthamoeba keratitis (amoeba)	Drinking water distribution pipe	UK	Tap water	89% of the study water samples have this pathogen. Severe eye infection in those who wear contact lens, and sometimes may lead to blindness.	Not regulated yet	[106]
	Acanthamoeba keratitis (amoeba)	Drinking water distribution pipe	Chicago, USA	Tap water	Forty-four cases in 2.5 years	Not regulated yet	[107]

	Legionella	Copper distribution pipe	New York, USA	Tap water	Infections of the central nervous system and eye in humans	Not Regulated Yet	[108, 109]
	Cryptosporidium	Drinking water distribution pipe	Milwaukee, USA	Tap water	403,000 cases showing gastrointestinal illness symptoms such as diarrhea, vomiting, cramps	Maximum Contaminant Level Goal (MCLG): zero	[109, 110]