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Using Probabilistic Modeling to Evaluate Human Exposure to Organotin in Drinking Water Transported by Polyvinyl Chloride Pipe

Anthony Fristachi,[1,*] Ying Xu,[2] Glenn Rice,[3] Christopher A. Impellitteri,[4] Heather Carlson-Lynch,[5] and John C. Little[6]

The leaching of organotin (OT) heat stabilizers from polyvinyl chloride (PVC) pipes used in residential drinking water systems may affect the quality of drinking water. These OTs, principally mono- and di-substituted species of butyltins and methyltins, are a potential health concern because they belong to a broad class of compounds that may be immune, nervous, and reproductive system toxicants. In this article, we develop probability distributions of U.S. population exposures to mixtures of OTs encountered in drinking water transported by PVC pipes. We employed a family of mathematical models to estimate OT leaching rates from PVC pipe as a function of both surface area and time. We then integrated the distribution of estimated leaching rates into an exposure model that estimated the probability distribution of OT concentrations in tap waters and the resulting potential human OT exposures via tap water consumption. Our study results suggest that human OT exposures through tap water consumption are likely to be considerably lower than the World Health Organization (WHO) "safe" long-term concentration in drinking water (150 μg/L) for dibutyltin (DBT)—the most toxic of the OT considered in this article. The 90th percentile average daily dose (ADD) estimate of $0.034 \pm 2.92 \times 10^{-4}$ μg/kg day is approximately 120 times lower than the WHO-based ADD for DBT (4.2 μg/kg day).

KEY WORDS: Drinking water; exposure assessment; leaching; organotin; probabilistic; PVC pipe

1. INTRODUCTION

Polyvinyl chloride (PVC) and chlorinated polyvinyl chloride (CPVC), hereinafter referred to as PVC, are the most commonly used pipe materials in U.S. and Canadian residential plumbing systems[(1)] because they are durable and resist biofilm formation. To produce these desired properties, several compounds are added to PVC during manufacturing—including mixtures of organotin (OT) compounds that act as stabilizers protecting the polymer from the high temperature and pressure encountered during the manufacturing process.[(2)] These OT stabilizers contain mono- and di-substituted alkyltin chloride species represented by the chemical formula R_nSnX_{4-n}, where R is either a methyl or butyl group bound to a tin atom (Sn), $n = 1$ or 2, and X is a mercaptoester (e.g., thioglycolate), a carboxylate (e.g., maleate), or a sulfide ligand.[(3)] Many stabilizer formulations include

[1] Battelle, Statistics and Information Analysis, Columbus, OH, USA.
[2] Department of Civil, Architectural and Environmental Engineering, The University of Texas at Austin, Austin, TX, USA.
[3] U.S. Environmental Protection Agency, Office of Research and Development, National Center for Environmental Assessment, Cincinnati, OH, USA.
[4] U.S. Environmental Protection Agency, Office of Research and Development, National Risk Management Research Laboratory, Cincinnati, OH, USA.
[5] Syracuse Research Corporation, Syracuse, NY, USA.
[6] Department of Civil & Environmental Engineering, Virginia Tech, Blacksburg, VA, USA.
*Address correspondence to Anthony Fristachi, P.O. Box 8086, Columbus, OH 43201, USA; antaknee@gmail.com.

mixtures of monomethyltin (MMT), dimethyltin (DMT), monobutyltin (MBT), and dibutyltin (DBT) chlorides.[4] These OT compounds do not react completely with the PVC polymer, and some OT can remain unbound in the polymer after manufacture. OT mixtures also are used to lubricate the pipes during manufacture, and residual OT may remain on the inner surface of the pipe.[2] During use, unbound OT can migrate toward the pipe surface and leach into the water being transported.[5] If OT leach from the pipe polymer, the largest accumulation would occur in waters where the ratio of inner pipe surface area to pipe volume is high, which occurs in small diameter residential pipes. This is a possible health concern because OT are potential human nervous system, developmental, and reproductive toxicants.[6]

A 1996 Health Canada pilot study reported low levels of total Sn, as MBT and DBT, in potable water transported through PVC pipes. Approximately 35% of the waters sampled exceeded the analytical detection limit (DL) of 5×10^{-4} μg Sn/L.[7] A follow-up study of recently installed (<6 months old) residential drinking water systems consisting solely of PVC pipe reported OT concentration levels ranging from less than the DL (5×10^{-4} μg Sn/L) to 0.291, 0.491, 0.029, and 0.052 μg Sn/L for MMT, DMT, MBT, and DBT, respectively.[8]

While the Health Canada studies demonstrate that OT compounds can occur in drinking waters passing through PVC pipes, these data are of limited utility for evaluating human OT exposures through contact with U.S. drinking waters because of the small number of samples and lack of data on the temporal variability of OT concentrations. Other researchers have relied on indirect evidence from measures of OT extracted from a 40-year-old PVC pipe that was used in a water distribution system to suggest that small quantities of OT leach from PVC pipes over time.[9]

We address this problem of insufficient occurrence data through a mathematical modeling approach, adapting a family of models to simulate the leaching of OT from PVC pipe into transported waters, then predicting the resulting concentrations in the transported drinking waters. These models are based on diffusion and convection mass-transfer theory and account for partitioning between the polymer and the external phase, which is defined as the water contacting the inner surface of the PVC pipe. The models require the input of several physical properties of the OT, the polymer, and the external phase. OT leaching is influenced by the mobility of the OT in the polymer relative to that of the external phase, the relative volumes and surface areas of the external phase to the polymer, and the degree of mixing in the external phase.[10] Finally, using a human exposure model capable of integrating the predicted leaching rates and OT concentrations with drinking water intake data, we estimate probability distributions of U.S. population exposures to OT mixtures through drinking contaminated tap water.

2. METHODS

2.1. Leaching Rate Model

The leaching process begins with diffusion of unbound OT within the PVC pipe polymer matrix at a rate that is proportional to the local concentration gradient.[11] When the unbound OT reaches the internal surface of the pipe, it partitions between the polymer phase and the external phase immediately adjacent to the pipe surface. OT then transfers through a thin diffusive boundary layer of water before reaching the bulk of the water flowing within the pipe.

We developed the mathematical models presented in this section under the assumption that Fick's 2nd law applies:[5]

$$\frac{\partial c}{\partial t} = D\frac{\partial^2 c}{\partial x^2}. \tag{1}$$

Simplifying approximations of the model include:[5,11]

- OT is distributed homogeneously in the polymer,
- the volume of the pipe and the water within is finite,
- no boundary resistance occurs between the polymer and water,
- the total amount of OT in polymer and water remains constant during the leaching,
- the diffusion constant (D) of OT is constant over time, and
- the water is well mixed.

Estimates of the leaching rate (M_t) per unit inner pipe surface area A at time t (μg/m^2 hr) are based on the mechanisms illustrated in Fig. 1. PVC pipe is the only source of OT considered (it is assumed that the amount of OT initially in the external phase [y_{in}] equals zero). Assuming simple partioning between the interior surface of the pipe and the water

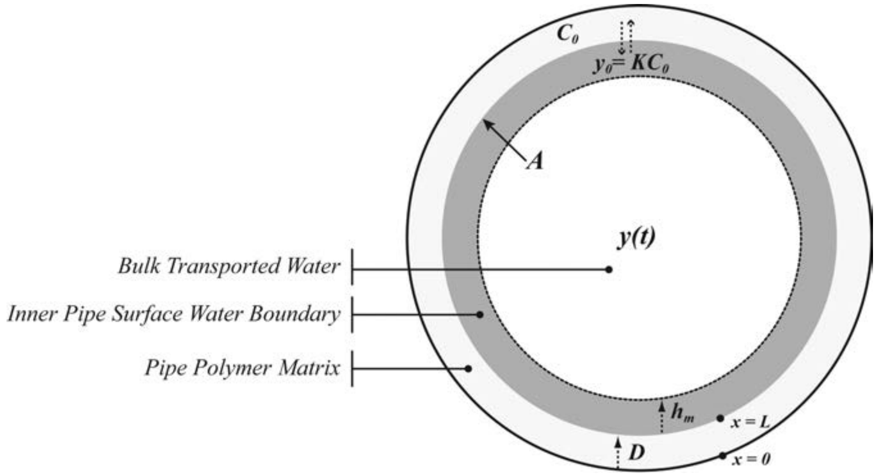

Fig. 1. Schematic representation of OT leaching mechanism in PVC pipe. The rate at which OT is leached M_t (μg/m^2/hr) is a function of inner pipe surface area A (m^2) and time t (hour). The leaching process begins with diffusion of unbound OT (C_0) within the PVC pipe polymer matrix at a rate proportional to the local concentration gradient, represented by the diffusion coefficient D (m^2/s). When the unbound OT reaches the internal surface of the pipe, it partitions between the polymer and the water immediately adjacent to the pipe surface explained by K, the material/water partition coefficient (dimensionless). OT then can transfer through a thin diffusive boundary layer of water into the bulk of the water flowing within the pipe $y(t)$, explained by h_m (m/sec) the mass transfer coefficient that is a function of Q, the water flow inside the pipe (m^3/sec).

immediately adjacent to the surface, we derived the following equation:

$$-Dp \times \frac{\partial C(x,t)}{\partial x} = h_m\left(\frac{C(x,t)}{K} - y(t)\right), \quad \text{for} \quad t > 0, \quad x = L, \tag{2}$$

where D_p is the polymer diffusion coefficient (m^2/s) of OT in the PVC pipe and $C(x, t)$ is the material-phase concentration of OT (μg/L) at time t (s) with respect to location x(m) in the pipe. K is the material/water partition coefficient (dimensionless) and $y(t)$ is the OT concentration in the recirculating water (μg/L). We assumed that K and D were independent of concentration as required for the model.[12] The mass transfer coefficient, h_m (m/s), which varies depending on pipe characteristics, temperature, and water flow rate,[13] is defined as:

$$h_m = D_w(0.023\mathrm{Re}^{0.83}Sc^{\frac{1}{3}})id^{-1} \tag{3}$$

where id is the inner pipe diameter (m), D_w is the OT diffusion coefficient in water (m^2/s), Re is the Reynolds number (dimensionless) defined as the ratio of the mean flow velocity (υ) to the viscosity of water (ν) in units of m/s multiplied by the ratio of the id to ν in units of m^2/s,[11] and Sc is the Schmidt number (dimensionless) defined as the ratio of ν to D_w, which is used to characterize fluid flows in which there are simultaneous momentum and mass diffusion convection processes.[11] Q is the water flow rate inside the pipe (m^3/s) estimated using the American National Standards Institute (ANSI) specifications for PVC[14] and CPVC[15] pipe. The accumulation of OT obeys the following mass balance, where V is the volume of water within the pipe (m^3):

$$\frac{dy(t)}{dt}V = A \times M_t. \tag{4}$$

Several laboratory leaching studies designed to simulate residential plumbing conditions over periods of days to weeks have measured OT concentrations (as total Sn) in waters flowing through PVC piping.[16–21] These studies suggest that several factors, such as flow rate, temperature, pH, the volume of transported water, and pipe surface area, influence the rate and extent of OT leaching. Each study reported a statistically significant rapid dissolution of the residual OT from the inner pipe surface. Once this residual OT was removed, a slower rate of OT leaching from the interior of the pipe into the water followed.

The leaching model was applied to results obtained by Impellitteri *et al.*,[21] who measured MMT, MBT, DMT, and DBT from 10-m pipe sections of three brands of 1-in. nominal size PVC pipe in a recirculating system over 180 days.[21] De-ionized water was introduced into the pipe and allowed to remain in place for several days before being drained and replaced with fresh water. Because the pipes were rinsed thoroughly before testing, we assumed that the contribution from residual OT on the interior surface of the pipe was negligible. The DL for the OT (μg L^{-1}) in this study were as follows: MMT 1.5×10^{-4}, DMT 7.0×10^{-5}, MBT 5.0×10^{-5}, and DBT 1.0×10^{-5}.[21] Leaching rates followed a roughly exponential decay function, with significant reductions during the first 4 h and steady-state concentrations achieved in approximately 12 h. Repeated leaching from the same pipe at a flow rate of 0.35 m^3/h resulted in decreasing Sn concentrations from 36.01 μg/L (MMT), 5.57 μg/L (DMT), 14.14 μg/L (MBT), and 53.27 μg/L (DBT) to below the DL in successive extractions carried out to 40 days, duration.[20] The analytical solution for M_t is:

$$\begin{aligned} C &= \frac{M_t}{A} \\ &= \left(\left[-D_p \sum_{m=1}^{\infty} \sin^2 \beta_m L \left(\frac{2\left(\beta_m^2 + H^2\right)}{L\left(\beta_m^2 + H^2\right) + H}\right)\right]\right. \\ &\quad \times \left[\left(\left(C_0 - K_{y(o)}\right) e^{-D\beta_m^2 t}\right)\right. \\ &\quad \left.\left. + \int_0^t e^{-D\beta_m^2 (t-\tau)} \left(Kdy(\tau)\right)\right]\right) A^{-1}. \end{aligned} \tag{5}$$

The parameters C_0 (9.2×10^7 μg/m^3), the initial uniform concentration of OT, and K (6.8×10^5) were derived from the results of Impellitteri *et al.*[21] Although K determines the maximum concentration that can be reached in the water, D_p is the factor that most influences the rate at which OT leaches from pipe. Based on an analysis of the data presented by Wu *et al.*[20] and Impelliteri *et al.*,[21] we were able to back-calculate a mean value for D_p of $1.56 \times 10^{-14} \pm 1.42 \times 10^{-14}$ m^2/h. Because we identified only two relevant studies and these studies did not directly measure D_p, the standard deviation unlikely captures our uncertainty in this parameter adequately. Finally, $H = h_m/KD_p$ and $\beta_m = (1, 2, \ldots, m)$ are the positive roots of the trigonometric identity $\beta_m \tan(\beta_m L) = H$. Because V, A, and L are usually known from the pipe dimensions, Equations (3) and (4) can be used to predict the changing OT concentration $y(t)$ in the recirculating water. Unfortunately, the data provided in the other extraction studies[16–19] were not suitable for deriving additional estimates of the model parameters.

M_t was calculated at 0.1 h intervals from $t_{\min} =$ day 0 to $t_{\max} =$ day 365. Flow rates (Q) can be extremely variable and are dependent on socioeconomic factors, individual water demands, residents' age and gender, the number of fixtures in a household, and climate.[22] To accommodate this variability, the simulation utilized a truncated normal distribution of faucet flow rates (m^3/h) [$\mu = 9.26$, $\sigma = 1.45$] and uniform probability distribution of faucet use time (hour) [min = 0, max = 0.15] reported in a comprehensive study on water use in 1,000 single-family, detached residential homes.[23] These distributions introduced temporal variability into the simulation that allows for realistic predictions of OT concentrations over time.

2.2. Exposure Model

The distribution of human exposure to OT in U.S. drinking waters are obtained from Monte Carlo simulations employing models that integrate OT concentrations calculated from the predicted distribution of leaching rates and surface areas with empirical body weight and tap water intake data. Spearman correlation tests (r) were used to quantify the relationships among exposure factors. Age is significantly correlated with body weight (BW) ($r = 0.698$, $p < 0.0001$) for a sample size of $n = 31{,}857$. To account for this potential correlation, the analysis is stratified into four kth life stages consisting of 14 ith age bins in the exposure estimates:

1. Infancy (birth to <1 month, 1 to <3, 3 to <6, and 6 to <12 months).
2. Childhood (1 to <2, 2 to <3, 3 to <6, and 6 to <11 years).
3. Adolescence (11 to <16 and 16 to <21 years).
4. Adulthood (21 to <30, 30 to <50, 50 to <70, and 70 + years).

The age bin notation "X to < Y" refers to the (Y–X) interval from an individual's X birthday until the day before their Y birthday. Age bins for infants and children are narrow (≤1 year) at younger ages when rapid developmental changes occur, and broaden with increasing age, based on current U.S. EPA guidance.[24] All estimates are stratified by gender. Exposure estimates also were calculated for single pregnancy events of 15 months (5-month preconception plus 10-month gestation) for women within the childbearing ages of 15 to <45 years. Because data used in this study include information on individuals up to the age of 85, we assume an average lifetime in the United States of 85 years. We also assume that individuals within a specific age bin receive the same daily OT exposure from drinking water.

The average daily dose (ADD) for each jth gender within an ith age bin due to ingestion of tap water (ADD_{ij}) in units of μg/kg-day is calculated as:

$$ADD_{ij} = C \times INTAKE = \left(\left[M_t \times \frac{1000\ L}{0.0634} \times \frac{24\ hours}{day} \times A\right] \times \left[\frac{IR_{ij}}{BW_{ij}}\right]\right), \quad (6)$$

where A is the distribution of inner surface areas of a 1-m section of pipe (m^2), IR_{ij} is the probability distribution of tap-water intake rates (L/day), and BW_{ij} is the probability distribution of body weights (kg).

The time-weighted ADD (Equation (7)) within each kth life stage (ADD_{jk}) is calculated by summing the individual doses for each age bin across life stages, weighted by the ratio of the uniform distribution of exposure duration ED (years), the length of time over which continuous or intermittent exposure occurs for each age bin, to the time spent in each life stage, the averaging time AT (years). These weights represent the proportion of an age bin in relation to the life stage an individual is assigned. For each life stage, these weights represent the proportion of a life stage in relation to an 85-year lifetime.

$$ADD_{jk} = \sum_{i=1}^{i_k} \left(\frac{ED_i}{AT_k} \times ADD_{ij}\right) \quad (7)$$

The time-weighted mean for each jth gender (ADD_j) is given by:

$$ADD_j = \sum_{i=1}^{i_j} \left(\frac{ED_i}{85} \times ADD_{ij}\right). \quad (8)$$

2.3. Development of Distributions

We used the following distributions in a Monte Carlo simulation to develop distributions of ADD_{ij}, ADD_{jk}, and ADD_j.

2.3.1. OT Concentrations

A quantile lognormal distribution of OT concentrations in drinking water (C_w) was developed from the product of the vector of M_t values and a random sample from the triangular distribution of the inner pipe surface area A of a 1-m length of PVC pipe. Arithmetic mean values for three commonly used nominal sizes of PVC[14] and CPVC[15] pipe (1/2 in. pipe [0.047] as the lower limit of the distribution, 1 in. pipe [0.080] as the upper limit of the distribution, and 3/4 in. pipe [0.047] as the mode of the distribution) were used to represent uncertainty in the surface area of residential PVC pipe. *Quantile* functions return a value x at which $p(x) = p_{lhs}$ given a particular probability distribution, where p_{lhs} is the vector of probabilities generated from a 10,000-iteration Latin hypercube sample (LHS).

The Kolmogorov-Smirnov D goodness-of-fit test for normality was applied to the log-scale and nonlog-scale data values of input parameters, with a significant D statistic resulting in the rejection of the assumption that the distribution is normal.[25] It is important to note that when the sample size is large, as is the case in this study ($n = 31{,}857$), even "unimportant" deviations from normality may be statistically significant by this and other tests.[25] For this reason, the final determination of the shape of the distributions was made based on visual inspection of the probability plots.

Estimates of C_w represent the expected OT concentrations in a 1-m PVC pipe with an average *id* of 0.19 m that can be applied to any x linear feet of piping within a residence. To develop a realistic estimate of the distribution of OT exposures from the consumption of drinking water, we reestimated OT concentrations based on data from a case study that estimated the amount of piping in a drinking water system for a "typical larger single-family home in California."[26] This piping system is comprised of different lengths of three commonly used nominal pipe sizes: 50.3 m [0.5 in.], 41.1 m [0.75 in.], and 18.3 m [1 in.] for a total length of 109.7 m, an inner pipe surface area of 6.38 m^2, and standing volume of 31 L. To account for the varying pipe diameters and lengths (L_i) and to incorporate the influence of pipe surface area, the predicted case study OT concentration (C_{cs}) was calculated as a surface area-weighted mean.

2.3.2. Drinking Water Consumption

U.S. population-weighted daily average direct tap water consumption rates IRa_{ij} (L/day) along with age, body weight, gender, and pregnancy status for each individual were obtained from the National Health and Nutrition Examination Survey for the years 1999–2006 (NHANES).[27–30] Tap water is defined as all water from a household tap consumed directly as a beverage or used to prepare foods and beverages.[31]

The data necessary for the calculation of indirect water consumption (IRb_{ij}) (i.e., the consumption of specific foods or beverages, as indicated by U.S. Department of Agriculture (USDA) food codes), and the amount of each food consumed per meal also was obtained from NHANES. Data on the amount of water per 100 g of the edible portion of food and beverages, as indicated by USDA food codes, was obtained from the USDA Food and Nutrient Database for Dietary Studies (FNDDS).[32–34] IRb_{ij} was calculated using the following equation:

$$IRb_{ij} = \left[\begin{array}{l} \sum_{i=1}^{n} (MEAL_{beverage} \times WATER) + \\ \sum_{i=1}^{n} \left(\left(1 + \frac{MOIST}{100} \right) \times MEAL_{food} \times WATER \right) \end{array} \right] 1000\, g^{-1} \quad (9)$$

where i corresponds to the different types of food or beverages consumed by an individual, n c corresponds to the total number of foods and beverages consumed during a 24-h period, $MEAL$ is the weight of food consumed (g), $WATER$ is the amount of tap water per 100 g edible portion of food, and $MOIST$ is the proportion increase or decrease in moisture (%) due to preparation. This approach is comparable to that of other studies that used food consumption survey data to estimate distributions of water ingestion.[35,36]

To produce statistically reliable estimates for demographic subdomains (e.g., sex and age), 2- and 4-year sample weights for each survey cycle were combined to construct 8-year sample weights.[37] NHANES sampling weights, reported in 2-year cycles, reflect the unequal probabilities of selection, adjustments for nonresponse, and adjustments for independent population controls to allow the calculation of unbiased nationally representative estimates.[37]

Quantile lognormal distributions of BW_{ij} and the sum of direct and indirect tap water consumption rates (IR_{ij}) were developed using population-weighted geometric mean and standard deviation estimates. Quantile uniform distributions of ED_{ij} were also developed. Tables I and II, respectively, show the distributions of BW_{ij}, IR_{ij}, and tap water ingestion for males and females.

2.4. Sensitivity Analysis

The primary purpose of performing a Monte Carlo simulation is to create a map from analysis inputs to analysis results that can be explored to determine the relationships between the uncertainty in the independent variables and the uncertainty in the dependent variables. This sensitivity analysis is needed to address the inherent interindividual uncertainty in the estimation of OT exposures due to variability in age, gender, body weight, and the amount of water consumed in a 24-hour period. The sensitivity analysis was performed by rank correlation of each input parameter with the model output.[38] Significant correlations were defined as r values associated with a p-value $\leq$the Bonferroni-adjusted p-value of α/k, where k equals the number of input parameters in the sensitivity analysis. The Bonferroni correction is a statistical adjustment to keep the experiment-wise error rate to a specified level of α for k number of comparisons.[39]

Tornado diagrams are used to summarize the impact of each ADD_{ij} on lifetime exposures for each gender. Based on the upper and lower limits of uncertainty, we ranked the variables from those that have the most impact (at the top) to those that have the least (at the bottom).[40] This analysis assumes that these variables are statistically independent and the output is monotonic.[40]

2.5. Computational Methods

The analytical solution for M_t shown in Equation (4) was determined using MatLab® v7.7 Release 2008b (The MathWorks, Natick, MA). We performed exposure model simulations and sensitivity analyses using SAS v9.1.3® (SAS Institute, Cary, NC). LHS package v. 0.5[41] in R® v. 2.9.1 (R Foundation for Statistical Computing, Vienna, Austria) generated random LHS probability vectors. Triangular distributions were generated using the *Triangle* package v.0.5[42] in R.

3. RESULTS

3.1. Leaching Rate

The mean M_t was estimated to be 12.26 ± 3.32 × 10^{-3} μg/m^2-day (90th percentile = 12.94 μg/m^2-day). Table III summarizes the leaching rate estimates. Fig. 2, where M_t is plotted as a function of time, illustrates the strength of utilizing

Table I. Distributions of Exposure Factors for Males

Age Bin/Life Stage	ED	N	Body Weight (kg) μ	Body Weight (kg) 90% CI	Intake Rate (L/day)[a] μ	Intake Rate (L/day)[a] 90% CI	Tap-Water Ingestion (L/kg-day)[a] μ	Tap-Water Ingestion (L/kg-day)[a] 90% CI	Tap-Water Ingestion (L/kg-day)[a] p 90
Birth to <1 month	0.083	41	4.77	(4.49, 5.07)	0.828	(0.585, 1.17)	0.173	(0.121, 0.249)	0.418
1 to <3 months	0.167	89	5.86	(5.56, 6.19)	0.632	(0.408, 0.979)	0.108	(0.07, 0.165)	0.378
3 to <6 months	0.25	167	7.55	(7.40, 7.71)	0.936	(0.793, 1.10)	0.124	(0.105, 0.146)	0.341
6 to <12 months	0.5	342	9.33	(9.18, 9.50)	1.147	(1.02, 1.28)	0.123	(0.11, 0.138)	0.309
Infants (birth to <12 months)	1	639	8.04	(7.87, 8.20)	0.990	(0.896, 1.09)	0.123	(0.112, 0.136)	0.334
1 to <2 years	1	488	11.55	(11.41, 11.7)	1.495	(1.37, 1.63)	0.129	(0.119, 0.141)	0.299
2 to <3 years	1	429	14.07	(13.89, 14.25)	1.509	(1.36, 1.68)	0.107	(0.097, 0.119)	0.262
3 to <6 years	3	873	18.53	(18.25, 18.81)	1.610	(1.51, 1.72)	0.087	(0.082, 0.093)	0.202
6 to <11 years	5	1377	30.83	(30.32, 31.34)	1.899	(1.81, 2.00)	0.062	(0.059, 0.065)	0.138
Children (1 to <11 years)	10	3167	22.43	(22.06, 22.8)	1.73	(1.67 1.80)	0.077	(0.074, 0.08)	0.219
11 to <16 years	5	2111	55.48	(54.64, 56.32)	2.44	(2.34 2.54)	0.044	(0.042, 0.046)	0.096
16 to <21 years	5	1990	75.78	(74.91, 76.66)	3.14	(2.98, 3.30)	0.041	(0.039, 0.044)	0.093
Adolescents (11 to <21 years)	10	4101	64.72	(63.98, 65.47)	2.76	(2.67, 2.85)	0.043	(0.041, 0.044)	0.094
21 to <30 years	9	1080	83.25	(82.15, 84.37)	3.84	(3.66, 4.03)	0.046	(0.044, 0.048)	0.106
30 to <50 years	20	2428	87.67	(86.98, 88.37)	3.72	(3.59, 3.85)	0.042	(0.041, 0.044)	0.101
50 to <70 years	20	2139	87.99	(87.24, 88.75)	3.50	(3.38, 3.63)	0.040	(0.038, 0.041)	0.090
70 to 85 years	15	1530	80.46	(79.74, 81.18)	2.77	(2.67, 2.88)	0.034	(0.033, 0.036)	0.077
Adults (21 to 85 years)	64	7177	86.18	(85.76, 86.61)	3.56	(3.49, 3.64)	0.041	(0.04, 0.042)	0.094
Time-weighted mean	85	15084	78.49	(83.15, 85.02)	3.29	(3.06, 3.35)	0.048	(0.036, 0.04)	0.111

[a]Estimates are based on water ingested *directly* as a beverage and water ingested *indirectly* in preparation of food or beverages on two nonconsecutive days. Water added to commercial foods and beverages or water occurring naturally in foods is not considered in the analyses. *Notes:* μ = mean; *CI* = confidence interval; ρ 90 = 90th percentile; N = sample size; *ED* = exposure duration in years.

Table II. Distributions of Exposure Factors for Females

Age Bin/Life Stage	ED	N	Body Weight (kg) μ	Body Weight (kg) 90% CI	Intake Rate (L/day)[a] μ	Intake Rate (L/day)[a] 90% CI	Tap-Water Ingestion (L/kg-day)[a] μ	Tap-Water Ingestion (L/kg-day)[a] 90% CI	Tap-Water Ingestion (L/kg-day)[a] p 90
Birth to <1 month	0.083	33	4.53	(4.35, 4.72)	0.683	(0.474, 0.985)	0.151	(0.105, 0.217)	0.380
1 to <3 months	0.167	64	5.58	(5.35, 5.82)	1.12	(0.941, 1.339)	0.201	(0.17, 0.238)	0.448
3 to <6 months	0.25	118	7.08	(6.88, 7.29)	0.817	(0.632, 1.06)	0.115	(0.089, 0.15)	0.359
6 to <12 months	0.5	322	8.84	(8.71, 8.99)	1.30	(1.18, 1.44)	0.147	(0.134, 0.163)	0.313
Infants (birth to <12 months)	1	537	7.68	(7.512, 7.85)	1.11	(1.02, 1.22)	0.145	(0.133, 0.158)	0.343
1 to <2 years	1	430	11.03	(10.87, 11.19)	1.61	(1.48, 1.75)	0.146	(0.134, 0.159)	0.312
2 to <3 years	1	459	13.29	(13.09, 13.49)	1.49	(1.38, 1.61)	0.112	(0.104, 0.121)	0.251
3 to <6 years	3	893	18.07	(17.8, 18.36)	1.47	(1.38, 1.57)	0.082	(0.076, 0.087)	0.193
6 to <11 years	5	1412	30.45	(29.91, 31)	1.67	(1.59, 1.76)	0.055	(0.052, 0.058)	0.131
Children (1 to <11 years)	10	3194	21.88	(21.51, 22.25)	1.59	(1.53, 1.64)	0.073	(0.07, 0.075)	0.207
11 to <16 years	5	2202	54.03	(53.33, 54.73)	1.94	(1.86, 2.03)	0.036	(0.034, 0.037)	0.080
16 to <21 years	5	1894	64.25	(63.44, 65.07)	2.32	(2.22, 2.43)	0.036	(0.035, 0.038)	0.082
Adolescents (11 to <21 years)	10	4096	58.82	(58.24, 59.4)	2.12	(2.055, 2.19)	0.036	(0.035, 0.037)	0.080
21 to <30 years	9	1504	69.69	(68.73, 70.67)	2.89	(2.76, 3.03)	0.041	(0.04, 0.044)	0.101
30 to <50 years	20	2712	73.52	(72.81, 74.24)	2.94	(2.84, 3.04)	0.040	(0.039, 0.041)	0.097
50 to <70 years	20	2206	75.17	(74.4, 75.94)	3.03	(2.93, 3.15)	0.040	(0.039, 0.042)	0.091
70 to 85 years	15	1495	66.92	(66.23, 67.62)	2.42	(2.33, 2.52)	0.036	(0.035, 0.038)	0.083
Adults (21 to 85 years)	64	7917	72.39	(71.98, 72.8)	2.88	(2.82, 2.93)	0.040	(0.039, 0.041)	0.094
Time-weighted mean	85	15744	66.96	(71.31, 73.1)	2.70	(2.51, 2.75)	0.047	(0.035, 0.038)	0.108
Pregnant (15 to 45 years)		1029	75.49	(73.78, 77.25)	3.13	(2.92, 3.36)	0.041	(0.039, 0.045)	0.106

See legend for Table I.

Table III. Predicted Leaching Rates and OT Concentrations for Various Time Intervals for a Period of 1 Year

Timeframe	N	M_t (μg/m^2-day)				C_w (μg/L)				C_{cs} (μg/L)			
		$\mu \pm$ 95% CI	Min	Max	p 90	$\mu \pm$ 95% CI	Min	Max	p 90	$\mu \pm$ 95% CI	Min	Max	p 90
0 to 24 hours	240	12.64 ± 0.079	10.71	13.82	13.60	0.799 ± 0.010	0.560	1.05	0.924	28.21 ± 0.176	23.90	30.83	30.33
1 to 30 days	6960	12.34 ± 0.012	9.80	13.63	13.00	$0.772 \pm 1.80\times10^{-3}$	0.520	1.05	0.899	27.53 ± 0.026	21.86	30.41	29.00
1 to 12 months	80400	$12.25 \pm 3.46\times10^{-3}$	8.66	13.78	12.94	$0.768 \pm 5.26\times10^{-4}$	0.442	1.07	0.895	$27.33 \pm 7.71\times10^{-3}$	19.33	30.73	28.86
Mean	87600	$12.26 \pm 3.32\times10^{-3}$	8.66	13.82	12.94	$0.738 \pm 5.05\times10^{-4}$	0.442	1.07	0.895	$27.35 \pm 7.40\times10^{-3}$	19.33	30.83	28.88

Notes: μ = mean; min = minimum value; max = maximum value; 95% CI = $100(1-\alpha)$ confidence interval; ρ 90 = 90th percentile.

a distribution of flow rates and water use to capture the variability in M_t during the MatLab simulation.

3.2. Concentration Term

The mean C_w was estimated to be $0.768 \pm 5.05 \times 10^{-4}$ μg/L (90th percentile = 0.895 μg/L). The mean C_{cs} was estimated to be $27.35 \pm 7.40 \times 10^{-3}$ μg/L (90th percentile = 28.88 μg/L). The concentrations increase during the first 24 h with a gradual decrease over the course of a year. This phenomenon reflects the gradual depletion of C_0 over time as M_t approaches steady state. Table III summarizes the predicted tap water OT concentrations.

We also estimated OT concentrations for residences where there is no water use during extended absences (e.g., vacation homes). M_t is predicted to reach a steady-state value of 0.523 μg/m^2-day after approximately 8 days, corresponding to an estimated OT concentration at first draw equal to 2.67 μg/L. OT concentrations are expected to return to the mean M_t value reported previously after flushing the piping system with clean water for an extended period. Flushing does not suppress the process of leaching—rather, the movement of the water prevents the accumulation of OT.[43] This phenomenon highlights two potential exposure periods of concern for this scenario: (1) initial high-level exposure and (2) chronic low-level exposures.

3.3. Per Capita Tap Water Ingestion

On a per unit BW basis (L/kg/day), infants younger than 1 month of age ingest, on average, approximately four times the amount of water as the adults. Water intake values for infants are considered representative of the water intake by infants fed with tap-water-reconstituted formula.[43] As age increases, mean indirect ingestion decreases and direct ingestion increases, reflecting the pattern of decreased use of baby formula and increased direct ingestion of water as children grow older. In general, adults over 21 years of age ingest a larger amount of tap water (L/day) than children and infants.

3.4. ADD

Table IV shows predicted OT exposures for a 1-m pipe with an average surface area of 0.06 m^2 (μg/kg-day) by life stage. The largest mean exposures were seen for male infants (birth to <1 month): 0.136 ± 0.053 μg/kg-day (90th percentile = 0.187μg/kg-day) and female infants (1 to <3 months):

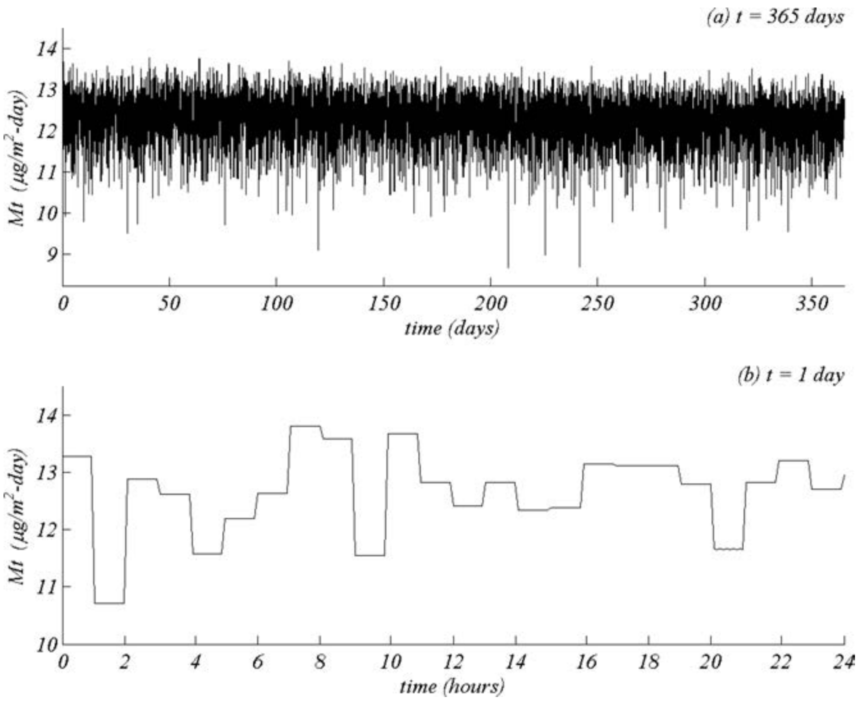

Fig. 2. (a) Distribution of leaching rates from the output of a MatLab simulation representing one year at $t = 0.10$ h intervals for a 1-m pipe with an average *id* of 0.016 m ($n = 87{,}600$); (b) a random 24-h sample of observations.

0.156 ± 0.041 μg/kg-day (90th percentile = 0.196 μg/kg-day). Overall, the mean exposure for infants (0.053 ± 0.034 μg/kg-day [90th percentile = 0.086 μg/kg-day]) was the largest among all life stages. Mean pregnant exposures were $0.04 \pm 8.37 \times 10^{-3}$ μg/kg-day (90th percentile = 0.048 μg/kg-day).

Table V shows predicted OT exposures by life stage for the case study. As expected, case study exposures were higher, highlighting the influence of surface area on OT concentrations. The largest overall mean exposures were seen for infant males (birth to <1 month): 4.69 ± 1.53 μg/kg-day (90th percentile = 6.16 μg/kg-day) and infant females (1 to <3 months): 5.38 ± 0.97 μg/kg-day (90th percentile = 6.32 μg/kg-day). Overall, the mean exposure for infants (1.83 ± 1.06 μg/kg-day [90th percentile = 2.86 μg/kg-day]) was the largest among all life stages. Mean exposures during pregnancy were 1.38 ± 0.10 μg/kg-day (90th percentile = 1.48 μg/kg-day).

3.5. Sensitivity Analysis

We examined the sensitivity of the model to its parameterization by calculating r between the ADD_j and the input parameters of OT concentration, drinking water intake, and exposure duration. Significant r were defined as all values associated with a p-value less than the Bonferroni-adjusted p-value of $(\alpha[0.05]/k)$. As expected, much of the variability was associated with the estimates of C_w for all exposure groups, effectively obscuring the contributions of other model parameters. Because of this influence, C_w was excluded from the final sensitivity analysis. The sensitivity analysis simulations resulted in similar results for males and females (r = 0.594 and 0.576), indicating that exposure duration was the most influential parameter. Figs. 3(a) and 3(b) present tornado diagrams constructed using the upper and lower limits of uncertainty for a lifetime exposure (all ADD_i) for each gender. For males, exposures during ages 21–30 years have the most impact on lifetime exposures and exposures during the ages 70–85 years have the least impact. For females, exposures during the ages 50–70 years have the most impact on lifetime exposures and exposures during the ages 11–16 years have the least impact.

4. DISCUSSION

The models employed here appear to characterize the variability of OT exposures via tap water consumption in the United States. The use of a probability distribution of water flow rate and water use in the leaching rate model allowed for the characterization of temporal variability in estimated OT. Because we were unable to define probability distributions for the other parameters used in the calculation of

Table IV. Distribution of Predicted OT Exposures per Unit 1-m Pipe with an Average Surface Area of 0.06 m^2 (μg/kg-day)

Age Bin	Males		Females	
	μ	p 90 ± 90% CI	μ	p 90 ± 90% CI
Birth to <1 month	0.136	$0.187 \pm 2.13 \times 10^{-3}$	0.119	$0.169 \pm 1.84 \times 10^{-3}$
1 to <3 months	0.086	$0.127 \pm 1.43 \times 10^{-3}$	0.156	$0.196 \pm 1.12 \times 10^{-3}$
3 to <6 months	0.096	$0.121 \pm 7.44 \times 10^{-4}$	0.090	$0.119 \pm 1.05 \times 10^{-3}$
6 to <12 months	0.095	$0.117 \pm 3.68 \times 10^{-4}$	0.114	$0.143 \pm 8.58 \times 10^{-4}$
Infants	0.049	$0.078 \pm 1.07 \times 10^{-3}$	0.058	$0.094 \pm 1.24 \times 10^{-3}$
1 to <2 years	0.100	$0.122 \pm 7.17 \times 10^{-4}$	0.113	$0.137 \pm 6.74 \times 10^{-4}$
2 to <3 years	0.083	$0.102 \pm 5.07 \times 10^{-4}$	0.087	$0.105 \pm 4.53 \times 10^{-4}$
3 to <6 years	0.067	$0.081 \pm 4.31 \times 10^{-4}$	0.063	$0.076 \pm 2.52 \times 10^{-4}$
6 to <11 years	0.048	$0.057 \pm 1.87 \times 10^{-4}$	0.042	$0.051 \pm 2.28 \times 10^{-4}$
Children	0.031	$0.049 \pm 4.84 \times 10^{-4}$	0.030	$0.047 \pm 3.66 \times 10^{-4}$
11 to <16 years	0.034	$0.041 \pm 2.26 \times 10^{-4}$	0.028	$0.033 \pm 1.39 \times 10^{-4}$
16 to <21 years	0.032	$0.039 \pm 1.73 \times 10^{-4}$	0.028	$0.034 \pm 1.26 \times 10^{-4}$
Adolescents	0.016	$0.029 \pm 2.36 \times 10^{-4}$	0.014	$0.024 \pm 2.83 \times 10^{-4}$
21 to <30 years	0.036	$0.043 \pm 1.53 \times 10^{-4}$	0.032	$0.039 \pm 2.03 \times 10^{-4}$
30 to <50 years	0.033	$0.039 \pm 1.50 \times 10^{-4}$	0.031	$0.037 \pm 1.71 \times 10^{-4}$
50 to <70 years	0.031	$0.037 \pm 1.65 \times 10^{-4}$	0.031	$0.038 \pm 1.33 \times 10^{-4}$
70 to 85 years	0.027	$0.032 \pm 1.08 \times 10^{-4}$	0.028	$0.034 \pm 1.44 \times 10^{-4}$
Adults	0.016	$0.024 \pm 2.14 \times 10^{-4}$	0.015	$0.024 \pm 2.55 \times 10^{-4}$
Time-weighted mean	0.024	$0.033 \pm 3.10 \times 10^{-4}$	0.025	$0.034 \pm 2.73 \times 10^{-4}$
Pregnant			0.040	$0.048 \pm 2.37 \times 10^{-4}$

Notes: μ = mean; σ = standard deviation of the mean; p90 = 90th percentile; and 90% CI = distribution-free confidence interval about the 90th percentile.

Table V. Distribution of Case Study OT Exposures (μg/kg-day)

Age Bin	Males		Females	
	μ	p 90 ± 90% CI	μ	p 90 ± 90% CI
Birth to <1 month	4.88	6.42 ± 0.058	4.28	6.00 ± 0.051
1 to <3 months	3.07	4.40 ± 0.042	5.60	6.58 ± 0.031
3 to <6 months	3.45	4.00 ± 0.018	3.24	4.15 ± 0.029
6 to <12 months	3.41	3.79 ± 0.010	4.09	4.51 ± 0.014
Infants	1.74	2.71 ± 0.033	2.07	3.24 ± 0.023
1 to <2 years	3.59	$3.92 \pm 7.30 \times 10^{-3}$	4.04	$4.41 \pm 9.96 \times 10^{-3}$
2 to <3 years	2.98	3.30 ± 0.010	3.12	$3.37 \pm 5.99 \times 10^{-3}$
3 to <6 years	2.41	$2.58 \pm 4.53 \times 10^{-3}$	2.26	$2.42 \pm 3.77 \times 10^{-3}$
6 to <11 years	1.71	$1.81 \pm 2.57 \times 10^{-3}$	1.52	$1.61 \pm 2.50 \times 10^{-3}$
Children	1.12	1.70 ± 0.012	1.08	1.62 ± 0.016
11 to <16 years	1.22	$1.29 \pm 1.24 \times 10^{-3}$	1.00	$1.05 \pm 1.49 \times 10^{-3}$
16 to <21 years	1.15	$1.22 \pm 2.66 \times 10^{-3}$	1.00	$1.06 \pm 1.97 \times 10^{-3}$
Adolescents	0.59	$1.00 \pm 7.67 \times 10^{-3}$	0.50	$0.845 \pm 6.77 \times 10^{-3}$
21 to <30 years	1.28	$1.36 \pm 2.35 \times 10^{-3}$	1.15	$1.22 \pm 2.09 \times 10^{-3}$
30 to <50 years	1.18	$1.24 \pm 1.91 \times 10^{-3}$	1.11	$1.17 \pm 1.62 \times 10^{-3}$
50 to <70 years	1.10	$1.17 \pm 1.33 \times 10^{-3}$	1.12	$1.18 \pm 1.67 \times 10^{-3}$
70 to 85 years	0.954	$1.01 \pm 1.59 \times 10^{-3}$	1.00	$1.06 \pm 1.87 \times 10^{-3}$
Adults	0.558	$0.84 \pm 6.09 \times 10^{-3}$	0.55	$0.824 \pm 7.06 \times 10^{-3}$
Time-weighted mean	0.867	$1.14 \pm 7.34 \times 10^{-3}$	0.89	$1.17 \pm 5.24 \times 10^{-3}$
Pregnant			1.44	$1.54 \pm 3.22 \times 10^{-3}$

Notes: See legend for Table IV. The piping system used in the case study consists of 109.7 m of three commonly used nominal pipe sizes (0.5, 0.75, and 1 in.) with a total inner pipe surface area of 6.38 m^2 and standing water volume of 31 L.

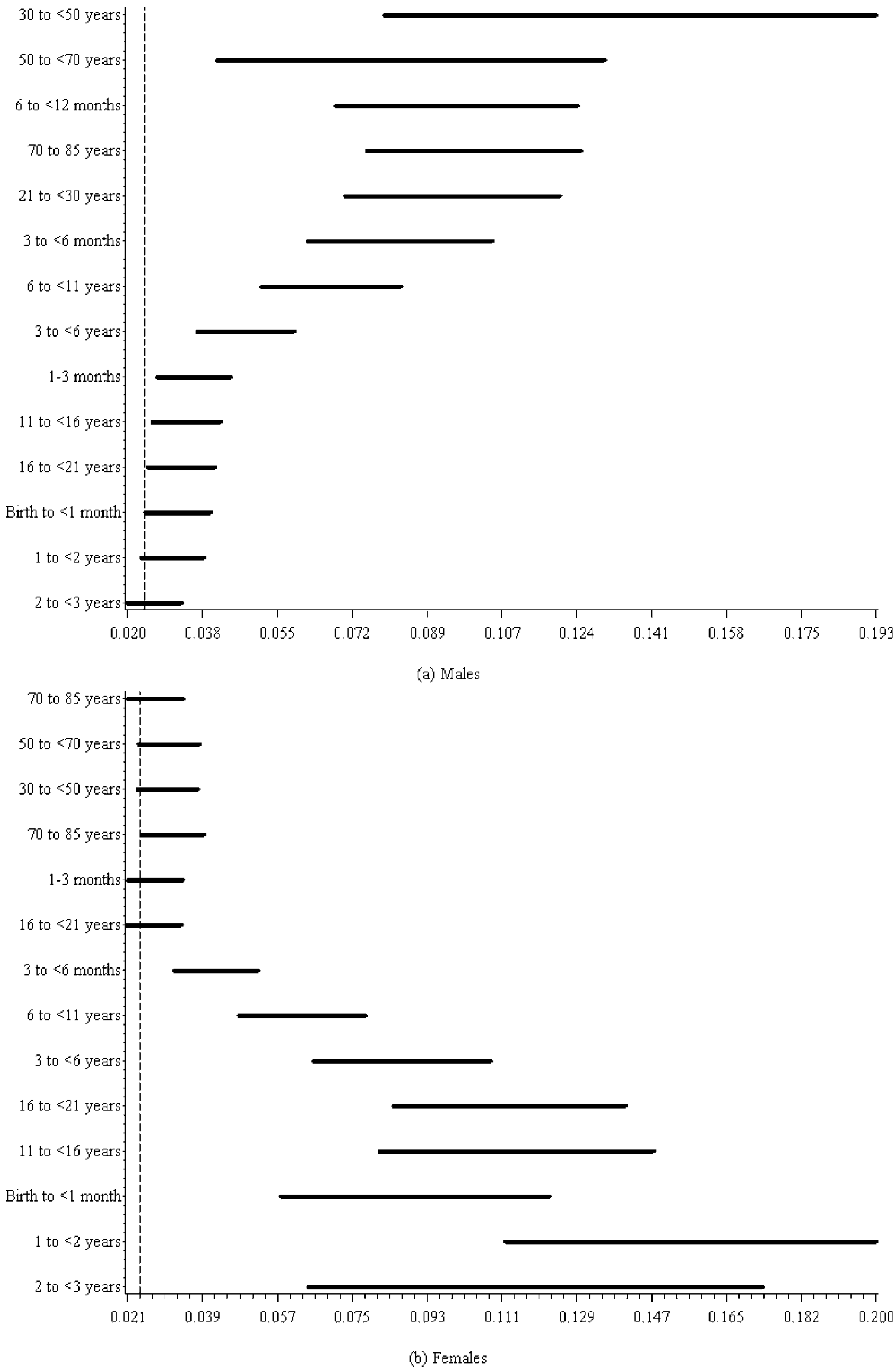

Fig. 3. Sensitivity analysis diagrams using 95% confidence intervals about the mean for lifetime exposure for (a) males and (b) females.

M_t, uncertainty about its prediction is not adequately characterized. The case study results show the effect of a high pipe surface area to water volume ratio, which can exist in residential plumbing, on OT concentration levels. Our distributions for model parameter values are from sources that reasonably describe the heterogeneity in U.S. domestic water uses. Implementation of the model required certain assumptions regarding the distributional fit of the input variables and the length of exposure during any given life stage. Our estimates are conservative and likely overestimate exposure.

Our study results suggest that human OT exposures through tap water consumption are likely to be considerably lower than the World Health Organization (WHO) "safe" long-term concentration in drinking water (150 μg/L) for DBT,[44] the most toxic of the OTs considered in this article. The estimated 90th percentile C_w (0.895 μg/L) and the estimated 90th percentile C_{cs} (28.88 μg/L) are approximately 20 and 550 times greater, respectively, than the highest level reported in occurrence studies (0.052 μg/L). The 90th percentile ADD estimate of $0.034 \pm 2.92 \times 10^{-4}$ μg/kg-day is approximately 125 times lower than the WHO-based ADD for DBT (4.2 μg/kg-day). The 90th percentile ADD estimate for our case study $1.15 \pm 6.29 \times 10^{-3}$ μg/kg-day is approximately four times lower than the WHO ADD for DBT. OT concentrations encountered in water from piping systems subject to extended period of nonuse, while higher than expected concentrations during normal use, are still well below the WHO level.

5. CONCLUSIONS

Our model results suggest that intakes associated with the ingestion of tap water contaminated with OT mixtures that leach from PVC pipe are below levels associated with adverse health effects. Although OT has been reported in a diverse array of consumer goods and foods, these exposure pathways were excluded from this drinking water analysis. Inhalation of OT originating in tap water as the result of volatilization during activities such as showering, cooking, and laundering is unlikely given their low volatility.[45] We identified no studies that provided quantitative estimates of dermal absorption of OT in humans or animals during showering or bathing. Additional analyses of these exposure pathways are needed to evaluate, comprehensively, total OT exposure.

The physical characteristics of a piping system (pipe diameter, pipe length, water demands throughout a system, and initial water quality concentrations) and between and within systems are rarely known precisely. We have attempted to capture this uncertainty in our model predictions. The quantity of PVC pipe used in a typical U.S. home is poorly characterized in the peer-reviewed literature. The type and quantity of OT used in PVC or CPVC pipe manufacturing is proprietary information and therefore exact values of the potential OT available for leaching (C_0) are uncertain.

The OT leaching model used in our study appears to provide reasonable estimates of OT leaching rates based on comparisons with the limited occurrence data. D_p, an important term in the OT leaching model, is estimated from two studies; given the limitations of these two studies for characterizing this parameter value, it is unlikely that we have adequately addressed the uncertainty in this parameter. Future OT drinking water exposure assessments should include information for these data gaps. The principles employed for calculating leaching rates could conceivably be adapted to other organic and inorganic additives within polymer pipes and tubing used to transport drinking water (e.g., phthalates and Bisphenol-A) and offer a novel method for estimating concentrations in lieu of measurement data. A thorough validation of the leaching rate model has not been conducted; therefore, we recommend that the models be tested against a variety of data.

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