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An application for relating *Legionella* shower water monitoring results to estimated health outcomes

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ABSTRACT

Exposure models are useful tools for relating environmental monitoring data to expected health outcomes. The objective of this study was to (1) compare two *Legionella* shower exposure models, and (2) develop a risk calculator tool for relating environmental monitoring data to estimated *Legionella* infection risks and Legionnaires' Disease (LD) illness risks. *Legionella* infection risks for a single shower event were compared using two shower *Legionella* exposure models. These models varied in their description of partitioning of *Legionella* in aerosols and aerosol deposition in the lung, where Model 1 had larger and fewer aerosol ranges than Model 2. Model 2 described conventional vs. water efficient showers separately, while Model 1 described exposure for an unspecified shower type (did not describe it as conventional or water efficient). A Monte Carlo approach was used to account for variability and uncertainty in these aerosolization and deposition parameters, *Legionella* concentrations, and the dose-response parameter. Methods for relating infection risks to illness risks accounting for demographic differences were used to inform the risk calculator web application ("app"). Model 2 consistently estimated higher infection risks than Model 1 for the same *Legionella* concentration in water and estimated deposited doses with less variability. For a 7.8-min shower with a *Legionella* concentration of 0.1 CFU/mL, the average infection risks estimated using Model 2 were 4.8×10^{-6} (SD=3.0×10^{-6}) (conventional shower) and 2.3×10^{-6} (SD=1.7×10^{-6}) (water efficient). Average infection risk estimated by Model 1 was 1.1×10^{-6} (SD=9.7×10^{-7}). Model 2 was used for app development due to more conservative risk estimates and less variability in estimated dose. While multiple *Legionella* shower models are available for quantitative microbial risk assessments (QMRAs), they may yield notably different infection risks for the same environmental microbial concentration. Model comparisons will inform decisions regarding their integration with risk assessment tools. The development of risk calculator tools for relating environmental microbiology data to infection risks will increase the impact of exposure models for informing water treatment decisions and achieving risk targets.

1. Introduction

1.1. *Legionella* disease burden and the role of the environment

Legionella species cause Pontiac fever and a more severe illness known as Legionnaires' Disease (LD). According to the U.S. Centers for Disease Control and Prevention (CDC), cases of LD have increased in the U.S. nearly nine-fold since 2000, and there were almost 10,000 reported cases in the US in 2018 (Centers for Disease Control and Prevention, 2018). This increase could be due to a myriad of factors, including increased testing, population susceptibility, and greater prevalence of *Legionella* in the environment. Despite alarming increases in LD cases, 90% of outbreaks may be preventable via water safety management programs (Centers for Disease Control and Prevention, 2016).

Of *Legionella* spp. that cause infection, most infections are attributable to *Legionella pneumophila* serogroup 1 (SG1) (Yu et al., 2002). In an

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international survey of community-acquired legionellosis cases that were confirmed using culture-based methods, 91.5% (465/508) were attributable to *L. pneumophila*, and, of these, 92% (428/465) were of SG1 (Yu et al., 2002). More recently, Amemura-Maekawa et al. (2018) found that 98% (419/427) of legionellosis patient isolates of *Legionella* spp. from the *Legionella* Reference Center in Japan were *L. pneumophila*, specifically (Amemura-maekawa et al., 2018). During an outbreak in the U.S. at an 89-bed acute care hospital, all cases were of *L. pneumophila* SG1 infections (Hanrahan et al., 1987). In conjunction with this outbreak investigation, 13 of 38 hospital water system samples were positive for *L. pneumophila* SG1, including showers, showerheads, and a hot water tank (Hanrahan et al., 1987). It should be noted that the widely used urinary antigen diagnostic test does not readily detect non-SG1 *L. pneumophila*, possibly resulting in testing bias for studies that implement this method (Byrne et al., 2018).

Several legionellosis epidemiological studies support a relationship between *L. pneumophila* presence in potable water in hospital buildings and nosocomial cases. One of the first studies exploring epidemiological evidence of *L. pneumophila* in hospitals and associated legionellosis cases reported that *L. pneumophila* was detected in potable water of 30% (3/10) of sampled sites (Best et al., 1983). While this suggested a relationship between *L. pneumophila* in potable water and infection risk, it also suggested that concentrations below detectable limits could still result in exposures posing meaningful infection risks. The health burden and cost of *L. pneumophila* make it an important focus of current healthcare-associated infection research. In a CDC report of outbreaks of waterborne disease, from 2011 to 2012, 15 of 18 total outbreaks were of legionellosis (Beer et al., 2015). Of 10 deaths resulting from these outbreaks, five were associated with healthcare environments (unspecified healthcare facilities, hospitals and long-term care facilities) (Beer et al., 2015). From 2013 to 2014, 63% (17/27) of waterborne disease outbreaks were attributable to *Legionella* spp. (McClung et al., 2017). Collier et al. (2012) estimated each episode of LD of inpatient Medicare Supplemental hospitalized cases and of commercial hospitalized cases to cost $26,741 and $38,363, respectively (Collier et al., 2012). The high burden and cost of these outbreaks, some of which are preventable, necessitates development and implementation of risk mitigation strategies.

1.2. Mitigation strategies

To mitigate *Legionella* spp. exposures and consequential infection risks, *Legionella* spp. water management programs are now an industry standard for large buildings, such as hospitals, long-term care, hotels, resorts, and other large facilities with a high density of people, and in 2018, a memo was published by the Centers for Medicare & Medicaid Services (CMS) describing facility requirements to "develop and adhere to policies and procedures that inhibit microbial growth in building water systems" in order to reduce *Legionella* risks (Centers for Medicare and Medicaid Services, 2018). Standard 188-2021 was published by the American National Standards Institute (ANSI) and the American Society of Heating, Refrigerating, and Air-Conditioning Engineers (ASHRAE), Legionellosis: Risk Management for Building Water Systems, providing information on compliance (ANSI/ASHRAE Standard 188-2018, 2018, Legionellosis: Risk Management for Building Water Systems, 2021). These programs include developing a management plan and ensuring the plan is effective. One means to make the plan effective is through "routine environmental sampling" (Centers for Disease Control and Prevention, n.d.). With increased environmental monitoring efforts, there is a growing need for guidance in interpreting monitoring results through a risk-based lens, especially interpretation of *Legionella* concentrations that fall below the limit of detection.

Risk targets, or goals to protect exposed individuals at specific risk levels, have been used in other microbial water quality contexts, where quantitative microbial risk assessment (QMRA) was used to inform intervention and monitoring strategies for drinking water to meet a 1/10,000 annual infection risk target (Macler and Regli, 1993; Signor and Ashbolt, 2009). More recently, advanced microbial risk assessment tools have been used to quantitatively ascribe the degree of infection risk associated with water aerosol-generating features including faucets, toilets, showers outdoor spray irrigation systems and cooling towers (Hamilton et al., 2018, 2019; Pepper and Gerba, 2018; Schoen and Ashbolt, 2011). These studies provide mechanistic insights into *Legionella* spp. exposure events that quantitatively relate a specific concentration of *L. pneumophila* (this specific species since this is what the dose-response curve data is fit to (Armstrong and Haas, 2007)) to infection risk. However, risk assessment models are often difficult to implement into practice. This has been improved by efforts to build web applications of QMRA models so that those without modeling or coding expertise can apply these models for decision-making or risk management strategy (Crank et al., 2019; Rocha-Melogno et al., 2022). The extension of these models for risk-based tool development will increase their potential impact for guiding monitoring and intervention strategies for achieving risk thresholds.

1.3. Study objective

To develop such a tool, more information is needed regarding the existing exposure models (Hamilton et al., 2019; Schoen and Ashbolt, 2011) and how they compare in their estimates of infection risk. Therefore, the objectives of this study were to (1.) compare infection risks from showers estimated by two model frameworks, (2.) explore reasons for discrepancies between risk estimates, and (3.) demonstrate proof of concept for a *L.* pneumophila risk app to be used by facilities managers in water management programs.

2. Methods

A simple exposure scenario describing a single showering event was used to compare two shower risk assessment models in their infection risk estimates. The estimated illness and infection risks for the Schoen and Ashbolt (2011) (Model 1) and Hamilton et al. (2019) (Model 2) models were compared using the same *L. pneumophila* concentrations in the water and shower durations. A Monte Carlo approach was used to account for variability and uncertainty in parameters describing aerosolization of *L. pneumophila*, inhalation rates, and the fractions of aerosols depositing in the alveolar region of the lung. Ten-thousand iterations were used, supported by Burmaster and Anderson (1994), and central tendencies of infection risk were reasonably stable with this number of iterations (Burmaster and Anderson, 1994). To conduct a sensitivity analysis, Spearman correlation coefficients were used to quantify monotonic relationships between input parameters and infection risks for both models, where a larger absolute value of a Spearman correlation coefficient indicated a stronger influence of the input parameter on the output (infection risk). Spearman correlation coefficients are also appropriate for nonparametric data.

2.1. Model 1 for estimating dose and infection risk

In Model 1, the concentration of *L. pneumophila* in the air (CFU/m^3) is a function of the concentration in the water (CFU/L) and a partitioning coefficient (CFU/m^3/CFU/L) (Eq. (1)) (Schoen and Ashbolt, 2011).

$$C_{air} = PC \cdot C_{water} \quad (1)$$

A partitioning coefficient was randomly sampled from a triangular distribution (minimum=1×10^{-5}, mode=1×10^{-4}, maximum=1.9×10^{-4}), informed by the low value and the best estimate value listed by Schoen and Asbolt (2011). To estimate the volume of air inhaled, an inhalation rate (m^3/hr) (B) was multiplied by the duration of the exposure. An inhalation rate was randomly sampled from a normal distribution (mean=1.2×10^{-2}, sd=2.5×10^{-3}, left-truncated at zero, m^3/min), informed by the U.S. Environmental Protection Agency's

Exposure Factors Handbook (U.S. Environmental Protection Agency, 2011).

$$V_{air} = B \cdot t \quad (2)$$

To estimate how the concentration of *L. pneumophila* in the air and the volume of air inhaled relate to dose, the fractions of aerosolized *L. pneumophila* in the aerosol size range of 1–5 μm, and the fraction of aerosols that reach the alveoli were multiplied by the concentration and volume inhaled. While the original model addresses other size ranges (5, 6 μm and 6–10 μm), there is evidence that particles >5 microns primarily deposit in upper and larger airways of the lung (Darquenne, 2020) and will not remain airborne for as long as particles less than 5 μm (Fennelly, 2020). In terms of other size ranges and deposition in the lung, 2-5 μm mostly deposits in the central and small airways and <2 μm in the alveolar region (Darquenne, 2020). Although we were interested in deposition in the alveolar region, we used 5 μm a cut off since this is the upper limit of the smaller range of particles explored in the original Schoen and Ashbolt model (1-5 μm) for which there are parameterized distributions (Schoen andand Ashbolt, 2011). It should be noted that not all aerosols in the size range of 1–5 μm in this model were assumed to deposit in the alveolar region of the lung: the fraction of total aerosols (1–5 μm) assumed to deposit in the alveolar region was randomly sampled from a triangular distribution (minimum=0, midpoint=0.2, maximum=0.54). The percent of 1-5 μm range aerosols containing *Legionella* was then randomly sampled from a uniform distribution with a minimum of 75% and a maximum of 100%.

The dose was then inputted into an exponential dose response curve with parameter k (the probability that a single organism survives and arrives at the infection site). This dose-response curve with an infection endpoint was used in the original work from Model 2 (Hamilton et al., 2019), informed by a dose-response study of guinea pig data originating from inhalation exposures (Armstrong and Haas, 2007; Muller et al., 1983). No dose-response curve was originally used in the development of Model 1, as risk was not a main output in that work (Schoen and Ashbolt, 2011). Therefore, the same dose-response curve was used in Models 1 and 2.

Table 1
Model parameters and sources.

Model	Parameter	Point Value or Distribution	Source
Both Models	k (dose-response curve parameter)	Lognormal (meanlog=-2.93, sdlog=0.49)	(Hamilton, et al., 2019)
	Inhalation rate (m^3/min)	Normal (mean=1.2×10^{-2}, sd=2.5×10^{-3}), left-truncated at zero	(U.S. Environmental Protection Agency, 2011)
Model 1	Flow rate (L/hr)	Triangular (min=350, mid=360, max=370)	(Schoen and Ashbolt, 2011)
	Partitioning coefficient (CFU/m^3/CFU/L)	Triangular (min=1×10^{-5}, mid=1×10^{-4}, max=1.9×10^{-4})	(Schoen and Ashbolt, 2011)
	Fraction of total aerosolized organisms in 1–5 um range (F_1) (unitless)	Triangular (min=0.5, mid=0.75, max=1)	(Schoen and Ashbolt, 2011)
	Fraction of total aerosols of size range 1–5 um deposited at alveoli (F_2) (unitless)	Triangular (min=0, mid=0.2, max=0.54)	
Model 2	Concentration of aerosols at diameter 1-2 (# aerosols/m^3)	Conventional shower: Lognormal (meanlog=17.5, sdlog=0.30) Water efficient shower: Lognormal (meanlog=18.1, sdlog=0.57)	(Hamilton et al., 2019)
	Concentration of aerosols at diameter 2-3 (# aerosols/m^3)	Conventional shower: Lognormal (meanlog=17.5, sdlog=0.17) Water efficient shower: Lognormal (meanlog=17.9, sdlog=0.64)	
	Concentration of aerosols at diameter 3-6 (# aerosols/m^3)	Conventional shower: Lognormal (meanlog=19.4, sdlog=0.35) Water efficient shower: Lognormal (meanlog=18.7, sdlog=0.52)	
	Deposition efficacies (fraction, unitless)	1 micron Uniform (min=0.23, max=0.25) 2 microns Uniform (min=0.40, max=0.53) 3 microns Uniform (min=0.36, max=0.62) 4 microns Uniform (min=0.29, max=0.61) 5 microns Uniform (min=0.19, max=0.52)	
	Percent aerosolized (percent, unitless)	F.1 = 17.50 F.2 = 16.39 F.3 = 15.56 F.4 = 6.67 F.5 = 3.89	

$$Dose = PC \cdot C_{water} \cdot B \cdot t \cdot F_1 F_2 \quad (3.1)$$

$$Dose = C_{air} \cdot V_{air} \cdot F_1 F_2 \quad (3.2)$$

$$P(infection) = 1 - e^{-k \cdot Dose} \quad (4)$$

Variables and their distributions can be seen in Table 1. The partitioning coefficient values (*PC*) and the fraction of *L. pneumophila* in aerosols in size range 1–5 (F_1) originate from experimental data in a hospital setting (Perkins et al., 2009). The fraction of aerosols in size range 1–5 that are then assumed to deposit in the lung originate from a chapter of *Concepts in Inhalation Toxicology* (Schlesinger, 1989).

2.2. Model 2 for estimating dose and infection risk

Using Model 2, the dose was estimated by multiplying the *L. pneumophila* concentration in the water at the fixture (C_{water}) by the breathing rate (B), duration of exposure (t), a sum of concentrations of aerosols ($C_{aer,i}$) of specific diameter sizes, i, by their volume sizes ($V_{aer,i}$) and a sum of the fraction of *L. pneumophila* in the aerosols of specific sizes (F_i) and the "deposition efficiency" (D_i) of aerosols of those sizes (Hamilton et al., 2019). The range of aerosol sizes explored here was from 1 to 5 μm to be consistent with Model 1 and due to mechanistic reasons described above, even though larger size ranges are explored in the original work (Hamilton et al., 2019). Parameters and their distributions and sources can be seen in Table 1.

$$Dose = C_{water} Bt \sum_{i=1}^{5} C_{aer,i} V_{aer,i} \sum_{i=1}^{5} F_i D_i \quad (5)$$

The concentration of aerosols ($C_{aer,i}$, number of aerosols with diameter i μm per m^3) of various sizes for water efficient or conventional showers originate from experimental studies (O'Toole et al., 2008, 2009). The fraction of aerosols with diameter i μm containing *L. pneumophila* (F_i) and the fraction of aerosols of that size that would then deposit in the lung (D_i) were also informed by experimental data and (Allegra et al., 2016; Heyder et al., 1986).

2.3. Relating infection risks to illness risks

Methodology described by Weir et al. (2020) was used to relate infection to illness risks (Weir et al., 2020). However, it should be noted that individual infection risks per group were not calculated and combined, as done by Weir et al. (2020). Rather, we directly estimate a population level risk. Briefly, the probability of illness ($P_{illness}$) was estimated by multiplying the "overall population" (as opposed to stratified by age or sex) probability of infection by "morbidity ratio proxy" (MR_G) for a specific group (Eq. (6)) (Weir et al., 2020).

$$P(illness)_G = P(infection) \cdot MR_G \quad (6)$$

The morbidity ratio is estimated by multiplying a national attack rate (AR) by the ratio of the incidence in a specific group (IR_G) to that of the total population (IR_P) (Eq. (7)).

$$MR_G = AR \cdot \frac{IR_G}{IR_P} \quad (7)$$

In this study, the groups included 8 age ranges, males and females, 4 races, and 2 ethnicity categories, based on available incidence data. While not measured in this study, it should be noted that differences in incidence across race and ethnicity may be due to a myriad of factors, including social determinants of health associated with increased Legionnaires' Disease risk (e.g., household income, living in older homes or rental properties), and higher incidence of Legionnaires' Disease among Black or African American individuals relative to White individuals has been reported in other studies (Barskey et al., 2022).

In a report of 2016-2017 data (Deven et al., 2020), the CDC reported a national incidence rate of 2.29/100,000 in 2017, which we used to inform IR_P. To our knowledge, a more recent CDC report providing a national incidence rate is not available. An estimated national attack rate of 0.05 was used, as this has been suggested by Weir et al. (2020) as a potential value for AR available from OSHA (Occupational Safety and Health Administration, n.d.; Weir et al., 2020). Since a wide range of inhalation rates representative for males and females of age ranges overlapping with the ranges here, it was assumed that the estimated $P_{infection}$ was representative of an "overall population risk" (Weir et al., 2020).

2.4. Comparing deposited doses based on airborne concentrations

We hypothesized the driver of differences between the two models would be in how partitioning is handled, where in Model 1, a ratio for partitioning of all sizes is used. However, Model 2 involves the use of size-specific partitioning coefficients. To explore how similarly they described deposition of aerosols in the lung, specifically, we assumed the same concentration of bacteria in the air and updated the models to only describe deposition of aerosols. Data from Allegra et al. (2020) were used to inform input parameters for Models 1 and 2 (Allegra et al., 2020; Hamilton et al., 2019; Schoen and Ashbolt, 2011). These parameters included the concentration of *Legionella* in the air that was experimentally measured using a simulated shower setup (2.9×10^3 bacteria/m^3) and the inhalation rate (7.5 m^3/min) (Allegra et al., 2020).

Because the concentration of air was used as an input as opposed to the concentration in the water, Eq. (1)) for Model 1 was not used for model comparison. For Model 2, Eq. (5) was altered, where the concentration of *Legionella* in the air was assumed to be equal to the product of the concentration of *Legionella* in the water (C_{water}) and the summation of the number of aerosols of size i per cubic meter of air multiplied by the volume of the aerosol of size i. Note that this means estimated deposited doses would be the same for conventional and water efficient showers.

2.5. App development

An interactive app was developed with RShiny, where flexible input parameters included $\log_{10}$ CFU/mL of *Legionella* in shower water, shower duration (min), risk threshold, shower type (conventional vs. water efficient), age, and sex. Age- and sex-specific inhalation rates were used to result in age- and sex-specific infection risk estimates. The app was then designed to output infection risks estimated over a range of *Legionella* concentrations for the same scenario (shower duration, shower type, age, and sex), with a point on the lines indicating the estimated mean infection risk for the specific scenario. A heatmap of illness risks in the form of cases/100,000 estimated for showers of this duration; shower type; and with the selected *Legionella* concentration were also outputted for both males and females of ages 55-64 yrs, 65-74 yrs, 75-84 yrs, and 85+ yrs; stratified by race (White, African American/Black, Asian/Pacific islander, Native American). Illnesses were not estimated for groups with less than 16 cases for informing incidence rates. These groups included Native American men or women, Asian/Pacific Islander women, and Asian/Pacific Islander men ages 75-84 years or 85+ (Table 2).

3. Results

3.1. Infection risks

Infection risks for conventional showers estimated with Model 2 were greatest, followed by infection risks for water efficient showers also estimated with Model 2, and, lastly, by infection risk estimates using model 1 (Fig. 1). Greater variability was seen for infection risk estimates using Model 1 in comparison to Model 2 (Fig. 1). These differences in infection risk translated to differences in *Legionella* concentrations that yielded a greater than 1/10,000 infection risk per shower event. It

Table 2
National attack and incidence rates and group-specific incidence rates of Legionnaires' Disease used for illness risk estimation.*

National Attack Rate			National Incidence Rate			Source
0.05			2.29/100,000			(Deven et al., 2020; Occupational Safety and Health Administration, n.d.)
Group-specific Incidence Rates						
Sex	Age	Native American	Asian/Pacific Islander	African American	White	Source
Female	55-64	1.60/100,000*	0.80/100,000	10.24/100,000	3.24/100,000	This study**
	65-74	3.44/100,000*	1.16/100,000	9.31/100,000	4.20/100,000	
	75-84	3.20/100,000*	1.97/100,000*	9.68/100,000	4.63/100,000	
	85+	12.45/100,000*	4.92/100,000*	10.10/100,000	5.84/100,000	
Male	55-64	4.33/100,000*	1.72/100,000*	17.22/100,000	6.20/100,000	
	65-74	6.26/100,000 *	3.22/100,000*	16.59/100,000	8.29/100,000	
	75-84	6.18/100,000*	2.53/100,000*	15.34/100,000	10.26/100,000	
	85+	0.00/100,000*	6.50/100,000*	15.65/100,000	11.89/100,000	

* Indicates there were less than 16 cases for the population, so illness risks were not estimated for these groups.
** Data provided by the Centers for Disease Control and Prevention.

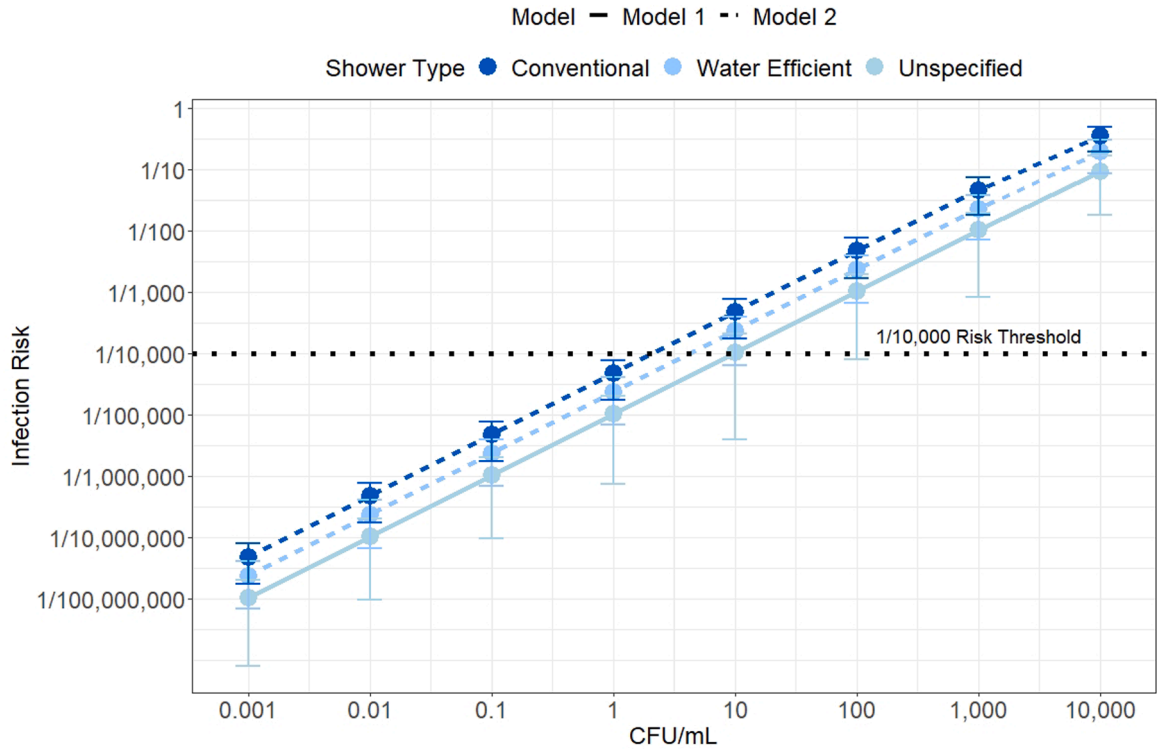

Fig. 1. Infection risks for a 7.8-min shower and a range of *L. pneumophila* concentrations (CFU/mL). "Unspecified" risk estimates come from Model 1, where the type of shower in the original work describing the model (Schoen and Ashbolt, 2011) does not specify the shower as conventional or water efficient.

should be noted that the 1/10,000 is an annual risk target not originally used to be a target per exposure (World Health Organization, 2004). However, this threshold and similar ones (5/10,000) have been used in other non-water-related QMRA contexts as a threshold for comparison for exposure-specific events (Harvey et al., 2021; Wilson et al., 2021). While Model 1 estimated infection risks straddling a 1/10,000 risk target for a *Legionella* concentration of 10 CFU/mL, this risk threshold was already surpassed for Model 2.

For a 7.8-min shower with a *Legionella* concentration of 0.1 CFU/mL, a concentration and shower duration used by Hamilton et al. (2019), the average infection risk for conventional showers was 4.8×10^{-6} (SD=3.0×10^{-6}) (Fig. 2). Water efficient showers corresponded to an average infection risk of 2.3×10^{-6} (SD=1.7×10^{-6}), and "unspecified showers" (showers from the Schoen and Ashbolt model that do not specify water efficient vs. conventional) using Model 1 corresponded to an average infection risk of 1.1×10^{-6} (SD=9.7×10^{-7}) (Fig. 2).

3.2. Comparison of deposited doses for same airborne concentration

When Models 1 and 2 were used to estimate deposition of *Legionella* in the lungs assuming the same concentration of airborne *Legionella* and disregarding differences in partitioning, the central tendencies of estimated deposited doses were similar, where the mean estimated doses for Models 1 and 2 were 4.0 CFU and 5.2 CFU, respectively (Fig. 3).

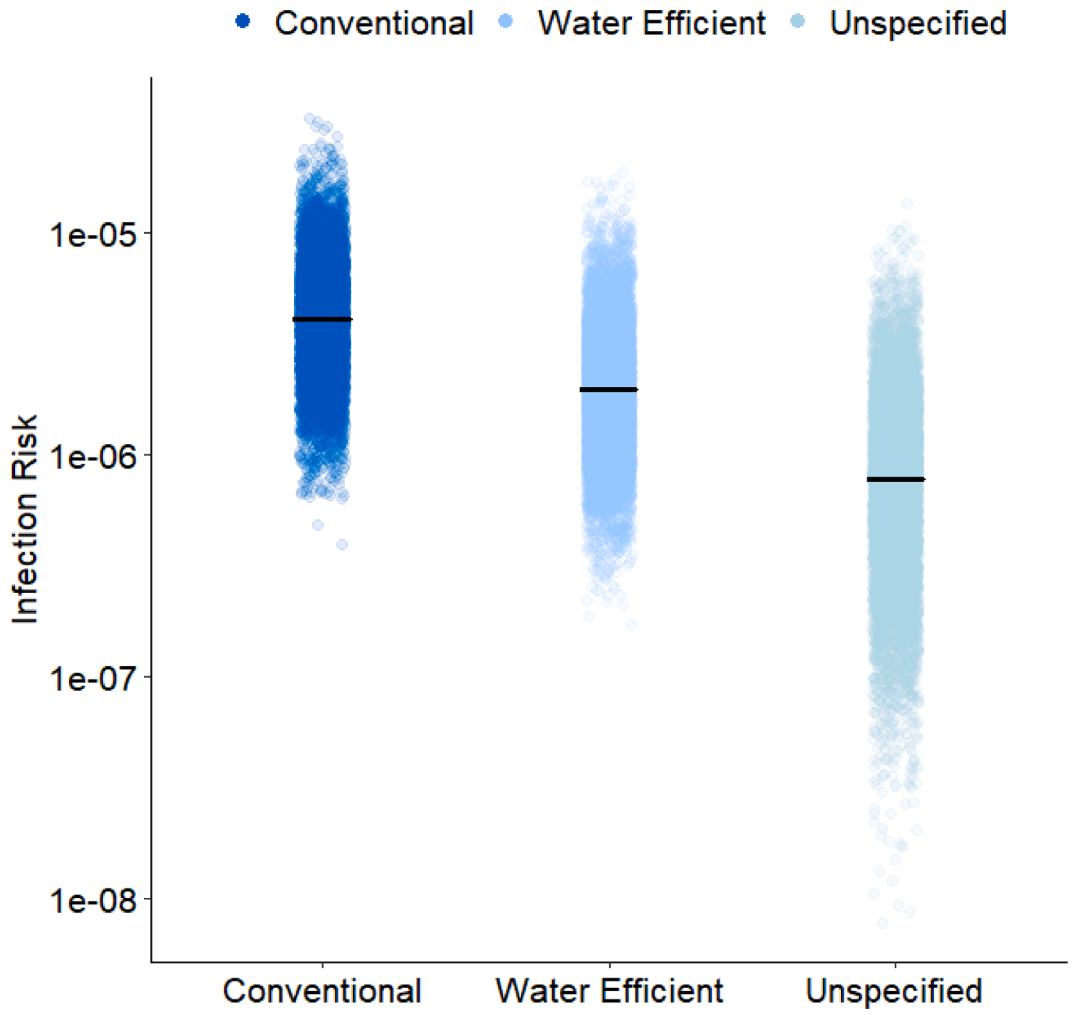

Fig. 2. Infection risks for a 7.8-min shower at a concentration of 100 *L. pneumophila* CFU/L*
*Conventional and water efficient infection risks were estimated with Model 2, while the unspecified shower type infection risks correspond to Model 1. Horizontal lines indicate the median of estimated infection risks.

However, when these distributions were compared with a Wilcoxon rank sum test, they were statistically significantly different (W=26774006, $p < 0.001$). It should be noted that this was a comparison of 10,000 iterations for each model and that a p-value is a function of sample size. Aside from the statistical implications, the overall similarity in magnitude of estimated deposited doses demonstrated that differences in infection risk between the models are likely driven by differences in describing partitioning as opposed to deposited dose. More variability in estimated dose was seen for Model 1 than for Model 2. We therefore used Model 2 for app development.

3.3. Sensitivity analysis

Of the parameters used to inform deposited dose, the factors with the greatest influence on infection risk for Model 1 were the dose-response curve parameter (k) (ρ=0.54), the partitioning coefficient (ρ=0.47), and the fraction of aerosols of sizes 1-5 μm that deposit in the alveolar region of the lung (ρ=0.58) (Fig. S1). For Model 2, the most influential factor in both the conventional and water efficient fixture models was the dose-response curve parameter (k) (ρ=0.82 for conventional and ρ=0.76 for water efficient), followed by the inhalation rate, B (ρ=0.36 for conventional and ρ=0.33 for water efficient) (Fig. S1). This may be due, in part, to smaller ranges of aerosol sizes where no one size drives infection risk (Fig. S1).

3.4. App development

Due to more conservative risk estimates (Figs. 1 and 2) and more refined aerosol size ranges (Table 1), we utilized the Model 2 for risk calculator application development. The calculator inputs included *Legionella* concentrations of $\log_{10}$ CFU/mL, shower duration (min), risk thresholds (1/1,000 to 1/1,000,000 varying by a power of ten), conventional vs. water efficient showers, age (years from 11 to 81), and the sex of the person taking the shower (male or female) (Fig. 4). Infection risk estimates based on inhalation rates for the age and sex selected informed by the U.S. Exposure Factors Handbook were then used to estimate infection risks for a range of *Legionella* concentrations, and the mean infection risk for the selected scenario was plotted (Fig. 4) (U.S. Environmental Protection Agency, 2011). If this risk was above the selected risk threshold (indicated by a dotted line), then the diamond was colored red as opposed to green when it was below the risk threshold. This allows for a fast interpretation of the infection risk for the scenario relative to the selected risk threshold. Illness risks were then plotted below, where a population-level infection risk (not specific to age or sex) was used in conjunction with case data (Table 2) to estimate illness risks (LD, specifically) for men and women of various age ranges and races for a shower with the selected duration and *Legionella* concentration (Fig. 4). A disclaimer was added to the app to communicate its scope of use: The Quantitative Microbial Risk Assessment (QMRA) models are developed from peer-reviewed publications and risk factors

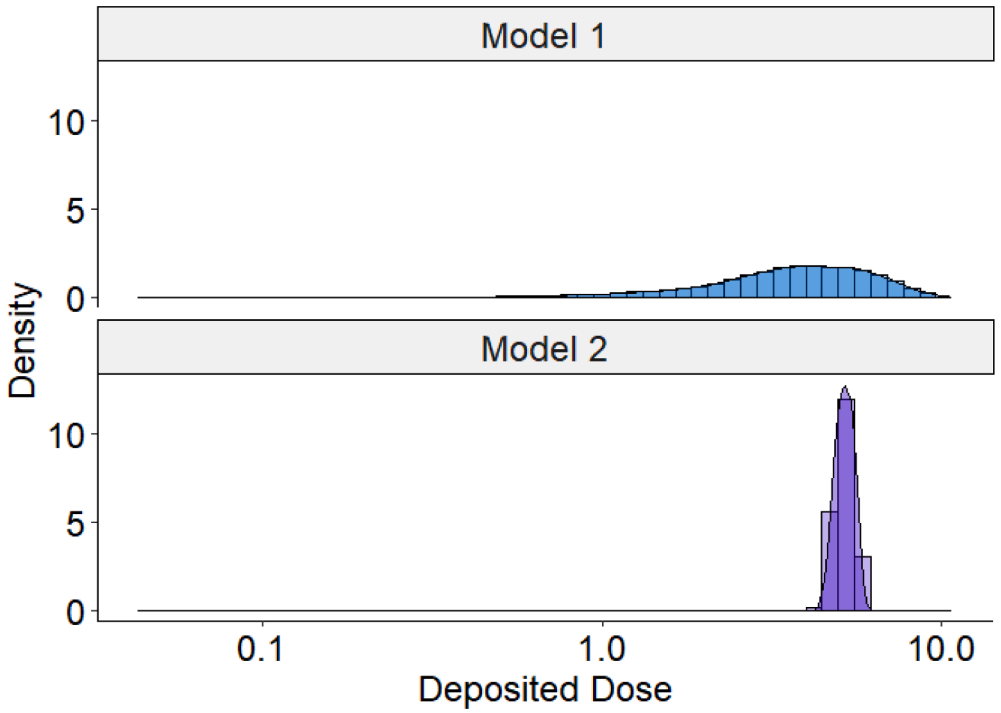

Fig. 3. Comparison of estimated deposited doses estimated by Models 1 and 2*
*These results reflect a shower scenario assuming 1 min of shower exposure, 2.9×10^3 *Legionella* CFU/m^3, and 7.5×10^{-3} m^3/min inhalation rate.

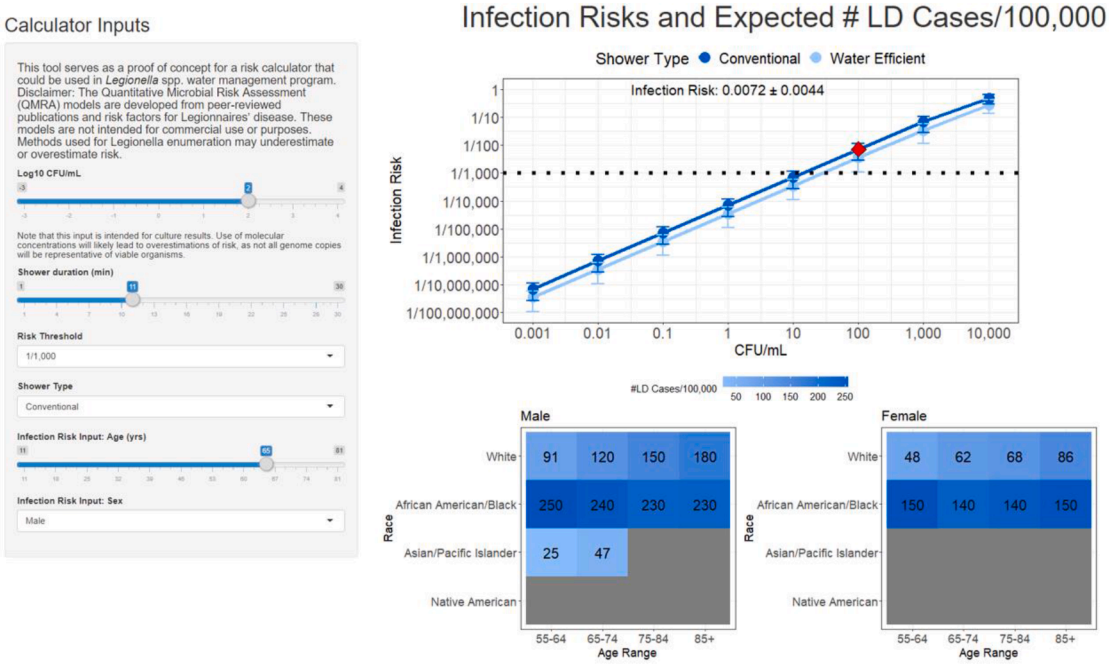

Fig. 4. App output using Model 2 per given calculator inputs indicated in the left menu. It should be noted that an annual risk threshold (1/10,000) is an option for comparing estimated risks from a single showering event. However, the tool is designed to let users define the risk threshold with more or less protective values.

for Legionnaires' disease. These models are not intended for commercial use or purposes. Methods used for *Legionella* enumeration may underestimate or overestimate risk.

4. Discussion

Two mechanistic models were compared in their estimation of *Legionella* exposures and subsequent infection risks during showering events. Model 2, which divides aerosols into smaller bin sizes than Model 1 for describing partitioning and deposition into the lung, produces more conservative risk estimates, where average risks for the conventional and water efficient showers were 4 and 2 times greater than risks estimated using Model 1 for a shower of the same duration and *Legionella* concentration (Fig. 2). Model 2 was utilized in development of the risk calculator tool because it resulted in more conservative risk estimates (Figs. 1 and 2), and was composed of more detailed aerosol

size parameters in development of a risk calculator tool (Table 1). Translation of risk assessment tools for interpreting environmental monitoring data is an important development for increasing the impact of mechanistic models for comparing anticipated health outcomes based on environmental conditions and relating these environmental monitoring data to risk threshold goals.

This study facilitates interpretation of *L. pneumophila* culture monitoring results in infection risk terms. The model developed by Hamilton et al. (2019) in the form of an interactive app will help building owners and operators determine risks of *Legionella* infection and inform decisions on changes that may be required in their water safety management program. While traditional culture methods are more typically used for environmental surveillance, it is recognized that some facilities use molecular methods for verifying the effectiveness of their water safety management program. Molecular methods may be favored due to faster results and greater sensitivity. One limitation of this method, however, is that not all detected genome copies represent live *L. pneumophila*. For example, Ditommaso et al. (2015) found that the mean log difference between the amount of *Legionella* detected with culture and with qPCR was 1.45 (standard deviation 0.24), or qPCR concentrations were approximately 28 times greater than those of culture (Ditommaso et al., 2015). Because these were artificial samples, more research is needed elucidating ratios of *Legionella* detected with molecular methods and culture methods in real-world samples.

Integrating Model 2 with the approach developed by Weir et al. (2020) for relating infection risks to demographically-specific illness risks using *Legionella* case data further extends the potential for a risk calculator tool to inform not only risk targets but also to evaluate risks for the most vulnerable populations (Gleason et al., 2017). Previously, the method developed by Weir et al. (2020) could only be applied to one demographic variable at one time due to available data not including intersections of these demographic groups. Using data provided by the CDC in this study, we were able to explore intersections of race, age, and sex as they relate to LD. However, even with this advancement in available data, a current limitation is a lack of *Legionella* case data, especially for specific racial groups, such as Native American individuals, making illness estimates potentially unreliable. It should be noted that the use of population-level health data is limited in that it does not necessarily capture risk of illness for immunocompromised individuals. Therefore, application of this type of tool in environments with immunocompromised individuals, such as in healthcare, could underestimate risks, and should be done with caution. A tool such as this may be more useful for large facilities that serve less susceptible populations, such as commercial buildings (e.g., hotels or conference centers) or institutional (e.g., university dormitories that contain single showers). Additionally, this tool would be more valuable if we had data to inform LD and Pontiac fever risks.

When developing QMRA or risk-based tools, it is important to consider how estimated risk outputs will be interpreted or influence future behavior or potential policies. For example, while the model we used to develop the tool in this work includes a 95% confidence interval, the interpretation of this interval could vary. If the model accurately captures reality, and the distributions adequately capture variability and uncertainty, the 95% confidence interval could communicate the certainty in the risk estimate. If there is uncertainty about whether the model captures reality or if the distributions capture uncertainty and variability accurately, the 95% confidence interval may only provide information regarding confidence about where the central tendency of the model output truly lies. Additionally, studies of the perception of uncertainty in risk contexts suggests that communicating uncertainty as a numerical range vs. with a visual depiction can influence risk perceptions or perceptions of the quality or accuracy of the risk assessment (Johnson and Slovic, 1995; van der Bles et al., 2019). Considering that the purposes of QMRA or health risk-based tools are generally (1) so that risk models are accessible to non-experts and (2) so risk models can be applied to protect human health with real-world influences on health outcomes, effective communication of risk outputs is paramount. Following the development of a tool, surveys, focus groups, interviews, and other methods are useful for determining the tool's interpretability and risk perceptions associated with its output. Therefore, before the official version of this tool would be released, more data will be needed regarding usability and interpretability of the tool in water management contexts and development of a user manual designed to address common questions or misconceptions.

Future development efforts to progress the utilization of risk assessment tools for *Legionella* to improve water safety plans or management strategies are warranted. Leveraging both *Legionella* spp. sampling results with technical-based information regarding potential risk and illness can improve upon existing water quality guidance values for *Legionella* spp. currently being used by building water quality managers. This combination can help advance concentration limit recommendations or criteria that may be based on judgment alone. More so, research to further single point-of-use QMRA models to estimate facility-level *Legionella* risks would help give building water quality managers better decision-making abilities for general water safety management such as water flushing or business re-openings following pandemic related shutdowns.

Public areas where consumers and tourists frequently visit may also experience increased risks of legionellosis with increasing temperature, relative humidity, and precipitation (De Giglio et al., 2019; Fisman et al., 2005). The favorability of environments for *Legionella* growth is influenced by sunlight intensity, rainfall, and water temperature (Beauté et al., 2016; Walker, 2018). Climate change and the potential for increased legionellosis risks highlight the need for education and awareness of exposure risks for everyday water activities (Walker, 2018). Accessible dissemination of risk-based knowledge is imperative for increasing public awareness and thereby protecting public health. Further development of user-friendly and digestible risk-based tools is an underutilized approach for addressing the increased need for interpretation of environmental monitoring results and understanding how behavior-related parameters (such as shower duration) and demographic variables influence risk. More data to inform these models, especially human behavior data, population-specific risk factors, and temporal and spatial variability of *Legionella* concentrations at points of use, will be useful for increasing the reliability of risk modeling tools. Additionally, while a 1/10,000 threshold is used in this study as a point of comparison for individual risks (as opposed to its use in drinking water as an annual risk threshold), acceptable risk thresholds may vary by context and community. More efforts are needed to characterize communities' acceptable risks so these may drive concentration thresholds and health in built environments.

5. Conclusion

This research adds to the body of knowledge demonstrating the value of QMRA in *Legionella* risk assessment. We recognize the limitations of the model as not all strains of *Legionella* spp. are equally infective and pathogenic. However this QMRA model will help inform building owners and operators of three important principles; (1) understand the value in enumerating *Legionella* in their premise plumbing system, (2) recognize that lower *Legionella* counts reduce infection risk and (3) zero risk is not achievable (a standard assumption in QMRA models), but actions taken as part of a water management program can reduce risk by factors of 10-fold or more, assuming a 10-fold reduction in concentration relates to a 10-fold reduction in risk.

Authors' contributions

All authors contributed to the intellectual development and writing of the manuscript. Additionally, AM Wilson, K Canter, and SE Abney contributed to the code development.

Declaration of Competing Interest

The authors declare no conflict of interest.

Data availability

Code can be accessed at https://github.com/awilson12/legionella_models.

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Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.watres.2022.118812.

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