Evaluating *Legionella* Risk Reduction Strategies in a Large Healthcare Setting: An Integrated Forward and Reverse QMRA Approach

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Abstract

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Legionella pneumophila is a leading cause of drinking water–associated outbreaks in the United States and presents a significant risk in healthcare facilities where complex plumbing systems and immunocompromised patient populations increase susceptibility to infection. Although water management programs and secondary disinfection systems are widely implemented, translating environmental monitoring data into meaningful health risk estimates remains challenging. This study evaluates Legionella risks at the University of Washington Medical Center (UWMC) Montlake Campus using an integrated Quantitative Microbial Risk Assessment (QMRA) framework. Environmental surveillance data collected between 2018 and 2021 from two major hospital buildings—Cascade Tower and Pacific Tower—were analyzed to characterize the occurrence and distribution of Legionella within the facility's water systems. Forward QMRA models were applied to estimate infection risks associated with exposure to aerosolized water from showers and handwashing sinks, incorporating measured Legionella concentrations, exposure scenarios, and established

dose–response relationships. In addition, a reverse QMRA approach was used to assess fixture-specific infection risks and determine the microbial concentrations corresponding to established health risk benchmarks. This analysis enabled comparison of potential infection risks associated with different fixtures and helped identify areas where targeted interventions may be most effective. The integrated QMRA framework provides a practical approach for translating environmental monitoring data into quantitative health risk estimates and supports evidence-based decision-making for Legionella management in complex healthcare water systems.

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CHAPTER ONE: Title, overall background, rationale, and study objectives

Dissertation title

Evaluating *Legionella* Risk Reduction Strategies in a Large Healthcare Setting: An Integrated Forward and Reverse QMRA Approach

Background

Legionella pneumophila was first identified in 1976 during a major pneumonia outbreak that occurred among attendees of the American Legion convention held at the Bellevue-Stratford Hotel in Philadelphia. The outbreak, which resulted in 221 cases and 34 deaths, triggered a joint investigation by the Pennsylvania Department of Health and the U.S. Centers for Disease Control and Prevention (CDC), leading to the identification of *L. pneumophila* as the causative agent of what became known as Legionnaires' disease[1–3]. Retrospective investigations later revealed earlier outbreaks are detected, such as the 1965 nosocomial pneumonia cluster at St. Elizabeths Hospital in Washington, D.C., where 81 patients developed severe pneumonia and 14 died. Archived tissue samples from this outbreak were re-analyzed in 1977, confirming the presence of *Legionella*[4]. These discoveries catalyzed decades of scientific inquiry into the microbiology and ecology of *Legionella* spp., emphasizing its relevance to public health and healthcare infrastructure. Notably, *Legionella* has been implicated in numerous nosocomial outbreaks, highlighting its persistence in complex hospital water systems and the elevated risk it poses to immunocompromised patients[4–6]. Moreover, in recent decades, *Legionella* has emerged as the leading cause of drinking water–associated outbreaks in the United States, accounting for the majority of hospitalizations and deaths linked to waterborne pathogens[7].

Much of the early research focused on understanding how engineered water systems—such as building plumbing, hot water storage tanks, and cooling towers—serve as reservoirs for *Legionella* proliferation. Conditions like warm water temperatures, stagnation, and biofilm formation create ideal niches for the bacteria's survival[2] . Biofilms are particularly significant as they shield *Legionella* from disinfection and enable long-term persistence within plumbing systems. These findings have been central to the development of modern *Legionella* control and prevention strategies in healthcare and public environments[2]

Recognizing these risks, major regulatory and standards organizations—including the CDC, OSHA, ASHRAE, and The Joint Commission—have established guidelines that emphasize proactive *Legionella* risk management[8–11]. These include comprehensive water management plans (WMPs), routine environmental monitoring, and secondary disinfection systems in high-risk settings like hospitals and long-term care facilities.

In response, UWMC's Water Management Committee implemented a dual disinfection strategy: cold water systems are treated using Nalco's electrolytic chlorine system, while hot water systems utilize LiquiTech's copper-silver ionization technology. These systems are supported by a robust infrastructure of monitoring and control, including real-time digital reporting, remote engineering management systems (REMS), and adherence to regulatory standards established by the Washington State Department of Health (DOH).

The integrated deployment of these technologies aligns with the hospital's broader infection control goals, especially considering its high-risk patient population, which includes organ transplant recipients and immunocompromised individuals. The current study leverages this infrastructure to conduct both forward-looking and retrospective quantitative microbial risk assessment (QMRA), offering a model for evaluating the real-world effectiveness of disinfection strategies in large, complex healthcare facilities.

UWMC Montlake Campus is a large academic hospital located within the University of Washington's main campus in Seattle. This study focuses on two primary structures—Cascade Tower and Pacific Tower—which together account for a significant portion of the hospital's patient care infrastructure. Cascade Tower, originally constructed in 1983 with expansions in 1999 and 2017, contains nine floors, including 12 operating rooms, a 33-bed intensive care unit (ICU), and an Organ Transplant Unit, totaling 249 patient beds. Pacific Tower dates back to 1952 (Unit 1) and 1956 (Unit 2), with later additions in the 1980s, and houses a 12-bed ICU, another Organ Transplant Unit, a cafeteria, and central sterilization facilities, totaling 77 patient beds. Both towers receive potable water from Seattle Public Utilities (SPU) through independent metered connections and have a history of *Legionella* colonization, making them ideal candidates for this study's risk assessment and remediation evaluation.

The University of Washington Medical Center (UWMC) Montlake Campus serves as a compelling case study of Legionella risk management in a large, urban, academic healthcare facility. UWMC houses a high proportion of immunocompromised patients, including organ transplant recipients, and has documented Legionella colonization in two of its largest towers. Between 2018 and 2021, Legionella was detected in 32% of Cascade Tower samples and 74% of Pacific Tower samples. A total of 199 samples (10%)were classified as poorly controlled or uncontrolled, all of which exceeded the 1 colony-forming unit (cfu)/mL threshold that typically triggers corrective action, underscoring the need for systemic intervention.

In contrast, Montlake Tower and the Surgery Pavilion, which are supplied by separate water systems, showed negligible levels of colonization. Montlake Tower had only two positive samples, both from a single sink that was isolated and removed in 2018. No further detections occurred after this intervention. The Surgery Pavilion recorded zero detections across all monitoring rounds during the same four-year period. Consequently, these two buildings were excluded from the secondary disinfection program, reinforcing the conclusion that Legionella colonization was isolated to specific infrastructure within the Cascade and Pacific Towers.

A targeted investigation of the Cascade Tower plumbing risers revealed that Legionella colonization was widespread throughout the vertical piping system. Although chlorine and temperature readings at distal outlets appeared normal after flushing, further analysis indicated malfunctioning recirculation systems, which are essential for maintaining thermal and disinfectant consistency across the plumbing network. The findings also suggested potential interface problems between hot and cold water systems, contributing to the creation of temperature zones favorable to Legionella proliferation.

Legionella species are responsible for two distinct illnesses: Legionnaires' disease, a severe form of pneumonia, and Pontiac fever, a milder, flu-like illness. Together, these are classified as legionellosis. Both conditions are transmitted primarily through inhalation of aerosolized water droplets or aspiration of contaminated water. Inhalation occurs when water contaminated with *Legionella* becomes aerosolized through fixtures such as showers, faucets, cooling towers, or decorative fountains. The incubation period for Legionnaires' disease typically ranges from 2 to 10 days, with an average of 5 to 6 days[12]. In immunosuppressed individuals, the incubation period may be longer[12,13]. This latency is important for determining the origin of infection. According to CDC guidelines, a case is classified as facility-acquired if the patient was present in a facility for 10 or more days prior to symptom onset, aligning with the known incubation period of the bacterium[14].

Engineered water systems are widely recognized as the primary reservoirs for *Legionella*, especially in large buildings such as hospitals and long-term care facilities. These systems often contain low-flow or stagnant zones where biofilm accumulates, providing shelter and nutrients for microbial communities, including *L. pneumophila*[15]. Chlorination and other disinfection strategies often fail to penetrate biofilms fully, allowing *Legionella* to persist even in treated water. Temperature plays a vital role in *Legionella* ecology, with growth favored between 25°C and 45°C, and survival possible in a broader range of 20°C to 50°C[3] .

Numerous studies have shown that cooling towers, whirlpool spas, humidifiers, and decorative fountains contribute to aerosol formation and subsequent inhalation risk[5,16,17]. These systems are capable of dispersing aerosols over large distances, even exceeding 1 kilometer in some outbreak scenarios[18]. Personal hygiene activities, such as showering or hand washing, are everyday sources of aerosol exposure, particularly in healthcare settings[13]. Additionally, aspiration of contaminated drinking water is a documented route of transmission in vulnerable hospital populations, while medical equipment, including respiratory therapy devices, can serve as vectors in nosocomial infections[6,19].

At UWMC investigation of the Cascade and Pacific Towers revealed several infrastructure-related risk factors consistent with this broader understanding. These included non-functioning hot water recirculation loops, stagnant plumbing risers, and suspected thermal crossovers between hot and cold water systems—conditions that promote ideal temperature ranges and flow dynamics for *Legionella* persistence. In addition, equipment such as handheld shower hoses, respiratory therapy devices, and ice machines were identified as priority monitoring sites by the facility's Water Management Committee, aligning with known transmission pathways in healthcare-associated outbreaks.

Accurate classification of Legionnaires' disease cases is crucial for infection control. The CDC defines a case as facility-acquired if symptom onset occurs 10 days or more after admission to a healthcare facility[14], this definition is based on the upper limit of the incubation period and assumes continuous exposure. However, patients may be exposed late during their hospital stay and develop symptoms after discharge—such cases still fall within the incubation window and may represent probable or possible healthcare-associated infections, depending on timing and risk assessment[4,13]. This helps distinguish between hospital-acquired and community-acquired infections and supports targeted public health responses.

Several environmental and infrastructural factors have been identified as contributors to *Legionella* outbreaks. Water pressure shocks—caused by plumbing repairs or system flushing—can dislodge biofilms and release bacteria into the water stream[20]. Construction activities near water mains or within facilities may introduce sediments, stagnate flow, or disrupt system integrity, all of which foster *Legionella* colonization[14]. Additionally, newly constructed or renovated facilities are particularly vulnerable due to periods of water stagnation before occupancy, allowing colonization of plumbing networks [14]. These findings underscore the need for proactive water safety planning during construction and maintenance.

Legionnaires' disease presents a growing threat to public health, especially in healthcare settings where vulnerable populations are concentrated. While the general population experiences a case fatality rate of around 10%, this risk increases significantly to approximately 25% among individuals with preexisting health conditions or compromised immune systems [12]. The inherent risks are amplified in institutional environments like hospitals and long-term care facilities, where complex plumbing systems can facilitate *Legionella* proliferation and aerosol exposure.

Despite national surveillance and regulatory efforts, the incidence of legionellosis continues to rise. Between 2009 and 2021, the U.S. Centers for Disease Control and Prevention (CDC) reported 536 outbreaks, resulting in 2,965 illnesses, 1,817 hospitalizations, and 224 deaths across the United States[7,21]. The number of reported cases has increased more than nine-fold since 2000, with seasonal peaks in summer and fall, yet year-round detection is now common[21,22]. However, the true scale of infection is likely underestimated—recent studies suggest that the actual incidence may be 1.8 to 2.7 times higher than reported, due to underdiagnosis and misclassification [7] .

The disease also carries significant economic consequences. Median hospitalization costs range from $26,000 to $38,000 per case, with the total national burden exceeding $434 million annually[22]. Given that *L. pneumophila* serogroup 1 causes the majority of clinical cases and is frequently detected in both hot and cold water systems, traditional control methods such as thermal disinfection and chlorination may not be sufficient[21,22]. These realities emphasize the need for a more proactive, predictive framework—such as Quantitative Microbial Risk Assessment (QMRA)—to assess risk, prioritize interventions, and better protect vulnerable populations in healthcare environments.

Rationale:

In the United States alone, an estimated 8,000 to 18,000 people are hospitalized each year with Legionnaires' disease, with a fatality rate of approximately 10%[21,22] among the general population, and significantly higher in individuals with underlying conditions such as chronic lung disease or immunosuppression. For healthcare-associated infections, the mortality rate is even higher—reaching nearly 25%[13] This increased vulnerability among hospital populations highlights a pressing need for more rigorous prevention strategies.

Despite the introduction of various national and institutional policies, including guidelines from the CDC, ASHRAE, and CMS, the incidence of legionellosis continues to rise [3,21,22]. This persistent upward trend suggests that current policies, while important, may be insufficiently implemented or adapted to the complexity of real-world water systems in large facilities like hospitals.

From 2000 to 2019, surveillance data revealed a steep rise in the crude national incidence of Legionnaires' disease, increasing from 0.42 to 2.71 cases per 100,000 people, with the rate peaking at 3.04 in 2018[21]. This rise has occurred despite increased awareness and improved diagnostic capabilities, indicating that underlying environmental and infrastructural factors remain unchecked. These statistics not only reflect a growing public health concern, but also emphasize the critical need for more proactive, data-driven, and site-specific risk assessment tools—especially in high-risk settings like healthcare facilities.

Recognizing this vulnerability, regulatory bodies such as the American Society of Heating, Refrigerating and Air-Conditioning Engineers (ASHRAE) and the Centers for Medicare and Medicaid Services (CMS) have mandated the implementation of comprehensive water management programs, notably through ASHRAE Standard 188-2018 and federal CMS guidelines[9,23,24]. These frameworks are a vital step toward institutionalizing *Legionella* risk management. However, in practice, many healthcare facilities continue to face challenges in operationalizing these policies. Implementation gaps often arise due to limited on-site expertise, insufficient risk assessment tools, or resource constraints that hinder long-term monitoring and evaluation.

One of the most persistent challenges in this space is the lack of clear, universally accepted thresholds that translate microbial concentrations into quantifiable health risks.

While the literature offers various suggested limits—for example, *L. pneumophila* concentrations between 10 and 10,000 CFU/mL in general use water systems, and even lower thresholds (e.g., 50 CFU/L) for high-risk patient areas like intensive care units [25,26], these numbers alone often lack context. Without a formalized, quantitative framework for interpreting such concentrations in relation to exposure frequency, aerosolization potential, and host susceptibility, facility managers are left to make critical public health decisions without the benefit of predictive modeling.

This gap between policy guidance and practical application has highlighted the urgent need for approaches like Quantitative Microbial Risk Assessment (QMRA), which can bridge the divide between environmental data and patient health outcomes. By translating microbial measurements into probabilistic infection risks, QMRA offers a scientifically grounded way to prioritize interventions, allocate resources, and ultimately reduce disease burden in healthcare settings.

QMRA as a Public Health Decision-Making Tool

QMRA provides a systematic approach to quantifying the health risks associated with exposure to microbial pathogens like *L. pneumophila*[27–29] . The QMRA process includes four steps: hazard identification, exposure assessment, dose-response modeling, and risk characterization[28,30]. This framework enables stakeholders to move beyond simple presence/absence data and develop evidence-based thresholds for action.

QMRA has been successfully applied in assessing microbial risks in drinking water, food systems, recreational water, and healthcare plumbing[31–33]. It allows integration of environmental concentration data, exposure pathways (such as inhalation or ingestion), and pathogen infectivity to estimate infection probability. For *Legionella*, dose-response models exist for serogroup 1 strains, enabling application in real-world settings[29,31,34]. Regulatory benchmarks—such as the EPA and WHO annual infection threshold of 1×10^{-4} infections per person—serve as comparison points for determining whether an exposure scenario poses unacceptable risk[12,34].

Despite its utility, no standardized protocol for *Legionella*-specific QMRA exists. Modeling assumptions, data availability, and system variability lead to wide variation in outcomes[32,34]. However, the use of surveillance data—such as that collected by hospitals for regulatory compliance—offers a valuable input for QMRA and helps contextualize pathogen concentrations in terms of actual health risk.

Study Purpose and Objectives

Given the increasing incidence of Legionnaires' disease, the complexity of healthcare plumbing systems, and the absence of standardized risk thresholds, this study aims to assess the health risks of *L. pneumophila* exposure in a healthcare setting using both forward and reverse QMRA approaches. Specifically, this study will:

1. Describe *Legionella* surveillance findings from the University of Washington Medical Center (UWMC) from 2018 to 2021;
2. Estimate infection risks associated with showers and hand sinks using the forward QMRA model;

3. Assessing Fixture-Specific Legionella Infection Risk at UWMC Using a Reverse QMRA Approach

By leveraging four years of environmental monitoring data, this research offers a novel and practical method for quantifying infection risks and informing evidence-based water safety interventions in complex healthcare environments.

CHAPTER TWO: Aim 1 - Legionella Surveillance at the University of Washington Medical Center: Trends and Findings from Routine Monitoring

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Abstract

Background: Legionella species remain a critical threat in healthcare environments due to their potential to cause severe pneumonia, especially in vulnerable patient populations. The University of Washington Medical Center (UWMC) has experienced recurrent detections of Legionella in clinical and environmental settings, and confirmed cases of Legionnaires' disease. This study describes multi-year environmental surveillance data for Legionella at UWMC, highlighting trends, risks, and control measures from 2018 to 2021

Methods: 1,895 water samples were collected across multiple UWMC buildings and analyzed using culture-based methods in accordance with CDC and ISO 11731 standards. We used 1456 of these water samples, taken from Cascade, Montlake, and Pacific, for this analysis. We classified them using the CDC's Routine Testing Interpretation Tool into three categories: well-controlled (0–0.9 CFU/mL), poorly controlled (1.0–9.9 CFU/mL), or uncontrolled (≥10 CFU/mL). Statistical analyses included log-transformation of Legionella concentrations, one-way ANOVA for annual comparisons, and distribution fitting using lognormal, Weibull, and gamma models.

Results: Overall, 86.3% (1257/1456) of samples were well-controlled, 6.0% (87/1456) poorly controlled, and 7.7% (112/1456) uncontrolled. The Pacific Wing accounted for 97% (193/199) of all poorly controlled and uncontrolled samples, while the Cascade and Montlake Wings maintained >99% control. Hot water systems showed the highest frequency of uncontrolled samples (9.3%).

Conclusion: These findings support continued vigilance and adaptive risk mitigation strategies in complex healthcare plumbing infrastructures.

Background

Legionnaires' disease, a severe form of pneumonia caused by *Legionella* species, remains a persistent global public health challenge[35]. *Legionella pneumophila*, the most clinically significant species, thrives in warm, stagnant water systems and can colonize complex plumbing networks, posing a particular risk in hospitals where immunocompromised patients are concentrated[36]. Despite advances in water management, healthcare-associated Legionnaires' disease (HCA-LD) continues to occur, with the Centers for Disease Control and Prevention (CDC) estimating that nearly 20% of reported cases in the United States are healthcare-associated[37–39]. This persistent burden highlights the need for rigorous, site-specific surveillance systems. In large academic medical centers, the challenge is compounded by the size and age of infrastructure, creating ideal conditions for bacterial proliferation and dissemination through aerosols generated from showers, sinks, and cooling systems[12].

The consequences of *Legionella* contamination pose significant risks in high-acuity medical centers, where vulnerable patient populations are routinely treated. Outbreaks in healthcare settings can disrupt clinical operations, prompt unit closures, and require extensive remediation efforts costing millions of dollars annually[38]. These operational consequences directly affect the continuity of care and strain already limited resources. For example, In the United States, an estimated 85–90% of the total economic burden of Legionnaires' disease is attributable to hospitalization and treatment costs, closely reflecting the UK study where 86% of outbreak expenses were for clinical care[40].. In addition to direct healthcare expenditures, reputational damage and regulatory scrutiny from public health authorities place significant administrative and financial burdens on health institutions. Thus, the detection and prevention of *Legionella* within healthcare environments represent both a medical and operational imperative[41].

Several environmental and operational factors contribute to the persistent colonization by *Legionella* in healthcare water systems. Key conditions include sub-optimal water temperatures that fall outside disinfection-effective ranges, stagnant or intermittently used plumbing lines, and biofilm formation, which collectively create a favorable ecological niche for *Legionella* survival and regrowth[42,43]. These risks are exacerbated by the presence of aging infrastructure and aerosol-generating fixture such as showers, faucets, and ice machines. In hospital environments like the UWMC, the complexity and scale of the water distribution network—including extended piping runs, large-volume storage tanks, and varied-use water systems—amplify these environmental vulnerabilities. Importantly, the clinical setting itself introduces compounding patient-related risk factors. Individuals with advanced age, chronic pulmonary disease, compromised immune systems, or those requiring ventilator support are significantly more susceptible to infection, even at relatively low levels of exposure[44].

In response to the risks associated with *Legionella* colonization in healthcare water systems, numerous interventions have been implemented across hospital settings. These strategies commonly include comprehensive water-management plans, regular sampling of both water sources and fixtures, chemical disinfection methods such as hyper-chlorination, mechanical system flushing, installation of point-of-use filters, and physical replacement of contaminated fixtures.

Over the past decade, UWMC has documented multiple *Legionella*-related events- including environmental detections, suspected or confirmed clinical cases, and findings requiring public health investigation or remediation—prompting repeated epidemiologic investigations and system-level interventions[45]. A major outbreak occurred in August, September 2016, resulted in five confirmed cases of Legionnaires' disease, including two fatalities—linked to the Cascade Tower[46]. Environmental sampling identified *Legionella* in ice machines and sink fixtures, confirming including localized amplification points within the potable water system[47]. Additional clinical cases in 2017 and 2018, although fewer in number, reinforced the persistence of colonization and suggested incomplete system clearance.

In response, UWMC implemented a series of aggressive mitigation measures, including hyper-chlorination, system flushing, point-of-use filtration, and intensified environmental surveillance. These events underscore the difficulty of of eradicating *Legionella* from large, complex hospital water systems and reinforces the critical need for sustained, data-driven environmental monitoring..

The present study is motivated by recurrent Legionella detections in both clinical and environmental settings at UWMC, some associated with confirmed disease[45]. Despite multiple interventions, little is known about longitudinal trends in environmental surveillance data and their alignment with infection risk and control measures. Using five years (2018–2022) of surveillance data from the Cascade Tower and affiliated facilities, this study aims to characterize temporal trends, assess variation by fixture type and location, and contextualize findings within implemented control strategies to inform proactive water safety management and prevention of healthcare-associated Legionella transmission.

Methods

Water Sampling and *Legionella* Analysis

Over the 4- year period, periodic monitoring was carried out from various water sources in the hospital facilities, with a total of 1,895 samples from 2018 to 2022. Microbial detection of *L Legionella* was performed according to the CDC method or ISO 11731 from the International Organization of Standardization[48]. Briefly, 1 L samples of bulk water from distal outlets were collected in sterile bottles with sodium thiosulphate (0.01%, *w/v*) to neutralize residual chlorine in the drinking water supplies. Sample collection and transportation were conducted by Pacific Industrial Hygiene LLC (www.pacificih.com), an environmental health consulting firm. Samples were delivered to Sound Microbiology Laboratory, a CDC ELITE-certified laboratory located on Bainbridge Island, Washington.

All samples were conveyed to the laboratory using insulated coolers to safeguard against substantial temperature fluctuations. Samples expected to arrive at the laboratory beyond a 72-hour were placed in refrigeration before transportation. Upon arrival, sample results were reviewed and accessed by the UWMC Director of Operations and Maintenance for ongoing risk assessment and mitigation planning.

Definitions: To evaluate the control status of potable water systems, we used the **CDC Routine Testing Interpretation Tool for Potable Water**, which classifies *Legionella* culture results into standardized performance categories (Table 1). This tool provides clear thresholds, expressed in colony-forming units per milliliter (CFU/mL), to indicate whether a system is well-controlled, poorly controlled, or uncontrolled. These categories serve as performance indicators of system management and are widely applied to interpret routine *Legionella* monitoring results in non-outbreak settings.

Table 1. CDC Potable Water Thresholds for Routine *Legionella* Testing Interpretation

Category	**Definition (CFU/mL)**	**Interpretation**
Well-Controlled	0–0.9 CFU/mL	Acceptable; indicates effective system control
Poorly Controlled	1.0–9.9 CFU/mL	Suboptimal; suggests need for further review or mitigation
Uncontrolled	≥10 CFU/mL	Unacceptable; corrective action generally recommended

Note: These thresholds apply to culture-based testing in potable water systems and are used as performance indicators, not direct measures of health risk (CDC, 2021).

Analysis techniques

Legionella concentration data were log-transformed to normalize the distribution, and descriptive statistics (mean ± standard deviation) were computed. Annual variations in *Legionella* contamination levels were assessed using a one-way analysis of variance (ANOVA), with statistical significance set at $p < 0.05$. When significant overall differences were detected, post-hoc pairwise comparisons, using Tukey's HSD test, were performed to identify specific years showing significant variation.

To further explore temporal and spatial trends, *Legionella* prevalence was summarized across quarterly intervals and by sample source type (e.g., faucets and showerheads). Year-to-year fluctuations in *L. pneumophila* concentrations among positive samples were visualized using boxplots, illustrating the distribution of concentration values for each surveillance year (2018–2021), with color coding distinguishing among serogroups.

We fitted lognormal, Weibull, and gamma distributions to assess best model fit. To enable log-scale visualization and modeling, nondetects were imputed as 0.025 CFU/mL—representing half of the minimum observed non-zero concentration (0.05 CFU/mL). This imputation was used solely for statistical and graphical purposes and does not reflect actual measured values. This imputation method may also contribute to slight discrepancies between raw category counts and visual trends in $\log_{10}$-scale plots.

The lognormal distribution describes data whose logarithm follows a normal distribution, often appropriate for environmental concentration data. The Weibull distribution is a continuous probability model frequently used for reliability and life-data analysis, allowing flexible representation of skewness. The gamma distribution represents a family of continuous, non-negative, right-skewed distributions suitable for variables with a lower bound of zero. These distributions provide the probabilistic framework for characterizing uncertainty and variability in *Legionella* concentration data and are widely applied in QMRA applications.

Results

Distribution of Legionella Concentrations

A total of 1,895 potable water samples were collected and analyzed from 2018–2021. *Legionella* concentrations were highly right-skewed (Table 2), with most values clustering near zero and a small proportion showing elevated levels. The geometric mean concentration was 0.11 CFU/mL (GSD = 7.88). Percentile analysis indicated that 75% of samples contained ≤ 0.05 CFU/mL, whereas the upper 5% reached concentrations up to 17.30 CFU/mL, highlighting a strong floor effect (large number of values accumulate near the lower limit of detection, limiting the ability to distinguish meaningful differences at the low end).

Table 1: Percentile Distribution of Legionella Concentrations (CFU/mL)

Percentile*	**Legionella Concentration (CFU/mL) Value**
25%	0.05
50% (Median)	0.05
75%	0.05
95%	17.30

*Percentile values describe the distribution of Legionella concentrations in water samples, indicating overall central tendency and variability. Values are reported in CFU/mL.

System Control Status

Based on CDC potable water performance categories, 86.3% of samples were *well-controlled* (0–0.9 CFU/mL), 6.0% were *poorly controlled* (1.0–9.9 CFU/mL), and 7.7% were *uncontrolled* (≥ 10 CFU/mL). Overall, these results indicate effective system control, with a small minority of samples exceeding actionable thresholds. The primary analysis focused on *L. pneumophila*, particularly serogroup 1 where data were available, as this species is most clinically relevant and most commonly associated with disease. Other *Legionella* species were detected infrequently, and available data on non-pneumophila species were limited by high rates of missingness and non-detects.

Temporal patterns showed stable control across years, with well-controlled proportions ranging from 78.9% (2020) to 91.4% (2018). Uncontrolled samples peaked in 2020 (n = 37) and 2019 (n = 34). By temperature, hot-water systems accounted for most uncontrolled samples (74/799), followed by cold (24/718) and warm (14/133) systems.

Wing-level stratification revealed that the Cascade Wing demonstrated exceptional control, with 99.4% (n = 858) of 863 samples classified as *well-controlled* and only one *uncontrolled* sample (0.1%). In contrast, the Pacific Wing exhibited persistently higher contamination levels, accounting for over 99% of all poorly controlled and uncontrolled samples. These differences were statistically significant (p<0.001) (Table 3).

Table 3: Distribution of Legionella Control Levels by Year, Water Temperature, and Wing

Variables		Well-Controlled*	Poorly Controlled*	Uncontrolled*
	Total	**1221**	**87**	**112**
Year	2018	524	26	23
	2019	272	26	34
	2020	195	15	37
	2021	266	20	18
Temperature	Cold	522	42	24
	Hot	490	37	74
	Warm	88	8	14
Wing	Cascade	858	4	1
	Montlake	234	1	0
	Pacific	165	82	111

**Legionella concentrations categorized as Well-Controlled (0–0.9 CFU/mL), Poorly Controlled (1.0–9.9 CFU/mL), and Uncontrolled (≥10 CFU/mL) according to CDC guidance. Counts represent the number of water samples in each category.*

The Legionella concentrations had a right-skewed distribution, with high outliers predominantly associated with Pacific Wing samples (Figure 1).

Wing-Level Patterns

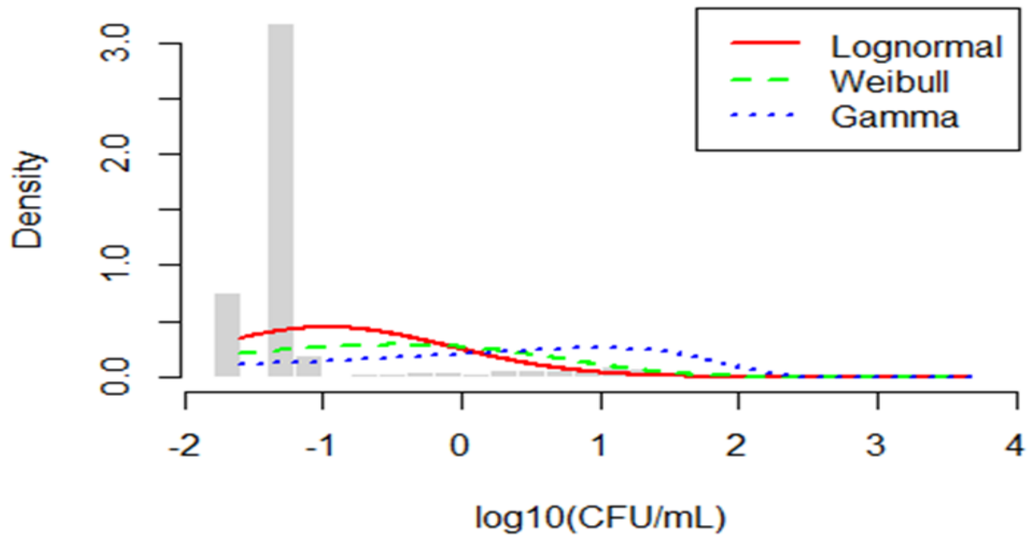

Figure 1: Distribution of log10-Transformed Legionella Concentrations with Lognormal, Weibull, and Gamma Fit Overlays

Distribution of Legionella Concentrations.

To formally evaluate distributional fit, lognormal, Weibull, and Gamma models were compared using Akaike Information Criterion (AIC) and Bayesian Information Criterion (BIC). The lognormal distribution had substantially lower AIC (–277.1) and BIC (–266.6) values compared to Weibull and Gamma, indicating superior model performance (Table 4).

Table 4. Model Fit Statistics (AIC and BIC) for Parametric Distributions Applied to Legionella Concentration Data

Distribution	Akaike Information Criterion (AIC)	Bayesian Information Criterion (BIC)
Lognormal	-277.1	–266.6

Weibull	729.76	740.3
Gamma	2046.6	2057.2

Note: Interpretation of the model summary: Lower AIC and BIC values indicate better model fit.

Temporal and Wing-Specific Trends

Quarterly trend analysis (Figure 2) revealed substantial spatial and temporal heterogeneity across hospital wings. Mean $\log_{10}$ CFU/mL levels and the percentage of uncontrolled samples (≥10 CFU/mL) were tracked quarterly from Q1 2018 to Q4 2021 across three hospital wings: Cascade, Montlake, and Pacific.

The Pacific wing demonstrated a notable and sustained increase in both contamination concentration and percent-positive samples.

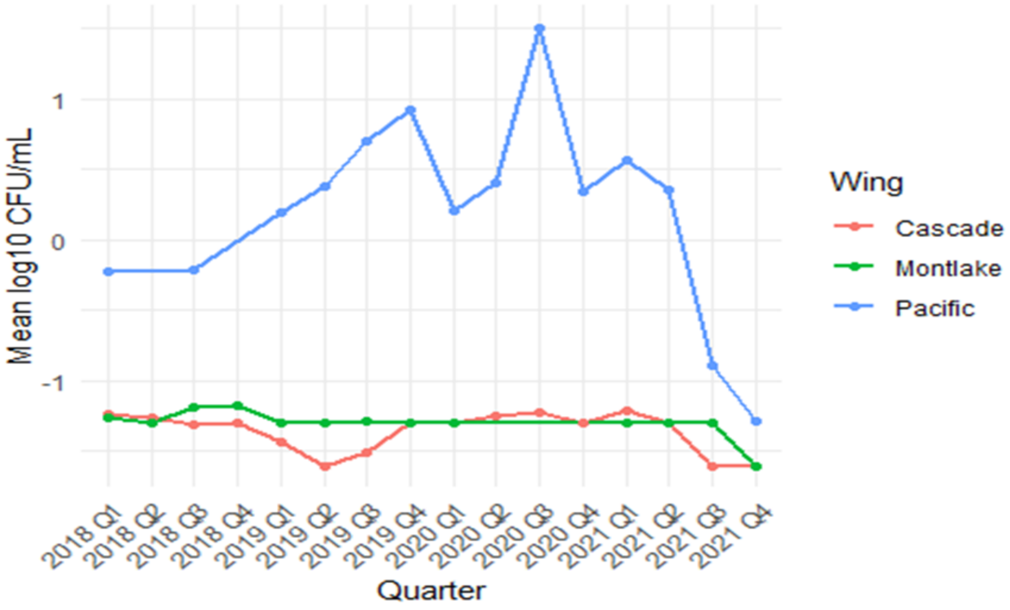

Figure 2: Quarterly Trends in log10 Legionella Concentration by Hospital Wing (2018-2021)

From Q2 2019 through Q1 2021, the percentage of uncontrolled samples exceeded the 30% threshold, with a peak around Q3 2020, indicating a prolonged period of inadequate microbial control. During this same interval, Pacific's mean $\log_{10}$ CFU/mL levels rose steadily, reaching a maximum above 1.5, before sharply declining after Q2 2021. By Q4 2021, both the concentration and percent-positive values had returned to levels consistent with controlled conditions.

In contrast, the Cascade and Montlake wings remained consistently well-controlled throughout the monitoring period. Mean $\log_{10}$ CFU/mL values for both wings remained below -1.0, with minimal variation.

A one-way ANOVA of $\log_{10}$-transformed concentrations indicated a significant overall effect of year ($F(3, 1891) = 98.21$, $p < 0.001$), though Tukey's HSD post-hoc comparisons revealed no significant pairwise differences.

The percentage of uncontrolled samples in these wings remained near zero across all quarters, never approaching the 30% threshold.

In addition to concentration trends, quarterly percent-positive rates and the percentage of "uncontrolled" samples (≥10 CFU/mL) were evaluated by wing, with a horizontal reference line at 30% to contextualize persistent exceedances. Only the Pacific Wing crossed the 30% threshold, doing so for multiple consecutive quarters from Q2 2019 through Q1 2021, peaking around Q3 2020. This indicates a sustained period of elevated risk and loss of control. In contrast, Cascade and Montlake remained well below the 30% threshold, with uncontrolled sample rates near zero across all quarters.

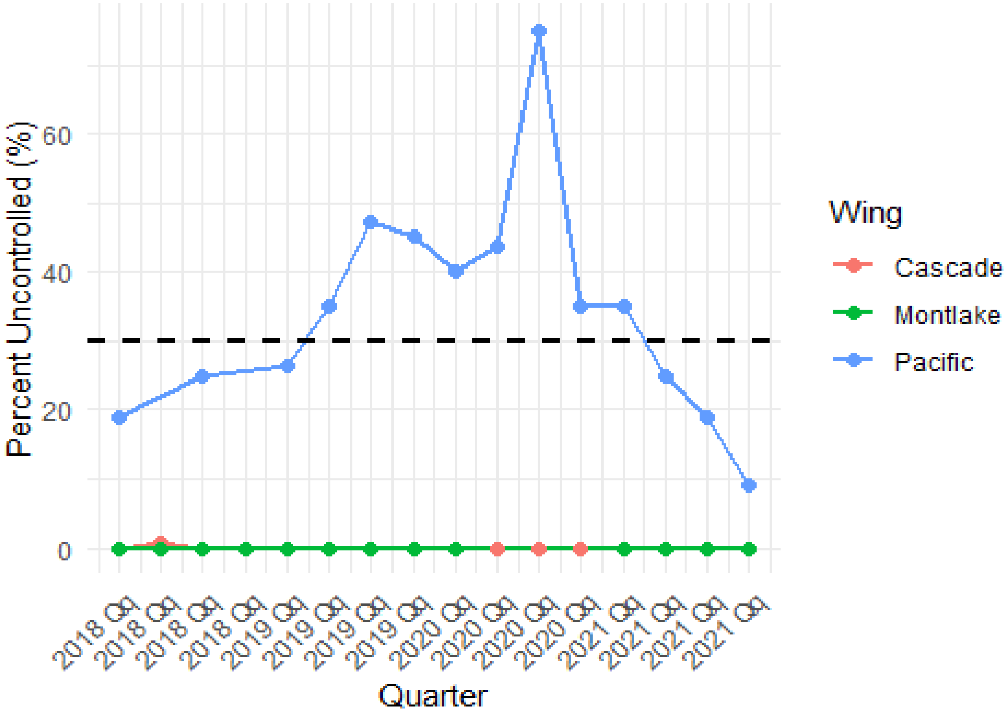

Figure 3: Percent Uncontrolled Samples Over Time by Wing (≥10 CFU/mL)

Discussion

Analysis of 1456 water samples collected between 2018 and 2021 demonstrates that Legionella concentrations at UWMC were predominantly low, with the vast majority of samples meeting CDC criteria for well-controlled systems. The distribution of concentrations was highly right-skewed, with most values near or below the limit of detection and infrequent but substantial exceedances. While overall system control was stable over time, a small proportion of samples exceeded actionable thresholds, driven almost entirely by hot-water systems within the Pacific Wing. In contrast, the Cascade and Montlake Wings maintained near-complete control throughout the study period, reflecting effective long-term mitigation. Distributional modeling further indicated that *Legionella* concentrations were best described by a lognormal distribution, consistent with environmental amplification processes that produce rare high-concentration events. Together, these findings highlight substantial spatial heterogeneity within an otherwise well-managed system and underscore the importance of sustained, wing-specific surveillance to identify localized vulnerabilities and guide targeted control strategies.

About 86% water samples were classified as well-controlled according to CDC thresholds, with only a small fraction exceeding actionable concentrations. These findings reflect a high standard of system performance and underscore the effectiveness of UWMC's comprehensive water safety program—characterized by regular monitoring, temperature regulation, flushing, and rapid response protocols. The proportion of well-controlled samples observed here is notably higher than in experimental or non-healthcare building studies, where *Legionella* detection rates frequently exceed 10–20% under suboptimal temperature or stagnation conditions[49]. This demonstrates that sustained water management efforts can achieve high levels of microbial control in complex healthcare environments.

The stability of system performance over time further indicates resilience in management practices, though transient increases in uncontrolled samples during 2019–2020 suggest that operational variability, environmental conditions, or maintenance disruptions may temporarily influence *Legionella* proliferation. Similar trends have been reported in other healthcare and commercial facilities, where seasonal temperature fluctuations, reduced occupancy, and interruptions in flushing routines, particularly during the COVID-19 pandemic, have been shown to contribute to microbial regrowth and increased *Legionella* detections[50] . These findings highlight the importance of maintaining consistent water use and temperature control, even during low-demand or partial occupancy periods, to prevent *Legionella* rebound.

Our findings clearly identify hot-water systems as the dominant source of elevated Legionella risk within the system.. This pattern is consistent with established *Legionella* ecology, as bacterial replication peaks within the 25–45 °C range[51]. Even in well-managed systems, hot-water loops remain critical control points requiring strict oversight of temperature maintenance, thermal disinfection, and fixture-level flushing. These findings emphasize that maintaining temperatures outside the optimal growth range—while ensuring scald prevention—should remain central to risk mitigation strategies.

Spatial variation across hospital wings revealed meaningful insights for targeted control. While the Cascade Wing achieved near-complete control, the Pacific Wing accounted for nearly all poorly controlled and uncontrolled samples, indicating localized system vulnerabilities. Differences of this magnitude within the same institution likely reflect structural or operational variations such as water loop design, stagnation zones, and differential maintenance histories. Cascade's consistently low levels of *Legionella* suggest that well-engineered hydraulic configurations, sustained monitoring, and timely interventions can maintain long-term control, even in high-risk zones.

Although the findings demonstrate that continuous environmental surveillance—coupled with responsive mitigation—can sustain low bacterial concentrations over multiple years, they also underscore that localized risk mapping within buildings is critical. High-performing zones such as Cascade can serve as benchmarks for identifying design or management strategies applicable to other areas as their sustained control likely reflects underlying differences in system hydraulics, stagnation potential, thermal regime stability, and the effectiveness and timeliness of operational monitoring and maintenance practices. Finally, they affirm that proactive maintenance and real-time data interpretation are more effective than reactive outbreak response models.

In summary, this study highlights the value of long-term surveillance in guiding evidence-based *Legionella* control strategies. UWMC's experience suggests that comprehensive water management programs, emphasizing consistent monitoring, temperature regulation, and system-specific intervention, can substantially reduce *Legionella* risk in healthcare facilities. Continued vigilance is warranted—particularly in hot-water loops and less-controlled zones—to sustain safe water systems and protect vulnerable patient populations.

Limitations

Several limitations should be acknowledged. First, the absence of pre-intervention baseline data restricts the ability to quantify direct improvements or measure the effectiveness of specific control interventions. As such, findings primarily characterize current control performance rather than changes over time. Second, reliance on culture-based methods may underestimate total *Legionella* burden, as these methods do not detect viable but non-culturable (VBNC) cells or account for differences in strain virulence[52]. Third, although the dataset spans multiple years, it may not fully capture short-term operational fluctuations—such as maintenance events, plumbing disruptions, or occupancy-related stagnation—that can transiently affect bacterial concentrations. Finally, the study was conducted within a single healthcare facility, which may limit generalizability to other institutions differing in water system design, scale, or local environmental conditions. Despite these limitations, the robust sampling framework and standardized analysis provide valuable insight into sustained *Legionella* control in a real-world healthcare context.

Strengths

Even with these limitations, our study has multiple strengths and our results are crucial for clinical care settings. This study represents one of the most comprehensive post-intervention Legionella surveillance assessments conducted in a healthcare setting, encompassing nearly 1,900 water samples collected over a four-year period. A major strength lies in the application of CDC-defined control thresholds, which allowed for standardized interpretation of results and meaningful comparison across years, water temperatures, and building zones. Stratification by facility wing and water temperature provided a granular understanding of localized system performance, highlighting spatial variability in Legionella risk within a complex hospital infrastructure. The long-term consistency in sampling frequency, analytical methods, and documentation reflects a well-established and sustained water management program, enhancing both data reliability and interpretability. Collectively, these features strengthen the study's capacity to evaluate longitudinal patterns in microbial control and inform practical improvements to healthcare water safety programs.

Conclusion

This study demonstrates that sustained and structured water management practices can effectively maintain *Legionella* control within complex healthcare environments. The multi-year surveillance at the UWMC highlights how continuous monitoring, temperature regulation, and systematic maintenance can keep bacterial levels well within acceptable limits. Differences observed across facility wings and water temperatures emphasize the importance of localized assessment and targeted interventions, particularly in hot-water systems where conditions favor bacterial growth. These findings reinforce the essential role of routine microbial surveillance as a cornerstone of *Legionella* risk management in healthcare settings. Long-term, data-driven approaches not only verify system performance but also enable timely identification of vulnerabilities before they result in patient exposure. The UWMC experience illustrates that proactive, rather than reactive, water management strategies are both achievable and sustainable, offering a model for similar institutions aiming to strengthen water safety and infection prevention efforts.

CHAPTER 3: Aim 2 - Estimating Legionellosis Risk in a Healthcare Facility Using Forward Quantitative Microbial Risk Assessment (QMRA): A Four-Year Surveillance Analysis (2018–2021)

Abstract

Legionella pneumophila is a critical opportunistic pathogen in healthcare environments, where immunocompromised individuals are at heightened risk of exposure to contaminated aerosols. Despite the recognized role of water fixtures in transmission, comparative risk profiles of different sources remain underexplored. This study aimed to quantify inhalation-related infection risks associated with *L. pneumophila* exposure from showerheads and hand sinks within a tertiary healthcare facility. We analyzed *Legionella pneumophila* surveillance data collected from the University of Washington Medical Center (2018–2021) using a forward Quantitative Microbial Risk Assessment (QMRA) framework. The model incorporated fixture-specific exposure parameters, including aerosol generation efficiency, water-to-air partitioning coefficients, exposure durations, and inhalation rates. Monte Carlo simulations (100,000 iterations) were conducted to estimate inhaled doses per exposure event for faucets and showers. Infection probabilities were then derived using an exponential dose–response model and extrapolated to annual infection risks based on typical fixture-use frequencies. R version 4.5.1 was used for analysis. The results demonstrate significantly higher infection risks from showerhead exposure compared to hand sinks, with annual risk values frequently exceeding recommended health-protective thresholds. These risks remained relatively stable across the four-year period, highlighting persistent exposure concerns despite ongoing water management efforts. Fixture-specific differences in aerosolization and exposure parameters critically influence *Legionella* infection risk in healthcare settings. This study underscores the need for targeted surveillance and control strategies that account for fixture type and temporal variability to better protect vulnerable populations.

Keywords: *Legionella pneumophila*, healthcare-acquired infections, QMRA, harrison, showerheads, hand sinks, exposure risk, infection modeling, risk assessment

Background

Legionellosis, a severe respiratory infection caused primarily by *Legionella pneumophila*, poses an ongoing public health challenge in healthcare environments. Vulnerable populations including immuno-compromised individuals, elderly patients, and those with chronic illness are especially susceptible. Transmission occurs through inhalation of contaminated aerosols containing *L. pneumophila,* which thrives in warm, stagnant water and colonizes biofilms within plumbing systems.

Healthcare facilities are especially at risk due to the prevalence of complex water systems and aerosol-generating fixtures such as showerheads and hand sinks. These fixtures differ in design, frequency of use, and aerosol dynamics, making fixture-specific risk assessment a critical component of infection prevention and control[25,53].

The University of Washington Medical Center (UWMC) presents a representative example of these challenges. The hospital comprises several interconnected buildings with infrastructure dating back to the 1950s, and includes multiple retrofitted plumbing systems[54]. Its domestic hot water network incorporates mixed-use risers, recirculation loops, storage tanks, and variable pressure zones, all of which contribute to fluctuating water age, stagnation potential, and inconsistent thermal performance. Although UWMC has implemented a comprehensive water management program involving thermal regulation, chemical disinfection, and selective fixture replacement, residual colonization risks persist due to the complexity and age of the system.

The facility maintains a large number of patient-use water fixtures, many of which are located near units housing immunosuppressed patients, further increasing exposure concern. Variations in fixture use and water flow create localized stagnation and biofilm growth, heightening the potential for aerosolized exposure. Despite preventive flushing and routine maintenance, these spatial and operational differences can lead to uneven Legionella control across hospital wings.

Many hospitals have adopted conventional water sampling – systematic monitoring and engineering controls – to reduce *Legionella* colonization, translating those efforts into actionable infection risk reduction remains a challenge. Most assessments focus on system-level conditions rather than quantifying risk at the fixture level, even though exposure dynamics vary substantially across sources. Without approaches that integrate microbial concentration data with real-world exposure scenarios, infection risk cannot be adequately quantified or mitigated [55] .

Quantitative Microbial Risk Assessment (QMRA) provides a structured, probabilistic framework for estimating infection risks from environmental pathogens, including *Legionella*. QMRA consists of four core components: hazard identification, exposure assessment, dose-response modeling, and risk characterization [55]. Previous studies have applied this approach successfully in residential, recreational, and healthcare settings, demonstrating that infection risk is influenced by system design, bacterial concentrations, aerosol characteristics, and user activity[56,57].

Among the species of *Legionella*, *L. pneumophila* serogroup 1, particularly the Philadelphia-1 strain, is most commonly implicated in human outbreaks. This strain is widely selected for QMRA modeling due to its documented epidemiological relevance and the availability of a well-characterized exponential dose–response curve [58,59]. While host susceptibility varies greatly, particularly in clinical settings, risk assessments often focus on infection probabilities rather than illness severity to ensure consistency and comparability across population groups.

This study hypothesizes that infection risks from *L. pneumophila* differ between hand sinks and showerheads due to variations in exposure duration, aerosol behavior, and water-to-air partitioning, which influence inhalation dose and infection probability. Using a forward QMRA framework and 2018–2021 surveillance data from the University of Washington Medical Center, the study quantifies fixture-specific infection risks, evaluates temporal trends, and informs targeted strategies for *Legionella* mitigation in healthcare water systems.

Methods

Data Source and Overview:

This analysis utilized *Legionella pneumophila* surveillance data collected from the University of Washington Medical Center (UWMC) between 2018 and 2021. The UWMC water management program routinely, quarterly, monitors *L. pneumophila* concentrations across multiple patient-care units, encompassing a range of fixtures including hand sinks and showerheads. Surveillance data included culture-based measurements of *L. pneumophila* (colony-forming units per liter, CFU/L), fixture type, sampling location, and collection date.

2.2 Quantitative Microbial Risk Assessment (QMRA) Framework:

A forward Quantitative Microbial Risk Assessment (QMRA) framework was applied to estimate infection probabilities associated with exposure to *L. pneumophila* aerosols. The QMRA followed the standard four-step structure outlined by Haas et al. (2014) (**Figure 1**, Modified from Kermani [18]):

2.2.1. Hazard Identification (legionellosis):

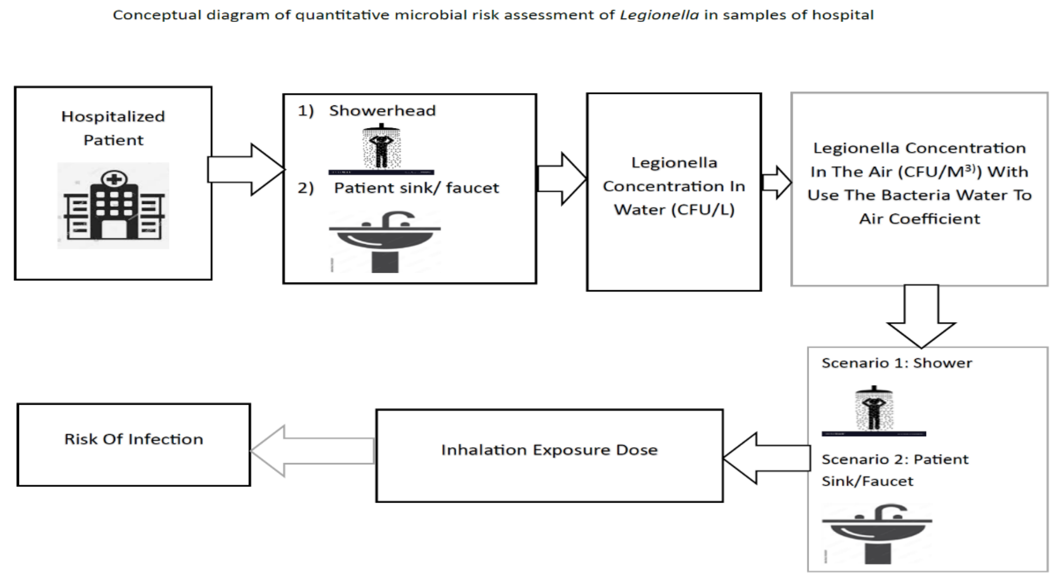

Figure 1: Conceptual diagram of quantitative microbial risk assessment of legionella in samples of hospital adapted from Modified from Kermani (Kermani et al., 2022)

Legionella pneumophila is an opportunistic waterborne pathogen that colonizes engineered water systems and can cause severe respiratory illness following inhalation of contaminated aerosols. Once inhaled, the organism reaches the lower respiratory tract, where it infects alveolar macrophages, leading to a range of disease outcomes—from mild, flu-like Pontiac fever to severe pneumonia (Legionnaires' disease). The case fatality rate of healthcare-associated Legionnaires' disease can exceed 25%, particularly among vulnerable populations. In this study, L. pneumophila serogroup 1 (sg1) was used as the reference strain for risk modeling. The log means and standard deviation concentration of *L. pneumophila* was calculated from surveillance data collected from UWMC.

2.2.2. Exposure Assessment:

The exposure assessment modeled two primary scenarios of patient-proximal aerosol exposure to *Legionella pneumophila*: (1) shower use and (2) faucet (hand sink) use. These fixtures differ significantly in exposure duration, aerosol emission efficiency, and the proportion of respirable droplets generated, all of which influence the inhaled dose. Each exposure scenario was modeled independently using a fixture-specific equation based on first-order mass transfer principles.

For **Model 1 (Shower exposure)**, the inhaled dose was calculated as:

$$D_{\text{shower}} = C_{\text{water}} \times PC_{\text{shower}} \times F_{1\text{–}5,\text{shower}} \times IR \times ET_{\text{shower}} \quad \text{Equation 1}$$

For **Model 2 (Faucet exposure)**, the corresponding dose equation was:

$$D_{\text{faucet}} = C_{\text{water}} \times PC_{\text{faucet}} \times F_{1\text{–}5,\text{faucet}} \times IR \times ET_{\text{faucet}} \quad \text{Equation 2}$$

In both models, *C_water* represents the concentration of *L. pneumophila* in water (cfu/L); *PC* is the water-to-air partitioning coefficient (L/m^3); $F_{1\text{–}5}$ denotes the fraction of aerosols within the respirable size range (1–5 µm); *IR* is the inhalation rate (m^3/min); and *ET* is the exposure duration (min). These two model equations [30,60] reflect the distinct exposure dynamics associated with each fixture and provide the foundational structure for risk estimation.

2.2.3. Exposure parameter distributions

Table 1: Input parameters and probability distributions for QMRA exposure modeling

Input Variables	Description	Unit	Characterization	Source and Comments
C_{water}	*L. pneumophila* sg1 concentration in water	Log(CFU/L)	lognormal distribution [1] $\mu \approx -2.4756$, $\sigma \approx 1.4935$)[2]	Based on a 4-year monitoring data (UWMC)

Input Variables	Description	Unit	Characterization	Source and Comments
PC	Sink partitioning coefficient	L/m^3	lognormal distribution [1] ($\mu = -13.3$, $\sigma = 3.49$) truncated on the interval [0, 2.35×10^{-3}]	Hamilton et al., 2019 [20]. Data analysis of 19 paired water and air samples from hot-water faucets
F $_{1\text{–}5}$	Percentage of aerosols in respirable range (1–5 μm) produced by faucet or shower	%	Faucet: 0.3% Shower: 4.4%	Hamilton et al., 2019. *Risk-based critical concentrations of Legionella pneumophila for indoor residential water uses*. Environ. Sci.: Water Res. Technol. 5(4):598–609[25].
IR	Inhalation rate	m^3/min	uniform distribution (min = 0.013, max = 0.017)	USEPA 2011 [31]. Inhalation rate for individuals engaging in light activities
ET	Sink use duration	Min	uniform distribution (min = 0.5, max = 1.5)	An assumption on the duration of an individual would stay in the toilet for hand washing (Wilson
ET	Shower use duration		Normal ($\mu = 7.8$ minutes, $\sigma = 0.02$)	Hamilton[25]

*[1] The lognormal distribution of each variable Y has been evaluated as exp(μ + σ*Z) where Z is a standardized normal variable with mean 0 and standard deviation 1, and μ and σ are, respectively, the mean and the standard deviation of a generic normal distribution.*

SOURCES: Federigi [61;] [2]log(CFU/mL) was convert to CFU/L for analysis.

Dose-Response modeling.

The probability of *L. pneumophila* infection was calculated using an exponential dose–response model [58]:

$$\boldsymbol{Probability\ of\ infection = 1 - e^{-k*Dose}} \qquad Equation\ 3$$

where P_{inf} is the probability of infection during a single use of the sink, D is the inhaled dose of *L. pneumophila* from the exposure assessment, and K as the likelihood of one cell to survive host barriers and successfully initiate an infection, which corresponds to k = 5.99E-02 for *L. pneumophila*[60,62], is the subclinical severity infection model.

The annual infection risk from exposure to *Legionella pneumophila* can be estimated using an exponential dose–response model. To determine the cumulative risk over a year, assuming independent and repeated exposures, the annual infection probability is calculated as

$$\boldsymbol{Probability\ of\ infection}_{\textbf{annual}}(\boldsymbol{P}_{\textbf{annual}}) = \mathbf{1} - (\mathbf{1} - \boldsymbol{P}_{\textbf{inf}})^{\boldsymbol{n}} \qquad Equation\ 4$$

Where n is the number of exposure event per year. Substituting the exponential model into this equation yields the simplified form $P_{\text{annual}} = 1 - e^{-kDn}$. This formulation allows for direct computation of yearly infection risk based on dose per event, frequency of exposure, and pathogen-specific virulence, enabling meaningful comparison across different water fixtures and use patterns in QMRA (**Figure 2**).

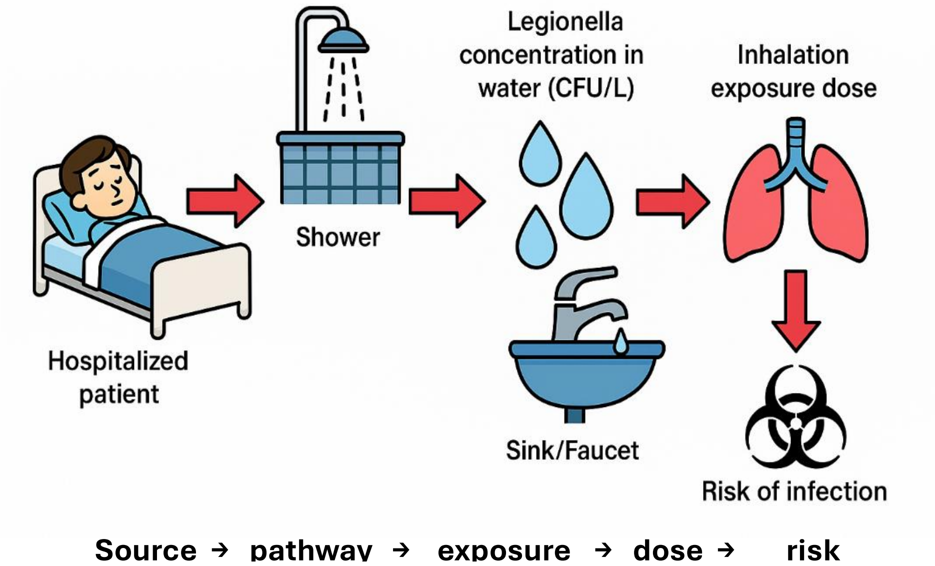

Figure 2: Conceptual diagram of QMRA of Legionella exposure for hospitalized patient

2.2.5 Exposure Scenario Modeling

To characterize patient-proximal inhalation risks, we compared two exposure routes—showers and faucets—using route-specific aerosol behavior. The QMRA converts measured/assumed water concentrations of *L. pneumophila* (lognormal) to airborne concentrations via a water-to-air partitioning coefficient (truncated lognormal; upper bound 2.35×10^{-3} L/m^3) and route-specific respirable fractions (lower for faucets, higher for showers). Inhaled dose is then calculated with uniform inhalation rates and durations appropriate to each activity (handwashing 0.5–1.5 min; showering 5–15 min). Infection probability is derived with an exponential dose–response model (k = 0.06). To capture variability and uncertainty, we performed a Monte Carlo simulation with 100,000 iterations, a number substantiated by Burmaster and Anderson[63], which produced stable central estimates.

Risk Characterization:

To estimate the annual risk of infection, single-use exposure doses derived from each fixture scenario (shower or faucet) were scaled based on expected fixture usage frequencies in a healthcare setting. The exponential dose–response model was applied to each calculated dose to yield the probability of infection per exposure event [55]. These event-based probabilities were then aggregated to reflect annual exposure, resulting in an annual infection risk per person for each fixture type. The resulting infection risk estimates were evaluated against internationally recognized health-based benchmarks. Specifically, risk acceptability was assessed relative to the United States Environmental Protection Agency (USEPA) threshold of 1×10^{-4} infections per person per year.

2.7. Sensitivity and uncertainty analysis

To account for uncertainty and variability in the input parameters, a Monte Carlo simulation was performed using 100,000 iterations. This simulation involved probabilistically sampling from the distributions of key input variables, including C_{water}, partitioning coefficient (PC), aerosol fraction (F_1–$_5$), inhalation rate (IR), and exposure duration (ET). This approach generated a full distribution of predicted infection risks for each scenario, allowing for the estimation of central tendency, upper percentiles, and confidence bounds.

In addition, sensitivity analysis was conducted using rank-order correlation coefficients between each input variable and the resulting infection risk output. This analysis identified the relative influence of each parameter on model outcomes, thereby highlighting the primary drivers of variability in infection risk estimates. A rank coefficient near ±1 indicates strong influence, while coefficients near 0 suggest minimal impact. This dual analysis approach enhances transparency and provides insight into model robustness, informing the interpretation and potential refinement of exposure assumptions.

Results

3.1 Distribution of Legionella pneumophila Concentrations in Water Samples

Measured concentrations of *Legionella pneumophila* serogroup 1 in water samples from the University of Washington Medical Center (UWMC) exhibited a lognormal distribution. On the natural log scale, the mean was approximately $\mu = -2.4756$, corresponding to ~0.084 CFU/mL in arithmetic terms. The standard deviation was $\sigma = 1.4935$, equating to a geometric standard deviation of approximately 0.74 CFU/mL.

3.2 Inhaled Dose Distribution by Fixture Type

When visualized on a $\log_{10}$ scale, the dose distributions for each fixture type exhibited near-symmetric patterns, though centered at distinctly different dose levels (Figure 3). Faucet exposure events clustered around $\log_{10}$ doses of ~–8 CFU, while shower exposures peaked near ~–6 CFU. The entire distribution for shower exposure was shifted approximately two orders of magnitude to the right, reinforcing the higher inhalation dose associated with showers. For faucet exposure, the median inhaled dose was ~1.7 × 10^{-12} CFU, with 95th and 99th percentiles reaching ~2.6 × 10^{-9} CFU and ~2.1 × 10^{-8} CFU, respectively. The maximum simulated faucet dose approached ~3.2 × 10^{-7} CFU. For

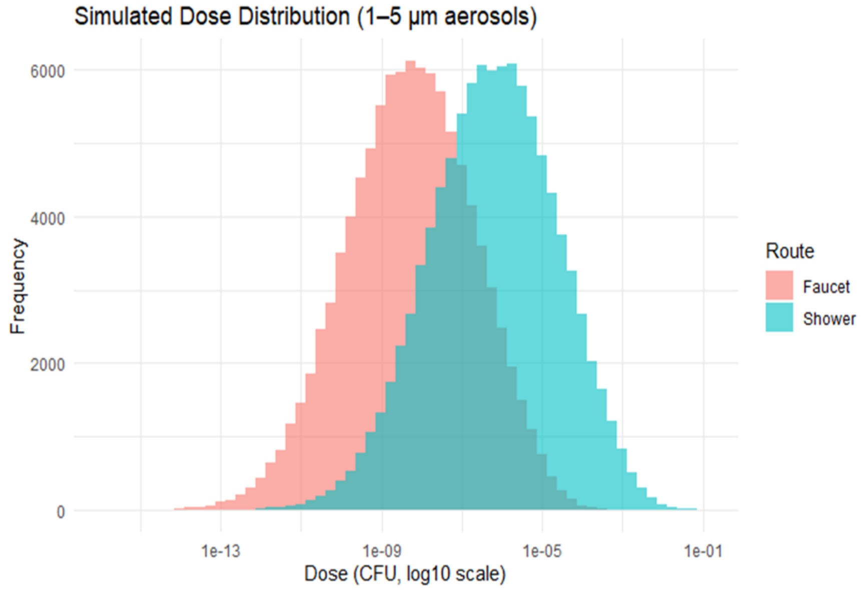

Figure 3: Simulated Inhaled Dose of Legionella pneumophila by faucet and

shower exposures, the median dose was higher at ~2.6 × 10^{-8} CFU, with 95th and 99th percentiles at ~4.2 × 10^{-6} and ~2.1 × 10^{-5} CFU, respectively. Maximum values exceeded ~3.8 × 10^{-4} CFU per exposure event. Shower exposures result in consistently higher doses due to longer exposure time and greater aerosolization efficiency (**Figure 3**).

These inhaled dose estimates provide the probabilistic input required for dose–response modeling in subsequent infection risk characterization steps of the QMRA.

3.3 Cumulative Distribution of Inhaled Dose

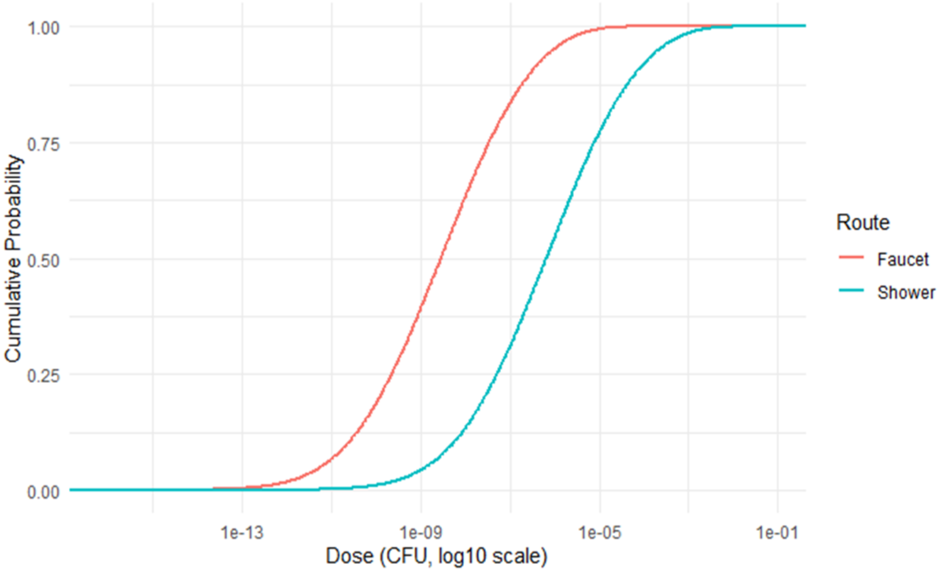

Figure 4: Cumulative distribution of simulated inhaled doses by fixture type (faucet vs. shower).

The cumulative distribution of simulated inhaled doses highlighted substantial differences between faucet and shower exposures (**Figure 4**). Faucet-associated doses were tightly clustered at the lower end of the dose range, with a median near 6 × 10^{-9} CFU and the 99th percentile remaining below 2 × 10^{-5} CFU. These results suggest that nearly all faucet exposures result in negligible inhalation of *L. pneumophila*.

In contrast, shower-associated doses were distributed several orders of magnitude higher. The median inhaled dose for showers was approximately 7 × 10^{-7} CFU, with the upper percentiles extending above 10^{-3} CFU per event. The broader spread of the shower curve reflects the influence of longer exposure durations and higher proportions of respirable aerosols (1–5 μm) during shower use. Collectively, these results reinforce that showers deliver substantially greater inhalation doses than faucets, confirming their dominant role in fixture-specific quantitative risk assessments.

3.4 Cumulative Distribution of Infection Risk

The cumulative distribution of infection risk per exposure event further distinguished faucet from shower pathways (**Figure 5**). Risks associated with faucet use remained consistently low across all simulations, with values concentrated between 10^{-13} and 10^{-7}. The median per-exposure infection probability from faucet use was approximately 1×10^{-11}, and 99% of simulated events did not exceed 10^{-7}.

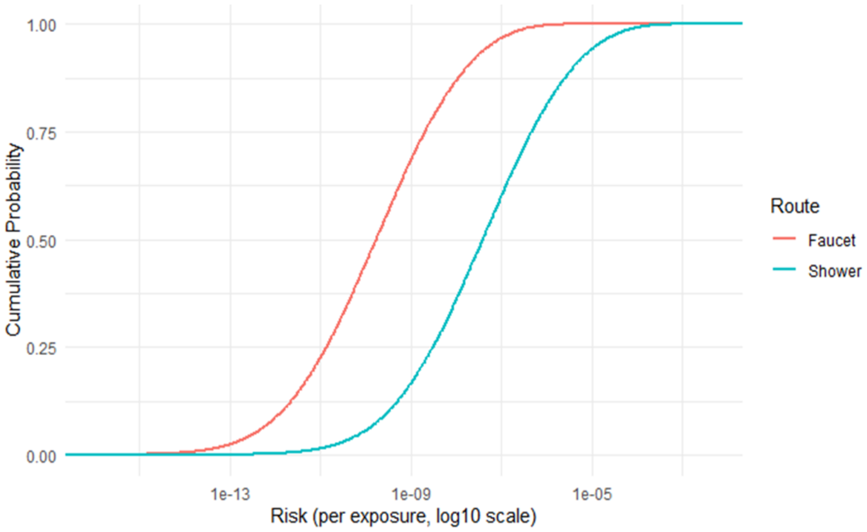

Figure 5: cumulative distribution of simulated infection risk by faucet and shower

Shower exposures, however, resulted in substantially higher infection probabilities. The distribution of per-exposure risk for showers was shifted several orders of magnitude to the right, with a median risk of ~1×10^{-6} and upper percentiles reaching into the 10^{-3} to 10^{-2} range. These findings emphasize the impact of both exposure duration and aerosol efficiency in shower scenarios.

3.5 Per-Exposure vs annual Infection Risk Estimates

The mean infection probability per faucet use was 1.81×10^{-6}, whereas the mean risk for a single shower exposure was 2.56×10^{-4}. This represents a difference of roughly two orders of magnitude, with showers posing a substantially higher risk of infection per event (**Table 2**).

Assuming one faucet use per day, the resulting annual infection risk was 6.365621×10^{-4}. If the same faucet was used three times daily, the annual risk increased proportionally to 1.80×10^{-3}. In contrast, a single daily shower resulted in a significantly higher annual infection probability of 3.86×10^{-2} (**Table 2**).

Table 2. Summary of estimated infection risks by fixture type and exposure frequency.

Scenario	**Mean per Exposure**	**Number of Exposures (n)**	**Annual infection Risk**
Faucet (1×/day)	1.81×10^{-6}	365	6.37×10^{-4}
Faucet (3×/day)	1.81×10^{-6}	1095	1.80×10^{-3}
Shower (1×/day)	2.56×10^{-4}	365	3.86×10^{-2}

3.6. Sensitively Analysis:

Spearman rank-order sensitivity analysis was conducted to identify the relative influence of model parameters on predicted *Legionella pneumophila* infection risk for faucet and shower exposures (Figure 7). For both exposure routes, the water-to-air partitioning coefficient (PC) emerged as the most influential variable, with strong positive correlations to infection risk (ρ = 0.903 for faucets; ρ = 0.907 for showers). This indicates that variation in aerosol generation efficiency is the primary driver of uncertainty in model outcomes.

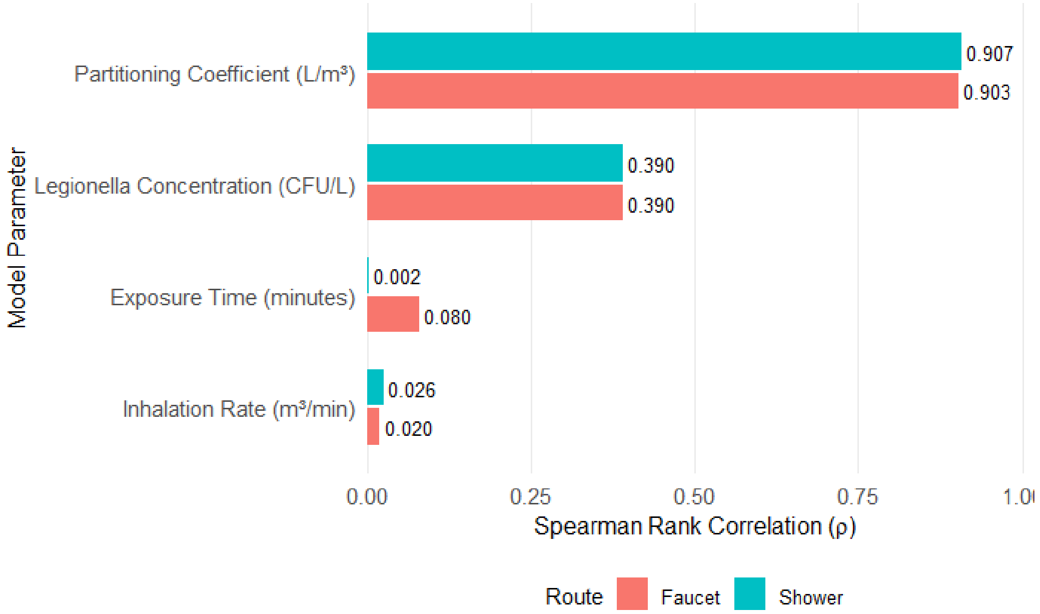

Figure 6: Rank-Order (Spearman) Sensitivity Analysis — Infection Risk faucet and shower

The Legionella concentration in water also exhibited a moderate positive correlation with infection risk (ρ ≈ 0.39), suggesting that higher bacterial loads in water modestly increase infection probability across both fixtures. This is an important point, and the sensitivity analysis supports it: the partitioning coefficient (PC) had the strongest rank correlation with infection risk in both routes (ρ ≈ 0.90), while water concentration had a moderate association (ρ ≈ 0.39). This pattern is plausible in this model because the inhaled dose is directly proportional to: $d \propto Cw \times PC \times F \times IR \times ET$ and the PC distribution was extremely wide and highly variable (lognormal with a large σ and truncation), which can dominate uncertainty even when concentration varies. In contrast, the concentration distribution—

especially after nondetect handling and pooling—may have relatively less influence on the output variability than expected.

In contrast, exposure time ($\rho = 0.08$ for faucets; $\rho \approx 0.002$ for showers) and inhalation rate ($\rho = 0.02$ for faucets; $\rho \approx 0.026$ for showers) had minimal influence, indicating that variations in duration or breathing rate contribute little to the overall risk variability.

Discussion

This quantitative microbial risk assessment (QMRA) revealed a clear differentiation in inhaled *Legionella pneumophila* doses and infection risks between faucet and shower exposures. Monte Carlo simulation results demonstrated that faucet-associated inhaled doses were extremely low, with a median of approximately 1.7×10^{-12} CFU and upper percentiles remaining below ~10^{-8} CFU, while shower exposures were several orders of magnitude higher, with a median of 2.6×10^{-8} CFU and upper percentiles exceeding 10^{-5} CFU per exposure. The cumulative dose distributions confirmed that shower exposures were consistently shifted to the higher end of the range, reflecting greater inhalation potential. These differences translated directly into infection probabilities, where the median per-exposure risk for faucets was on the order of 10^{-11}, compared with 10^{-6}–10^{-3} for showers. When aggregated across typical daily use frequencies, annualized infection risks from showers (~0.16%) were at least an order of magnitude greater than those from frequent faucet use. Collectively, these findings establish that showers represent the dominant inhalation pathway for *L. pneumophila* in healthcare water systems, underscoring their central role in exposure and infection prevention strategies.

The observed disparity between faucet and shower exposures is consistent with prior research identifying showers as the principal source of *Legionella* aerosolization in built water systems. Previous QMRA studies (Quon et al., 2021; Tang, 2025) have similarly identified showers as a primary source of exposure, reinforcing the role of fixture design and usage characteristics in shaping inhalation risk. Showerheads produce finer and more respirable droplets (1–5 μm) compared to faucets, which primarily generate larger droplets that settle rapidly and contribute little to inhalation exposure[25,64]. The mechanical design of showerheads, including narrow nozzles and elevated spray pressures, enhances aerosol generation and dispersal, facilitating greater bacterial entrainment into the air. In healthcare and residential settings, *Legionella* amplification within biofilms of distal outlets such as showerheads has been well documented, further elevating exposure potential[64,65]. Additionally, prolonged exposure durations during showering, combined with the close proximity of the breathing zone to the aerosol plume, compound the inhaled dose received per event. These mechanisms collectively explain why showers contribute disproportionately to overall inhalation risk, even when *L. pneumophila* concentrations in water are comparable across fixtures[25,64].

These findings have direct implications for *Legionella* control and water management practices in healthcare facilities. The dominance of showers as an inhalation exposure pathway underscores the need for fixture-specific surveillance and mitigation strategies. Routine monitoring programs often focus on bulk water sampling; however, these results suggest that distal outlets—particularly showerheads—should be prioritized for sampling, disinfection, and maintenance[25]. Engineering controls such as temperature management, point-of-use filtration, and periodic thermal or chemical disinfection can effectively reduce *Legionella* colonization and aerosol release from shower systems[66]. In addition, regular replacement or cleaning of showerheads, implementation of secondary disinfection systems (e.g., monochloramine or chlorine dioxide), and staff awareness of flushing protocols are critical to maintaining microbial control[67]. From a risk management perspective, probabilistic QMRA modeling provides a valuable tool for quantifying infection risk across fixture types and identifying where interventions yield the greatest health benefit. Integrating these quantitative insights into hospital water safety plans can enhance decision-making, optimize resource allocation, and ultimately reduce the likelihood of healthcare-associated legionellosis[68].

While the results clearly differentiate the relative infection risks associated with faucet and shower exposures, interpretation must account for model assumptions and uncertainties in input parameters. The Monte Carlo framework was developed to capture variability in environmental concentrations, aerosol generation efficiency, and human exposure behaviors; however, several parameters—such as the partitioning coefficient, inhalation rate, and exposure duration—were derived from literature-based distributions rather than site-specific measurements. To evaluate model robustness, a rank-order (Spearman) sensitivity analysis was conducted.

For faucet exposures, the water-to-air partitioning coefficient (PC) exhibited the strongest positive correlation with infection risk ($\rho = 0.903$, $p < 0.001$), followed by Legionella concentration in water ($\rho = 0.39$, $p < 0.001$). Exposure time ($\rho = 0.08$, $p < 0.001$) had a weak but statistically significant effect, while inhalation rate contributed minimally ($\rho = 0.02$, $p < 0.001$). Similarly, for shower exposures, the partitioning coefficient remained the dominant driver ($\rho = 0.907$, $p < 0.001$), with Legionella concentration in water again showing moderate influence ($\rho = 0.39$, $p < 0.001$). In contrast, inhalation rate and exposure duration had negligible effects ($\rho < 0.03$). These results demonstrate that infection risk variability is primarily governed by factors influencing aerosol generation and microbial concentration rather than by physiological or behavioral parameters. The sensitivity analysis enhances model transparency and highlights key parameters—particularly partitioning efficiency and waterborne Legionella levels—for targeted monitoring and data collection in future studies aimed at improving model precision and reducing uncertainty.

This study offers several key strengths in estimating *Legionella pneumophila* infection risk in healthcare water systems using the QMRA framework. First, it leverages four years (2018–2021) of real surveillance data from the UWMC, providing robust, context-specific insight into *L. pneumophila* behavior within a complex healthcare water system. The use of a large-scale Monte Carlo simulation (100,000 iterations) represents a significant methodological advantage, enabling the characterization of uncertainty and variability in exposure conditions that simpler deterministic models cannot capture. Furthermore, this research advances existing knowledge by comparing two clinically relevant inhalation exposure routes—showers and faucet—and quantifying infection risk both per exposure and on an annualized basis. Explicit modeling of the tails of the dose distribution underscores how a small number of high-exposure events can drive infection probabilities, providing critical insight for risk mitigation and water safety planning.

Despite these strengths, several limitations should be acknowledged. The study focused exclusively on *L. pneumophila* serogroup 1, which, although epidemiologically significant, does not account for other *Legionella* species that may contribute to healthcare-associated disease. Some model parameters—such as aerosol partitioning coefficients, droplet retention fractions, and exposure frequencies—were drawn from published literature rather than site-specific measurements, introducing potential uncertainty into exposure estimates. In addition, the model estimates infection risk but does not link these estimates to observed clinical outcomes, limiting opportunities for epidemiological validation. The environmental sampling frequency, while extensive, may not have fully captured short-term fluctuations in *Legionella* concentrations, potentially underrepresenting transient high-risk events. Another limitation is the homogeneous treatment of host susceptibility; the model does not account for patient-specific factors such as age, immune status, or comorbidities that can substantially modify infection risk in hospital populations. Finally, as a single-institution study conducted at UWMC, the findings may not be generalizable to facilities with differing infrastructure, climate, or water management practices. Nonetheless, the modeling framework and methodological approach remain broadly applicable and provide a valuable foundation for future multi-site risk assessments and the refinement of hospital water safety programs.

Conclusions

This study applied a quantitative microbial risk assessment (QMRA) framework to estimate Legionella pneumophila infection risks from faucet and shower exposures in a healthcare setting. Analysis of four years of surveillance data from the University of Washington Medical Center, combined with Monte Carlo simulation, indicated that shower exposures consistently resulted in markedly higher inhaled doses and infection risks than faucet exposures, with annual risk estimates on the order of 10^{-2} for showers compared with 10^{-3}–10^{-4} for faucets. These differences were driven primarily by longer exposure durations and greater aerosolization efficiency during shower use. Overall, the findings confirm showers as the dominant inhalation exposure pathway. The findings also highlight that infection risk variability is primarily governed by water-to-air partitioning and Legionella concentration in water, underscoring the need to prioritize these parameters in monitoring and control efforts.

CHAPTER 4: Aim 3- Assessing Fixture-Specific Legionella Infection Risk at UWMC Using a Reverse QMRA Approach

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Abstract

Background: Legionnaires' disease remains a critical health concern in healthcare settings, particularly for immunocompromised patients. Despite existing CDC guidance defining "controlled" *Legionella* levels as <0.9 CFU/mL, evidence suggests that this threshold may be insufficiently protective for hospital environments. This study aimed to evaluate the effectiveness of monitoring and mitigation strategies at the University of Washington Medical Center (UWMC) using a reverse Quantitative Microbial Risk Assessment (QMRA) approach, with a focus on deriving fixture-specific risk-based *Legionella* concentration thresholds.

Methods: We applied a reverse quantitative microbial risk assessment (QMRA) framework at the University of Washington Medical Center (UWMC) to estimate fixture-specific critical concentrations of *Legionella pneumophila* associated with an annual infection risk threshold of 1×10^{-4}. Using an exponential dose-response model and fixture-specific inhalation exposure assumptions for faucets and showers, we conducted forward Monte Carlo simulations (n = 10,000) to estimate infection risk probabilities across a range of water concentrations. The resulting critical concentrations—defined as the highest allowable concentration at which infection risk remains below the benchmark—were then compared against CDC guidance and previously published residential risk-based thresholds.

Results: The estimated infection risk from faucet use (1×/day and 3×/day) was 3.43×10^{-6} and 1.03×10^{-5}, respectively—both well below the regulatory benchmark of 10^{-4}. In contrast, shower use at 1×/day reached the benchmark risk level, with a corresponding critical concentration of 0.5806 CFU/L. Forward QMRA modeling identified fixture-specific critical concentrations of approximately 10 CFU/L for faucets and 0.58 CFU/L for showers. These findings confirm that shower exposure reaches the benchmark risk at substantially lower Legionella concentrations than faucet use due to higher aerosolization and inhalation volumes. While faucet exposures did not reach the benchmark within the tested concentration range (0–10 CFU/L), shower use clearly intersected the 10^{-4} risk threshold at sub-CFU/L levels. These results underscore the importance of implementing fixture-specific control strategies, particularly in high-risk environments such as healthcare facilities, where even low-level Legionella exposures may pose a measurable infection risk.

Conclusion: Reverse QMRA effectively identified fixture-specific critical concentrations, revealing that showers pose a higher infection risk at lower Legionella levels than faucets. These findings support the need for tailored, exposure-based management strategies in healthcare settings and call for updated guidelines that reflect the vulnerability of high-risk populations.

Key words: Reverse QMRA, *Legionella pneumophila*, Critical concentration, Healthcare-associated infections and Water safety plan

Introduction

Legionnaires' disease, caused by the opportunistic waterborne pathogen *Legionella pneumophila*, presents a substantial and growing public health challenge. The disease is most commonly acquired through inhalation of aerosolized water droplets contaminated with the bacterium, with sources including showers, cooling towers, decorative fountains, and other engineered water systems[12]. Clinical outcomes range from mild, flu-like Pontiac fever to severe and potentially fatal pneumonia, especially among older adults and immunocompromised individuals. The overall case fatality rate is approximately 10% in the general population, rising to 25% among individuals with underlying health conditions, such as chronic lung disease, cancer, or organ transplant recipients.[12,69.] According to data reported to the US Centers for Disease Control and Prevention (CDC) through the National Outbreak Reporting System (NORS), between 2009 and 2021, there were 536 outbreaks resulting in 2,965 illnesses, 1,817 hospitalizations, and 224 deaths from Legionnaires' disease in the US[21].[70] These figures are widely believed to underrepresent the true burden of disease due to underdiagnosis and limited environmental surveillance. According to Gleason & Cohn (2022), CDC's NORS data from 2009–2019 recorded 322 outbreaks, 1,923 illnesses, 1,112 hospitalizations, and 143 deaths from Legionnaires' disease. The authors emphasize underreporting due to "lack of testing and inconsistent environmental surveillance[71].

The critical concentration of *L. pneumophila* defined as the bacterial load in water at which the risk of infection becomes significant, requiring preventive or corrective action is 10 to 10,000 CFU/mL (10^4–10^7 CFU/L) in both cold and hot water sources[25], with a lower threshold of less than 0.05 CFU/mL (50 CFU/L) recommended for setting with hospitalized patients[26]. Recent studies highlight the importance of designing and maintaining water systems and cooling towers to prevent contamination and outbreaks[72]. Given the vulnerability of sick and immunocompromised patients, implementing a robust water quality management program is essential in settings such as hospitals, healthcare facilities, and elderly care homes[23,59,69]. Regulatory bodies like the Centers for Medicare and Medicaid Services (CMS) mandate the implementation of prevention programs, including *Legionella* risk assessments as per ASHRAE 188-2018 standards[23,24], to mitigate the risk of waterborne diseases[9].

A notable example of such vulnerability occurred at the University of Washington Medical Center (UWMC) in Seattle, where a Legionnaires' disease outbreak between 2015 and 2016 led to multiple confirmed infections and fatalities among hospitalized patients[73]. The outbreak, which infected five patients in the hospital's Cascade Tower in August and September, tragically resulted in two deaths, while three patients fortunately survived[73]. The outbreak prompted extensive environmental and epidemiological investigations, revealing persistent *Legionella* colonization in parts of the hospital's water distribution system. This event underscored the critical need for continuous environmental surveillance, secondary disinfection, and proactive water management in healthcare settings—particularly those serving immunocompromised populations.

QMRA was created to measure the health risks posed to individuals due to exposure to particular waterborne pathogens[28,74–76]. This approach has been widely applied to public health issues[22]. QMRA is a useful tool in assessing and determining concentration limits for microbial contamination in water and food-borne pathogens[28]. QMRA integrates pathogen occurrence, infectivity, and exposure data to estimate the probability of infection and subsequent infection, illness, or other adverse outcomes[77,78] using hazard identification, exposure assessment, dose–response, and risk characterization, offering insights beyond epidemiological studies alone[30]. QMRA can be invaluable for evaluating Legionnaires' disease risk, particularly given the prevalence of Legionella in plumbing systems.

In this study, we applied a reverse QMRA approach not to retrospectively validate past interventions, but rather to proactively identify fixture-specific critical concentrations at which infection risk reaches a defined threshold. This modeling effort aimed to support UWMC in refining its internal action levels by translating environmental *Legionella* concentrations into clinically relevant risk metrics. Rather than assuming that meeting general population standards ensures safety for all, this approach aligned exposure estimates with infection probability targets tailored to vulnerable hospital populations. The resulting insights may help UWMC reassess its surveillance triggers and better integrate risk-informed thresholds into its Water Safety Plan, particularly for aerosol-generating fixtures such as showers.

Methods

2.1 Quantitative Microbial Risk Assessment (QMRA) Framework

To estimate fixture-specific critical concentrations of *Legionella pneumophila* in the UW Medical Center (UWMC) potable water system, we applied a forward Monte Carlo simulation approach within a reverse QMRA framework, using site-specific exposure parameters and a standard exponential dose-response model. The goal was to identify the maximum concentration of *L. pneumophila* (i.e., critical concentration) that would not exceed a regulatory infection risk threshold of 1 × 10^{-4} infections per person per year.

Table 2: Reverse QMRA Model Variables and Assumptions

Parameter	Description	Value / Distribution	Source / Notes
r	Dose-response parameter (infectivity rate) for *Legionella pneumophila*	0.0599	Armstrong and Haas (2007); EPA standard QMRA models
P_annual	Annual infection risk benchmark	1×10^{-4}	Regulatory benchmark; used in EPA and WHO guidance
C	Concentration of *L. pneumophila* in water (CFU/L)	Range: 0–10 CFU/L	Simulated to identify critical concentration
V	Inhaled volume per exposure	**Faucet**: rlnorm(meanlog = log(0.001), sdlog = 0.3) **Shower**: rlnorm(meanlog = log(0.5), sdlog = 0.3)	Fixture-specific aerosolized water intake
n	Number of exposure events per year	Faucet (1x/day): 365 Faucet (3x/day): 1095 Shower (1x/day): 365	Based on daily use frequencies
partitioning	Fraction of *L. pneumophila* aerosolized and inhaled	runif(10000, 0.001, 0.01)	Uniform distribution assumed
dose	Total inhaled dose per exposure (CFU)	C × V × partitioning × n	Derived during simulation
P_infection	Probability of infection per exposure	1 - exp(-r × dose)	Exponential dose-response model
P_annual	Annual probability of infection	1 - (1 - P_infection)^n	Based on number of exposures
C_crit	Critical concentration (CFU/L) required to reach target risk	Computed iteratively to find C where P_annual ≈ 1×10^{-4}	Reverse QMRA calculation

2.2 Dose-Response Model and Exposure Scenarios

Infection probability was modeled using the exponential dose-response equation:

$$P_{\text{infection}} = 1 - \exp\left(-k \cdot d\right)$$

where:

$P_{\text{infection}}$= infection probability per exposure

k= dose-response infectivity parameter for *L. pneumophila* (0.0599)

d= dose (CFU) = concentration × inhaled volume × aerosol partition factor

To account for repeated daily exposures, annual infection risk was derived as:

$$P_{\text{annual}} = 1 - (1 - P_{\text{infection}})^{n}$$

where $n$represents the number of exposures per year (365 for once daily; 1,095 for thrice daily).

We modeled two primary fixture types: faucets (low aerosol exposure) and showers (high aerosol exposure). Inhaled volumes and aerosol partition factors were based on published literature values and tailored to each fixture.

2.3 Monte Carlo Simulation Approach

Rather than using the closed-form algebraic solution for critical concentration, we implemented a forward Monte Carlo simulation using 10,000 iterations per scenario. At each candidate concentration value, the model simulated variability in inhaled dose using a lognormal distribution and then computed the resulting infection probability using the exponential model. The process was repeated across a wide range of concentrations (0.001 to 100 CFU/L). For each fixture-use scenario:

Simulated annual infection risks were estimated.

The critical concentration was identified as the lowest concentration at which the mean estimated risk matched the 10^{-4} benchmark.

This approach accommodates dose variability and allows for a probabilistic rather than deterministic identification of thresholds.

2.4 Application to UWMC Mitigation Strategy Evaluation

Using pre-defined post-mitigation concentration data collected from routine surveillance, we compared measured *L. pneumophila* levels to the modeled fixture-specific critical concentrations. This allowed us to assess whether current conditions at UWMC meet the benchmark risk threshold, and whether risk reductions achieved after intervention are sufficient from a public health protection perspective.

2.5 Integration with Existing Regulatory Categories

Finally, we compared our QMRA-based risk thresholds with existing CDC concentration categories for controlled (<1 CFU/mL), poorly controlled (1–9.9 CFU/mL), and uncontrolled (≥10 CFU/mL) systems. This comparison informed whether UWMC-specific targets suggest the need for refined concentration categories for healthcare settings serving high-risk populations.

Results

3.1. Fixture-specific infection risk estimates

Using the exponential dose-response model within a forward Monte Carlo simulation framework, the estimated infection risk from faucet use remained well below the regulatory benchmark of 10^{-4}. Specifically, the modeled risks were 3.43×10^{-6} for once-daily faucet use and 1.03×10^{-5} for three-times-daily use.

In contrast, daily shower exposure reached the benchmark risk level, with an estimated infection probability of approximately 1.0×10^{-4}. These findings highlight the elevated risk associated with fixtures that generate higher aerosol volumes, such as showers.

Table 3: Estimated Infection Risk by Fixture Type

Fixture Type	**Use Frequency**	**Estimated Infection Risk**	**Within 10^{-4} Benchmark?**
Faucet	1×/day	3.43×10^{-6}	Yes
Faucet	3×/day	1.03×10^{-5}	Yes
Shower	1×/day	$\sim 1.0 \times 10^{-4}$	At Benchmark

3.2. Forward QMRA-derived critical concentrations

Critical concentration was defined as the Legionella pneumophila level at which the modeled annual infection risk intersects the 10^{-4} benchmark. Rather than relying on a closed-form algebraic solution, concentrations were identified numerically through forward Monte Carlo simulation.

Results demonstrated clear fixtures specific differences. Shower exposure reached the benchmark at a substantially lower concentration (0.5806 CFU/L), whereas faucet exposures did not reach the benchmark within the evaluated range and required concentrations of approximately 10 CFU/L to approach comparable risk levels.

Table 4: Fixture Specific Critical Concentrations

Fixture Type	**Critical Concentration (CFU/L)**	**Estimated Risk**
Faucet (1×/day)	10	3.43×10^{-6}
Faucet (3×/day)	10	1.03×10^{-5}
Shower (1×/day)	0.5806	$\sim 1 \times 10^{-4}$

3.3. Comparison with regulatory guidance

When expressed in CFU/mL, the shower-based critical concentration corresponds to 0.00058 CFU/mL, which remains well below the CDC "controlled" category upper bound of 0.9 CFU/mL. This suggests that existing categorical thresholds may not fully capture fixture-specific exposure risks in healthcare environments, particularly for aerosol-generating fixtures.

3.4. Implications for hospital risk management

The results indicate that uniform concentration categories may not adequately reflect exposure variability across fixture types. Shower use demonstrated markedly higher sensitivity to concentration changes compared to faucets, supporting the adoption of fixture-specific, risk-based targets rather than single system-wide thresholds. Such an approach aligns with modern water safety planning principles and offers a more protective framework for healthcare facilities serving vulnerable populations.

Discussion

This study applied a forward Monte Carlo-based Quantitative Microbial Risk Assessment (QMRA) approach to evaluate the annualized infection risk of Legionella pneumophila from daily water use through different fixtures in a healthcare setting[25,30]. QMRA has been widely used to quantify infection risks from waterborne pathogens and to establish exposure-based action thresholds, particularly in environments serving immunocompromised populations. Our findings provide fixture-specific estimates of infection probability and identify the critical concentrations at which *Legionella* presence becomes a concern under the widely used benchmark of *10^{-4} annual risk*. The results also raise important questions about the adequacy of current regulatory thresholds when applied uniformly across fixture types in vulnerable populations.

Consistent with previous literature, our results reveal significant differences in infection risk based on fixture type and use frequency. Previous QMRA studies have shown that fixture-specific aerosolization and exposure pathways strongly influence *Legionella* infection risk, even when water concentrations are comparable[25,30]. Faucet use, even at three times per day, remained well below the 10^{-4} risk benchmark, with modeled probabilities of 3.43×10^{-6} (1x/day) and 1.03×10^{-5} (3x/day). In contrast, shower use approached the 10^{-4} threshold even with once-daily exposure, with a modeled risk of approximately 1.0×10^{-4}. This observation is consistent with prior findings that showers generate higher respirable aerosol volumes and promote deeper pulmonary deposition, resulting in elevated infection risk relative to other fixtures[25]. This underscores the higher-risk profile of fixtures associated with greater aerosol generation, longer exposure durations, and deeper pulmonary inhalation pathways.

Rather than solving algebraically for a "reverse" critical concentration, we used forward Monte Carlo simulation to identify the exposure concentration at which the infection risk intersects the 10^{-4} benchmark. Monte Carlo–based QMRA approaches have been widely used to identify risk thresholds for *Legionella pneumophila*, particularly when exposure variability and uncertainty cannot be adequately captured by closed-form solutions[25,30].Results show that Showers reached this risk level at a Legionella concentration of 0.5806 CFU/L and Faucets required much higher concentrations (~10 CFU/L) to approach the same risk level and still remained below the benchmark. Previous QMRA studies similarly report that aerosol-generating fixtures such as showers reach benchmark infection risks at substantially lower concentrations than low-aerosol fixtures, underscoring the importance of fixture-specific risk assessment[25]. This contrast confirms that fixture sensitivity to microbial concentration varies widely, and using a single uniform concentration limit across all fixture types may lead to underestimation of risk from high-exposure devices, particularly in healthcare settings where susceptible individuals are at greater risk.

When our critical concentration values are expressed in CFU/mL (e.g., 0.00058 CFU/mL for showers), they fall well below the CDC’s “controlled” system upper limit of 0.9 CFU/mL. CDC guidance defines these categorical thresholds primarily for system management and outbreak response, rather than for fixture-specific or exposure-based infection risk estimation[14,59]. This discrepancy—over 1,500-fold lower—suggests that CDC's categorical framework may not sufficiently reflect exposure intensity or user vulnerability. While CDC guidance remains practical for general environmental monitoring, it lacks fixture specificity and does not account for the high transmissibility via aerosol inhalation from showering. Previous risk-based assessments have demonstrated that aerosol-generating fixtures such as showers can pose elevated infection risks at concentrations well below population-level action thresholds, particularly in healthcare settings[25,30]. Besides, global benchmarks like those from the WHO (<1 CFU/mL) or ISO 11731 similarly provide broad population-level thresholds but lack granularity for use in risk-based water safety plans for healthcare institutions. International guidance documents emphasize that facilities serving immunocompromised populations may require more conservative, exposure-specific targets than those intended for the general population[34,59]. Our results support calls for refined, use-specific targets to prevent infections in environments serving immunocompromised individuals.

The stark difference in critical concentrations between faucets and showers confirms that uniform monitoring thresholds are insufficient for accurately assessing Legionella infection risks in healthcare settings. Previous QMRA studies have demonstrated that infection risk varies substantially by fixture type due to differences in aerosol generation, exposure duration, and inhalation pathways, even when water concentrations are similar[25,30]. A more nuanced, risk-based management framework is needed—one that accounts for the specific exposure dynamics of each fixture type. This includes detailed modeling of fixture-specific exposure characteristics such as aerosol volume, duration of use, and frequency, which significantly influence infection risk. Risk-based frameworks for *Legionella* control increasingly emphasize exposure-informed modeling rather than reliance on single concentration-based thresholds, particularly in complex building water systems[75].

Moreover, infection benchmarks should be adjusted to reflect the vulnerability of high-risk hospital populations, potentially adopting more conservative targets such as an annual infection risk threshold of $\leq 10^{-5}$. Several authors have noted that acceptable risk benchmarks for immunocompromised populations may need to be more stringent than those applied to the general public, given the elevated severity and mortality associated with healthcare-associated legionellosis[34,59]. Surveillance strategies must also prioritize high-aerosol-generating devices like showers, ensuring they are monitored more frequently than lower-risk fixtures.

In addition, proactive interventions tailored to fixture type—such as maintaining appropriate hot water temperatures, installing point-of-use filters, and enforcing scheduled maintenance—are crucial to mitigate risks. Multiple studies have demonstrated that fixture-level interventions, including thermal control, filtration, and targeted maintenance, are effective at reducing *Legionella* amplification and transmission in healthcare water systems[26,31,55]. This approach is in strong alignment with contemporary water safety planning (WSP) principles and regulatory frameworks, including ASHRAE 188-2018 and CMS hospital water safety mandates. Water safety frameworks emphasize context-specific, risk-based control measures that prioritize high-risk fixtures and vulnerable populations rather than relying solely on system-wide concentration limits [57,59]These guidelines emphasize the importance of context-specific risk assessments, particularly in settings with highly vulnerable patients, and support the development of more protective, evidence-based water quality standards. A major strength of this study lies in its application of forward Monte Carlo simulation to estimate both infection probabilities and critical concentration thresholds for Legionella pneumophila. Probabilistic QMRA methods have been widely recommended for capturing uncertainty in pathogen occurrence, exposure, and dose–response relationships, particularly in complex building water systems[55,75]. This modeling approach, which utilized 100,000 simulation iterations, significantly improves robustness by capturing uncertainty across a range of inputs, including dose-response parameters, microbial concentrations, and exposure scenarios. Unlike static or deterministic methods, this probabilistic framework enables a more nuanced assessment of risk variability. Importantly, the study also incorporated fixture-specific exposure parameters—such as inhaled aerosol volume, usage duration, and frequency—thereby enhancing the real-world relevance of the modeled scenarios for faucets and showers in healthcare settings.

However, several limitations should be acknowledged. First, while infection probabilities were estimated, the model did not account for clinical severity or outcomes such as hospitalization or mortality. Previous studies have noted that QMRA frameworks focused solely on infection probability may underestimate public health impact when disease severity and outcomes vary substantially across populations, particularly among immunocompromised patients[34,55]. This limits the ability to weigh risks based on the differential health impacts of infection—especially critical in settings serving immunocompromised individuals. Second, key exposure parameters (e.g., aerosol fractions and inhalation rates) were derived from published literature rather than facility-specific measurements, which may reduce context-specific accuracy. Uncertainty in aerosolization efficiency and inhalation exposure has been identified as a major limitation in Legionella QMRA studies, particularly when site-specific measurements are unavailable [57]. Third, the model did not incorporate empirical dose-response data from actual hospital outbreaks, which limits its validation against real-world clinical outcomes. The lack of outbreak-linked dose–response data remains a recognized gap in Legionella risk assessment and constrains direct validation of modeled infection risks[30,31]

Future research should aim to overcome these limitations by integrating severity-adjusted health metrics, such as Disability-Adjusted Life Years (DALYs) or hospitalization rates, into the risk framework. Incorporating severity-weighted outcomes into QMRA has been recommended to better inform decision-making in high-risk settings and to prioritize interventions based on overall health burden rather than infection probability alone[33,55]Additionally, pairing environmental sampling with clinical case surveillance in healthcare facilities would enhance the empirical validation of QMRA tools and support the development of more context-sensitive infection control strategies.

Conclusion

This study demonstrates that sustained and structured water management practices can effectively maintain *Legionella* control within complex healthcare environments. The multi-year surveillance at the University of Washington Medical Center highlights how continuous monitoring, temperature regulation, and systematic maintenance can keep bacterial levels well within acceptable limits. Differences observed across facility wings and water temperatures emphasize the importance of localized assessment and targeted interventions, particularly in hot-water systems where conditions favor bacterial growth.

These findings reinforce the essential role of routine microbial surveillance as a cornerstone of *Legionella* risk management in healthcare settings. Long-term, data-driven approaches not only verify system performance but also enable timely identification of vulnerabilities before they result in patient exposure. The UWMC experience illustrates that proactive, rather than reactive, water management strategies are both achievable and sustainable, offering a model for similar institutions aiming to strengthen water safety and infection prevention efforts.

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Appendix:1

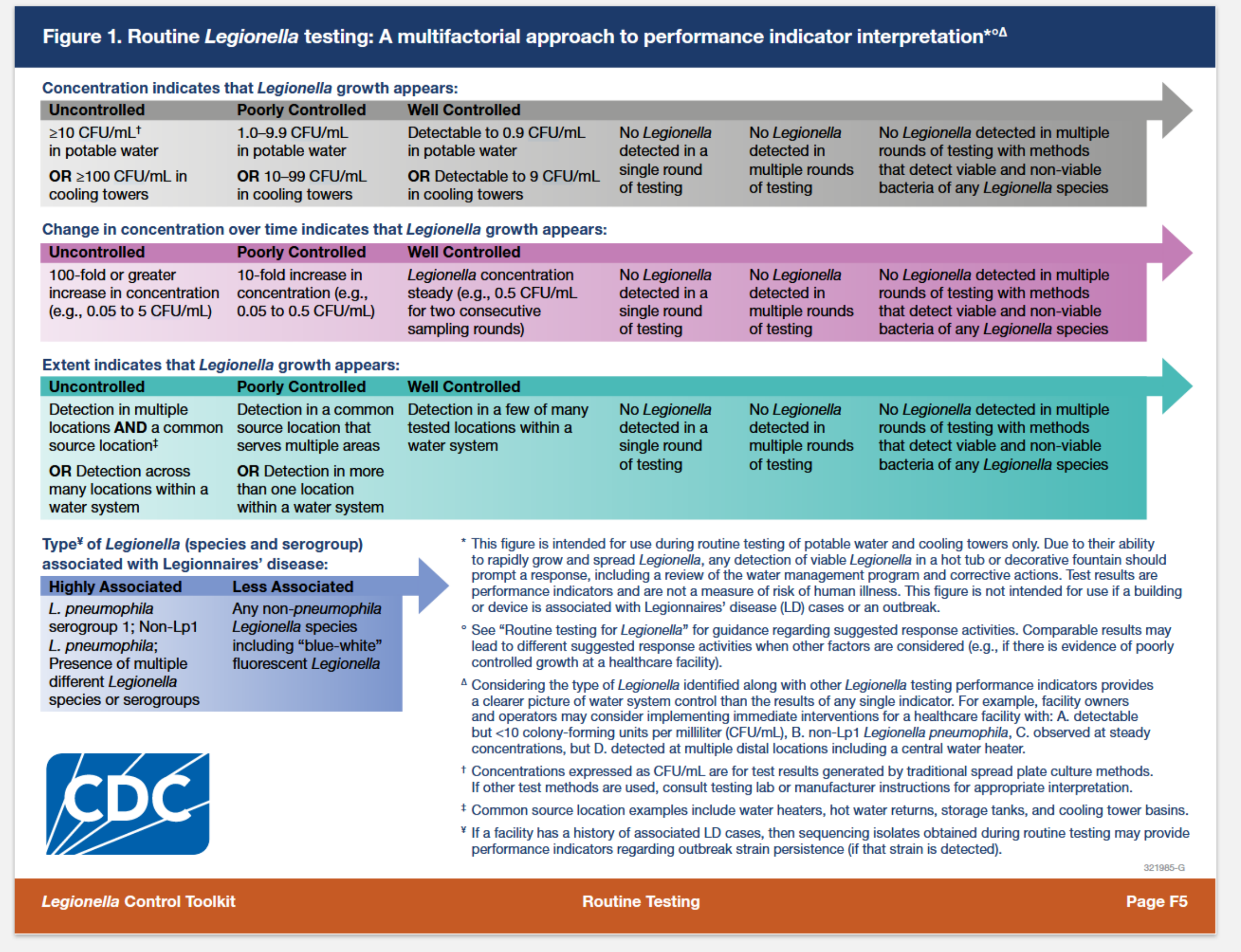

Figure 1. Routine *Legionella* testing: A multifactorial approach to performance indicator interpretation*°Δ

Concentration indicates that *Legionella* growth appears:

Uncontrolled	Poorly Controlled	Well Controlled			
≥10 CFU/mL† in potable water **OR** ≥100 CFU/mL in cooling towers	1.0–9.9 CFU/mL in potable water **OR** 10–99 CFU/mL in cooling towers	Detectable to 0.9 CFU/mL in potable water **OR** Detectable to 9 CFU/mL in cooling towers	No *Legionella* detected in a single round of testing	No *Legionella* detected in multiple rounds of testing	No *Legionella* detected in multiple rounds of testing with methods that detect viable and non-viable bacteria of any *Legionella* species

Change in concentration over time indicates that *Legionella* growth appears:

Uncontrolled	Poorly Controlled	Well Controlled			
100-fold or greater increase in concentration (e.g., 0.05 to 5 CFU/mL)	10-fold increase in concentration (e.g., 0.05 to 0.5 CFU/mL)	*Legionella* concentration steady (e.g., 0.5 CFU/mL for two consecutive sampling rounds)	No *Legionella* detected in a single round of testing	No *Legionella* detected in multiple rounds of testing	No *Legionella* detected in multiple rounds of testing with methods that detect viable and non-viable bacteria of any *Legionella* species

Extent indicates that *Legionella* growth appears:

Uncontrolled	Poorly Controlled	Well Controlled			
Detection in multiple locations **AND** a common source location‡ **OR** Detection across many locations within a water system	Detection in a common source location that serves multiple areas **OR** Detection in more than one location within a water system	Detection in a few of many tested locations within a water system	No *Legionella* detected in a single round of testing	No *Legionella* detected in multiple rounds of testing	No *Legionella* detected in multiple rounds of testing with methods that detect viable and non-viable bacteria of any *Legionella* species

Type¥ of *Legionella* (species and serogroup) associated with Legionnaires' disease:

Highly Associated	Less Associated
L. pneumophila serogroup 1; Non-Lp1 *L. pneumophila*; Presence of multiple different *Legionella* species or serogroups	Any non-*pneumophila Legionella* species including "blue-white" fluorescent *Legionella*

* This figure is intended for use during routine testing of potable water and cooling towers only. Due to their ability to rapidly grow and spread *Legionella*, any detection of viable *Legionella* in a hot tub or decorative fountain should prompt a response, including a review of the water management program and corrective actions. Test results are performance indicators and are not a measure of risk of human illness. This figure is not intended for use if a building or device is associated with Legionnaires' disease (LD) cases or an outbreak.

° See "Routine testing for *Legionella*" for guidance regarding suggested response activities. Comparable results may lead to different suggested response activities when other factors are considered (e.g., if there is evidence of poorly controlled growth at a healthcare facility).

Δ Considering the type of *Legionella* identified along with other *Legionella* testing performance indicators provides a clearer picture of water system control than the results of any single indicator. For example, facility owners and operators may consider implementing immediate interventions for a healthcare facility with: A. detectable but <10 colony-forming units per milliliter (CFU/mL), B. non-Lp1 *Legionella pneumophila*, C. observed at steady concentrations, but D. detected at multiple distal locations including a central water heater.

† Concentrations expressed as CFU/mL are for test results generated by traditional spread plate culture methods. If other test methods are used, consult testing lab or manufacturer instructions for appropriate interpretation.

‡ Common source location examples include water heaters, hot water returns, storage tanks, and cooling tower basins.

¥ If a facility has a history of associated LD cases, then sequencing isolates obtained during routine testing may provide performance indicators regarding outbreak strain persistence (if that strain is detected).

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Legionella Control Toolkit Routine Testing Page F5

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