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# Quantitative Performance Evaluation of Interventions for Pathogens and Chemical Contaminants in Building Water Systems: A Review and Meta-Analysis

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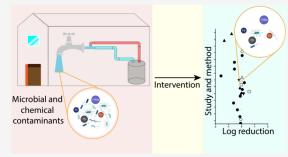
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ABSTRACT: Building water systems are associated with variable water age and temperatures, causing water quality concerns. Legionella spp., nontuberculous mycobacteria (NTM), and Pseudomonas spp. are known to inhabit and grow in these systems for which building-level interventions are often required to reduce their concentrations and detections. Other contaminants such as metals and disinfection byproducts (DBPs) are also health concerns. Interventions are typically flushing, temperature manipulation, responsive facility-level interventions (e.g., chemical disinfection and heat shock), or point-of-use devices. A systematic literature review was conducted to summarize interventions targeting pathogen control, and subsequent meta-analysis quantified their respective log



reduction values (LRVs). Across the studies (n = 45), Legionella spp. was the primary target (n = 45), and studies varied from laboratory benchtops/pipe racks to hospitals and residential or commercial buildings. Additional measurements and LRVs for heavy metals (e.g., copper, lead, and iron) and DBPs such as trihalomethanes (THMs) were evaluated. The findings pointed to the importance of contextual conditions and incoming water quality in playing a role in both pathogen occurrence and intervention effectiveness. Common interventions such as recommissioning flushing and increased temperature should be further examined for their impacts on pathogens besides Legionella spp. and their contribution to biofilm sloughing and pathogen regrowth. Trade-offs, such as increased metal leaching in parallel with pathogen inactivation, should be examined in context with intervention and building water quality conditions.

#### 1. INTRODUCTION

Building water systems, often referred to as premise or premises plumbing, are drinking water pipe networks specific to a property and in buildings, with distribution through water heaters and to end users and devices such as showers and faucets. Premise plumbing has been defined as the portion of a water system, including both hot and cold water, various devices (e.g., hot water heater, HVAC humidifier), fixtures (e.g., showers, faucets), and drains (e.g., sinks, toilets) connected to the main distribution system via service lines. These systems, while using incoming drinking water, vary by design and use and can be characterized by high temperatures, stagnation zones and higher water ages, and decreased disinfection residuals. Such water quality concerns at the building level can contribute to a number of adverse water quality outcomes and potential health risks.

A number of waterborne microorganisms such as *Legionella* spp., nontuberculous mycobacteria (NTM), and *Pseudomonas* spp. are known to inhabit and grow in building plumbing and water systems.<sup>7</sup> These microorganisms are often broadly

referred to as opportunistic premise plumbing pathogens, drinking water-associated pathogens that can cause infections in immunocompromised or otherwise susceptible individuals, environmental (saprozoic) pathogens of engineered water systems, or accidental pathogens. These genera and taxonomic groups such as NTM include both pathogens and non-pathogens; for example, the NTM group includes over 150 officially recognized species. They are commonly found in natural, as well as, built environments such as building water systems and predominantly pose a human health risk due to indoor building exposures (often from aerosols produced by water fixtures), especially in individuals with underlying health conditions but not exclusively in these populations. Together,

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infections from Legionella pneumophila, Mycobacterium avium, and Pseudomonas aeruginosa cause \$2.39 billion in annual healthcare costs in the United States. 13 Due to both their ability to form symbiotic relationships with other biofilm-dwelling microorganisms such as free-living amoeba and the capacity for survival in low-nutrient environments in a viable but nonculturable (VBNC) state, these bacteria can persist in engineered water systems for long periods of time, are resilient in the presence of intermittent and/or low level disinfectants, survive at elevated temperatures, and persist in biofilms. 14–16

Legionella spp. is one of the most widely studied bacteria in engineered water systems today as it is associated with waterborne respiratory outbreaks of Legionnaire's Disease and Pontiac Fever.<sup>17</sup> Legionnaire's Disease is one of the leading waterborne illnesses in the United States, with an increased risk to smokers, those who are immunocompromised, and those with underlying or chronic diseases. <sup>17</sup> There are more than 60 known Legionella species, 18 with L. pneumophila accounting for over 88% of cases in the U.S. and Europe, often with cases of Legionnaire's Disease being confirmed through the urinary antigen test and identified as Legionella pneumophila serogroup 1 in over 90% of U.S. cases. 19 Nearly 10,000 official cases were reported in the United States in 2018 and continue to trend upward, with a 95% hospitalization rate and 10% mortality rate of official cases.<sup>20</sup> As a result, Legionella is typically the focus of building water management plans and/or interventions, often at the expense of other considerations such as chemical contaminants (e.g., heavy metals or disinfection byproducts [DBPs]) or sustainability. While no drinking water regulation exists for Legionella spp. and not all Legionella species are pathogenic, many studies have established monitoring approaches and risk-based targets based on its presence in building water systems, linking its potential presence to an established concentration threshold for intervention. 11,12

Water quality management interventions are any action or control measure that is implemented to limit, reduce, or eliminate contaminants in buildings. Building-level interventions are typically focused on flushing, system water temperature manipulation (e.g., water heater set point controls or thermostatic mixing valve settings), responsive facility-level interventions after a problem is identified (e.g., chemical disinfection, heat shock), or point-of-use (POU) treatment device implementation (e.g., faucet filters, reverse osmosis units, or UV disinfection units).<sup>23</sup> Recommended disinfection strategies for pathogens in building water systems, such as Legionella spp., can include chlorine, monochloramine, chlorine dioxide, copper-silver ionization, ultraviolet (UV) light disinfection, and ozone.3 The scales and application of these methods varies, such as with ozone which is used in drinking water treatment around the world, and less as an onsite disinfectant for buildings since it rapidly decays, producing no disinfectant residual.3 Advancing quantitative, evidence-based water quality management in buildings is key, especially for pathogens, as reduction of their occurrence is critical for reducing acute infection risks. 21,24,25 While water management plans are recommended by numerous building water guidance documents, <sup>4,26,27</sup> there is currently no standardized approach to address water quality improvement in building water systems, due in part to complexities and heterogeneities of building types and their associated water conditions, inconsistencies in regulatory paradigms (e.g., the Lead and Copper Rule (40 CFR 141.80) vs guidelines for Legionella spp. 22), and logistical challenges

related to defining and evaluating successful intervention

Trade-offs among water quality contaminants can result from various management interventions, <sup>28</sup> and novel approaches to reduce these hazards holistically are needed as there is still uncertainty regarding their prediction and control. Additional data are needed to quantitatively evaluate predictors of the prevalence of pathogens in building water systems as well as the effects of water use, stagnation, and control measures at multiple scales, including consideration of uncertainties. <sup>29,30</sup> To date, a quantitative evaluation of the effectiveness of reported pathogen interventions and of the unintended consequences of pathogen control measures on chemical contamination in building water systems has not been performed.

Given the importance of quantitative treatment reduction requirements in the water treatment and reuse schemes, 31,32 there is a potential for increasing efforts to quantify the risks and benefits of different in-building water quality management strategies to better inform decision-making. Identification and quantification of effective measures for reducing and preventing pathogen growth in building water systems are therefore a critical first step in establishing more evidence-based water quality management approaches. To advance a quantitative understanding of the efficacy of building water control measures, we conducted a systematic review and meta-analysis of the literature addressing intervention measures, with a focus on the control of bacteria, (primarily Legionella spp., NTM, and Pseudomonas spp.) and effects on holistic water quality in situations where data are at the minimum reported for pathogens. In this context, "holistic" was defined and used by Proctor et al. (2022) to refer to the interconnectedness of health impacts, cost, and energy with regard to water quality and approaches to its maintenance and design. Our objectives were therefore to 1) review and synthesize studies on water quality interventions at different single building scales, focusing on studies that quantified pathogens and secondarily on other health-relevant contaminants (heavy metals, DBPs) and their potential trade-offs; 2) quantify the effectiveness of reported control measures based on measurements made before and after a water quality intervention; 3) for studies where additional contaminant information was available, quantify simultaneous contaminant removal or increase; and 4) identify the conditions which affected the success of water quality interventions. By compiling this information, the overall goal of this work is to critically evaluate in-building water quality intervention measures to inform the design of water management plans.

## 2. INTERVENTION AND CONTROL MEASURES FOR BUILDING WATER SYSTEMS

For this review, the PRISMA process was used to screen and collect literature data, resulting in 45 papers for data extraction. Study characteristics are provided in Table 1, and a more detailed description of this process and methodology is given in the Supporting Information. The goal of this study was to summarize and compare the effectiveness of implemented control measures quantitatively through log-reduction of pathogens and chemical contaminants (for inclusion criteria and data extraction details, see the Supporting Information, methods section). This allowed for normalization across studies including pathogens, metals, and DBPs regardless of the scale and units of measurement for direct comparison before and after the treatment. Log-reduction values (LRVs) are commonly used to assess unit process performance, particularly in water/

Table 1. Summary of Reviewed Studies, Control Measures, and Targeted Parameters

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		lab										49			>						>	>		>	>					>
		source	Baron et al. (2015) <sup>129</sup> Bedard et al. (2016) <sup>98</sup> Berthelot et al. (1998) <sup>52</sup>	Best et al. $(1983)^{105}$ Blanc et al. $(2005)^{54}$	Borella et al. (2016) <sup>59</sup>	Chen et al. $(2007)^{33}$ Ciesielski et al. $(1984)^{96}$	Coniglio et al. (2018) <sup>134</sup>	De Giglio et al. $(2021)^{84}$ Duda et al. $(2014)^{97}$	Edelstein et al. $(1982)^{85}$	Flannery et al. $(2006)^{3}$ Greenwald et al. $(2022)^{95}$	Grimard-Conea et al. (2022) <sup>94</sup>	Grimard-Conea & Prevost (2023) <sup>64</sup>	Hirsh et al. $(2020)^{139}$ Hozalski et al. $(2020)^{102}$	Huang et al. (2023) <sup>103</sup>	Ji et al. (2018) <sup>50</sup>	Joshi et al. $(2023)^{57}$	Kim et al. $(2023)^{-1}$ Liu et al. $(1998)^{82}$	Lytle et al. $(2021)^{71}$	Makin & Hart $(1990)^{136}$	Marchesi et al. $(2012)^{69}$	Marchesi et al. $(2013)^{70}$	Meegoda et al. (2023)	Moore et al. $(2006)^{22}$ Orsi et al. $(2014)^{65}$	Rhoads et al. (2015) <sup>55</sup>	Rhoads et al. (2017) <sup>83</sup>	Rhoads et al. $(2020)^{100}$ Rhoads et al. $(2022)^{101}$	Richard & Boyer (2021) <sup>104</sup>	Serrano-Suárez et al. (2013) <sup>117</sup>	Snyder et al. $(1990)^{68}$	Thomas et al. (2004) <sup>15</sup>

DBPs metals positive detections) concentration pathogen target intervention method commercia hospital lab Zacheus & Martikainen (1996)<sup>58</sup> van der Kooij et al. (2005)<sup>51</sup> Unterberg et al. (2021)<sup>53</sup> Wang et al. (2012)<sup>138</sup> Xue et al. (2020)<sup>139</sup>

Table 1. continued

was tewater treatment and reuse systems. They are especially useful in assessing risk-based criteria and human health protection.  $^{35,36}$ 

We applied this concept as a simplification to the reviewed interventions and treatments in engineered water systems to assess their treatment performance in reducing pathogen concentrations and to compare the results across methods and contaminants. First, we define and outline the types of interventions reviewed below. For each of the interventions, Table 2 highlights expected and demonstrated impacts (as an increase or decrease) to pathogens and contaminants reviewed in this study. Based on our approach and assessment of log-reductions, a positive LRV is a decrease in concentration after intervention or treatment, and a negative LRV is an increase. Specific equations and assumptions for these values are outlined in the Supporting Information.

2.1. Physical Treatment. 2.1.1. Flushing. Building and engineered water system complexities and variable water use patterns can lead to increased stagnation and water age, which is a contributing factor to the presence and growth of waterborne pathogens.<sup>37,38</sup> One of the simplest and most common methods of removing contaminants is flushing the system. Flushing for these purposes has previously been defined as running water through components to turn over water in building water systems to remove contamination.<sup>39</sup> It is common practice to reduce the water age within the system and to remove contaminants after any periods of prolonged stagnation. In practice, the water is left running on either the "cold" or "hot" setting for a designated period (e.g., 5 min) before postflush samples are taken. Flushing was used as the sole method (n = 18)or in combination with another method (n = 9) in the majority of the studies reviewed (n = 27/45).

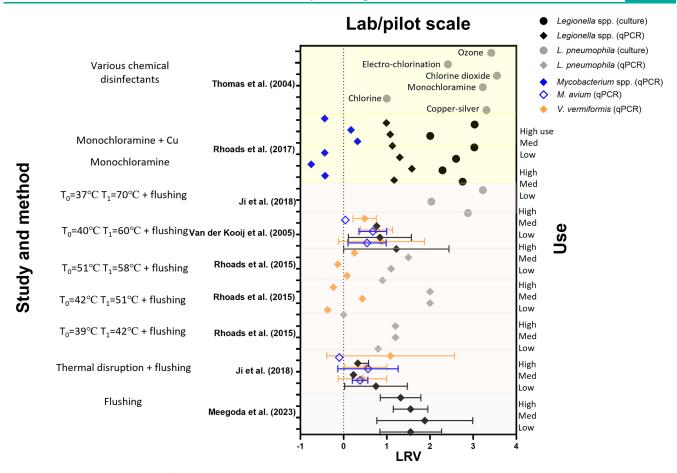
2.1.2. Thermal Disinfection. Temperature plays a key role in the growth and proliferation of opportunistic pathogens as they have been shown to grow in a wide range of temperatures.<sup>40-</sup> However, exposure to high temperatures can be an effective tool for inactivation and eradication within plumbing systems. It has been shown that temperatures above 55-60 °C are generally adequate for control. 43-45 Despite this, in many cases, Legionella spp. have demonstrated persistence, thermotolerance, and regrowth at temperatures up to 70 °C (Table 2).46-48 For many systems in which the water heater setting was 55-60 °C, an increase to a higher set point temperature (typically 55 °C across the network or 60 °C at the outlet) was implemented and is referred to as the "set point change" in this review. Set point change simply refers to the new temperature setting of the hot water heater and does not necessarily mean that the water is delivered to the tap or distal point at the indicated temperature, and still recirculation and heat transfer dynamics may impact consistent temperature maintenance.<sup>49</sup> This change is usually accompanied by flushing to compare with preheated or firstflush concentrations.

Some applications using higher temperatures (65–75 °C) for a short period of time are referred to as "thermal shock" or a "superheat" method of thermal disinfection.  $^{50,51}$  Studies which utilized set point change specified adjusting the water heater temperature setting. "Superheating" referred to increased water temperature above 65 °C or increased heat and flushing using an external circulation system. Thermal disinfection in the form of thermal/heat shock,  $^{50}$  superheat,  $^{52-54}$  or water heater set point change  $^{50,51,55-59}$  was used by 11 total studies.

2.1.3. Point of Use (POU) Filtration. Adding a point of use filter at distal outlets and taps is used to remove contaminants at

Table 2. Identified Intervention Effects and Expected Outcomes of Contaminants Included in This Review

intervention	impacts on pathogens (e.g., Legionella)	impacts on metals	impacts on disinfection byproducts
Flushing	$\downarrow$ Physical removal from plumbing, reintroduction of lower age water with higher chlorine residual (if chlorinated) $^{37}$	↑↓ Depending on pipe materials, water chemistry, and flushing procedure, flushed water may remove metals or cause increased leaching 140,141	↓ Increased water age can contribute to higher DBP concentrations, but flushing has demonstrated reduction of concentrations.
	$\uparrow$ May reintroduce higher temperature water and nutrients to shock the system into stimulating biomass growth after low use periods $^{5.50,94,101}$		
Thermal disinfection	$\downarrow$ Thermal inactivation of <i>Legionella</i> spp. is generally found to be adequate above 55–60 $^{\circ}$ C <sup>43–45</sup>	$\uparrow$ Higher temperatures increase lead solubility <sup>143</sup>	† Higher temperatures result in increased reaction rates for trihalomethane formation and volatilization 144
	$\uparrow$ Water in stagnant/ dead legs has temperature increased to stimulate growths (not all water is exposed to sufficiently high temperatures), and demonstrated persistence, thermotolerance, and regrowth at temperatures up to $70^{\circ}\text{C}^{\text{Ho}-48,142}$		
Point of use filtra- tion	$\downarrow$ Physical removal at distal points $^{60,61}$	$\uparrow$ Physical removal at distal points $^{146}$	$\ensuremath{\downarrow}$ Physical removal or adsorption at distal points $^{147}$
	↑ Pathogens can colonize filters <sup>145</sup>	$\uparrow$ Increase in iron concentrations from filter material leaching $^{146}$	$\uparrow$ Increase in DBP production from biofilms on aged filters $^{147}$
Chlorine residual	↓ Effective oxidant for pathogen disinfection <sup>148</sup>	$\uparrow$ Precipitation of plumbing materials, such as lead <sup>151</sup>	$\uparrow$ Reacts with organic matter to produce DBPs $^{152}$
	† May not sufficiently reduce resistant bacteria or penetrate biofilms, <sup>149</sup> may decay more quickly at higher temperatures <sup>150</sup> or when exposed to iron or copper corrosion and cause subsequent pathogen regrowth <sup>120,121</sup>		
Monochloramine	↓ Control of pathogens with better biofilm penetration and efficiency than free chlorine residual <sup>71</sup> ↑ Precipitation of plumbing materials, such as lead <sup>151</sup>	$\uparrow$ Precipitation of plumbing materials, such as lead $^{151}$	↓ Tendency to not form DBPs; thus a transition from chlorine residual to monochloramine should result in decreased concentrations. <sup>125</sup>
	† Some bacteria like NTM are more resistant to monochloramine and increase		
Copper—silver ion- ization	$\downarrow$ Pathogen control through dosing of copper and silver ions $^{154}$	$\uparrow$ Interaction with plumbing materials causing deposition and corrosion $^{155}$	N/A
Ozone	$\downarrow$ Demonstrated reductions of <i>Legionella</i> spp. in onsite applications <sup>40</sup>	N/A	N/A
Hydrogen peroxide	Hydrogen peroxide $\;\;\downarrow\;$ Demonstrated reductions of Legionella pneumophila $^{90}$	N/A	N/A



**Figure 1.** Log reduction values (LRVs) of measured bacteria and amoebae (*V. vermiformis*) for intervention measures at the lab and pilot scale. Bacteria concentrations were reported as CFU per volume (culture) or as gene copies per volume (molecular) as measured by qPCR.

the point-of-use rather than at the source. Although it can be expensive to implement throughout an entire facility, POU filters have proven to be effective treatment options when used and maintained correctly. POU filters are utilized in two studies in this review. <sup>59,62</sup>

**2.2.** Chemical Disinfection. 2.2.1. Chlorine Residual. While its usage in water treatment and distribution is not ubiquitous, 63 free chlorine has been demonstrated as an intervention method at the building level. It is usually associated with a residual measurement after leaving a treatment plant but in this study is assessed as a form of additional onsite treatment and/or secondary disinfection. Onsite, the addition of supplemental chlorine residual in various forms and through different technologies is an option for chemical disinfection and pathogen removal. Similar to thermal shock, "shock chlorination" has been used as a short-term control measure and is the addition of chlorine to exceed maximum allowable free chlorine concentrations in drinking water, such as adding up to 20 to 50 mg/L.64 Hyperchlorination is performed through additional chlorine, either intermittent or continuous, to ensure 0.5-1.0 mg/L at distal points throughout the system.<sup>65</sup> Electrochlorination was assessed in one study. 15 As a form of continuous hyperchlorination, electrochlorination achieves free chlorine concentrations 0.5–1.0 mg/L through production of chlorine solution by electrolyzing a side-stream of salt water. 66 Chlorine dioxide can control pathogens and has demonstrated improved biofilm disinfection when compared to free chlorine.<sup>6</sup> As a gaseous solution, it is injected into the water supply as with chlorine and is generated onsite chemically or electrochemically.

However, it can react with corrosion processes in pipes, may break down to form DBPs, and has higher maintenance and costs compared to free chlorine (Table 2). Chlorine disinfection was used by five studies in this review, usually as "shock" chlorination, 15,59,64,65,68 and chlorine dioxide was used by four studies. 15,59,69,70

2.2.2. Monochloramine. By adding ammonia to chlorinated water, the use of monochloramine can be an effective secondary disinfectant for drinking water distribution and building water systems. When compared with free chlorine, monochloramine is thought to penetrate biofilms more efficiently and therefore provide better control of Legionella spp. Monochloramine residuals demonstrate better persistence as well, as free chlorine may decay more quickly at higher temperatures or when reacting with iron. Instances have been reported where a switch from a free chlorine residual to monochloramine was performed, resulting in a lower prevalence and reduced concentrations of Legionella spp. as well as a decreased number of reported infections. Several studies in this review utilize this intervention method (n = 12).

2.2.3. Copper/Silver lonization. Copper—silver ionization is a process that uses an electric current with a copper and silver electrode to disperse positively charged ions into the water supply. These ions then electrostatically bind with biofilms and cell membranes, destroying them in the process, thus reducing the levels of *Legionella* spp. in the system. Much like chlorination, a residual level of ions must remain in water to be effective. These levels vary by water quality, but generally are around 0.2 and 0.8 mg/L for copper and between 0.02 and 0.08

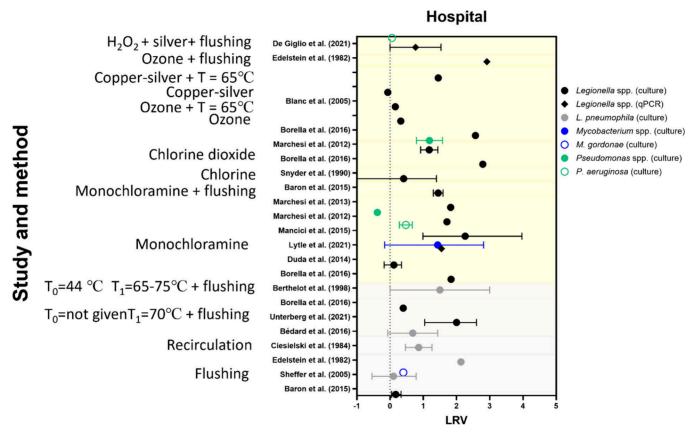


Figure 2. Log reduction values (LRV) for measured bacteria concentrations across intervention measures in hospitals.

mg/L for silver,  $^{78,79}$  although the total dosing will depend on the water chemistry. Copper and/or silver ionization was used by six studies in this review.  $^{15,54,80-83}$ 

2.2.4. Ozone. Ozone has become a popular method of water and wastewater treatment, often utilized in combination with hydrogen peroxide and UV for the advanced oxidation of wastewater. It is a strong oxidant and disinfectant, with mechanisms for cell lysis.<sup>84</sup> This biocidal activity has shown to be greater than free chlorine at much lower concentrations (around 0.1 mg/L vs 1 mg/L free chlorine).85,86 However, studies have suggested it be used in tandem with free chlorine or other methods due to its lack of a residual effect over time.<sup>54</sup> While it is more commonly implemented in larger scale municipal drinking water or wastewater treatment, 87,88 ozone was used as a control method for building water systems in a few (n = 3) studies in this review, often to compare with free chlorine efficacy. Blanc et al. (2004) and Edelstein et al. (1982) assessed the efficacy of onsite ozone disinfection in a hospital on Legionella spp. and L. pneumophila, respectively. 54,85 The first was located in Switzerland and was tested on water without free chlorine and a residual ozone concentration around 0.3 mg/L, and the second contained free chlorine residual around 0.1 mg/ L. The third study, Thomas et al. (2004), applied ozonation to a laboratory pipe rack setup to reduce *L. pneumophila*. 15

2.2.5. Hydrogen Peroxide. Similarly to ozone, hydrogen peroxide is an advanced oxidation process and also is occasionally used as an in-building disinfectant. <sup>89</sup> Casini et al. (2017)<sup>90</sup> note its stability at higher temperatures, higher oxidation potential than chlorine dioxide, lower corrosive properties, and reduced overall costs than more traditional disinfection methods, such as chlorine. It has been used for cleaning and disinfection of dental units <sup>91,92</sup> and has been

applied for municipal water treatment in building water systems. <sup>81</sup> It was applied by one study in this review as continuous treatment with both hydrogen peroxide and silver ions in a university hospital. <sup>81</sup>

## 3. PATHOGEN LOG REDUCTION VALUES (LRVs) ACROSS DIFFERENT BUILDING TYPES

From the selected studies, the extracted concentration data were further sorted based on the scale and setting of the research (lab/pilot scale [n = 6], hospital [n = 23], or residential/commercial [residential, n = 3], [commercial n = 15]) and on the method of intervention used.

Lab/Pilot Scale. Laboratory scale studies generally applied control measures to recirculating tap water in pipe racks on a small scale to reduce Legionella spp. (Figure 1). Ji et al. (2018),<sup>50</sup> Rhoads et al. (2015), 55 and Rhoads et al. (2017) 83 all acclimated their rigs to local municipal drinking water prior to experimentation. Ji et al. (2018) investigated the effects of two thermal disinfection methods, thermal disruption and heat shock. For both methods, concentrations were measured before and after a 30 min flushing event during which the water heater set point was 60 °C, before being changed to 40 °C. For heat shock, the system had been operating at 40 °C, and for thermal disruption the system had already been operating at 60 °C, thus effectively utilizing a simple flushing event followed by lowering the set point temperature. The authors illustrated their results as several samplings, and the LRVs shown here (Figure 1, "thermal disruption" and " $T = 60^{\circ}$ C") are based on the average and standard deviation of log reduction across all samples. Rhoads et al. (2015) also evaluated water heater set point change, from a control temperature of 39 °C to 42, 51, and 58 °C. 55 Rhoads et al. (2017) utilized chemical disinfection, comparing the impacts

### Residential/commercial

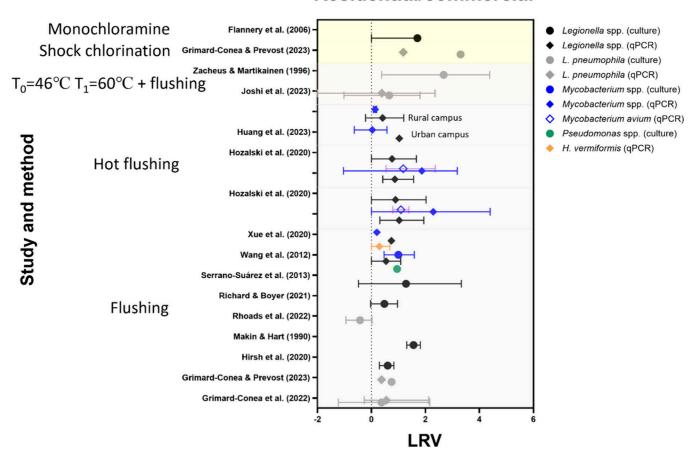


Figure 3. Log reduction values (LRV) for measured bacteria or amoebae (*H. vermiformis*) concentrations across intervention measures in residential or commercial buildings.

of monochloramine with or without additional dosed copper ions. 83 Interestingly, higher temperatures (60 °C or higher) did not necessarily correspond to higher LRVs for flushing when compared to "cold" (unheated) or lower temperature water heater set changes. Reintroduction of warmer temperature water (40–60 °C) throughout the system without thorough biomass eradication may unintentionally cause bacterial regrowth. 47,51 A review of temperatures in hotel plumbing and their effect on Legionella spp. yielded a recommendation that maintaining temperatures of 55-59 °C in the building water system was adequate to control *Legionella*. 93 This maintenance is often difficult due to pipe lengths and patterns and could carry a potential scalding risk at the point of use. Thus, recommended temperatures for thermal disinfection and control of pathogens have demonstrated effectiveness after thermal shock and flushing procedures but are often difficult to put into regular practice due to concerns over scalding, energy, and cost impacts, and uncertainties of thorough temperature exposure.

Thomas et al. (2004) and Van der Kooij et al. (2005) both inoculated their systems with *L. pneumophila* either directly<sup>51</sup> or by mixing river water with drinking water and allowing for regrowth. Thomas et al. (2004) compared multiple chemical disinfectants, yielding LRVs between 1 and 3.55 for all trials. Van der Kooij (2005) compared copper (Cu), stainless steel (SS), and cross-linked polyethylene (PEX) piping rigs using a superheat (SPC to 70 °C) and flush intervention midstudy. While the various materials demonstrated different rates of *L. pneumophila* growth, the midstudy superheat and flush event

was successful in all three cases for immediate pathogens, with LRVs between 2.0 and 3.3, but saw rapid regrowth in the days following.

Across all studies, the impacts of control measures yielded log reductions of all *Legionella* species (Figure 1, LRV up to 3.55). The only negative log reductions, indicating lack of pathogen removal, were using copper and monochloramine for mycobacteria (as low as -0.75 LRV), <sup>83</sup> and various SPCs for *V. vermiformis* and *M. avium* (as low as -0.37 and -0.1, respectively). <sup>55</sup>

Both culture and molecular (qPCR) results were reported across the studies. Studies which reported both, such as Rhoads et al. (2017), noted lesser impacts of treatment on gene copy numbers (as represented in this study by a smaller LRV). This is likely because qPCR detects live (culturable and/or metabolically active) but also dead and viable but nonculturable (VBNC) cells. Large discrepancies between culture and qPCR concentrations may be accounted for by the VBNC cells from less favorable conditions (stagnant or higher temperatures), which was also reported in other studies in this review, <sup>94,95</sup> among other factors such as different assay detection limits, the number of target genes per cell genome, and analytical process recoveries as a function of sample characteristics.

**3.2. Hospitals.** Nineteen studies applied control measures in hospital water systems, and the results of LRV calculation are shown in Figure 2. As with lab-scale studies, there was a variety of physical and chemical disinfection methods, and often a combination of the two (such as ozone and increased

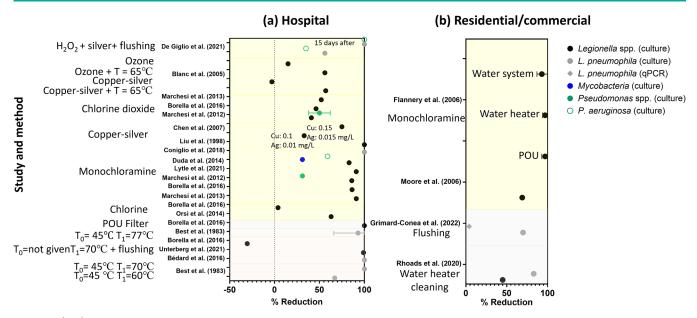


Figure 4. (a, b) Percent reduction of positive detections based on intervention method and treatment setting.

temperature <sup>54</sup>). Overall, LRVs ranged from -1.9 to 4.4. One study reduced L. pneumophila by constant recirculation through the water heater system. <sup>96</sup> A negative LRV was observed for one case of thermal disinfection and flushing for L. pneumophila, copper—silver ionization interventions on Legionella spp., <sup>54</sup> and monochloramine on Legionella spp., <sup>97</sup> Pseudomonas spp., <sup>69</sup> and Mycobacterium spp., <sup>71</sup> all measured by culture.

Two studies evaluated the performance of point-of-use filters for pathogen removal in a hospital setting,  $^{59,62}$  in addition to other methods. This method proved to be successful, resulting in no detection of *Legionella* spp. after implementation. Sheffer et al.  $(2005)^{62}$  conducted a study of flushing using POU filters in a hospital, noting that *Legionella* spp. was not detected in any filtered samples before and after the flushing event; no LRV was estimated in this case.

The limit of detection was "unacceptably high" for Bédard et al. (2016), where thermal disinfection was used. <sup>98</sup> For example, in one of their studied subsystems, a reduction of at least 1.4 LRV was observed, when substituting a 1000 CFU/L limit of detection for nondetect observations (n=1). In another subsystem studied by the authors, suboptimal recirculation was observed with large temperature differences across the plumbing sections. Inability to maintain the high flush temperatures may have allowed for L. pneumophila regrowth in these sections. System A (water for one hospital wing) began the study with 10-times higher L. pneumophila counts than System B (a separate hospital wing) and therefore may have also influenced these observations.

While Blanc et al.  $(2005)^{54}$  demonstrated LRV of -0.068 to 1.45 (Figure 2), they reported that neither ozone nor coppersilver ionization reduced the number of positive detections of *Legionella* spp., likely attributed to a lack of residual ozone over time and low copper-silver ion concentrations. The demonstration of monochloramine disinfection by Marchesi et al.  $(2012)^{69}$  showed the concentration of monochloramine used was effective in reducing *Legionella* spp. but had no significant effect on *Pseudomonas* spp. (LRV = -0.38). In this case, chlorine dioxide was a more effective method for reduction of both pathogens (LRV = 0.79 to 1.58).

**3.3. Residential/Commercial.** The remaining studies (n = 16) involved measures conducted in residential or commercial settings, often in homes or university buildings (Figure 3). The majority utilized flushing (n = 13), one flushed with increased temperature (SPC), <sup>57</sup> two used chemical disinfection through shock chlorination <sup>64</sup> and monochloramine, <sup>99</sup> and one study conducted a thorough cleaning of water heater systems. <sup>100</sup>

On average, flushing reduced the pathogens for all cases of "after" measurements except one study. 101 In this study, 101 impacts of stagnation and a recommissioning flushing event were measured. L. pneumophila numbers were higher in the 1-2weeks after this recommissioning flushing, when compared with both first-flush samples and flushed samples before the flushing event. The flushing events for all temperatures also demonstrated the greatest variation (Figure 3). For Legionella spp., flushing LRVs ranged from -1.02 to 4.38 for culture-based methods and from -2.36 to 2.36 for molecular-based methods. Large ranges were also observed for mycobacteria (LRV −1.04 to 4.4). Flushing was the most practiced method of intervention; it also had the greatest variability in pathogen reductions. Flushing is intended to clear out the plumbing system, particularly to remove the accumulation of contaminants in dead-end areas where stagnation occurs. Yet, these dead-end areas in complex networks are difficult to manage and predict, which was illustrated by the lower effectiveness of flushing for a hot water system with more distal points (Table S1). 98 Several of the residential/commercial buildings required recommissioning flushing after a period of low-use or stagnation, such as during the COVID-19 pandemic (n = 5 studies). <sup>94,101–104</sup> Regular or routine flushing is recommended, but after such periods of stagnation or low use, a recommissioning flushing event may actually increase pathogen concentrations. This first flush is noted to potentially reintroduce higher temperature water and an influx of nutrients, which have been shown to shock the system into stimulating biomass growth after low use periods and was demonstrated in several of the studies. 5,50,94,101 This may explain the range of results and error bars below zero (Figure 3).

For chemical disinfection in residential/commercial buildings, LRVs were positive (Figure 3), with shock chlorination

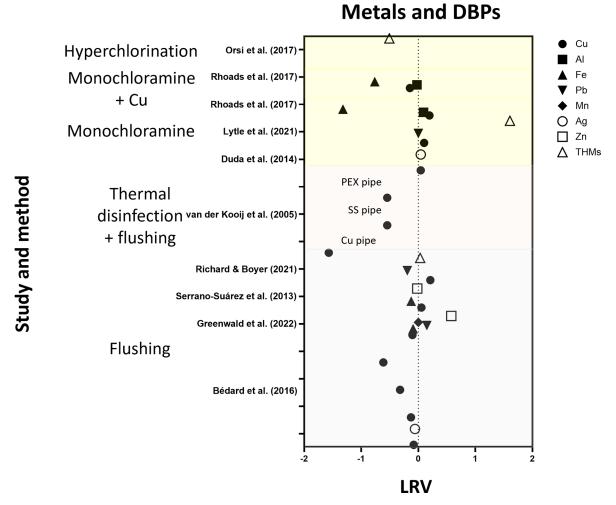


Figure 5. Log reduction of reported concentrations of metals and trihalomethanes across all studies.

resulting in LRVs of 3.3 and 1.2 for culture and molecular detection of *L. pneumophila*, respectively,<sup>64</sup> and an average of 1.7 for *Legionella* spp.<sup>73</sup>

3.4. Reductions for Pathogen Prevalence (Percent Positive Detections). The percent reduction of positive detections was quantified from the studies that reported this in addition to concentrations (n = 9) or only reported prevalence data (n = 7) and illustrated in Figure 4 similarly to Figures 1–3. Similar trends and patterns in pathogen reduction were noted compared with studies reporting quantitative data. When thermal disinfection studies were compared, increasing the temperature was more effective in reducing the number of detections. For example, a 70 °C heat shock followed by flushing had a 100% reduction in positive detections for Bédard et al. (2016), <sup>98</sup> and increasing from 60 to 70 °C reduced the number of detections, resulting in 100% reduction at the higher temperature. 105 However, one study 59 reported the detections between the start and end of the entire study duration (6 months) and found superheating and flushing to be the most unreliable due to excessive regrowth after 2 weeks of treatment, eventually exceeding the initial detections by over 30% (Figure 4). Prevalence data and distal site positivity for Legionella spp. are useful for hospitals in particular for evaluating legionellosis risk, and a 30% site positivity has shown to be an appropriate threshold. 106,107 The instances where a hospital intervention did not result in positivity below 30% were ozonation and coppersilver ionization (56% and 93%), <sup>54</sup> chlorine dioxide (56%, 61%,

and 46% for various systems), <sup>69,70</sup> and hydrogen peroxide and silver ions (46%, although after 15 days of treatment it was reduced to 0%). <sup>97</sup>

**3.5. Other Contaminants.** In addition to pathogens, several reviewed studies also measured metals (n = 9) and DBPs (n = 3) before and after their interventions. The LRVs of both metals and DBPs across all studies are illustrated in Figure 5 and Figures S1–S3 in the Supporting Information.

3.5.1. Metals. While several of the studies (n=9) measured specific metals pre- and postintervention, the interplay between metals and pathogens in building water systems was underexplored. The most commonly observed metal was copper (n=8), likely due to its interactions with and inhibition of bacteria, through the use of copper ion dosing or copper—silver ionization as a control measure, or through corrosion from copper piping. These efforts resulted in increased copper post-treatment (LRV -1.57 to -0.15, Figure 5). Flushing results varied between positive and negative LRVs regardless of the pipe material. This may have been due to accumulation rates observed on pipe inner surfaces and subsequent removal through flushing, depending on the source water concentrations. Iron, copper, and aluminum were observed to increase over time in a copper system due to increased deposition corrosion. 83

Stagnation causes increased dissolution of metals into the water from the plumbing system or hot water tanks. <sup>109–111</sup> Heavy metals in drinking water cause adverse health effects <sup>112</sup> and are regulated in drinking water. <sup>113</sup> Contributing factors to

Table 3. Summary of Studies Which Monitored Multiple Contaminants before and after Control Measures<sup>a</sup>

source	intervention	Legionella	Mycobacteria	Pseudomonas	amoeba	metals	DBPs
Bédard et al. (2016) <sup>98</sup>	Heat shock and flushing	±				+	
De Giglio et al. (2021) <sup>81</sup>	Hydrogen peroxide, silver ions, and flushing	_		_			
Duda et al. (2014) <sup>97</sup>	Monochloramine	_	_	_		±	
Huang et al. $(2023)^{103}$	Flushing	_	_				
Ji et al. $(2018)^{50}$	Thermal disruption and heat shock	-	_		-		
Lytle et al. (2021) <sup>71</sup>	Monochloramine	_	_			_	
Mancici et al. (2015) <sup>137</sup>	Monochloramine	_		_			
Marchesi et al. (2012) <sup>69</sup>	Monochloramine	_		+			ND
	Chlorine dioxide	_		_			ND
Orsi et al. (2014) <sup>65</sup>	Hyperchlorination	_					+
Rhoads et al. (2015) <sup>55</sup>	SPC and flushing	-			+		
Rhoads et al. (2017) <sup>83</sup>	Monochloramine and copper ionization	_	+			+	
Richard & Boyer (2021) <sup>104</sup>	Flushing	_				±	_
Serrano-Suárez et al. (2013) <sup>117</sup>	Flushing	±		_		±	
Sheffer et al. $(2005)^{62}$	Flushing	±	_				
van der Kooij et al. $(2005)^{51}$	Superheat and flush	_				+	
Wang et al. (2012) <sup>138</sup>	Flushing	-	_		-		
Xue et al. $(2020)^{139}$	Flushing	_	_				

<sup>&</sup>quot;Symbols indicate a reduction (-), increase (+), not detected (ND), or not performed (blank) for each study.

increased exposures are variations at distal points due to water use patterns and seasonal variations. 114 As with pathogens, a single flushing event aimed at lowering concentrations of metals (lead and copper) only provided temporary benefits, as stagnation and subsequent first-draws resulted in higher concentrations. 115,116 Moreover, some metals such as iron or zinc are critical for bacterial growth, and Serrano-Suárez et al. (2013)<sup>117</sup> found a logistic relationship between Legionella spp. and iron concentrations above 0.095 ppm. While a detailed discussion of chemical mechanisms is addressed elsewhere,  $^{118,119}$  the importance of the relationship between metals (copper and iron), pH, and Legionella spp. is acknowledged here. A study in Flint, MI also indicated iron corrosion as a key contributor for reducing and/or removing chlorine residuals. 12 In plumbing conditions with increasing iron or iron corrosion (such as lower pH<sup>121</sup>), iron appears to be a key player in stimulating Legionella spp. proliferation and provides useful information alongside other factors in monitoring plans. Other studies have shown the demand for free chlorine residual (and thus decay of chlorine) from copper oxides and subsequent Legionella spp. growth. 122,123 Further investigation between elevated metal concentrations, biomass growth or inhibition, water chemistry, and stagnation or management interventions is recommended to improve water quality prediction, control, and trade-off evaluation.

3.5.2. Disinfection Byproducts. Four studies measured DBPs and are also included in Figure 5. Marchesi et al. (2013) measured haloacetic acids (HAAs) and trihalomethanes (THMs) in a hospital system after using monochloramine and chlorine dioxide to reduce Legionella spp. contamination. No HAAs were detected, and THMs were low (<1  $\mu$ g/L). Richard and Boyer (2021)<sup>104</sup> found a slight reduction in THM concentrations after flushing in school buildings (LRV = 0.033). Lytle et al. (2021)<sup>71</sup> did not observe additional THM production during their study after adding a monochloramine disinfection system to a hospital facility (Figure 5). Based on all distal sites, there was an average LRV of 1.6 after the implementation of monochloramine in the facility treatment system. Orsi et al. (2014) applied shock and continuous hyperchlorination in an old hospital building and measured an

increase in THMs (LRV = -0.51, 15 days after shock hyperchlorination of 20–50 ppm free chlorine for 1–2 h). <sup>65</sup>

While the use of chemical disinfection methods can be effective for interventions related to Legionella spp. and other pathogens, there is a lack of investigation of their simultaneous impact on DBPs and subsequent relationships between DBPs and Legionella spp. or other pathogens within the plumbing system. Free chlorinated water can result in increased DBPs such as THMs and HAAs, and thus it can be difficult to achieve a balance between adequate disinfection and minimal production of DBPs. 124 Monochloramine has become an increasingly popular secondary disinfectant to replace chlorine, as studies have shown it can better penetrate biofilms, kill biofilm bacteria Legionella spp. and Pseudomonas spp., and carry fewer taste and odor-inducing concerns.<sup>71</sup> The studies reviewed here demonstrated its effectiveness in reducing Legionella spp. and had higher LRVs when compared directly with free chlorine. 15 Another advantage of monochloramine over free chlorine is the tendency not to form THMs and other DBPs. 125 Few studies investigated DBPs in conjunction with their interventions, but Thomas et al. (2004) observed a reduction of THMs after switching from chlorine to monochloramine. 15 Despite these advantages and a switch to monochloramine showing effective reduction of L. pneumophila, monochloramine has also led to increases in HPC, mycobacteria, and lead leaching, and should continue to be evaluated for building water system applications. 67,126,127

**3.6. Contaminant Trade-Offs.** For trade-off evaluation, more research is needed to understand the effects of varied water quality parameters and of different intervention methods on the intended outcomes. Table 3 briefly summarizes the identified trade-offs as a list of all studies which measured both pathogens and other contaminants, indicating mixed results. One evident trade-off in this review was the increase of other pathogens or amoebae in parallel with a reduction of *Legionella* spp. Rhoads et al. (2015) observed increased *V. vermiformis* concentrations in their laboratory setup (recirculating pipe to simulate household water systems) of flushing and increased temperatures, demonstrating that while the measures reduced *Legionella* spp. immediately, amoeba persistence could play a role in *Legionella* 

spp. regrowth even at the higher temperatures.<sup>55</sup> The use of chloramines for disinfection demonstrated a trade-off of controlling Legionella spp. but may have contributed to mycobacteria growth in one case.<sup>83</sup> This was shown to be consistent with an earlier study demonstrating increased mycobacteria colonization after the introduction of monochloramine. The interactive effects of metal ions and plumbing materials, chemical disinfectants, temperature, and pathogens can be both beneficial with regard to intervention and control, and result in adverse and/or longer term outcomes and is an area where additional data generation could aid in disentangling these factors. 7,83,128 While Orsi et al. (2014) demonstrated a 63% reduction of Legionella spp. detection after shock and continuous hyperchlorination in an old hospital building, the authors measured an increase of THMs from 2.71 to 8.7  $\mu$ g/L, 15 days after shock hyperchlorination.<sup>65</sup> THMs continued to increase up to 10.7  $\mu$ g/L after continuous hyperchlorination, and the authors noted that it may be necessary to implement warnings or special equipment in some hospital units to reduce free chlorine levels and to note safety concerns.

The focus of our meta-analysis was immediate before and after measurements to quantify contaminant reduction. However, in many cases, follow-up investigations in longer-term studies demonstrated regrowth, indicating a lack of eradication of colonization within biofilms in the systems. While this has been demonstrated and can be expected (Table 2), it is still an unintended consequence of the studied interventions. For example, Legionella spp. regrowth over time postintervention was observed for copper-silver, 15 incorrect dosing of monochloramine, 129 and thermal disinfection and flushing. Rohr et al. (1999)<sup>130</sup> found that L. pneumophila built up resistance to ionization treatment over time (>1 year) in the investigated hospital system, demonstrating copper-silver as a short-term solution. In addition to ineffective biofilm eradication, biomass and bacterial regrowth may occur due to treatments which lack residual disinfectant and inadequately reduce pathogens, 15,129 and the futility of short-term flushing and/or thermal disinfection measures to completely intervene in all legs of a building water and plumbing system at the desired temperature. 98 In terms of intervention, there comes trade-offs of cost, time, sustainability (especially in terms of water wastage during flushing) and health risk when identifying both the contaminants to monitor and target, and the method of intervention or water safety plan thereafter. Not accounting for longitudinal data in this study is a limitation and plays a role in assessing water quality over time, especially when locating the source, drivers, or amplifying factors of contamination.

#### 4. OUTLOOK AND RECOMMENDATIONS

In this review and meta-analysis of interventions for building water systems, LRVs for different methods of interventions were quantified and compared across pathogens, metals, disinfection byproducts, and study scale. All studies (n=45) assessed the impacts of their approaches on *Legionella* spp. or *L. pneumophila*, further highlighting its role as a priority monitoring target. The decision of which pathogen targets to monitor (e.g., whether to focus on monitoring *L. pneumophila* or *Legionella* spp.) depends on the context (e.g., research vs other end-uses). In the hospital studies, *Legionella* spp. was more commonly measured than *L. pneumophila*. This approach provides conservatism in a high risk setting but might be modified when applied to other less risky settings (e.g., commercial and institutional buildings).

One common thread throughout the studies, scales, and treatments was the variability in treatment efficacy and questions regarding the time scales of the intervention benefit, as in many cases, there was measured regrowth or rebounding effect in the weeks or months following an intervention. Many efforts were designed based on intervention after an issue was identified, but additional studies focused on preventative efforts that maintain cost effectiveness and reliability would also be beneficial for water management planning. As many of these interventions (e.g., recommissioning flushing) are designed to reactively address water quality problems rather than to identify root causes or prevent long-term water quality disbenefits, it is recommended to consider the relationship between building water management plan measurement values (e.g., exceedances of water quality criteria) and actions prior to plan implementation, while also iteratively revising the approach in response to site-specific data. While flushing or other interventions may reduce pathogen concentrations after a water quality adverse event is identified, the potential regrowth in the weeks or months following suggests that physical intervention methods (heat and flushing) are not solely adequate as longer-term control measures. Based on the reviewed data, additional research on timing, long-term impacts, and reoccurrence of contaminants under varying conditions is needed to inform more nuanced water management plan development. Within this approach, extending intervention testing to situations that inform proactive, preventative-based, rather than reactive approaches would be beneficial. Of the 17 studies that measured multiple contaminants, over half (n = 10)indicated some degree of mixed effects on contaminant reductions. Due to the time and resources involved in performing interventions within buildings, attention should be paid to potential trade-offs to ensure that effective plans are put into place.

Prior literature have demonstrated the relationship between metals and corrosion (such as iron and copper oxides), pH levels, and their impacts on decaying chlorine residuals. 117,120,122,123 Monitoring disinfectant residual may provide monitoring benefits as it can correlate with some pathogens, but does not guarantee control of all pathogens potentially present in the system. 95,102,132 The combined measurement of pH, metals, and disinfectant residuals in applicable systems is beneficial for understanding factors that affect pathogen or biomass proliferation. Overall, monochloramine demonstrated benefits across multiple pathogens, with LRVs up to 3.97 for Legionella spp., 2.81 for mycobacteria, and 0.67 for Pseudomonas spp. However, one study reported an increased level of mycobacteria colonization in the presence of monochloramine. As the transition from a chlorine to a monochloramine residual is explored for pathogen control and reduced DBPs, it should be further examined in the context for its impacts on metals and other pathogens.

Our meta-analysis focused on calculating LRVs from building water interventions or treatments. Due to dissimilarities across studies, quantification of LRVs is valuable for evidence-based water management plans. Future work can improve the quantification of uncertainty in comparing studies across heterogeneous plumbing environments. Timing plays a critical role in comparing before and after treatment detections and concentrations, particularly with regard to fluctuations in the plumbing environment such as temperature or water chemistry changes. Longer contact times with chemical disinfectants are expected to provide benefits for pathogen reduction but can also

result in greater variability across pathogen measurements, depending on the method and targeted pathogen. For example, De Giglio et al. (2021) had complete removal (zero positive detections) after 15 days of exposure to hydrogen peroxide and silver ions, an improvement after first implementation and the first week's sampling. However, ozone and copper—silver ionization was shown to have little effect on reducing *Legionella* spp. in longer time scales, possibly due to low residual concentrations or changes in pathogen persistence mechanisms. Al The contextualization of treatment methods, setting, building age, initial conditions, and time are needed and play a key role in understanding building water quality and effective management solutions and deciding on a method of intervention or action going forward.

Finally, this review was limited by data reporting and availability. The quantitative evaluation of LRVs limited the systematic review of literature, which clearly measured and presented concentrations of pathogens before and after interventions or treatment. Despite the putative benefits of water management plans and interventions, knowledge gaps persist regarding the behavior of control measures at different scales, within complex environments, and for representative detection methods. Methods and approaches for both intervention and detection varied, especially in reporting nondetects due to varying limits of detection. For the purposes of this review and estimation of LRVs, individual values which were reported as zero, less than the limit of detection, or "nondetect" were replaced with the reported limit of detection, where available, to calculate the appropriate LRV based on an obvious reduction from the "before" concentration. This was the case in ~ 13% of data points. While more sophisticated censoring methods would improve the estimation of reductions and our analyses, 133 the data for each study was limited, often to averages and ranges, rather than more complete distributions. While the use of LRVs allowed us to synthesize conclusions and identify treatment impacts across studies, its use toward single building systems can be improved upon in the future (such as in a water safety or management plan) with location-specific concentrations alongside meta-data such as temperature, disinfectant concentration, time since treatment or intervention, and the limit of detection.

#### ASSOCIATED CONTENT

#### Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acsestwater.4c00269.

Figure S1. Identification and initial screening of studies addressing building water system pathogen intervention measures using PRISMA; Figure S2. The results of the review for intervention methods illustrated as the percent of each study scale/category implementing each method; Figure S3. Concentrations of copper before and after interventions; Figure S4. Concentrations of all other heavy metals before and after interventions; Figure S5. Concentrations of THMs before and after interventions (PDF)

Table S1. Data file for all extracted LRV data from premise plumbing studies (n = 45); literature review and inclusion criteria; data extraction and evaluation (XLSX)

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