



Potential for nontuberculous mycobacteria proliferation in natural and engineered water systems due to climate change: A literature review

S.M. Blanc^{a,*}, D. Robinson^b, N.L. Fahrenfeld^a

^a Civil & Environmental Engineering, Rutgers, The State University of New Jersey, 500 Bartholomew Road, Piscataway, NJ 08854, United States

^b Geography, Rutgers, The State University of New Jersey, 54 Joyce Kilmer Avenue, Piscataway, NJ 08854, United States

ARTICLE INFO

Keywords:

NTM
Aerosol
System dynamics
Water quality
Opportunistic pathogen

ABSTRACT

Nontuberculous mycobacterial (NTM) infections are costly, difficult to treat, and increasing in prevalence. Given this, there is a desire to understand the potential relationships between NTM in water sources and climate change stressors. To address this need, a critical literature review was performed. Connections were made between NTM fate and transport, climate change, engineering decisions, and societal changes, and uncertainties highlighted. Environmental conditions discussed with respect to NTM risk included changing temperature, humidity, salinity, rainfall, and extreme weather events. NTM risk was then considered under climate/societal scenarios described by Intergovernmental Panel on Climate Change (IPCC) scientists. Findings indicate that the resilience of NTM under a variety of environmental conditions (e.g., warm temperatures, eutrophication) may increase their net prevalence in water environments under climate change, increasing exposure. Water management decisions may also influence exposure to NTM as water scarcity is expected to result in increased reliance on reclaimed water. Water managers may control risk of exposure through innovative water treatment processes and equitable water management decisions, turning towards an integrated One Water approach to reduce and/or mitigate the impacts of de facto reuse. Future research recommendations are provided including studies into potential changes to NTM fate and transport in uniquely impacted climates (e.g., boreal regions), and investigations into the relative risk of managed aquifer recharge as compared to no action.

1. Introduction

1.1. Disease impact

Infections caused by nontuberculous mycobacteria (NTM) have gained increasing attention over the past several decades in medical and engineering fields due to their high cost [23], difficult treatment [28], and increasing prevalence [111]. NTM, otherwise referred to as “atypical mycobacteria,” “environmental mycobacteria,” or mycobacterial species other than *Mycobacterium tuberculosis* and *Mycobacterium leprae*, are ubiquitous in water and soil environments and include many opportunistic pathogens such as those in the *Mycobacterium avium* complex (MAC) [46]. Exposures to NTM species by immunocompromised individuals can result in a variety of infection and disease outcomes including pulmonary disease, as well as extrapulmonary and disseminated diseases [28,40,153]. Cases of NTM infections and disease come with a high price tag. A US Centers for Disease Control (US CDC) study estimated that NTM infections were the costliest primarily water-

based infections, costing \$1.53 billion in direct healthcare costs in the US in 2014 [23]. Between 1994 and 2014, NTM positive culture rates across five US states nearly doubled, increasing from 8.2 to 16 cases per 100,000 persons per year [37]. Due to the increasing instances of disease [37] and prevalence in drinking water systems [45], *M. avium* has been included in all four US Environmental Protection Agency (USEPA) Drinking Water Contaminant Candidate Lists (CCL-4) (USEPA, 2016). While concerns about NTM disease typically focus on immunocompromised individuals who comprise a large fraction of patients, researchers have recently noted that NTM disease prevalence is increasing in immunocompetent populations, raising the public health concern around these bacteria [129].

1.2. The nexus of pathogen, climate, and human interactions - A roadmap to risk analysis

The majority of NTM infections are believed to be acquired through human-environment interactions, such as by inhalation of infected

* Corresponding author.

E-mail address: sophia.blanc@rutgers.edu (S.M. Blanc).

<https://doi.org/10.1016/j.cacint.2021.100070>

Received 14 April 2021; Received in revised form 21 June 2021; Accepted 24 June 2021

Available online 28 June 2021

2590-2520/© 2021 The Authors.

Published by Elsevier Ltd.

This is an open access article under the CC BY-NC-ND license

(<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

particles and bioaerosols [44]. NTM have been identified in soils [32,79], household dust [30], freshwater sources [119], public water supplies [81,147] and in plumbing biofilms in homes using public and private well water supplies [12,49,58,151,155]. As environmental bacteria, NTM can be expected to be influenced by changing climatic conditions. Since the dawn of the industrial revolution, emissions of greenhouse gases such as carbon dioxide (CO₂) and methane (CH₄) have increased, leading to an accelerated increase in average global land and ocean temperatures at a rate of approximately 0.2 °C per decade [5]. Increases in atmospheric carbon dioxide and global temperatures have rippling effects [70]. Some of these include increases in humidity, intense precipitation and drought, changes in sea level, increases in the frequency and/or intensity of natural disasters, and extended warm seasons. These changes lead to numerous secondary, or cascading effects such as increased flooding, saltwater intrusion, mold exposure, and water and food instability [5]. Coastal regions are particularly affected by climate change, and in the US, these are many of the same regions (e. g., Hawaii, Louisiana, California, Florida) with the majority of NTM infections [2,31,131]. Researchers from the Intergovernmental Panel on Climate Change (IPCC) suggest that the trajectory of global emissions [5] and the associated societal and population dynamics [98,114] are highly likely to influence the magnitude of the abovementioned effects.

As cases of NTM disease continue to climb, global climate change accelerates, and population dynamics shift, there is an urgent need to understand how risk of NTM infections might be expected to change in the coming decades. Literature reviews have been published that synthesize information about NTM epidemiology and ecology [42,65,96,104,107], and specifically about NTM and natural disasters [64]. However, there remains a gap in the literature as to how the combination of changing climates and human dynamics might influence NTM risk, despite evidence that climate [21,137] and societal [88] factors can influence NTM disease, and that these factors influence each other [114]. Therefore, the overarching objective of this review is to synthesize the wealth of information about NTM, climate, and human system dynamics to characterize the processes that may influence future human risk of NTM infections from water and aerosol sources. The specific goals of this review are to capture the primary interactions occurring at the interface of several systems, to highlight the gaps in understanding how the systems function and interact, and to identify potential scenarios that might lead to different levels of future risk. This analysis is intended to support future model-based risk analyses of NTM, as well as to inform decision making by water managers to mitigate potential risk.

2. Literature review

2.1. Biological, ecological, and physiological characteristics

To hypothesize how risk of NTM infections might change under future circumstances, some key characteristics that affect the survival of NTM must be understood. First, NTM have an outer membrane rich in lipids and composed of mycolic acids that provide them with an array of survival-enhancing qualities including hydrophobicity, impermeability, and slow growth [16]. Because of their hydrophobicity, NTM tend to form biofilms on surfaces such as pipe walls or soil particles [121], to which they can also adsorb due to their negative surface charge [11,18,92]. NTM can survive and replicate within several protozoan species [130], primarily free-living amoeba in both the trophozoite and cyst phases [9,22,33,109,133]. Some NTM species can adapt by sharing genetic information through plasmid-mediated horizontal gene transfers [95]. Biofilms provide an ideal habitat for NTM to share antibiotic resistance genes (ARGs) as well as metal resistance genes (MRGs) [76,90]. NTM also have other adaptive capabilities that aid in survival, such as the ability to enter a stationary phase of reduced cell activity under starvation [125] and acid stresses [14]. They are known to survive typically extreme environments, such as acidic [14], warm [120],

oligotrophic [125,159], and microaerobic environments [44,78].

There are currently more than 190 known NTM species [28] that can be divided into two major groups: slow and rapid growing [57,126]. The most clinically relevant species vary by region across the globe and have changed over time [63]. However, several slow and rapid growing species are currently of widespread clinical interest. Slow growing commonly pathogenic *Mycobacterium* species include *M. avium*, *M. intracellulare*, *M. kansasii*, *M. marinum*, *M. malmoense*, and *M. xenopi*; and rapid growing species include *M. fortuitum*, *M. abscessus*, and *M. chelonae* [44]. Another important slow-growing species, *M. goodii*, is ubiquitous in drinking water environments but is less frequently implicated in disease. These species are generally small (1–3 µm), acid-fast, tubular cells [56] that exhibit varying degrees of resistance to treatments in humans and to environmental stresses.

Environmental concentrations of NTM species vary depending on the location, measurement method, and sample matrix (Table 1). As an example, both the Finland brook study [69] and the southeastern US swamp study [79] cultivated mycobacteria from water and found average values that differed by two orders of magnitude, owing to different environmental conditions. Moreover, measurements for abundance of mycobacteria in aerosols are not readily comparable to those for water or biofilms, even in the same study, due to differences in measurement units [79]. For these reasons, future investigations that seek to calculate quantitative risk analyses of NTM should consider the specific location, source, predicted transmission route, and species of interest for the exposure assessment. Some researchers have already attempted a quantitative microbial risk assessment (QMRA) for NTM species or have investigated dose–response relationships, and future work may consider building off of those studies [17,26,59,61,115].

2.2. Climate change considerations

2.2.1. Temperature

For NTM in surface water or shallow groundwater environments [132], warmer temperatures could provide more favorable conditions given that NTM species survive and grow better in warm waters than in cold [53,139]. For example, NTM were found to be more prevalent in southeastern US waters as compared to waters in the northeastern US, an observation that researchers attributed to the relatively longer period of time that water in the southeast spends above 15.5 °C and the smaller time period that it spends below 9.4 °C [53]. Similarly, MAC species were found in greater abundance in warm water [27], such as surface water during warm seasons [79]. Correlations were observed between temperature and mycobacteria detected by qPCR in a coastal lagoon [71]. During increasingly frequent extreme heat events [5], NTM species may be uniquely adaptable. Some species (e.g., *M. xenopi*) have been shown to survive in extremely warm waters, at temperatures as high as 60 °C [120]. Disease risk for some NTM species can be greater in warmer or tropical regions [21,31,64,65,110,123]. For example, in Queensland, Australia, infections by *M. abscessus* occurred in a hotspot in a tropical subregion [21]. A 16-year study in Australia also found cyclical associations between seasonal temperatures and disease, finding decreased incidence of disease by different NTM species several months (3–6) after increased temperatures [137].

As home plumbing systems are considered transmission routes, one might consider how changing temperatures influence NTM in water once it is treated and within a distribution system. Several studies have reported seasonal increases in NTM in drinking water distribution systems during warm times of the year [89,108,136,146] and correlations between water temperature and mycobacteria abundance [87,113], suggesting that increased temperature carries potential to increase NTM abundance in these engineered systems as it provides a more suitable environment for survival [89]. Considering climate change, Walker [149] suggests that longer periods of warmer temperatures within buildings could result in increased regrowth in pipes as building operators struggle to maintain in-pipe water temperatures below 20 °C. This

Table 1

Measurements of mycobacteria across several studies spanning decades, geographics locations, sample types, and measurement methods. Note, this table is not exhaustive.

Data measured	Value	Unit	Matrix	Sample origin	Reference
Culture counts (range, average, and standard deviation)	Range: 0 – 10 ⁶ $\bar{x}$ = 4.06 × 10 ⁵ σ = 1.49 × 10 ⁶	CFU/cm ²	Biofilm	DWTP ^a and home plumbing, Germany and France	[121]
	Range: 10 – 2200 $\bar{x}$ = 618 σ = 603	CFU/L	Water	Peatland influenced brook, Finland	[69]
	Range: 0 – 4.8 × 10 ⁴ $\bar{x}$ = 2.11 × 10 ⁴ σ = 1.83 × 10 ⁴	CFU/L	Water	Swamps, Southeastern US	[79] ^b
	Range: 0 – 1.65 $\bar{x}$ = 0.82 σ = 0.74	CFU/cm ² /hr	Ejected droplets	Swamps, Southeastern US	[79] ^b
	Range: 0 – 66.1 $\bar{x}$ = 24.5 σ = 26.3	CFU/m ³ /hr	Aerosol	Swamps, Southeastern US	[79] ^b
Culture Range	1 – 50 (78) 51 – 500 (21) > 500 (1)	CFU/L (% of samples)	Water	DWDS ^c , France	[82]
Culture Presence/Absence	4/16 (25)	P/A (%)	Biofilm	DWTP ^a , Spain	[24]
	46/165 (28)		Biofilm	Home plumbing, US	[43]
	5/12 (42)		Water	SW ^c , Spain	[24]
	4/55 (7)		Water	DWTP ^a , Spain	[24]
	2/10 (20)		Water	DWDS ^c , Spain	[24]
	5/16 (31)		Water	DW, GW ^d , US	[25]
	32/89 (36)		Water	DW, SW ^d , US	[25]
	41/60 (68)		Water	DWDS, GW ^d , France	[82]
	33/48 (69)		Water	DWDS ^c , SW ^d , France	[82]
	30/36 (83)		Water	DWDS ^c , mixed, France	[82]
	90/142 (63)		Water	Chlorinated SW ^c , Czech Republic	[143]
	45/195 (24)		Water	Home plumbing, US	[43]
	Range: < 4.5 × 10 ² – 2.4 × 10 ⁴ $\bar{x}$: < quantitation		Biofilm	No disinfectant residual DWDS ^c , SW ^d , US	[148] ^h
	Range: 6.0 × 10 ² – 4.8 × 10 ⁶ $\bar{x}$: 9.3 × 10 ⁴		Biofilm	Chloraminated DWDS ^c , SW ^d , US	[58]
	Range: < 200 – 7.76 × 10 ⁶ Range: 2.0 × 10 ⁴ – 1.3 × 10 ⁷		Water	Chloraminated DWDS ^{c,e} mixed, US	[58]
qPCR	Range: 8.6 × 10 ² – 4.4 × 10 ⁷	copies <i>atpE</i> gene/L	Water	No disinfectant residual DWDS ^c , mixed, Netherlands	[146] ^h
	Range: 10 ⁴ – 10 ⁷ $\bar{x}$ = 10 ^{5.78} σ = 10 ^{0.72}	myco16 ^f gene copies/L	Water	SWSS ^g , China	[84] ^h
	Range: 6.7 × 10 ³ – 1.9 × 10 ⁸ $\bar{x}$ = 2.16 × 10 ⁵	myco16 ^f gene copies/L	Water	Chlorinated DWDS point-of-use, mixed, China	[89] ^h
		copies <i>atpE</i> gene/L	Water	Lakes, France	[119]

^a DWTP = drinking water treatment plant.

^b focused on *M. avium*, *M. intracellulare*, and *M. scrofulaceum*.

^c DWDS = drinking water distribution system.

^d DW = drinking water, SW = surface water, GW = groundwater; if SW or GW not listed, information was not available in referenced paper.

^e samples from premise plumbing in homes connected to the DWDS.

^f myco16 refers to the *Mycobacterium* spp. -specific fragment of the 16S rRNA gene.

^g SWSS = secondary water supply system, which refers to water storage and pressure systems connected to larger buildings, such as rooftop tanks.

^h Evaluated for but did not find *M. avium*-specific genes in any samples.

has already been observed as an issue in the United Kingdom in the context of *Legionella* [149], which is sensitive to disinfectant residual that degrades at warmer temperatures [122]. However, NTM have been found to resist or be selected for by disinfection [41,128], so the impact that disinfectant degradation may have on NTM remains uncertain. Further, as stated in Section 2.1, NTM can live within amoeba, some of which (e.g., *Vermamoeba*) have been found in greater abundance in drinking water distribution systems during warmer seasons [33], indicating potential for NTM to enhance survival by living within the

amoebas that also prefer warmer conditions.

2.2.2. Humidity

In humid environments, NTM may be more likely to survive and transport in aerosols that remain suspended for longer periods of time. With increased temperatures, increases in humidity have been observed and are projected to continue in already humid regions of the world [10]. A study by Lin and Marr [86] found increased survival with relative humidity for bacteria in aerosols, including *M. smegmatis*. Aerosol

droplets can resist full evaporation, retaining liquid water for up to an hour when the relative humidity is higher than 55%. This suggests that if NTM aerosolize in humid environments, these microorganisms may have ample time to transport through air in the remaining liquid [86].

2.2.3. Sea level rise

Rising temperatures also have important implications for NTM due to the secondary effect of sea level rise, influencing salinity gradients in estuaries and the saltwater/freshwater interface in aquifers [70]. Research suggests that most NTM species appear in greater abundance in waters with lower salinity [27], and that salinity above 3 g/L can inhibit replication of most NTM species [53]. In a coastal lagoon study, a negative correlation between salinity and mycobacteria gene abundance was one of three factors (along with total nitrogen and dissolved oxygen) used to build a model to predict measured values with 83% agreement, suggesting that the negative association is important to understanding mycobacteria abundance in waters with a salinity gradient [71]. During storms with winds and heavy precipitation, mixing of saltwater and freshwater may result in greater aerosol production efficiency [64,105]. As the salinity gradient migrates inland, this could result in more aerosols forming closer to the land where more people may be exposed via inhalation. Therefore, although the abundance of NTM species in mixed saltwater/freshwater zones may be expected to generally decrease as the salinity gradient migrates inland, the potential for greater aerosolization efficiency and exposure complicates risk predictions.

2.2.4. Precipitation, hydrology, and water quality

Increases in heavy precipitation are projected to lead to increases in flooding and runoff [5] that can elevate turbidity and nutrient concentrations, and decrease oxygen content in receiving waters [70]. Due to their hydrophobic membranes that enable attachment to particle surfaces [11,19], increased turbidity may lead to increased abundance of NTM in receiving surface waters (Fig. 1). Previous work supports this positive association between NTM and turbidity [47,71,145]. NTM have also been associated with various metals, such as nickel, chromium, and iron, potentially for similar mechanistic reasons [117]. Nickel and chromium, as examples, are common to urban stormwater runoff [112],

suggesting potential for NTM concentrations in receiving water to increase with increased runoff carrying metal pollution. However, this could be complicated by increased flushing rates, which may reduce concentrations of the abovementioned pollutants, underscoring the importance of local models and understanding [70]. Additionally, the increase in nutrients as a result of increased runoff could create eutrophic conditions that have previously been correlated with mycobacteria gene concentrations [71]. This could be because of the capacity of NTM to survive under anoxic or anaerobic stresses that other organisms cannot [107], as well as their preference for warm water associated with eutrophic conditions [70]. Although NTM are often considered oligotrophic [41], they can adapt to nearly opposite environmental conditions imposed by increased runoff [71]. This indicates that increased precipitation intensity resulting in eutrophication may increase NTM in receiving surface water environments. Combined sewer overflows (CSOs) are also a concern with respect to increased runoff, as stormwater and wastewater flow together and carry pathogens directly to receiving water bodies [106]. Further, periods of intense precipitation have the potential to create sanitary sewer overflows, resulting in more concentrated waterbody contamination with pathogens including NTM [94].

Increases in precipitation intensity also carry the potential for increased flooding and associated impacts to shallow, unconfined groundwater [70]. Similar to the discussion above, increased flooding could result in increased transport of contaminants (e.g., nutrients, organic matter, metals, microorganisms) that can introduce the contaminants to shallow groundwater as the subsurface becomes saturated [38,80]. Because NTM adhere to surfaces [11,15], there is uncertainty about how efficiently they may be removed by soils during infiltration. Flooding could also lead to waterlogging, blocking off air flow between the atmosphere and subsurface, creating anoxic conditions [39,80] for which NTM are well suited [44,107]. Alternatively, in other situations, flooding could introduce oxygenated water into the water table. However, oxidation of associated nutrients and organic matter could consume the oxygen nonetheless, again resulting in reduced oxygen conditions [157]. Flooding of typically unsaturated soils also may release naturally accumulated salts into aquifers, potentially increasing salinity [38], a factor that could negatively influence NTM survival [71],

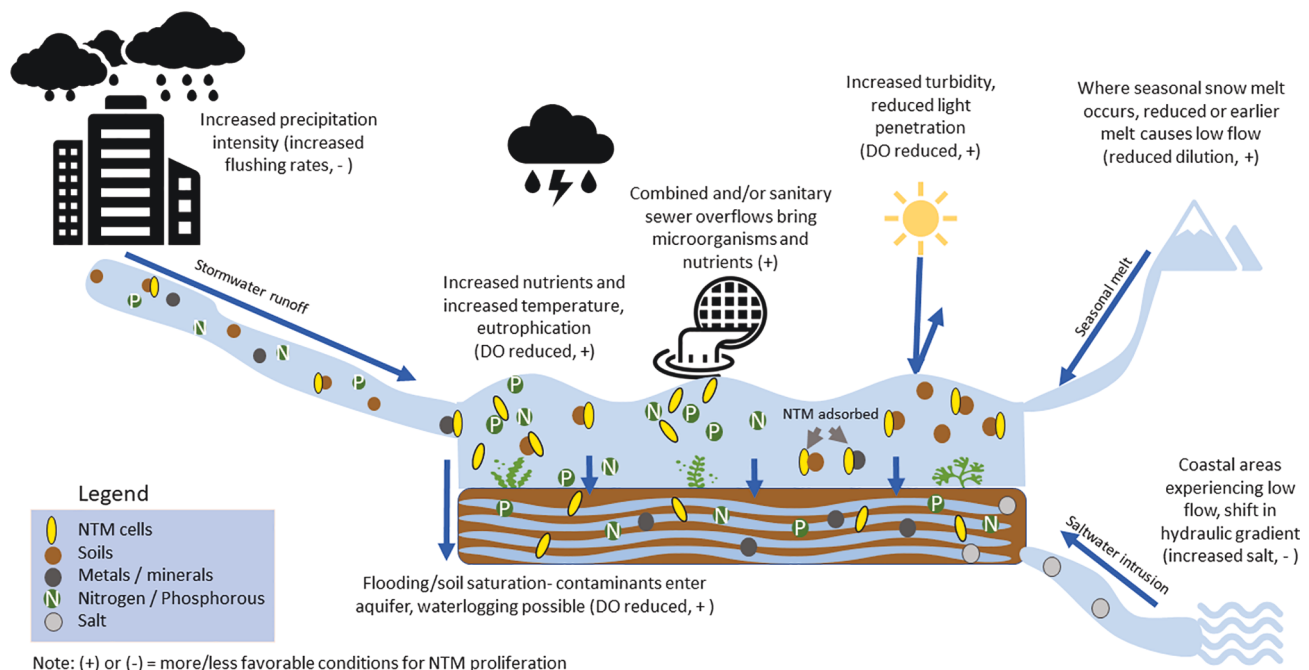


Fig. 1. Simplified conceptual model of hydrological relationships affecting NTM proliferation. Evaporation and groundwater residence time effects, discussed in Section 2.2.4, are not included in this diagram. Aerosols, not discussed in this section, are also not included.

as described above.

In regions where precipitation is projected to decrease or flow to be seasonally reduced, water quality and NTM considerations differ from those discussed for increasingly wetter conditions. When surface water flow decreases as a result of drought or reduced snowpack, the volume of water available to dilute pollutants (e.g., nutrients, organic matter, microorganisms) [152] introduced to surface water by wastewater decreases [70]. Cultivable NTM [74] and biomolecular detection of mycobacteria genes [6,20] have been observed in wastewater effluents. Therefore, low flows, exacerbated by potential increases in evapotranspiration rates, could allow for increased concentrations of NTM in water sources simply by way of less dilution of wastewater effluents. In regions with high rates of de facto water reuse, therefore, this could degrade source water quality with respect to NTM. In areas with combined sewers, low flow as a result of drought would likely accompany a decrease in CSOs, decreasing associated microbial loads in connected water bodies. However, in areas with low flow due to earlier and reduced snow melt, CSOs may still occur with precipitation events, and would be met with less water available for dilution, increasing microbial concentrations [72]. In groundwater, where reduced precipitation and increased evapotranspiration also decrease flow and lower the water table, there are changes in the hydraulic gradient where aquifers meet surface water [80,141]. In coastal areas, this could lead to increased saltwater intrusion, as has been seen in areas of California [7], expected to negatively influence the suitability of the habitat for NTM [80]. At the headwaters, decreased baseflow from cooler groundwater into streams could result in increased surface water temperature [38], favorable for NTM [79]. Decreased flow in aquifers could also lead to increased residence time and, therefore, contact time between subsurface rock and water, increasing the opportunity for minerals to leach [38]. Minerals related to rocks such as hematite and goethite were previously associated with NTM abundance [117]. Therefore, decreased groundwater flow has the potential to increase or decrease NTM abundance, depending on whether salinity or mineral concentrations control their survival and growth.

2.2.5. Natural disasters

With tropical cyclones, there is potential for increased aerosolization of NTM as freshwater, saltwater, and soils mix, as well as for transport of the bioaerosols with cyclone winds [64]. According to the IPCC, it is likely that the average tropical cyclone wind speed and precipitation will increase in coming decades [50]. Thus, as wind intensity of cyclones is projected to increase with climate change [50], so too might NTM exposure through bioaerosols. A recent study of climatic factors and NTM disease found associations that supported this idea. Associations between heavy rainfall and disease differed in direction between humid, tropical storm environments and arid environments: risk in humid environments increased and risk in arid environments decreased, both with several months lag time [137]. The researchers suggested that this may be because the humid environments were subject to tropical storms with strong winds capable of transporting aerosolized NTM far distances. The abundance of aerosolized NTM as a result of rainfall impact may further be related to factors such as raindrop velocity, soil type, and surface temperature [75]. In addition, Honda et al. [64] suggested that the relationship between NTM and amoeba may further contribute to infection risk post-disaster, as NTM within amoeba may better survive when displaced from originating water sources by cyclones. Previous investigations of spatial clusters of NTM disease have found hotspots in regions with frequent disasters, such as in Florida, Hawaii, and Louisiana, suggesting that increased exposure to extreme events may relate to risk [2]. Additional details on the potential relationships between NTM and natural disasters can be found in a review by Honda et al. [64]. These authors also acknowledge that, to fully assess risk in this context, additional factors such as changes in host susceptibility with trauma and food/water insecurity need to be considered and better understood as NTM are primarily opportunistic pathogens and may find more suitable

hosts during disaster periods [64].

2.3. Changes in engineering and water management practices

Meeting water demands while adapting to challenges including reduced snowpack, unpredictable rainfall, and saltwater intrusion, as well as potential increased water requirements for energy production, will require flexibility and creativity [7]. Adaptations to these stresses, as with any water management changes, will influence the prevalence and abundance of contaminants, including NTM. Control of NTM in this section focuses on mitigation of opportunistic pathogenic NTM species to reduce exposure and subsequent infection. However, it should be noted that some evidence exists suggesting that early exposure to pathogenic NTM may have positive effects on allergy and asthma development [100]. Some practical adaptation choices to address the challenges of water scarcity and water quality are discussed in this section as specifically related to NTM risk.

2.3.1. Managing water scarcity with reclaimed water

As water resources become more stressed and water reclamation trends continue upward [54], there are several considerations to reduce the risk of exposure to NTM. Water reclamation or reuse includes wastewater reuse, as well as reclamation of stormwater for uses such as washing, irrigating, cooling, toilet flushing, or even drinking [55]. Wastewater reuse today occurs both intentionally through extensive treatment and redistribution [6,13] and non-intentionally (de facto reuse) by way of poor sanitation [68] and low flow rivers that accept wastewater effluents while feeding drinking water influents [115].

To reduce NTM in reclaimed wastewater, several studies suggest that some current practices may be insufficient [6,73]. For example, treatment including biological reactors, microfiltration, and chlorination selected for mycobacteria in wastewater effluents [20]. In another study, when conventional treatments, membrane bioreactors (MBR), and disinfection reduced NTM at the wastewater treatment plant, they regrew to densities 10 times those of fecal indicators along the redistribution system, similar to behavior in potable water systems [74]. Based on existing knowledge about the resistance of NTM to disinfection and tendencies for regrowth [41,85,102,151,154], these observations are not surprising. In contrast, studies suggest that a treatment train including conventional treatments in addition to reverse osmosis (RO) may be effective at removing NTM, other pathogens, and even ARGs that contribute to their virulence [13,62,127]. This could be because RO exploits the negative charge of NTM [92] to exclude the cells [156]. Challenges to this type of treatment, however, do exist. The high cost, energy intensity, production of RO concentrates, and potential for dangerous disinfection byproducts formed by advanced oxidation processes (AOPs) that typically follow RO are all practical concerns [118]. These challenges could be overcome by implementation of alternative treatments, such as nanofiltration, that similarly take advantage of NTMs' negative charge to exclude them from finished water, but with less drawbacks in terms of energy usage and cost [156]. Disinfection by UV rather than chemical disinfectants could also be employed, though the effectiveness of UV varies by NTM species [83]. Further, Falkinham [41] highlights that this may result in mutations that require investigation. Temperature management could also be considered to control NTM. However, while treating with heat above 53 °C has been found to control MAC species, other species (e.g., *M. xenopi*), and MAC in other experiments [120], have been found to resist temperatures above that [97].

Even if treatments successfully reduce NTM concentrations in reclaimed water at the treatment plant, potential for regrowth along redistribution systems remains a concern. One reason for this is thought to be availability of nutrients in reclaimed water. Although NTM are often considered to be oligotrophic [41] and studies have shown that assimilable organic carbon (AOC) may not be a limiting nutrient for all NTM [89,159], others suggest that severely limiting AOC (<10 µg/L)

may inhibit growth of the most clinically relevant and likely to be regulated MAC species [97,146]. Studies of reclaimed water treated conventionally and with MBR have found relatively high AOC concentrations (range 45–3200 µg/L, median 450 µg/L), suggesting that additional processes would need to be undertaken to drastically lower the concentrations [152]. Chemical disinfectants increase AOC concentrations [91,152]. Thus, controlling microbial growth by engineering low nutrient conditions rather than by using disinfectants, as is done in the Netherlands [146], would likely reduce AOC throughout redistribution [52].

Reducing corrosion in the redistribution system may also reduce the likelihood of NTM proliferation by controlling the surface area available for attachment and preventing additional nutrients from entering the system [97]. Corrosion control could also reduce the virulence of the surviving NTM by limiting horizontal gene transfer of ARGs and MRGs [76,90,103]. However, corrosion control mechanisms should be thoughtfully considered because research has also shown that phosphates, often used for corrosion control, may aid the growth of NTM in distribution system biofilms [48,51,159]. Another challenge that is particularly relevant when considering reclaimed water distribution in the context of climate change is maintaining a cool temperature to limit growth activity of NTM in biofilms [51]. While this remains a challenge, potential solutions such as providing a minimum pipe to subsurface depth or distance from electric cables, or providing shade or vegetation cover above distribution pipes can be investigated for efficacy and practicality [3]. Considering the finding that temperature is a more important factor than nutrient levels in controlling *M. avium* growth [139], a practical temperature control approach could be high-impact if achieved.

In addition to using reclaimed wastewater, rainwater reclamation is another strategy to make use of finite water resources in areas facing unreliable water supply. This can be done through rainwater catchment systems, such as roof-harvested rainwater systems that direct rainwater from a building's roof into a barrel, tank, or collection channel for uses including washing, toilet flushing, showering, irrigating, or drinking [59]. The water quality of roof-harvested rainwater has been investigated for risk of exposure to opportunistic pathogens, including NTM. Some studies have found NTM species, including *M. avium* and *M. intracellulare*, frequently in roof-harvested rainwater [59,60], while others in different locations found them seldom or did not find them at all [4,158]. A comprehensive QMRA for MAC species in roof-harvested rainwater resulted in the conclusion that use of roof-harvested rainwater can be low risk if used for car and clothing washing, or toilet flushing, but that it should not be used for drinking, irrigating, or showering [59]. Importantly, the QMRA suggested that the cumulative risk reflective of solely relying on roof-harvested rainwater was higher than acceptable (10^{-4}), suggesting that risk of infection could increase if no other water sources were available [59]. Thus, as water resources become more scarce in some regions, water managers may consider ways to ensure that residents do not rely solely on untreated roof-harvested rainwater, as is already the case in 13.6% of households in Queensland, Australia [1].

2.3.2. Reclaimed water storage/artificial aquifer recharge

There is much uncertainty around the potential for proliferation of NTM as a result of managed artificial recharge. Some researchers suggest that storing reclaimed water in a high quality aquifer can improve water quality through natural microbial processes [34,36], while others suggest that introducing reclaimed water into a clean aquifer may result in unintended consequences, such as distribution of ARGs [62]. While Harb et al. [62] suggest that the original groundwater microbiome dictates the final recharged aquifer microbiome, they also report evidence of wastewater influence by way of ARGs, highlighting uncertainties in the extent of wastewater influence. This could be cause for concern about potential acquisition of ARGs because NTM are capable of horizontal gene transfer [95]. However, both NTM and ARGs have been

identified in aquifers without the influence of managed artificial recharge [82,93,144], and some of the water treatments described in Section 2.3.1 may reduce the likelihood of additional ARGs and NTM entering aquifers. In contrast, unmanaged artificial aquifer recharge via disposal of wastewater or stormwater into aquifers without water quality considerations could have negative effects in terms of NTM and other pathogens [36]. For this reason, intentional water reclamation and recharge is a preferred option from a water quality and water quantity standpoint as it provides control and conserves water [35]. When considering intentional infiltration of stormwater through wetlands, research has indicated that high temperatures and nutrient levels can result in NTM presence in the connected aquifer [71,138]. Thus, Jacobs et al. [71] suggest that steps taken to reduce eutrophication in wetlands may also benefit the water quality of aquifers below, which could potentially reduce NTM prevalence.

2.4. Related societal dynamics

Changing societal dynamics feed into climate change, influence water management decisions, and affect host exposure and susceptibility to opportunistic infections. Political will and associated policies that curb climate change by shifting energy and industrial practices will influence the magnitude of the abovementioned climate challenges [98]. Increases in population density and urbanization trends already influence air and water temperatures via the urban heat island effect [116]. For example, in Minnesota urbanization increased shallow groundwater temperatures by 3 °C compared to temperatures in agricultural areas [132]. This increased temperature could provide a more supportive environment for NTM survival and growth [120] and is driven in large part by the presence of heat trapping land cover, such as pavements [132]. Moving forward, urbanization and associated impervious land cover combined with increased wastewater loads (associated with increased population density) may also impact water quality through increased nutrients (e.g., nitrogen and phosphorous) from runoff and wastewater, potentially resulting in eutrophication [67]. Implementation of stormwater best management practices (BMPs), such as rain gardens and bioswales, could offset increases in runoff, but the impact to eutrophication, and ultimately to NTM concentrations, would be complicated by the reduction in flow available for nutrient dilution [124]. Urbanization, often concentrated in coastal and riverine areas, also exposes more people and their water sources to floods and natural disasters [70], both of which may lead to greater exposure to environmental pathogens, including NTM [64]. Population density, a proxy for urbanization, has been associated with NTM disease prevalence in several studies [88,101,137].

Increased temperature and population may also increase energy and water demands [5]. Water requirements for energy and food production (e.g., biofuel crop production) may further stress water resources affected by droughts and rainfall unpredictability, requiring more water reclamation and storage [5,7]. With proper water management (i.e., conservation, 'One Water' integrated cooperative management among stakeholders) and treatment processes, increased reliance on reclamation and artificial aquifer recharge could result in minimal changes or improvements in NTM exposure risk [59,127]. In the absence of comprehensive management and treatment, increased NTM exposure from reclaimed or unmanaged aquifer recharge is also possible [6,74].

The impacts of climate and societal change also influence individuals and their risk to opportunistic infections. With increased exposure to extreme weather events, individuals experience trauma and food/water insecurity that stress their immune systems, increasing susceptibility to opportunistic infections including those by NTM [64]. Disaster events also may lead to mold and associated mycobacteria growth, potentially increasing exposure to NTM [140]. Individual immune response also declines with age, suggesting that as the global population ages, vulnerability to opportunistic NTM infections will increase [41,111]. Access to equitable healthcare and education also influence infection

outcomes by enabling or preventing access to adequate treatment [88,111].

2.5. Potential scenarios for consideration

To synthesize the information discussed thus far, scenarios are provided that characterize potential outcomes of NTM risk in the context of the detailed shared socioeconomic pathways (SSPs) developed by IPCC scientists [98,114]. Fig. 2 shows the system dynamics involved that can be applied to any of the SSPs, following the direct (green) and inverse (red) relationships. These scenarios represent merely a few of the infinite potential pathways and outcomes of future change. They are a result of assumptions combined with quantitative information. It is worth noting that all SSP scenarios result in an emissions pathway higher than RCP 4.5, a radiative forcing level that was previously considered ‘middle of the road’ [70]. Three out of five scenarios are described in Table 2 below. The most sustainable future is described by SSP1 and is characterized by a swift transition to clean energy, low resource demand, and globally cooperative nations that enable adaptation and mitigation of climate change [99,114]. Under this scenario, the worst impacts of climate change are avoided, and global cooperation supports efforts to improve health and wellbeing, ultimately implying reduced risk of NTM and other opportunistic infections. SSP2 and SSP3 provide less optimistic futures for the environment and for NTM, mainly

due to an inability to manage finite water resources and innovate or distribute management solutions equitably.

2.6. Uncertainties and recommendations for future work

As with any projections and scenario analyses, there are many uncertainties involved in the scenarios described and in their interpretation with respect to NTM. Uncertainties involved in modeling due to stochasticity and gaps in knowledge impact climate change projections as well as predictions of NTM abundance under different conditions. Uncertainties also exist with respect to the choices that humans will make as well as the ultimate effect of those choices. For example, in SSP1, innovation is key and there are uncertainties as to how successful innovative efforts may be at tackling challenges including energy efficiency and water quality/quantity. There are uncertainties about how social behaviors and interactions with the environment (e.g., time spent outside) will change in the future, which may also influence vulnerability and relative risk. Although robust modeling efforts by IPCC scientists attempt to delineate the extent of uncertainties, there will always be potential surprises given the large number of interacting factors involved in all climate and SSP projections.

To close some of the remaining knowledge gaps, several future research recommendations are provided in Table 3. For example, study is warranted of potential relationships between thawing permafrost over

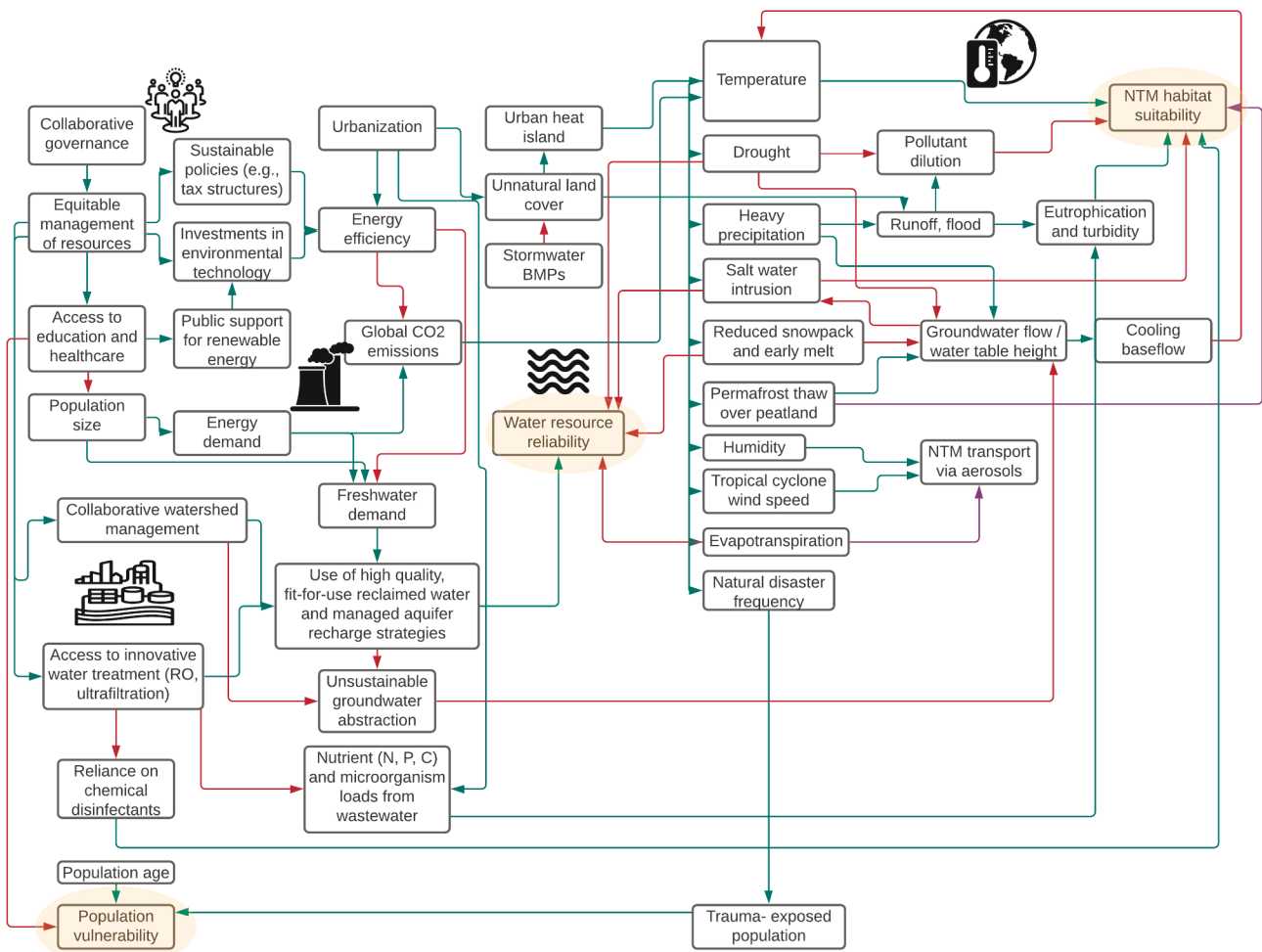


Fig. 2. Systems affecting NTM fate and transport considering climate and societal changes. Green arrows indicate a direct relationship (+), red arrows indicate an inverse relationship (-), and purple arrows indicate uncertain relationships. Yellow ovals indicate key nodes that affect the system outcome and connect to other nodes that may be points of intervention. The left side of the figure represents societal and engineering dynamics, and the right represents climate/natural environment dynamics. Note, although the connections here are informed by the studies reviewed for this analysis, there are many uncertainties. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

Table 2

SSPs considered with respect to NTM. Descriptions for the SSPs were obtained from O'Neill et al. [99] and Riahi et al. [114] and represent a few of many potential pathways and outcomes. Interpretations for NTM are an extension of the literature review and discussion in the previous sections.

Scenario	Description	Potential implications for NTM
SSP1	Cooperative governance, sustainable development, urbanization, equity, healthcare and education access, lower population, clean energy, innovation for environmental technologies, sharp cut in resource demand. Low mitigation and adaptation challenges Radiative forcing $\sim 5 \text{ W/m}^2$	Cooperation reduces de facto reuse by embracing a One Water approach, reducing pathogen exposure. Innovation and equity bring improved water treatment and reclamation practices to more people, reducing NTM exposure. Temperatures continue to rise, supporting NTM in most natural environments, except for those with increased salinity. Heightened focus on wellbeing and equity reduces vulnerability and adverse infection outcomes during disaster times.
SSP2	No major changes from status quo, slow movements towards sustainable development, innovation proceeds slowly without major breakthroughs, resource demand reduces slowly, inequality persists, urbanization remains at pace and does not accelerate. Medium challenges to mitigation and adaptation Radiative forcing $\sim 6.5 \text{ W/m}^2$	Lack of major innovation and persistent inequality suggest that improved water treatment and management strategies fail to reach all populations, allowing de facto reuse and existing inadequate treatment options to persist in practice. Pressure on water resources continues, resulting in greater reliance on reclaimed water, but without new management practices, potentially exposing more people to NTM. Continuing urbanization trends allow greater impervious cover and increase urban heat island effect, exacerbating eutrophication and flood challenges in highly populated areas, potentially exposing more people to NTM in affected water sources and flood water.
SSP3	Regional rivalries, resurgent nationalism, focus on national security at the expense of environmental issues, inequality persists, technological investments decline, population grows in developing countries and stabilizes in industrial, urbanization and economic growth stabilize. High challenges to mitigation and adaptation Radiative forcing $\sim 7.2 \text{ W/m}^2$	Climate change accelerates with a high level of radiative forcing, exacerbating warming, humidity, evapotranspiration, sea level rise, natural disaster intensity and/or frequency, extreme precipitation and drought, and all of the associated effects on water scarcity and NTM. Nationalism prevents cooperative water management, stressing water resources and increasing reliance on inadequately treated reclaimed water. Inequalities prevent increases in education and access to healthcare, increasing vulnerability, and resulting in worse outcomes for those exposed to NTM.

peatlands in boreal regions [142] and NTM concentrations in connected freshwater systems. Previous reports have associated NTM abundance with peatland drainage areas [69] and the organic acids found in peat [77], but no conclusive evidence exists regarding how permafrost thaw might affect that dynamic or human populations downstream. As another example, future work is recommended about the relationships between evapotranspiration and NTM transport through air to understand why evapotranspiration is related to disease risk in some regions [2]. Understanding the mechanisms behind NTM survival and transport in aerosols in arid climates where rates of evapotranspiration are projected to increase would inform the potential for changes in risk.

Collaborations between patients, medical professionals, environmental microbiologists, engineers, and climatologists may facilitate a more complete understanding of likely transmission routes, exposure

Table 3

Research recommendations.

Topic	Suggested research	Related references, if applicable
Climate-related data collection	- Effect of thawing permafrost over peatlands in boreal regions on NTM concentrations in connected freshwater. - Relationships between climate change and water quality in developing parts of the world. - Effects of climate change, land use, and water abstraction on groundwater hydrology and quality in diverse regions. - Impact of climate change on exposure routes (NTM aerosolization efficiency and transport)	[69,77,142] [70] [70] [75,86,137]
NTM fate and transport	- NTM in connected water and air environments over extended time periods and diverse environmental conditions. - Improved NTM measurement techniques for species-level and viability analyses in a variety of environments. - Relationships between: NTM, soils, temperature, nutrients, metals, salinity, and oxygen (in natural and engineered systems) - Effects of evapotranspiration on NTM transport through air - Changes in UV irradiation and effects on NTM survival	[12] [2] [8,29]
Water conservation	- Safety of reclaimed water/engineered recharge with respect to pathogens (NTM) - Comparative risk analysis of water conservation practices vs. no action	[6,35,73]
Reclaimed water treatment/distribution	- Effects of UV disinfection on NTM control - Use of alternative corrosion inhibitors to prevent biofilm growth. - Use of pipe protection for temperature control (e.g., shade, minimum clearance distances). - Practicality of disseminating advanced water treatment systems around the globe. - Development of innovative, accessible water treatment solutions. - Potential effects on proliferation of other pathogens of concern as a result of NTM treatment methods.	[41] [66,76] [3] [150]
Modeling	- Models to determine critical limits of controlling factors for NTM fate and transport. - Models to translate gene concentrations into viable NTM cell counts.	

levels, and dose–response parameters necessary for QMRA. A public health reporting requirement for NTM infections does not exist in most of the world, and if implemented, would enhance the understanding of these relationships by providing more data on the prevalence of NTM infections. Consistent reporting would also inform potential relationships between disease incidence and public health interventions or climatic events, would facilitate better cost analyses, and would aid in evaluating changes in epidemiology [134,135].

3. Conclusions

- Climate change may lead to a net increase in NTM exposure from water sources due to their adaptability to environmental conditions imposed by warming temperatures as well as their ability to be easily aerosolized. Infection risk may also increase due to their opportunistic nature that may benefit from an increasingly stressed population.
- Engineering solutions exist, such as reverse osmosis and nano-filtration, that could reduce exposure to NTM from reclaimed water sources. Potential solutions must be evaluated in the context of the whole microbiome, given that NTM control may lead to increased proliferation of other pathogens. More research is also needed to understand regrowth during distribution of reclaimed water and potential solutions, as well as the practicality of making these solutions accessible worldwide.
- Equitable and sustainable socioeconomic choices may provide an opportunity for water managers to collaboratively manage water resources through One Water practices and innovation that reduce contamination by unmanaged wastewater, reducing risk of infection by pathogens including NTM.
- More field data is needed to understand impacts of climate change on water quality broadly, and to specifically understand NTM fate and transport as a function of environmental factors, as well as relevant exposure routes.
- Collaborative studies that merge knowledge across fields of expertise would support better understanding of relative risk of infection by pathogens including NTM in a complex global change landscape.

CRedit authorship contribution statement

S.M. Blanc: Conceptualization, Methodology, Investigation, Formal analysis, Funding acquisition, Visualization, Writing - original draft, Writing - review & editing. **D. Robinson:** Conceptualization, Writing - review & editing. **N.L. Fahrenfeld:** Conceptualization, Project administration, Supervision, Writing - review & editing.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgements

Thanks to Carrie Ferraro and Jeanne Herb for providing critical review of the article. Thanks to Melissa Tu, Sasha Monti, and Ian Roback for their assistance with data collection.

Funding

This work was supported by a grant from the National Science Foundation Award # 1633557 (Coastal Climate Risk & Resiliency Traineeship). The funders had no role in the study design, data collection, interpretation, writing of the article, or decision to publish.

References

- [1] ABS 2013 Environmental Issues: Water Use and Conservation, Australian Bureau of Statistics Canberra.
- [2] Adjemian J, Olivier KN, Seitz AE, Falkinham III JO, Holland SM, Prevots DR. Spatial clusters of nontuberculous mycobacterial lung disease in the United States. *Am J Respir Crit Care Med* 2012;186(6):553–8.
- [3] Agudelo-Vera C, Avvedimento S, Boxall J, Creaco E, de Kater H, Di Nardo A, et al. Drinking water temperature around the globe: understanding, policies, challenges and opportunities. *Water* 2020;12(4):1049.
- [4] Albrechtsen H-J. Microbiological investigations of rainwater and graywater collected for toilet flushing. *Water Sci Technol* 2002;46(6–7):311–6.
- [5] Allen M, Antwi-Agyei P, Aragon-Durand F, Babiker M, Bertoldi P, Bind M, et al. Technical Summary: Global warming of 1.5° C. An IPCC Special Report on the impacts of global warming of 1.5° C above pre-industrial levels and related global greenhouse gas emission pathways, in the context of strengthening the global response to the threat of climate change, sustainable development, and efforts to eradicate poverty; 2019. <https://www.ipcc.ch/sr15/>.
- [6] Amha YM, Anwar MZ, Kumaraswamy R, Henschel A, Ahmad F. Mycobacteria in municipal wastewater treatment and reuse: microbial diversity for screening the occurrence of clinically and environmentally relevant species in arid regions. *Environ Sci Technol* 2017;51(5):3048–56.
- [7] Ashbolt NJ. *Adaptation and Mitigation Strategies for Climate Change*. Tokyo: Springer; 2010. p. 71–82.
- [8] Bais A, McKenzie R, Bernhard G, Aucamp P, Ilyas M, Madronich S, et al. Ozone depletion and climate change: impacts on UV radiation. *Photochem Photobiol Sci* 2015;14(1):19–52.
- [9] Barker J, Brown M. Trojan horses of the microbial world: protozoa and the survival of bacterial pathogens in the environment. *Microbiology* 1994;140(6):1253–9.
- [10] Barreca AI. Climate change, humidity, and mortality in the United States. *J Environ Econ Manage* 2012;63(1):19–34.
- [11] Bendinger B, Rijnaarts HH, Altendorf K, Zehnder AJ. Physicochemical cell surface and adhesive properties of coryneform bacteria related to the presence and chain length of mycolic acids. *Appl Environ Microbiol* 1993;59(11):3973–7.
- [12] Blanc S, Pender D, Vinnard C, Gennaro M, Fahrenfeld N. Nontuberculous Mycobacteria in the Biofilm Microbiome of Private Well and Premise Plumbing. *Environ Eng Sci* 2021. <https://doi.org/10.1089/ees.2020.0528>.
- [13] Böckelmann U, Dörries H-H, Ayuso-Gabella MN, de Marçay MS, Tandoi V, Levantesi C, et al. Quantitative PCR monitoring of antibiotic resistance genes and bacterial pathogens in three European artificial groundwater recharge systems. *Appl Environ Microbiol* 2009;75(1):154–63.
- [14] Bodmer T, Miltner E, Bermudez LE. *Mycobacterium avium* resists exposure to the acidic conditions of the stomach. *FEMS Microbiol Lett* 2000;182(1):45–9.
- [15] Bolster C, Cook K, Haznedaroglu B, Walker S. The transport of *Mycobacterium avium* subsp. *paratuberculosis* through saturated aquifer materials. *Lett Appl Microbiol* 2009;48(3):307–12.
- [16] Brennan PJ, Nikaido H. The envelope of mycobacteria. *Annu Rev Biochem* 1995;64(1):29–63.
- [17] Breuninger KJ, Weir MH. Development of an interspecies nested dose-response model for *Mycobacterium avium* subspecies *paratuberculosis*. *Risk Anal* 2015;35(8):1479–87.
- [18] Brooks RW. Soil as a possible origin of organisms of the *Mycobacterium avium*, *M. intracellulare*, and *M. scrofulaceum* (M) complex in southeastern United States. Virginia Polytechnic Institute and State University; 1983.
- [19] Brooks RW, George KL, Parker BC, Falkinham III JO, Gruft H. Recovery and survival of nontuberculous mycobacteria under various growth and decontamination conditions. *Can J Microbiol* 1984;30(9):1112–7.
- [20] Chen X, Lang XL, Xu A-L, Song Z-W, Yang J, Guo M-Y. Seasonal variability in the microbial community and pathogens in wastewater final effluents. *Water* 2019;11(12):2586.
- [21] Chou MP, Clements AC, Thomson RM. A spatial epidemiological analysis of nontuberculous mycobacterial infections in Queensland, Australia. *BMC Infect Dis* 2014;14(1):279.
- [22] Cirillo JD, Falkow S, Tompkins LS, Bermudez LE. Interaction of *Mycobacterium avium* with environmental amoebae enhances virulence. *Infect Immun* 1997;65(9):3759–67.
- [23] Collier SA, Deng L, Adam EA, Benedict KM, Beshearse EM, Blackstock AJ, et al. Estimate of burden and direct healthcare cost of infectious waterborne disease in the United States. *Emerg Infect Dis* 2021;27(1):140–9.
- [24] Corsaro D, Pages GS, Catalan V, Loret J-F, Greub G. Biodiversity of amoebae and amoeba-associated bacteria in water treatment plants. *Int J Hyg Environ Health* 2010;213(3):158–66.
- [25] Covert TC, Rodgers MR, Reyes AL, Stelma GN. Occurrence of nontuberculous mycobacteria in environmental samples. *Appl Environ Microbiol* 1999;65(6):2492–6.
- [26] Cui Q, Fang T, Huang Y, Dong P, Wang H. Evaluation of bacterial pathogen diversity, abundance and health risks in urban recreational water by amplicon next-generation sequencing and quantitative PCR. *J Environ Sci* 2017;57:137–49.
- [27] Dailloux M, Laurain C, Weber M, Hartemann P. Water and nontuberculous mycobacteria. *Water Res* 1999;33(10):2219–28.
- [28] Daley CL, Iaccarino JM, Lange C, Cambau E, Wallace Jr RJ, Andrejak C, et al. Treatment of Nontuberculous Mycobacterial Pulmonary Disease: An Official ATS/ERS/ESCMID/IDSA Clinical Practice Guideline. *Clin Infect Dis* 2020;71(4):e1–36.
- [29] David HL. Response of mycobacteria to ultraviolet light radiation. *Am Rev Resp Dis* 1973;108(5):1175–85.
- [30] Dawson D. Potential pathogens among strains of mycobacteria isolated from house-dusts. *Med J Aust* 1971;1(13):679–81.
- [31] De Groot MA, Huijtt G. Infections due to rapidly growing mycobacteria. *Clin Infect Dis* 2006;42(12):1756–63.
- [32] De Groot MA, Pace NR, Fulton K, Falkinham III JO. Relationships between *Mycobacterium* isolates from patients with pulmonary mycobacterial infection and potting soils. *Appl Environ Microbiol* 2006;72(12):7602–6.
- [33] Delafont V, Bouchon D, Héchard Y, Moulin L. Environmental factors shaping cultured free-living amoebae and their associated bacterial community within drinking water network. *Water Res* 2016;100:382–92.
- [34] Dillon P. Water recycling via managed aquifer recharge in Australia. *Boletín Geológico y Minero* 2009;120(2):121–30.

- [35] Dillon P, Stuyfzand P, Grischek T, Lloria M, Pyne R, Jain R, et al. Sixty years of global progress in managed aquifer recharge. *Hydrogeol J* 2019;27(1):1–30.
- [36] Dillon P, Toze S, Page D, Vanderzalm J, Bekele E, Sidhu J, et al. Managed aquifer recharge: rediscovering nature as a leading edge technology. *Water Sci Technol* 2010;62(10):2338–45.
- [37] Donohue MJ. Increasing nontuberculous mycobacteria reporting rates and species diversity identified in clinical laboratory reports. *BMC Infect Dis* 2018;18(1):163.
- [38] Earman S, Dettinger M. Potential impacts of climate change on groundwater resources—a global review. *J Water Clim Change* 2011;2(4):213–29.
- [39] Estop-Aragonés C, Knorr KH, Blodau C. Controls on in situ oxygen and dissolved inorganic carbon dynamics in peats of a temperate fen. *J Geophys Res Biogeosci* 2012;117(G2).
- [40] Falkinham III J. Epidemiology of infection by nontuberculous mycobacteria. *Clin Microbiol Rev* 1996;9(2):177.
- [41] Falkinham III J. Surrounded by mycobacteria: nontuberculous mycobacteria in the human environment. *J Appl Microbiol* 2009;107(2):356–67.
- [42] Falkinham III JO. Impact of human activities on the ecology of nontuberculous mycobacteria. *Future Microbiol* 2010;5(6):951–60.
- [43] Falkinham III JO. Nontuberculous mycobacteria from household plumbing of patients with nontuberculous mycobacteria disease. *Emerg Infect Dis* 2011;17(3):419–24.
- [44] Falkinham III JO. Ecology of nontuberculous mycobacteria—where do human infections come from? Thieme Medical Publishers; 2013, p. 095–102.
- [45] Falkinham III JO. Environmental sources of nontuberculous mycobacteria. *Clin Chest Med* 2015;36(1):35–41.
- [46] Falkinham III JO. Current epidemiologic trends of the nontuberculous mycobacteria (NTM). *Curr Environ Health Rep* 2016;3(2):161–7.
- [47] Falkinham III JO, Norton CD, LeChevallier MW. Factors influencing numbers of *Mycobacterium avium*, *Mycobacterium intracellulare*, and other mycobacteria in drinking water distribution systems. *Appl Environ Microbiol* 2001;67(3):1225–31.
- [48] Fang W, Hu J, Ong S. Influence of phosphorus on biofilm formation in model drinking water distribution systems. *J Appl Microbiol* 2009;106(4):1328–35.
- [49] Feazel LM, Baumgartner LK, Peterson KL, Frank DN, Harris JK, Pace NR. Opportunistic pathogens enriched in showerhead biofilms. *Proc Natl Acad Sci* 2009;106(38):16393–9.
- [50] Field CB, Barros V, Stocker TF, Dahe Q. Managing the risks of extreme events and disasters to advance climate change adaptation: special report of the intergovernmental panel on climate change. Cambridge University Press; 2012.
- [51] Garner E, McLain J, Bowers J, Engelthaler DM, Edwards MA, Pruden A. Microbial ecology and water chemistry impact regrowth of opportunistic pathogens in full-scale reclaimed water distribution systems. *Environ Sci Technol* 2018;52(16):9056–68.
- [52] Garner E, Zhu N, Strom L, Edwards M, Pruden A. A human exposome framework for guiding risk management and holistic assessment of recycled water quality. *Environ Sci Water Res Technol* 2016;2(4):580–98.
- [53] George KL, Parker BC, Gruft H, Falkinham III JO. Epidemiology of infection by nontuberculous mycobacteria: II. Growth and survival in natural waters. *Am Rev Resp Dis* 1980;122(1):89–94.
- [54] Ghernaout D. Increasing trends towards drinking water reclamation from treated wastewater. *World J Appl Chem* 2018;3:1–9.
- [55] Ghernaout D, Elboughdiri N, Al Arni S. Water Reuse (WR): Dares, restrictions, and trends. *Appl Eng* 2019;3:159–70.
- [56] Glaser KC, Hetrick ND, Molestina RE. Evidence for a previously unrecognized mycobacterial endosymbiont in *Acanthamoeba castellanii* Strain Ma (ATCC® 50370™). *J Eukaryot Microbiol* 2011;58(1):75–6.
- [57] Griffith DE, Akshami T, Brown-Elliott BA, Catanzaro A, Daley C, Gordin F, et al. An official ATS/IDSA statement: diagnosis, treatment, and prevention of nontuberculous mycobacterial diseases. *Am J Respir Crit Care Med* 2007;175(4):367–416.
- [58] Haig S-J, Kotlarz N, Kalikin LM, Chen T, Guikema S, LiPuma JJ, et al. Emerging investigator series: bacterial opportunistic pathogen gene markers in municipal drinking water are associated with distribution system and household plumbing characteristics. *Environ Sci Water Res Technol* 2020;6(11):3032–43.
- [59] Hamilton KA, Ahmed W, Toze S, Haas CN. Human health risks for *Legionella* and *Mycobacterium avium* complex (MAC) from potable and non-potable uses of roof-harvested rainwater. *Water Res* 2017;119:288–303.
- [60] Hamilton KA, Parrish K, Ahmed W, Haas CN. Assessment of water quality in roof-harvested rainwater barrels in greater Philadelphia. *Water* 2018;10(2):92.
- [61] Hamilton KA, Weir MH, Haas CN. Dose response models and a quantitative microbial risk assessment framework for the *Mycobacterium avium* complex that account for recent developments in molecular biology, taxonomy, and epidemiology. *Water Res* 2017;109:310–26.
- [62] Harb M, Wang P, Zarei-Baygi A, Plumlee MH, Smith AL. Background antibiotic resistance and microbial communities dominate effects of advanced purified water recharge to an urban aquifer. *Environ Sci Technol Lett* 2019;6(10):578–84.
- [63] Hoefsloot W, Van Ingen J, Andrejak C, Ångeby K, Bauriaud R, Bemer P, et al. The geographic diversity of nontuberculous mycobacteria isolated from pulmonary samples: an NTM-NET collaborative study. *Eur Respir J* 2013;42(6):1604–13.
- [64] Honda JR, Bernhard JN, Chan ED. Natural disasters and nontuberculous mycobacteria: a recipe for increased disease? *Chest* 2015;147(2):304–8.
- [65] Honda JR, Viridi R, Chan ED. Global environmental nontuberculous mycobacteria and their contemporaneous man-made and natural niches. *Front Microbiol* 2018;9(2029).
- [66] Huang C, Sun PP, Won J, Wang Y, Boppart SA, Nguyen TH. Effect of Nonphosphorus Corrosion Inhibitors on Biofilm Pore Structure and Mechanical Properties. *Environ Sci Technol* 2020;54(22):14716–24.
- [67] Huang C, Wang X, Yang H, Li Y, Wang Y, Chen X, et al. Satellite data regarding the eutrophication response to human activities in the plateau lake Dianchi in China from 1974 to 2009. *Sci Total Environ* 2014;485:1–11.
- [68] Huo C, Dar AA, Nawaz A, Hameed J, Pan B, Wang C. Groundwater contamination with the threat of COVID-19: Insights into CSR theory of Carroll's pyramid. *J King Saud Univ-Sci* 2021;33(2):101295.
- [69] Iivanainen E, Martikainen P, Väänänen P, Katila M-L. Environmental factors affecting the occurrence of mycobacteria in brook waters. *Appl Environ Microbiol* 1993;59(2):398–404.
- [70] IPCC. Climate Change 2014: Synthesis Report. Core Writing Team, R.K.P.A.L.A.M., editor. Geneva, Switzerland; IPCC; 2014.
- [71] Jacobs J, Rhodes M, Sturgis B, Wood B. Influence of environmental gradients on the abundance and distribution of *Mycobacterium* spp. in a coastal lagoon estuary. *Appl Environ Microbiol* 2009;75(23):7378–84.
- [72] Jalliffier-Verne I, Leconte R, Huaranga-Alvarez U, Madoux-Humery A-S, Galarnau M, Servais P, et al. Impacts of global change on the concentrations and dilution of combined sewer overflows in a drinking water source. *Sci Total Environ* 2015;508:462–76.
- [73] Jjemba P, Johnson W, Bukhari Z, LeChevallier M. Review of the leading challenges in maintaining reclaimed water quality during storage and distribution. *J Water Reuse Desal* 2014;4(4):209–37.
- [74] Jjemba PK, Weinrich LA, Cheng W, Giraldo E, LeChevallier MW. Regrowth of potential opportunistic pathogens and algae in reclaimed-water distribution systems. *Appl Environ Microbiol* 2010;76(13):4169–78.
- [75] Joung YS, Ge Z, Buie CR. Bioaerosol generation by raindrops on soil. *Nat Commun* 2017;8(1):1–10.
- [76] Kimbell LK, Wang Y, McNamara PJ. The impact of metal pipe materials, corrosion products, and corrosion inhibitors on antibiotic resistance in drinking water distribution systems. *Appl Microbiol Biotechnol* 2020. <https://doi.org/10.1007/s00253-020-10777-8>, 1–16.
- [77] Kirschner Jr RA, Parker BC, Falkinham III JO. Humic and fulvic acids stimulate the growth of *Mycobacterium avium*. *FEMS Microbiol Ecol* 1999;30(4):327–32.
- [78] Kirschner Jr. RA, Parker BC, Falkinham III JO. Epidemiology of infection by nontuberculous mycobacteria. *Mycobacterium avium*, *Mycobacterium intracellulare*; 1992, p. 271–5.
- [79] Kirschner Jr RA, Parker BC, Falkinham III JO. Epidemiology of infection by nontuberculous mycobacteria: *Mycobacterium avium*, *Mycobacterium intracellulare*, and *Mycobacterium scrofulaceum* in acid, brown-water swamps of the southeastern United States and their association with environmental variables. *Am Rev Resp Dis* 1992;145(2_pt_1):271–5.
- [80] Kløve B, Ala-Aho P, Bertrand G, Gurdak JJ, Kupfersberger H, Kværner J, et al. Climate change impacts on groundwater and dependent ecosystems. *J Hydrol* 2014;518:250–66.
- [81] Kotlarz N, Rockey N, Olson TM, Haig S-J, Sanford L, LiPuma JJ, et al. Biofilms in full-scale drinking water ozone contactors contribute viable bacteria to ozonated water. *Environ Sci Technol* 2018;52(5):2618–28.
- [82] Le Dantec C, Duguet J-P, Montiel A, Dumoutier N, Dubrou S, Vincent V. Occurrence of mycobacteria in water treatment lines and in water distribution systems. *Appl Environ Microbiol* 2002;68(11):5318–25.
- [83] Lee E-S, Yoon T-H, Lee M-Y, Han S-H, Ka J-O. Inactivation of environmental mycobacteria by free chlorine and UV. *Water Res* 2010;44(5):1329–34.
- [84] Li H, Li S, Tang W, Yang Y, Zhao J, Xia S, et al. Influence of secondary water supply systems on microbial community structure and opportunistic pathogen gene markers. *Water Res* 2018;136:160–8.
- [85] Li W, Wang F, Zhang J, Qiao Y, Xu C, Liu Y, et al. Community shift of biofilms developed in a full-scale drinking water distribution system switching from different water sources. *Sci Total Environ* 2016;544:499–506.
- [86] Lin K, Marr LC. Humidity-dependent decay of viruses, but not bacteria, in aerosols and droplets follows disinfection kinetics. *Environ Sci Technol* 2019;54(2):1024–32.
- [87] Ling F, Whitaker R, LeChevallier MW, Liu W-T. Drinking water microbiome assembly induced by water stagnation. *ISME J* 2018;12(6):1520–31.
- [88] Lipner EM, Knox D, French J, Rudman J, Strong M, Crooks JL. A geospatial epidemiologic analysis of nontuberculous mycobacterial infection: an ecological study in Colorado. *Ann Am Thoracic Soc* 2017;14(10):1523–32.
- [89] Liu L, Xing X, Hu C, Wang H. One-year survey of opportunistic premise plumbing pathogens and free-living amoebae in the tap-water of one northern city of China. *J Environ Sci* 2019;77:20–31.
- [90] Liu S, Gunawan C, Barraud N, Rice SA, Harry EJ, Amal R. Understanding, monitoring, and controlling biofilm growth in drinking water distribution systems. *Environ Sci Technol* 2016;50(17):8954–76.
- [91] Liu X, Wang J, Liu T, Kong W, He X, Jin Y, et al. Effects of assimilable organic carbon and free chlorine on bacterial growth in drinking water. *PLoS ONE* 2015;10(6):e0128825.
- [92] Lytle D, Frieth C, Covert T. Electrophoretic mobility of *Mycobacterium avium* complex organisms. *Appl Environ Microbiol* 2004;70(9):5667–71.
- [93] Machado A, Bordalo A. Prevalence of antibiotic resistance in bacteria isolated from drinking well water available in Guinea-Bissau (West Africa). *Ecotoxicol Environ Saf* 2014;106:188–94.
- [94] Nasrin T, Sharma AK, Muttill N. Impact of short duration intense rainfall events on sanitary sewer network performance. *Water* 2017;9(3):225.

- [95] Nguyen KT, Piastro K, Gray TA, Derbyshire KM. Mycobacterial biofilms facilitate horizontal DNA transfer between strains of *Mycobacterium smegmatis*. *J Bacteriol* 2010;192(19):5134–42.
- [96] Nishiuchi Y, Iwamoto T, Maruyama F. Infection sources of a common non-tuberculous mycobacterial pathogen, *Mycobacterium avium* complex. *Front Med* 2017;4:27.
- [97] Norton CD, LeChevallier MW, Falkinham III JO. Survival of *Mycobacterium avium* in a model distribution system. *Water Res* 2004;38(6):1457–66.
- [98] O'Neill BC, Oppenheimer M, Warren R, Hallegatte S, Kopp RE, Pörtner HO, et al. IPCC reasons for concern regarding climate change risks. *Nat Clim Change* 2017;7(1):28–37.
- [99] O'Neill BC, Kriegler E, Ebi KL, Kemp-Benedict E, Riahi K, Rothman DS, et al. The roads ahead: Narratives for shared socioeconomic pathways describing world futures in the 21st century. *Global Environ Change* 2017;42:169–80.
- [100] Obihara CC, Kimpen JL, Beyers N. The potential of Mycobacterium to protect against allergy and asthma. *Current allergy and asthma reports* 2007;7(3):223–30.
- [101] Olivier KN, Weber DJ, Wallace Jr RJ, Faiz AR, Lee J-H, Zhang Y, et al. Nontuberculous mycobacteria: I: multicenter prevalence study in cystic fibrosis. *Am J Respir Crit Care Med* 2003;167(6):828–34.
- [102] Oriani AS, Sierra F, Baldini MD. Effect of chlorine on *Mycobacterium gordonae* and *Mycobacterium chubuense* in planktonic and biofilm state. *Int J Mycobacteriol* 2018;7(2):122.
- [103] Pal C, Bengtsson-Palme J, Kristianson E, Larsson DGJ. Co-occurrence of resistance genes to antibiotics, biocides and metals reveals novel insights into their co-selection potential. *BMC Genomics* 2015;16(1):964.
- [104] Parikh A, Vinnard C, Fahrenfeld N, Davidow AL, Patrawalla A, Lardizabal A, et al. Revisiting John Snow to meet the challenge of nontuberculous mycobacterial lung disease. *Int J Environ Res Public Health* 2019;16(21):4250.
- [105] Parker BC, Ford MA, Gruft H, Falkinham III JO. Epidemiology of infection by nontuberculous mycobacteria: IV. Preferential aerosolization of *Mycobacterium intracellulare* from natural waters. *Am Rev Resp Dis* 1983;128(4):652–6.
- [106] Patz JA, Vavrus SJ, Uejio CK, McLellan SL. Climate change and waterborne disease risk in the Great Lakes region of the U.S. *Am J Prev Med* 2008;35(5):451–8.
- [107] Pereira AC, Ramos B, Reis AC, Cunha MV. Non-tuberculous mycobacteria: Molecular and physiological bases of virulence and adaptation to ecological niches. *Microorganisms* 2020;8(9):1380.
- [108] Perez-Martinez I, Aguilar-Ayala DA, Fernandez-Rendon E, Carrillo-Sanchez AK, Helguera-Repetto AC, Rivera-Gutierrez S, et al. Occurrence of potentially pathogenic nontuberculous mycobacteria in Mexican household potable water: a pilot study. *BMC Res Notes* 2013;6(1):531.
- [109] Prasad BK, Gupta S. Preliminary report on the engulment and retention of mycobacteria by trophozoites of exenically grown *Acanthamoeba castellanii* Douglas, 1930. *Curr Sci* 1978;47(7):245–7.
- [110] Ramsay K, Stockwell R, Bell S, Kidd T. Infection in cystic fibrosis: impact of the environment and climate. *Exp Rev Resp Med* 2016;10(5):505–19.
- [111] Ratnatunga CN, Lutzky VP, Kupz A, Doolan DL, Reid DW, Field M, Bell SC, Thomson RM, Miles JJ. The Rise of Non-Tuberculosis Mycobacterial Lung Disease. *Front Immunol* 2020;11.
- [112] Reddy KR, Xie T, Dastgheibi S. Removal of heavy metals from urban stormwater runoff using different filter materials. *J Environ Chem Eng* 2014;2(1):282–92.
- [113] Revetta R, Gomez-Alvarez V, Gerke T, Santo Domingo J, Ashbolt N. Changes in bacterial composition of biofilm in a metropolitan drinking water distribution system. *J Appl Microbiol* 2016;121(1):294–305.
- [114] Riahi K, van Vuuren DP, Kriegler E, Edmonds J, O'Neill BC, Fujimori S, et al. The shared socioeconomic pathways and their energy, land use, and greenhouse gas emissions implications: an overview. *Glob Environ Change* 2017;42:153–68.
- [115] Rice G, Wright JM, Boutin B, Swartout J, Rodgers P, Niemuth N, et al. Estimating the frequency of tap-water exposures to *Mycobacterium avium* complex in the US population with advanced AIDS. *J Toxicol Environ Health, Part A* 2005;68(11–12):1033–47.
- [116] Rizwan AM, Dennis LY, Chunho L. A review on the generation, determination and mitigation of Urban Heat Island. *J Environ Sci* 2008;20(1):120–8.
- [117] Robinson ST. Geological and geochemical controls on non-tuberculous mycobacterium transmission: examples from Hawaii. MS: Brigham Young University; 2019.
- [118] Roccaro P. Treatment processes for municipal wastewater reclamation: The challenges of emerging contaminants and direct potable reuse. *Curr Opin Environ Sci Health* 2018;2:46–54.
- [119] Roguet A, Thieria C, Catherine A, Bressy A, Varrault G, Bouhdmane L, et al. Importance of local and regional scales in shaping mycobacterial abundance in freshwater lakes. *Microb Ecol* 2018;75(4):834–46.
- [120] Schulze-Röbbecke R, Buchholtz K. Heat susceptibility of aquatic mycobacteria. *Appl Environ Microbiol* 1992;58(6):1869–73.
- [121] Schulze-Röbbecke R, Janning B, Fischeder R. Occurrence of mycobacteria in biofilm samples. *Tuber Lung Dis Off J Int Union Tuber Lung Dis* 1992;73(3):141–4.
- [122] Sebakova H, Kozisek F, Mudra R, Kaustova J, Fiedorova M, Hanslikova D, et al. Incidence of nontuberculous mycobacteria in four hot water systems using various types of disinfection. *Can J Microbiol* 2008;54(11):891–8.
- [123] Sherrard LJ, Tay GT, Butler CA, Wood ME, Yerkovich S, Ramsay KA, et al. Tropical Australia is a potential reservoir of non-tuberculous mycobacteria in cystic fibrosis. *Eur Respir J* 2017;49(5).
- [124] Small GE, Niederluecke EQ, Shrestha P, Janke BD, Finlay JC. The effects of infiltration-based stormwater best management practices on the hydrology and phosphorus budget of a eutrophic urban lake. *Lake Reservoir Manage* 2019;35(1):38–50.
- [125] Smeulders MJ, Keer J, Speight RA, Williams HD. Adaptation of *Mycobacterium smegmatis* to stationary phase. *J Bacteriol* 1999;181(1):270–83.
- [126] Stahl DA, Urbance JW. The division between fast- and slow-growing species corresponds to natural relationships among the mycobacteria. *J Bacteriol* 1990;172(1):116–24.
- [127] Stamps BW, Leddy MB, Plumlee MH, Hasan NA, Colwell RR, Spear JR. Characterization of the microbiome at the world's largest potable water reuse facility. *Front Microbiol* 2018;9:2435.
- [128] Steed KA, Falkinham III JO. Effect of growth in biofilms on chlorine susceptibility of *Mycobacterium avium* and *Mycobacterium intracellulare*. *Appl Environ Microbiol* 2006;72(6):4007–11.
- [129] Stout JE, Koh W-J, Yew WW. Update on pulmonary disease due to non-tuberculous mycobacteria. *Int J Infect Dis* 2016;45:123–34.
- [130] Strahl ED, Gillaspie GE, Falkinham JO. Fluorescent acid-fast microscopy for measuring phagocytosis of *Mycobacterium avium*, *Mycobacterium intracellulare*, and *Mycobacterium scrofulaceum* by *Tetrahymena pyriformis* and their intracellular growth. *Appl Environ Microbiol* 2001;67(10):4432–9.
- [131] Strollo SE, Adjemian J, Adjemian MK, Prevots DR. The burden of pulmonary nontuberculous mycobacterial disease in the United States. *Ann Am Thoracic Soc* 2015;12(10):1458–64.
- [132] Taylor CA, Stefan HG. Shallow groundwater temperature response to climate change and urbanization. *J Hydrol* 2009;375(3–4):601–12.
- [133] Thomas V, Loret JF, Jousset M, Greub G. Biodiversity of amoebae and amoebae-resisting bacteria in a drinking water treatment plant. *Environ Microbiol* 2008;10(10):2728–45.
- [134] Thomson R, Donnan E, Konstantinos A. Notification of nontuberculous mycobacteria: an Australian perspective. *Ann Am Thoracic Soc* 2017;14(3):318–23.
- [135] Thomson R, Donnan E, Unwin S. Nontuberculous Mycobacterial Lung Disease. Time to Get a Grip! *Am Thoracic Soc* 2015.
- [136] Thomson RM, Carter R, Tolson C, Coulter C, Huygens F, Hargreaves M. Factors associated with the isolation of Nontuberculous mycobacteria (NTM) from a large municipal water system in Brisbane, Australia. *BMC Microbiol* 2013;13(1):89.
- [137] Thomson RM, Furuya-Kanamori L, Coffey C, Bell SC, Knibbs LD, Lau CL. Influence of climate variables on the rising incidence of nontuberculous mycobacterial (NTM) infections in Queensland, Australia 2001–2016. *Sci Total Environ* 2020;740:139796.
- [138] Tjandraatmadja G, Kaksonen A, Gonzalez D, Barry K, Vanderzalm J, Puzon G, et al. Managed aquifer recharge and stormwater use options: investigation of stormwater impact on water quality and distribution infrastructure. Goyder Institute for Water Research Technical Report Series. 2014. 14/8.
- [139] Torvinen E, Lehtola MJ, Martikainen PJ, Miettinen IT. Survival of *Mycobacterium avium* in drinking water biofilms as affected by water flow velocity, availability of phosphorus, and temperature. *Appl Environ Microbiol* 2007;73(19):6201–7.
- [140] Torvinen E, Meklin T, Torkko P, Suomalainen S, Reiman M, Katila M-L, et al. Mycobacteria and fungi in moisture-damaged building materials. *Appl Environ Microbiol* 2006;72(10):6822–4.
- [141] Treidel H, Martin-Bordes JL, Gurdak JJ. Climate change effects on groundwater resources: a global synthesis of findings and recommendations. CRC Press; 2011.
- [142] Turetsky MR, Wieder RK, Williams CJ, Vitt DH. Organic matter accumulation, peat chemistry, and permafrost melting in peatlands of boreal Alberta. *Écoscience* 2000;7(3):115–22.
- [143] Ulmann V, Kralikova A, Dziedzinska R. Mycobacteria in water used for personal hygiene in heavy industry and collieries: a potential risk for employees. *Int J Environ Res Public Health* 2015;12(3):2870–7.
- [144] Unno T, Kim J, Kim Y, Nguyen SG, Guevarra RB, Kim GP, et al. Influence of seawater intrusion on microbial communities in groundwater. *Sci Total Environ* 2015;532:337–43.
- [145] Vaerewijck MJ, Huys G, Palomino JC, Swings J, Portaels F. Mycobacteria in drinking water distribution systems: ecology and significance for human health. *FEMS Microbiol Rev* 2005;29(5):911–34.
- [146] van der Wielen PW, van der Kooij D. Nontuberculous mycobacteria, fungi, and opportunistic pathogens in unchlorinated drinking water in the Netherlands. *Appl Environ Microbiol* 2013;79(3):825–34.
- [147] Waak MB, Hozalski RM, Hallé C, LaPara TM. Comparison of the microbiomes of two drinking water distribution systems—with and without residual chloramine disinfection. *Microbiome* 2019;7(1):1–14.
- [148] Waak MB, LaPara TM, Halle C, Hozalski RM. Nontuberculous mycobacteria in two drinking water distribution systems and the role of residual disinfection. *Environ Sci Technol* 2019;53(15):8563–73.
- [149] Walker J. The influence of climate change on waterborne disease and *Legionella*: a review. *Perspect Public Health* 2018;138(5):282–6.
- [150] Wang H, Edwards MA, Falkinham III JO, Pruden A. Probiotic approach to pathogen control in premise plumbing systems? A review. *Environ Sci Technol* 2013;47(18):10117–28.
- [151] Wang H, Masters S, Hong Y, Stallings J, Falkinham III JO, Edwards MA, et al. Effect of disinfectant, water age, and pipe material on occurrence and persistence of *Legionella*, mycobacteria, *Pseudomonas aeruginosa*, and two amoebas. *Environ Sci Technol* 2012;46(21):11566–74.
- [152] Weinrich LA, Jjemba PK, Giraldo E, LeChevallier MW. Implications of organic carbon in the deterioration of water quality in reclaimed water distribution systems. *Water Res* 2010;44(18):5367–75.
- [153] Wolinsky E. Nontuberculous mycobacteria and associated diseases. *Am Rev Resp Dis* 1979;119(1):107–59.

- [154] Xu J, Tang W, Ma J, Wang H. Comparison of microbial community shifts in two parallel multi-step drinking water treatment processes. *Appl Microbiol Biotechnol* 2017;101(13):5531–41.
- [155] Xue J, Zhang B, Lamori J, Shah K, Zabaleta J, Garai J, et al. Molecular detection of opportunistic pathogens and insights into microbial diversity in private well water and premise plumbing. *J Water Health* 2020;18(5):820–34.
- [156] Yangali-Quintanilla V, Maeng SK, Fujioka T, Kennedy M, Li Z, Amy G. Nanofiltration vs. reverse osmosis for the removal of emerging organic contaminants in water reuse. *Desalin Water Treat* 2011;34(1–3):50–6.
- [157] Yu Q, Wang Y, Xie X, Currell M, Pi K, Yu M. Effects of short-term flooding on arsenic transport in groundwater system: A case study of the Datong Basin. *J Geochem Explor* 2015;158:1–9.
- [158] Zhang X, Xia S, Zhao R, Wang H. Effect of temperature on opportunistic pathogen gene markers and microbial communities in long-term stored roof-harvested rainwater. *Environ Res* 2020;181:108917.
- [159] Zhu J, Liu R, Cao N, Yu J, Liu X, Yu Z. Mycobacterial metabolic characteristics in a water meter biofilm revealed by metagenomics and metatranscriptomics. *Water Res* 2019;153:315–23.