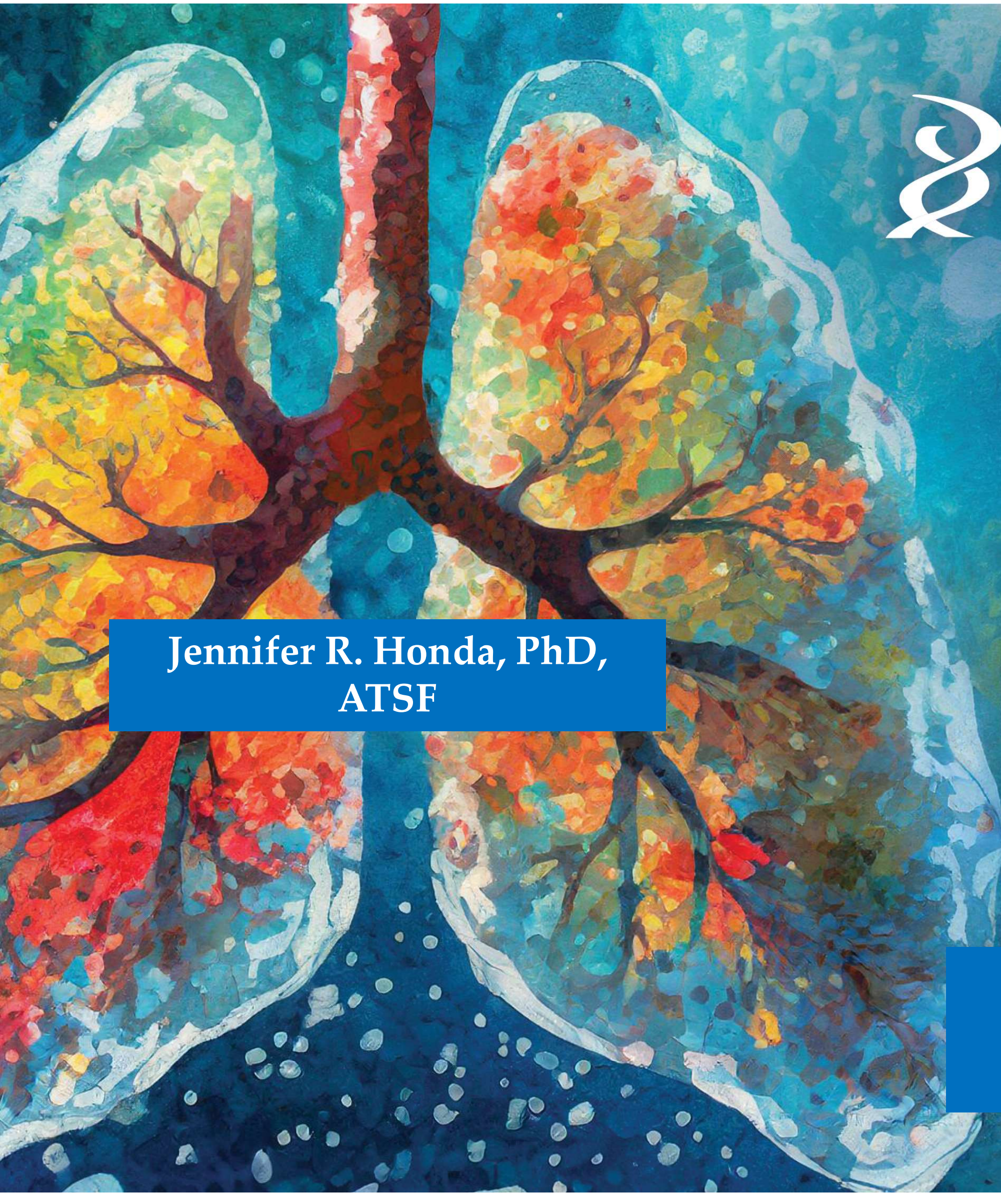


National Jewish Health®

Breathing Science is Life.®

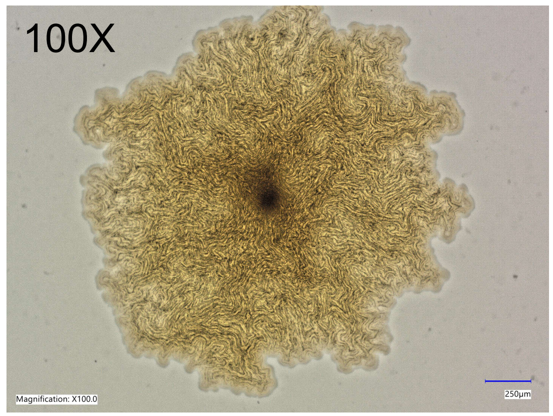
NTM Lecture Series

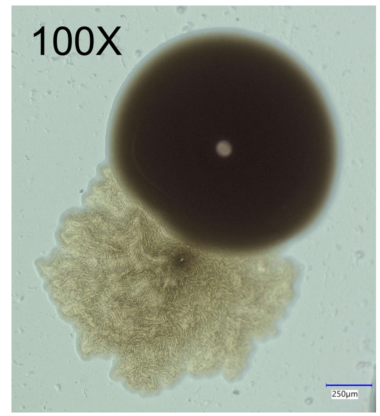
for Patients and Families

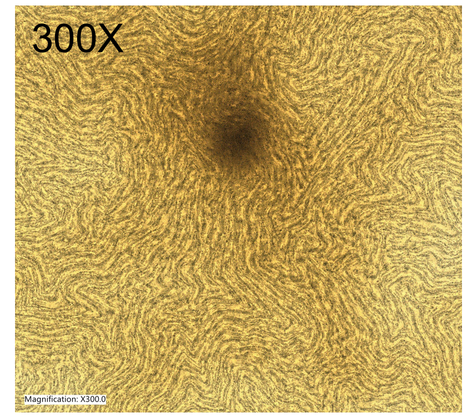
How we should think about our environment

Jennifer R. Honda, PhD, ATSF

NTM Microbiology 101







- NTM are bacteria with a thick and heavy protective outer covering [1]
  - Adherence to plumbing pipe surfaces [2]
  - Broad resistance to disinfectants, chemicals, and antibiotics [3]
  - Can be biofilm pioneers [4]
- Resistant to low pH of stomach [5]
- Withstand exposure to high temperatures (50-60 ºC); *M. avium* tolerates 45℃ [4]
- Metal resistance [6].

Adaptable

[1] Brennan, *et al*., Annu Rev Biochem, 1995; [2] Mullis, *et al.,* J Appl Micro, 2013; [3] Rastogi *et al.,* Antimicr Agents Chemo 1981; [4 5] Falkinham *et al*., Clin Chest Med, 2002; [5] Portaels *et al.,* Ann Microb, 1992; [6] Falkinham *et al*., Antim Agents Chemo 1984.

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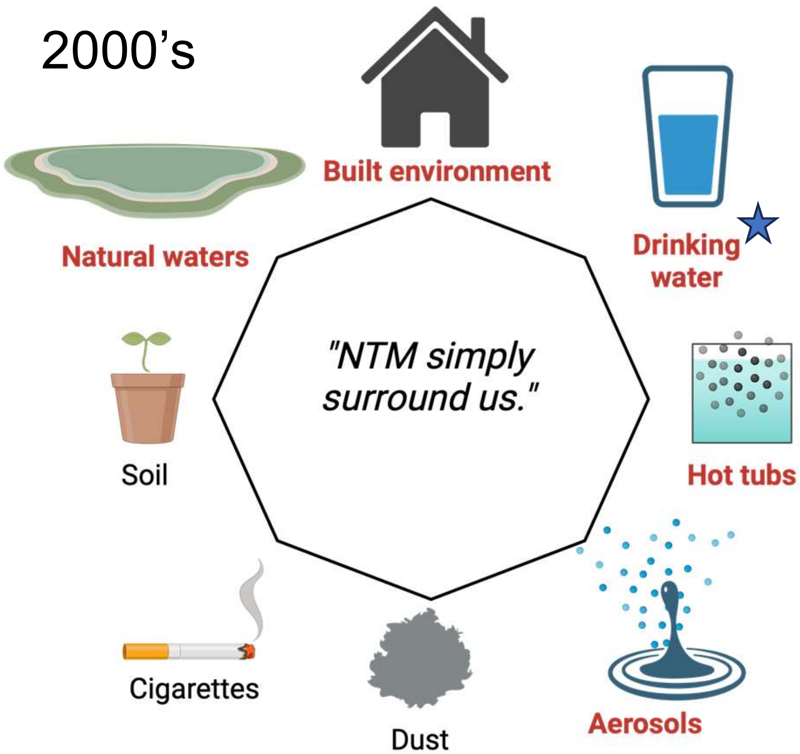
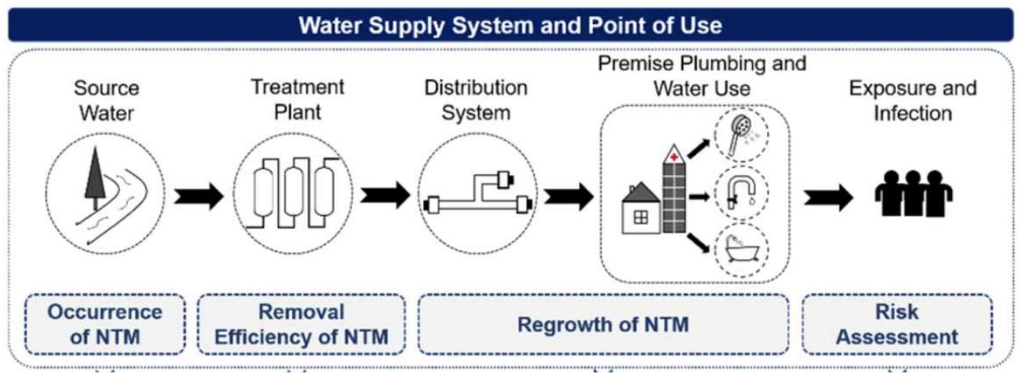
NTM environments, 2000's



One of the most serious waterborne infections. [1,2]



"We predict an increasing incidence of interactions between humans and mycobacteria in the coming years. [3]

[6] Faklinham et al., J Appl Micro, 2009; [1] Gan et al.. H2O Open Journal, 2022; [2] Collier, *et al.,* Estim Burden HealthCare, 2021; [3] Falkinham *et al.*, Clin Chest Med, 2002; Primm *et al.*, 2004
Image created in BioRender

NTM Identified From Drinking Water Systems Globally

Location:	% NTM recovery:	Species:	Reference:
Mexico	**16% (19/120)**	*M. mucogenicum* most common; *M. avium*, **no *M. abscessus***	Perez, *et al.,* BMC Res Notes, 2013
Greece	**22% (42/197)**	*M. chelonae* most common; **no M. *abscessus***	Tsintzou, et al., Water, Air, Soil Poll, 2000
USA	**33% (46/139)**	9 species, *M. mucogenicum* most common; **no M. *abscessus***	Covert, *et al.,* AEM 1999
Colombia	**50% (9/18)**	*M. mucogenicum* most common; **no M. *abscessus***	Dávalos, *et al.,* Env Res & Public Health, 2021
Argentina	**52% (64/124)**	*M. gordonae* most common	Oriani, *et al.,* Int J. Mycobacter, 2019
Australia	**62% (236/384)**	*M. gordonae* most common; ***M. abscessus* identified**	Thomson, *et al.,* BMC Microb, 2013
Paris, France	**72% (104/144)**	*M. gordonae* and *M. nonchromogenicum* most common; Potentially pathogenic, 16%; **no *M. abscessus*.**	Le Dantec, *et al.,* AEM, 2002

Which species of NTM is found, matters.

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"Anonymous" no longer

- Inhalation from the environment – shower water and soil aerosols; spa exposures [1,2 3,4]
- Oral ingestion – drinking water [5]
  - Survival in stomach acid and reflux into the lung
- Aerosols from ultrasonic humidifier use [6]
- Dermal contact [7]
- Hospital ice and ice machines [8]
- Heater-cooler devices [9] and bronchoscopes [10]
- Biofilms in water lines in dental drilling and cleaning devices [11,12]
- Glass, copper, galvanized steel, PVC [13, 14, 15]

[1] Thomason *et al.,* Appl Env Microi*,* 2013; [2] Gebert *et al*., mBio, 2018; [3]Uwamino, *et al.,* J Infect Chemoth; 2020; [4] Nakanaga, *et al.,* J Clin Micro, 201; [5] Hamilton, *et al.,* Water Research, 2017; [6] Hamilton *et al.,* J Med Microbio, 2018;[7] Patel *et al.,* Case Rep Dermatol Med, 2013; [8] Millar *et al.,* Int J Mycobacteria, 2020; [9] Sax *et al*., Clin Infect Dis, 2015; [10] Gubler et al., Chest, 1992; [11] Schulze-Robbecke, *et. al.,* Tubercle Lung Dis, 1995; [12] Wang *et al*., Eur Resp J, 1995; [13] Steed, *et al.,* Appl Env Micro*,* 2006; [14] du Moulin, *et al., JAMA*, 1988; [15] George, *et al.,* Am Rev Respir Dis 1980.

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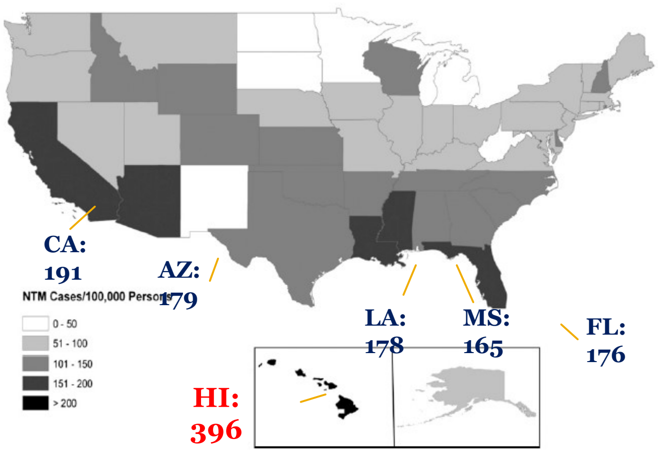
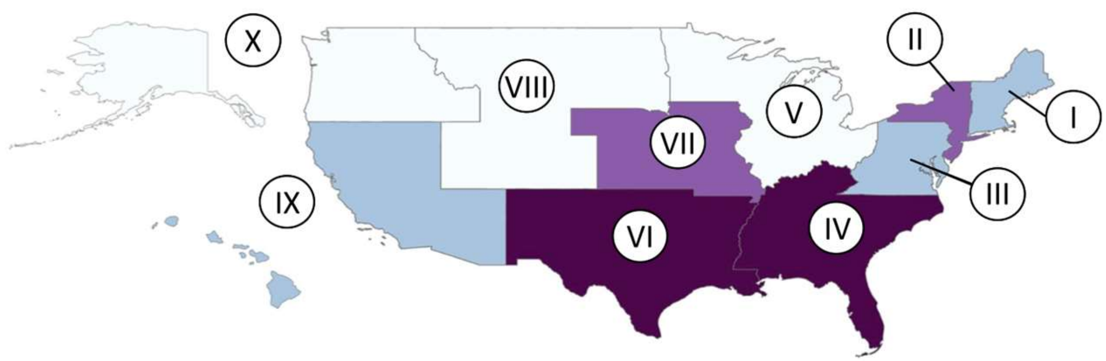
Where you live may matter

NTM national prevalence – 1997-2007 [1]



396 cases/100,000 population
among persons > 65 years-old

NTM culture positivity (%); 2019-2022
National Commercial Lab [2]



[1] Adjemian, *et al.,* AJRCCM, 2012; [2] Marshall *et al.*, BMC infectious Disease, 2002

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What’s new regarding NTM in the environment

- Greater **water age** (combined time in distribution system and home plumbing stagnation time) promotes *M. avium* [1]
- *M. abscessus* **hot water persistence** is higher at residences than office buildings; *M. intracellulare* hot water occurrence is influenced by water age and square footage; *M. avium’s* hot water occurrence is affected by **distances between tank and tap** [2]
- Presence of certain **metals** - as molybdenum increases, MAC infections increase by 45% (OR); molybdenum associated with disease risk in CO; as vanadium increases, *M. abscessus* infections increase by 41% (OR). [3]
- **Low risk for hospital** transmission of *M. abscessus* at an Adult Cystic Fibrosis Program [4]

[1] Haig *et al.,* mBio, 2018, [2] Donohue, *et al.,* Science Total Environment, 2022; Lipner, *et al*., Annals ATS, 2021; Gross et al., ERJ, 2024

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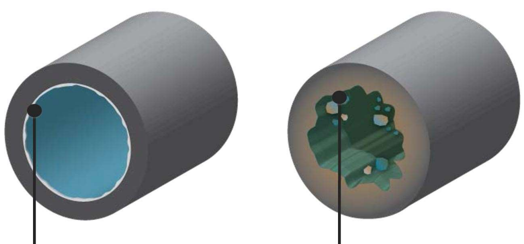
Freshwater features that may contribute to NTM

***Mycobacterium avium* in Community and Household Water, Suburban Philadelphia, Pennsylvania, USA, 2010–2012**

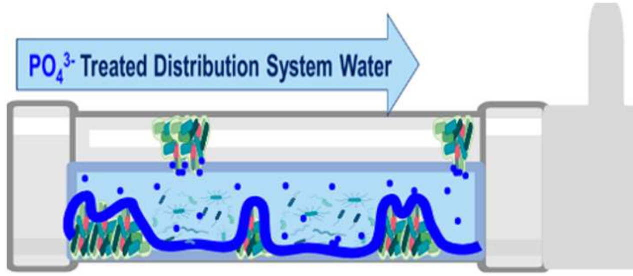
Leah Lande, David C. Alexander, Richard J. Wallace, Jr., Rebecca Kwait, Elena Iakhiaeva, Myra Williams, Andrew D.S. Cameron, Stephen Olshefsky, Ronit Devon, Ravikiran Vasireddy, Donald D. Peterson, Joseph O. Falkinham, III

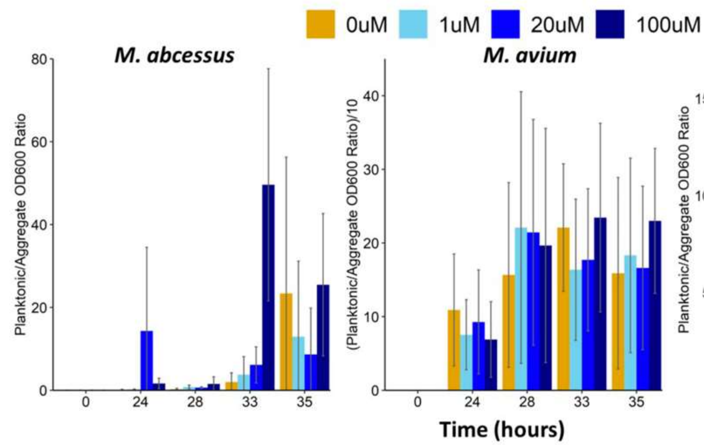
Many drinking water systems commonly add orthophosphates to reduce the release of metals and control for lead and copper in pipes. [1]

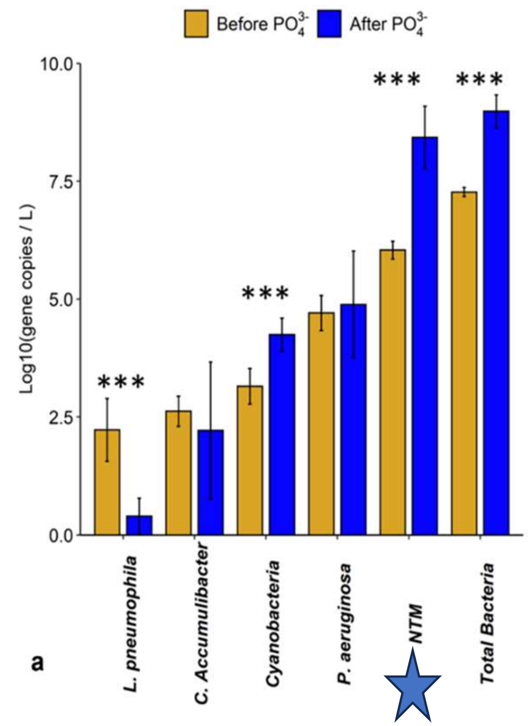


A protective layer of *Orthophosphate* forms to prevent pipe corrosion.

Lack of corrosion control allows lead to leach from pipes into water.







Lande *et al*., EID, 2019; [1] Pittsburgh Water and Sewer Authority, 2019; [2] Spencer-Williams, et al., Env Science and Tech., 2023

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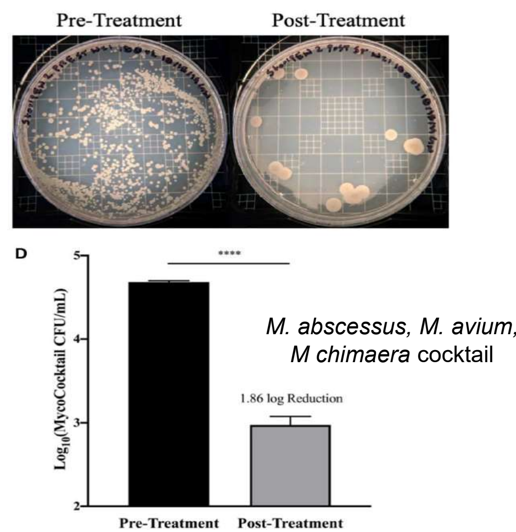
Longstanding suggestions on how to reduce exposures

- Clean showerheads and faucet taps regularly.
- Avoid misting showerheads
- Ventilate bathrooms, showers, other steam areas.
- Use a water filter.
- Raise the temperature of household water heater and drain.
- Avoid humidifiers.
- Wear dust mask.
- Reduce acid reflux.
- Self-supplied water (*e.g.*, wells, collected rainwater) is a protective factor, Virginia [5]

- Avoid dusts from soil * [1, 2]
- Boil water for 10min before use [3].
- Use of UV water bottles [4]

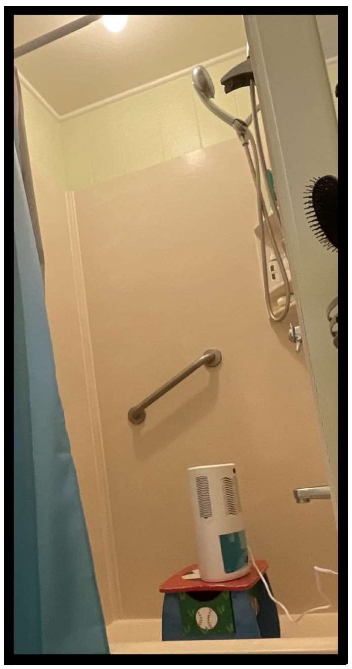
UV Water Bottles reduce NTM from drinking water



Falkinham, Clin Chest Med, 2015; Honda, Clin Chest Med, 2023; [1] Hamada *et al.,* Int J Myco 2016; [2], Reed *et al,* Am J Epidem, 2006; [3] Falkinham, WhiteJ, 2013; [5] Norton, *et al.,* Frontiers in Public Health, 2020; [5] Mullen, *et al*, EID, 2024.

Reducing shower humidity reduces aerosolized NTM

Saturated vapor pressure is a climate variable that affects NTM prevalence [1,2,3]



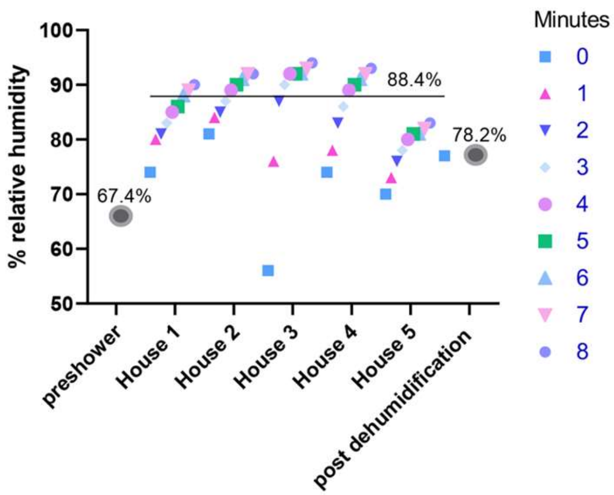


Table 1 Dehumidification reduced *Mycobacterium chelonae* aerosolization, sampling round 1 (37 °C)

	Biofilm		Air		
House:	**Showerhead biofilm (swab):**	**Showerhead biofilm (swab), post- disinfection**	**Pre shower air (SAS):**	**Post shower air (SAS):**	**Post de-humidi-fication (SAS):**
1	***M. chelonae***	No NTM	No NTM	***M. chelonae***	No NTM
2	No NTM	No NTM	No NTM*	No NTM*	No NTM*
3	No NTM	No NTM	No NTM	No NTM	No NTM
4	No NTM	No NTM	No NTM*	No NTM*	No NTM
5	No NTM	No NTM	No NTM*	No NTM*	No NTM

(*) Limitation - indicates instances where mold overgrowth likely reduced NTM detection

Kostecki, *et al.*, BMC Research Notes, 2024

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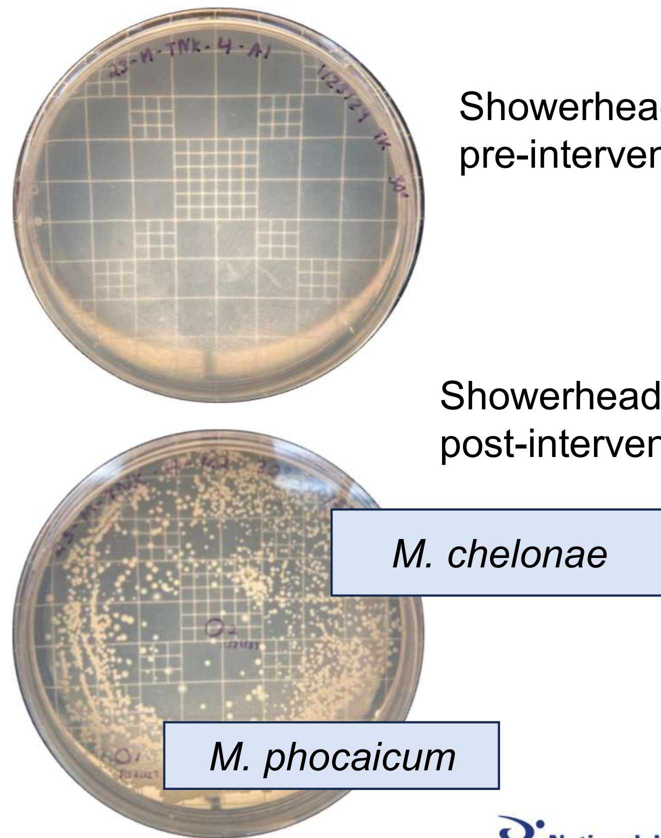
Showerhead filters do not reduce NTM, a pilot

	Biofilm		Water
House:	Pre-intervention Showerhead biofilm (swab):	Post-intervention Showerhead biofilm (filter):	Post-intervention Showerhead water:
1	No NTM		*M. gordonae*
4	No NTM	Pending	*M. phocaicum, M. chelonae*
5	No NTM		*M. porcinum*
6	No NTM		No NTM



Showerhead, pre-intervention

Showerhead, post-intervention

Unpublished

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Antimicrobial showerheads do not impact aerosolization

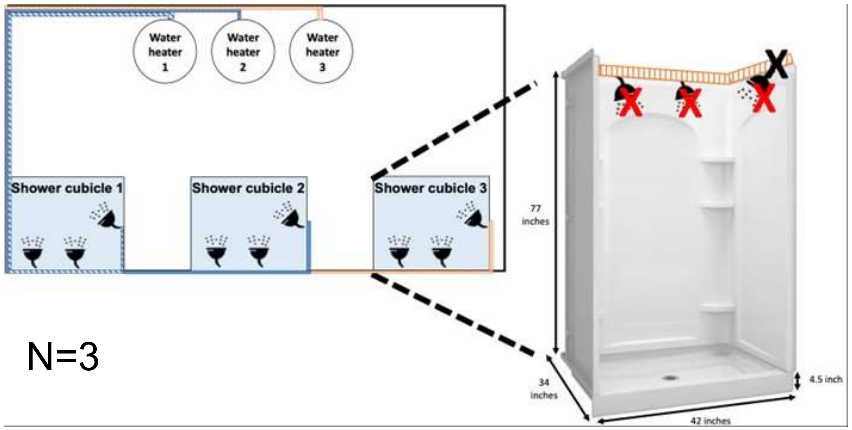
Pitell and Haig, Fronters in Microbiome, 2024;

1. Proprietary multistage antimicrobial filter
2. Antimicrobial silver-embedded
3. Conventional plastic

Drinking water associated pathogens did not differ between showerhead type.

Each peaked as showerhead aged.

# of days of showerhead operation important.



N=3

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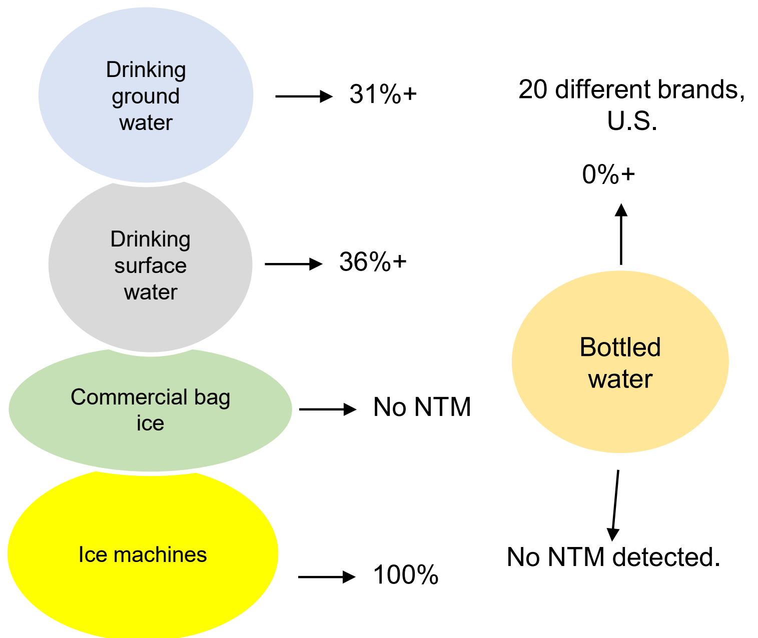
Expand Drinking Water Awareness



Bottled Water (Honda Lab)

Water Tested:	Type of water (Source = U.S.A.) unless noted:	Characteristic:	Results:
1	Bottled Water, Brand 1	Natural spring water	None
2	Bottled Water, Brand 2	Purified water	None
3	Bottled Water, Brand 3	Natural spring water	None
4	Bottled Water, Brand 4	Water from snow	None
5	Bottled Water, Brand 5	Volcanic rock filtered water	*Mycobacterium neoaurum* *Mycobacterium phocaicum*
6	Bottled Water, Brand 6	Volcanic rock filtered water	None
7	Bottled Water, Brand (non-U.S.A)	Volcanic rock filtered water	None
8	Distilled water	Commercially available	None
9	Sink faucet 1	Municipal water, Colorado	*Mycobacterium abscessus*
10	Sink faucet 2	Municipal water, Colorado	None
11	Sink faucet 3	Municipal water, Colorado	None
12	Water fountain	Municipal water, Colorado	None
13	Wall mounted water bottle filling station	Municipal water, Colorado	None

Holtzman, *et al,* J Food Protect 1997
Covert, *et al,* AEM, 1999
Totaro, *et al,* J Water Health, 2018
https://www.bottledwater.org/public/CCL4%20Microbes%20of%20Interest%20in%20Drinking%20Water_0.pdf0
Honda Lab, unpublished.

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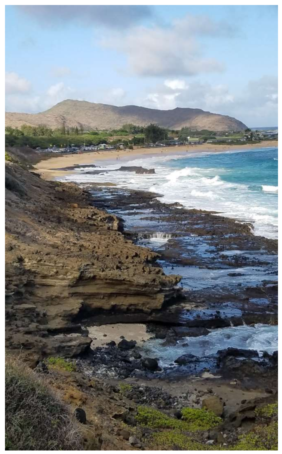
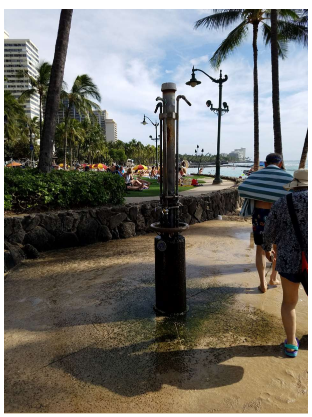
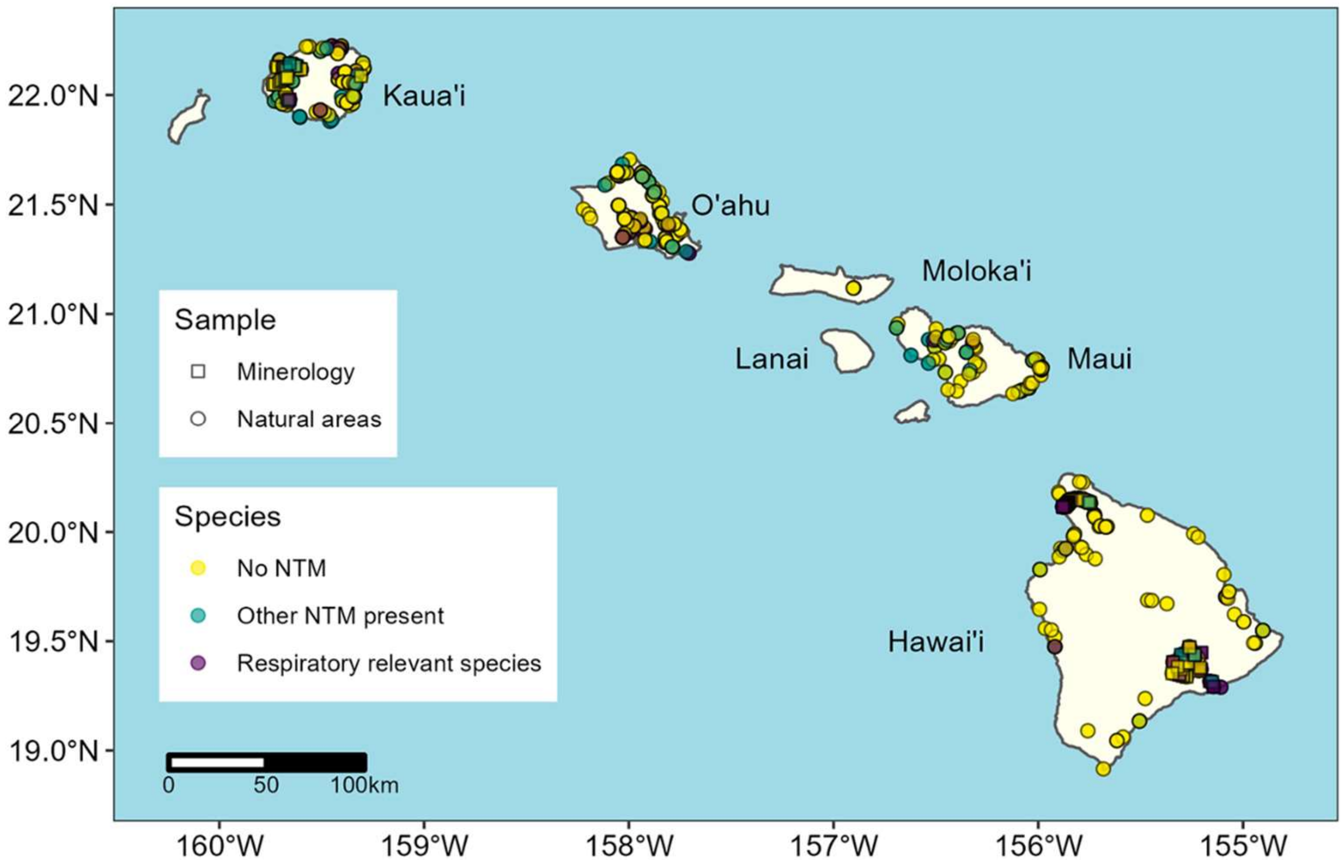
Aloha Hawai'i – Teaching us about NTM

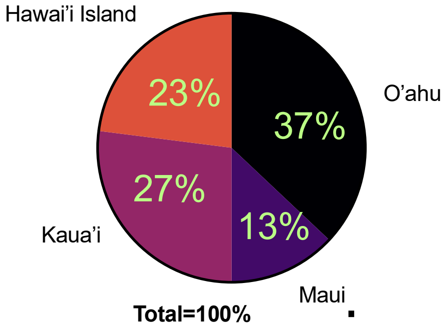



1. Enrichment in the built environment (Honda *et al*., Plos Neg Trop 2016; Virdi, *et al*, Microorganisms, 2020)
2. Preference for iron minerals, hematite in soil and aversion to gibbsite (Glickman *et al*., App Env Micro, 2020)
3. Like highly expansive, moist soils containing high iron oxides and hydroxides (Parsons *et al*., Appl Env Micro, 2022)
4. Vanadium in groundwater increases MAC lung disease risk (Lipner *et al*., Env Epi, 2022)
5. Water transport from riparian zones into losing stream stretches, aquifers, and into homes (Nelson *et al*., Geohealth, 2021).
6. Local feral pigs harbor pathogenic NTM species. (Hendrick, et al, in preparation.)

Larger cities are NTM hot spots



Island distribution
766 total NTM+ samples



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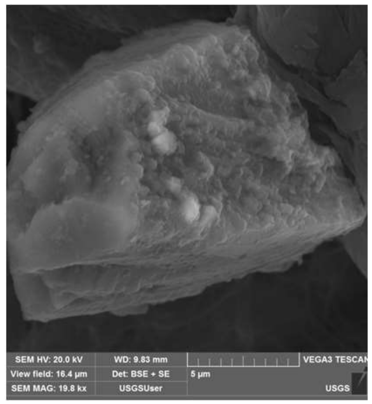
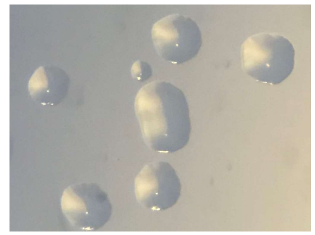
Active volcanism contributes to NTM

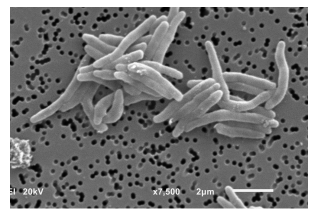
Kīlauea volcano, Hawai'i Island, 2018

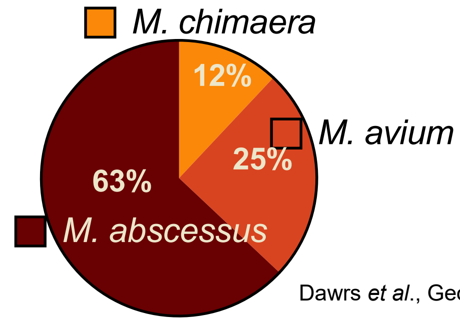
Photo credit: USGS

Kīlauea ash, SEM





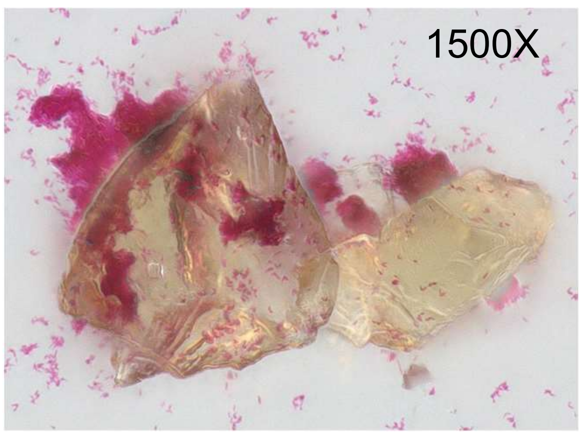


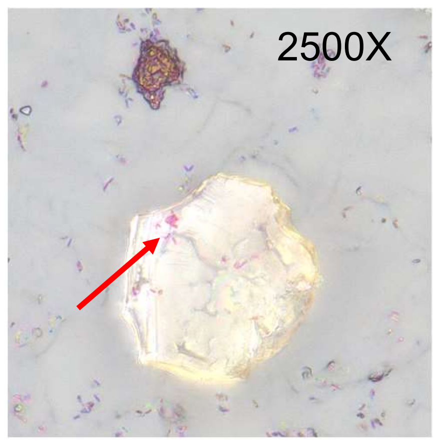


Dawrs *et al*., GeoHealth, 2023

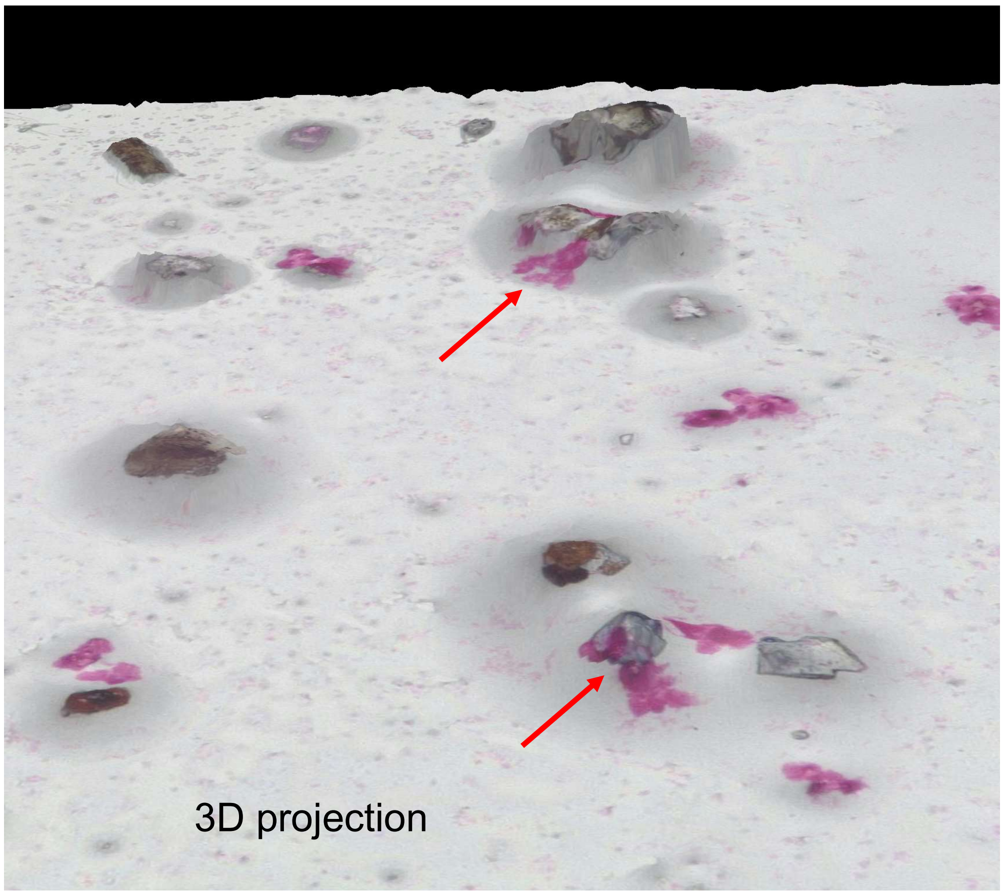
Total = 8 NTM recovered from Kilauea ash

AFB





Active volcanism contributes to NTM



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NTM and the Lāhainā wildfire

The Lāhainā Maui wildfire is earmarked both as the *worst natural disaster in Hawai'i history* and the *deadliest U.S. wildfire in over 100 years.*

August 2023

https://www.sfchronicle.com/climate/article/maui-fire-before-after-photos-18290051.php.

February, 2024, Lāhainā

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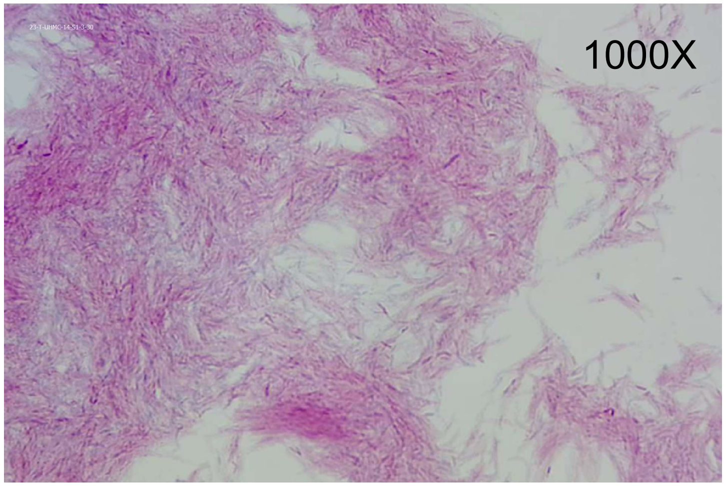
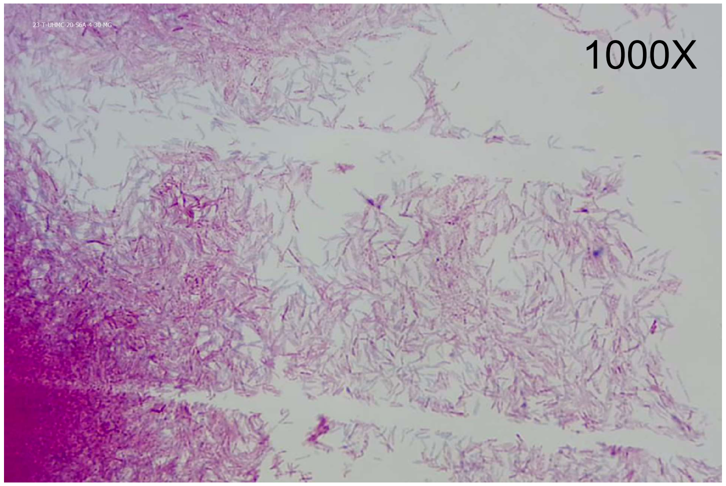
NTM and the Lāhainā wildfire

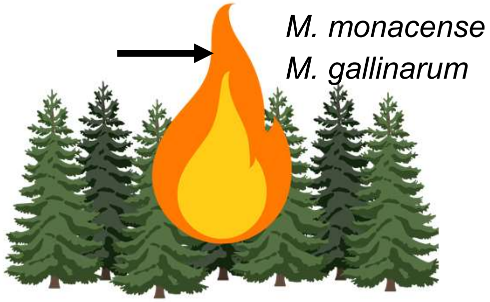
Soil and ash (burnt ground)
Non-household



Soil and ash (burnt ground)
Household



Wildfire ash, Kansas



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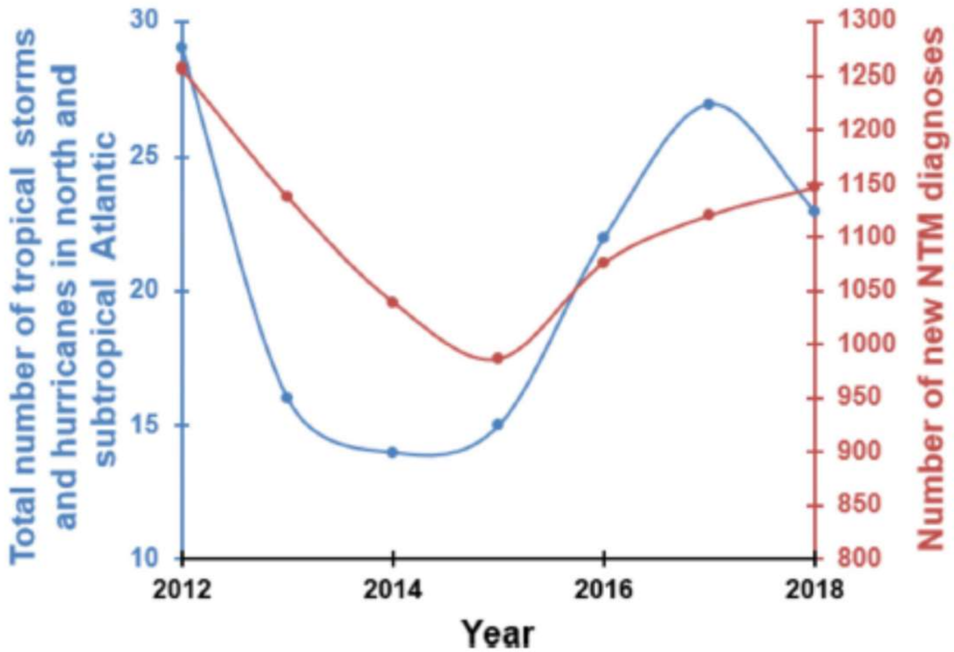
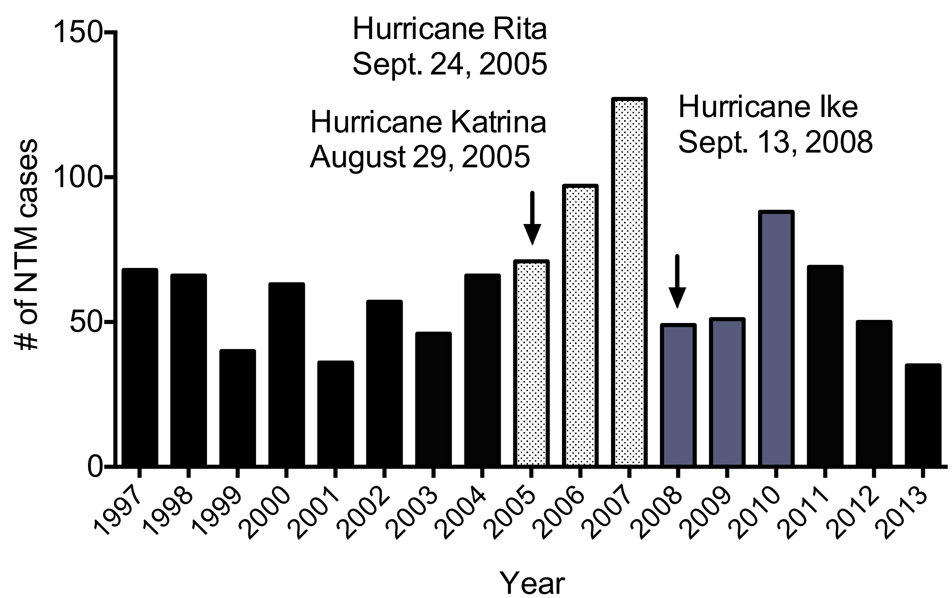
In addition to volcanic eruptions and wildfires…..

Tropical storms



Hurricanes



Honda *et al*, 2015; Kambali, *et al.*, 2021

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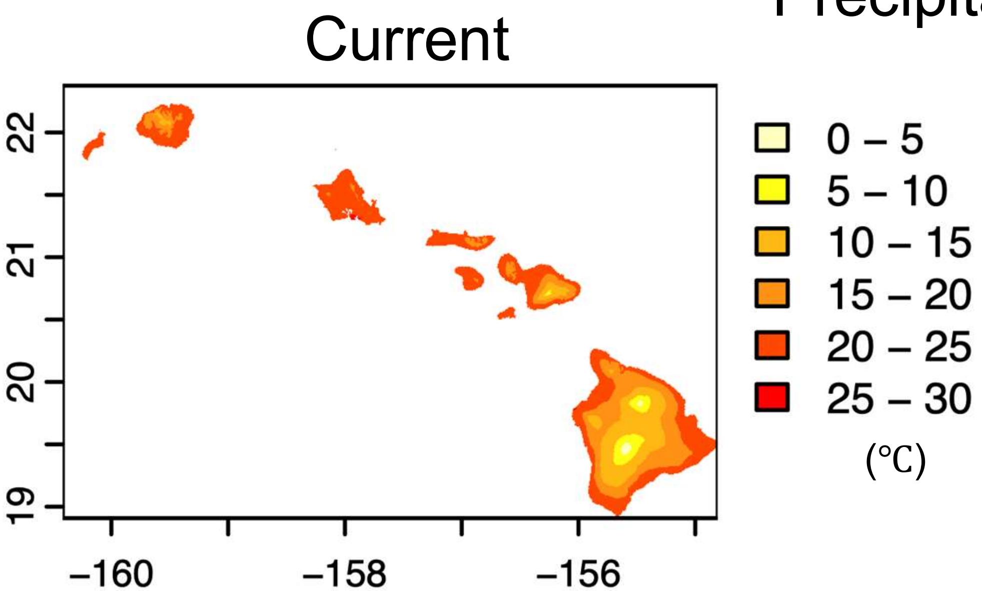
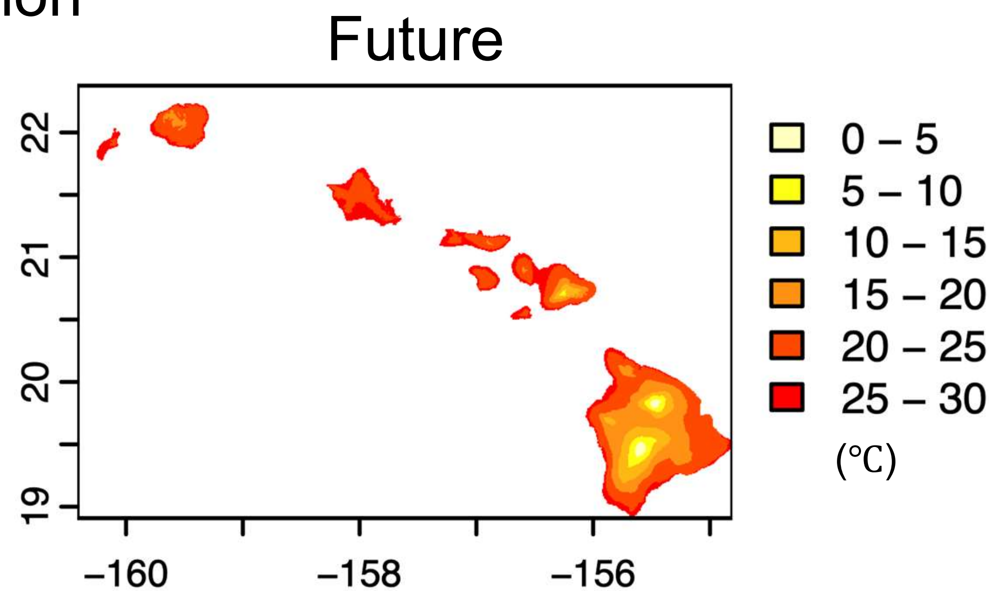
Our environments will likely get warmer

Precipitation





Ecological niche modeling

Unpublished

** Joshua Banta, PhD, University of Texas Health Science Center at Tyler

Jim Crooks, PhD, National Jewish Health

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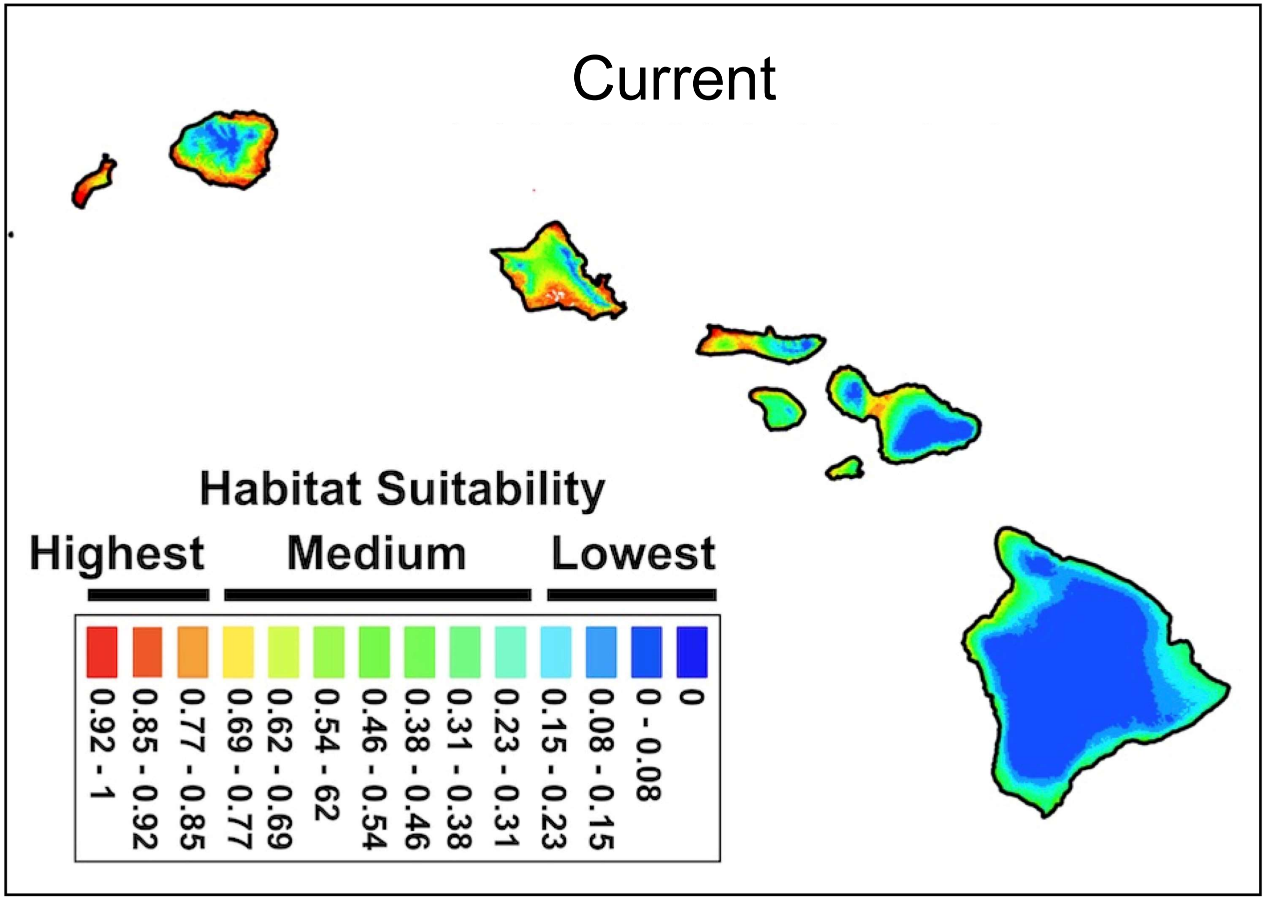
M. abscessus in Hawai'i



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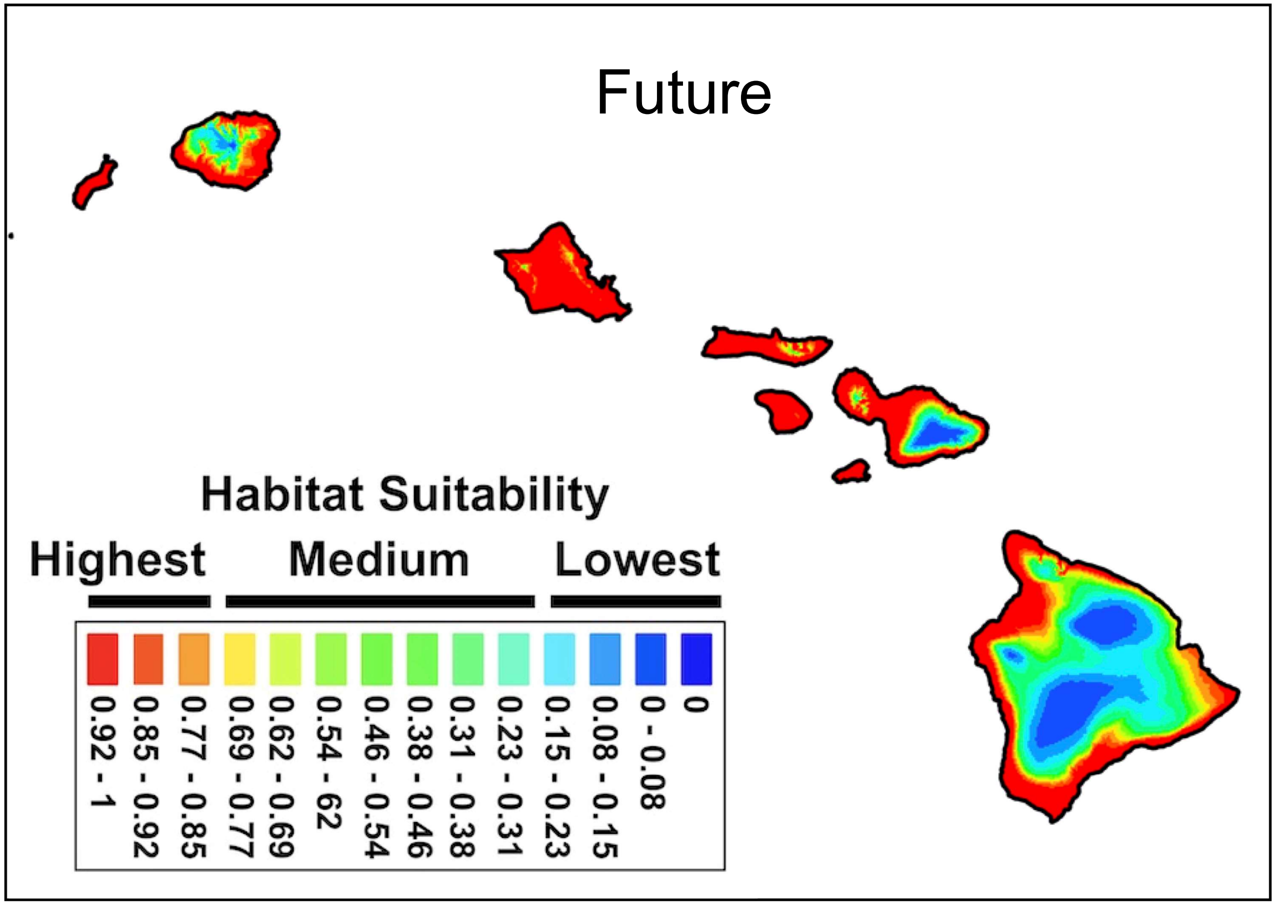
M. abscessus in Hawai'i



Future climate data from the years 2041 - 2070 based on the IPSL-CM6A-LR climate model and a shared socioeconomic pathway

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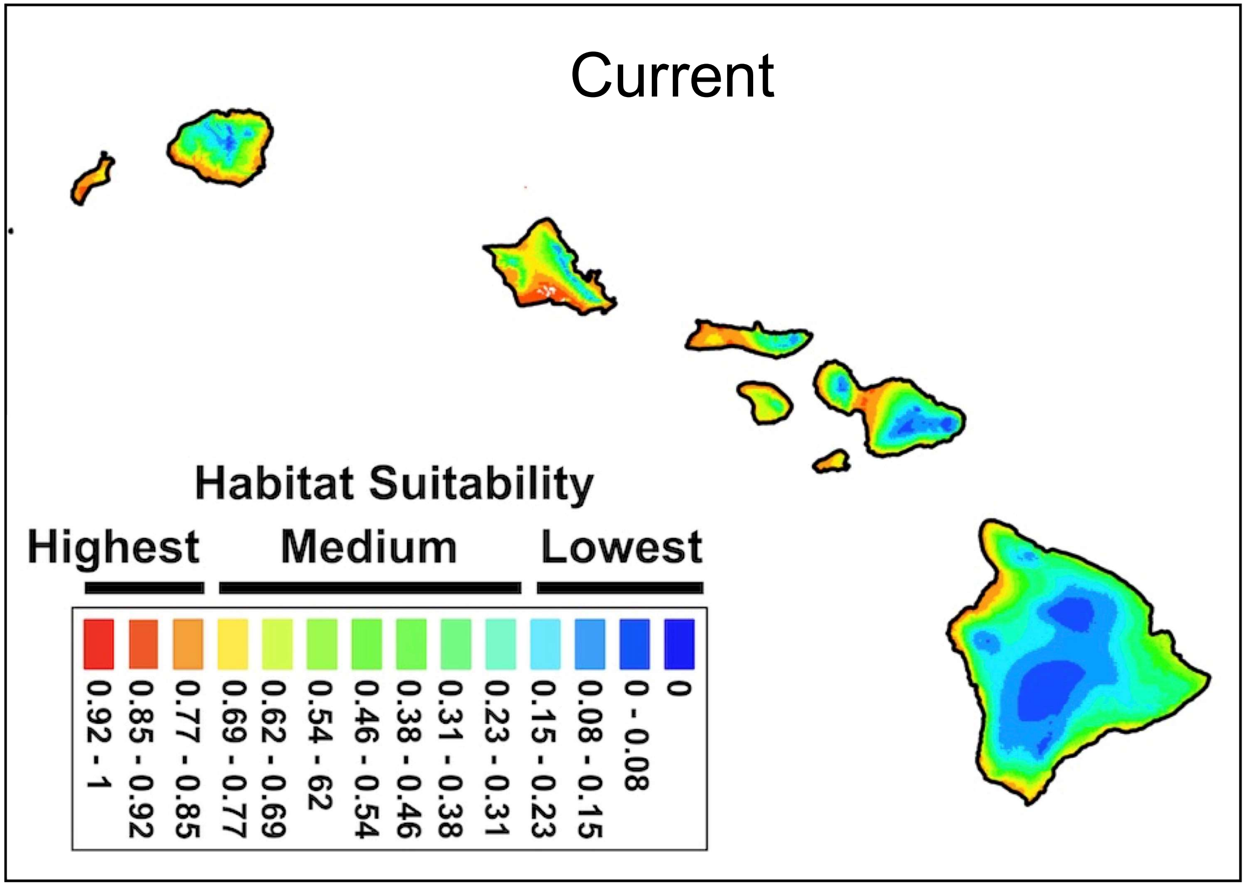
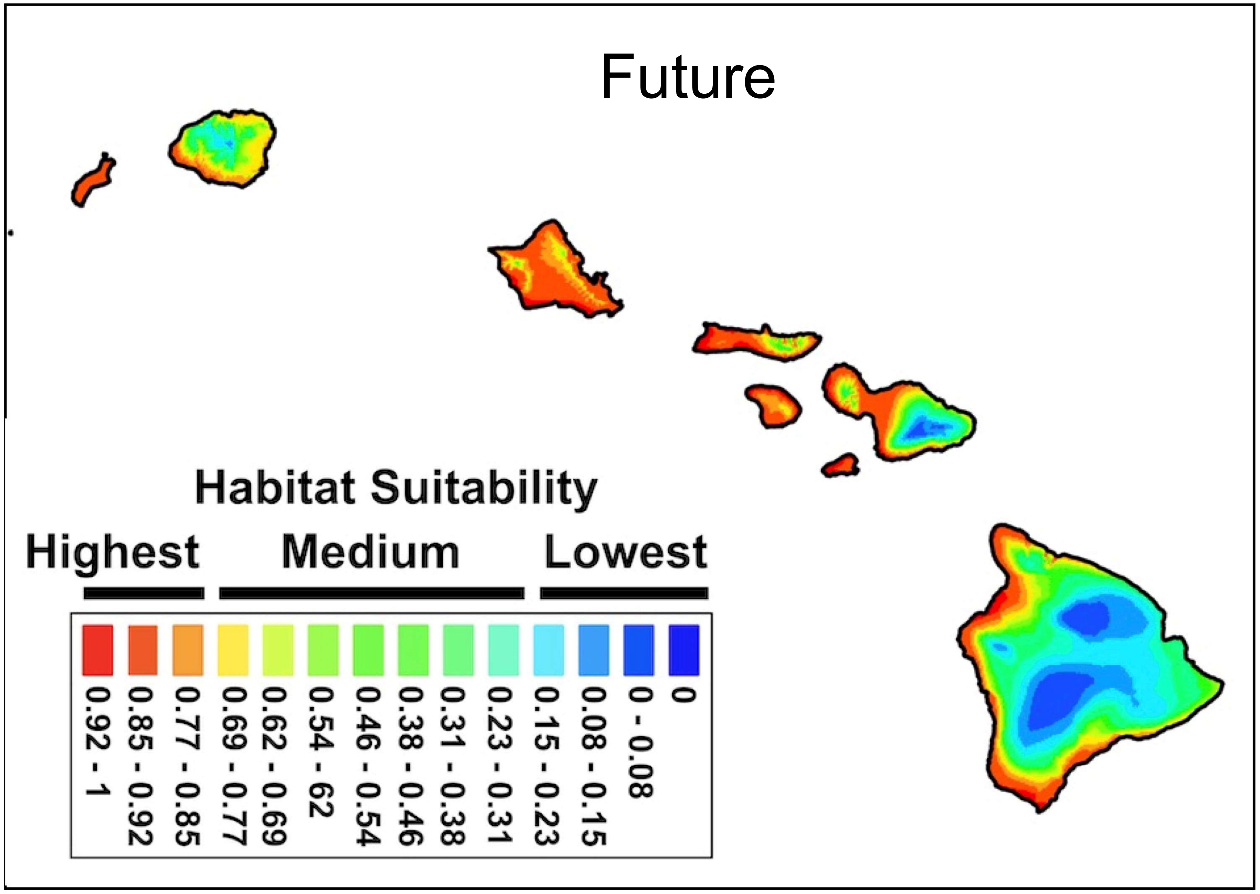
M. gordonae in Hawai'i



M. gordonae in Hawai'i



Future climate data from the years 2041 - 2070 based on the IPSL-CM6A-LR climate model and a shared socioeconomic pathway

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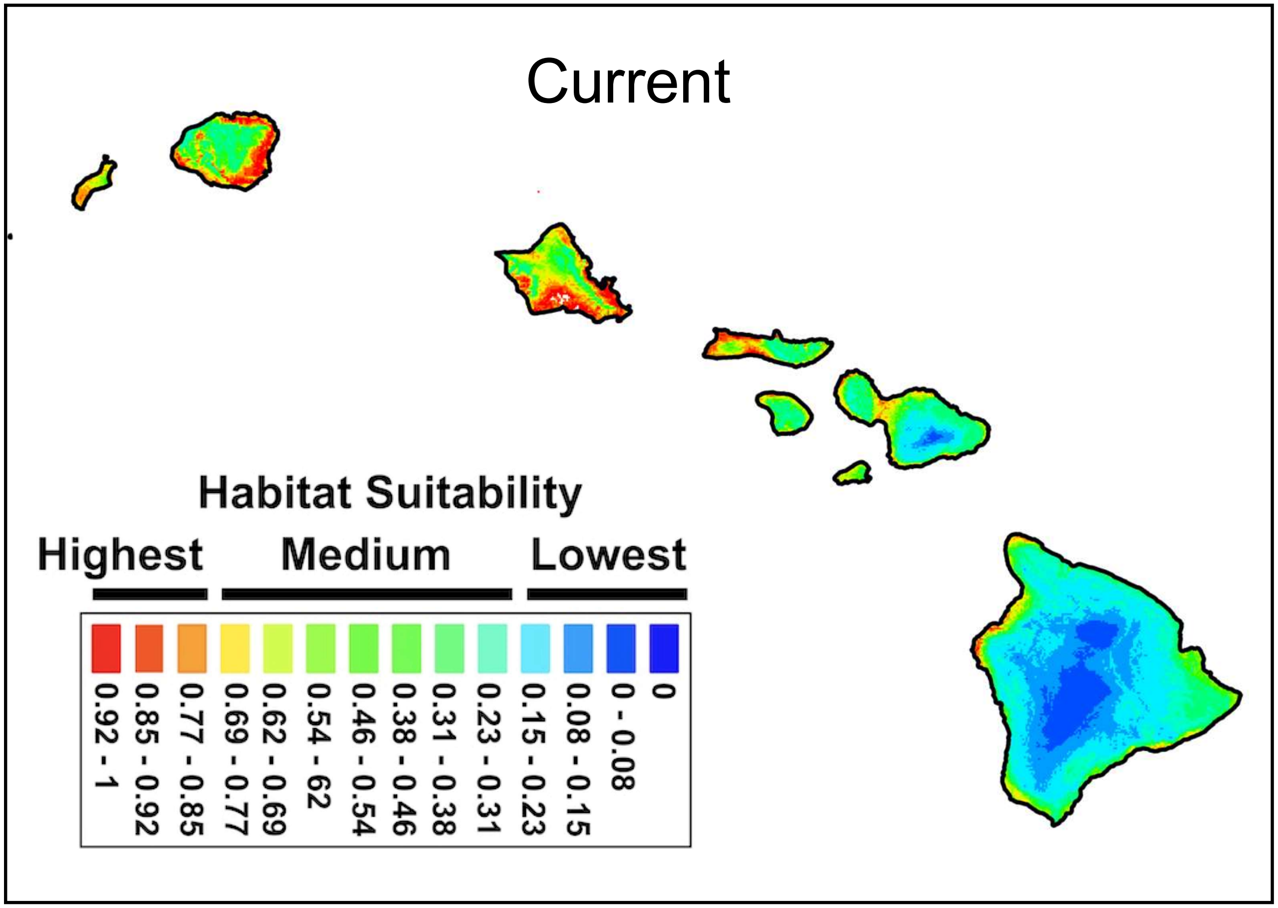
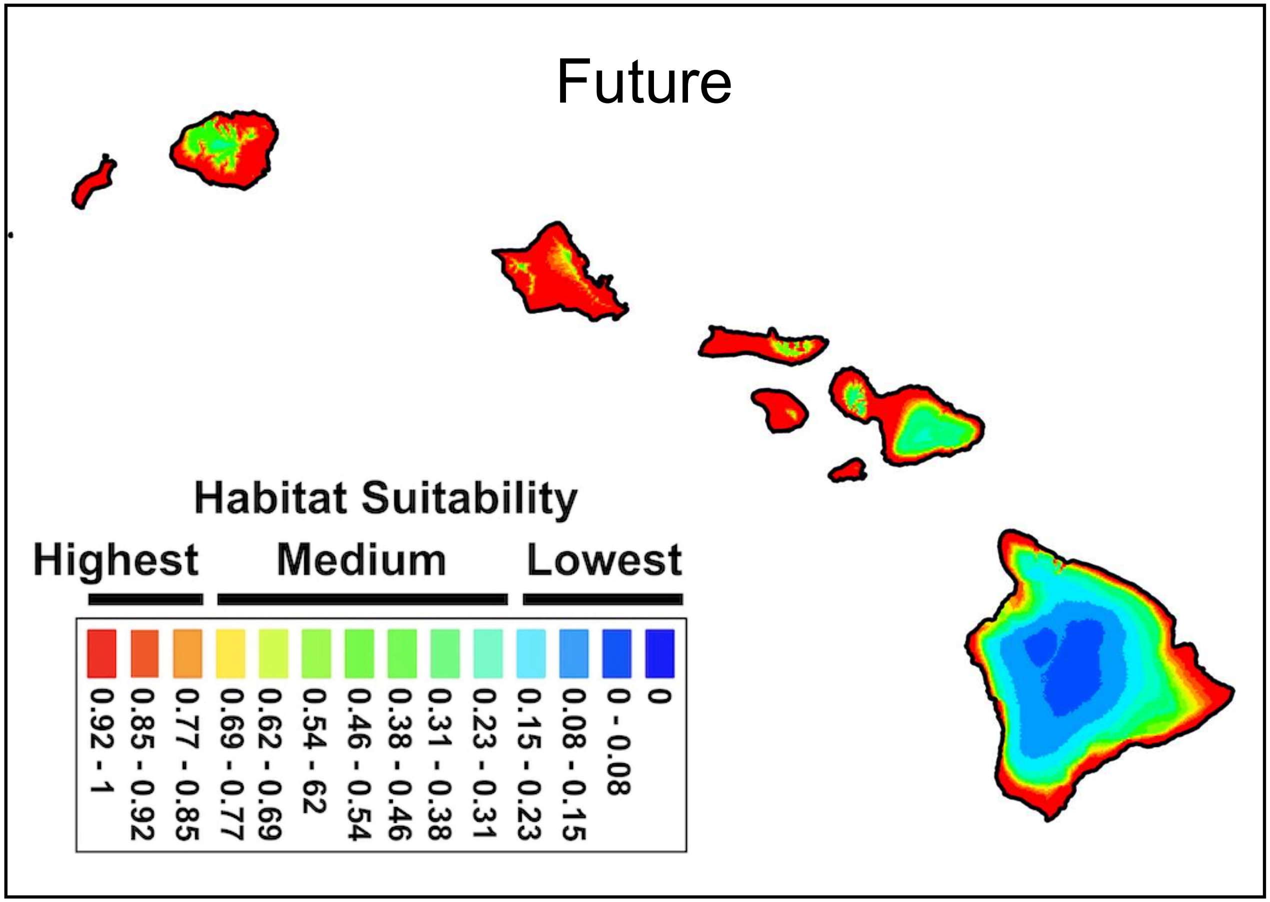
M. chelonae in Hawai'i

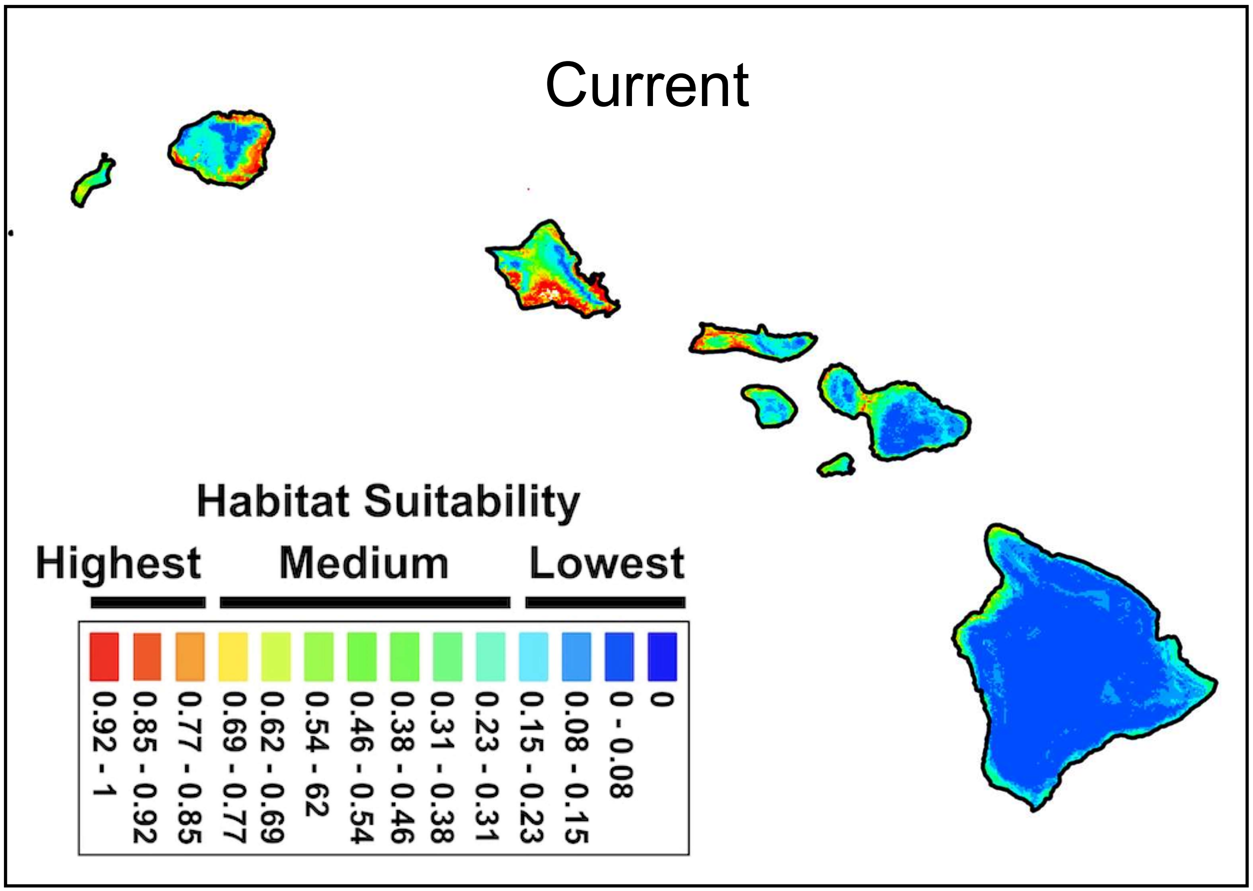


M. chelonae in Hawai'i

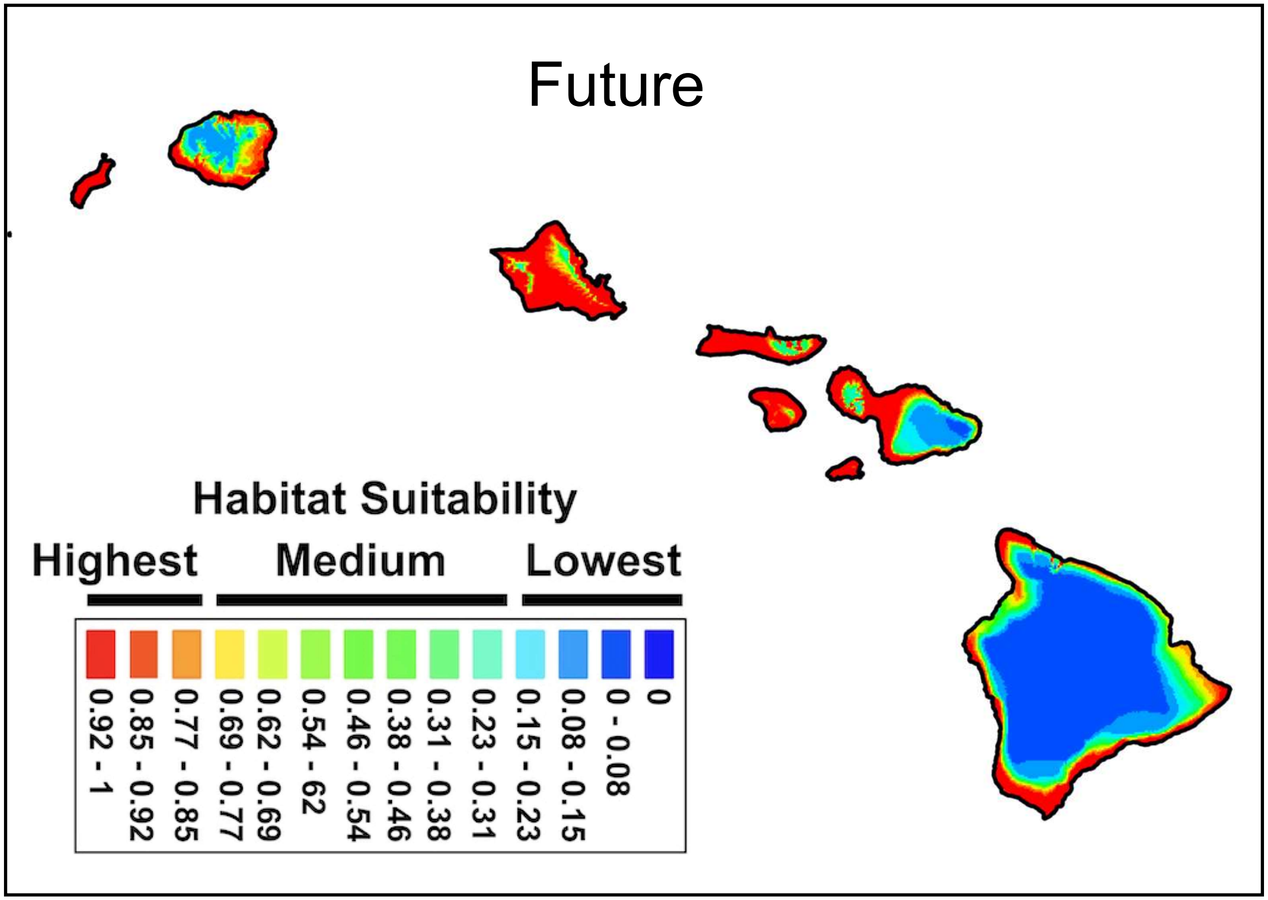


Future climate data from the years 2041 - 2070 based on the IPSL-CM6A-LR climate model and a shared socioeconomic pathway

M. chimaera in Hawai'i



M. chimaera in Hawai'i



Future climate data from the years 2041 - 2070 based on the IPSL-CM6A-LR climate model and a shared socioeconomic pathway

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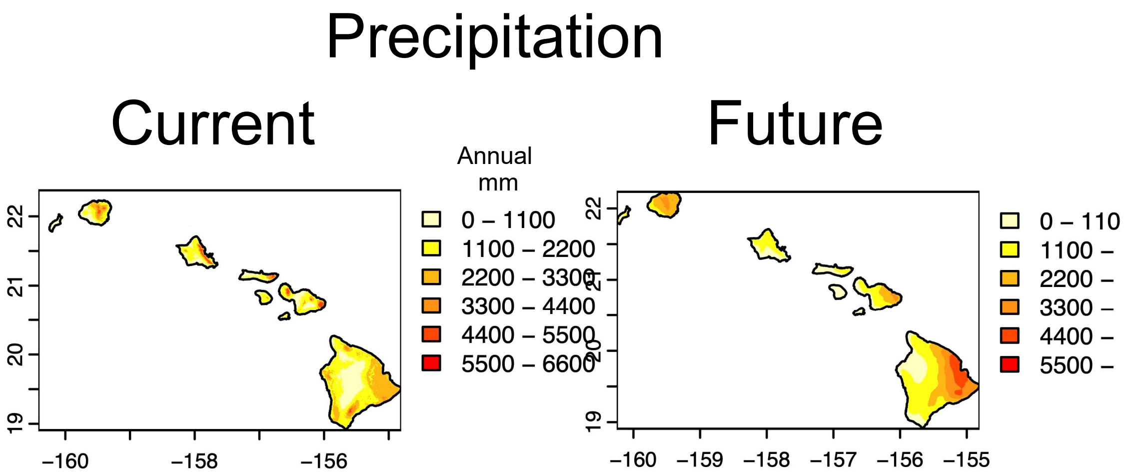
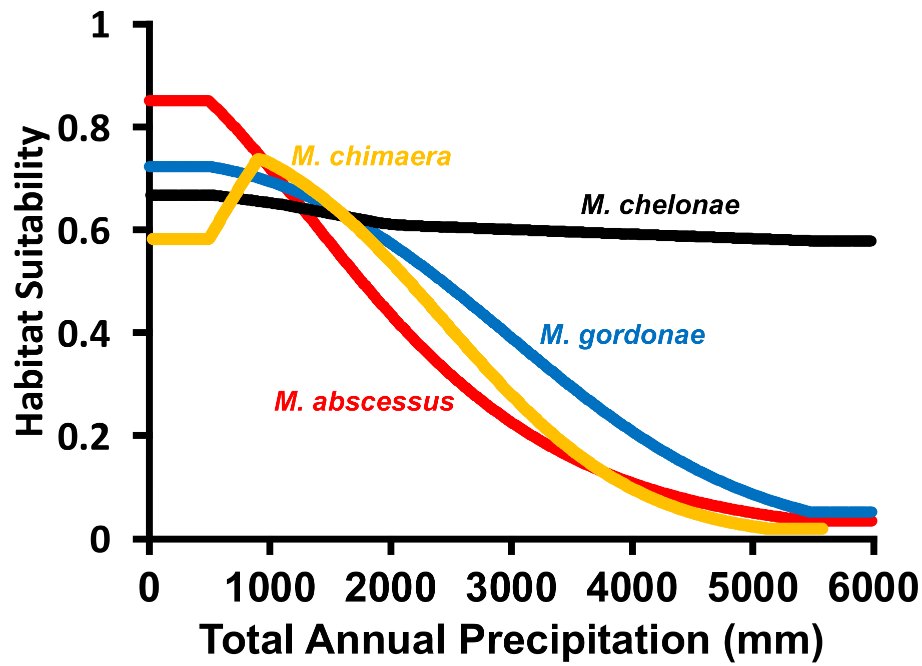
Colonization of *M. chelonae* across areas with wide ranges of precipitation





Among people with CF in FL: Precipitation and NTM

(Foote, *et al.*, PloS One, 2021)

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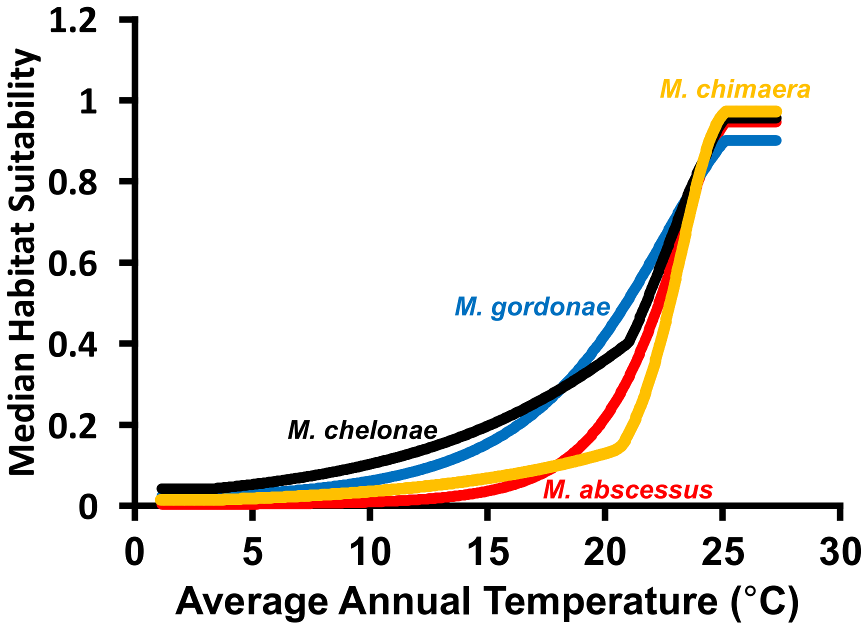
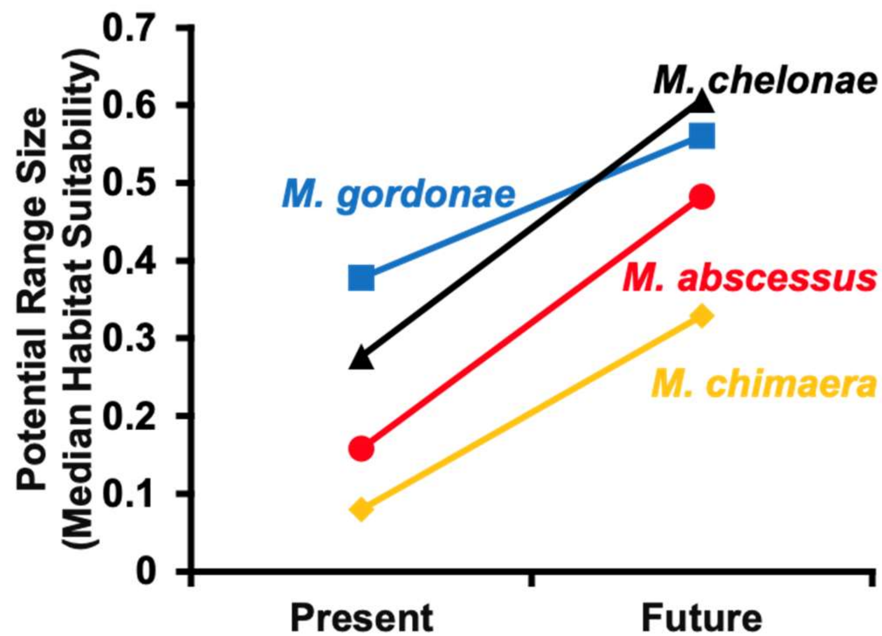
Emergence of NTM under future climates

M. chimaera will thrive in hotter climates.



Greater NTM emergence under future climates.



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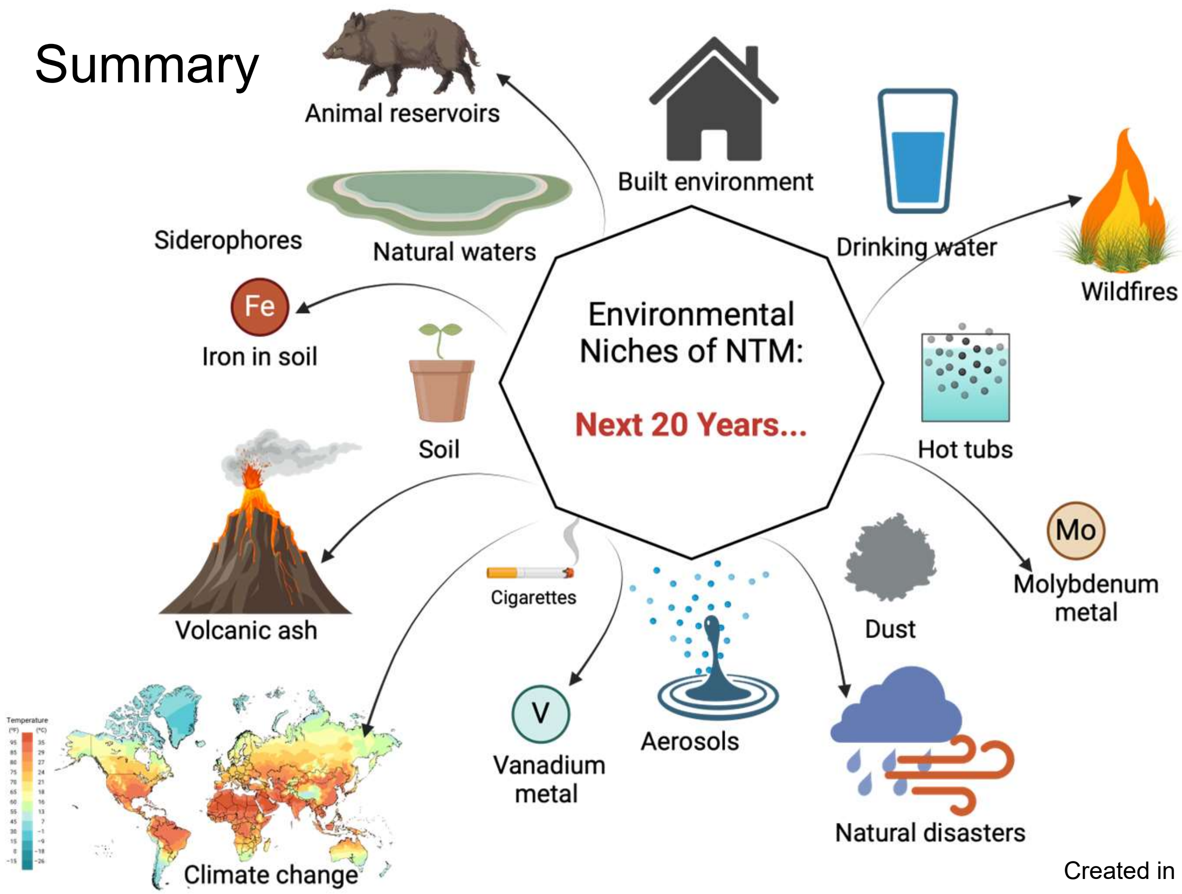
Conclusions

Summary



Created in BioRender

Future directions

"We predict an increasing incidence of interactions between humans and mycobacteria in the coming years.

↓

Climate changes may be increasingly recognized pressures for the emergence of environmentally acquired NTM.

Acknowledgements

Honda Lab
Rachel N. Wilsey
Tiana N.M. Koch
Kristin T. Dean
Madelyn M. Terrell
Lianghao Ding, PhD
Adrian Hornby, PhD

Prior Lab Members
Stephanie Dawrs
Ravleen Virdi
Grant Norton
Charmie Vang
Jobel Matriz

U of Texas, Tyler
Julie Philley, MD
PJ McShane, MD
Richard Wallace, MD
Barbara Brown-Elliott
Joshua Banta, PhD

National Jewish Health

** Edward D. Chan, MD
** Michael Strong, PhD
** Nabeeh A. Hasan, PhD
** L. Elaine Epperson, PhD
** James Crooks, PhD
Cody M. Glickman
Melissa Lowe
Jo Hendrick
Brady Holst
Scott Alper, PhD
Rebecca Davidson, PhD
Fan Jia, PhD
Human Cell Core

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**Josh Banta, PhD

University of Idaho
Leda Kobziar, PhD

NTM Hawai'i Consortium: 'Iolani School, The Kamehameha Schools, Seabury Hall, Kailua High School, Waianae High School, Kapa'a High School, Island School, University of Hawai'i at Hilo, University of Hawai'i Maui College, Brigham Young University Laie, Mike Burnett, Homeschoolers, Department of Tropical Medicine University of Hawai'i, Hawai'i Division of Wildlife

Brigham Young University
Dept. of Geological Sciences
Provo, UT
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Schuyler Robinson
Leeza Brown

Hawai'i Volcano Observatory
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North Carolina State University
Krishna Pacifici, PhD
Arielle Parsons, PhD

Volcano Science Center,
US Geological Survey
David E. Damby, PhD

Kaiser Permanente, Hawai'i
Stacey Honda, MD
Vanessa Simiola

Lahaina Wildfire Team
Chris Shuler, PhD, Julynn Li, Kellie Cole, Pacific Whale Foundation, U of Hawai'i Maui College, Renee Takeuchi, PhD (USGS, CA), Community scientists, All Hands Hawai'i Network

Funding: Padosi Foundation, NSF Ecology, Evolution and Infectious Disease (#1743587), NIH R21AI171587, NSF RAPID for Lahaina, Maui #2345008, UT Stars Award, UT Recruitment Funds.

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“Flat Stanley” Travels with our “Flat Stanley”

Ho’okipa Beach Park , Maui

Haleakalā , Maui

Waipuilani Park, Maui

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