

# Antimicrobial Resistance in a Warming World – What Should We Expect?

Alex Wong

March 7, 2023

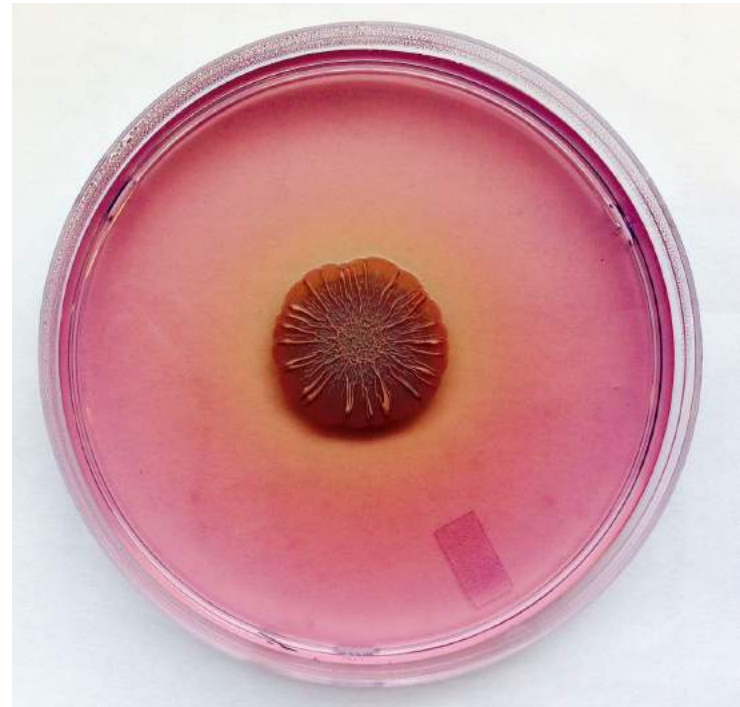


INSTITUTE FOR ADVANCING  
HEALTH THROUGH AGRICULTURE

# First, an Introduction

## Microbial Genomics and Evolution

- What genes and mutations cause resistance?
- What are the impacts of resistance genes/mutations on bacteria?
- Molecular methods for pathogen surveillance (SARS-CoV-2; *Salmonella*)
- Implications for policy



# First, an Introduction

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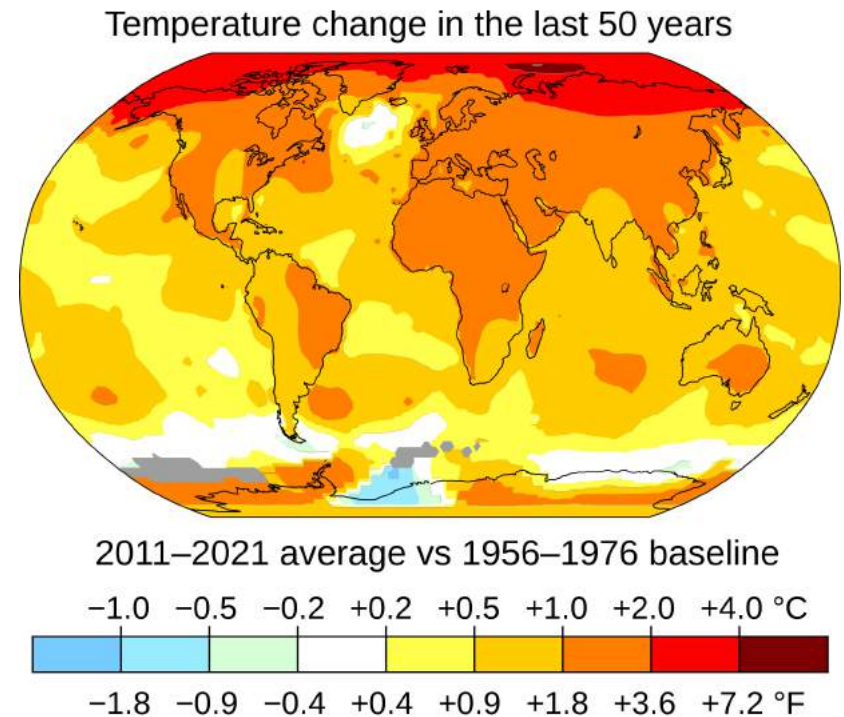
Carleton University: 2013 - 2022

Texas A&M Fort Worth: 2022 - ???



# Today

- Work in progress: AMR in a warming world
- What are the expectations?
- Mechanisms?
- Funding?



# Climate Change Impacts on Infectious Disease

(b) Observed impacts of climate change on human systems

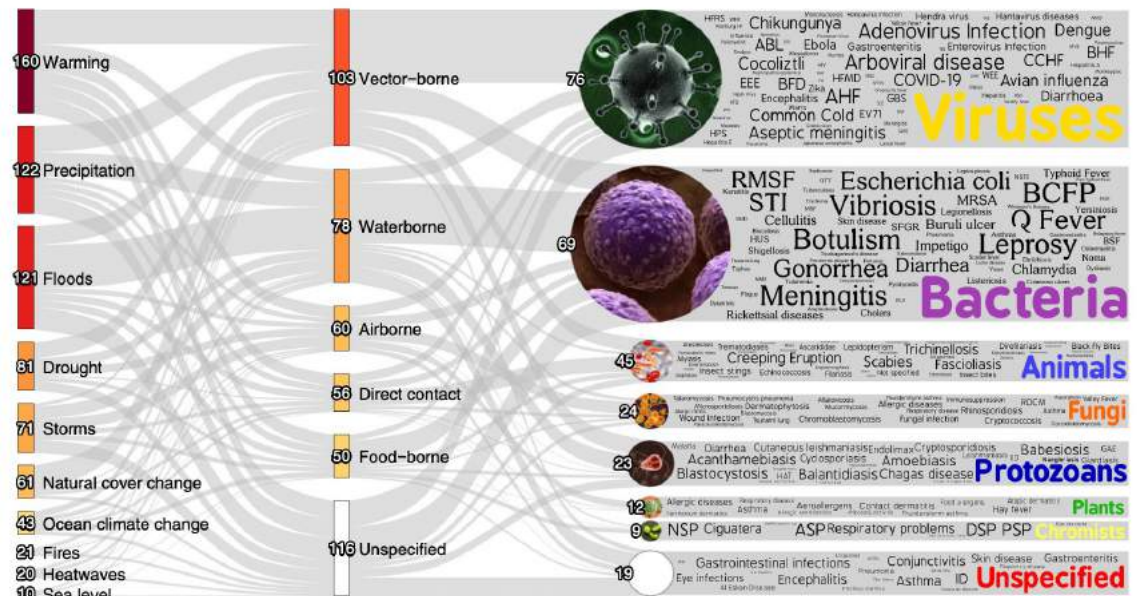
Human systems	Impacts on water scarcity and food production				Impacts on health and wellbeing				Impacts on cities, settlements and infrastructure			
	Water scarcity	Agriculture/crop production	Animal and livestock health and productivity	Fisheries yields and aquaculture production	Infectious diseases	Heat, malnutrition and other	Mental health	Displacement	Inland flooding and associated damages	Flood/storm induced damages in coastal areas	Damages to infrastructure	Damages to key economic sectors
Global	±	-	○	-	-	-	-	-	-	-	-	-
Africa	-	-	-	-	-	-	○	-	-	-	-	-
Asia	±	±	-	-	-	-	-	-	-	-	-	-
Australasia	±	-	±	-	-	-	-	not assessed	-	-	-	-
Central and South America	±	-	±	-	-	-	not assessed	-	-	-	-	-
Europe	±	±	-	±	-	-	-	-	-	-	-	-
North America	±	±	-	±	-	-	-	-	-	-	-	-
Small Islands	-	-	-	-	-	-	○	-	-	-	-	-
Arctic	±	±	-	-	-	-	-	-	-	-	-	±
Cities by the sea	○	○	○	-	○	-	not assessed	-	○	-	-	-
Mediterranean region	-	-	-	-	-	-	not assessed	-	±	-	○	-
Mountain regions	±	±	-	○	-	-	○	-	-	na	-	-

Observed global and regional impacts on human systems attributed to climate change.

2022 IPCC Report



# Climate Change Impacts on Infectious Disease

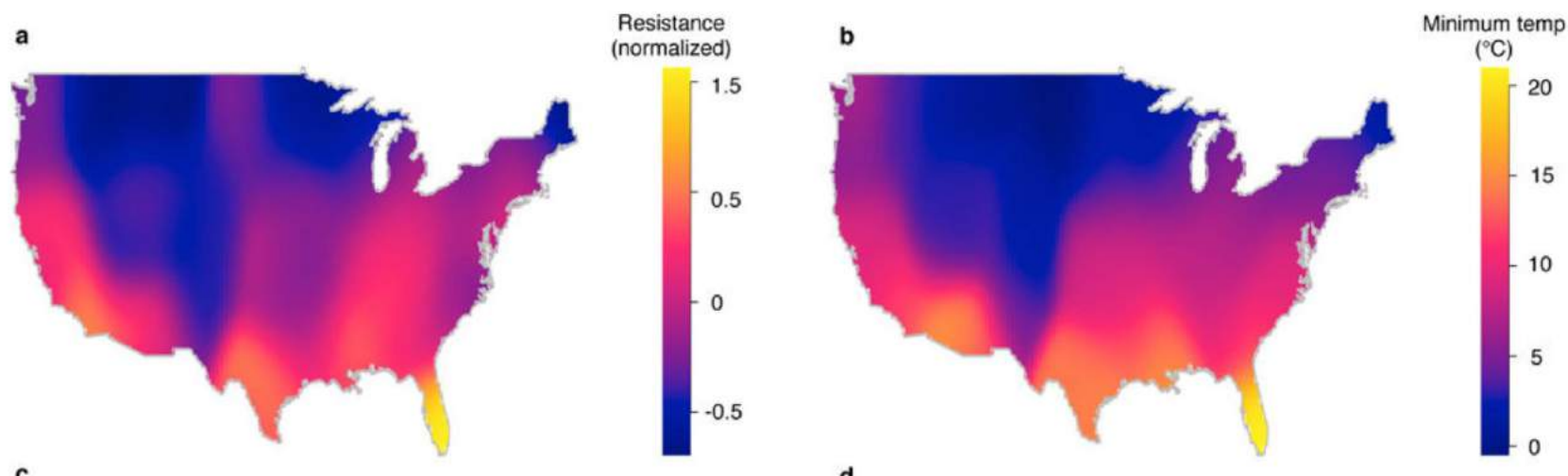


Pathogenic diseases aggravated by climactic hazards.  
Mora et al. 2022 Nat Clim Chang 12: 869.



How Will Climate Change Impact AMR?

# Clinical AMR Prevalence Correlates With Temperature

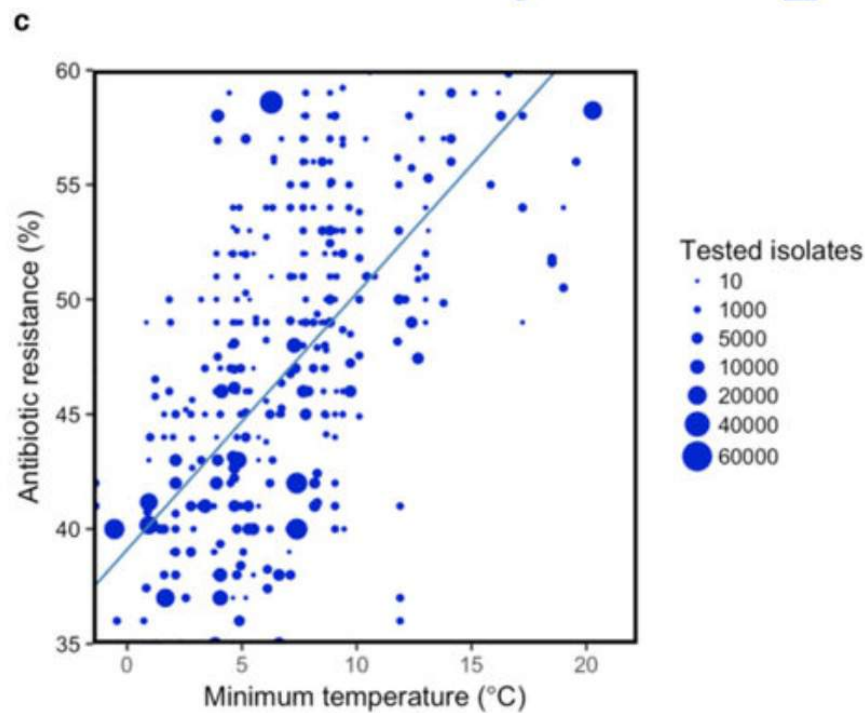


Resistance prevalence for *E. coli*

MacFadden et al. 2018 *Nat Clim Chang* 8(6): 510–514. doi:10.1038/s41558-018-0161-6.



# Clinical AMR Prevalence Correlates With Temperature



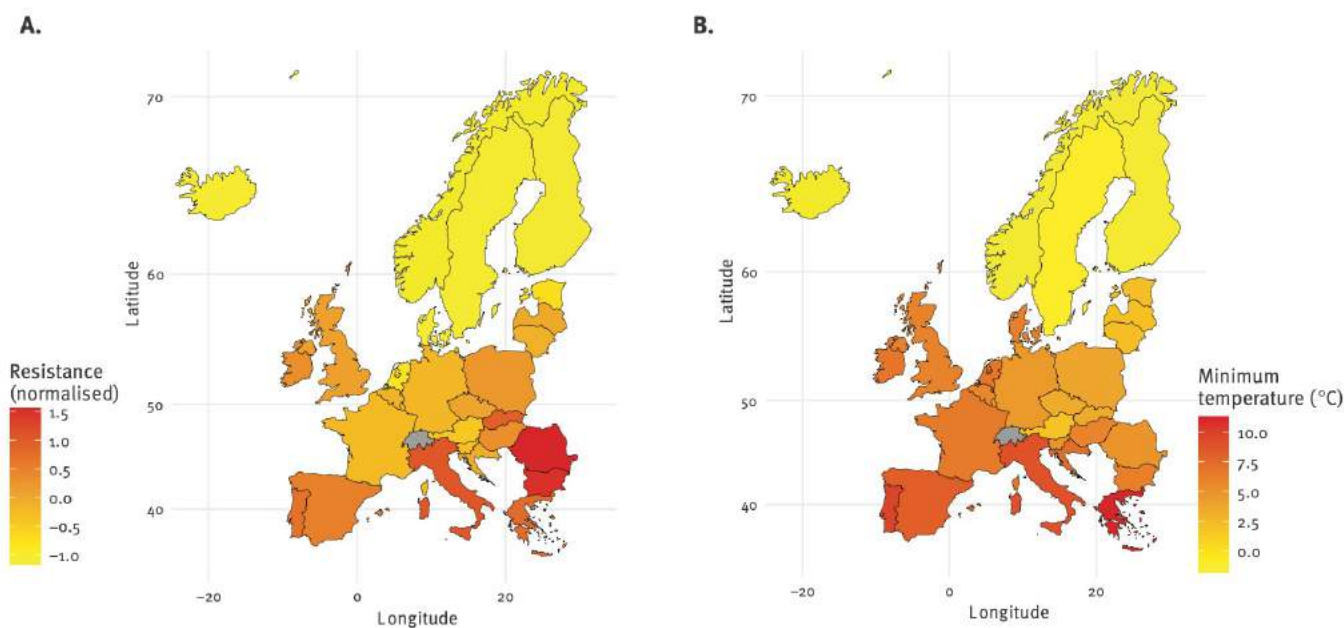
Amoxicillin resistance in *E. coli*

MacFadden et al. 2018 *Nat Clim Chang* 8(6): 510–514. doi:10.1038/s41558-018-0161-6.

# What About Confounding Variables?

- Lots of other variables correlate with temperature...
- MacFadden (USA) - temperature/AMR correlation is robust to acquisition source (inpatient vs. in+out), prescription rate, population density, laboratory standard (CLSI vs. other)

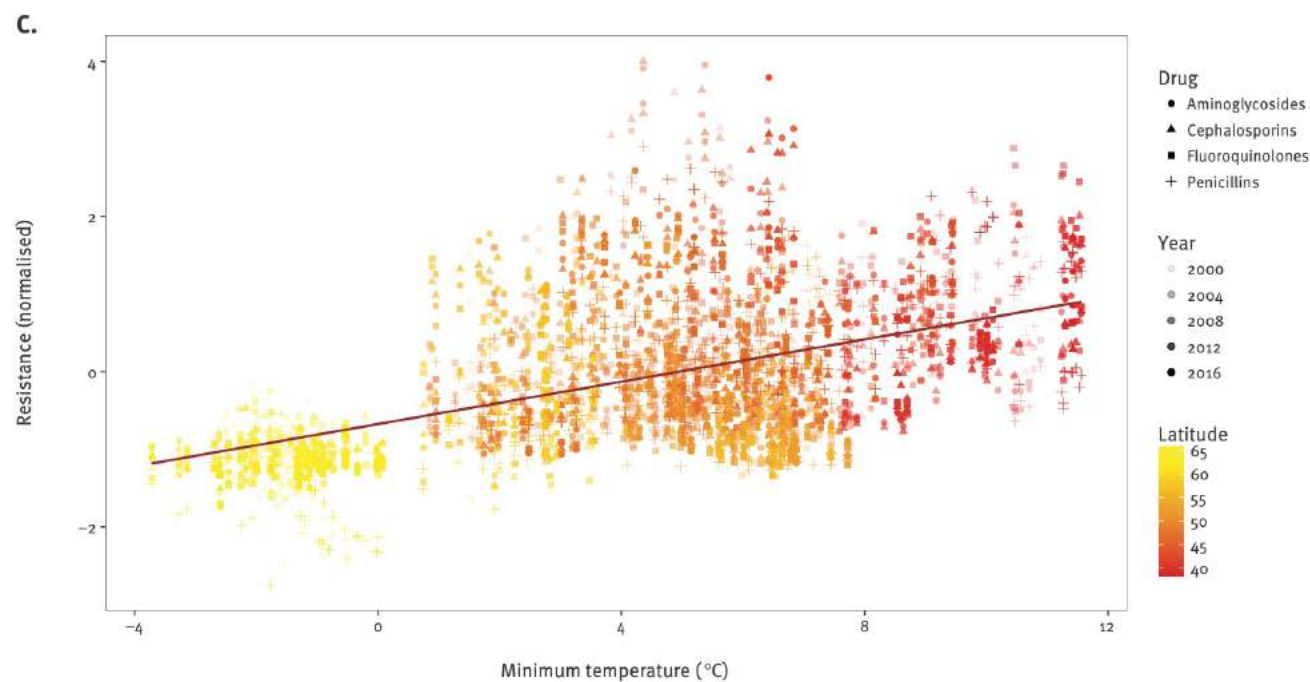
# Clinical AMR Prevalence Correlates With Temperature



Resistance prevalence for three common pathogens (*E. coli*, *K. pneumoniae*, *S. aureus*)

McGough et al. 2020 Euro Surveill. 2020;25(45):pii=1900414. <https://doi.org/10.2807/1560-7917.ES.2020.25.45.1900414>

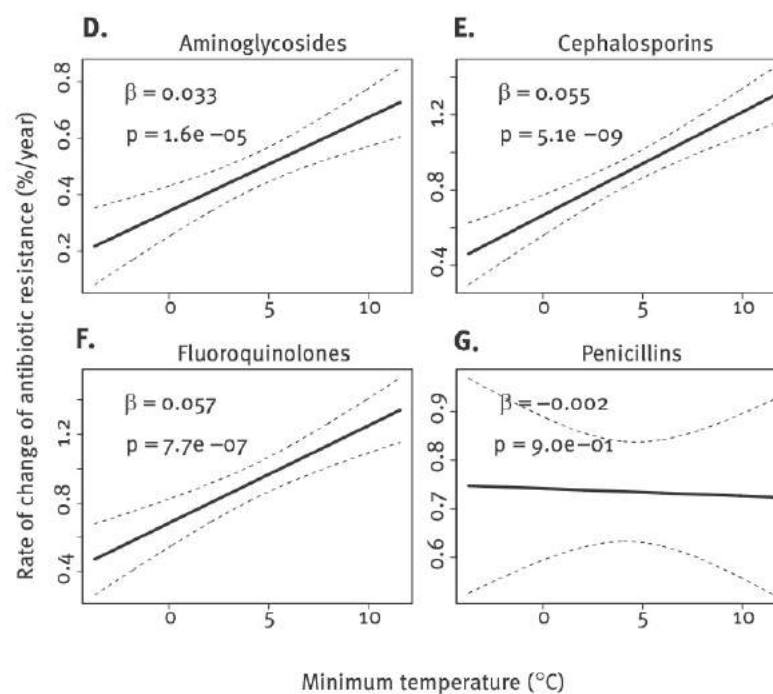
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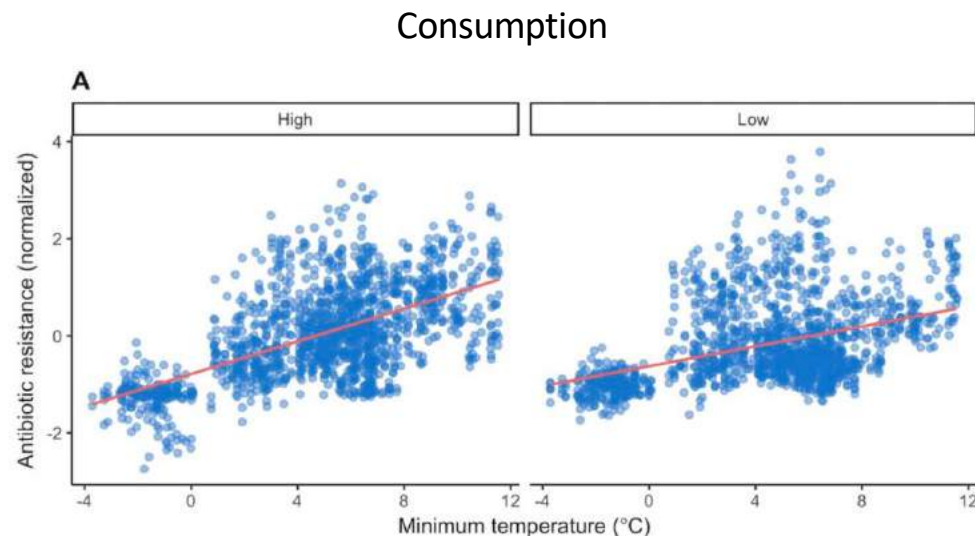
# Rate of Change in AMR Prevalence Correlates with Temperature



McGough et al. 2020 Euro Surveill. 2020;25(45):pii=1900414. <https://doi.org/10.2807/1560-7917.ES.2020.25.45.1900414>

# What About Confounding Variables?

- Lots of other variables correlate with temperature...
- McGough (Europe) – temperature/AMR correlation is robust to antibiotic consumption, population density

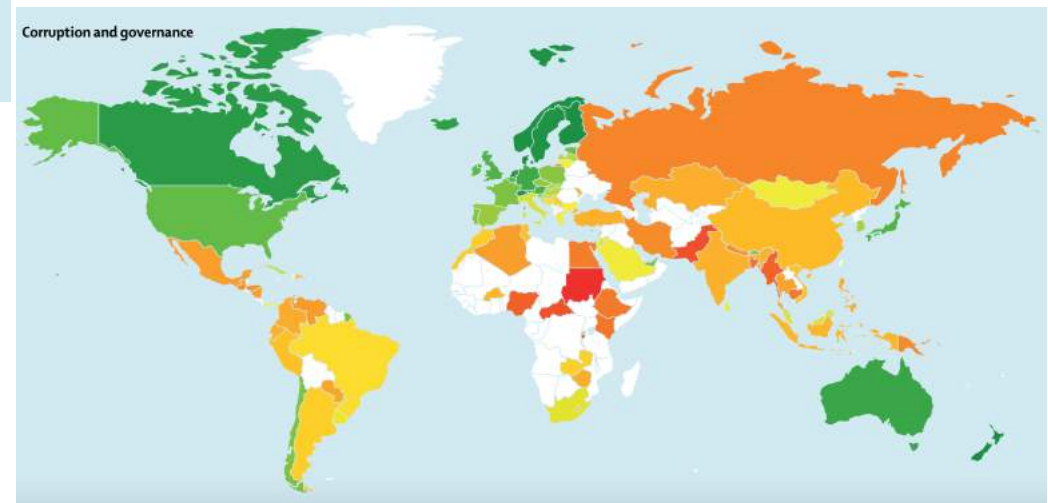
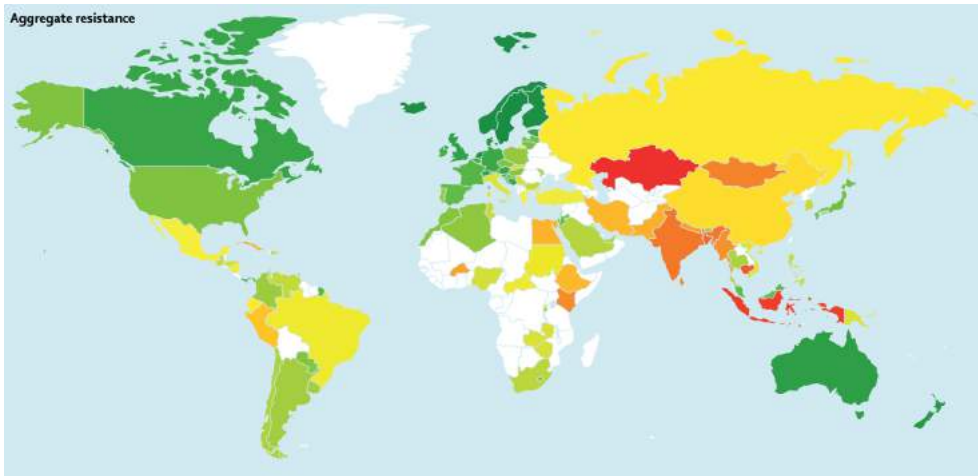




# What About Confounding Variables?

- Lots of other variables correlate with temperature...
- Governance? GDP?
  - Collignon (2018) – Worldwide by country
    - Temperature correlates with AMR prevalence in univariate analyses
    - In multivariate analyses, most important predictors are governance, GDP, infrastructure

# Governance



# What About Confounding Variables?

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- Governance? GDP?
  - Collignon (2018) – Worldwide by country
    - Temperature correlates with AMR prevalence in univariate analyses
    - In multivariate analyses, most important predictors are governance, GDP, infrastructure
  - Kaba (2020) – Europe by country
    - In multivariate analyses, temperature remains an important predictor even after accounting for governance, GDP

# What About Confounding Variables?

- Lots of other variables correlate with temperature...
- Socio-economic factors need further work
- Other factors remain to be investigated
  - Use of antibiotics in animals

# Summary so far

## **Prevalence of AMR correlates with temperature**

- Further work needed on confounders

# Summary so far

## **Prevalence of AMR correlates with temperature**

- Further work needed on confounders
- Mechanisms?



# Climate and AMR prevalence - Mechanisms

Effects of temperature/climate on...

- **Microbial physiology**
- Transmission, e.g., through human behaviour
- Environmental transmission, e.g., dust particles
- Health care delivery
- Microbial communities
- Socio-economic factors
- ...

# Direct Effects on Microbial Physiology

- Many resistant microbes spend part of their life cycles in the environment
  - Water, surfaces
  - Ambient temperature could impact the fitness of resistant microbes
  - Horizontal gene transfer rates

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- This is part of what my lab works on...

# Systematic investigation of the fitness effects of AMR mutations in *E. coli*



Dr. Aaron Hinz

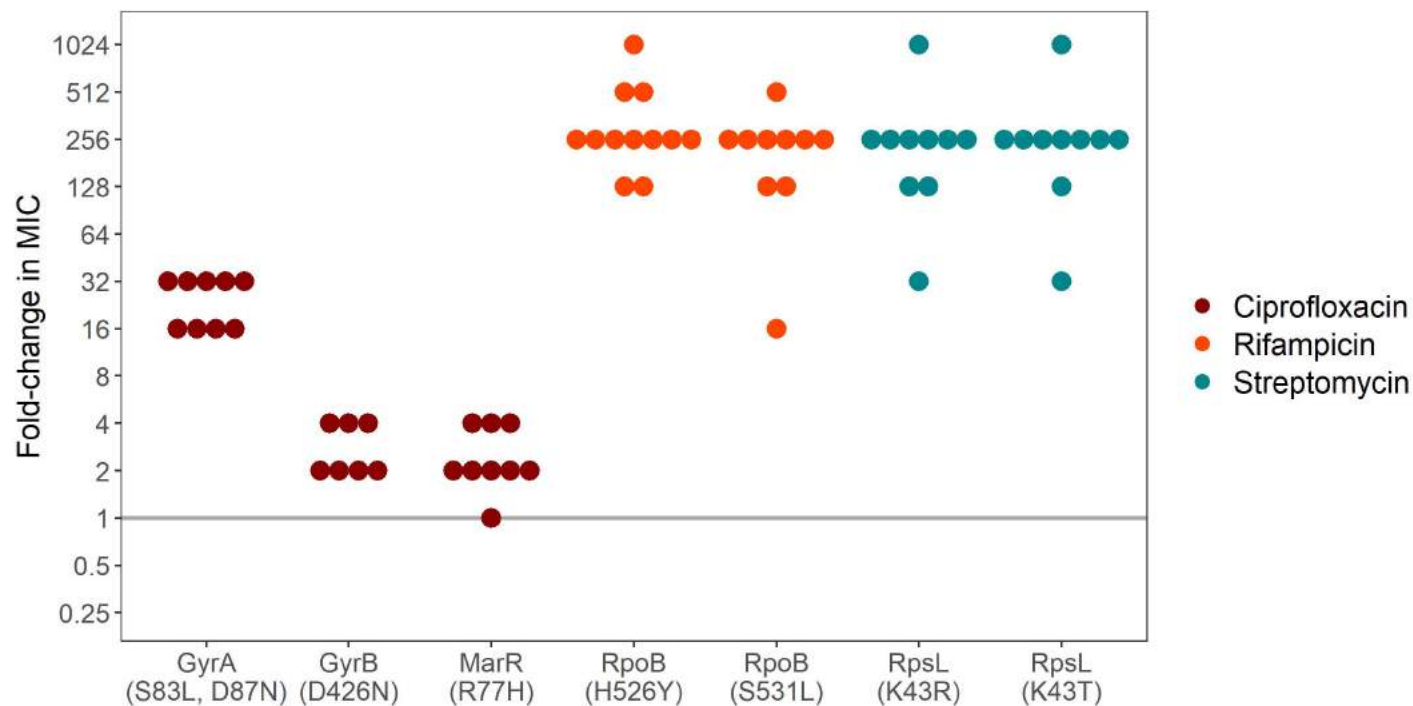
With Claudia Bank, Isabel Gordo,  
Thomas Bataillon, Rees Kassen

- What are the fitness effects of AMR mutations...
  - ...across different genetic backgrounds?
  - ...in different environments?
- And can we predict those fitness effects?

# Systematic investigation of the fitness effects of AMR mutations in *E. coli*

		Fluoroquinolone target		Multidrug Efflux	Rifampicin target		Aminoglycoside Target	
		<i>gyrA</i>	<i>gyrB</i>	<i>marR</i>	<i>rpoB</i>		<i>rpsL</i>	
		S83L, D87N	D426N	R77H	H526Y	S531L	K43T	K43R
Lab strain Enteric (EHEC)	MG1655							
	OLC682							
	OLC809							
	OLC969		Failed				Resistant	Resistant
Extra-intestinal (ExPEC)	GZ 1							
	GZ 2							
	GZ 4					Failed		
	GZ 5							
	GZ 6		Failed				Resistant	Resistant
	GZ 10	Resistant	Resistant	Resistant				
	GZ 13	Resistant	Resistant	Resistant				
	GZ 15	Resistant	Resistant	Resistant				
Total		9	7	9	12	10	10	10

# Consistent Effects of AMR mutations on resistance

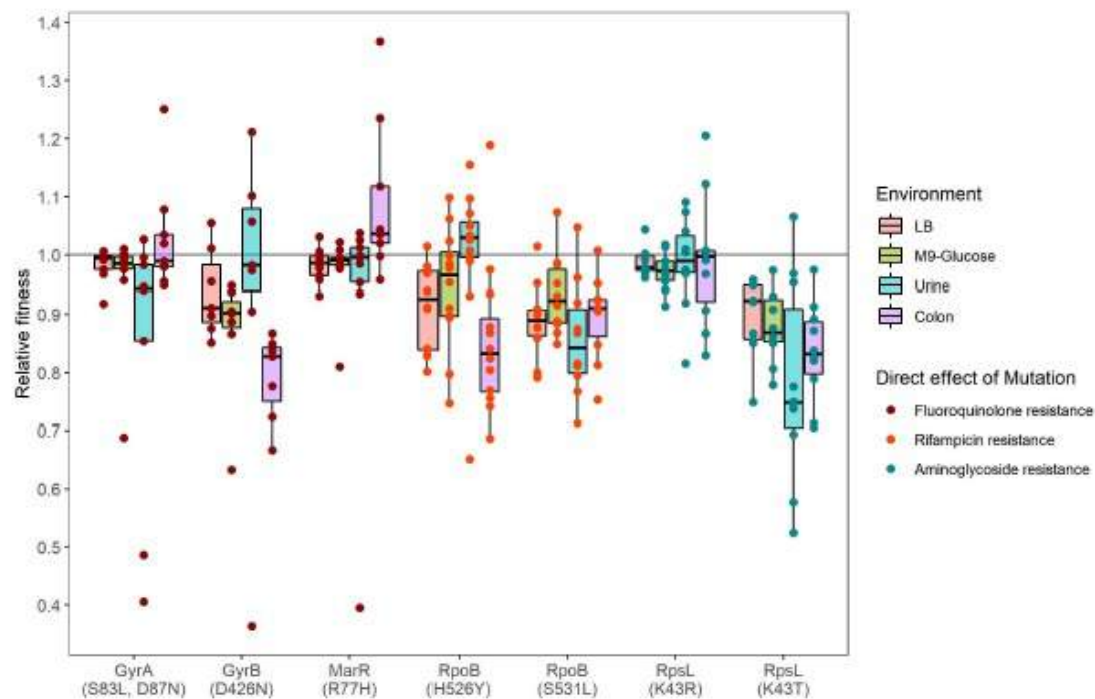




# Genotype and environment effects on fitness

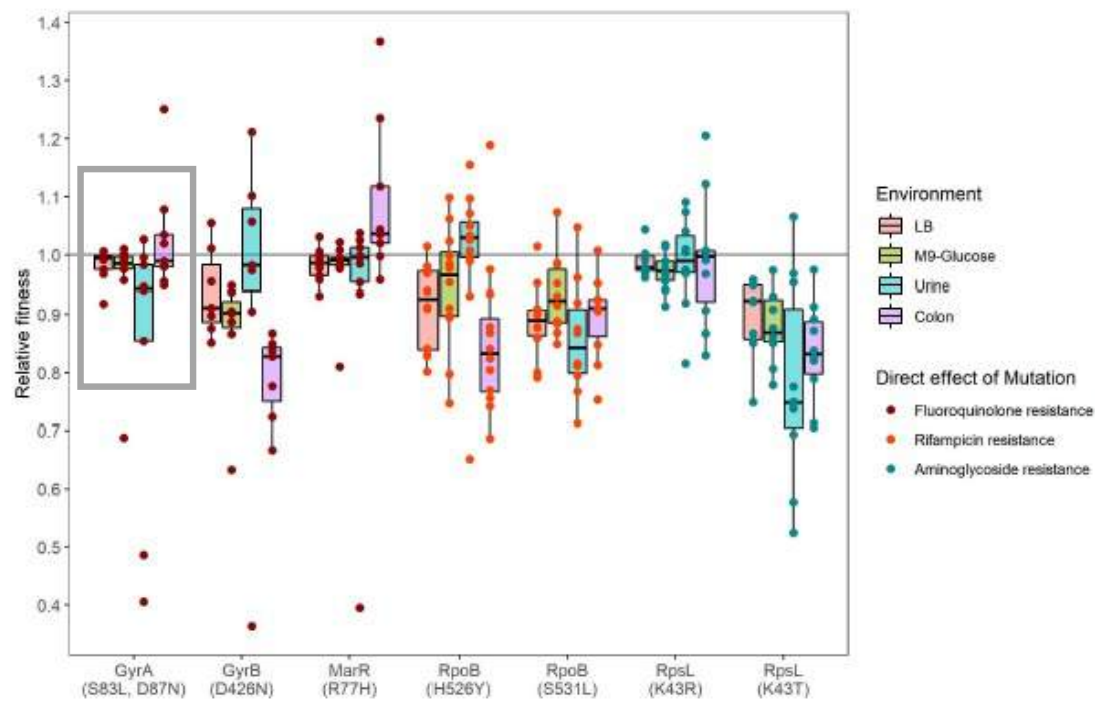
- 7 resistance alleles
- 12 genetic backgrounds
- 4 environments: Lysogeny broth (LB), M9 + glucose, synthetic urine, synthetic colon

# Effects of resistance mutations across genotypes and environments



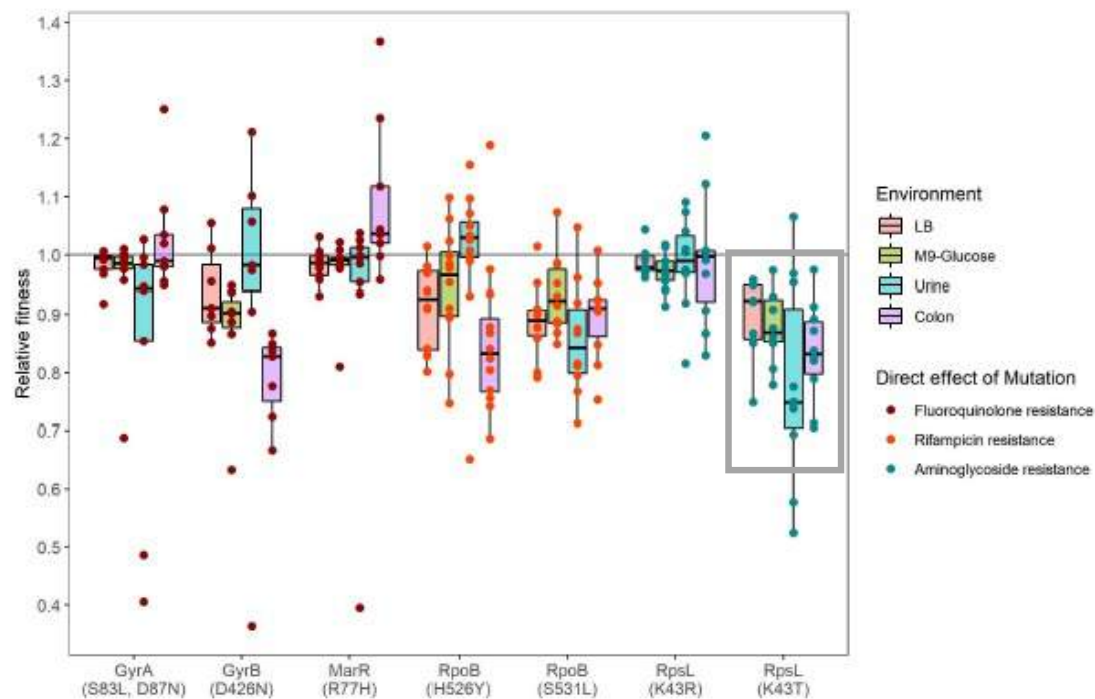
Hinz et al. in preparation

# Some mutations incur few costs



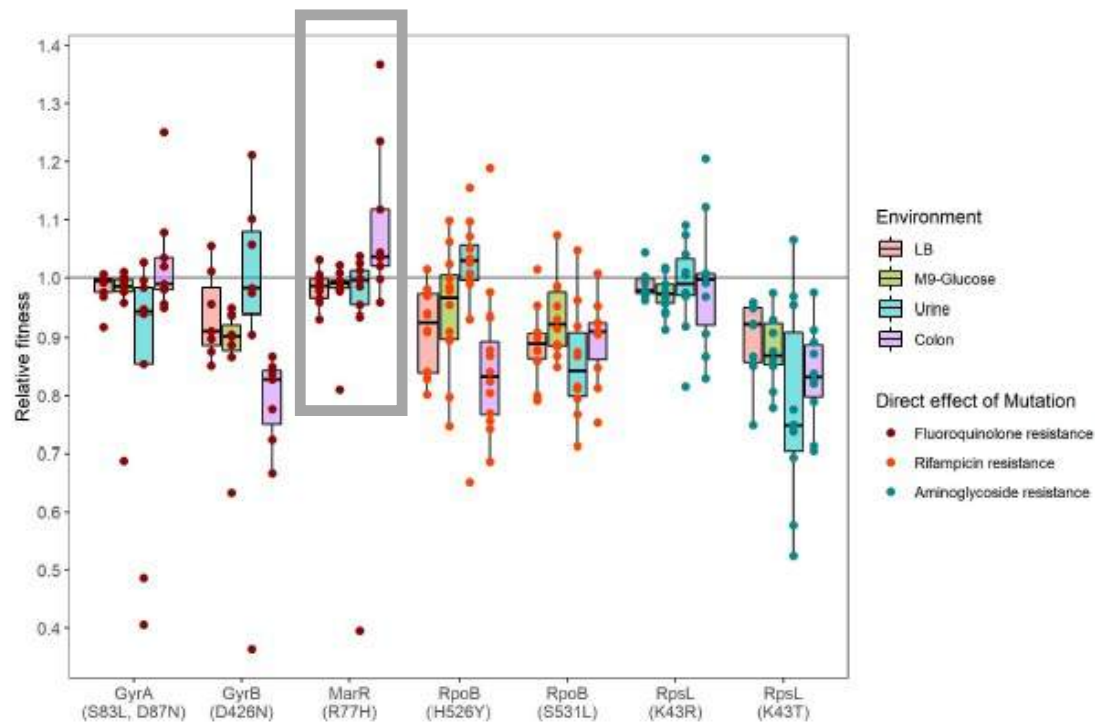
Hinz et al. in preparation

# Some mutations are broadly costly



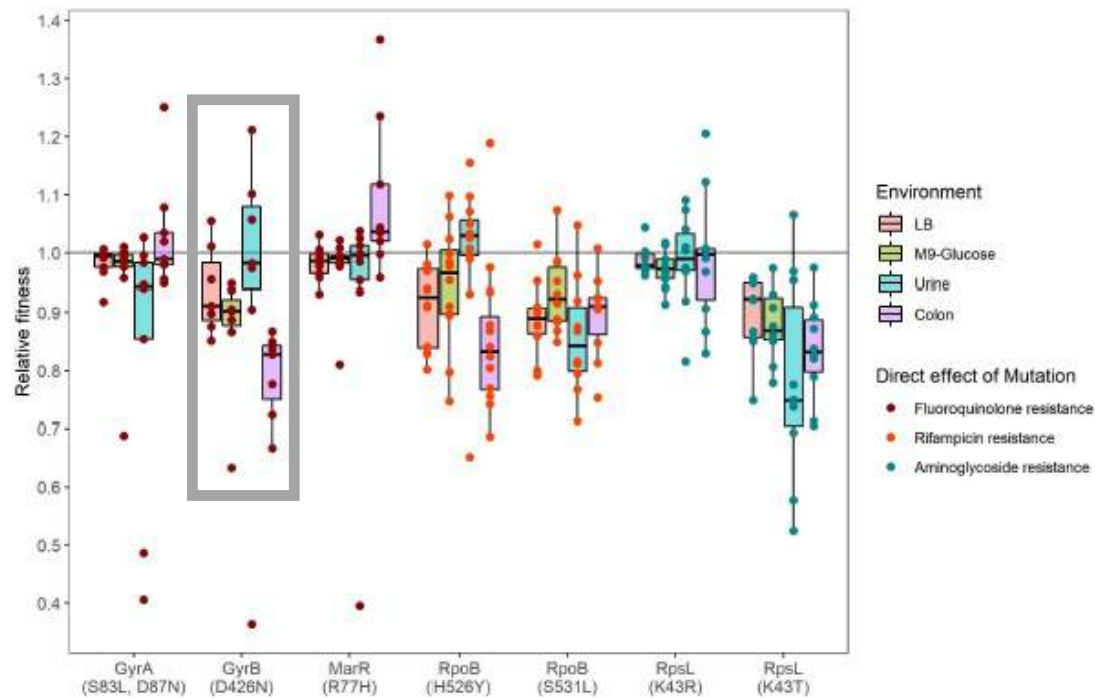
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# Genotype and environment effects on fitness costs



Hinz et al. in preparation

# Genotype and environment effects on fitness costs



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  - **Ambient temperature could impact the fitness of resistant microbes**
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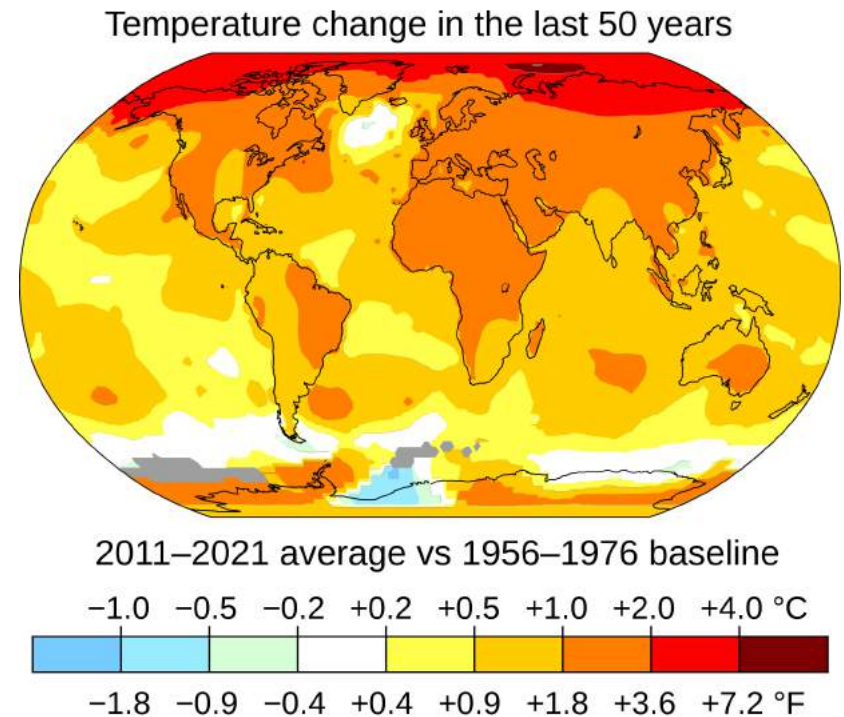
# Urbanization and AMR

- Climate change drives urbanization, particularly in the developing world
- Urbanization can increase AMR through
  - Population density -> higher transmission
  - Greater antibiotic use -> higher rates of emergence
- Arne Ruckert



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# Burroughs-Wellcome Fund – Climate Change Initiatives

Application Deadline

**Jul 22, 2022**

## Climate and Health Interdisciplinary Awards (CHI)

BWF's Climate and Health Interdisciplinary Awards (CHI) provide \$375,000 over three years to support collaborative exploratory work that opens new ground for comprehensively assessing or mitigating the impacts of climate change on human health. These awards are open to both individual scientists and multi-investigator teams. Early career faculty and postdoctoral fellows nearing their transition to independence are especially encouraged to apply, whether individually or within teams. Only U.S. and Canadian citizens, permanent residents, and temporary residents may apply, and applications must be submitted by U.S. or Canadian institutions.

[LEARN MORE](#)

[APPLY NOW](#)

Rolling Application Deadline

**Apr 12, 2023**

## Climate Change and Human Health Seed Grants

Small grants to promote the growth of new connections between scholars, practitioners, educators, and/or communicators working to understand, spread the word about, and mitigate the impacts of climate change on human health. Proposals will be accepted on a rolling basis from September 1, 2021 through July 12, 2023. Review will be conducted quarterly. After each quarterly review, we will support, decline, or send proposals back to applicants for revision, but may hold some proposals over for a future review. Recommended revisions may include suggestions that separate groups of applicants submitting similar proposals work together to develop a single proposal or that applicants consider becoming involved in efforts aligned with work funded in earlier quarters.

# Acknowledgements

Aaron Hinz

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Derek MacFadden

Ade Oladeinde

Alexandra Ponette-Gonzalez

Arne Ruckert

Mauricio Santillana

Morgan Scott



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# Discussion

- Confounders
- Mechanisms
- Other considerations

