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

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Texas A&M AgriLife | INSTITUTE FOR ADVANCING HEALTH THROUGH AGRICULTURE

# First, an Introduction

Microbial Genomics and Evolution

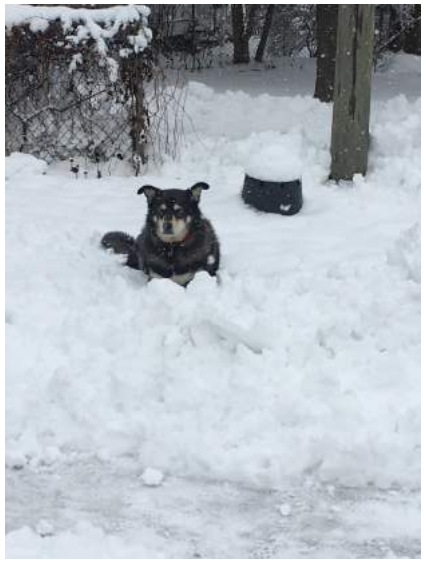
- What genes and mutations cause resistance?
- What are the impacts of resistance genes/mutations on bacteria?
- Molecular methods for pathogen surveillance (SARS-CoV-2; *Salmonella*)

- Implications for policy

# First, an Introduction

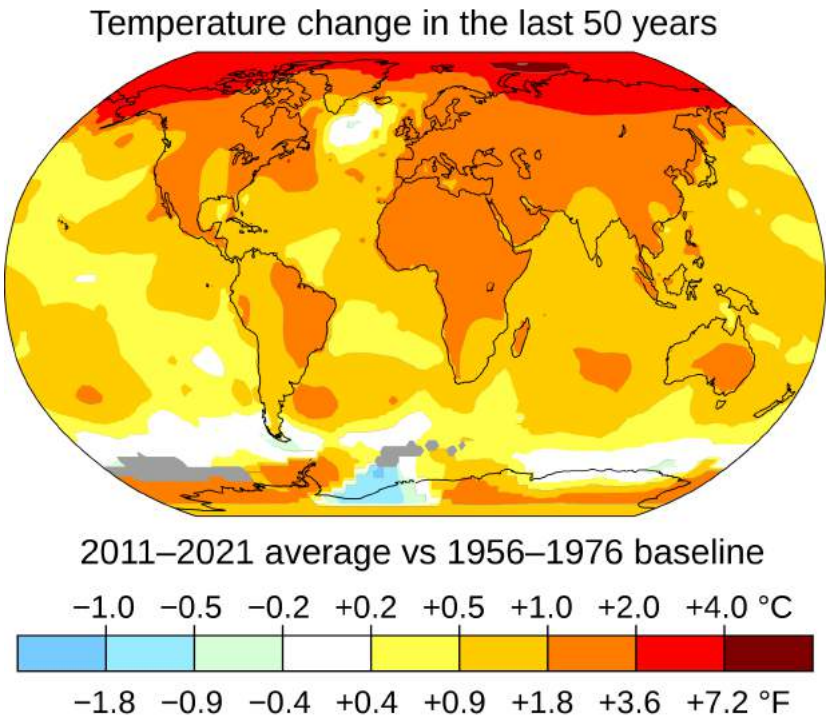
Carleton University: 2013 - 2022

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

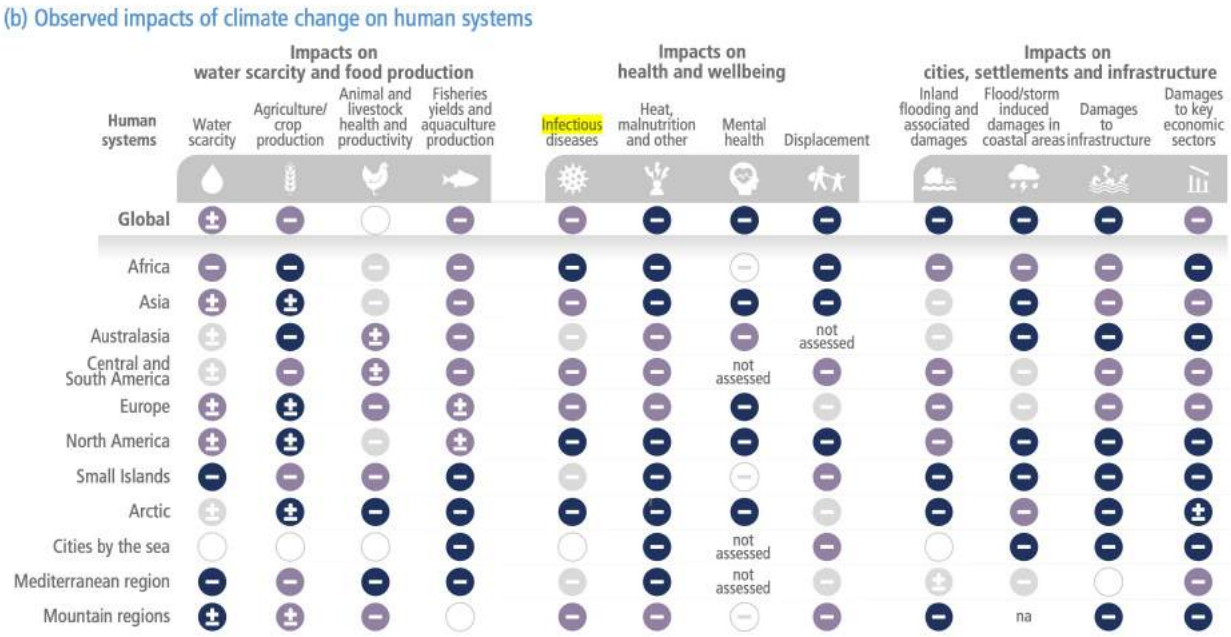


# Today

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



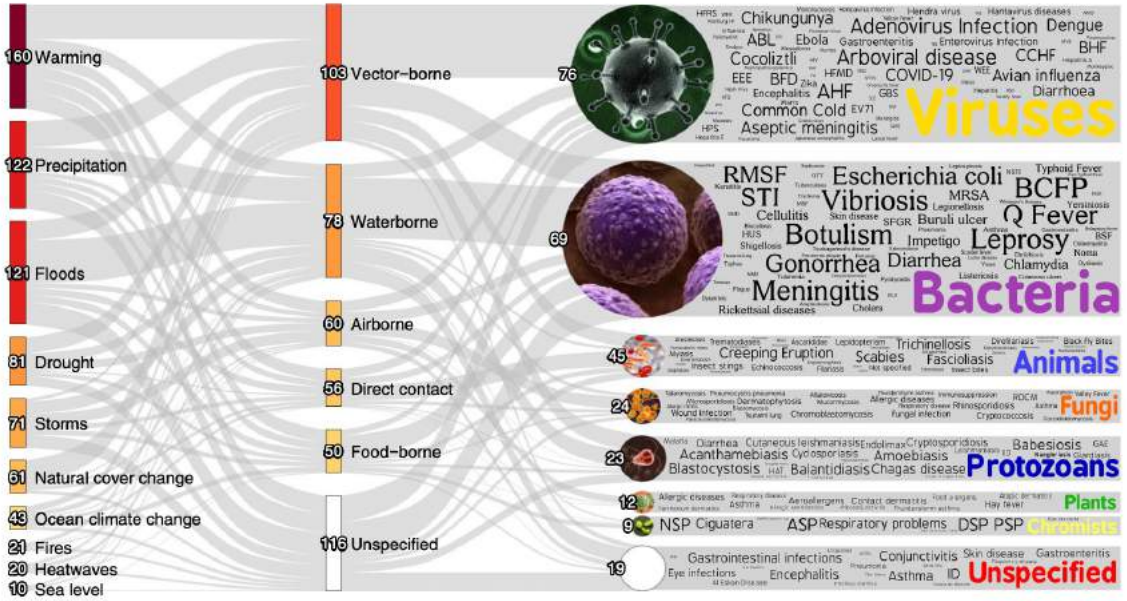
# Climate Change Impacts on Infectious Disease




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

2022 IPCC Report

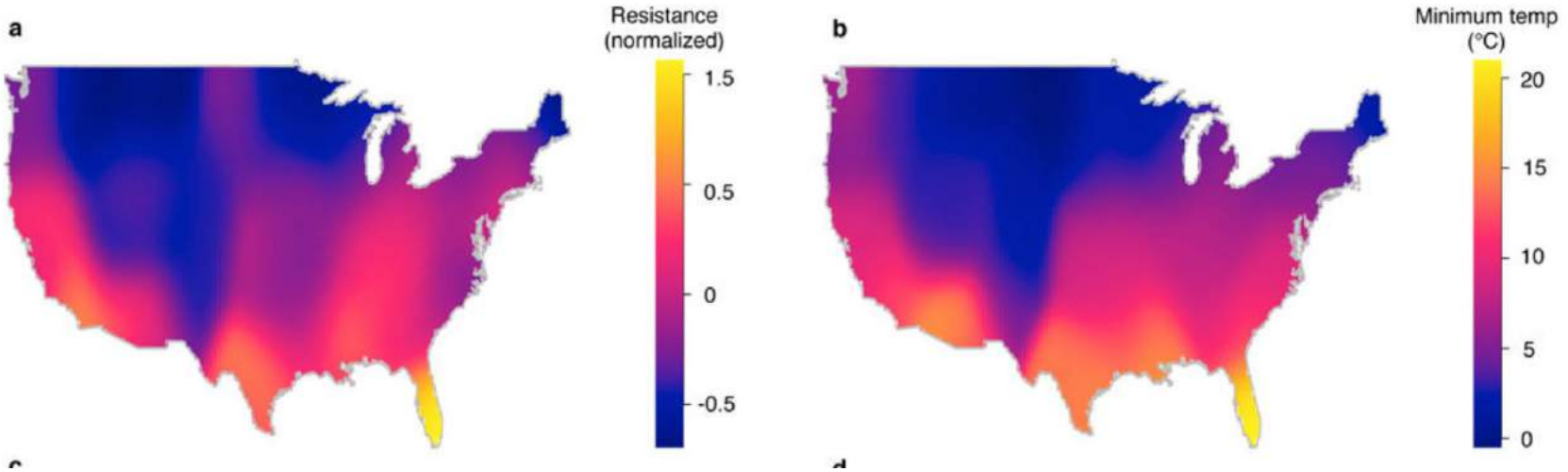
# Climate Change Impacts on Infectious Disease




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

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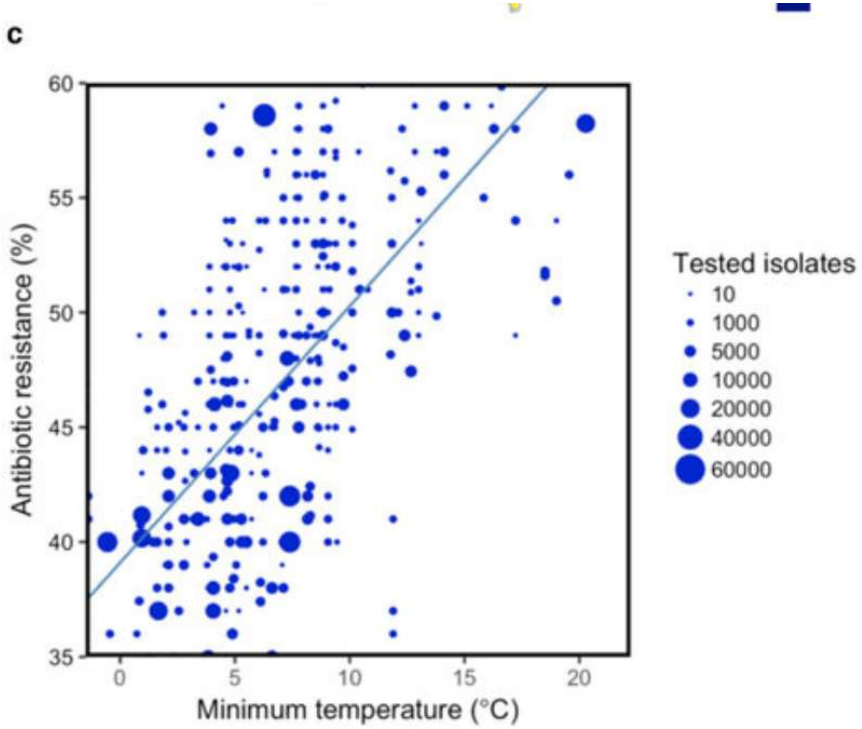


Amoxicllin resistance in *E. coli*

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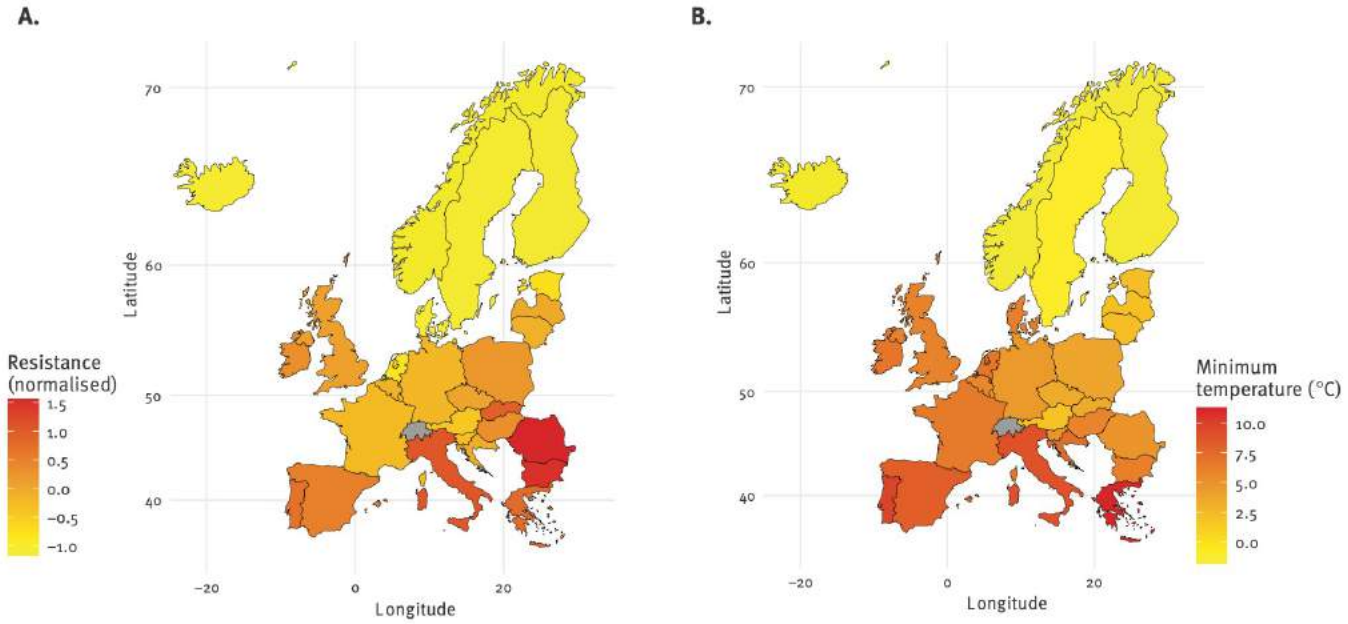
# What About Confounding Variables?

- 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*)
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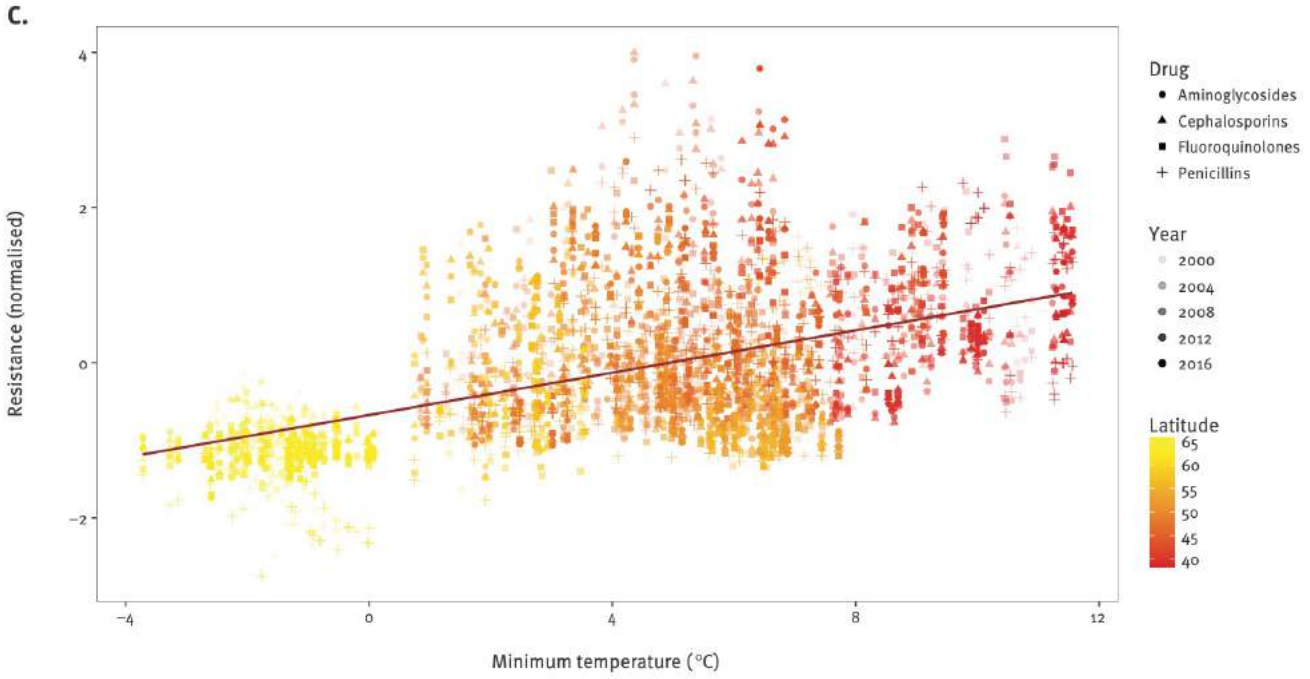


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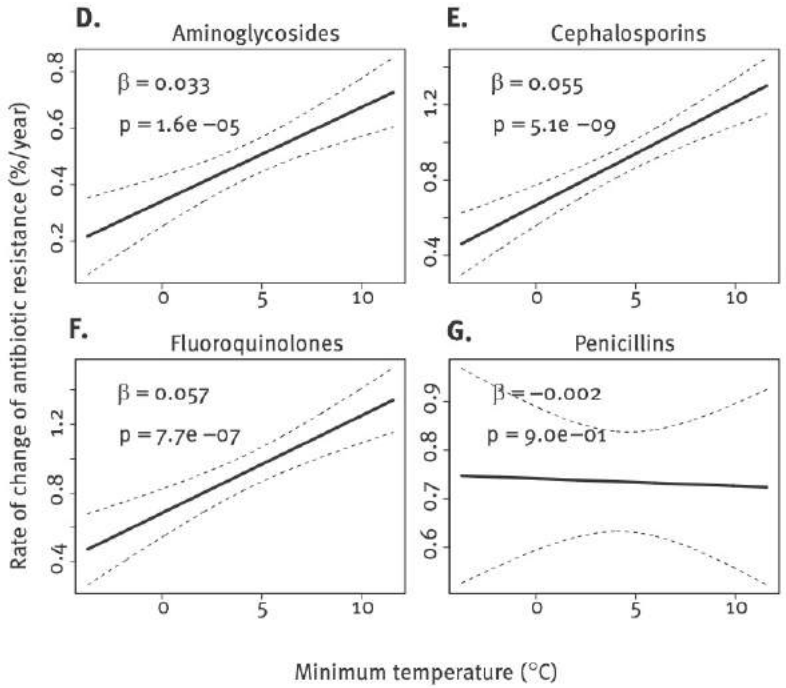
# Rate of Change in AMR Prevalence Correlates with Temperature

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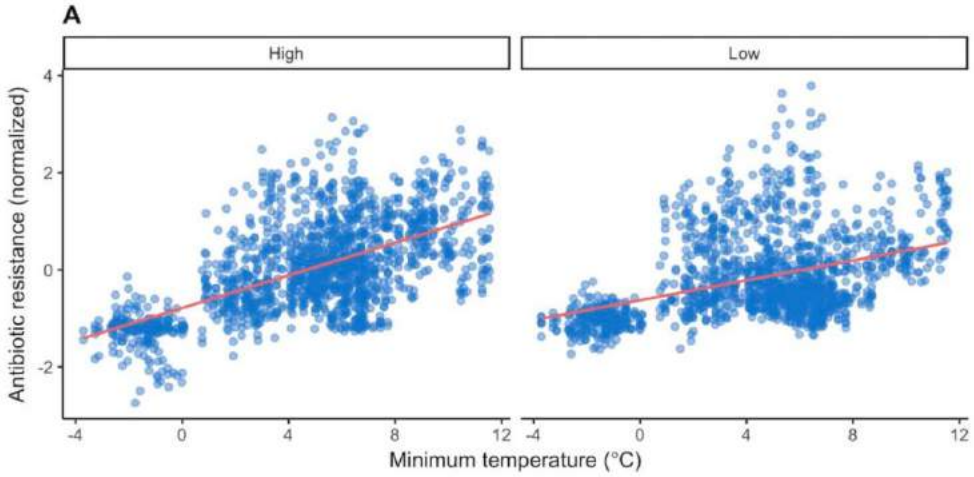
# What About Confounding Variables?

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

Consumption

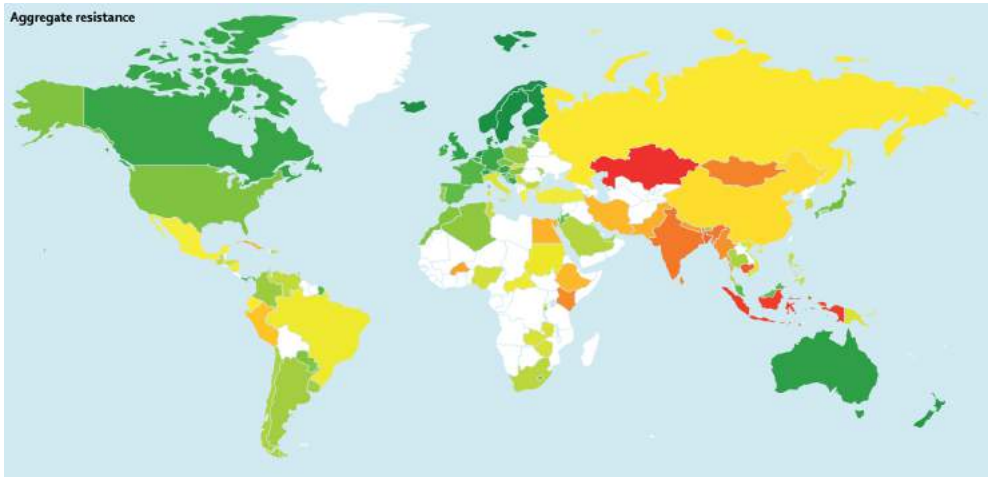


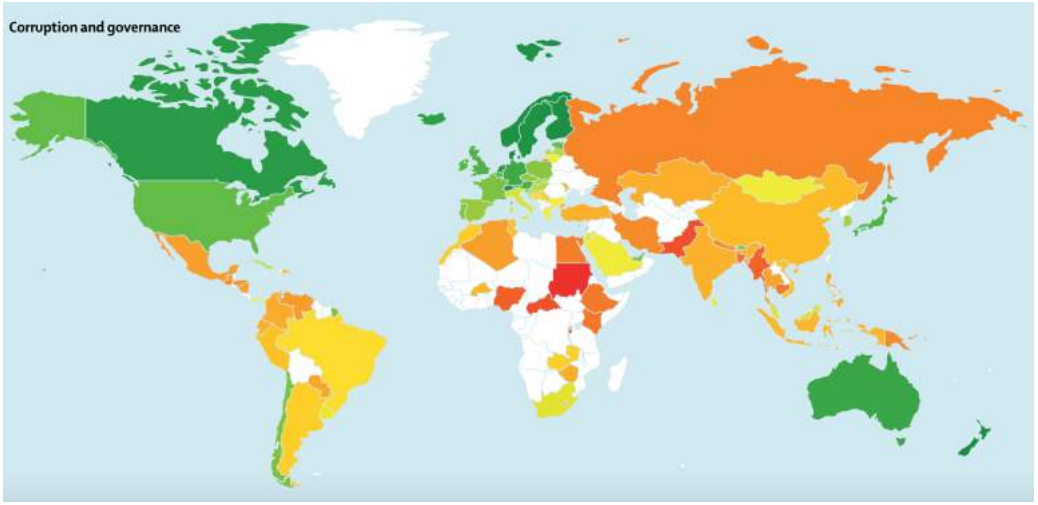
# What About Confounding Variables?

- 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



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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

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**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

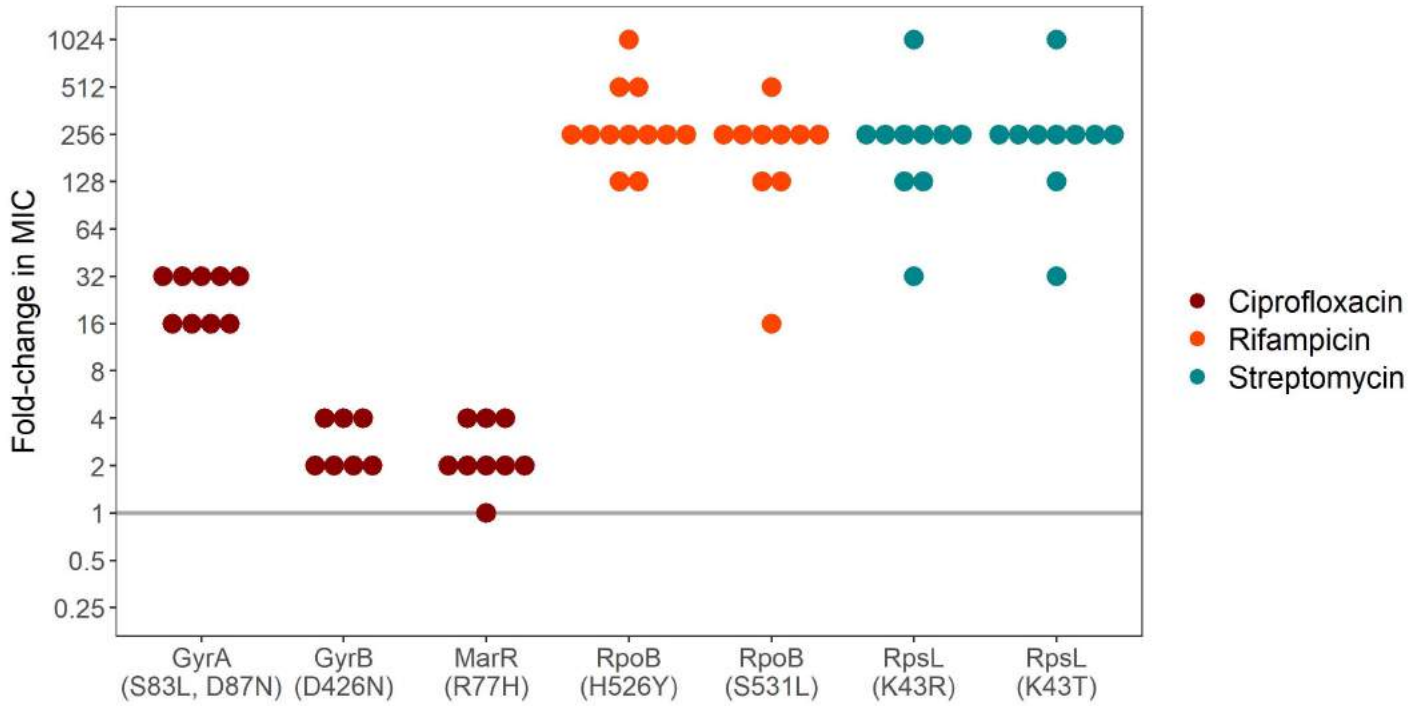
With Claudia Bank, Isabel Gordo, Thomas Bataillon, Rees Kassen

- 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 | |
|---|---|---|---|---|---|---|---|---|
| | | *gyrA* | *gyrB* | *marR* | *rpoB* | | *rpsL* | |
| | | S83L, D87N | D426N | R77H | H526Y | S531L | K43T | K43R |
| Lab strain | MG1655 | | | | | | | |
| Enteric (EHEC) | 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 |

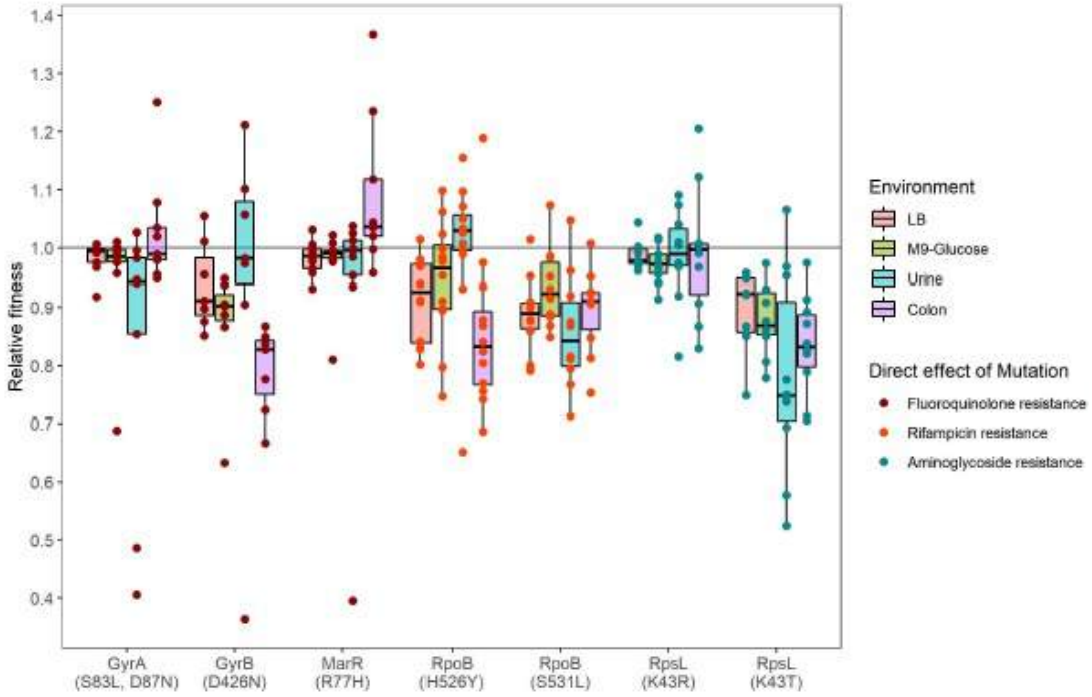
# Consistent Effects of AMR mutations on resistance



# Genotype and environment effects on fitness

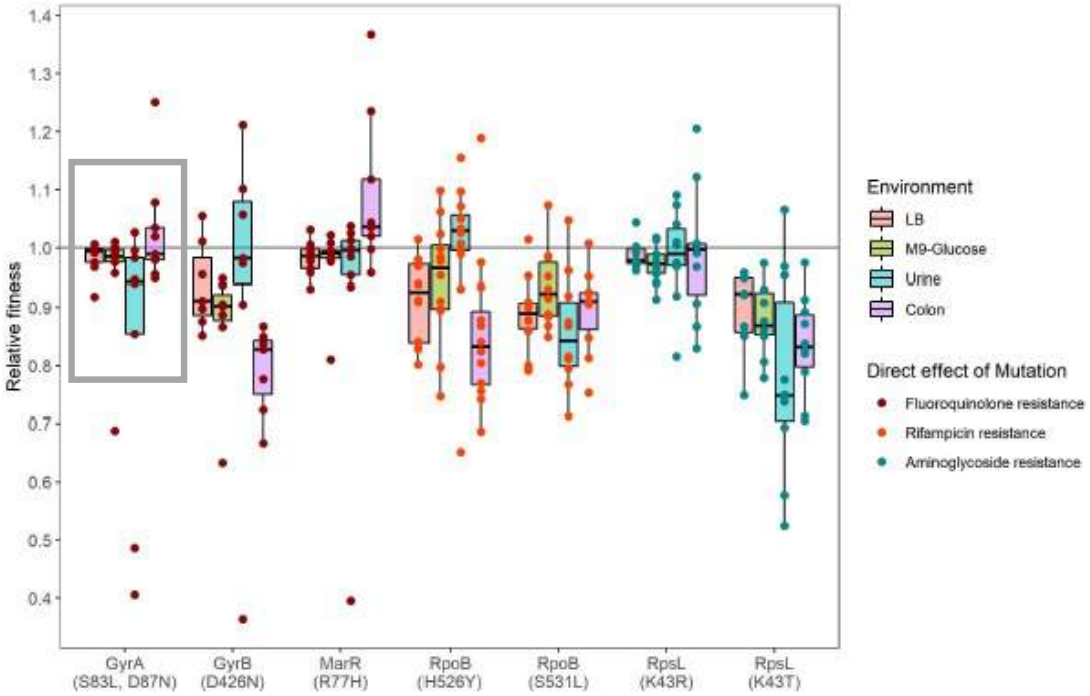
- 7 resistance alleles
- 12 genetic backgrounds
- 4 environments: Lysogeny broth (LB), M9 + glucose, synthetic urine, synthetic colon

# Effects of resistance mutations across genotypes and environments




Hinz et al. in preparation

# Some mutations incur few costs

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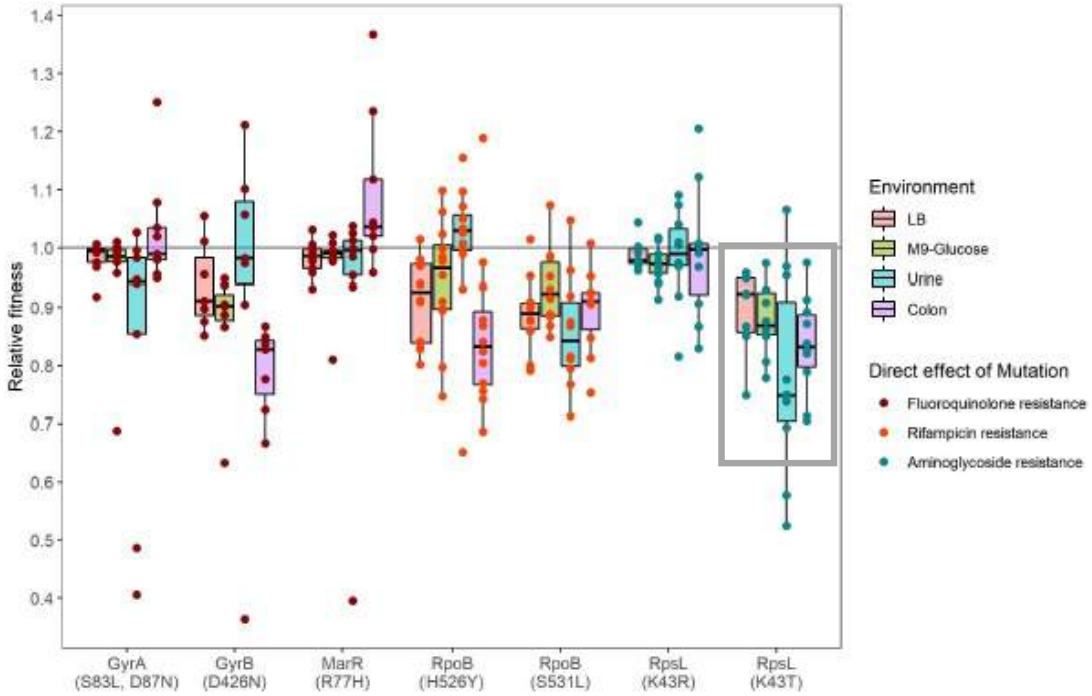
# Some mutations are broadly costly

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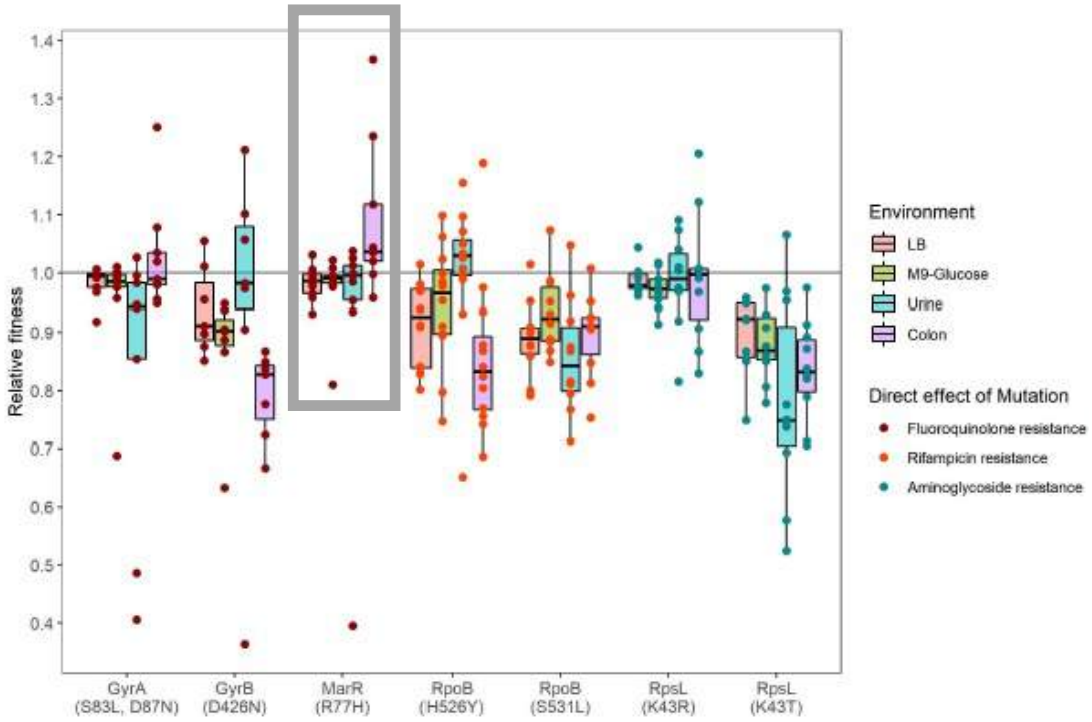


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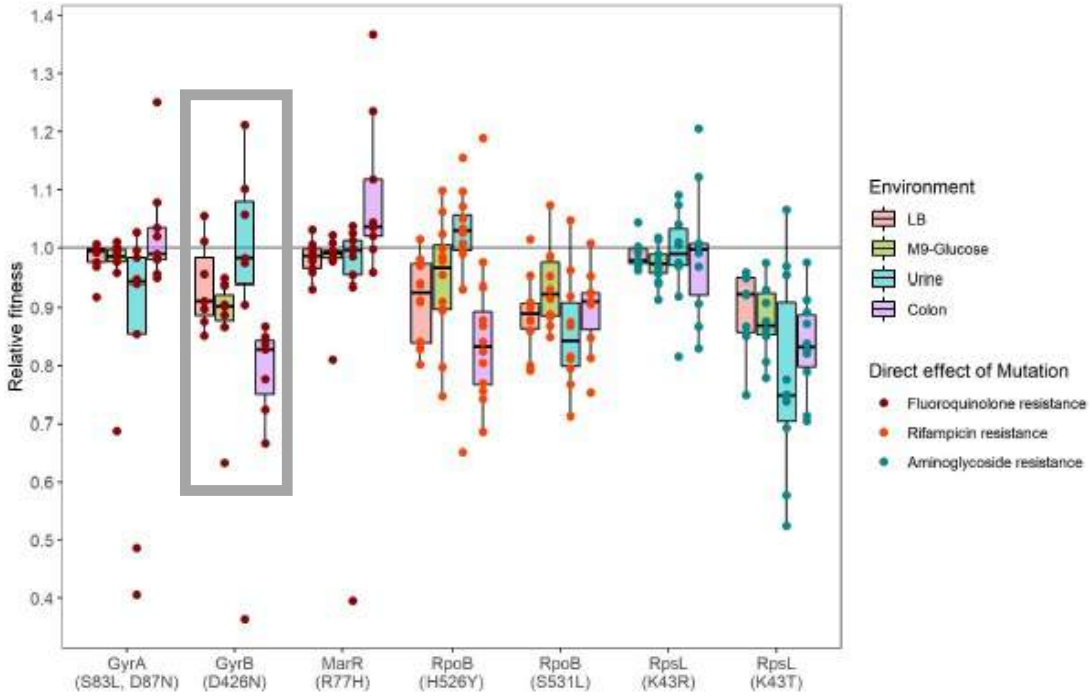


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- Environmental transmission, e.g., dust particles
- Health care delivery
- Microbial communities
- **Socio-economic factors**
- …

# 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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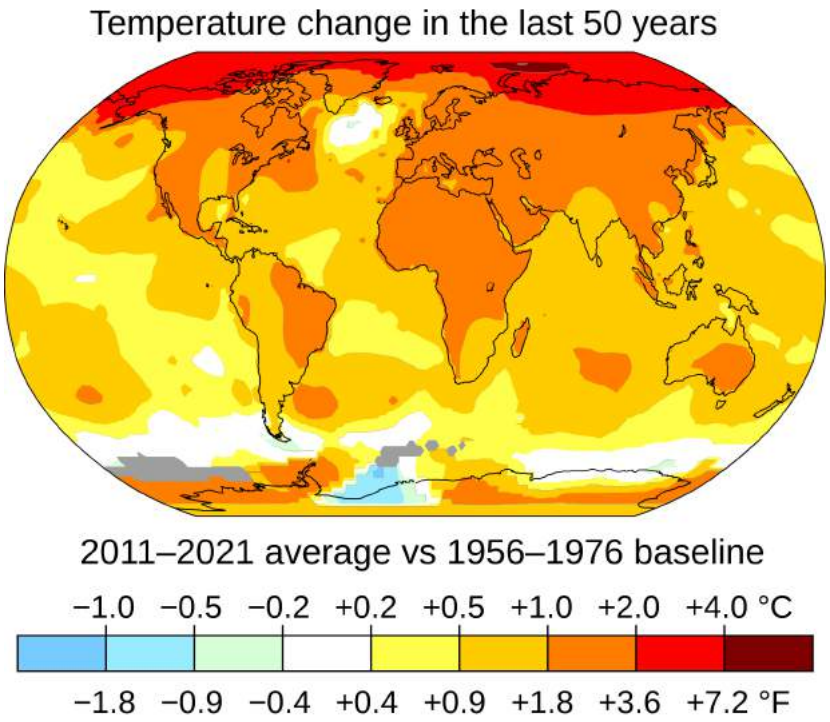
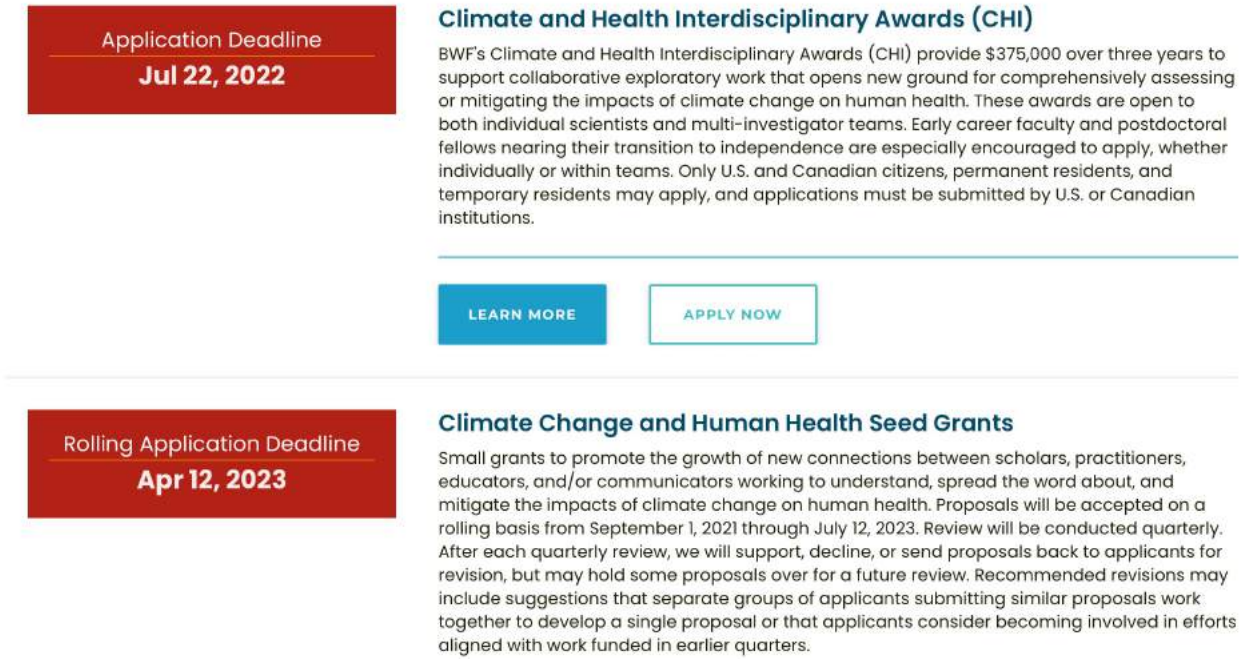


# Burroughs-Wellcome Fund – Climate Change Initiatives



# Acknowledgements


Aaron Hinz

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Ade Oladeinde
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Arne Ruckert
Mauricio Santillana
Morgan Scott



NSERC CRSNG

CIHR IRSC
Canadian Institutes of Health Research | Instituts de recherche en santé du Canada

jpiamr

Texas A&M AgriLife | Institute for Advancing Health through Agriculture

Carleton University

# Discussion

- Confounders
- Mechanisms
- Other considerations