

Ambient Temperature Associated with Variation in Cystic Fibrosis Lung Disease

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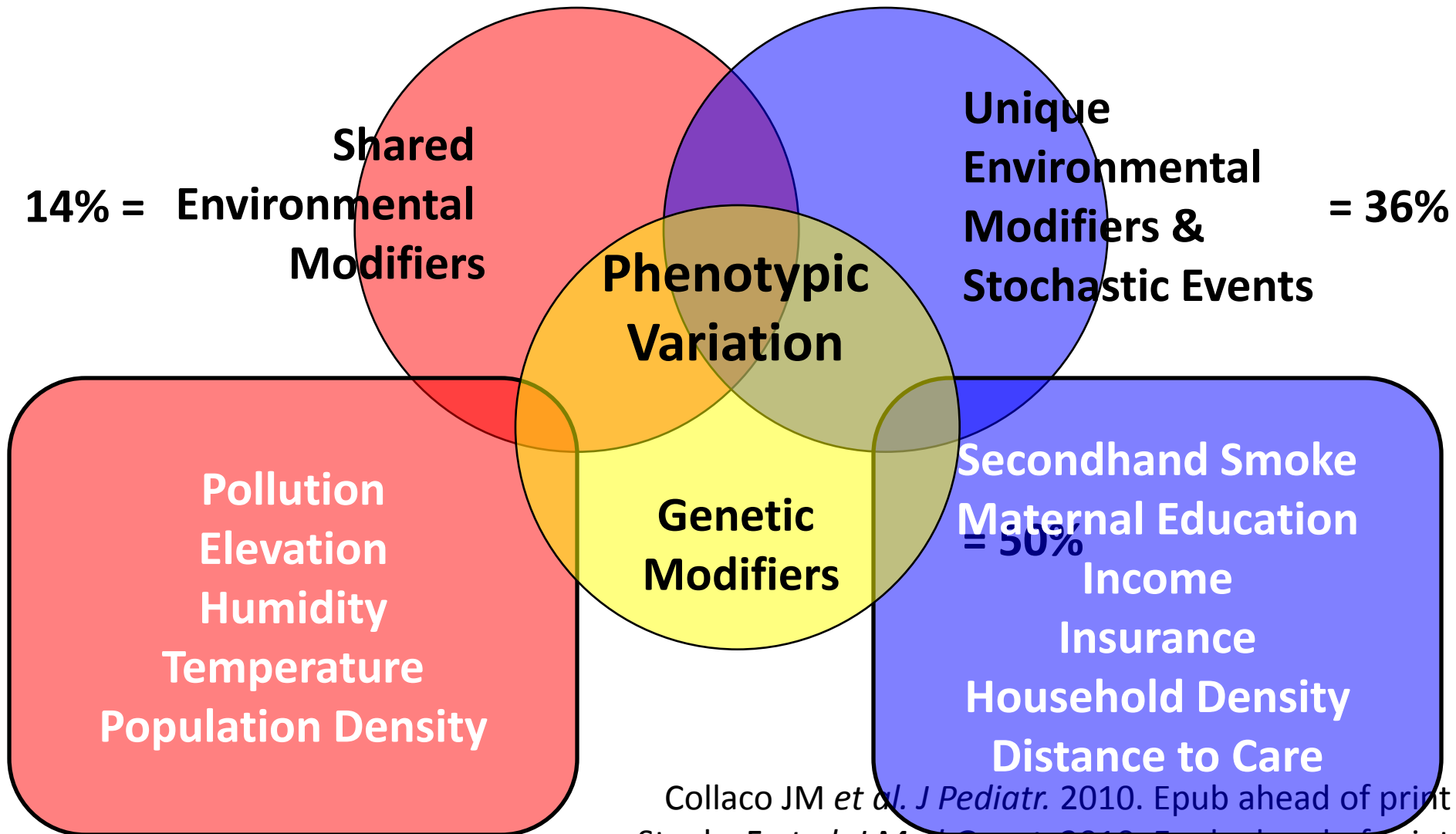
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M E D I C I N E

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Disclosures

- Funding Sources
 - U.S. Cystic Fibrosis Foundation
 - Flight Attendant Medical Research Institute
 - National Institutes of Health

Non-CFTR Sources of Variation in CF Lung Disease



CF Twin-Sibling Study

- 1658 twins and siblings with CF (817 families) enrolled, primarily from U.S., but also Australia and Scotland [P.I. Garry Cutting]
- Study includes ~90% of twins with CF in U.S. and ~60% of siblings
- Study Population n = 1378
 - Excluded
 - No lung function data (n = 191)
 - No U.S. zip code (n = 43)
 - Active smoking (n = 46)

CF Foundation Patient Registry (Replication Population #1)

- Data provided for calendar year of 2007 by the U.S. Cystic Fibrosis Foundation (n=24,799)
- Exclusions
 - In Twin-Sibling Study (n = 1435)
 - No lung function data (n = 5341)
 - No U.S. zip code (n = 318)
 - Active smoking (n = 315)
- Study Population (n = 17,390)
 - This includes 7189 Caucasian, F508del homozygous individuals

Modeling Methods

Predictors		
<u>Demographics</u>	<u>Micro-Environment</u>	<u>Macro-Environment</u>
Sex <i>CFTR</i> Genotype Race/Ethnicity Age at Diagnosis Age at FEV₁	Secondhand Smoke Lack of Insurance Maternal Education Estimated Income Medicaid vs. Private Insurance Household Density	Pollution: PM _{2.5} Distance to CF Care Population Density Relative Humidity Elevation Temperature

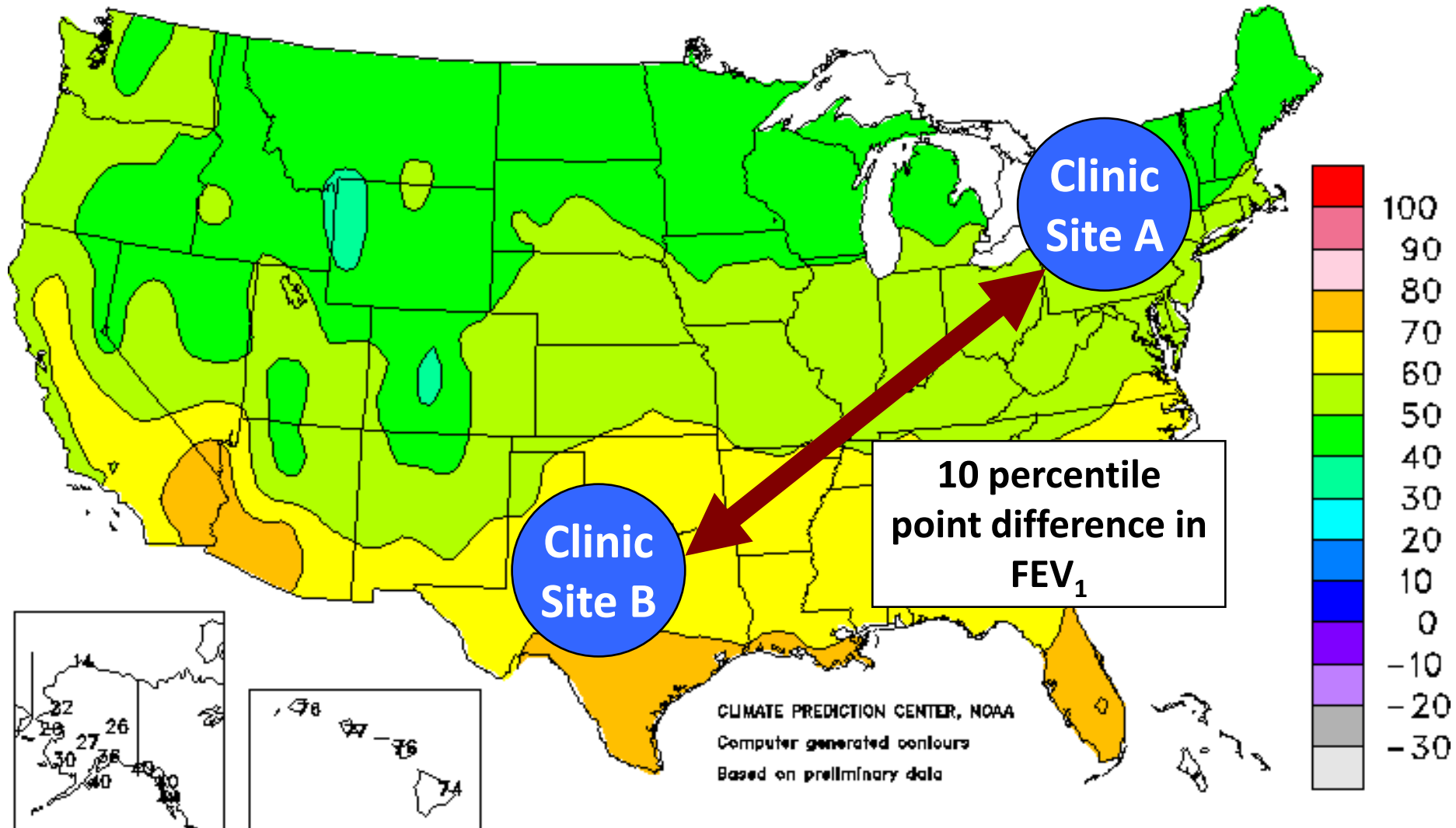
- Univariate regression modeling (GEE) clustered by family to account for familial relationships
- Outcome: CF-Specific FEV₁ percentile (not survival corrected)
- Predictors in bold were significant in univariate modeling and were used for multivariate regression modeling

Multivariate Coefficient (<i>p</i> Value)	Twin Sibling Study	
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Variable	Preliminary	
n	1167	
Model <i>p</i> value	<0.0001	
Model r	0.22	
Age at PFT (yrs)	-0.31	(0.005)
Maternal Education	1.25	(0.19)
Log Income (\$)	1.35	(0.82)
Insurance Status	-6.44	(0.001)
Household Density	0.97	(0.10)
Log Elevation (m)	1.57	(0.34)
Temperature (°F)	-0.31	(0.023)

Average Temperature (°F)

JAN - DEC 2006



Possible Connection between Temperature and Lung Function?

- NACFC 2009: ACFBAL Study update strengthened a suspicion...the presence of *Pseudomonas aeruginosa*

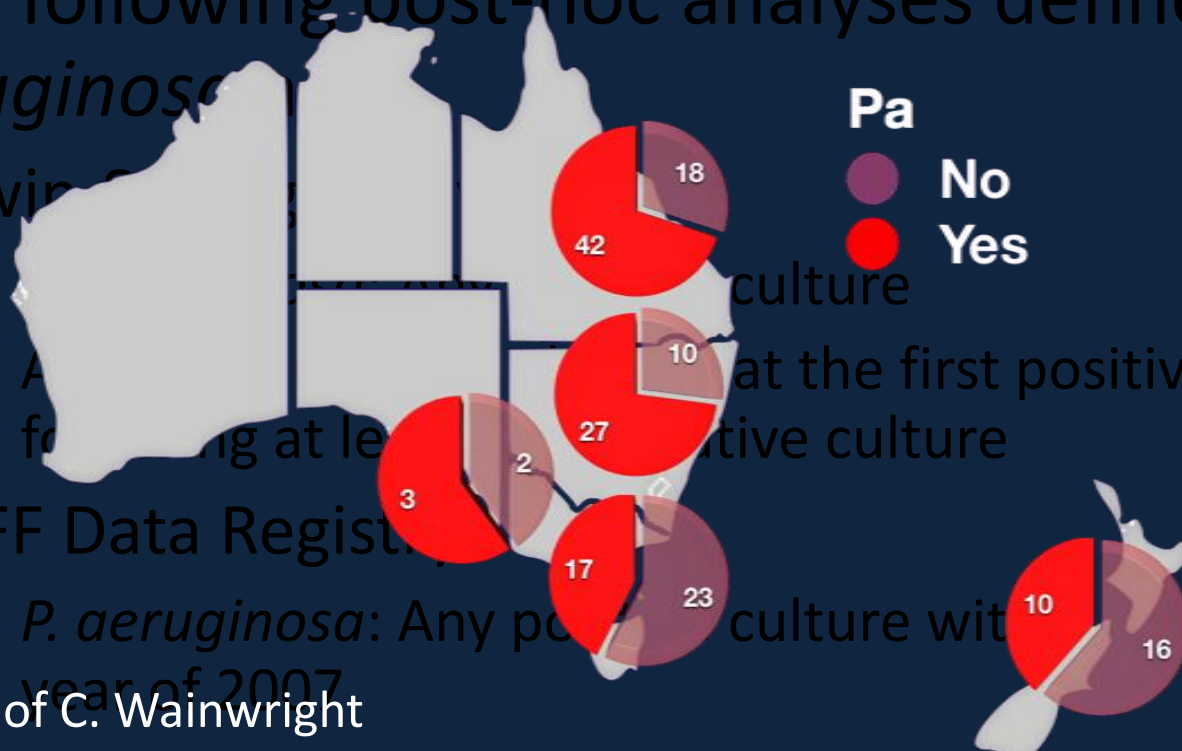
- The following post-hoc analyses define *P. aeruginosa*

– Twin Study

- Any *P. aeruginosa* culture
- Any *P. aeruginosa* at the first positive culture
- Any *P. aeruginosa* found at least one positive culture

– CFF Data Register

- *P. aeruginosa*: Any positive culture with a positive calendar year of 2007

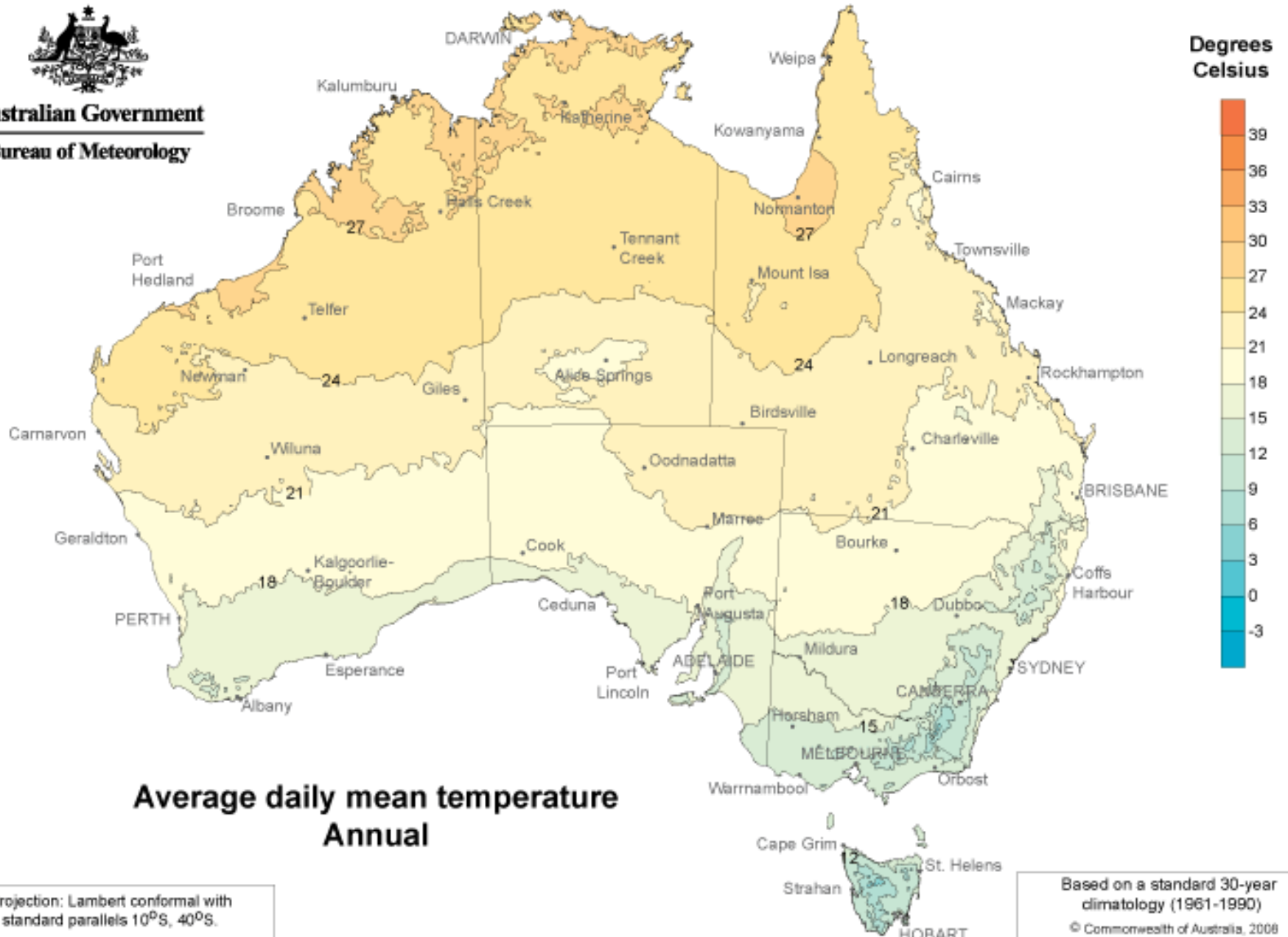


Australian CF BAL Study (Replication Population #2)

- Data provided by Dr. Claire Wainwright
- Prospective collection of infants with CF who receive serial respiratory cultures (n = 170)
- Total Population n = 168
 - Excluded
 - No Australian postcode (n = 2)



Australian Government
Bureau of Meteorology



Higher Prevalence of *P. Aeruginosa* Seen at Warmer Temperatures

<i>P. aeruginosa</i> (% Positive)	Mean Annual Temperature Quartiles				ANOVA <i>p</i> value
	Coldest	Cold	Warm	Warmest	
Twin-Sibling Study (n = 1372)	85.3	85.0	88.4	92.9	0.005
CFF Data Registry (n = 6501) [White, F508del Homozygotes]	60.8	64.4	62.6	65.5	0.020
ACFBAL Study (n = 168)	40.5	54.8	71.4	73.8	0.005

Earlier Acquisition of *P. Aeruginosa* Seen at Warmer Temperatures

<i>P. aeruginosa</i> Age of Acquisition (Yrs)	Mean Annual Temperature Quartiles				ANOVA <i>p</i> value
	Coldest	Cold	Warm	Warmest	
Twin-Sibling Study (n = 916)	7.6 (± 7.5)	6.2 (± 6.5)	6.3 (± 5.8)	6.3 (± 5.0)	0.04
ACFBAL Study (n = 91)	2.7 (± 1.5)	2.8 (± 1.4)	2.1 (± 1.4)	1.9 (± 1.4)	0.10

Conclusions

- Ambient temperature is correlated with lung function in the United States
- Ambient temperature is also associated with prevalence of *P. aeruginosa* in U.S. and Australia
- Benchmarking may need to account for geographic factors leading to variation
- Ambient temperature may need to be considered as a covariate in large genetic studies of CF lung function

Acknowledgments

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 - John McGready
 - Kathleen Naughton
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 - Claire Wainwright