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*The role of phylogenetic lineage in  
Escherichia coli O157:H7 risk:  
location, location, location*

Gillian A. M. Tarr<sup>1</sup>, Smriti Shringi<sup>2</sup>, Jon Wakefield<sup>1</sup>, Amanda Phipps<sup>1</sup>, Thomas E. Besser<sup>2</sup>, Phillip I. Tarr<sup>3</sup>, Peter Rabinowitz<sup>1</sup>,  
Jonathan Mayer<sup>1</sup>

<sup>1</sup>University of Washington, <sup>2</sup>Washington State University, <sup>3</sup>Washington University in St. Louis



Center for  
One Health Research

# Acknowledgements

Washington State Department of Health

Hanna Oltean

Washington State University

Besser Lab team

University of Washington

Allison Black

Center for One Health Research team

## Research Support

U.S. Department of Agriculture 2009-04248 and 2010-04476

National Institutes of Health T32ES015459





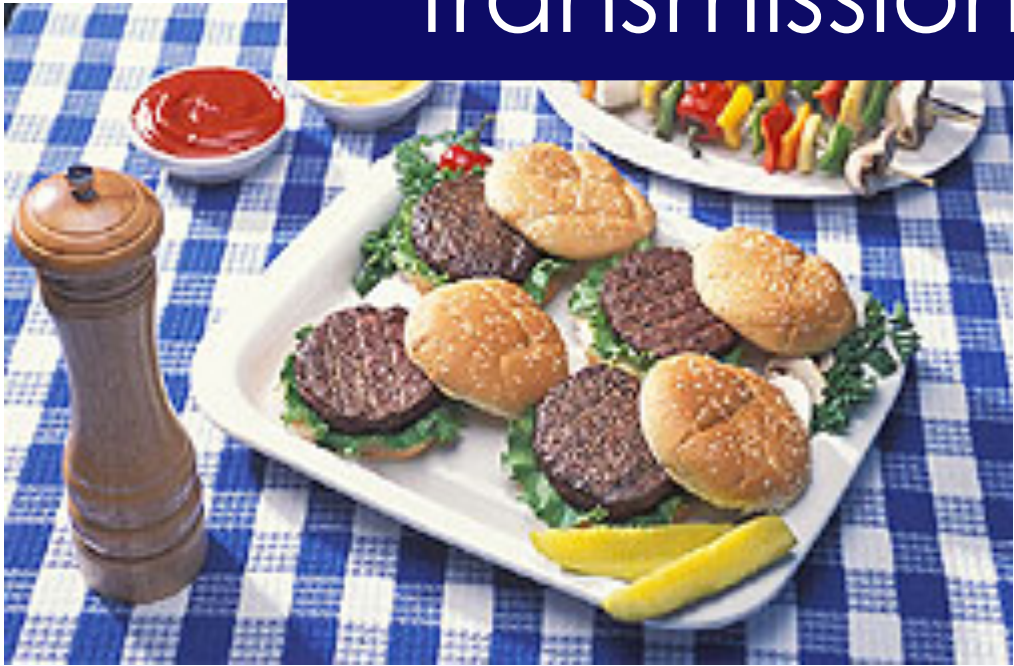


Reservoir  
 -cattle  
 -sheep  
 -goats

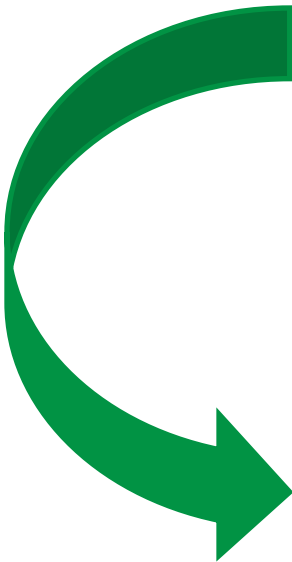


Environmental  
 contamination

Foodborne  
 transmission



*E. coli* O157 infections  
 -gastroenteritis  
 -bloody diarrhea  
 -hemolytic uremic  
 syndrome  
 -kidney failure

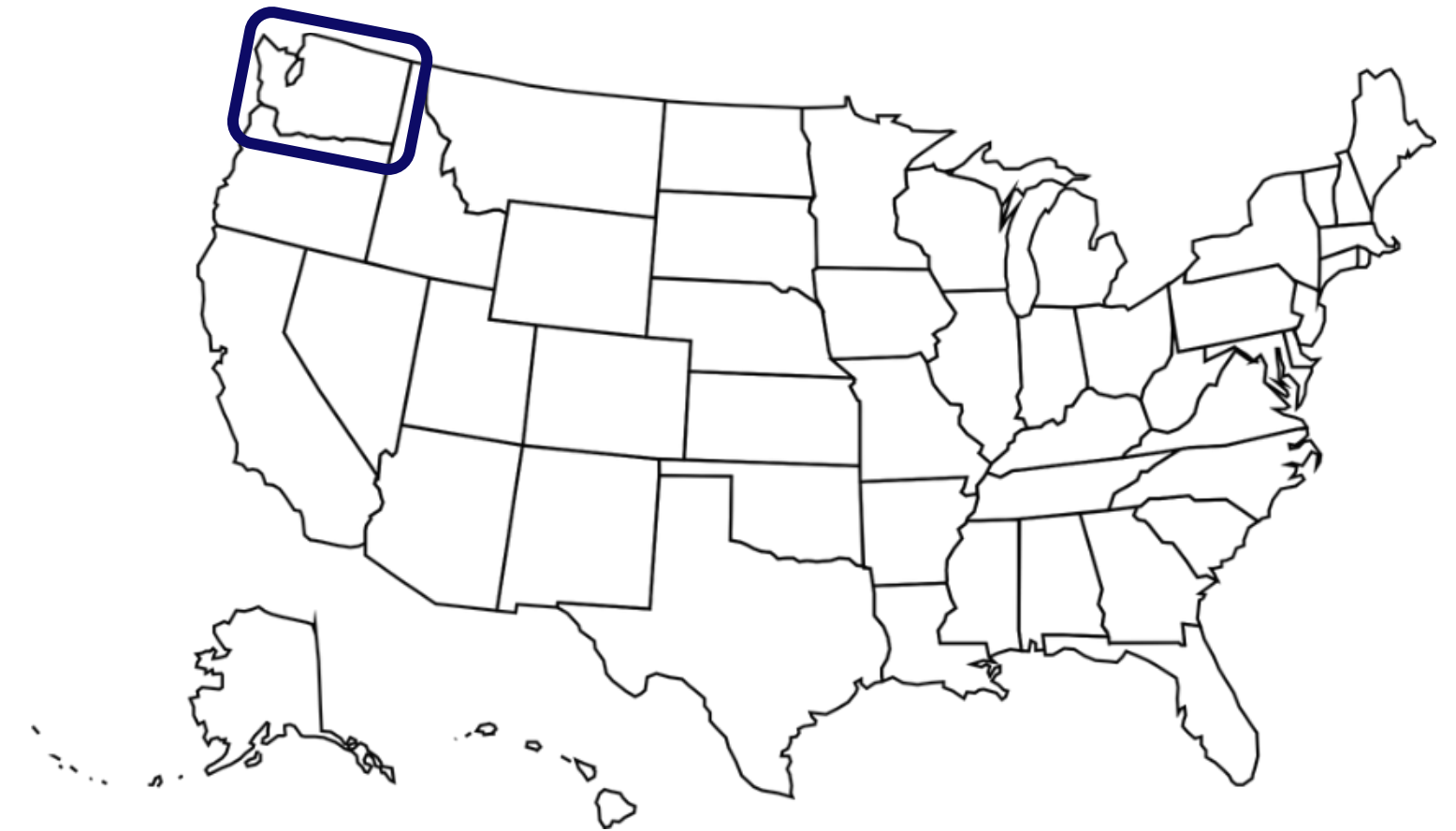


Overarching Question:  
Do “local” bacteria contribute  
significantly to reported *E. coli* O157  
infections?

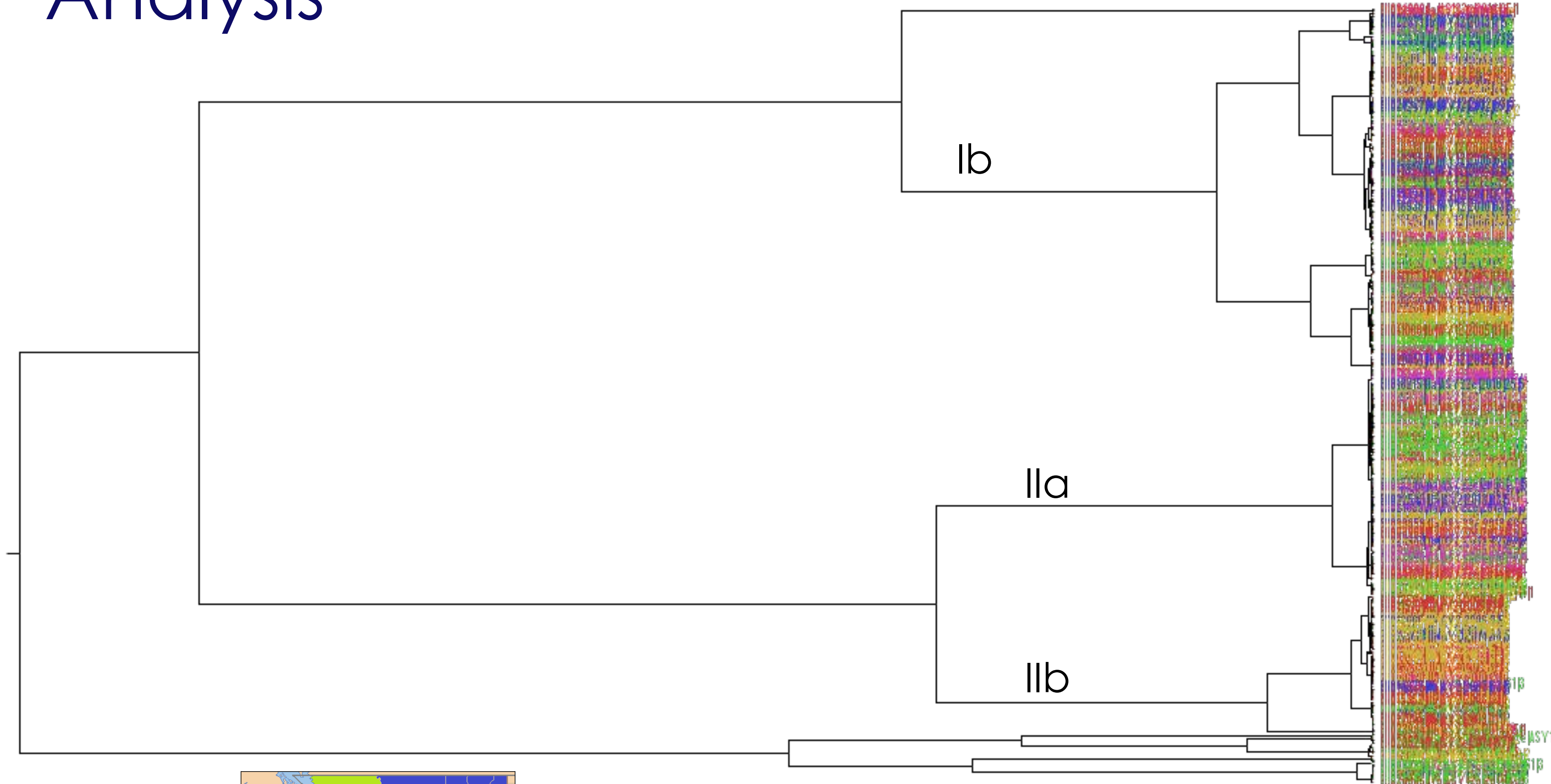


# Study Setting & Design

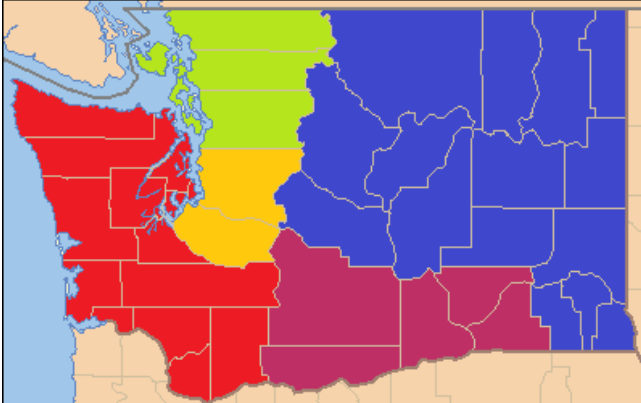
- Washington State
  - 71,362 mi<sup>2</sup> or 184,827 km<sup>2</sup>
  - Population 7.1 million
  - Rural: 96% area, 16% population
- 1,160 *E. coli* O157 cases
  - Culture-confirmed
  - Reported to public health jurisdictions
  - 2005-2014
- Home address geocoded to census block group
  - 4,783 block groups in Washington
  - Each with ~1,500 people



# Phylogeographic Discrete Trait Analysis



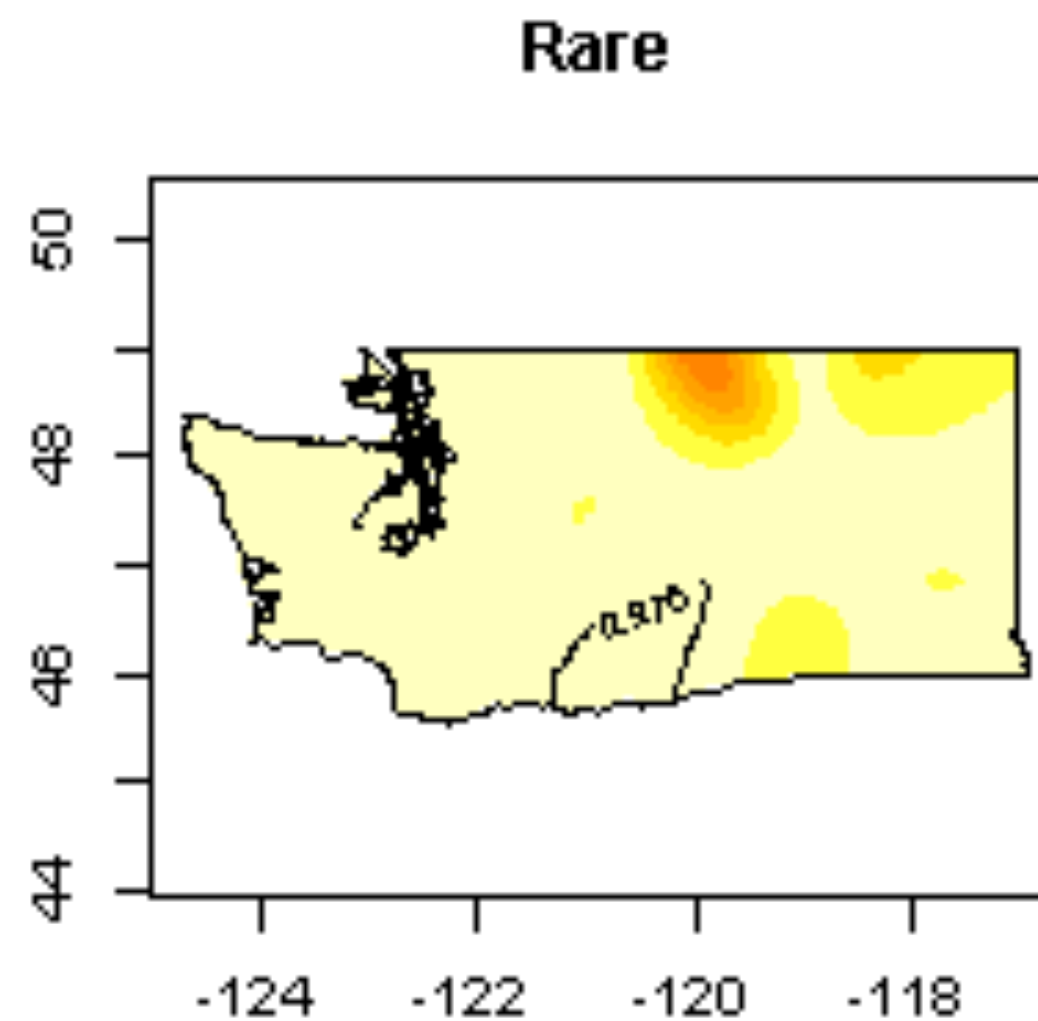
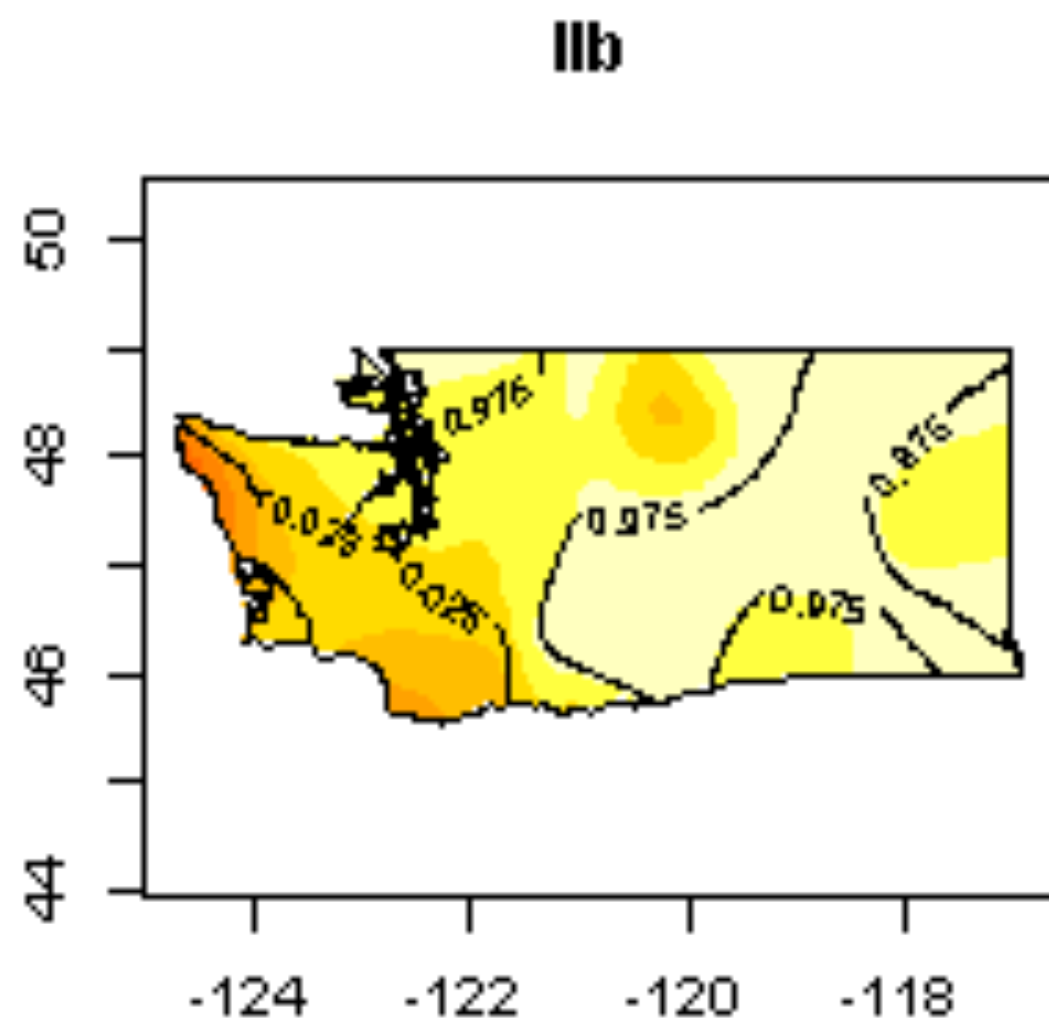
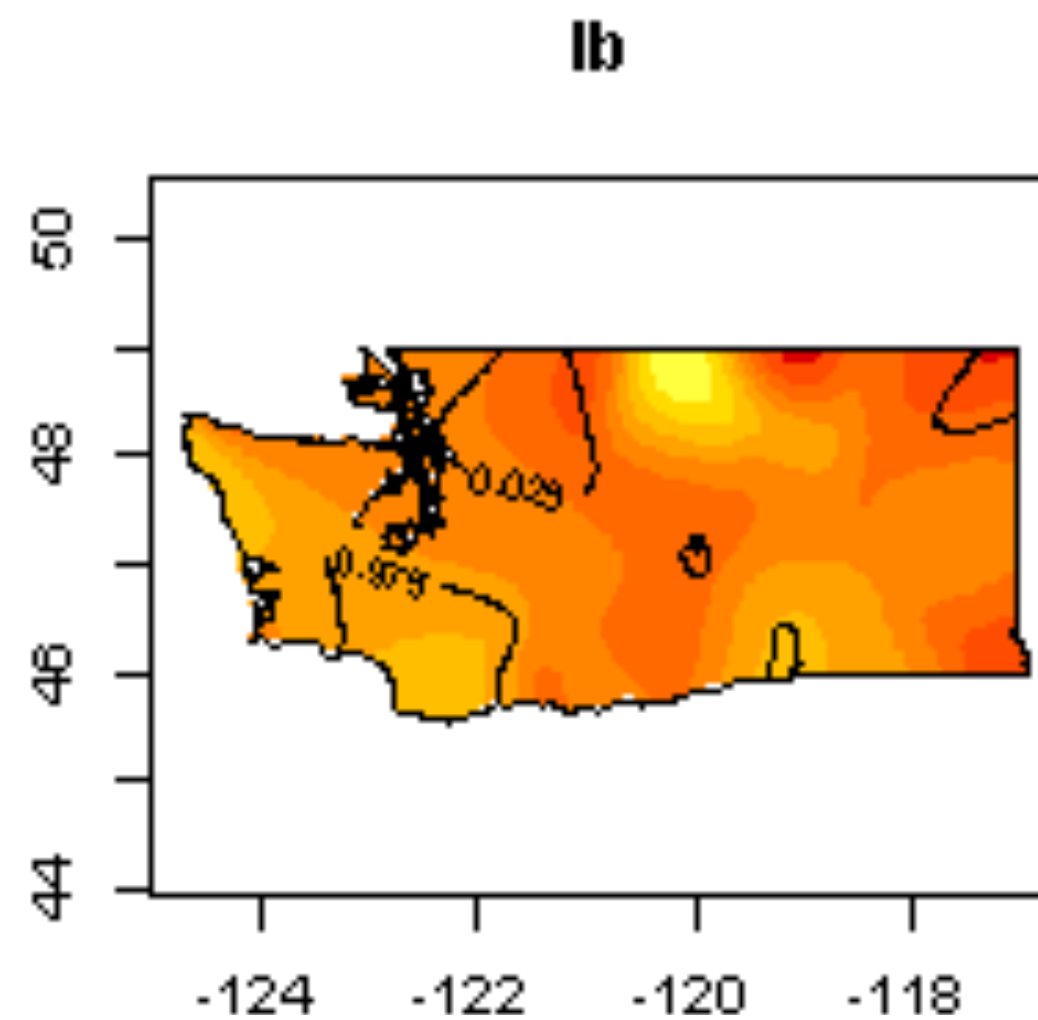
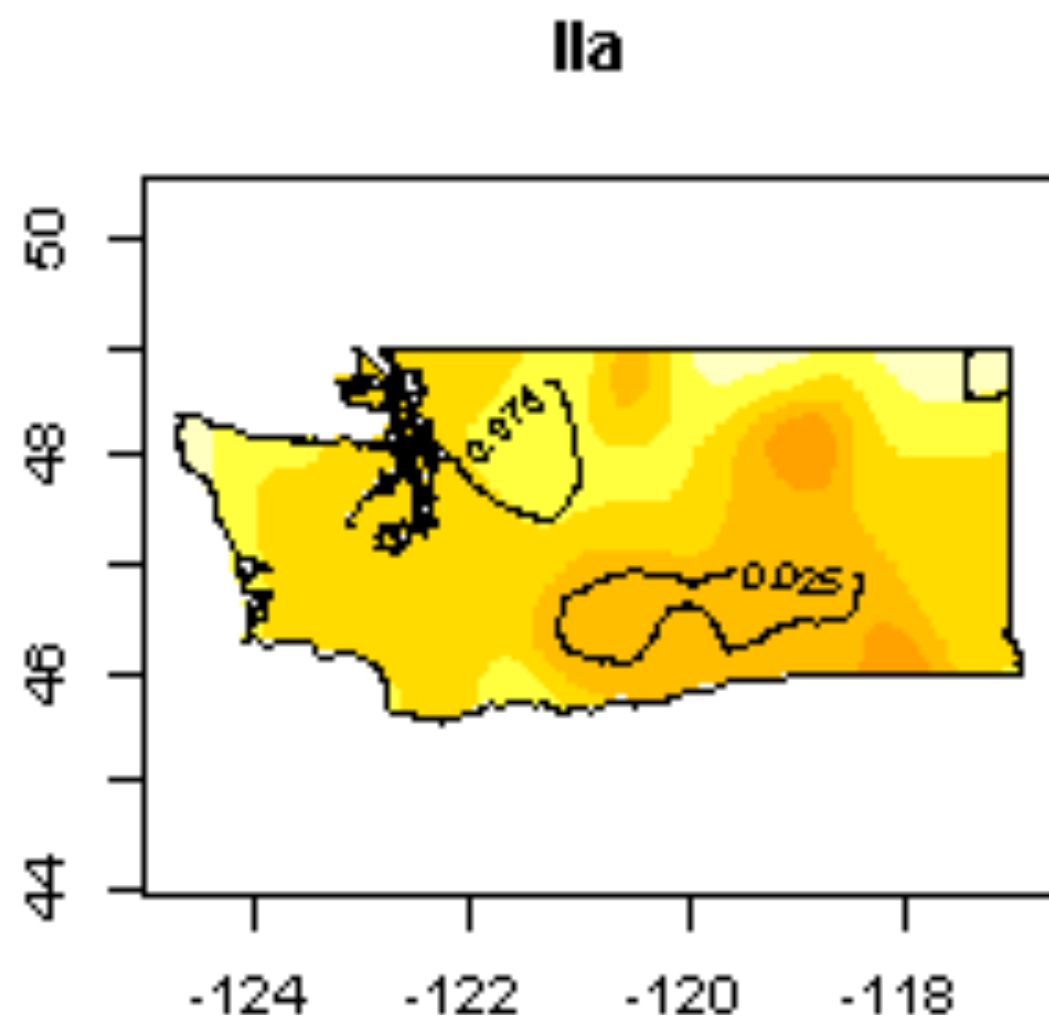
n=477



700.0



# *E. Coli* O157 Infections are Spatially Segregated by Phylogenetic Lineage



Kernel estimation:  
 $p = 0.001$

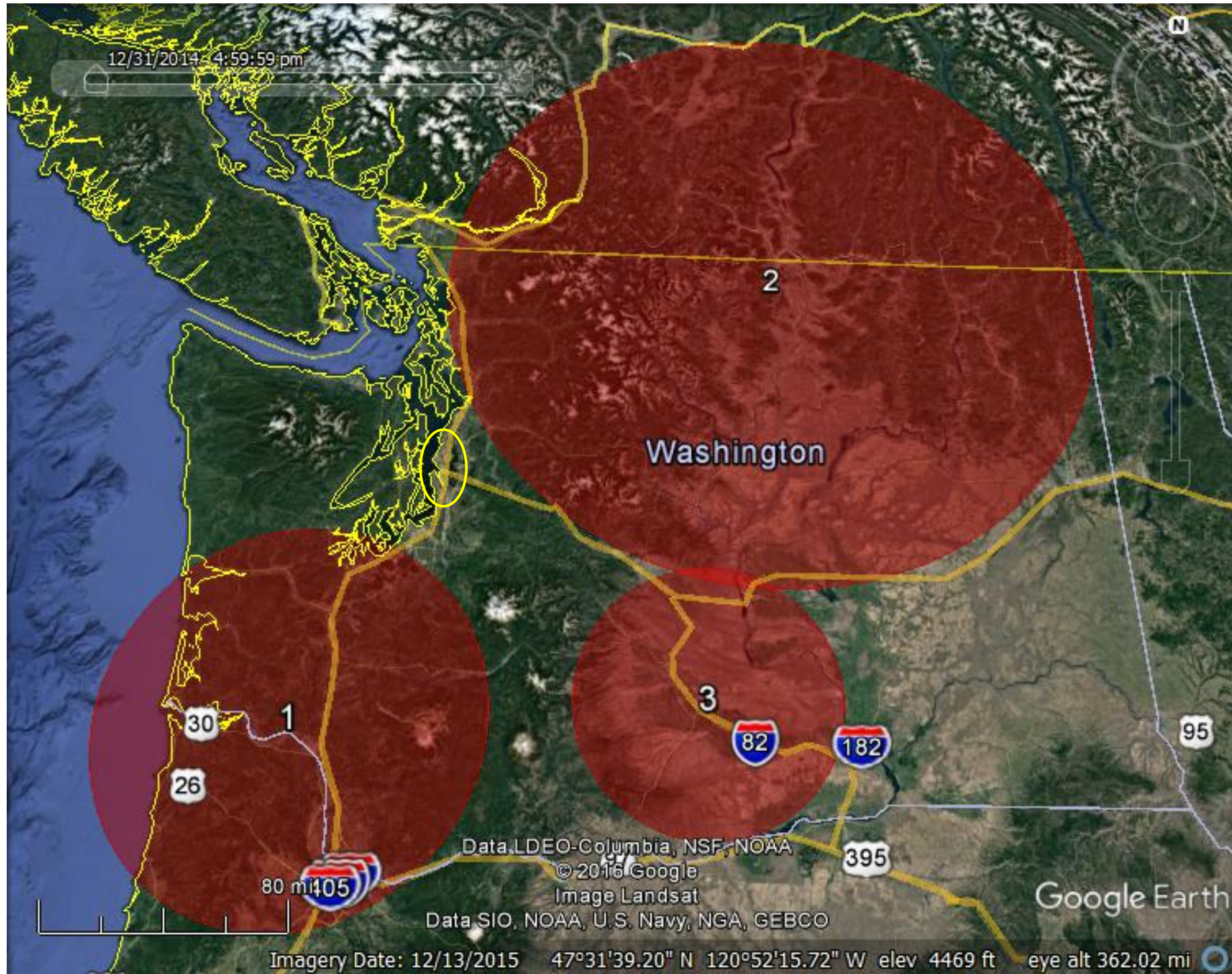
Nearest-neighbor:  
 $p < 0.001$

Multinomial GAM:  
IIa  $p = 0.127$   
IIb  $p < 0.001$   
Rare  $p = 0.691$





# Clusters Echo Segregation Pattern



CLUSTER 1  
203 cases,  $p = 0.001$   
Relative risk (RR):  
*Ib* 0.66, *Ila* 0.94,  
***Ilb* 2.59**, Rare 0.80

CLUSTER 2  
185 cases,  $p = 0.001$   
RR: ***Ib* 1.37**, *Ila* 0.65,  
*Ilb* 0.29, Rare 1.88

CLUSTER 3  
79 cases,  $p = 0.006$   
RR: *Ib* 1.14, ***Ila* 1.70**,  
*Ilb* 0.13, Rare 0

$n=1,111$





# Conclusions & Further Work

- The segregation of reported cases by phylogenetic lineage suggests that there are important local drivers of STEC O157 infection
  - Lineage IIb is spatially segregated in the southwest corner of the state, with some potential segregation of Ib and IIa in particular areas
  - The main animal-production centers are dominated by lineages Ib and IIa, with little IIb
  - Lineage IIb shows other differences, as well: age distribution, secondary attack rate, virulence
- Potential hypotheses need further exploration
  - Specific bacterial lineages may have taken hold in particular areas (“phylogenomic founder effect”)
  - Or specific lineages could be associated with different risk factors
- WGS could provide greater phylogenetic resolution and more precise environmental risk assessment



Extra Slides





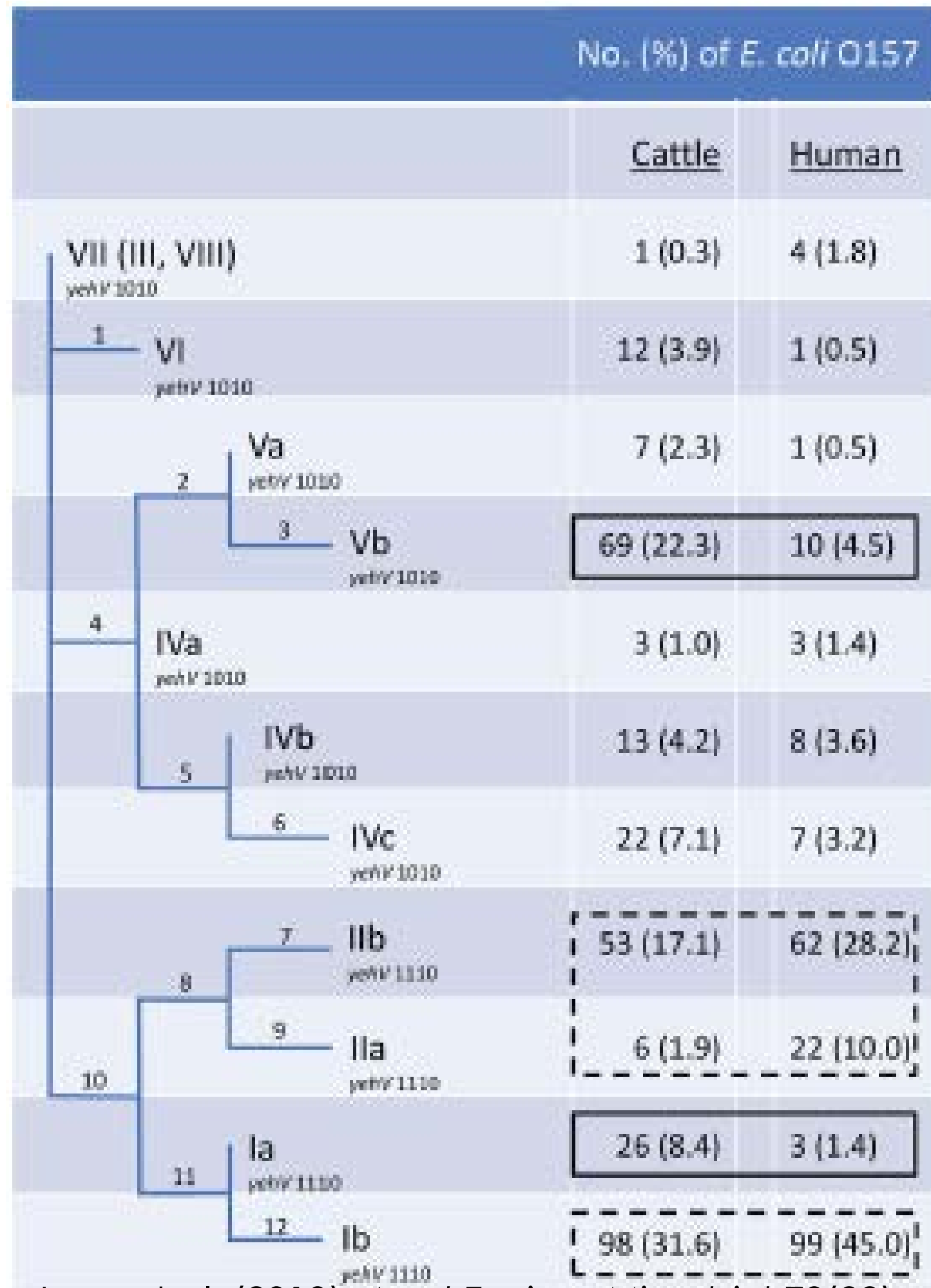
# *E. coli* O157:H7



- Gram-negative bacteria
- One of the Shiga toxin-producing *E. coli* (STEC)
- Produces gastrointestinal illness
  - Severe abdominal pain, bloody diarrhea
- Causes hemolytic uremic syndrome (HUS) in 6-10% of cases
  - Can result in kidney failure and death (CF: 3-5%)
- Global STEC annual burden: 2.8 million (Majowicz et al. *Foodborne Pathog Dis*, 2014)
  - STEC O157 : ~350,000
- ~40% of reported cases in children <10yo
  - HUS incidence in this age group is ~15%



# Phylogenetic Lineages



Jung et al. (2013). *Appl Environ Microbiol* 79(22): 7036-7041.

- Established 48-plex SNP assay used to assign lineage/lineage group:
  - Ib
  - IIa
  - IIb
  - Rare
- 1,121 isolates assigned a lineage





# Spatial Segregation

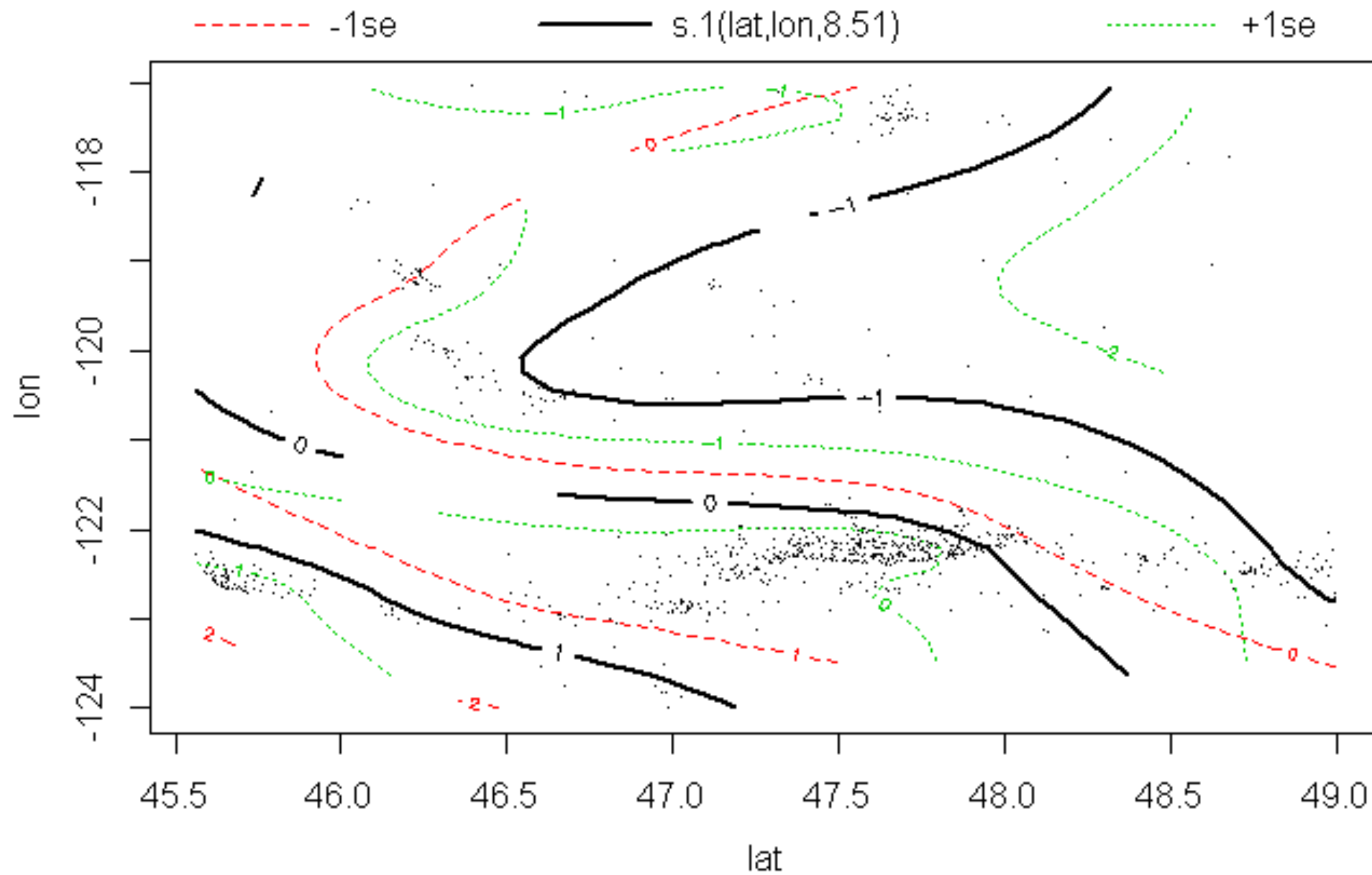
Are there geographic areas in which lineages of a given type are more likely to be found together than in the proportions expected based on the statewide distribution of lineages?

## *Analytic Methods*

- Tests of spatial segregation:
  - Kernel estimation method (Diggle et al. 2005)
  - Nearest-neighbor contingency table method (Dixon 2002)
- Model of the risk surface:
  - Multinomial general additive model (GAM)
- Segregated cluster identification:
  - Multinomial spatial scan statistics (Jung et al. 2008)



# Risk Surface



Multinomial  
GAM:  
*Ila*  $p = 0.127$   
*Ilb*  $p < 0.001$   
*Rare*  $p = 0.691$

