Regional distribution of *Escherichia coli* antibiotic resistance among outpatients in Washington state, 2013-2019

Hannah Fenelon[1], Stephen E. Hawes[1], Hema Kapoor[2], Ann Salm[2], Jeff Radcliff[2], Peter Rabinowitz[1]

[1]University of Washington, Seattle, WA; [2]Quest Diagnostics, Secaucus, NJ

Contact information:
Hannah Fenelon; hfenelon@uw.edu

Introduction

- *E. coli* is one of the most common bacterial infections in the United States and costs an estimated $5 billion in direct and indirect costs annually[1].
- Antibiotic resistance in *E. coli* is increasing and UTIs caused by antibiotic resistant *E. coli* cause significant disease burden.
- Potential drivers of resistance include clinical prescribing practices and use of antibiotics in agriculture.
- Geographic variation in resistance of *E. coli* in the outpatient setting is poorly understood.

Methods

Data

- Quest Diagnostics outpatient urinary *E. coli* isolates from Washington state from 2013-2019.
- The first isolate from each unique individual was included in the analysis and a complete case analysis for each antibiotic was done.

Methods

- Exposure: nine Public Health Emergency Preparedness Regions (PHEPRs) of Washington state (Figure 1).
    - Central region was selected as the reference group because it had the most isolates and contains Seattle.
- Outcome: antibiotic susceptibility, as determined by the Clinical and Laboratory Standards Institute (CLSI)[2], was binarized to susceptible (susceptible) or non-susceptible (resistant or intermediate) for 5 antibiotics:
    - ampicillin (AMP)
    - ciprofloxacin (CIP)
    - ceftriaxone (CRO)*
    - gentamicin (GEN)
    - trimethoprim / sulfamethaxazole (SXT)
- Logistic regression with robust standard errors was performed with the PHEPRs and adjusted for year of collection, sex at birth, and age group to get prevalence odds ratios (PORs).
- *CLSI CRO breakpoints changed

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Figure 1: Map of Washington state with the nine PHEPRs outlined

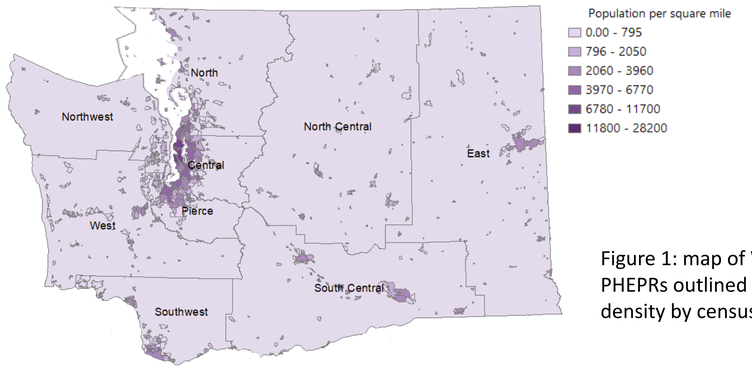

Figure 1: map of Washington with the PHEPRs outlined and the population density by census populated areas[3,4].

Table 1: Regression results for antibiotic non-susceptibility of five antibiotics

Antibiotic		Ampicillin (n=40,042)	Ciprofloxacin (n=40,214)	Ceftriaxone (n=40,017)	Gentamicin (n=40,217)	Trimethoprim / sulfamethaxazole (n=40,170)
Crude non-susceptibility proportion		0.37	0.10	0.03	0.05	0.18
	n (%)	Prevalence Odds Ratio (95% Confidence Interval)				
PHEPR						
Central	8097 (20.1)	*Ref.*	*Ref.*	*Ref.*	*Ref.*	*Ref.*
East	2783 (6.9)	0.89 (0.81-0.98)	0.73 (0.62-0.85)	0.46 (0.35-0.60)	0.71 (0.57-0.88)	0.67 (0.59-0.75)
North	7451 (18.5)	0.82 (0.76-0.88)	0.81 (0.72-0.90)	0.61 (0.51-0.72)	0.83 (0.72-0.97)	0.76 (0.70-0.83)
North Central	474 (1.2)	0.78 (0.64-0.95)	0.64 (0.46-0.90)	0.20 (0.06-0.63)	**0.86 (0.56-0.1.31)**	0.76 (0.59-0.97)
Northwest	1300 (3.2)	0.79 (0.70-0.90)	0.70 (0.57-0.86)	0.42 (0.26-0.65)	0.70 (0.53-0.93)	0.57 (0.48-0.67)
Pierce	5962 (14.8)	0.84 (0.78-0.90)	0.78 (0.70-0.87)	0.65 (0.53-0.78)	0.69 (0.59-0.81)	0.70 (0.64-0.76)
South Central	1189 (3.0)	0.88 (0.77-1.00)⊥	0.80 (0.65-0.99)	**0.78 (0.57-1.08)**	**0.98 (0.75-1.28)**	0.84 (0.72-0.99)
Southwest	7857 (19.5)	0.79 (0.74-0.84)	0.67 (0.60-0.75)	0.57 (0.48-0.68)	0.66 (0.57-0.77)	0.66 (0.61-0.72)
West	5104 (12.7)	0.84 (0.78-0.91)	0.73 (0.65-0.82)	0.61 (0.49-0.75)	0.75 (0.64-0.89)	0.70 (0.64-0.76)
Year of collection						
2013	4271 (10.6)	*Ref.*	*Ref.*	*Ref.*	*Ref.*	*Ref.*
2014	3499 (8.7)	**1.02 (0.93-1.12)**	**0.93 (0.80-1.08)**	**1.11 (0.63-1.94)**	**1.19 (0.96-1.47)**	**1.00 (0.91-1.11)**
2015	4086 (10.2)	1.17 (1.06-1.28)	**1.12 (0.97-1.29)**	5.37 (3.52-8.18)	**1.20 (0.98-1.48)**	**1.04 (0.95-1.14)**
2016	4313 (10.7)	1.15 (1.05-1.26)	**1.07 (0.93-1.24)**	6.48 (4.28-9.80)	**1.18 (0.97-1.43)**	**1.08 (0.99-1.19)**
2017	7656 (19.0)	1.14 (1.05-1.24)	**1.08 (0.95-1.23)**	6.60 (4.40-9.89)	**1.13 (0.94-1.37)**	**1.02 (0.94-1.11)**
2018	7563 (18.8)	1.12 (1.03-1.21)	**1.03 (0.90-1.17)**	7.20 (4.81-10.78)	**1.18 (0.98-1.43)**	**1.05 (0.96-1.14)**
2019	8829 (22.0)	1.15 (1.06-1.25)	**1.01 (0.89-1.15)**	7.36 (4.93-10.97)	**1.18 (0.98-1.42)**	1.09 (1.01-1.19)
Sex						
Female	37628 (93.6)	*Ref.*	*Ref.*	*Ref.*	*Ref.*	*Ref.*
Male	2589 (6.4)	0.92 (0.87-0.97)	1.39 (1.24-1.56)	1.73 (1.44-2.08)	1.29 (1.09-1.52)	**1.06 (0.95-1.17)**
Age Group (years)						
19-50	18326 (44.8)	*Ref.*	*Ref.*	*Ref.*	*Ref.*	*Ref.*
0-18	3781 (9.3)	**0.96 (0.89-1.04)**	0.62 (0.53-0.72)	0.74 (0.57-0.94)	**0.85 (0.71-1.02)**	**0.94 (0.85-1.03)**
>50	18110 (44.3)	0.93 (0.89-0.97)	1.59 (1.49-1.71)	1.47 (1.31-1.66)	1.15 (1.04-1.26)	0.91 (0.87-0.97)

⊥ This confidence interval does not include 1.00 but due to rounding 1.00 is the upper limit for the table. Bold indicates the POR is not significant at the alpha = 0.05 level.

Results

- The analysis included 40,217 isolates.
- More than 50% of isolates were from three regions: Central, North, and Pierce.
- Overall, non-susceptibility for each antibiotic varied greatly, ranging from 3.2% for ceftriaxone to 37.0% for ampicillin.
- There were significant differences in non-susceptibility by region for all antibiotics, controlling for year of isolate collection, sex, and age.
    - Ceftriaxone saw the largest differences in non-susceptibility compared to the Central region.
    - Ampicillin saw the smallest differences in non-susceptibility compared to the Central region.
- Adjusted PORs for antibiotic non-susceptibility for ampicillin, ciprofloxacin and trimethoprim-sulfa were consistently 10%-35% lower odds compared to the Central region, all but one of which are significantly different.
- Adjusted POR for non-susceptibility was higher for males than females for AMP, CIP, CRO, and GEN.
- Higher adjusted POR of non-susceptibility for ceftriaxone for recent years (2015-2019) compared to 2013.
- There was increasing non-susceptibility with age for CIP and CRO.

Conclusions

- The highest rates of non-susceptibility were found in regions with more urban areas, suggesting a link between factors associated with urbanization and non-susceptibility.
- Due to significant geographic variation in non-susceptibility, efforts in antimicrobial stewardship in the outpatient setting should rely on local resistance patterns, using tools such as local antibiograms.

References

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