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Ella M. Meumann
Royal Melbourne Hospital, ella.meumann@gmail.com

Brett G. Mitchell
Avondale College of Higher Education, brett.mitchell@avondale.edu.au

Louise Cooley
Royal Hobart Hospital, louise.cooley@dhhs.tas.gov.au

Alistair McGregor
Department of Health and Human Services TAS, alistair.mcgregor@dhhs.tas.gov.au

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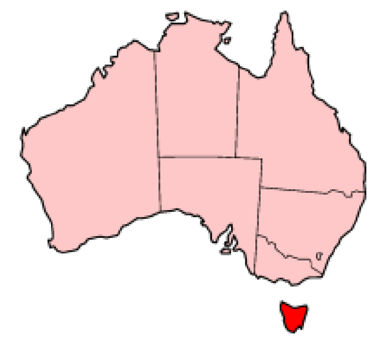
Urinary *Escherichia coli* susceptibility profiles and their association with community antibiotic use in Tasmania, Australia

Ella Meumann[a,c], Brett Mitchell[b], Alistair McGregor[a], Emma McBryde[c], Louise Cooley[a]

[a]*Department of Infectious Diseases & Microbiology, Royal Hobart Hospital, Hobart, Australia;* [b]*Avondale College of Higher Education, Cooranbong, Australia;* [c]*Victorian Infectious Diseases Service, Royal Melbourne Hospital, Melbourne, Australia*



Introduction

- Bacterial resistance to antibiotics is increasing, but varies greatly in different geographical locations.
- Antimicrobial use is considered the major factor driving this increase.
- This study aims to assess urinary *Escherichia coli* susceptibility patterns in the Australian island-state of Tasmania, and explore their relationship with community antibiotic use.

Methods

- The susceptibility profiles of all urinary *E. coli* isolates between January 2010 and December 2012 in Tasmania were included; this was a population-based study.
- Susceptibility testing had been done using disc diffusion with CDS methodology[1], with the exception of 2011 & 2012 isolates from one laboratory, which were tested using EUCAST methodology[2].
- Isolates were classified as either "susceptible" or "not susceptible" (intermediate or resistant) to each antibiotic tested.
- Only the 1st isolate from each patient, each year was included in the analyses for geographical and temporal differences.
- The number of PBS-subsidised prescriptions for amoxycillin, amoxycillin-clavulanate and cephalexin in Tasmania each month was downloaded from the PBS website[3], and converted to defined daily doses (DDDs) per 1,000 population per day[4,5]. This represents antibiotic use by concession card holders.

Table 2. Logistic regression models* assessing season and lag in resistance after antimicrobial use.

	Odds Ratio	Confidence Interval
Outcome: Amoxycillin resistance		
Season (peak July)	1.17	1.09-1.26
Amoxycillin use, 2-month lag	1.12	1.06-1.17
Outcome: Amoxycillin-clavulanate resistance		
Amoxcycillin-clavulanate use, 2-month lag	1.26	1.04-1.52
Amoxcycillin-clavulanate use, 3-month lag	1.17	0.97-1.40
Outcome: Cephalexin resistance		
Season (peak July)	1.17	0.99-1.38

***Methods for Logistic Regression**

- Season was transformed from month of year (1 to 12), into a sine wave taking on values between -1 and +1, with the peak in July and nadir in January to represent anticipated increased risk associated with winter months.
- The number of isolates not susceptible each month was assumed to have a binomial distribution determined by the proportion resistant and the number of isolates collected for the month.
- The outcome variable was the proportion of isolates not susceptible to the antimicrobial each month.
- Predictors assessed included time, season, antimicrobial use (DDDs per 1,000 population per day) in the same month, and antimicrobial use 1, 2 and 3 months prior.
- Univariate and multivariate logistic regression models were created. Only predictors with P≤0.1 were included in the final model.

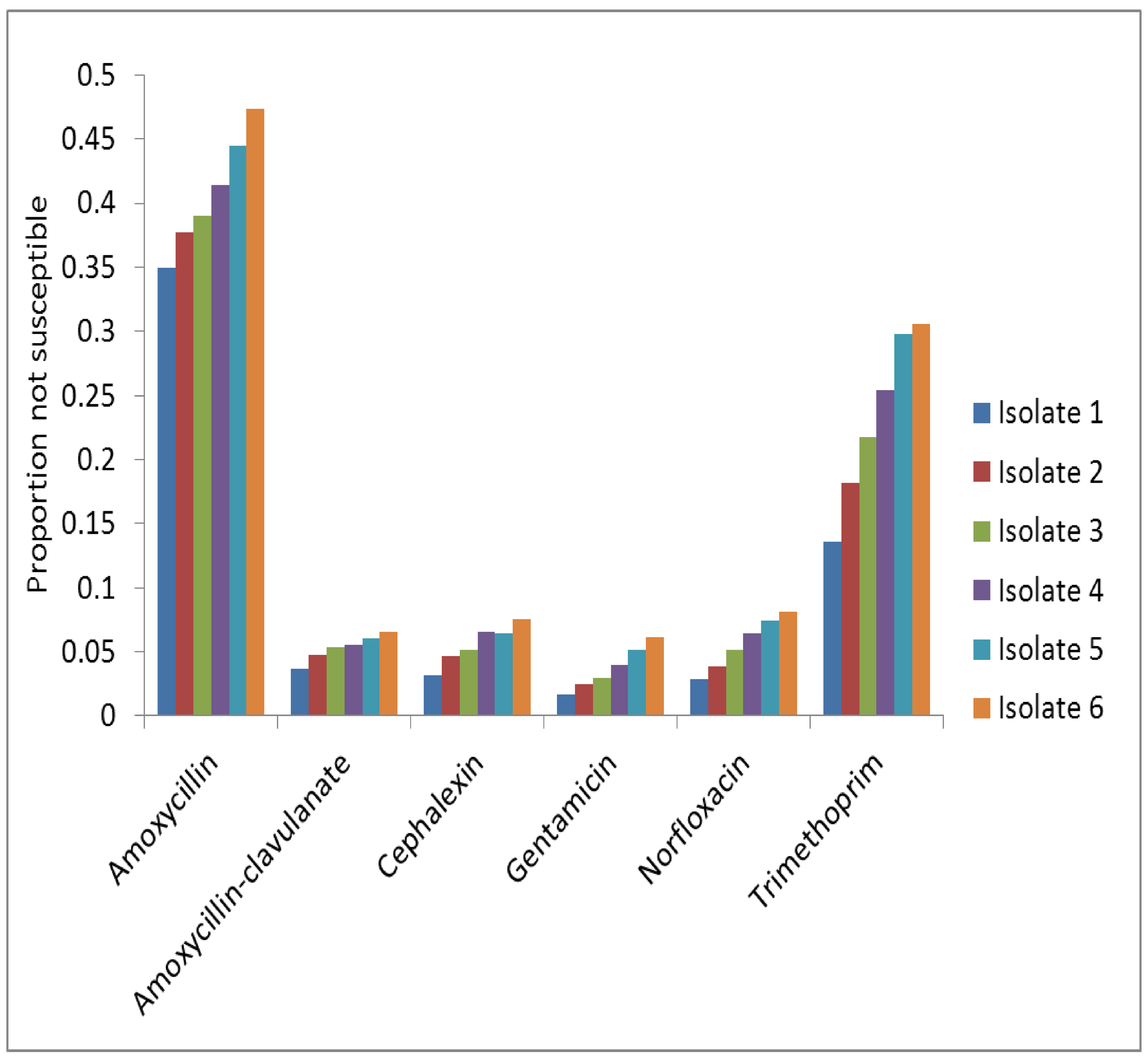


Figure 2. Antimicrobial resistance in recurrent *E. coli* isolates.

Table 1. Suseptibility profile of urinary *E. coli* isolates in Tasmania.

Antibiotic	Proportion Not Susceptible			P-Value
	South	North	Northwest	
Amoxycillin	35.7%	33.8%	35.6%	<0.01
Amoxycillin-clavulanate	4.6%	3.6%	2.2%	<0.01
Cephalexin	3.6%	3.4%	2.7%	0.01
Gentamicin	1.9%	1.9%	1.4%	0.03
Norfloxacin	4.0%	2.4%	1.7%	<0.01
Trimethoprim	14.7 %	13.5%	14.2%	0.03

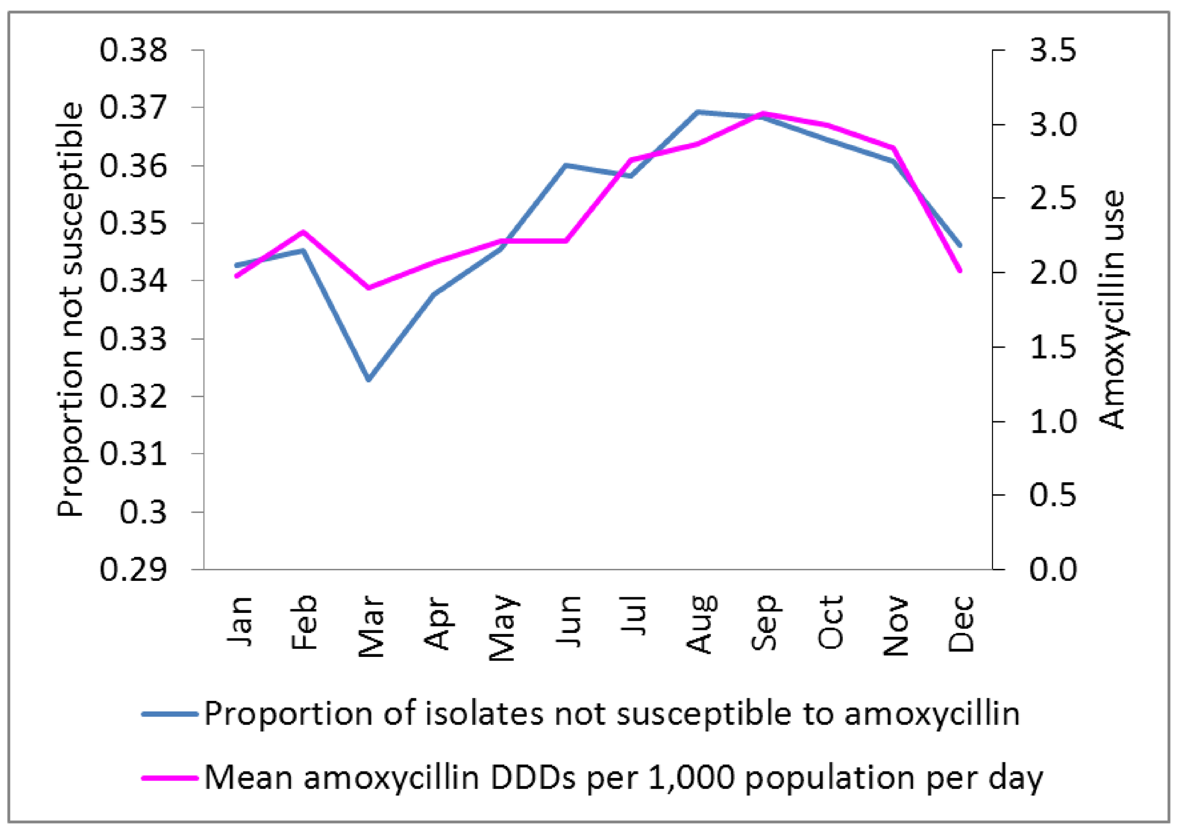


Figure 1. Amoxycillin use and *E. coli* resistance to amoxycillin.

Results

- There were 42,691 isolates included in total; 32,920 isolates were included in the analyses for geographical and temporal differences.

Geographical differences

- Antimicrobial resistance levels were low and regional differences were small, although resistance to amoxycillin-clavulanate, cephalexin and norfloxacin was greater in the South than the North and Northwest of Tasmania (Table 1).

Temporal changes

- The proportion of *E. coli* isolates not susceptible to amoxycillin-clavulanate increased from 3.4% in 2010 to 4.2% in 2012 (P=0.01), but there was no increase in resistance to other antibiotics detected when analysed using linear regression.
- There was an increase in the proportion of *E. coli* isolates not susceptible to amoxycillin from 34.2% during Summer/Autumn to 36.1% during Winter/Spring (P<0.01) (Figure 1).
- Amoxycillin use increased from 2.07 DDDs per 1,000 population per day in Summer/Autumn to 2.79 in Winter/Spring (P<0.01)(Figure 1).
- The results of logistic regression models further evaluating the effect of season and lag in resistance after antibiotic use are shown in Table 2.

Recurrent isolates

- 7,653 patients had *E. coli* isolated on multiple occasions during the study.
- The proportion of *E. coli* isolates not susceptible to each antimicrobial tested increased with each episode (Figure 2).

Conclusions

- *E. coli* resistance to antimicrobials is lower in Tasmania than reported elsewhere in Australia, which may be due to Tasmania's isolated geographical location.
- There was no increase in antibiotic resistance detected during this 3-year study, with the exception of minimal increase in amoxycillin-clavulanate resistance.
- An increase in amoxycillin use and resistance was identified during winter and spring, which may be due to treatment of respiratory tract infections.
- Increased resistance to amoxycillin and amoxycillin-clavulanate was seen following a 2-month lag after increased use of each of these antimicrobials.
- The increase in antimicrobial resistance in recurrent isolates is likely to be a result of antimicrobial treatment in patients with recurrent urinary tract infection.

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