Contribution of socio-economic factors in the spread of antimicrobial resistant infections in Australian primary healthcare clinics

Teresa M. Wozniak [a,b,*], Will Cuningham [b], Katie Ledingham [c], Karen McCulloch [d,e]

[a] Australian e-Health Research Centre CSIRO, Brisbane, Queensland, Australia
[b] Menzies School of Health Research, Charles Darwin University, Darwin, Northern Territory, Australia
[c] Department of Science, Innovation, Technology and Entrepreneurship, University of Exeter Business School, Exeter, United Kingdom
[d] Department of Infectious Diseases, Melbourne Medical School, University of Melbourne at the Peter Doherty Institute for Infection and Immunity, Melbourne, Victoria, Australia
[e] WHO Collaborating Centre for Viral Hepatitis, Victorian Infectious Diseases Reference Laboratory, Royal Melbourne Hospital at the Peter Doherty Institute for Infection and Immunity, Melbourne, Victoria, Australia

A R T I C L E   I N F O

A B S T R A C T

Objectives: To effectively contain antimicrobial-resistant (AMR) infections, we must better understand the social determinates of health that contribute to transmission and spread of infections.

Methods: We used clinical data from patients attending primary healthcare clinics across three jurisdictions of Australia (2007–2019). *Escherichia coli (E. coli)*, *Klebsiella pneumoniae (K. pneumoniae)*, *Pseudomonas aeruginosa* (*P. aeruginosa*) and *Staphylococcus aureus (S. aureus)* isolates and their corresponding antibiotic susceptibilities were included. Using multivariable logistic regression analysis, we assessed associations between AMR prevalence and indices of social disadvantage as reported by the Australian Bureau of Statistics (i.e., remoteness, socio-economic disadvantage and average person per household).

Results: This study reports 12 years of longitudinal data from 43 448 isolates from a high-burden low-resource setting in Australia. Access to health and social services (as measured by remoteness index) was a risk factor for increased prevalence of third-generation cephalosporin-resistant (3GC) *E. coli* (odds ratio 5.05; 95% confidence interval 3.19, 8.04) and methicillin-resistant *S. aureus* (MRSA) (odds ratio 5.72; 95% confidence interval 5.02, 6.54). We did not find a positive correlation of AMR and socio-economic disadvantage or average person per household indices.

Conclusion: Remoteness is a risk factor for increased prevalence of 3GC-resistant *E. coli* and MRSA. We demonstrate that traditional disease surveillance systems can be repurposed to capture the broader social drivers of AMR. Access to pathogen-specific and social data early and within the local regional context will fill a significant gap in disease prevention and the global spread of AMR.

1. Introduction

The COVID-19 pandemic demonstrates that inequalities in health are profound and that social determinants of health unequally affect morbidity and mortality in affected patients [1,2]. In the midst of this pandemic, the threat of antimicrobial resistance (AMR) is worsening [3,4]. Each year an estimated 5 million people die with an antimicrobial resistant (AMR) infection, a number greater than the number of deaths from HIV/AIDS and malaria combined [5]. Without effective action, antibiotics may become 'only a fact of historic interest' [6].

Like COVID-19 and other infectious diseases [7–11], AMR disproportionately affects people who live in areas of poverty and overcrowding and who are economically or socially underprivileged [12–14]. In Australia, this is reflected by a high prevalence of infectious diseases amongst people living in regional and remote areas, compared with major cities [15]. Despite a high overall health status of many Australians, people living in regional and remote areas continue to experience comparatively poor health outcomes [16], have high rates of AMR [17] and experience persistent social inequalities [18].

* Corresponding author: Australian e-Health Research Centre (AEHRC), Level 7, 296 Herston Road, Herston 4029 Brisbane, Queensland, Australia.
E-mail address: teresa.wozniak@csiro.au (T.M. Wozniak).

Antibiotic resistance refers to the ability of bacteria to change in ways that render antibiotics ineffective against infections. While global efforts to reduce antibiotic consumption are essential in preserving the limited therapeutic options, it is hypothesized that reduction of antibiotic consumption will not be sufficient to control AMR because of contagion—the spread of resistant strains and genes [14]. Contagion is facilitated by poor sanitation, limited access to clean water and inadequate healthcare expenditure [14]. In Australia, the observed reduction of antibiotic use for some infections [19] and exceedingly high rates of community-acquired AMR in remote settings [20] supports this hypothesis. Unpacking the social determinants of health that contribute to transmission and spread of AMR is necessary to more effectively support treatment of patients and to mitigate risks of further spread. Co-design with community and collaboration with diverse sectors (e.g., health, housing) are core to containment of AMR, as is working with diverse kinds of information systems, which must include disease surveillance platforms. Similar to current efforts to monitor antibiotic use [21,22] alongside AMR prevalence as an identified risk factor for infection, data on socio-economic drivers should be routinely collected and reported to reduce the health burden.

Drawing on data from a resource-poor and remote setting within a high-income country, we argue that remoteness is contributing to the spread of AMR. Specifically, this work contributes to a more nuanced picture of the complexity of AMR inequality and raises important implications for global AMR research and surveillance practices.

2. Material and Methods

2.1. Study setting

This study was set within rural and remote northern tropical Australia, defined as the area north of the Tropic of Capricorn, which includes three separate jurisdictions: far north-western Australia, Northern Territory and far north Queensland. The Australian Bureau of Statistics (ABS) boundaries were categorized as Statistical Area Level 3 (SA3), with populations of 30 000 to 130 000 people [23]. We used data from the recently established HOTspots surveillance system, hereafter referred to as *HOTspots*. HOTspots is a laboratory-based geospatial surveillance system that collates antibiotic susceptibility data for critical pathogens across northern Australia [17].

2.2. Bacterial isolates

Bloodstream, urinary tract, respiratory and skin and soft tissue specimens were collected from patients attending primary healthcare clinics. All clinical isolates of *Escherichia coli (E. coli)*, *Klebsiella pneumoniae (K. pneumoniae)*, *Pseudomonas aeruginosa* (*P. aeruginosa*) and *Staphylococcus aureus (S. aureus)* and their corresponding antibiotic susceptibilities were analysed between 1 January 2007 and 31 December 2019. There were four groups of resistant organisms analysed, which include third-generation cephalosporin (3GC)-resistant *E. coli*; 3GC-resistant *K. pneumoniae*; ceftazidime-resistant *P. aeruginosa*; and methicillin-resistant *S. aureus* (MRSA).

2.3. Identification and susceptibility tests

Two widely used international susceptibility method systems, Clinical and Laboratory Standards Institute (CLSI) and European Committee on Antimicrobial Susceptibility Testing (EUCAST), were used by the participating laboratories. Susceptibility results were determined by VITEK 2 (bioMerieux, France). Data from Western Australia and Northern Territory were provided with CLSI-interpreted values (Susceptible, Intermediate and Resistant) using

2017 CLSI M100-S27 Performance Standards for Antimicrobial Susceptibility Testing (27th Edition). Data from Queensland were provided with CLSI-interpreted values (Susceptible, Intermediate and Resistant) for years 2008 to 2012, and 2019 EUCAST interpreted values for the years 2012 onwards. Participating pathologies are all accredited under regularly audited national testing guidelines and the National Quality Assurance and Quality Control program. Data were restricted to the first bacterial isolate per patient per year and categorized as 'resistant' or 'susceptible'. Additional clinical information was not available. Participating pathologies infer 3GC resistance from resistance to ceftazidime and/or ceftriaxone and methicillin resistance in *S. aureus* from resistance to oxacillin in laboratories in the Western Australia, cefoxitin in Northern Territory laboratories and flucloxacillin and cefoxitin in Queensland laboratories.

2.4. Antibiotic prescribing

Data from the National Antimicrobial Utilisation Surveillance Program [24] were used to investigate the correlation between antibiotic use and the rate of resistant isolates in hospital. NAUSP collects data from over 220 major Australian public and private hospitals and provides a standardized measurement of antimicrobial use as per World Health Organization defined daily doses (DDDs) per 1000 occupied bed days (OBDs) [25]. We used total hospital antimicrobial utilization rates measured as DDD consumed each month per 1000 OBD for 3GC within one region of our study setting (Northern Territory). We calculated a correlation coefficient between the rate of 3GC-resistant *E. coli* in blood isolates and the rate of 3GC usage.

2.5. Socio-economic risk factors

We used the socio-economic indexes from ABS that rank areas in Australia according to relative socio-economic advantage and disadvantage. The indexes are based on information from the five-yearly ABS census data and include 'Remoteness index', 'Index of relative socioeconomic disadvantage' and 'Average number of persons per household'.

2.5.1. Remoteness index
Remoteness index is a categorical variable that measures access to services (including health and social services) as measured by the Australian Statistical Geography Standards. It is classified into five categories: (1) major cities, (2) inner regional, (3) outer regional, (4) remote and (5) very remote [16].

2.5.2. Index of relative socioeconomic disadvantage
Index of relative socioeconomic disadvantage is a numerical variable that indicates relative disadvantage and compiles the percentage of people in low-income households; the percentage of occupied dwellings without Internet connection; the percentage of families with children under 15 years of age with unemployed parents; and the rate of unemployment. Index of relative socioeconomic disadvantage ranks areas on a continuum from most disadvantaged (Category 1) to least disadvantaged (Category 10) [26].

Low index score	High index score
Most disadvantaged	Most advantaged

2.5.3. Average person per household
Average person per household is an estimate of the number of persons per household within a region derived from ABS census data [26]. The average number of persons per household and the population density of each region were included to provide a high-level indication of overcrowding and its effect on AMR prevalence.

Table 1
AMR in primary healthcare, northern Australia, 2007–2019

Region	Proportion resistant, % (number of susceptibility tests)			
	3GC-resistant *E. coli*	3GC-resistant *K. pneumoniae*	Ceftazidime-resistant *P. aeruginosa*	MRSA
West				
Kimberley	17.00 (300)	7.06 (85)	2.62 (648)	52.16 (7834)
Pilbara	9.20 (174)	2.38 (42)	2.63 (228)	43.88 (2525)
Centre				
Gove	1.37 (73)	0.00 (22)	0.00 (32)	11.31(222)
Darwin	5.14 (389)	1.49 (67)	2.22 (45)	12.33 (521)
Tennant Creek	5.41 (111)	2.08 (48)	0.00 (27)	29.16 (464)
Katherine	0.73 (413)	0.00 (57)	4.92 (61)	20.88 (1297)
Alice Springs	6.08 (148)	0.00 (35)	0.00 (24)	26.63 (338)
East				
Torres and Cape	1.48 (3254)	0.64 (622)	1.08 (558)	27.36 (11993)
Cairns & Hinterland	0.96 (836)	2.11 (95)	1.54 (130)	24.1 (1357)
Northwest	6.33 (221)	2.17 (46)	1.96 (51)	34.32 (373)
Townsville	4.93 (406)	1.89 (53)	1.46 (205)	6.73 (773)

Fig. 2 provides summary measures of socio-economic risk factors for each region of interest.

2.6. Statistical analysis

We merged the HOTspots data set and the ABS data set in RStudio by aligning against the common variable of 'region'. We performed multivariable logistic regression analysis to assess association with individual socio-economic risk factors. The proportion resistant was the dependent variable (i.e., the number of resistant isolates divided by the total number of isolates tested) and the specified social factor the independent variable according to the following formula:

$$\log\left(\frac{y_i}{1 - y_i}\right) = \beta_0 + \beta_i x_i$$

where y_i refers to the proportion of resistant isolates for the ith organism/antibiotic combination listed in Table 1 and denotes the social factor on interest.

A correlation coefficient (r) between all independent variables was derived prior to performing multivariable regression analyses. For strong correlation, defined as absolute |r| > 0.7, the specified independent variable was excluded from multivariable analysis. After exclusion of any variables based on pairwise correlations, the following formula was used for the multivariable analysis:

$$\log\left(\frac{y_i}{1 - y_i}\right) = \beta_0 + \beta_1 x_1 + \beta_2 x_2 + \beta_3 x_3 + \mu_i$$

where y_i refers to the proportion of resistant isolates for the ith organism/antibiotic combination; x_1 = remoteness index, x_2 = index of relative socioeconomic disadvantage and x_3 = average persons per household. $\beta_i's$ represent the coefficients corresponding to each social factor with β_0 being the intercept. An odds ratio (OR) was derived for each independent variable. All analyses were carried out in RStudio [27].

2.7. Ethics

The study was conducted and approved by the Human Research Ethics Committee of the Northern Territory Department of Health and Menzies School of Health Research (HREC-2018-3084) as well as the Queensland Health Public Health Act 2005 (Section 280). All data were analysed in strict compliance with the requirements of the National Statement on Ethical Conduct in Human Research (2007) guidelines.

3. Results

The study reports laboratory data from 43 448 primary healthcare isolates collected over 12 years (2007–2019). This includes samples from blood (n = 1045, 2.4%), urine (n = 13 023, 30.0%), skin and soft tissue (n = 26 776, 61.6%), respiratory (n = 1426, 3.3%) and other sites (n = 1178, 2.7%).

3.1. Antimicrobial resistance patterns

There was geographical variation from west to east in resistant *E. coli*, *K. pneumoniae*, *P. aeruginosa* and *S. aureus* (Fig. 1, Table 1). The highest prevalence amongst the studied AMR pathogens was for MRSA patients (Fig. 1D), and the western part of Australia had consistently high rates of AMR across all four studied pathogens. The prevalence of MRSA ranged from 52% in the west (Kimberley region) to 6.7% in the east (Townsville region of far north Queensland). In the Northern Territory, the prevalence of MRSA ranged from 29.2% (Tennant Creek) to 11.3% (Gove). Rates of 3GC-resistant *E. coli* also demonstrated geographical variation, with a range of 9.2% (Pilbara region) in the west to 0.7% in the centre (Katherine region) (Fig. 1A). There was less geographical variation for 3GC-resistant *K. pneumoniae* (Fig. 1B) and ceftazidime-resistant *P. aeruginosa* (Fig. 1C).

3.2. Antimicrobial resistance and antibiotic utilization

We did not identify a linear relationship (correlation coefficient = -0.02 [P = 0.88]) between antibiotic utilization and the rate of *E. coli* 3GC resistance (Fig. 2). We show that in one region of northern Australia (Northern Territory) between 2015 and 2019 there was a decline in consumption of third-generation cephalosporin antibiotics in a tertiary healthcare setting and an increase in the rate of 3GC-resistant *E. coli* blood isolates. Antimicrobial utilization data are currently not available to assess the effect in the primary healthcare setting.

3.3. Remoteness and socio-economic disadvantage

Estimates of socio-economic risk factors derived for each region are shown in Fig. 3 and Table 2. They show that 75% (9 out of 12) regions within our study setting of northern Australia are categorized as very remote, and the remaining 25% are remote (Darwin, Townsville, Cairns and Hinterland) (Fig. 3A). The relative socio-economic disadvantage is varied across northern Australia, with three regions indicating households with high disadvantage (i.e., low income, minimal qualification and low-skill occupation
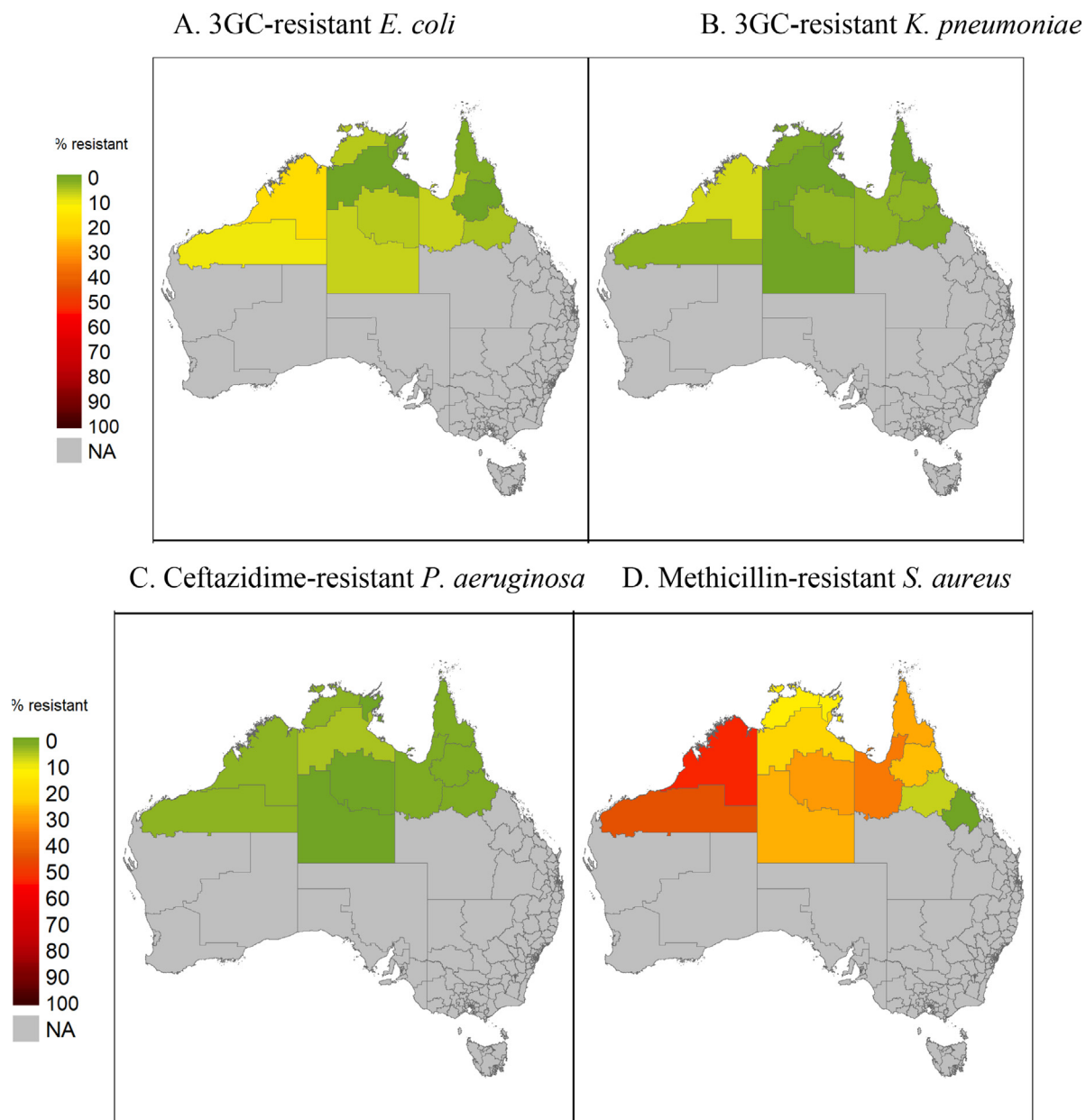
A. 3GC-resistant *E. coli*

B. 3GC-resistant *K. pneumoniae*

C. Ceftazidime-resistant *P. aeruginosa*

D. Methicillin-resistant *S. aureus*

Fig. 1. Proportion of resistant isolates from primary healthcare, northern Australia 2007–2019. (A) 3GC-resistant *E. coli*. (B) 3GC-resistant *K. pneumoniae*. (C) Ceftazidime-resistant *P. aeruginosa*. (D) Methicillin-resistant *S. aureus*. Source: HOTspots surveillance platform.

Table 2
The socio-economic risk factors, northern Australia 2016

Region	Remoteness index	Index of socio-economic disadvantage	Average person per household	Population density (persons/sq m)
West				
Kimberley	Very remote	5.00	2.93	2.80
Pilbara	Very remote	5.75	2.80	0.12
Centre				
Gove	Very remote	4.43	4.10	0.43
Darwin	Remote	6.77	2.70	46.50
Tennant Creek	Very remote	1.89	3.20	0.02
Katherine	Very remote	2.90	3.30	0.06
Alice Springs	Very remote	4.13	2.8	0.07
East				
Torres and Cape	Very remote	2.69	3.00	
Cairns & Hinterland	Remote	4.28	2.46	11.56
Northwest	Very remote	4.49	2.70	0.10
Townsville	Remote	4.24	2.57	0.69

NOTE: Index of socioeconomic disadvantage ranges from 1 = most disadvantaged to 10 = least disadvantaged.
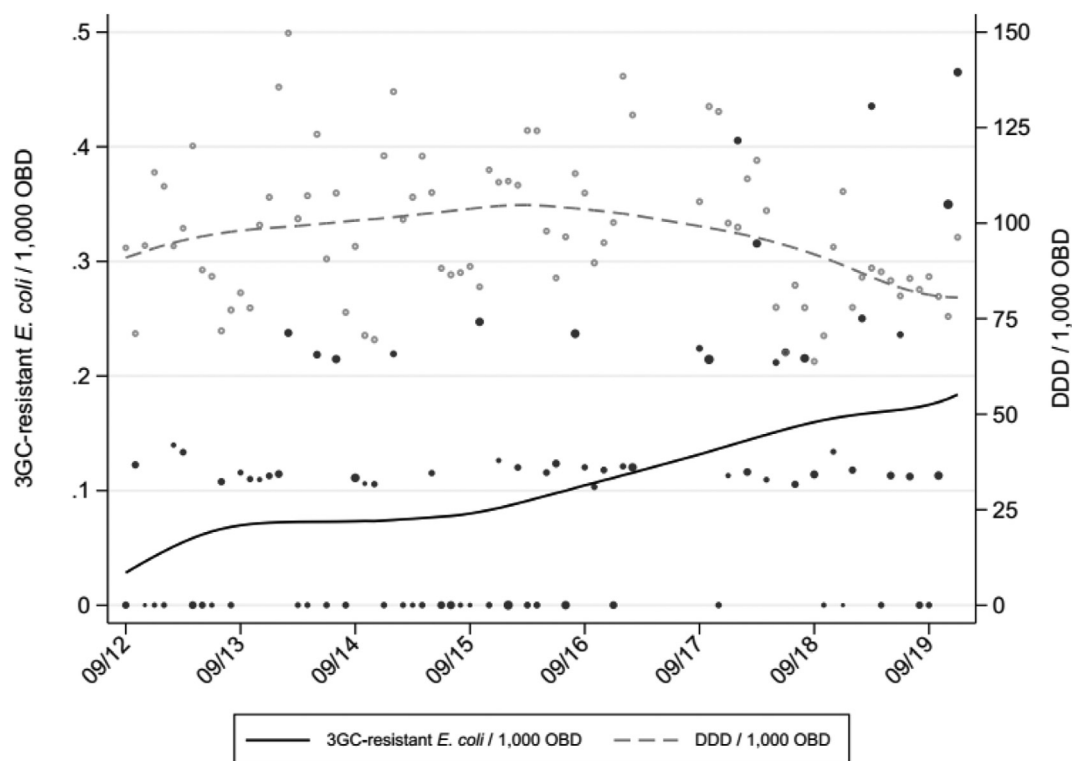
Fig. 2. Correlation of antimicrobial usage and prevalence of 3GC-resistant *E. coli*, northern Australia 2012–2019. DDD, defined daily dose; OBD, occupied bed-days; 3GC-resistant *E. coli* data from HOTspots; antibiotic data from National Antimicrobial Utilisation Surveillance Program.

measured as an index score of 1.8–2.9); eight regions with moderate disadvantage (index score 4.13–5.75); and one region (Darwin, index score 6.77) with lower disadvantage (Fig. 3B). There were no regions included in northern Australia with a relative socio-economic disadvantage index score greater than 7 (where a score of 10 indicates the least disadvantaged regions). The greatest number of persons per household in our study setting was in Gove, situated in northern NT, with an average of 4–4.5 persons per household, and Katherine (3.3 persons per household), compared to the national average of 2.6 persons per household (Fig. 3C).

3.4. Antimicrobial resistance, remoteness and socio-economic disadvantage

In multivariable logistic regression analysis, we found that the prevalence of 3GC-resistant *E. coli* (OR 5.05; 95% confidence interval [CI] 3.19, 8.04) and MRSA (OR 5.72; 95% CI 5.02, 6.54) increased with remoteness (Table 3). A similar pattern was evident for 3GC-resistant *K. pneumoniae* and ceftazidime-resistant *P. aeruginosa*, albeit not statistically significant. Prevalence of AMR was not positively correlated with the index of socio-economic disadvantage or the average persons per household measure. Using these indexes, we found that the odds of AMR pathogens increased in regions with less socio-economic disadvantage (3GC-resistant *E. coli* [OR 1.93, 95% CI 1.71, 2.18]; 3GC-resistant *K. pneumoniae* [OR 1.57, 95% CI 1.03, 2.35]; MRSA [OR 1.35, 95% CI 1.31,1.38]) (Table 3). The results for ceftazidime-resistant *P. aeruginosa* were not statistically significant.

4. Discussion

We demonstrate the feasibility of integrating traditional disease surveillance systems with other data sets to build a more comprehensive view of the AMR threat. Mapping geospatial locations [17] with sociodemographic information can identify pockets of

Table 3

Analysis of socio-economic risk factors for isolates from primary healthcare, 2007–2019

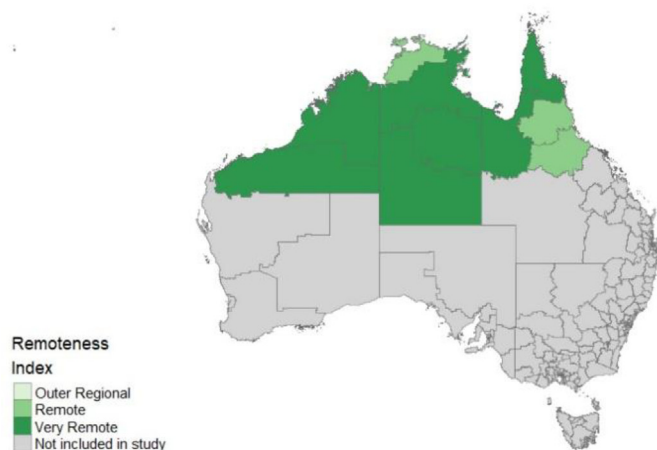| Socio-economic risk factors for all regions	OR (95% CI)
Access to health and social services (Remoteness index)	
3GC-resistant *E. coli*	**5.05 (3.19, 8.04)**
3GC-resistant *K. pneumoniae*	2.95 (0.61, 15.89)
Ceftazidime resistant PA	1.43 (0.51, 5.02)
MRSA	**5.72 (5.02, 6.54)**
Index of socioeconomic disadvantage[a]	
3GC-resistant *E. coli*	**1.93 (1.71, 2.18)**
3GC-resistant *K. pneumoniae*	**1.57 (1.03, 2.35)**
Ceftazidime-resistant *P. aeruginosa*	1.28 (0.96, 1.73)
MRSA	**1.35 (1.31, 1.38)**
Average persons per household	
3GC-resistant *E. coli*	**0.40 (0.16, 0.90)**
3GC-resistant *K. pneumoniae*	0.22 (0.00, 2.75)
Ceftazidime-resistant *P. aeruginosa*	0.94 (0.09, 4.15)
MRSA	**0.39 (0.31, 0.48)**

NOTE: Bold indicates a significant finding.
3GC, third-generation cephalosporin; MRSA, methicillin-resistant *Staphylococcus aureus*.
[a] High index indicates low disadvantage.

health inequity and lead to a better understanding of drivers of AMR. Our study found that the odds of MRSA (OR 5.72, 95% CI 5.02, 6.54) and 3GC-resistant *E. coli* (OR 5.05, 95% CI 3.19, 8.04) infections were increased with increasing remoteness. Using 12 years of data from primary healthcare facilities across three jurisdictions of northern Australia, we report striking geographical variation in AMR prevalence. Persistent clusters of high MRSA and 3GC-resistant *E. coli* in the west, with prevalence of 52% and 17%, respectively, are especially concerning. Temporal trends in *S. aureus* epidemiology have been previously shown in this region and are believed to be related to changes in dominant MRSA clones both within and between jurisdictions [17,29]. Whilst it has been

A. Remoteness index

B. Index of Socio-economic Disadvantage
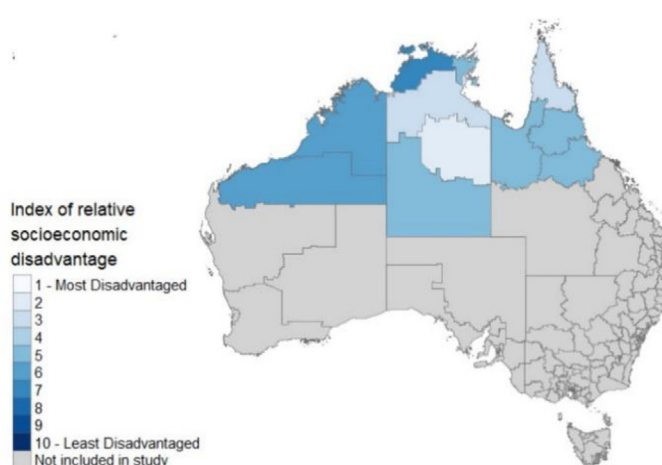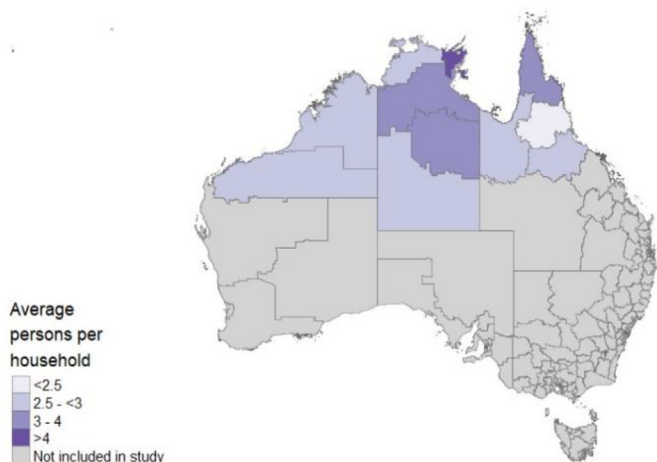

C. Average person per household

Fig. 3. The socio-economic risk factors by region, northern Australia 2016. (A) Remoteness index. (B) Index of Socio-economic Disadvantage. (C) Average person per household.

shown that socio-economic, environmental and cultural factors are likely to contribute to ill health in regional Australia [30], reasons for such disparity in AMR prevalence between remote and urban Australia remains ill-defined. A systematic approach is needed.

Health inequity of people living in remote regions is likely a combination of several factors. In regional Australia, limited access to health and social services, coupled with a high burden of chronic diseases and complex socio-demographic factors, contribute health disparities [31]. Previous studies have shown that inadequate hygiene practices can promote the spread of infections and result in chronic sequelae such as stunting, blindness, hearing loss, rheumatic heart disease and renal failure in this setting [32]. Environments such as unmaintained housing and malfunctioning 'health hardware', including bathroom, kitchen and laundry facilities, all contribute to poorer health outcomes often experienced by Australians living in rural regions [32–34].

There are a number of potential explanations for the observed negative correlation between increasing AMR prevalence and the index of socio-economic disadvantage in this study. We focused on examining correlation of AMR with the index of socio-economic disadvantage in remote and very remote populations, with 72%

of the population categorized as moderate to high socio-economic disadvantage and greater than 80% residing in very remote or remote regions. We did not compare against regions of higher socio-economic status and may have masked the effect of AMR on socio-economic disadvantage in our study. In addition, our study raises an important issue of reflexivity surrounding the use of categories such as the index of socio-economic disadvantage to understand the social dynamics of disease. We used the Australian Bureau of Statistics index of socio-economic disadvantage, which is measured using census data [23]. Despite concerted efforts to improve procedures through the Indigenous Enumeration Strategy, this index may significantly undercount Aboriginal and Torres Strait Islander people, notably those in remote areas, the young, the mobile and the socially marginalized [35,36]. Hence, in remote regions and where a high proportion of the population are Aboriginal and Torres Strait Islander people, a more appropriate measure of social disadvantage (or advantage) should be a considered to better capture the region-specific social determinants of health.

Our findings suggest that the relationship between antibiotic usage—a commonly considered key driver of AMR [37]—and the development of resistance is not clear. In our study, a decline in

the defined daily dose of third-generation cephalosporins did not correlate with increased 3GC-resistant *E. coli* resistance in regional hospital patients. Due to scarcity of antibiotic utilisation data from primary healthcare settings [31], we were unable to determine patterns in patients from our study population. However, a long history of guideline-based remote healthcare delivery is evident across northern Australia, showing high appropriateness of antimicrobial use compared with urban general practice settings [38]. Despite high appropriateness of antimicrobial use in regional Australia, we and others [17,29] report high AMR in this setting. Hence, it is the critical that we better define drivers of AMR in remote primary healthcare in Australia and other settings.

In this study we present an opportunity to approach AMR prevention and containment from a more holistic framework, and one that brings together much needed granularity of the societal context within which resistant pathogens interact. Currently, there are few information systems and evaluated platforms that aid in planning and delivery of AMR prevention programs whilst monitoring their effect on health [39]. We have previously described the HOTspots platform for aggregating, analysing and disseminating AMR surveillance data on bacterial pathogen [17]. We propose that the HOTspots platform could be repurposed to integrate other data sets such as access to health and social services measured by the remoteness index. Geocoding of postcode or statistical area level (as shown in this study) provides a means of appending area-based data to public health databases such as the Australian Statistical Geography Standards, the Socio-Economic Indexes for Areas and the National Social Housing survey [23,40]. Additionally, geocoding data from community-based programs with particular focus on programs that aim to improve housing, health hardware and environmental health would be desirable.

This was an exploratory study that aimed to determine if there are any associations between the selected (administrative) socio-economic risk factors and AMR prevalence in northern Australia. The analysis does not include an exhaustive list of social factors but rather serves as a starting point. Using the average persons per household from the ABS data set as a proxy for overcrowding is limiting and does not indicate the quality of the household that should be explored in future studies. It is also important to note that we cannot conclude that an area with low ranking on the socio-economic disadvantage index has a low proportion of advantaged people as this is not measured, only that there is a high proportion of disadvantage [26]. Due to the nature of how the index of socioeconomic disadvantage is derived, future studies would benefit from looking into associations between AMR and more specific measures of social inequalities. In the absence of more detailed clinical information, we were not able to confirm the presence of an active infection for patients with urinary or respiratory tract pathogens. Hence, the current study includes all specimen types based on positive culture and may suffer from misclassification bias. That is, in the absence of clinical data to confirm infection, it is probable that some skin and soft tissue samples may have been categorized as infections but were, in fact, colonisations. However, the HOTspots surveillance system used the accepted and published microbiological criteria for a positive culture and includes density of bacteria, which equates to an infection [41,42].

For long-term sustainability, the commitment of local stakeholders is essential, and sustainable collaborations between health, housing and the environment will be key. Issues requiring attention include strengthening our understanding of measures of social disadvantage (or advantage) and the diversity of programs that target primordial drivers of infectious disease, their feasibility, and the ways in which they may influence actions against AMR in different contexts. These efforts should be concurrent to work in strengthening monitoring of antibiotic use and appropriateness, in particular in Australian primary healthcare where antibiotic stewardship activities are currently not mandated [31]. Additionally, service coordination is key for successful navigation of healthcare systems, which are often complex. By integrating a wider variety of services in primary healthcare, such as housing or employment services, the need for coordination is particularly important to support the implementation. Positioning AMR containment within a social and health context will mean that policies to reduce social inequality and to improve health outcomes become interchangeable. Although true for all populations, it is especially salient in obtaining health support and resources for socially disadvantaged populations, given their vulnerability in terms of political and economic influence.

Disparities and inequities in health are not caused by one single factor and, as such, cannot be eliminated by a single intervention. Therefore, to ignore social determinates of resistant infection would be to ignore a major source of variation in health and society [43]. Access to socio-demographic and socio-economic data early and within the local regional context will fill a significant gap in disease prevention and spread. We show that socio-economic stratification is an appropriate analysis for an epidemiologist seeking to understand the effect of resistance on a population. Fundamental to the success of this work is the need to have integrated platforms with health, social and, if possible, economic data. This will not only create accountability for public health and governments but also allow community-based organizations, healthcare providers and citizens to contribute innovative solutions to the whole of community response.

Ethical approval

Human Research Ethics Committee of the Northern Territory Department of Health and Menzies School of Health Research (HREC-2018-3084) as well as the Queensland Health Public Health Act 2005.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Funding

References

[1] Tsai J, Wilson M. COVID-19: a potential public health problem for homeless populations. Lancet Public Health 2020;5:e186–7. doi:10.1016/S2468-2667(20)30053-0.

[2] Abrams EM, Szefler SJ. COVID-19 and the impact of social determinants of health. Lancet Respiratory Medicine 2020;8:659–61. doi:10.1016/S2213-2600(20)30234-4.

[3] Ching C, Zaman MH. Development and selection of low-level multi-drug resistance over an extended range of sub-inhibitory ciprofloxacin concentrations in *Escherichia coli*. Sci Rep 2020;10:8754. doi:10.1038/s41598-020-65602-z.

[4] Hsu J. How COVID-19 is accelerating the threat of antimicrobial resistance. BMJ 2020;369:m1983. doi:10.1136/bmj.m1983.

[5] Antimicrobial Resistance CollaboratorsGlobal burden of bacterial antimicrobial resistance in 2019: a systematic analysis. Lancet 2022;399:629–55. doi:10.1016/S0140-6736(21)02724-0.

[6] Levy S. The Antibiotic Paradox: How Miracle Drugs and Destroying the Miracle. Springer; 2013.

[7] Noppert GA, Kubale JT, Wilson ML. Analyses of infectious disease patterns and drivers largely lack insights from social epidemiology: contemporary patterns

and future opportunities. J Epidemiol Comm Health 2017;71:350–5. doi:10.1136/jech-2016-207967.

[8] Klovdahl AS. Social networks and the spread of infectious diseases: the AIDS example. Soc Sci Med 1985;21:1203–16. doi:10.1016/0277-9536(85)90269-2.

[9] Malosh RE, Noppert GA, Zelner J, Martin ET, Monto AS. Social patterning of acute respiratory illnesses in the Household Influenza Vaccine Evaluation (HIVE) Study 2014–2015. Epidemiol Infect 2019;147:e185. doi:10.1017/S0950268819000748.

[10] de Glanville WA, Thomas LF, Cook EAJ, Bronsvoort BMC, Wardrop N, Wamae CN, et al. General contextual effects on neglected tropical disease risk in rural Kenya. PLoS Negl Trop Dis 2018;12:e0007016. doi:10.1371/journal.pntd.0007016.

[11] DeLacy J, Dune T, Macdonald JJ. The social determinants of otitis media in Aboriginal children in Australia: are we addressing the primary causes? A systematic content review. BMC Public Health 2020;20:492. doi:10.1186/s12889-020-08570-3.

[12] Allegranzi B, Nejad SB, Combescure C, Graafmans W, Attar H, Donaldson L, et al. Burden of endemic health-care-associated infection in developing countries: systematic review and meta-analysis. Lancet 2011;377:228–41. doi:10.1016/S0140-6736(10)61458-4.

[13] Laxminarayan R, Duse A, Wattal C, Zaidi AKM, Wertheim HFL, Sumpradit N, et al. Antibiotic resistance: the need for global solutions. Lancet Infect Dis 2013;13:1057–98 0.1016/S1473-3099(13)70318-9.

[14] Collignon P, Beggs JJ, Walsh TR, Gandra S, Laxminarayan R. Anthropological and socioeconomic factors contributing to global antimicrobial resistance: a univariate and multivariable analysis. Lancet Planet Health 2018;2:e398–405. doi:10.1016/S2542-5196(18)30186-4.

[15] Gibney KB, Cheng AC, Hall R, Leder K. Sociodemographic and geographical inequalities in notifiable infectious diseases in Australia: a retrospective analysis of 21 years of national disease surveillance data. Lancet Infect Dis 2017;17:86–97. doi:10.1016/S1473-3099(16)30309-7.

[16] https://www.aihw.gov.au/reports/rural-remote-australians/rural-and-remote-health; 2022. [Accessed May 2022].

[17] Wozniak TM, Cuningham W, Buchanan S, Coulter S, Baird RW, Nimmo GR, et al. Geospatial epidemiology of Staphylococcus aureus in a tropical setting: an enabling digital surveillance platform. Sci Rep 2020;10:13169. doi:10.1038/s41598-020-69312-4.

[18] Turrell G, de Looper M, Oldenburg B. Health inequalities in Australia: morbidity, health behaviours, risk factors and health service use. Health Inequalities Monitoring Series No. 2. Canberra: Queensland University of Technology and the Australian Institute of Health and Welfare; 2006.

[19] Australian Commission on Safety and Quality in Health Care. AURA 2021: fourth Australian report on antimicrobial use and resistance in human health. https://www.safetyandquality.gov.au/publications-and-resources/resource-library/aura-2021-fourth-australian-report-antimicrobial-use-and-resistance-human-health; 2021. [Accessed May 2022].

[20] Tong SY, Varrone L, Chatfield MD, Beaman M, Giffard PM. Progressive increase in community-associated methicillin-resistant Staphylococcus aureus in Indigenous populations in northern Australia from 1993 to 2012. Epidemiol Infect 2015;143:1519–23. doi:10.1017/S0950268814002611.

[21] Krockow EM, Colman AM, Chattoe-Brown E, Jenkins DR, Perera N, Mehtar S, et al. Balancing the risks to individual and society: a systematic review and synthesis of qualitative research on antibiotic prescribing behaviour in hospitals. J Hosp Infect 2019;101:428–39. doi:10.1016/j.jhin.2018.08.007.

[22] Broom A, Broom J, Kirby E, Gibson A, Davis M. Antibiotic optimisation in 'the bush': local know-how and core-periphery relations. Health Place 2017;48:56–62. doi:10.1016/j.healthplace.2017.09.003.

[23] Australian Bureau of Statistics. Australian statistical geography standard. https://www.abs.gov.au/websitedbs/D3310114.nsf/home/Australian+Statistical+Geography+Standard+(ASGS); 2018. [Accessed May 2020]

[24] South Australia Health Australian Commission on Safety and Quality in Health Care. National antimicrobial utilisation surveillance program: 2019 key findings. Sydney: ACSQHC; 2021.

[25] WHO Collaborating Centre for Drug Statistics Methodology. Definitions and general considerations. https://www.whocc.no/ddd/definition_and_general_considera/; 2018. [Accessed Nov 2021]

[26] Australian Bureau of Statistics Socio-Economic Indexes for Areas (SEIFA) technical paper 2016. Australian Bureau of Statistics; 2016. https://www.abs.gov.au/ausstats/abs@.nsf/mf/2033.0.55.001. [Accessed Jun 2020].

[27] RStudio: Integrated Development for R. 2020.

[29] Coombs GW, Daley DA, Lee YT, Pearson JC, Robinson JO, Nimmo GR, et al. Australian Group on Antimicrobial Resistance Australian Staphylococcus aureus sepsis outcome programme annual report, 2014. Commun Dis Intell Q Rep 2016;40:E244–54.

[30] Hendrickx D, Bowen AC, Marsh JA, Carapetis JR, Walker R. Ascertaining infectious disease burden through primary care clinic attendance among young Aboriginal children living in four remote communities in Western Australia. PLoS One 2018;13:e0203684. doi:10.1371/journal.pone.0203684.

[31] Bowen AC, Daveson K, Anderson L, Tong SY. An urgent need for antimicrobial stewardship in Indigenous rural and remote primary health care. Med J Aust 2019;211 9–11.e1. doi:10.5694/mja2.50216.

[32] Ali SH, Foster T, Hall NL. The relationship between infectious diseases and housing maintenance in Indigenous Australian households. Int J Environ Res Public Health 2018;15:2827. doi:10.3390/ijerph15122827.

[33] Edney LC, Afzali HHA, Cheng TC, Karnon J. Estimating the reference incremental cost-effectiveness ratio for the Australian health system. Pharmacoeconomics 2018;36:239–52. doi:10.1007/s40273-017-0585-2.

[34] Bailie RS, Stevens M, McDonald EL. The impact of housing improvement and socio-environmental factors on common childhood illnesses: a cohort study in Indigenous Australian communities. J Epidemiol Comm Health 2012;66:821–31.

[35] Morphy F. Agency, contingency and census process: observations of the 2006 Indigenous enumeration strategy in remote Aboriginal Australia. ANU Press; 2007. [Accessed Feb 2020]. doi:10.22459/CAEPR28.12.2007.

[36] Anderson I, Robson B, Connolly M, Al-Yaman F, Bjertness E, King A, et al. Indigenous and tribal peoples' health (the Lancet-Lowitja Institute Global Collaboration): a population study. Lancet 2016;388:131–57. doi:10.1016/S0140-6736(16)00345-7.

[37] Klein EY, Van Boeckel TP, Martinez EM, Pant S, Gandra S, Levin SA, et al. Global increase and geographic convergence in antibiotic consumption between 2000 and 2015. Proc Natl Acad Sci U S A 2018;115:E3463–70. doi:10.1073/pnas.1717295115.

[38] Cuningham W, Anderson L, Bowen AC, Buising K, Connors C, Daveson K, et al. Antimicrobial stewardship in remote primary healthcare across northern Australia. PeerJ 2020;8:e9409. doi:10.7717/peerj.9409.

[39] Wernli D, Jorgensen PS, Parmley EJ, Troell M, Majowicz S, Harbarth S, et al. Evidence for action: a One Health learning platform on interventions to tackle antimicrobial resistance. Lancet Infect Dis 2020. doi:10.1016/S1473-3099(20)30392-3.

[40] Australian Institute of Health and Welfare. National Social Housing Survey: a summary of national results 2016. https://www.aihw.gov.au/reports/housing-assistance/national-social-housing-survey-summary-2016; 2017. [Accessed May 2020]

[41] Wang JL, Chen SY, Wang JT, Wu GHM, Chiang WC, Hsueh PR, et al. Comparison of both clinical features and mortality risk associated with bacteremia due to community-acquired methicillin-resistant Staphylococcus aureus and methicillin-susceptible S. aureus. Clin Infect Dis 2008;46:799–806. doi:10.1086/527389.

[42] Centers for Disease Control Prevention. National healthcare safety network (NHSN) patient safety component manual. https://www.cdc.gov/nhsn/pdfs/pscmanual/pcsmanual_current.pdf; 2018. [Accessed May 2020]

[43] Marmot M. Social justice, epidemiology and health inequalities. Eur J Epidemiol 2017;32:537–46. doi:10.1007/s10654-017-0286-3.