MICROBIOLOGY AUSTRALIA, 2021, **42**, 104–110
https://doi.org/10.1071/MA21031

Escherichia coli: placing resistance to third-generation cephalosporins and fluoroquinolones in Australia and New Zealand into perspective

Rhys T White

School of Chemistry and Molecular Biosciences and Australian Infectious Disease Research Centre, The University of Queensland, Brisbane, Qld 4072, Australia; *and* Australian Centre for Ecogenomics, The University of Queensland, Brisbane, Qld 4072, Australia. Tel.: +61 7 3365 8549; Email: rhystwhite@gmail.com

Abstract. At least 300 million urinary tract infections (UTIs) occur annually worldwide. Uropathogenic *Escherichia coli* (UPEC) are the leading cause of UTIs. The discovery of antibiotics has revolutionised modern medicine. Yet, overusing antibiotics has accelerated the emergence of antimicrobial resistance (AMR), with UPEC driving the dissemination of AMR globally. Resistance to broad-spectrum antibiotics like third-generation cephalosporins (3GCs) and fluoroquinolones threatens public health. Extended-spectrum β-lactamase (ESBL)-producing *E. coli* precipitate resistance, particularly when these antibiotics are used as empirical therapies against UPEC. In response, the Centers for Disease Control and Prevention in the United States have listed ESBL-producing Enterobacterales, such as *E. coli* as a severe threat. Additionally, the World Health Organization have classified 3GCs and fluoroquinolones as the highest priority (critically important antimicrobials), where these therapies are only recommended following susceptibility testing. The present report demonstrates the distributions of *E. coli* cases with resistance to 3GC and fluoroquinolones in Australia and New Zealand and contextualises trends with European reports. This investigation emphasises the value of epidemiology and the justification of evidence-based interventions using data as an essential resource for reducing resistance to our 'first-line' antibiotics.

Received 25 March 2021, accepted 21 July 2021, published online 8 September 2021

The burden of antimicrobial resistance

Antimicrobial resistance (AMR) is a well established global priority due to the increasing impacts on public health. Across the United States (US), at least 2.8 million antimicrobial-resistant infections occur each year[1]. Globally, antimicrobial-resistant infections cause more than 700 000 deaths annually, with 10 million deaths expected by 2050[2]. The increasing incidence and global dissemination of AMR are: (1) limiting treatment options; (2) resulting in prolonged illnesses; (3) increasing morbidity and mortality; and (4) increasing healthcare-related costs on a global scale[3,4]. In Australia, an estimated 200 000 healthcare-associated infections occur annually, including multidrug-resistant infections[5]. The same healthcare-associated infections are estimated to generate healthcare costs between A$2–3 billion (US$1 = A$1.11[6]) and contribute to 7000 deaths annually[5].

Increasing AMR rates affect current antimicrobial therapeutic guidelines, particularly as third-generation cephalosporins (3GCs) are recommended as 'first-line' treatments to avoid prescribing 'last-line' antibiotics such as carbapenems and colistin. In response, the World Health Organization has devised a list of highest priority, critically important antibiotics, which includes 3GCs and fluoroquinolones[7]. Extended spectrum β-lactamase (ESBL)-producing organisms inactivate broad spectrum 3GC antibiotics. Additionally, the US Centers for Disease Control and Prevention (CDC) listed ESBL-producing Enterobacterales (ESBL-E) as a serious threat. In 2017, the CDC predicted that ESBL-E accounted for the deaths of 9100 individuals in the US, with 197 400 confirmed cases, and an attributable healthcare cost of US$1.2 billion[1] (US$1 = A$1.31[6]). In New Zealand, ESBL-producing *Escherichia coli* incidence rates increased from 3.7 per 100 000 in the early to mid-2000s[8,9] to 113.8 per 100 000 in the early to mid-2010s[10]. Furthermore, the Australian Commission on Safety and Quality in Health Care (ACSQHC) have reported a 55.5% increase in fluoroquinolone-resistant *E. coli* between 2015 (n = 11 094/149 916, 7.4%) and 2018 (n = 17 253/169 145, 10.2%)[11]. These data from the US, New Zealand, and Australia represents a serious concern, as resistance to fluoroquinolones may indicate resistance to one of the last available oral treatment options. This is particularly concerning for low socio-economic, disadvantaged, and under-resourced communities across regional, rural, and remote regions who rely on these antimicrobials. These communities are at a higher risk of infections

for which quinolones are indicated. For example, non-ototoxic ciprofloxacin ear drops are the mainstays of treatment for chronic suppurative otitis media, which affects 9 in 10 Aboriginal and Torres Strait Islander peoples younger than 3 years of age in remote Northern Territory (Australia) communities[12].

Antimicrobial therapy and incidence epidemiology of urinary tract infections

With increasing AMR rates impacting public health, common infections are becoming more persistent and harder to treat. These include urinary tract infections (UTIs), which are typically self-limiting and are one of the most frequently occurring bacterial infections. The Institute for Health Metrics and Evaluation estimates 391.3 million UTIs occurred worldwide in 2017, mostly reported among females (Figure 1*a*)[13]. UTI-associated healthcare costs are at least GB£4 billion[14] (US$1 = GB£0.65[6]) annually. If undiagnosed or untreated, UTIs can progress to systemic bacteraemia infections, which can trigger sepsis and septic shock. Gram-negative bacteria are a common cause of UTIs[15]. In 2018 for example, *E. coli* was the predominant (n = 2948/8797, 33.5%) cause of UTIs and bacteraemia across Australia[15]. Most of these *E. coli* cases were defined as community-onset (n = 2425/2948, 82.3%; culture collected ≤48 h after admission) rather than hospital-onset (n = 523/2948, 17.7%; >48 h after admission)[15]. Acute UTIs are treated empirically within the first 48 h of symptoms using a 3–14-day course of oral antibiotics (i.e. trimethoprim/sulfamethoxazole, cephalexin, nitrofurantoin, ciprofloxacin, or amoxicillin with clavulanate)[16]. Hospitalisation

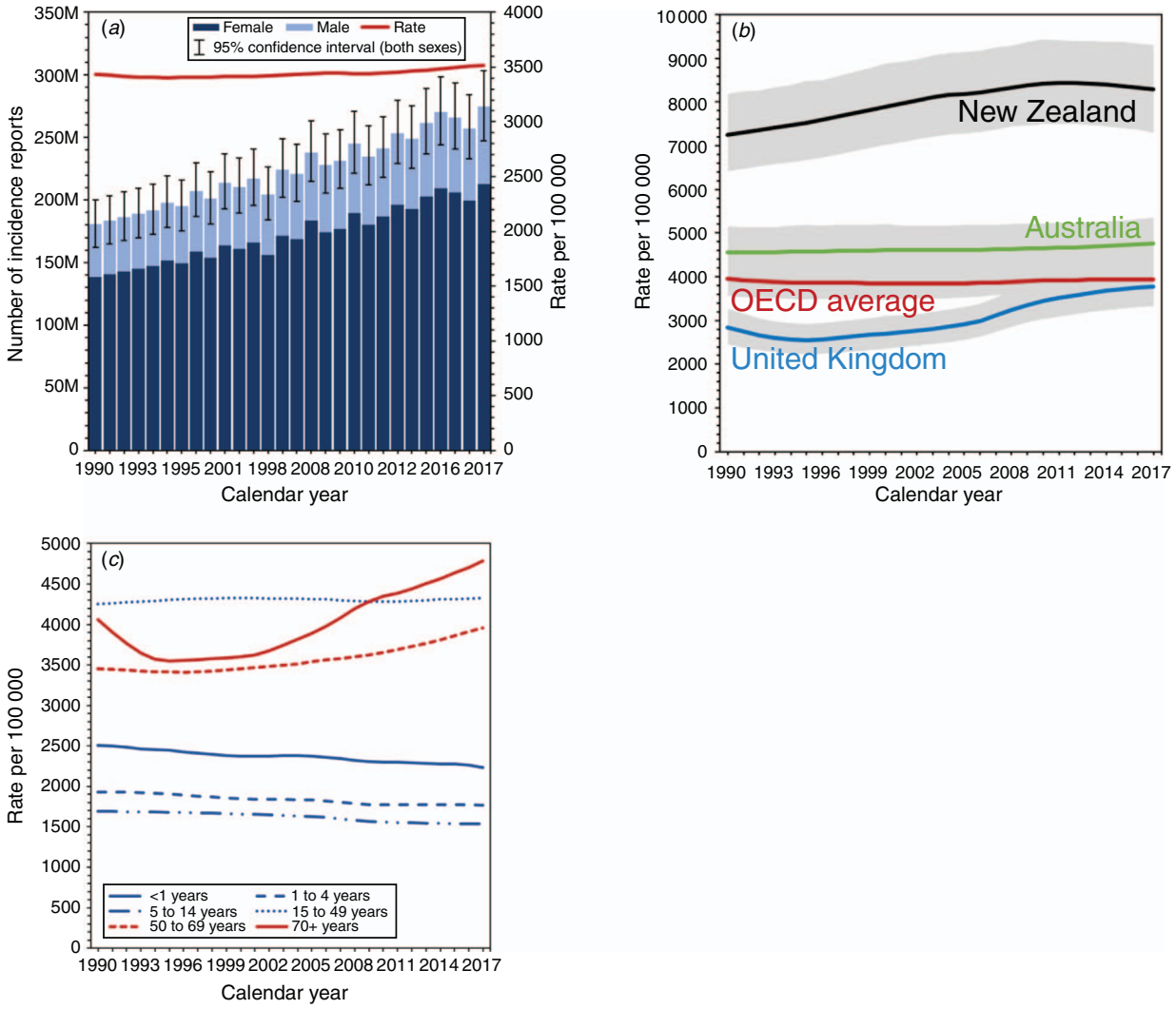

Figure 1. Global burden of urinary tract infections. (*a*) Global incidences reported, males (light blue) and females (navy) all ages, 1990 to 2017. Error bars represent the 95% confidence interval for total counts of infections reported in both sexes. The incidence rate per 100 000 is represented by the red line. (*b*) Age-standardised incidence rate in males and females from 1990 to 2017. Colour lines represents the point estimates for the incidence rate per 100 000 people for: the average from Organisation for Economic Co-operation and Development (OECD) member countries (red), Australia (green), New Zealand (black), and the United Kingdom (blue). Grey shading represents the 95% confidence intervals. (*c*) Global number of incidences by age group, males and females all ages, 1990 to 2017. Age groups are represented by corresponding line patterns with age groups 50–69 and 70+ highlighted in red (legend). Data retrieved from the Global Burden of Disease Collaborative Network[13].

for UTI can often result in the inappropriate use of broad-spectrum antimicrobials[17]. The increasing empiric use of broad-spectrum antibiotics may drive multidrug-resistant infections, particularly in recurrent cases of UTIs[18].

While changes among the annualised global age-standardised incidence rate over the past 27 years are negligible[13], increases have been observed in countries where mechanisms are in place for reporting UTIs, such as the United Kingdom, Australia, and New Zealand (Figure 1*b*). In 2017, the annualised incidence was substantially higher in New Zealand (8290 per 100 000) when compared with Australia (4759 per 100 000) and the average from 36 Organisation for Economic Co-operation and Development (OECD) member countries (3928 per 100 000). Meanwhile, incidence across all OECD member countries has remained stable, with approximately 1 case per 25 persons. Notably, the epidemiology of UTIs has changed, with increases in incidence in persons aged 50+ years (Figure 1*c*), raising concerns as the proportion of persons aged 65+ years across Australia and New Zealand has increased over the past two decades. While older persons are at higher risk of UTIs, over-diagnosis has been reported in these age groups[19]. Historical statistics in New Zealand show that one in every nine persons were aged 65+ years in 1996 compared with one in seven persons in 2017[20]. Similarly, in Australia, one in every eight persons were aged 65+ years in 1997 compared with one in six persons in 2017[21]. These groups are more susceptible to age-related decline in immune system function and other age-related health co-morbidities. This susceptibility leads to greater morbidity and poorer, undesirable health outcomes such as urosepsis and mortality in as little as 12 h from the onset of illness.

Coordinating national data on antimicrobial resistance across Australia and New Zealand

In 2014, the ACSQHC established the Antimicrobial Use and Resistance in Australia (AURA) Surveillance System to coordinate local and national data collection and analyses on AMR across Australia. AURA encompasses a national collaboration of clinicians and microbiologists known as the Australian Group on Antimicrobial Resistance (AGAR) (www.agargroup.org). AGAR is historically responsible for using standardised methodologies to undertake ongoing targeted surveillance of AMR within clinically relevant pathogens. Recently, AGAR has focused on the Gram-negative Sepsis Outcome Program, which involves collections of AMR and demographic data on isolates cultivated from patient episodes of bacteraemia. Similarly, in New Zealand, the Institute of Environmental Science and Research Ltd (ESR), contributes to the national public health surveillance of AMR among human pathogens (https://surv.esr.cri.nz/index.php). The ESR are responsible for the antimicrobial susceptibility testing and epidemiological typing of clinically relevant pathogens, including ESBL-E. The national public health surveillance into ESBL-E across New Zealand is monitored through an established network of hospitals and pathology laboratories, which conduct periodic point-prevalence surveys of isolates from throughout the country which commenced in 1996. Both the AURA and ESBL-E schemes across Australia and New Zealand, respectively, review resistance in pathogens found in blood cultures. This allows for a direct comparison with European countries that regularly release comparable data from the European Antimicrobial Resistance Surveillance Network (EARSNet) scheme[22].

Resistance to 3GC and fluoroquinolones in *E. coli* is lower in Australia and New Zealand compared with European countries

A standardised definition to measure antimicrobial usage (AU) across jurisdictions is called the Defined Daily Dose (DDD). This is essentially the total units of antibiotics that have been used, divided by a DDD correction factor that is reviewed by the World Health Organization every 3 years (https://www.whocc.no/atc_ddd_index/). With the DDD definition, comparisons between AU in Australia and Europe can be made from data collected from AURA and EARSNet. Although Australia has an overall downward trend in AU since 2016, Australia remains in the top seven countries for AU when compared with Europe[11]. For example, at least two in five hospital patients across Australia received antibiotic treatment on any given day in 2014; where 24.3% of prescriptions were noncompliant with guidelines and 23.0% were inappropriate[23]. These undesirable prescribing habits may have arisen because of the lack of timely susceptibility testing, which has been described as 'too slow to guide logical choice of antibiotic therapy in critically ill patients'[5]. While some bacterial infections are still susceptible to various antibiotics (or combinations of antibiotics), this extensive use has to some degree contributed to the acquisition of AMR in most bacterial pathogens, whether multidrug-resistant or not[24,25]. Most European countries observed an increase in the rates of resistance to fluoroquinolones and 3GC in *E. coli* between 2016 and 2018. In comparison, the rates across Australia and New Zealand remain relatively low (Figure 2). The prevalence of fluoroquinolone resistance in *E. coli* across Australia increased between the start of 2016 (14.0%) and end of 2017 (14.4%). In contrast, resistance to 3GCs across Australia decreased between the same period of 2016 (11.8%) and 2017 (11.5%). Conversely, fluoroquinolone-resistant *E. coli* across New Zealand increased 6-fold over the same period (2.0% in 2016 compared with 12.0% in 2017). Additionally, in New

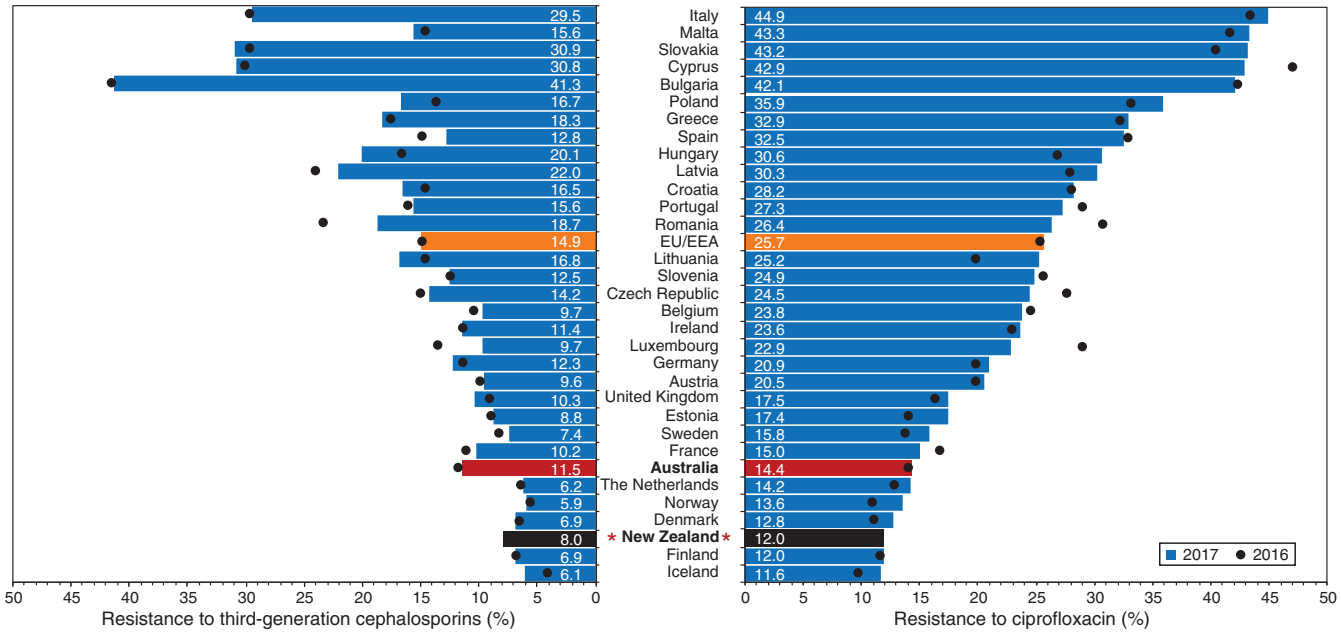

Figure 2. Prevalence of *Escherichia coli* resistant to third-generation cephalosporins (left) and ciprofloxacin (right) in Australia, New Zealand, and European countries, 2016 and 2017. European Union (EU) and European Economic Area (EEA) countries' population-weighted mean percentages are highlighted in orange, Australia in red, and New Zealand in black. For New Zealand, data represents isolates from 2015 only. Adapted from 'AURA 2019: third Australian report on antimicrobial use and resistance in human health' by the Australian Commission on Safety and Quality in Health Care (ACSQHC). Sydney, Australia: ACSQHC (2019).

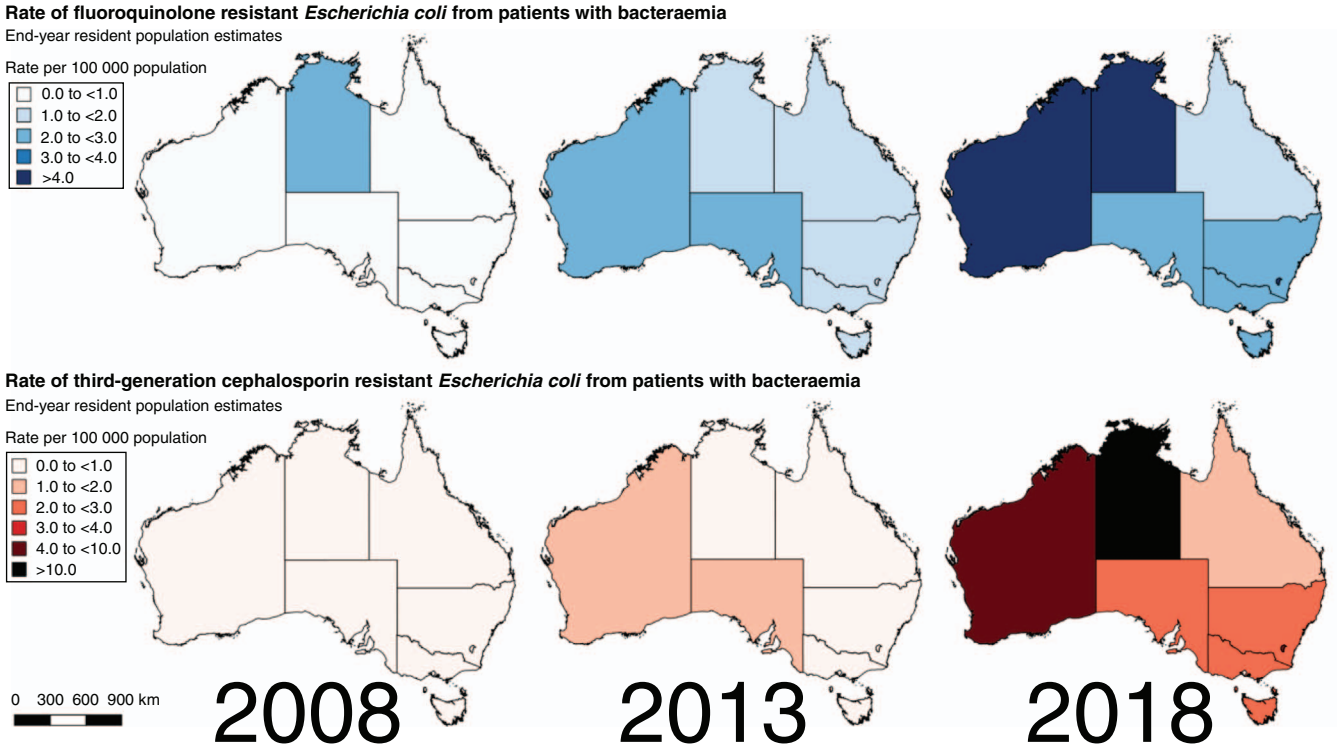

Figure 3. Annualised incident rates of resistance to fluoroquinolones (blue) and third-generation cephalosporins (red) amongst *Escherichia coli* from bacteraemia cases across Australia, 2008 to 2018. Incidence is expressed as rate per 100 000 based on the estimated resident population, States and Territories, from the Australian Bureau of statistics (Copyright © 2018 by the Commonwealth of Australia). Adapted from the 'Gram-negative Survey 2008 Antimicrobial Susceptibility Report' by the Australian Group on Antimicrobial Resistance (AGAR). Canberra, Australia: AGAR (2011); 'Gram-negative Survey 2013 Antimicrobial Susceptibility Report' by AGAR. Canberra, Australia: AGAR (2014); and 'Gram-negative Sepsis Outcome Programs 2018 report' by AGAR. Canberra, Australia: AGAR (2019).

Zealand there was a 4-fold increase in the incidence of 3GCs resistant infections (2.0% in 2016 compared with 8.0% in 2017). Nevertheless, the prevalence of resistance to fluoroquinolones and 3GCs across both Australia and New Zealand remained below the population-weighted averages (25.7% and 14.9%, respectively) of the European Union and European Economic Area countries' (Figure 2).

Comparisons of AMR in *E. coli* across Australia and New Zealand

ACSQHC uses reports like the AURA 2019 to survey the volume of AU within hospitals, the community, and aged care homes[11]. Notably, the total AU rate has increased from 22 DDDs per 1000 population in 2000 to 24 in 2009[26]. However, generally AU rates in Australia have been on a downward trend since 2010[11]. While AU is overall declining, *E. coli* with resistance to critical antibiotics like ciprofloxacin (an oral fluoroquinolone) and ceftriaxone (an injectable 3GC) are increasing (Figure 3). In contrast, metrics collected between 2016 and 2018 demonstrate a decline in the number of community dispensing rates under the government-subsidised medications Pharmaceutical Benefits Scheme. While 41.5% (n = 10 215 109) of the Australian population received at least one prescription for antimicrobials in 2017, the age-standardised rates of antimicrobial prescriptions dispensed per 1000 inhabitants decreased by 4.7% from 1120 in 2016 to 1067 in 2017[11]. Similarly, there was a decline in the number of residents in Australian aged care homes who were prescribed at least one antimicrobial between 2016 and 2018. While 8.8% (n = 1087/12 307) of residents in aged care homes received at least one prescription for antimicrobials in 2017, the rates of antimicrobial prescriptions dispensed per 1000 aged care home residents decreased from 98.6 in 2016 to 88.3 in 2017[11].

In New Zealand, surveillance conducted by the ESR reveals that the total-hospital AU rate has increased from 17 in DDDs per 1000 population per day in 2006 to 26 in 2012, before stabilising between 2012 and 2015[27]. This is also reflected by the longitudinal trend of increasing ESBL-producing clinical *E. coli* between 2006 (n = 56/87, 64.4%)[28] and 2016 (n = 386/521, 74.0%)[29]. The annualised rate of ESBL-producing *E. coli* circulating New Zealand is has also increased nation-wide, particularly between 2008 and 2013 (Figure 4). However, the data show reductions in major metropolitan areas in contrast to the increase observed in rural regions.

Conclusion

Since the discovery of penicillin, antibiotic treatments have revolutionised modern medicine and will forever impact global public health. Today, antimicrobials are extensively used against bacterial infections worldwide. The rapid emergence of resistance to 'first-line' and readily accessible antimicrobials like fluoroquinolones and third-generation cephalosporins requires urgent action. It is essential to place the prevalence of antimicrobial resistance into perspective and identify key indicators of their burden. From a clinical perspective, the appropriateness of antimicrobial use must be improved by supporting 'antibiotic stewardship' through initiatives at the local, national, and international level. This will reduce undesirable prescribing habits. While resistance to fluoroquinolones and third-generation cephalosporins is lower in Australia and New Zealand compared with European countries, *E. coli* with resistance ciprofloxacin (an oral fluoroquinolone) and ceftriaxone (an injectable

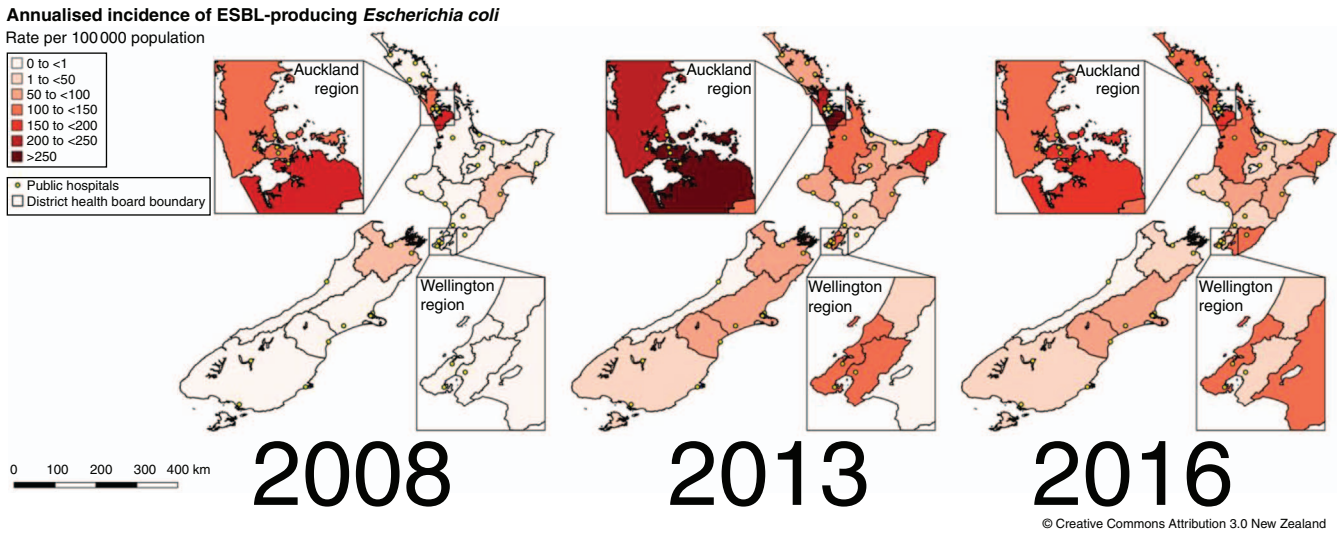

Figure 4. Extended-spectrum β-lactamase (ESBL)-producing *Escherichia coli* annualised incidence rates by district health board, New Zealand, 2008 to 2016. Incidence is expressed as rate per 100 000 based on the estimated resident population, District Health Boards, from Statistics New Zealand's data which are licensed for re-use under the Creative Commons Attribution 4.0 International licence. Incidence rates for (i) Capital & Coast and Hutt; and (ii) Canterbury and South Canterbury District Health Boards are combined. Adapted from the 'Annual survey of extended-spectrum β-lactamase (ESBL)-producing Enterobacteriaceae, 2008' by the Institute of Environmental Science and Research Ltd. (ESR). Wellington, New Zealand: ESR (2009); 'Annual survey of extended-spectrum β-lactamase (ESBL)-producing Enterobacteriaceae, 2013' by the ESR. Wellington, New Zealand: ESR (2014); and '2016 survey of extended-spectrum β-lactamase-producing Enterobacteriaceae' by the ESR. Wellington, New Zealand: ESR (2018).

third-generation cephalosporin) are increasing. It is important to maintain the decline in antimicrobial usage rates across hospitals, the community, and aged care homes as reported in Australia. Here, I have emphasised current trends in antimicrobial resistance and shown that work is still required to reduce the incidence of resistance to fluoroquinolones and third-generation cephalosporins.

Conflicts of interest

The author declares no conflicts of interest.

Declaration of funding

This research did not receive any specific funding.

Acknowledgements

The author thanks Scott Beatson (The University of Queensland) and Melinda Ashcroft (The Peter Doherty Institute for Infection and Immunity at The University of Melbourne) for constructive criticism of the manuscript. The author acknowledges Kristin Dyet (Communicable Disease Group at the Institute of Environmental Science and Research Ltd) for providing additional metadata for these analyses.

References

1. Centers for Disease Control and Prevention (2019) Antibiotic resistance threats in the United States, 2019. US Department of Health and Human Services, Centres for Disease Control and Prevention: Atlanta, GA, USA. https://www.cdc.gov/drugresistance/biggest-threats.html (accessed 9 July 2021).
2. O'Neill J. (2014) Review on antimicrobial resistance. Antimicrobial resistance: tackling a crisis for the health and wealth of nations. Wellcome Trust & UK Government: London, UK. https://amr-review.org/Publications.html (accessed 9 July 2021).
3. Holmberg, S.D. *et al*. (1987) Health and economic impacts of antimicrobial resistance. *Rev. Infect. Dis.* **9**, 1065–1078. doi:10.1093/clinids/9.6.1065
4. Munoz-Price, L.S. *et al*. (2013) Clinical epidemiology of the global expansion of *Klebsiella pneumoniae* carbapenemases. *Lancet Infect. Dis.* **13**, 785–796. doi:10.1016/S1473-3099(13)70190-7
5. Gilbert, L. *et al*. (2014) Healthcare infection prevention and control really is everyone's business. *Microbiol. Aust.* **35**, 3–4. doi:10.1071/MA14002
6. Organisation for Economic Co-operation and Development (2021) Exchange rates (indicator). Organisation for Economic Co-operation and Development: Paris, France. https://data.oecd.org/conversion/exchange-rates.htm (updated 6 July 2021; accessed 9 July 2021).
7. World Health Organization & WHO Advisory Group on Integrated Surveillance of Antimicrobial Resistance (AGISAR) (2017) Critically important antimicrobials for human medicine: ranking of antimicrobial agents for risk management of antimicrobial resistance due to non-human use. 5th edn. World Health Organization: Geneva, Switzerland. https://apps.who.int/iris/handle/10665/255027 (accessed 9 July 2021).
8. The Institute of Environmental Science and Research Ltd (2003) Extended-spectrum β-lactamases (ESBLs) in Enterobacteriaceae confirmed in 2002. Wellington, New Zealand: Institute of Environmental Science and Research Ltd. https://surv.esr.cri.nz/antimicrobial/esbl.php (accessed 9 July 2021).
9. The Institute of Environmental Science and Research Ltd (2008) Annual survey of extended-spectrum β-lactamase (ESBL)-producing Enterobacteriaceae, 2007. Wellington, New Zealand: Institute of Environmental Science and Research Ltd. https://surv.esr.cri.nz/antimicrobial/esbl.php (accessed 9 July 2021).
10. Dyet, K. *et al*. (2015) Annual survey of extended-spectrum β-lactamase (ESBL)-producing Enterobacteriaceae, 2014. Institute of Environmental Science and Research Ltd: Wellington, New Zealand. https://surv.esr.cri.nz/antimicrobial/esbl.php (accessed 9 July 2021).
11. Australian Commission on Safety and Quality in Health Care (2019) AURA 2019: third Australian report on antimicrobial use and resistance in human health. Australian Commission on Safety and Quality in Health Care: Sydney, NSW, Australia. https://www.safetyandquality.gov.au/our-work/antimicrobial-resistance/antimicrobial-use-and-resistance-australia-surveillance-system/aura-2019 (accessed 9 July 2021).
12. Leach, A.J. *et al*. (2021) Otitis media guidelines for Australian Aboriginal and Torres Strait Islander children: summary of recommendations. *Med. J. Aust.* **214**, 228–233. doi:10.5694/mja2.50953
13. James, S.L. *et al*. (2018) Global, regional, and national incidence, prevalence, and years lived with disability for 354 diseases and injuries for 195 countries and territories, 1990–2017: a systematic analysis for the Global Burden of Disease Study 2017. *Lancet* **392**, 1789–1858. doi:10.1016/S0140-6736(18)32279-7
14. Harding, G.K.M. and Ronald, A.R. (1994) The management of urinary infections – what have we learned in the past decade. *Int. J. Antimicrob. Agents* **4**, 83–88. doi:10.1016/0924-8579(94)90038-8
15. Australian Group on Antimicrobial Resistance (2019) Gram-negative Sepsis Outcome Program 2018 report. Australian Group on Antimicrobial Resistance: Sydney, NSW, Australia. https://www.safetyandquality.gov.au/publications-and-resources/resource-library/agar-sepsis-outcome-programs-2018-report (accessed 9 July 2021).
16. Jarvis, T.R. *et al*. (2014) Assessment and management of lower urinary tract infection in adults. *Aust. Prescr.* **37**, 7–9. doi:10.18773/austprescr.2014.002
17. Wawrysiuk, S. *et al*. (2019) Prevention and treatment of uncomplicated lower urinary tract infections in the era of increasing antimicrobial resistance – non-antibiotic approaches: a systemic review. *Arch. Gynecol. Obstet.* **300**, 821–828. doi:10.1007/s00404-019-05256-z
18. Forde, B.M. *et al*. (2019) Population dynamics of an *Escherichia coli* ST131 lineage during recurrent urinary tract infection. *Nat. Commun.* **10**, 3643. doi:10.1038/s41467-019-11571-5
19. Woodford, H.J. and George, J. (2009) Diagnosis and management of urinary tract infection in hospitalized older people. *J. Am. Geriatr. Soc.* **57**, 107–114. doi:10.1111/j.1532-5415.2008.02073.x
20. Statistics New Zealand (2019) Estimated total population by sex, year ended 31 December 1926–2018 and 30 June 1937–2018. Statistics New Zealand: Wellington, New Zealand. https://www.stats.govt.nz/topics/population (accessed 9 July 2021).
21. Australian Bureau of Statistics (2019) 'Table 59. Estimated resident population by single year of age, Australia' [time series spreadsheet], Australian demographic statistics. Australian Bureau of Statistics: Canberra, ACT, Australia. https://www.abs.gov.au/AUSSTATS/abs@.nsf/DetailsPage/3101.0Jun%202019 (updated 19 December 2019; accessed 9 July 2021).
22. European Centre for Disease Prevention and Control (2017) Antimicrobial resistance surveillance in Europe 2016: annual report of the European Antimicrobial Resistance Surveillance Network (EARS-Net). European Centre for Disease Prevention and Control: Stockholm, Sweden. https://www.ecdc.europa.eu/en/publications-data/antimicrobial-resistance-surveillance-europe-2016 (accessed 9 July 2021).
23. Australian Commission on Safety and Quality in Health Care (2016) Antimicrobial prescribing practice in Australian hospitals: results of the 2015 National Antimicrobial Prescribing Survey. Australian Commission on Safety and Quality in Health Care: Sydney, NSW, Australia. https://www.safetyandquality.gov.au/publications-and-resources/resource-library/antimicrobial-prescribing-practice-australian-hospitals-results-2015-hospital-national-antimicrobial-prescribing-survey (accessed 9 July 2021).
24. Laxminarayan, R. and Heymann, D.L. (2012) Challenges of drug resistance in the developing world. *BMJ* **344**, e1567. doi:10.1136/bmj.e1567
25. Laxminarayan, R. *et al*. (2013) Antibiotic resistance-the need for global solutions. *Lancet Infect. Dis.* **13**, 1057–1098. doi:10.1016/S1473-3099(13)70318-9
26. Organisation for Economic Co-operation and Development (2011) Health at a Glance 2011: OECD Indicators. Organisation for Economic Co-operation and Development Publishing: Paris, France. https://www.oecd-ilibrary.org/social-issues-migration-health/health-at-a-glance-2011_health_glance-2011-en (accessed 9 July 2021).

27. Williamson, D.A. *et al*. (2016) Antibiotic consumption in New Zealand, 2006–2014. The Institute of Environmental Science and Research Ltd: Porirua, New Zealand. https://surv.esr.cri.nz/surveillance/antibiotic_consumption.php?we_objectID=4331 (accessed 9 July 2021).

28. Heffernan, H. *et al*. (2006) Prevalence of extended-spectrum β-lactamases among urinary *Escherichia coli* and *Klebsiella* in New Zealand in 2006. Institute of Environmental Science and Research Ltd: Porirua, New Zealand. https://surv.esr.cri.nz/antimicrobial/esbl.php (accessed 9 July 2021).

29. Heffernan, H. *et al*. (2018) 2016 survey of extended-spectrum β-lactamase-producing *Enterobacteriaceae*. Antimicrobial Reference Laboratory and Health Group, Institute of Environmental Science and Research Ltd: Porirua, New Zealand. https://surv.esr.cri.nz/antimicrobial/esbl.php (accessed 9 July 2021).

Biography

Rhys White is working towards completing his PhD in Genomics and Bioinformatics at The University of Queensland, Australia. Rhys graduated with a BSc (Hons) from Cardiff University (United Kingdom) in 2016. Before commencing his PhD, Rhys started his career with Public Health Wales where he refined his analytical skills alongside clinicians. Rhys' research interests are in microbial genomics where he uses comparative genomic approaches to better understand the evolution, emergence, and dissemination of global Enterobacterales.

*MICROBIOLOGY AUSTRALIA, 2021, **42**, 110–115*
https://doi.org/10.1071/MA21033

Influenza B viruses: underestimated and overlooked

Marios Koutsakos[A,D] *and Stephen J Kent*[A,B,C]

[A]Department of Microbiology and Immunology, University of Melbourne, at the Peter Doherty Institute for Infection and Immunity, Melbourne, Vic. 3000, Australia
[B]Melbourne Sexual Health Centre and Department of Infectious Diseases, Alfred Hospital and Central Clinical School, Monash University, Melbourne, Vic. 3004, Australia
[C]ARC Centre for Excellence in Convergent Bio-Nano Science and Technology, University of Melbourne, Parkville, Vic. 3010, Australia
[D]Tel.: +61 3 9035 4179; Email: marios.koutsakos@unimelb.edu.au

Abstract. Influenza B viruses circulate globally every year causing respiratory disease with significant clinical and socio-economic impacts. IBV are considered exclusive human pathogens with no established animal reservoirs, which suggests with concerted effort it may be possible to eradicate this virus from human circulation. However, this requires a deeper understanding of IBV virology and immunology and the design of vaccines that induce universal immunity to antigenic variants of IBV.

Received 16 July 2021, accepted 19 August 2021, published online 6 September 2021

Introduction

Influenza A and B viruses (IAV and IBV) circulate annually causing seasonal epidemics around the world. Influenza viruses are single-stranded negative sense RNA viruses with segmented genomes belonging to the family of *Orthomyxoviridae*[1]. They replicate is the respiratory tract and cause influenza disease which can vary from asymptomatic and mild upper respiratory tract disease to severe lower respiratory tract disease and in some cases fatal disease[1]. Although IAV exists in a wide range of animal hosts, IBV does not have an established animal reservoir[2]. The potential of antigenically novel IAV viruses to 'jump' from animals into humans and cause severe disease, and is some instances global pandemics, has placed IAV in the spotlight. The lack of an established animal reservoir, and therefore lack of pandemic potential, for IBV has left this type of influenza virus considerably underestimated and overlooked. However, IBV has substantial health and socio-economic impacts annually. Additionally, the lack of an animal reservoir means that it may be possible to eradicate this virus from human circulation with highly effective, broadly protective vaccines and broad population coverage. To achieve that, a thorough understanding of IBV virology and immunology is needed.