COVID-19 restrictions limited interactions of people and resulted in lowered *E. coli* antimicrobial resistance rates

Peter Collignon (p) 1,2*, John Beggs³ and Jennifer Robson⁴

¹Microbiology Department, ACT Pathology, Canberra Hospital, Garran, Australia; ²Medical School, Australian National University, Canberra, Australia; ³Independent researcher, Melbourne, Australia; ⁴Microbiology and Molecular Pathology, Sullivan Nicolaides Pathology, Brisbane, Australia

Received 3 April 2024; accepted 5 July 2024

Background: Antibiotic resistance is rising globally and is a major One Health problem. How much person-to-person transmission or 'contagion' contributes to the spread of resistant strains compared with antibiotic usage remains unclear. As part of its COVID-19 response, Australia introduced strict people movement restrictions in early 2020. Along with internal lockdown measures, movement of people into Australia from overseas was severely restricted. These circumstances provided a unique opportunity to examine the association of people movements with changes in resistance rates.

Methods: Monthly resistance data on over 646 000 *Escherichia coli* urine isolates from 2016 till 2023 were modelled for statistical changes in resistance trends during pre-lockdown, lockdown and post-lockdown periods. Data were available for three clinical contexts (community, hospital and aged-care facilities). Data were also available for antibiotic usage volumes and movements of people into Australia.

Results: In 2020, arrivals into Australia decreased by >95%. Antibiotic community use fell by >20%. There were sharp falls in trend rates of resistance for all antibiotics examined after restrictions were instituted. This fall in trend rates of resistance persisted during restrictions. Notably, trend rates of resistance fell in all three clinical contexts. After removal of restrictions, an upsurge in trend rates of resistance was seen for nearly all antibiotics but with no matching upsurge in antibiotic use.

Conclusions: Restricting the movement of people appeared to have a dramatic effect on resistance rates in *E. coli.* The resulting reduced person-to-person interactions seems more closely associated with changes in anti-biotic resistance than antibiotic usage patterns.

Introduction

Antimicrobial resistance (AMR) has been rising globally for decades, including in Australia. Numerous factors are associated with, or implicated in, this rise. Essentially there are two main factors that drive increasing AMR levels. These are the volume of antibiotics used, and the spread of resistant bacteria from person to person and through the environment (e.g. via water, food and animals). ^{1–5} We call the latter 'contagion'. It has been repeatedly shown that resistant bacteria readily spread globally, with travel a major factor in this spread. ^{1–7}

Escherichia coli is the most common cause of serious bacterial infections in people. On a global scale, E. coli and the resistance

genes carried can spread widely. Poor sanitation and poor drinking water quality are major factors facilitating this spread. Travellers have higher carriage rates of resistant $E.\ coli$, particularly after visiting areas with poor infrastructure and sanitation. Carriage of these resistant bacteria can persist for 6 months or more, and potentially also spread to other people. $^{1-10}$

E. coli spreads readily within and between different sectors (people, animals and ecosystems). It is an important AMR indicator in the context of a One Health approach when it comes to better managing and controlling the development and spread of AMR at global and local levels.¹¹

The importance of infection control and prevention in limiting the infectious spread of resistant microbes is well established at the

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microlevel of the individual hospital. However, when the discussion of infection control is framed in the context of total socioeconomic systems such as nations, little is known that can inform public policy. Unanswered questions remain about the scale of importance of 'contagion' compared with antibiotic usage.

Australia, as part of its COVID-19 pandemic response, put in place restrictions in early 2020, including severe restrictions to limit the number of returning citizens and residents. Few non-Australian citizens or permanent residents were allowed entry. This resulted in a marked reduction (>95%) in the number of people coming into Australia compared with 2019. Additionally, nearly all persons entering Australia went into hotel quarantine for 14 days, and so prevented any returning traveller having any interactions in the community for that period. International borders were not formally reopened until 21 February 2022 (for fully vaccinated visa holders). Furthermore, State governments introduced extensive State border closures, regional quarantines, and other lockdowns measures such as stay-at-home orders, essential-worker-only orders and school closures. 12-14

There was ongoing debate and uncertainty as to whether COVID-19 would cause an increase in resistance levels because of a link with the potential increased use of antibiotics and excessive demand on healthcare infrastructure. ^{5,15–21} Compared with Australia, resistance rates are much higher in most other countries, especially in Asia. We hypothesized previously in this journal that once major COVID-19 restrictions were in place that stopped the movement of travellers entering countries that have higher socioeconomic status, safe water and good health infrastructure, that a lowering of resistance rates of *E. coli* would occur. ²¹

The stringent restrictions put in place in early 2020 created a unique natural experiment to investigate the relative role of contagion: were restrictions that reduced people movement associated with changes in antibiotic resistance rates?

Methods

E. coli susceptibility data from a large private pathology company (Sullivan Nicolaides Pathology) based in Queensland, but also servicing northern New South Wales (NSW), were analysed on a month-by-month basis on urine isolates. To avoid any selection bias, all the following routinely tested antibiotics were examined: amoxicillin, cefalexin, cefpodoxime, ciprofloxacin, ceftriaxone, co-trimoxazole, gentamicin, nitrofurantoin and trimethoprim. Although susceptibility data for amoxicillin/ clavulanic acid were reported, due to changes in antibiotic formulation and supply shortage of test cards, protocols were changed in March 2021, the middle of the lockdown period, making reliable time series comparisons unusable for that antibiotic. These antibiotics were chosen as, in the main, they are generally recommended for empirical treatment of UTIs. Cefpodoxime is used as a screen to detect ESBL production and hence the requirement for extended susceptibility testing for more resistant organisms.

Resistance data are available separately for three different contexts, namely aged-care facilities, hospitals and the community. This makes it possible to identify differences in resistance profiles and possible changes in rates among these different clinical usage contexts.

People movement restrictions were categorized into three time periods. Estimates reported here adopt March 2020 as the commencement of lockdown/travel restrictions, and January 2022 as the start of the post-lockdown/restrictions period. Results are not materially sensitive to moving these dates 1 month either way.

Data on *E. coli* resistance, respiratory virus numbers, antibiotic usage volumes and overseas traveller numbers are publicly available. ^{14,22,23}

It is not sufficient to simply examine average resistance rates in the three subperiods, pre-COVID-19, lockdown and post-lockdown. For example, if resistance rates trend up, then trend down, then trend up again, the average rates of resistance may look very similar in all three time periods. In this situation, subperiod average rates of resistance do not reveal the underlying changes taking place.

This paper explicitly models and examines the trends in antibiotic resistance of *E. coli* before, during and after the COVID-19 lockdown/border closure periods for Australia. Data are monthly percent of isolates testing resistant to each drug. The time series relationship can be expressed as:

Resistance =
$$\beta_0 + \beta_1 t_{All} + \beta_2 t_{Lockdown} + \beta_3 t_{Post\ Lockdown}$$

The trend variable $t_{\rm All}$ is the time measured in months from the start of the sample, $t_{\rm Lockdown}$ is the time measured in months from the start of lockdown and zero before lockdown, and $t_{\rm Post\ Lockdown}$ is the time measured in months from the end of lockdown and zero before the end of lockdown.

The model is illustrated in Figure 1. The coefficient β_0 is the regression intercept term and corresponds to the point value of the resistance rate in the month before the start of the sample, that is $t_{All}\!=\!0$. The coefficient β_1 is the pre-COVID-19 monthly trend in resistance, β_2 is the change in the monthly trend during the lockdown, and β_3 is the subsequent change in monthly trend after lifting lockdowns. The lockdown period has been treated as spanning the period from March 2020 until and including December 2021. Coefficients and P values were estimated by the ordinary least squares method.

Pre-COVID-19, and in line with global trends, a rising resistance trend is expected for many drugs ($\beta_1 > 0$). However, effective antimicrobial stewardship programmes are expected to have also created falling resistance ($\beta_1 < 0$) in some drugs and in some clinical contexts.

The trend in AMR is expected to improve (β_2 < 0) if domestic and international travel restrictions are imposed, as this will limit the opportunity for the introduction and spread of both resistant novel strains and those carrying known resistance. If resistance had been rising prior to lockdowns, the implementation of lockdown measures is likely to cause it to rise more slowly or to revert to a falling trend. Resistance is predicted to continue falling during lockdown, albeit more quickly than it did before. If resistance had been rising pre-lockdown, it is expected to rise more slowly or reverse to a falling trend. If resistance had been falling pre-lockdown it is expected to continue falling but at a faster rate during lockdown.

Post-lockdown, the increase in international and domestic travel is postulated to cause a deterioration (i.e. a rise) in the trend rate of resistance ($\beta_3 > 0$).

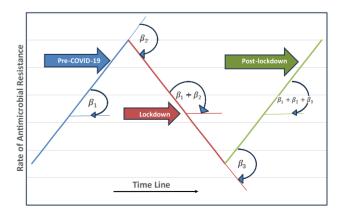


Figure 1. Illustration of role of model coefficients describing the trend.

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Table 1. Mean average monthly sample sizes and average resistance rates of *E. coli* by clinical context and drug (2016 to 2023)

	Average monthly isolates tested			Average monthly resistance rate (%)			
Drug	Aged care	Community	Hospital	Aged care	Community	Hospital	
Amoxicillin	292	6019	423	47.2	40.8	46.5	
Cefalexin	290	5987	368	13.8	7.6	13.4	
Cefpodoxime	216	3460	231	11.2	6.2	10.7	
Ceftriaxone	123	2977	411	23.5	9.7	10.7	
Ciprofloxacin	292	6014	423	14.6	8.9	13.7	
Co-trimoxazole	292	6015	423	24.9	20.7	23.7	
Gentamicin	123	2982	411	12.8	5.9	6.9	
Nitrofurantoin	292	6011	410	1.7	0.7	1.0	
Trimethoprim	292	6015	410	28.5	23.2	26.2	

Results

Antibiotic resistance rates

Resistance data were available monthly from January 2016 until mid-December 2023. In total, 646439 *E. coli* urine isolates were examined (577817 from the community, 40600 from hospitals and 28022 from the aged-care sector). Their average resistance rates are given in Table 1. Resistance rates for all antibiotics were much higher in the aged-care sector and lowest in the community.

Results for the estimated trend coefficients using the ordinary least squares methods are summarized in Table 2 and discussed below. For clarity, it is beneficial to start by looking at the model estimates in the context of a single drug example before looking at the overall findings. Let's examine cefalexin use in aged-care facilities as an example (see Figure 2). Prior to the lockdowns, resistance to this drug was rising ($\beta_1 > 0$) at a rate of 0.035% per month. After lockdowns/restrictions introduction in early 2020, the relative resistance trend improved ($\beta_2 < 0$) by -0.172% per month. This change was large enough to cause absolute resistance rate then to trend down ($\beta_1 + \beta_2 < 0$) at -0.138% per month. With the end of lockdowns at the end of 2021, the relative resistance trend worsened ($\beta_3 > 0$) by 0.311% per month. This post-lockdown change was large enough to cause the absolute resistance rate trend to head up again $(\beta_1 + \beta_2 + \beta_3 > 0)$ at 0.173% per month. In this instance, the post-lockdown resistance was rising at a higher rate than it had been pre-lockdown. The graphs showing these trends for cefalexin and all other antibiotics and in all clinical contexts are in the Supplementary data, available at JAC-AMR Online.

Pre-lockdown estimated trends in resistance (β_1) are shown in Table 2 (column 3), for each drug and clinical context. Of the 27 instances, 7 cases showed falling resistance rates in the pre-COVID-19 period, but only in 1 of these cases, amoxicillin in community context, was the improvement statistically significantly different from zero change. Amoxicillin is a widely used first-line drug in general practice clinics, and recent programmes to improve stewardship in community clinics may have been showing signs of success. Of the remaining 21 instances in the pre-lockdown period that showed resistance rates rising, 11 were statistically significant rises in resistance (P < 0.05).

During lockdown, estimated changes in the direction of resistance during lockdowns (β_2) are shown in Table 2 (column 4). Results show that the AMR trend improved for all nine antimicrobials

and for all three clinical contexts (i.e. hospital, aged-care facility and community). Furthermore, the changing trend was statistically significant in 21 of the 27 drug and clinical contexts analysed.

Post lockdown, all 27 cases in Table 2 (column five) showed a worsening of the trend rate of resistance ($\beta_3 > 0$). In 24 cases, this worsening change in the trend rate of resistance was significantly different from zero. Clearly, post lockdown, and with the return of international travellers, resistance rates quickly started rising again and generally at more rapid rates than pre-COVID-19. Interestingly, amoxicillin, which showed the largest improving trend rate of resistance during the lockdown period (-0.219% per month), also had the largest rising trend rate of resistance post-lockdown (+0.388%)

Summarized overall results by drug and clinical environment are in Tables 3 and 4, which show simple group averages of the estimated trend coefficients. The first column shows the monthly percentage point trend in resistance—overall about 0.023% increase per month. The second column shows the change in the trend rate during lockdown—overall about a 0.136% decrease per month. The third column shows the change in the trend rate that occurred post lockdown—an increase of 0.271% per month.

Overseas arrivals into Australia

Figure 3 displays data indicating the significant decrease of more than 95% in foreign arrivals into Australia during the COVID-19 lockdown period. Overseas arrivals into Australia fell initially by 41% between February and March 2020 after visitor restrictions were placed on countries with known COVID-19 outbreaks, then on 20 March 2020, Australian borders were closed to all noncitizens and non-residents.

In the post-lockdown period, domestic travel increased slowly from the fourth quarter of 2021. International arrival numbers began to increase from November and December 2021. International borders were not formally reopened until 21 February 2022 (for fully vaccinated visa holders).

For our analysis, we adopted January 2022 as the start of the post-lockdown period.

Antibiotic use

For Australia, community antibiotic use per 1000 people dropped by over 20% in 2020 compared with 2019 (see Figure 4). There had been already a steady decrease in antimicrobial prescriptions

Table 2. Estimated coefficients of monthly trends in rate of resistance for each drug by clinical context

	Drug	Trend bet		Change in tr start of lock		Change in t		Trend dur lockdow	_	Trend aft lockdow	
Clinical context	Drug	β_1		β_2		β_3		$\beta_1 + \beta_2$		$\beta_1 + \beta_2 + \beta_3$	
Aged-care facility	Amoxicillin	0.003		-0.171	*	0.307	*	-0.169	*	0.139	*
Aged-care facility	Cefalexin	0.035		-0.172	*	0.311	*	-0.138	*	0.173	*
Aged-care facility	Cefpodoxime	0.005		-0.069		0.219	*	-0.064		0.155	*
Aged-care facility	Ceftriaxone	0.051		-0.235	*	0.587	*	-0.184	*	0.403	*
Aged-care facility	Ciprofloxacin	0.041		-0.113		0.255	*	-0.072		0.183	*
Aged-care facility	Co-trimoxazole	-0.025		-0.177	*	0.498	*	-0.202	*	0.296	*
Aged-care facility	Gentamicin	0.105	*	-0.165	*	0.219	*	-0.060		0.158	*
Aged-care facility	Nitrofurantoin	0.005		-0.044	*	0.031		-0.039	*	-0.008	
Aged-care facility	Trimethoprim	-0.021		-0.169	*	0.503	*	-0.190	*	0.313	*
Community	Amoxicillin	-0.026	*	-0.222	*	0.462	*	-0.248	*	0.214	*
Community	Cefalexin	0.028	*	-0.100	*	0.165	*	-0.072	*	0.093	*
Community	Cefpodoxime	0.030	*	-0.081	*	0.165	*	-0.051	*	0.114	*
Community	Ceftriaxone	0.041	*	-0.155	*	0.363	*	-0.114	*	0.249	*
Community	Ciprofloxacin	0.060	*	-0.118	*	0.229	*	-0.057	*	0.172	*
Community	Co-trimoxazole	-0.006		-0.150	*	0.332	*	-0.156	*	0.176	*
Community	Gentamicin	0.037	*	-0.114	*	0.222	*	-0.077	*	0.145	*
Community	Nitrofurantoin	-0.003		-0.010		0.010		-0.013		-0.002	
Community	Trimethoprim	0.000		-0.166	*	0.358	*	-0.166	*	0.192	*
Hospital	Amoxicillin	0.035		-0.265	*	0.396	*	-0.231	*	0.165	*
Hospital	Cefalexin	0.052	*	-0.197	*	0.281	*	-0.145	*	0.136	*
Hospital	Cefpodoxime	0.037	*	-0.184	*	0.348	*	-0.147	*	0.201	*
Hospital	Ceftriaxone	0.045	*	-0.145	*	0.203	*	-0.100	*	0.103	*
Hospital	Ciprofloxacin	0.087	*	-0.160	*	0.218	*	-0.073		0.145	*
Hospital	Co-trimoxazole	-0.016		-0.086		0.233	*	-0.102	*	0.131	*
Hospital	Gentamicin	0.028	*	-0.076	*	0.138	*	-0.048		0.090	*
Hospital	Nitrofurantoin	0.000		-0.025		0.040		-0.024	*	0.016	
Hospital	Trimethoprim	-0.001		-0.111		0.215	*	-0.112	*	0.103	

^{*}Indicates statistical significance at 95% confidence level. *P* values are calculated for the null hypothesis of coefficient (or relevant sum of coefficients) to equal to zero against the alternative hypothesis they are not equal to zero. Numerical values are shown in Supplementary data Tables.

per 1000 people prior to 2019. There was a further slight fall in 2021 compared with 2020. Antibiotic use in 2023 appears similar to use in 2022 and remained lower than the usage in 2019. ^{22,24,26}

Community usage data in different states in Australia are available.²² In Queensland (from where most of the resistance data used in this study are derived), usage rates dropped by just over 20% from 2019 to 2020. Usage rates remained at a slightly lower level in 2021 and rose slightly in 2022 (at around 800 prescriptions per 1000 people).²²

In Australia, the number of antimicrobial prescriptions supplied under the Pharmaceutical Benefits Scheme (PBS) and Repatriation PBS (RPBS) decreased by 25.3% from 2019 to 2021, while it increased by almost 10% from 2021 to 2022.²²

Hospital use of antibiotics fell slightly (3.5%) in 2020 for inpatients, compared with 2019 [from 893.5 to 862.0 DDDs/1000 occupied bed days (OBDs)] but increased by about 6% in 2021 (to 906 DDDs/1000 OBDs) compared with 2019. Antibiotic use in hospitals in Australia had been rising slightly per OBDs per year from 2017 to 2019 (see details in Supplementary data).

For the aged-care sector, data are not as robust as for the community and hospital sectors. But prescription per aged-care resident

appears to have risen during the lockdown period (see Figure S5) but this was mainly driven by an increased use of topical antifungals (clotrimazole). The percentage of residents prescribed an antimicrobial in 2020 were higher compared with 2019 and rose again in 2021. The use of oral systemic antibiotics, however, was likely similar from 2019 to 2022 (see Supplementary data). 22,27

Discussion

Antibiotic resistance rates were rising prior to the COVID-19 period. There were then dramatic decreases in the trend rate of resistance of *E. coli* during the lockdown periods, but followed by rapid increases in the rate after the COVID-19 lockdown periods ended in Australia. This pattern was seen in all the antibiotic resistance rates analysed and coincided with the introduction of travel and other restrictions in Australia in March 2020. These results are strong evidence that the lockdown period had the powerful effect of improving the trend rate of resistance for *E. coli*. We therefore conclude that those restrictions were an important contributor to the major recent changes in trend rates of resistance seen in Australia in *E. coli*.

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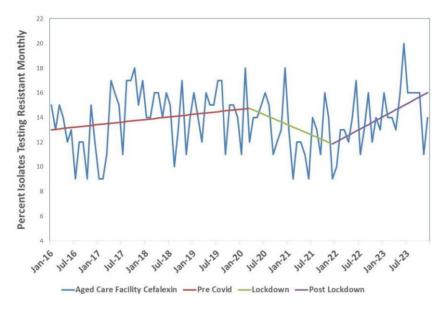


Figure 2. AMR rate of E. coli isolates for cefalexin in aged-care facilities and fitted trends.

Table 3. By clinical context: average across all nine drugs of estimated coefficients of monthly trends in rate of resistance

	Trend before lockdown	Change in trend at start of	Change in trend at end of	Trend during lockdown	Trend after lockdown
Clinical	tochdown	tochdown	tochdown	tochdown	$\beta_1 + \beta_2 +$
Context	β_1	β_2	β_3	$\beta_1 + \beta_2$	β3
Aged-care facility	0.022	-0.146	0.325	-0.124	0.201
Community	0.018	-0.124	0.256	-0.106	0.150
Hospital	0.030	-0.139	0.230	-0.109	0.121
Overall average	0.023	-0.136	0.271	-0.113	0.158

There were many factors that will have influenced the AMR levels seen in Australia after restrictions were introduced and these confounders make cause and effect more difficult to ascertain. The most obvious factor was the marked 95% reduction in overseas travellers and returning residents into Australia. But there was also less movement of people within Australia following state and territory border restrictions occurring at various times, and different movement restrictions within States themselves including lockdowns. 12-14 The prolonged closures of places where people more frequently gather, such as clubs, bars, restaurants etc., also decreased interactions among people.

Data also suggest there was a large fall (over 20%) in antibiotic usage in the community during this period, likely because of lower numbers of respiratory infections overall, lower numbers of people visiting doctors and because of the increased use of telemedicine, all of which are associated with lower numbers of antibiotic prescriptions on a population basis. There were many fewer respiratory infections seen during the winters of 2020 and 2021.

There was no influenza transmission in the community during those winters in Australia. The small number of influenza diagnoses occurred almost entirely in returning visitors whilst in quarantine. Other respiratory viruses (except for rhinovirus) also had dramatic reductions, including parainfluenza virus, adenovirus, human metapneumovirus and respiratory syncytial virus (RSV). ^{23,28} This meant for at least the first year after April 2020, there were fewer presentations to doctors for respiratory tract infections and therefore fewer antibiotics prescribed per patient visit.

Of note, we saw a drop in resistance during the lockdown period, not only in community isolates but also in hospital and aged-care facility isolates (and where resistance rates were much higher). This was despite likely unchanged systemic oral antibiotic usage during the lockdown period in aged care, and increased use in hospitals in 2021 (see Figures S4 and S5).^{22,25,27}

Pre-lockdown, community antibiotic use was decreasing, but conversely resistance was increasing. Post-lockdown, community antibiotic usage did not rise markedly but again, conversely resistance rates rapidly rose and at an even steeper rate than was occurring in the pre-lockdown period. These inconsistencies in the rates of rise or fall in resistance rates, with rises and falls in antibiotic usage, imply that changes in antibiotic usage were not the main factor behind the changes seen in the *E. coli* resistance levels in our study.

Not many studies have looked at the impact of changes in antibiotic resistance rates or trends in *E. coli* associated with decreases in antibiotic usage on a population basis. In two studies (one in Scotland and another in England), ^{29,30} there were no falls seen in antibiotic resistance after reductions in antibiotic usage. What was seen was just a reduction in the rate of rise of resistance. Another study modelled what the effects of usage and then decreases in antibiotic usage would have on a population basis in the EU. It showed that a decrease in usage had little identifiable impact, even over a period of 4 years.³¹

Those results are in marked contrast to this current study where, following lockdowns, not only was there a sharp fall in

Table 4. By drug: average across all three clinical contexts of estimated coefficients of monthly trends in rate of resistance	Table 4. By	v drua: average across	all three clinical contexts	of estimated coefficients of	f monthly trends in rate of resistance
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Drug	Trend before lockdown eta_1	$\frac{\text{Change}}{\text{lockdown}} \text{ in trend at start of } \\ \text{lockdown}$ β_2	<u>Change</u> in trend at end of lockdown β ₃	Trend during lockdown $\beta_1 + \beta_2$	Trend after lockdown $\beta_1 + \beta_2 + \beta_3$
Amoxicillin	0.004	-0.219	0.388	-0.216	0.172
Cefalexin	0.038	-0.157	0.252	-0.118	0.134
Cefpodoxime	0.024	-0.111	0.244	-0.087	0.157
Ceftriaxone	0.046	-0.178	0.384	-0.133	0.252
Ciprofloxacin	0.063	-0.130	0.234	-0.067	0.167
Co-trimoxazole	-0.016	-0.137	0.354	-0.153	0.201
Gentamicin	0.057	-0.119	0.193	-0.062	0.131
Nitrofurantoin	0.001	-0.026	0.027	-0.025	0.002
Trimethoprim	-0.007	-0.148	0.358	-0.156	0.202
Overall average	0.023	-0.136	0.271	-0.113	0.158

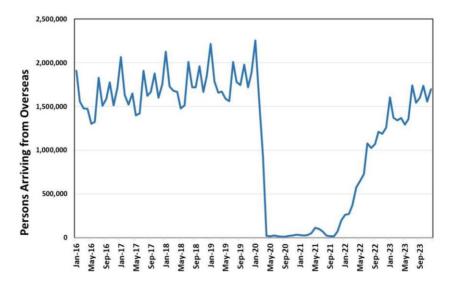


Figure 3. Monthly overseas arrivals into Australia (January 2016 to December 2023).

the trend rate of resistance, the net trend rate of resistance after lockdown ($\beta_1 + \beta_2$) became negative for all drugs in all clinical contexts. The average trend rate fell from 0.023% per month prelockdown to -0.136% post-lockdown, which equals -0.107% per month or approximately -1.3% per annum.

Following the lifting of lockdowns, not only was there a sharp rise in the trend rate of resistance, the net trend rate of resistance after lockdown ended ($\beta_1+\beta_2+\beta_3$) became positive for 25 of the 27 drug and clinical context combinations (the exception was nitrofurantoin in aged-care and community sectors). The simple average trend rate for all antibiotics went from -0.107% per month during lockdown up to a post-lockdown rate of 0.023% -0.136%+0.271, which equals +0.164% per month or approximately an increase in the rate of resistance of 1.9% per annum.

There are many limitations to our study. We only examined *E. coli* and so these results may not be the same as for other common bacteria e.g. *Staphylococcus aureus*. We have looked at bug–drug combinations for *E. coli* but these can't be interpreted as applying to bacteria we haven't examined. We only have data for Queensland

and northern NSW, so this may not be the same for other parts of Australia, other fully developed countries and in particular less developed countries. The largest percentage reduction in movements of people were on people entering Australia. However, there were also frequent and extended State border closures that severely restricted the internal movements of Australian residents. How much this contributed to the changes in resistance rates seen compared with international travellers, we can't determine.

However, taken together our results suggest that restrictions on the movements of people, especially on people entering Australia from overseas, were much more likely to be the major factor in the fall in resistance rates seen in Australia during the COVID-19 restrictions period, rather than changes in antibiotic usage volumes. The rapid rise in resistance seen commencing in 2022 once these restrictions were removed, but without a major rise in community antibiotic use from 2021 compared with 2022, also suggests that movement of people was a bigger factor for this rise in resistance rates seen, rather than antibiotic usage changes in the community. Plus, we saw drops in rates of

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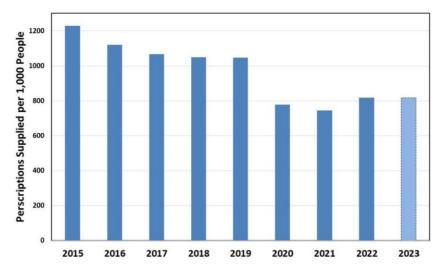


Figure 4. Community antimicrobial prescriptions supplied per age-standardized 1000 people. Data used are from Analysis of 2015–2022 PBS and RPBS Antimicrobial Dispensing Data, Australian Commission on Safety and Quality of Health Care October 2023 (Figure 3.22).²² Data for 2023 are an annualized pro rata estimate based on the first 8 months of 2023 compared with the same period in 2022 and scaled for Australian Bureau of Statistics estimate on population growth. Data for 2023 extracted from PBS and RPBS Section 85.^{24,25}

antibiotic resistance in the hospital and aged-care sector despite apparent increases or no changes in systemic antibiotic usage volumes, respectively. However, unravelling the exact magnitude and relative different contributions will require further study.

In conclusion, we saw a major drop in resistance levels in *E. coli* isolates following the introduction of movement and other restrictions because of COVID-19. Community antibiotic usage also dropped during these restrictions. However, we think this decrease in resistance is more likely related to less person-to-person transmission, through the infection prevention effects of the restrictions and in the major limitation of overseas travellers coming into Australia, rather than a direct effect of antibiotic usage changes because we also saw drops in resistance rates in the hospitals and aged-care sectors, despite no decreases in antibiotic use volumes. Conversely, when lockdown restrictions were removed, resistance rates spiked in all three sectors, and this happened at a time when very little more antibiotic was being used.

Acknowledgements

We would like to thank Dr Nadine Hillock and the NAUSP team for assistance with access and interpretation of recent hospital usage data and to Professor Christina Vandenbroucke-Grauls for very helpful critiques on the draft of our paper.

Funding

This study was supported by internal funding.

Transparency declarations

P.C. is Chair of Healthcare Associated Infection Expert group with the Australian Commission on Safety and Quality in Healthcare, both on infection control issues and antibiotic resistance and usage; he is also a member of the Infection Control Expert Group (ICEG) that provided advice

on infection control and prevention issues to Australian Government bodies, Federal Health department and Chief Health Officers during the COVID-19 pandemic from 2020 to 2022. J.B. and J.R.: no conflicts to declare.

Author contributions

The study was conceived and planned by all three authors (P.C., J.B. and J.R.). J.R. obtained the resistance data in a monthly format. Statistical analysis, and compilation of tables and figures were done by J.B. Interpretation of results was done by all three authors. The paper was written up by all three authors.

Supplementary data

Figures S1 to S5 and Tables S1 to S3 are available as Supplementary data at JAC-AMR Online.

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