Prescribing Antimicrobial Drugs for Acute Gastroenteritis, Primary Care, Australia, 2013–2018

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Learning Objectives

Upon completion of this activity, participants will be able to:

- Distinguish the rate of antibiotic prescriptions for AGE in the current study
- Assess variables associated with higher rates of antibiotic prescriptions for AGE
- Analyze trends in antibiotic prescribing for AGE
- Identify the most common antibiotic class prescribed in cases of AGE

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During 2013–2018, antimicrobial drugs were prescribed for 6.8% of cases of acute gastroenteritis encountered in general practice in Australia, including 35.7% of *Salmonella* infections and 54.1% of *Campylobacter* infections. During that time, prescriptions for acute gastroenteritis decreased by 2.0%. Managing infectious gastroenteritis in general practice will require greater antimicrobial stewardship.

Worldwide every year, acute gastroenteritis causes a loss of ≈89.5 million disability-adjusted life-years and 1.45 million deaths (*1*). In 2010, an estimated 16.6 million persons in Australia (population 22 million [*2*]) were affected, and ≈1.1 million of these persons sought care at a general practice (*3*,*4*). The most common cause of acute gastroenteritis is viral infection; therefore, antimicrobial drugs are not routinely recommended (*5*–*7*). Even for some common bacterial causes of acute gastroenteritis (e.g., nontyphoidal *Salmonella* and *Campylobacter* infections), antimicrobial therapy is not required for most patients because these infections are usually self-limiting (*8*).

Overuse of antimicrobial drugs for treating upper respiratory tract infections (mostly caused by viruses) has been well described (*9*,*10*) but not as much for acute gastroenteritis (*11*). Knowing the extent and pattern of antimicrobial drug use for acute gastroenteritis can help determine whether interventions to improve antimicrobial drug use for this specific clinical scenario are warranted.

We examined prescription of antimicrobial drugs for acute gastroenteritis in primary care practice in Australia during 2013–2018. The study was approved by the MedicineInsight Independent External Data Governance Committee (reference no. 2019-030: December 23, 2019) and the University of New South Wales Human Research Ethics Committee (no. HC190886).

The Study

We extracted clinical encounters for cases (including multiple episodes/patient) of acute gastroenteritis, nontyphoidal *Salmonella* infection, and *Campylobacter* infection recorded by MedicineInsight, a national primary healthcare database in Australia (https://www.nps.org.au/medicine-insight) during 2013–2018 and examined whether an antimicrobial drug was prescribed on the day of diagnosis (Appendix, https://wwwnc.cdc.gov/EID/article/27/5/20-3692-App1.pdf). Antimicrobial drugs were prescribed for 6.8% (6,652/98,496) of cases of acute gastroenteritis, including 35.7% (391/1,096) cases of nontyphoidal *Salmonella* infection and 54.1% (1,066/1,969) cases of *Campylobacter* infection.

Antimicrobial drug prescriptions for acute gastroenteritis increased with patient age (<10 years, 3.8%; ≥65 years, 13.7%) (Table 1). Antimicrobial drugs were more likely to be prescribed for those with than without the following: fever or no temperature measurement, a requested fecal sample test, underlying conditions, or a record of bacterial or parasitic infection. Antimicrobial drugs were less likely to be prescribed for those with a record of viral infection. Prescribing also differed by practice remoteness; prescribing was higher in practices in more remote areas than in cities. During the study period, the trend toward antimicrobial drug prescribing decreased from 7.8% to 5.8% (p<0.001). Similar findings were observed for children <10 years of age (Appendix Table 1).

The greatest reductions in antimicrobial drug prescriptions were found for those ≥65 years of age (2.8% absolute reduction from 13.4% to 10.6% (p = 0.049). The next greatest reductions were for those 30–49 years of age (2.4% absolute reduction from 8.3% to 5.9%; p = 0.006), 10–29 years (from 6.7% to 4.8%; p<0.001), and <10 years (from 4.8% to 3.0%; p = 0.03) (Figure 1).

For patients with nontyphoidal *Salmonella* infection (Appendix Table 2), prescriptions for antimicrobial drugs were more likely for those 30–49 than those <10 years of age (41.7% vs. 34.1%; p = 0.02) and in practices in outer regional or remote areas than in cities. Trend analysis of antimicrobial drug prescriptions for patients with nontyphoidal *Salmonella* infection suggested a significant reduction; absolute reduction was 11.4% (from 42.1% in 2013 to 30.7% in 2018; p = 0.01). For patients with *Campylobacter* infection (Appendix Table 3), antimicrobial drugs were more likely to be prescribed for female than male patients (56.8% vs. 51.7%; p = 0.02). We observed no significant reduction in antimicrobial drug prescriptions for patients with *Campylobacter* infection (55.8% to 57.1%; p = 0.81).

Of the 6,652 acute gastroenteritis cases for which antimicrobial drugs were prescribed, a reason was recorded for 42.9% (2,854/6,652), including 80.4% (2,295/2,854) for acute gastroenteritis, 1.1% (30/2,854) for other gastrointestinal illnesses, 5.7% (162/2,854) for respiratory tract infections, 1.8% (50/2,854) for urinary tract infections, and 11.1% (317/2,854) for other reasons. Of the 6,652 acute gastroenteritis cases for which antimicrobial drugs were prescribed, 7,159 prescriptions were written: 1 for 92.9% (6,179/6,652) of cases and ≥2 (range 2–5) for 7.1% (473/6,652). The predominant class of drug prescribed for acute gastroenteritis

was nitroimidazoles (41.6% of total; Table 2), of which metronidazole accounted for the most prescriptions (24.7% of total; Appendix Table 4).

Prescriptions of cephalosporins, quinolones, and nitroimidazoles decreased significantly over the study period (Figure 2). The greatest reduction was for nitroimidazoles (absolute reduction from 3.9% to 2.3%; p = 0.001), followed by quinolones (1.3% to 0.8%; p = 0.02) and cephalosporins (0.7% to 0.5%; p = 0.049). However, prescriptions of macrolides increased significantly (0.6% to 1.0%; p = 0.01).

For the 391 cases of nontyphoidal *Salmonella* infection, a total of 418 prescriptions were written: 1 for 93.1% (364/391) and 2 for 6.9% (27/391). No dominant antimicrobial drugs were prescribed for patients with nontyphoidal *Salmonella*; most commonly prescribed were quinolones (30.4% of total; Table 2). For 1,066 cases of *Campylobacter* infection, 1,165 prescriptions were written: 1 for 91.0% (970/1,066) and ≥2 (range 2–4) for 9.0% (96/1,066). The predominant antimicrobial drugs prescribed for *Campylobacter* infections were macrolides (70.9%

Table 1. Proportion of cases of acute gastroenteritis for which antimicrobial drugs were prescribed overall and according to various characteristics, Australia, 2013–2018

Characteristic	No. prescriptions/no. cases (%)	Adjusted odds ratio (95% CI)	p value*
Overall	6,652/98,496 (6.8)		
Age, y			
<10	762/20,130 (3.8)	Referent	
10–29	1,774/30,695 (5.8)	1.56 (1.42–1.71)	<0.001
30–49	2,065/29,315 (7.0)	1.87 (1.71–2.05)	<0.001
50–64	1,093/11,369 (9.6)	2.46 (2.21–2.73)	<0.001
≥65	958/6,987 (13.7)	3.27 (2.88–3.71)	<0.001
Sex			
M	3,098/47,892 (6.5)	Referent	
F	3,554/50,604 (7.0)	1.02 (0.97–1.08)	0.41
Aboriginal or Torres Strait Islander			
No	5,076/74,978 (6.8)	Referent	
Yes	145/2,516 (5.8)	0.98 (0.82–1.17)	0.82
Unknown	1,431/21,002 (6.8)		
Concession card holder			
No	3,447/56,841 (6.1)	Referent	
Yes	1,820/22,177 (8.2)	1.04 (0.97–1.12)	0.31
Unknown	1,385/19,478 (7.1)		
Fever, temperature >38.5°C			
No	1,748/30,312 (5.8)	Referent	
Yes	71/566 (12.5)	2.75 (2.09–3.60)	<0.001
Not recorded	4,833/67,618 (7.1)	1.14 (1.07–1.21)	<0.001
Fecal sample test requested			
No	4,832/86,085 (5.6)	Referent	
Yes	1,820/12,411 (14.7)	2.75 (2.58–2.92)	<0.001
Etiology			
Not recorded	5,820/79,799 (7.3)	Referent	
Viral	342/17,896 (1.9)	0.30 (0.27–0.34)	<0.001
Bacterial	483/790 (61.1)	19.49 (16.66–22.80)	<0.001
Parasitic	7/11 (63.6)	24.12 (6.22–93.59)	<0.001
Underlying conditions†			
No	5,314/85,970 (6.2)	Referent	
Yes	1,338/12,526 (10.7)	1.09 (1.00–1.19)	0.04
No visits to general practitioner in past year			
0–7	5,000/74,630 (6.7)	Referent	
8–14	950/14,332 (6.6)	1.02 (0.94–1.10)	0.60
≥15	702/9,534 (7.4)	0.95 (0.86–1.04)	0.28
Remoteness of practice			
Major city	4,421/69,557 (6.4)	Referent	
Inner regional	1,172/16,438 (7.1)	0.97 (0.90–1.04)	0.35
Outer regional or remote	1,059/12,501 (8.5)	1.21 (1.12–1.30)	<0.001
Year of diagnosis			
2013	1,238/15,845 (7.8)	Referent	
2014	1,258/16,681 (7.5)	0.92 (0.84–1.00)	0.046
2015	1,165/16,912 (6.9)	0.84 (0.77–0.92)	<0.001
2016	1,143/17,613 (6.5)	0.77 (0.71–0.84)	<0.001
2017	1,008/16,995 (5.9)	0.71 (0.65–0.78)	<0.001
2018	840/14,450 (5.8)	0.71 (0.65–0.78)	<0.001

*Adjusted for all variables listed in the table.
†Any medical history of diabetes mellitus, arthritis, or chronic kidney disease.

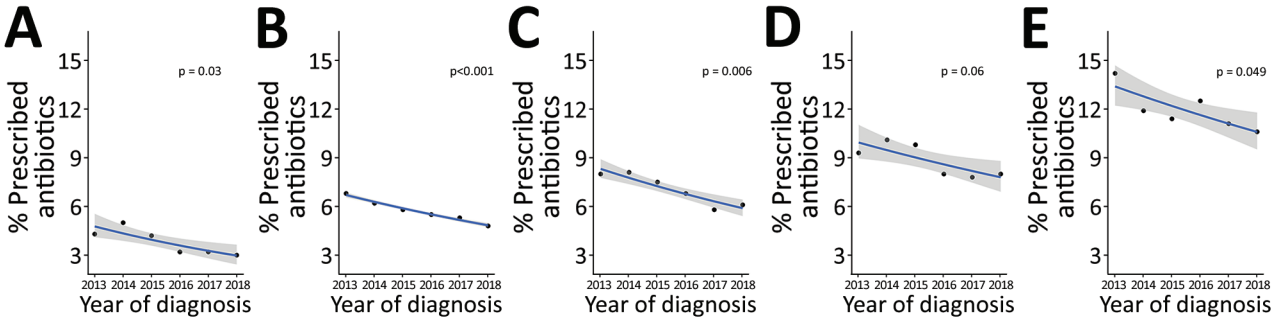

Figure 1. Proportion of acute gastroenteritis cases for which antimicrobial drugs were prescribed, by year of diagnosis and patient age, Australia, 2013–2018. A) <10 y; B) 10–29 y; C) 30–49 y; D) 50-64 y; E) ≥65 y.

of total; Table 2), of which most were azithromycin (44.4% of total; Appendix Table 4).

Conclusions

In this large study of patient clinical encounters in general practices in Australia, we found that antimicrobial drugs were prescribed for 6.8% of all cases of acute gastroenteritis but for 35.7% of nontyphoidal *Salmonella* infections and 54.1% of *Campylobacter* infections. Over the 6-year study period, the absolute proportion of cases for which antimicrobial drugs were prescribed for acute gastroenteritis decreased by 2%.

Of the few studies reporting on how often antimicrobial drugs are prescribed for acute gastroenteritis, estimates range from 8.5% of 2,089 cases in a sentinel surveillance sample from primary care in Switzerland in 2014 (*12*) to 65% in a survey of 237 physicians in China in 2012 (*13*). Our results were most similar to the estimates reported from the Switzerland study, which also found that antimicrobial drugs were more likely to be prescribed for older patients and those with fever (*12*).

In Australia, treatment guidelines recommend that empirical prescription of antimicrobial drugs is of no benefit for acute gastroenteritis and is indicated only for patients with manifestations of severe disease, those who are immunocompromised, returned travelers of all ages, or children in whom systemic bacterial infection is suspected (*7*). Our results suggest that general practitioners are more likely to

Table 2. Classes of antimicrobial drugs prescribed for cases of acute gastroenteritis, nontyphoidal *Salmonella* infection, and *Campylobacter* infection, Australia, 2013–2018

Case type, drug class	No. prescriptions	Proportion of total prescriptions, %
Acute gastroenteritis, 7,159 cases		
Nitroimidazoles	2980	41.6
Quinolones	1059	14.8
Penicillins	901	12.6
Macrolides	799	11.1
Cephalosporins	561	7.8
Sulfonamides and trimethoprim	445	6.2
Tetracyclines	295	4.1
Amphenicols	109	1.5
Nontyphoidal *Salmonella* infection, 418 cases		
Quinolones	127	30.4
Macrolides	105	25.1
Penicillins	88	21.0
Sulfonamides and trimethoprim	59	14.1
Nitroimidazoles	21	5.0
Cephalosporins	13	3.1
Tetracyclines	4	1.0
Amphenicols	1	0.2
Campylobacter infection, 1,165 cases		
Macrolides	826	70.9
Quinolones	243	20.9
Nitroimidazoles	58	5.0
Tetracyclines	12	1.0
Penicillins	10	0.9
Cephalosporins	8	0.7
Sulfonamides and trimethoprim	5	0.4
Amphenicols	3	0.3

*Ten prescriptions for acute gastroenteritis are not shown: 7 for nitrofurantoin, 2 for tobramycin and 1 for methenamine.

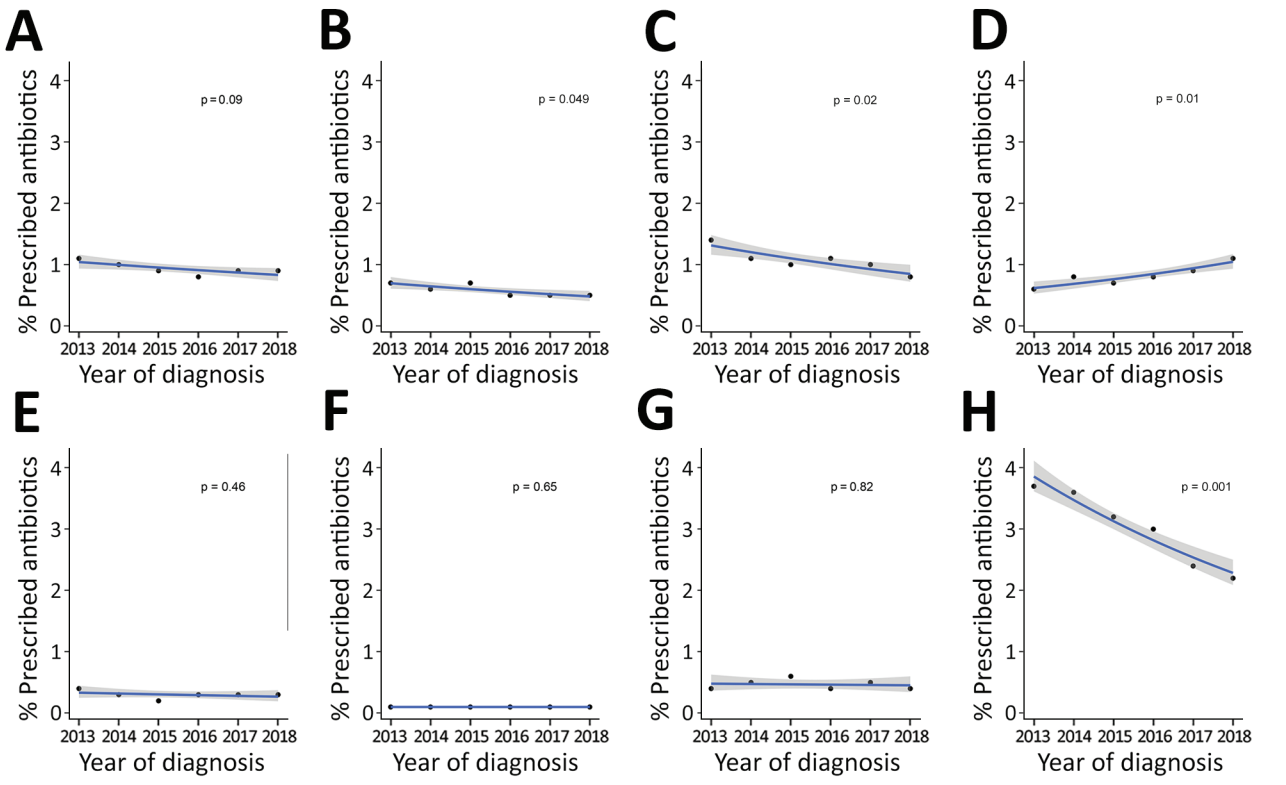

Figure 2. Trend in antimicrobial drug prescriptions for cases of acute gastroenteritis, by year and antimicrobial therapeutic class, Australia, 2013–2018. Ten prescriptions acute gastroenteritis are not shown: 7 for nitrofurantoin, 2 for tobramycin, and 1 for methenamine. A) Penicillins; B) cephalosporins; C) quinolones; D) macrolides; E) tetracyclines; F) amphenicols; G) sulfonamides and trimethoprim; H) nitroimidazoles.

adhere to guidelines and that antimicrobial drugs are more likely to be prescribed for patients who are older, those with underlying conditions, and those with systemic symptoms (e.g., fever). However, the substantial numbers of patients without these indications for whom antimicrobial drugs were still prescribed suggests overuse of antimicrobial drugs for acute gastroenteritis.

Reassuringly, we did find reduced antimicrobial drug prescriptions for acute gastroenteritis during the 6-year study period. This finding is consistent with that of an earlier study that used the same dataset and found an overall reduction in the proportion of patients for whom systemic antimicrobial drugs were prescribed: from 31.7% in 2015 to 26% in 2017 (*14*). This reduction has been attributed to a series of antimicrobial stewardship programs implemented during 2009–2014, which included educational and advertising campaigns aimed at general practitioners and consumers (*15*). Our results suggest that these antimicrobial stewardship programs may have reduced antimicrobial drug prescriptions for acute gastroenteritis.

Given the estimated 1.1 million cases of acute gastroenteritis seen in general practices in Australia annually (*3*), we estimate that nationwide ≈74,000 antimicrobial drugs are prescribed for acute gastroenteritis every year. Because most of these drugs are probably unnecessary, our findings highlight the need for greater antimicrobial stewardship to support management of infectious gastroenteritis in primary care.

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Data and more information may be obtained from MedicineWise MedicineInsight (https://www.nps.org.au/medicine-insight).

About the Author

Dr. He is a postdoctoral research fellow at the School of Population Health, University of New South Wales. He has research interests in infections and reproductive health as well as large-scale prospective cohorts and data-linkage studies.

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Appendix

Methods

Participants, data sources and definitions

MedicineInsight is an Australian national primary health care database of longitudinal de-identified electronic health records established in 2011. A detailed description of the database has been published previously (*1*). In 2018, MedicineInsight had 662 participating practices, representing approximately 8.2% of all general practices in Australia and 2.3 million regular patients (*1*). The dataset consists of practice and patient information including demographics, diagnosis, encounter reason, observations recorded, pathology requests, and prescription data. While data are anonymised, each patient, site and provider have a unique identifying number which can be used to link all the records held in the database for an individual.

For this study, a simple random sample of 25% of all patients with records between 1st January 2013 and 31st December 2018 was used. To ensure data quality, practices were excluded from analyses if they had low patient volume (less than 100 records in any diagnosis, encounter reason or prescription tables in any study year). From the remaining practices, we extracted clinical encounter records for cases of acute gastroenteritis, non-typhoidal salmonella or campylobacter infection. These were defined based on specific terms in the encounter reason or diagnosis fields (see Appendix Table 5). Multiple encounters with the same case definition within 30 days were counted as the same episode. For each episode that met our case definition, we examined whether there was an antibiotic prescribed on the day of diagnosis (see Appendix Figure 1 for the distribution of antibiotic prescribing date in relation to case diagnosis date) and if there was, we examined the class of antibiotic prescribed and the reason for prescription.

Antibiotics were identified by their medicine active ingredients and categorised based on the Anatomical Therapeutic Chemical Classification System (*2*).

Analysis

For each of acute gastroenteritis, non-typhoidal *Salmonella* and *Campylobacter*, we estimated the proportion of encounters where antibiotics were prescribed on the diagnosis date overall and then by various patient characteristics. These included age at encounter (<10, 10-29, 30-49, 50-64, 65+ years), sex (male, female), Indigenous status (no, yes), concession card holders referring to people with a Pensioner Concession Card, a Commonwealth Seniors Health Card or a Health Care card (no, yes), smoking (never, past, current), fever >38.5 ^{o}C (no, yes, not recorded), stool sample test requested (not recorded, yes), etiology (not recorded, viral, bacterial, parasitic), comorbidity (any medical history of diabetes, arthritis, or chronic kidney disease: no, yes), number of GP visits for clinical encounters in year prior to diagnosis (0-7, 8-14, 15+), and year of diagnosis (2013, 2014, 2015, 2016, 2017, 2018). Practice characteristics included practice remoteness (major city, inner regional, outer regional or remote). To account for multiple episodes in the same patient, generalised estimating equations (GEE) with exchangeable correlation structure was used to estimate characteristics associated with higher likelihood of antibiotic prescribing. Crude and adjusted odds ratios (ORs) were calculated with corresponding 95% confidence intervals (95% CI). A two-sided P value lower than 0.05 was considered statistically significant.

To understand the trends in antibiotic prescriptions over the study period, the proportions of antibiotic prescriptions by the year of diagnosis were then modelled with log-linear regression overall, by age and antimicrobial therapeutic classes. For the calculation of absolute reduction and increase, we used the first minus the last fitted value.

All analyses were performed using R version 3.5.1 (*3*).

Appendix Table 1. Proportion of episodes of acute gastroenteritis prescribed antibiotics overall and according to various characteristics for the children younger than 10 years.

Variable	N Prescribed/N acute gastroenteritis (%)	Adjusted Odds Ratios (95% CI)	P value*
Overall	762/20130 (3.8)		
Sex			
Male	410/10666 (3.8)	Ref	
Female	352/9464 (3.7)	0.97 (0.83, 1.12)	0.64
Aboriginal or Torres Strait Islander			
No	568/14680 (3.9)	Ref	
Yes	42/732 (5.7)	1.51 (1.10, 2.09)	0.01
Unknown	152/4718 (3.2)		
Concession card holder			
No	443/13007 (3.4)	Ref	
Yes	152/3788 (4.0)	1.16 (0.96, 1.41)	0.12
Unknown	167/3335 (5.0)		
Fever (>38.5 ^{o}C)			
No	245/7137 (3.4)	Ref	
Yes	21/277 (7.6)	2.37 (1.51, 3.71)	<0.001
Not recorded	496/12716 (3.9)	1.13 (0.96, 1.32)	0.13
Stool sample test requested			
No	599/17252 (3.5)	Ref	
Yes	163/2878 (5.7)	1.64 (1.36, 1.97)	<0.001
Etiology			
Not recorded	636/14622 (4.3)	Ref	
Viral	71/5387 (1.3)	0.35 (0.27, 0.44)	<0.001
Bacterial	55/119 (46.2)	19.77 (13.46, 29.05)	<0.001
Comorbidity#			
No	759/20057 (3.8)	Ref	
Yes	3/73 (4.1)	1.09 (0.34, 3.46)	0.88
Number of GP visit in last year			
0-7	583/14801 (3.9)	Ref	
8-14	128/3633 (3.5)	0.89 (0.73, 1.09)	0.26
15+	51/1696 (3.0)	0.77 (0.57, 1.03)	0.08
Remoteness of practice			
Major city	501/14991 (3.3)	Ref	
Inner regional	127/3309 (3.8)	1.14 (0.93, 1.40)	0.20
Outer regional or remote	134/1830 (7.3)	2.33 (1.91, 2.84)	<0.001
Year of diagnosis			
2013	131/3064 (4.3)	Ref	
2014	159/3210 (5.0)	1.17 (0.92, 1.48)	0.19
2015	153/3632 (4.2)	0.99 (0.78, 1.26)	0.96
2016	116/3606 (3.2)	0.74 (0.57, 0.96)	0.02
2017	118/3742 (3.2)	0.73 (0.57, 0.94)	0.02
2018	85/2876 (3.0)	0.69 (0.52, 0.92)	0.01

#Comorbidity refers to any medical history of diabetes, arthritis, or chronic kidney disease.
*Adjusted for all the variables listed in the table.

Appendix Table 2. Proportion of episodes of non-typhoidal *Salmonella* prescribed antibiotics overall and according to various characteristics, 2013-2018

Variable	N Prescribed/N non-typhoidal salmonella (%)	Adjusted Odds Ratios (95% CI)	P value*
Overall	391/1096 (35.7)		
Age (years)			
<10	101/296 (34.1)		
10-29	79/208 (38.0)	1.32 (0.89, 1.96)	0.17
30-49	111/266 (41.7)	1.56 (1.08, 2.27)	0.02
50-64	49/160 (30.6)	0.96 (0.59, 1.55)	0.85
65+	51/166 (30.7)	0.95 (0.54, 1.69)	0.87
Sex			
Male	163/483 (33.7)		
Female	228/613 (37.2)	1.18 (0.90, 1.54)	0.23
Aboriginal or Torres Strait Islander			
No	306/841 (36.4)		
Yes	8/23 (34.8)	0.93 (0.42, 2.06)	0.86
Unknown	77/232 (33.2)		
Concession card holder			
No	193/579 (33.3)		
Yes	103/301 (34.2)	1.30 (0.87, 1.95)	0.21
Unknown	95/216 (44.0)		
Fever (>38.5 ^{o}C)			
No	49/97 (50.5)		
Yes	3/6 (50.0)	1.25 (0.27, 5.73)	0.78
Not recorded	339/993 (34.1)	0.45 (0.28, 0.72)	<0.01
Stool sample test requested			
Not recorded	351/989 (35.5)		
Yes	40/107 (37.4)	0.95 (0.60, 1.52)	0.84
Comorbidity#			
No	310/857 (36.2)		
Yes	81/239 (33.9)	1.13 (0.73, 1.75)	0.60
Number of GP visits in last year			
0-7	234/631 (37.1)		
8-14	97/250 (38.8)	1.12 (0.81, 1.55)	0.49
15+	60/215 (27.9)	0.70 (0.47, 1.04)	0.08
Remoteness of practice			
Major city	224/650 (34.5)		
Inner regional	78/267 (29.2)	0.81 (0.57, 1.14)	0.23
Outer regional or remote	89/179 (49.7)	1.96 (1.30, 2.94)	<0.01
Year of diagnosis			
2013	53/126 (42.1)		
2014	82/222 (36.9)	0.73 (0.45, 1.16)	0.18
2015	76/200 (38.0)	0.86 (0.53, 1.38)	0.52
2016	73/224 (32.6)	0.66 (0.41, 1.05)	0.08
2017	64/184 (34.8)	0.74 (0.45, 1.21)	0.23
2018	43/140 (30.7)	0.59 (0.34, 1.02)	0.06

#Comorbidity refers to any medical history of diabetes, arthritis, or chronic kidney disease.

*Adjusted for all the variables listed in the table.

Appendix Table 3. Proportion of episodes of *Campylobacter* prescribed antibiotics overall and according to various characteristics, 2013-2018

Variable	N Prescribed/N campylobacter (%)	Adjusted Odds Ratios (95% CI)	P value*
Overall	1066/1969 (54.1)		
Age (years)			
<10	139/271 (51.3)		
10-29	241/446 (54.0)	1.22 (0.89, 1.66)	0.21
30-49	285/497 (57.3)	1.33 (0.98, 1.81)	0.07
50-64	205/362 (56.6)	1.23 (0.87, 1.74)	0.23
65+	196/393 (49.9)	1.00 (0.67, 1.48)	1.00
Sex			
Male	529/1023 (51.7)		
Female	537/946 (56.8)	1.24 (1.03, 1.50)	0.02
Aboriginal or Torres Strait Islander			
No	832/1528 (54.5)		
Yes	18/24 (75.0)	2.35 (0.91, 6.12)	0.08
Unknown	216/417 (51.8)		
Concession card holder			
No	529/1008 (52.5)		
Yes	319/609 (52.4)	0.96 (0.74, 1.24)	0.75
Unknown	218/352 (61.9)		
Fever (>38.5 ^{o}C)			
No	88/139 (63.3)		
Yes	6/6 (100.0)		
Not recorded	972/1824 (53.3)		
Stool sample test requested			
Not recorded	990/1841 (53.8)		
Yes	76/128 (59.4)	1.28 (0.88, 1.87)	0.20
Comorbidity#			
No	789/1465 (53.9)		
Yes	277/504 (55.0)	1.13 (0.86, 1.47)	0.39
Number of GP visits in last year			
0-7	560/1047 (53.5)		
8-14	279/497 (56.1)	1.11 (0.88, 1.39)	0.38
15+	227/425 (53.4)	1.00 (0.77, 1.30)	0.98
Remoteness of practice			
Major city	636/1219 (52.2)		
Inner regional	262/466 (56.2)	1.13 (0.89, 1.44)	0.33
Outer regional or remote	168/284 (59.2)	1.25 (0.93, 1.69)	0.14
Year of diagnosis			
2013	116/208 (55.8)		
2014	174/319 (54.5)	0.90 (0.63, 1.29)	0.56
2015	198/375 (52.8)	0.87 (0.62, 1.23)	0.44
2016	204/357 (57.1)	1.06 (0.75, 1.51)	0.74
2017	170/353 (48.2)	0.77 (0.54, 1.11)	0.16
2018	204/357 (57.1)	1.09 (0.77, 1.56)	0.62

#Comorbidity refers to any medical history of diabetes, arthritis, or chronic kidney disease.
*Adjusted for all the variables except fever listed in the table.

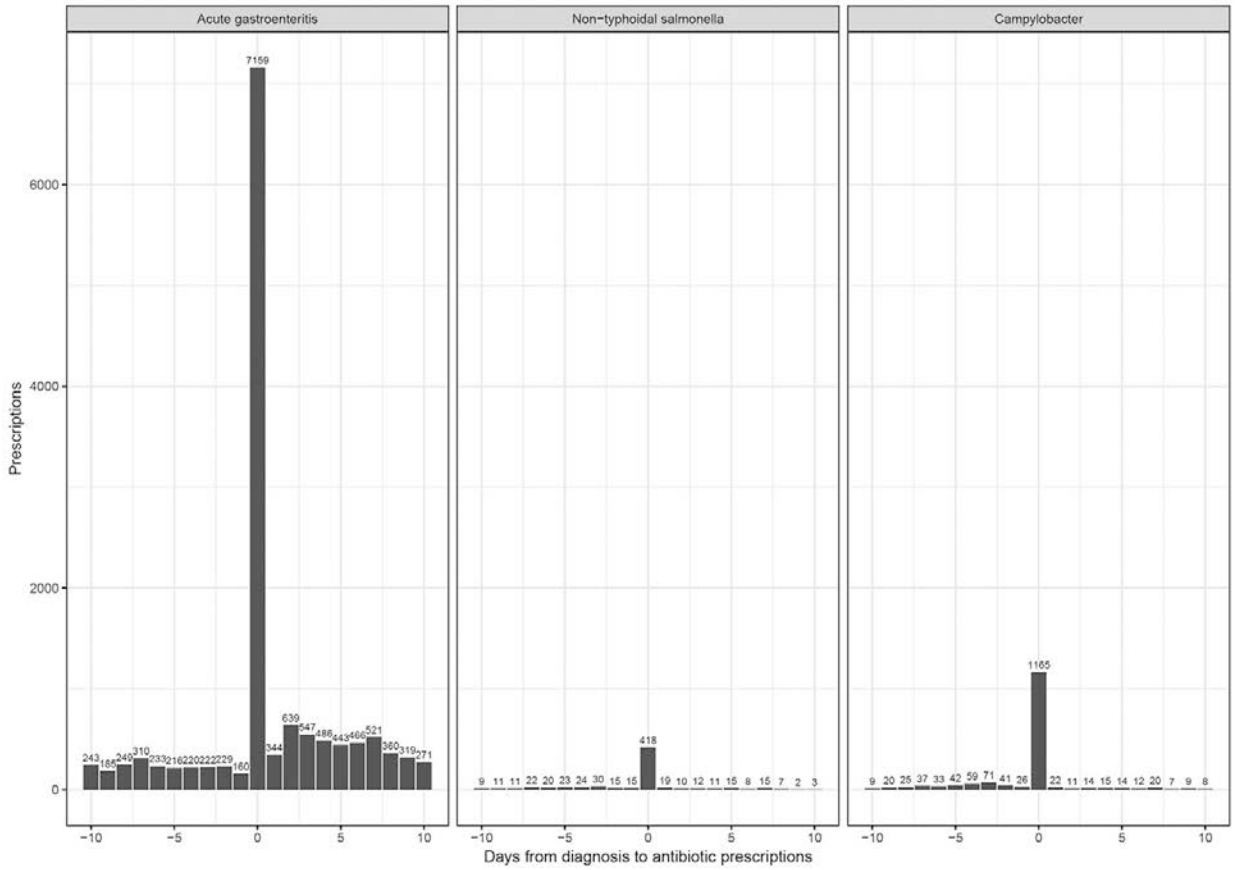
Appendix Table 4. The five most prescribed antibiotics/antimicrobials for episodes of acute gastroenteritis, non-typhoidal salmonella and campylobacter infections.

Variable	Number of prescriptions	Proportion of total prescriptions (%)
Acute gastroenteritis (n=7159)		
Metronidazole	1771	24.7
Tinidazole	1067	14.9
Norfloxacin	602	8.4
Ciprofloxacin	457	6.4
Amoxicillin	452	6.3
Non-typhoidal *Salmonella* (n=418)		
Azithromycin	93	22.2
Ciprofloxacin	91	21.8
Amoxicillin	66	15.8
Norfloxacin	36	8.6
Sulfonamides and trimethoprim	31	7.4
Campylobacter (n=1165)		
Azithromycin	517	44.4
Erythromycin	156	13.4
Norfloxacin	140	12.0
Erythromycin	132	11.3
Ciprofloxacin	103	8.8

Appendix Table 5. Terms used to identify a diagnosis of acute gastroenteritis, non-typhoidal salmonella, and campylobacter.

Variable	Terms for inclusion	Terms for exclusion
Acute gastroenteritis	“gastro”, “gastroenteritis”, “gastro enteritis”, “gastroentritis”, “gastro enterities”, “gastro-enteritis”, “gastroentrist”	"chronic", “likely”, “letter”, “refer”, “referral”, “gastroscopoy”, “upset”, “tiredness”, “or”, “skype”, “gastroschisis”, “gastroenterologist”, “gastro-intestinal”, “protection”, “cancer”, “gastroprotective”, “gastrojejunostomy”, “gastroenterostomy”, “bleeding”, “gastrosleeve”, “gastrostasis”, “muscle”, “torn”, “travel”, “?”, "cramp", "plasty"
Non-typhoidal *Salmonella*	“salmonella”, "salmonellosis"	“typhi”, "paratyphi", “immunization”, “?”, “age”, “post”, “suspicion”, “immunology”, “post”, “review”, “recall”, “trip”, “was”, “urine”, “vaccination”
Campylobacter	“campylobacter”, “notification”	“?”, “not”, “suspected”, “contact”, “likely”, “previous”, “post”, “resolved”

We used the following algorithm to include records of these infections:
1. had any of the inclusion terms in any of the following fields: encounter reason or diagnosis;
2. but was not accompanied by any of the exclusion terms.



Appendix Figure. Timing of the antibiotics prescription in relation to presentation for acute gastroenteritis, non-typhoidal *Salmonella* and *Campylobacter* infections.

References

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