Improving community antibiotic prescribing to keep antibiotics working in Aotearoa New Zealand

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ABSTRACT

Antibiotic resistance, principally a consequence of the human use of antibiotics dispensed in the community, is a relentlessly growing threat to human health in Aotearoa New Zealand. Reducing the prescription of antibiotics for conditions in which they confer no benefit is the most effective method of slowing the spread of antibiotic resistance. In Aotearoa New Zealand, as in many other nations, antibiotic "treatment" of acute respiratory tract infections is the most important component of unnecessary antibiotic use.

Because of the ethnic inequities in the incidence and consequences of infectious diseases in Aotearoa New Zealand, Māori and Pacific patients should receive antibiotic treatment more frequently than patients of other ethnicities. However, Māori and Pacific people who present to their doctor with conditions that do not require antibiotic treatment deserve the same excellent treatment as anyone else and should not be prescribed an antibiotic when it will provide no benefit. Setting annual goals for reductions in community antibiotic dispensing has been an effective method to encourage sustained improvements in antibiotic prescribing in other nations, and may help to quickly reduce inappropriate antibiotic prescribing in Aotearoa New Zealand.

Antibiotic resistance poses a threat to human health in Aotearoa New Zealand

Antibiotic resistance is widely expected to pose a steadily growing threat to human health in the coming decades.[1–4] Recent examples of the rapid spread of antibiotic resistance in Aotearoa New Zealand include mupirocin resistance in *Staphylococcus aureus*[5] and ciprofloxacin resistance in *Neisseria gonorrhoeae*.[6] During the 1990s, approximately 200,000 15g tubes of "Bactroban" (mupirocin) were dispensed annually, approximately equivalent to one tube per 17 residents of Aotearoa New Zealand each year. In 8 years, the prevalence of mupirocin resistance in strains of *S. aureus* tested by the Auckland community laboratory went from <5% to >20%.[5] Between 2000 and 2012, the proportion of isolates of *N. gonorrhoeae* in Aotearoa New Zealand that were resistant to ciprofloxacin increased from less than 2% to more than 40%.[6] Similar rapid increases in the prevalence of ciprofloxacin resistance occurred in many other nations.

Other important examples include the rapid spread of extended-spectrum beta-lactamase producing (ESBL+ve) *Escherichia coli, Klebsiella pneumoniae* and related Gram-negative bacteria. Seven ESBL+ve bacteria were isolated from patients in Aotearoa New Zealand in 1998; by 2012, more than 5,000 ESBL+ve bacteria were isolated each year.[7] These bacteria are resistant to most readily available oral antibiotics, and commonly require treatment with meropenem or another closely related carbapenem antibiotic, administered intravenously.[8] However, resistance to meropenem is also increasing rapidly. The number of people in Aotearoa New Zealand who had a meropenem-resistant *E. coli, K. pneumoniae* or related bacterium isolated increased from one person in 2009 to 223 people in 2023.[9]

There are very limited options for treating these carbapenem-resistant bacteria. Once strains of *E. coli, K. pneumoniae* and *P. aeruginosa* with resistance to carbapenems spread widely in Aotearoa New Zealand, as they have elsewhere, we will be faced with large numbers of patients with common infections such as pyelonephritis and cholecystitis that are almost untreatable and therefore likely to be fatal. The future is illustrated by a 2014–2015 survey of long-term care facilities across the United States, which reported that 24.6% (946/3,846) residents were colonised with carbapenem-resistant *K. pneumoniae*.[10] Infections with these bacteria were four times more likely to be fatal than infections with *K. pneumoniae* that were carbapenem susceptible.[11]

The risk of infections caused by extensively

resistant organisms will have severe implications for the use of the many medical treatments that increase patients' risk of severe infections, such as chemotherapy for haematologic cancers. It will also have implications for many surgical procedures, such as organ transplantation, that rely on the ability to successfully treat post-operative infections. A report commissioned by the United Kingdom's [UK] prime minister in 2014 predicted that by 2050 world-wide deaths attributable to antimicrobial resistance would surpass those attributable to cancer.[12]

The magnitude of the antibiotic resistance threat differs greatly between nations, with the threat expected to be greatest in those nations that have had very high rates of antibiotic use in the preceding decades. In developed countries, antibiotics dispensed by community pharmacies comprise 85–95% of all antibiotic consumption, with antibiotics dispensed for hospital inpatients comprising the remaining 5–15%.[13] Figure 1 shows the rates of community antibiotic dispensing, measured in defined daily doses (DDDs)/1,000 population/day, during 2018 for a range of European nations[14] and Aotearoa New Zealand.[15] In Greece, Spain, France, Poland and Aotearoa New Zealand the rates of community antibiotic dispensing were more than twice as high as they were in Sweden, Austria and the Netherlands.

High rates of antibiotic use in Aotearoa New Zealand have resulted in high rates of antibiotic resistance

The national rate of community dispensing of beta-lactam antibiotics (penicillins and cephalosporins) during 2018 in Aotearoa New Zealand was 12.9 DDDs/1,000 population/day, more than four times the rate in the Netherlands (2.9), and more than twice the rates in Norway (5.6) and Sweden (5.8)[14,15] (Figure 2a). A likely consequence of the high national rate of use of beta-lactam antibiotics in Aotearoa New Zealand in recent decades is that in 2018 methicillin-resistant *S. aureus* (MRSA) comprised 12.7% of all *S. aureus* isolates in Aotearoa New Zealand,[16] a much higher prevalence than in the Netherlands (1.2%), Sweden (1.9%) or Norway (0.9%).[17] In Belgium, Greece, France and Spain the rates of community beta-lactam antibiotic use were comparable or greater than those in Aotearoa New Zealand,[14] and the prevalence of MRSA in some of these nations was even higher than in Aotearoa New Zealand.[17] If we continue to have high rates of beta-lactam antibiotic use, the prevalence of MRSA in Aotearoa New Zealand is likely to increase to be similar to the high prevalence in Greece, Spain and Italy. Our ability to successfully treat *S. aureus* infections will fall.

The high national rate of community use of beta-lactam antibiotics in recent decades in Aotearoa New Zealand has also led to a high prevalence of reduced susceptibility to penicillin in *Streptococcus pneumoniae* in Aotearoa New Zealand (24%),[16] similar to the prevalence in Spain (18.5%) and France (29.1), and very much higher than the prevalence in the Netherlands, Norway and Sweden[17] (≤5%) (Figure 2b). The reduced susceptibility of *S. pneumoniae* to penicillin has important implications for the treatment of patients with bacterial meningitis and other invasive infections. The same trend of reduced susceptibility to penicillin, secondary to high rates of beta-lactam use, has also been observed in strains of *Neisseria meningitidis* isolated in Aotearoa New Zealand.[18]

The example of ciprofloxacin clearly shows the other side of this story. In recent decades, Aotearoa New Zealand has had a low national rate of community use of ciprofloxacin and other quinolone antibiotics (0.4 DDDs/1,000 population/day).[15] The low rate of use of quinolone antibiotics in Aotearoa New Zealand is the likely cause of the very low prevalence of ciprofloxacin resistance in *E. coli* (0.6%)[16] (Figure 3). In nations with high rates of use of quinolone antibiotics, such as Greece (2.9), Spain (2.7), Italy (2.7) and Bulgaria (2.8),[14] the prevalence of ciprofloxacin resistance in *E. coli* is very much higher (approximately 30–40%).[17]

Antibiotic use in animals is a minor contributor to antibiotic resistance in humans in Aotearoa New Zealand

Antibiotic use in farming has undoubtedly made a significant contribution to the emergence of antibiotic resistance. However, in most developed countries, including Aotearoa New Zealand, the rate of antibiotic use in humans (total kg antibiotic dispensed/total kg human biomass) greatly exceeds that in animals (total kg antibiotic dispensed/total kg farmed animal biomass), and antibiotic use in animals is generally thought to contribute relatively little to the rates of antibiotic resistance in human pathogens.[19] The total weight of antibiotics used in animals and in humans was

Figure 1: Community antibiotic dispensing in 16 European nations and Aotearoa New Zealand during 2018.[14,15]

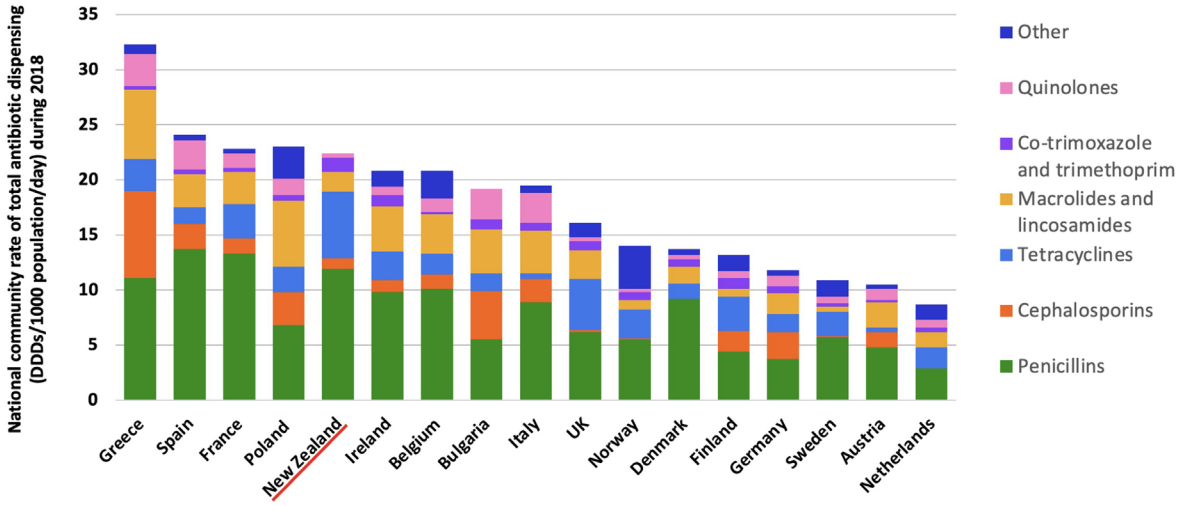


Figure 2: Prevalence of methicillin-resistance in *S. aureus* (a), and of reduced susceptibility to penicillin in *S. pneumoniae* (b), in relation to rates of community dispensing of beta-lactam antibiotics (penicillins plus cephalosporins)

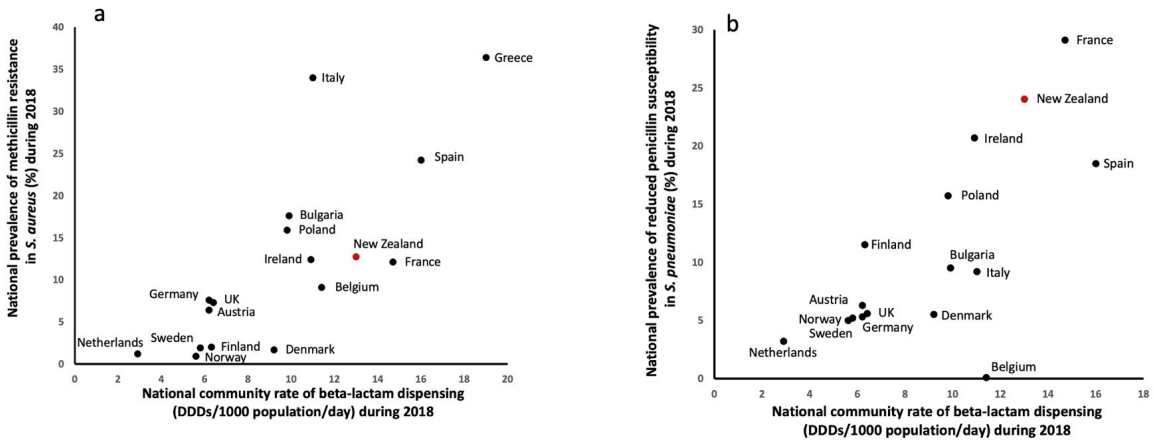


Figure 3: Prevalence of ciprofloxacin resistance in *E. coli* in relation to rates of community dispensing of quinolone antibiotics in 16 European nations and Aotearoa New Zealand during 2018.[14–17]

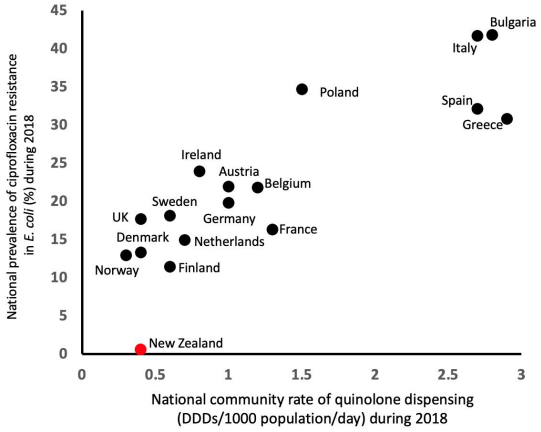


Figure 4: The proportion of consultations for an acute upper respiratory tract infection at 111 general practices in Aotearoa New Zealand during 2014 that were associated with dispensing of an antibiotic during the subsequent 7 days. Each column represents one general practice. An antibiotic was dispensed to at least 50% of patients at approximately two thirds of practices.[25]

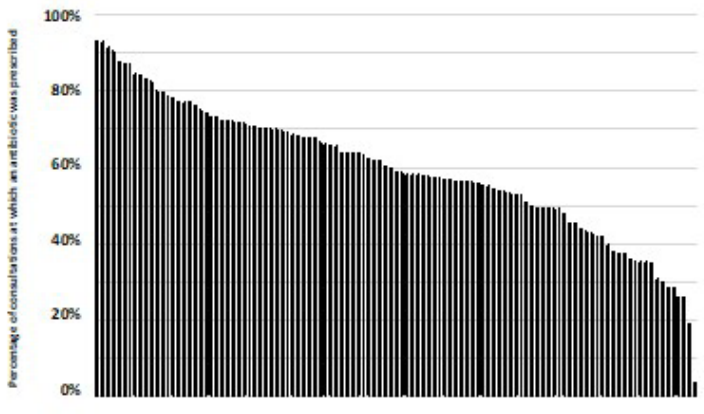
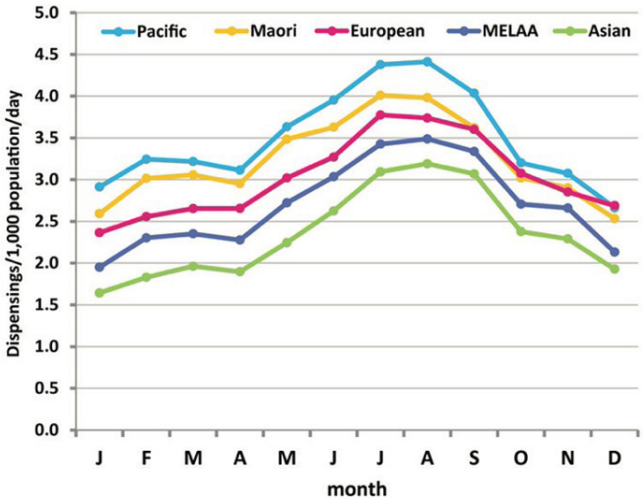


Figure 5: Rate of community antibiotic dispensing in relation to ethnicity and season in Aotearoa New Zealand during 2015.[26]



estimated for 30 countries, including Aotearoa New Zealand, during 2012. The rate of antibiotic use in animals in Aotearoa New Zealand was very low in comparison to the rates in other countries for which data was available.[20] In 2015, the New Zealand Veterinary Association published an ambitious goal that "*By 2030 New Zealand Inc. will not need antibiotics for the maintenance of animal health and wellness*".[21] Between 2017 and 2022, total antibiotic use in animals or plants in Aotearoa New Zealand fell by 42% from 71,361kg to 41,033kg.[22]

Reducing community antibiotic use that provides nil or minimal health benefit is a wise way to slow the spread of antibiotic resistant bacteria

All antibiotic use helps to select for the survival and spread of antibiotic-resistant bacteria within a community. However, it is only the inappropriate use of antibiotics that we should try to reduce. There are some good reasons why community rates of antibiotic use are higher in Aotearoa New Zealand than in many other nations. For example,

in Aotearoa New Zealand a relatively high proportion of the population are young, and a high proportion suffer socio-economic deprivation.

However, there is plenty of evidence that in all communities in Aotearoa New Zealand a large proportion of antibiotic use provides nil or minimal benefit. In developed countries, antibiotic "treatment" of people with viral respiratory tract infections comprises the largest proportion of inappropriate antibiotic dispensing.[23,24] A 2014 study reported that an antibiotic was dispensed following 61% (31,082/50,691) of consultations for acute respiratory tract infections at 111 general practices in Aotearoa New Zealand[25] (Figure 4). In comparison with many other countries, this is a very high rate of antibiotic prescribing for patients with acute respiratory tract infections.

A commonly used measure of the relative amount of inappropriate prescribing of antibiotics for people with acute respiratory tract infections is the proportional increase in dispensing of antibiotics during the colder months (April–September) when compared with dispensing of antibiotics during the warmer months (October–March). Total per capita antibiotic dispensing was 26% higher in the winter months than in the summer months in Aotearoa New Zealand during 2014–2015[26] (Figure 5). The winter increase in antibiotic dispensing was broadly similar regardless of ethnicity: 35% in Asian people, 31% in Middle Eastern, Latin American and African people, 29% in Pacific people, 28% in Māori people and 25% in European people.[26]

Much lower winter increases in antibiotic dispensing are seen in some other nations such as Denmark (12%) and the UK (14%).[26] These data strongly suggest that there is a clear opportunity to achieve significant reductions in inappropriate antibiotic dispensing in all ethnic groups in Aotearoa New Zealand.

Large UK studies strongly suggest that reducing community antibiotic consumption is safe

It is likely that most doctors will be concerned that any reduction in their per capita rate of antibiotic prescribing will create an increased risk of adverse outcomes for their patients. However, this is an understandable misconception. A study of 45 million person-years of observation at 610 UK general practices during 2005 to 2014 evaluated the safety of a policy to reduce antibiotic prescribing for respiratory tract infections in primary care. Slightly more than 50% of patients who presented with a respiratory tract infection were prescribed an antibiotic. The study suggested that, for a practice with 7,000 registered patients, a 10% reduction in the rate of antibiotic prescribing for patients presenting with respiratory tract infections would result in one more case of pneumonia each year, and one more case of peritonsillar abscess each decade.[23] A subsequent larger study of 66 million person-years of follow-up at 706 UK general practices during 2002 to 2017, by the same UK team, found no association between rates of antibiotic prescribing for any indication and subsequent risk of serious bacterial infections. Patients who attended practices that prescribed antibiotics less frequently did not have a higher rate of serious bacterial infections. This study reported that the number needed to treat to prevent one episode of sepsis was almost 30,000 in children aged 0–4, and was >250 in men aged ≥85 years, and >350 in women aged ≥85 years.[27]

A recent Aotearoa New Zealand study also suggests that reducing antibiotic treatment is safe

There was an overall 36% reduction in the number of antibiotic prescriptions dispensed in the community during weeks 15–20 in 2020—early in the COVID-19 epidemic—compared to the same 5-week periods in 2017, 2018 and 2019. The magnitude of the reductions during 2020 when compared with 2019 was 29% in Māori, 44% in Pacific people, 47% in Asian people and 25% in people of all other ethnicities. These large reductions in community antibiotic dispensing were not associated with any subsequent increase in admissions to hospital for pneumonia, peritonsillar abscess or rheumatic fever.[28]

Community antibiotic dispensing has been reducing in Aotearoa NZ in recent years

The per capita annual rate of community antibiotic dispensing increased steadily (by about 5% per year) in Aotearoa New Zealand until 2015, but since then it has declined. The average annual decline in Aotearoa New Zealand between 2015 and 2018 (4.6%) was broadly similar to the magnitude of the decline seen during the same period in Australia (6.5%), Denmark (3.6%) and the UK (3.2%)[15] (Figure 6).

The rate of decline was greater in children aged

Figure 6: Rates of total community antibiotic dispensing in Aotearoa New Zealand and other countries during 2013–2018.[15]

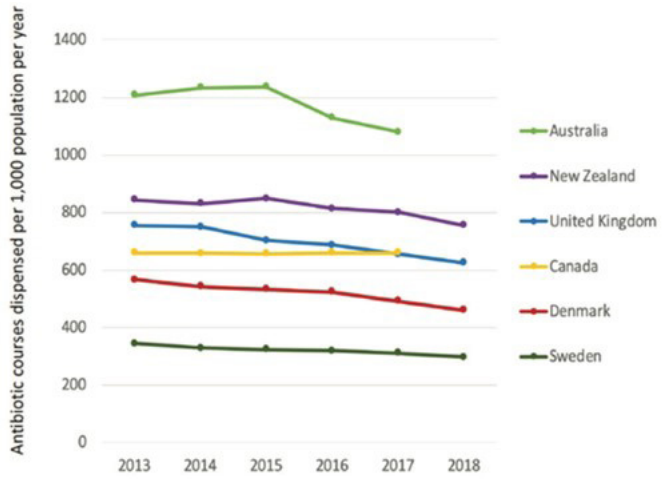


Figure 7: Rates of total community antibiotic dispensing in relation to patients' (a) ethnicity and (b) level of socio-economic deprivation (1 = least deprived, 5 = most deprived) in Aotearoa New Zealand during 2013–2018.[15]

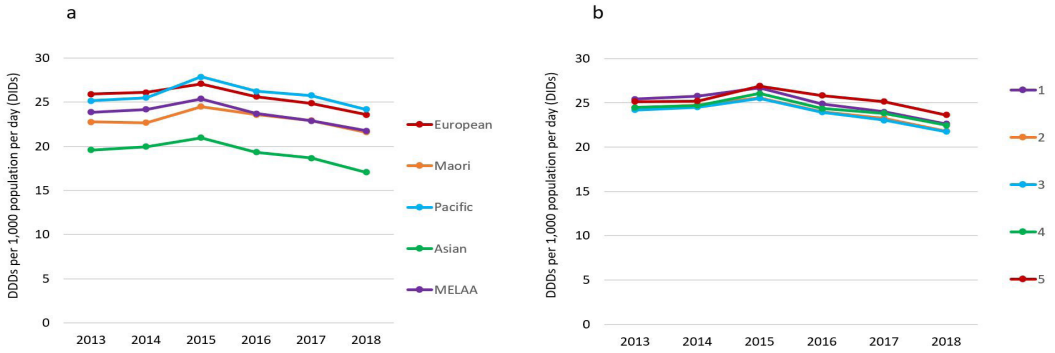


Figure 8: Percentage change between 2015 and 2018 in the rate of community antibiotic dispensing for each DHB (a) and each PHO (b).[15]

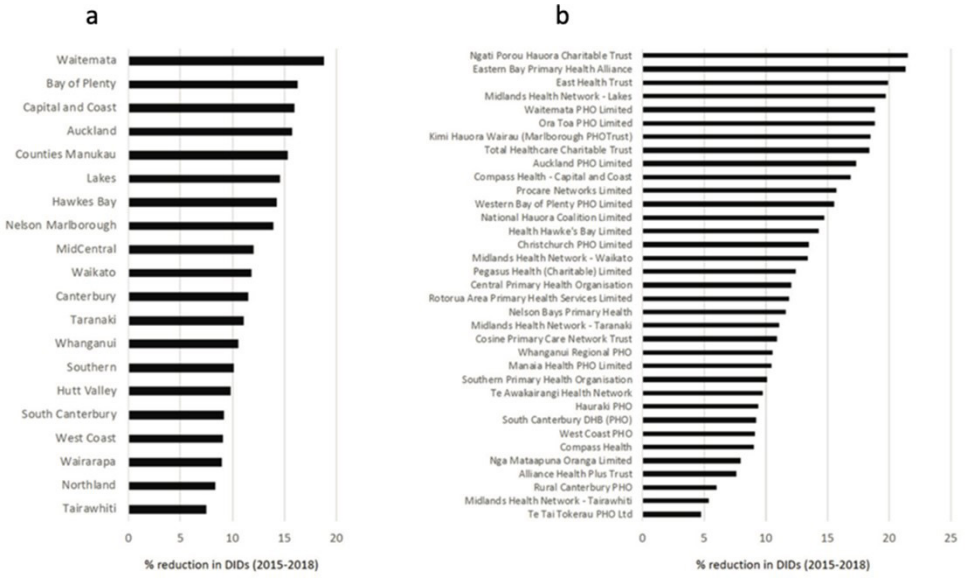
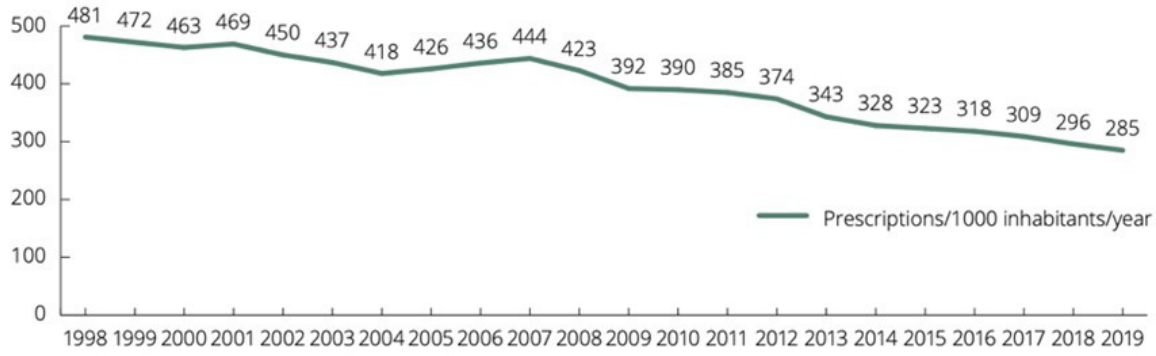


Figure 9: Swedish annual rate of community antibiotic dispensing 1998–2019.[32]



0–4 years than in other age groups. The rate of decline was similar regardless of patients' ethnicity or level of socio-economic deprivation (Figure 7).[15]

The rate of decline in total community antibiotic dispensing varied considerably with regard to primary health organisations (PHO), and to a lesser degree with regard to District Health Board (DHB)[15] (Figure 8).

The large declines in rates of community antibiotic dispensing in all PHOs and all DHBs between 2015 and 2018 suggest that there is a widespread, sustained awareness of the safety, and of the benefits, of reducing inappropriate antibiotic dispensing in Aotearoa New Zealand.

Recommending goals for reductions in community antibiotic dispensing has been very successful in France, England and Sweden

In 2002, the French National Health Insurance launched a long-term, nation-wide campaign to decrease total antibiotic use in the community by 25%. During the next 5 years there was a 26.5% reduction in the number of antibiotic prescriptions.[29]

In 2015, the National Health Service England stated that it would financially reward clinical commissioning groups (CCGs; the English "equivalent" of DHBs) for improvements in the quality of the services they provide in primary care. To be eligible for the Quality Premium payment there needed to be a ≥1% reduction in the number of antibiotic prescriptions compared with the number of prescriptions for the same CCG in 2013–2014, and a ≥10% reduction in the number of broad-spectrum antibiotic prescriptions compared with the number for the same CCG in 2013–2014. Twenty-three months after the intervention there had been an overall 8.2% decrease in total antibiotic prescriptions, and an overall 18.9% decrease in broad-spectrum antibiotic prescriptions.[30]

In 2009, when approximately 400 community antibiotic prescriptions were dispensed per 1,000 inhabitants each year, the Swedish antimicrobial stewardship programme set a national target of fewer than 250 antibiotic prescriptions dispensed per 1,000 inhabitants per year.[31] In 2020, this target was achieved in 19 out of 21 regions[32] (Figure 9).

As previously discussed, and as illustrated in Figure 6, the annual rates of antibiotic dispensing in Aotearoa New Zealand during 2013–2018 were approximately 800 per 1,000 inhabitants—2.7 times higher than in Sweden (approximately 300) and approximately 1.5 times higher than in Denmark (approximately 500).[15] Some might suggest that the differences in antibiotic dispensing rates between these two Scandinavian nations and Aotearoa New Zealand relate to the differences in the rates of deprivation in each of these nations. However, in Aotearoa New Zealand in recent years the level of community antibiotic consumption has hardly differed at all in relation to patients' level of socio-economic deprivation[15] (Figure 7b). The least deprived in Aotearoa New Zealand, as well as the most deprived in Aotearoa New Zealand, all have rates of community antibiotic dispensing that are very much higher than the average rates in Sweden and Denmark.

Improved community antibiotic prescribing can reduce health inequities in Aotearoa New Zealand

The rates of admission to hospital for an infectious disease during 1989–2008 were approximately

twice as high in Māori and Pacific people as in people of other ethnicities in Aotearoa New Zealand,[33] and the rates of admission to hospital for a first episode of rheumatic fever during 2000–2018 were 24 times higher for Pacific and 12 times higher for Māori people than for people of European and other ethnicities.[34] Reducing rates of community antibiotic prescribing for serious bacterial infections, and for *S. pyogenes* pharyngitis, would be certain to worsen health outcomes for Māori and Pacific people. Instead, we need to increase rates of community antibiotic prescribing for all Māori and Pacific people with conditions that require antibiotic treatment.[25]

However, Māori and Pacific people who present to their doctor with conditions that do not require antibiotic treatment deserve the same high-quality treatment as anyone else, and should not be prescribed an antibiotic when it will provide no benefit. As previously discussed, and as illustrated in Figure 5, antibiotic prescribing for Māori and Pacific people increases dramatically during the winter, as it does for people of other ethnicities. Reducing this antibiotic treatment of people with winter upper respiratory tract infections, whether they are Māori or Pacific peoples or other, should be a goal for all general practitioners.

Finally, the fact that the Ngāti Porou Hauora Charitable Trust and the Eastern Bay Primary Health Alliance were the two PHOs with the greatest reductions in rates of community antibiotic dispensing during 2015–2018[15] (Figure 7) suggests that Māori health organisations, and the communities that they serve, see advantages in reducing inappropriate antibiotic prescribing. The fact that community antibiotic dispensing reduced by approximately 22% over a period of 3 years in both these PHOs suggests that the doctors serving these communities have found many opportunities to improve their prescribing practices.

Conclusion

Continued high rates of community antibiotic dispensing will lead to ever higher rates of antibiotic resistance and worse health outcomes for people with infectious diseases in Aotearoa New Zealand in the coming decades. Comparisons with other developed nations suggest that total community antibiotic dispensing could safely be reduced by at least 25% in Aotearoa New Zealand, principally by reducing antibiotic prescribing for people with self-limiting respiratory tract infections, regardless of ethnicity.

However, there is a pressing need to increase the rates of antibiotic treatment for Māori and Pacific people with infectious diseases that do benefit from antibiotic treatment. Despite the incidence of many treatable infectious diseases being disproportionately high in Māori and Pacific people, they currently do not receive commensurately higher rates of community antibiotic prescribing. Therefore, when caring for Māori and Pacific people, healthcare providers need to increase their antibiotic prescribing for those conditions in which antibiotic treatment will be helpful, and decrease their prescribing for those conditions in which antibiotic treatment provides no benefit.

Healthcare providers should take every opportunity to educate their patients about the need for changes in antibiotic prescribing in Aotearoa New Zealand. Reducing the frequency with which patients with self-limiting respiratory tract infections present to their healthcare providers will have benefits for patients and for healthcare providers. Patients will also benefit from increased knowledge of those conditions for which antibiotic treatment is beneficial.

COMPETING INTERESTS
None.

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