# Antimicrobial Stewardship and Infection Control:

## Limiting the burden of antimicrobial resistance in New Zealand

New Zealand College of Public Health Medicine Policy Statement

## Policy statement

The New Zealand College of Public Health Medicine (NZCPHM) recognises that antimicrobial resistance (AMR) is an increasing health threat of significance, both globally and to New Zealand.

The NZCPHM supports antimicrobial stewardship being a national priority, requiring widespread commitment and leadership from all sectors in New Zealand[1,2] – using a 'One Health'[3] approach that recognises ecosystems and the development of AMR in humans and AMR in other species are linked inextricably.[4]

In line with World Health Organization (WHO) recommendations,[5,6,7] the NZCPHM calls for New Zealand to have a national plan for AMR that is comprehensive and sufficiently financed. Such planning should incorporate:

- preventing infections;
- improving antimicrobial prescribing and stewardship, in both community and healthcare settings;
- public education;
- national, DHB-level monitoring and surveillance activities;
- suitable regulation of agricultural and veterinary use (and improving stewardship) of antimicrobials;
- a national strategy that links with international efforts; and
- new research to identify the most effective methods to revive and sustain the effectiveness of existing antimicrobial agents.

The NZCPHM also calls for international governance structures, treaties and targets.[4,8]

The NZCPHM supports work by cross government, multi-agency, multi-sector groups to develop a strategic framework and implementation plan for New Zealand, led jointly by the Ministry of Health (MoH) and Ministry for Primary Industries (MPI) with a commitment to have a national action plan in place by May 2017.[9]

The NZCPHM also supports in general the AMR policies of the New Zealand Veterinary Association (NZVA), The Royal New Zealand College of General Practitioners (RNZCGP), and The Royal Australasian College of Physicians (RACP).[10,11,12]

## Background

The increasing emergence and spread of antimicrobial resistance (AMR) is an international health concern and burden on individual countries.[7,13,14,15,16,17,18] For example, each year in the United States of America (USA) it is estimated that at least two million people become infected with bacteria that are resistant to antibiotics and at least 23,000 people die as a direct result of these infections.[19] AMR is a leading global health issue that "threatens the very core of modern medicine and the sustainability of an effective, global public health response to the enduring threat from infectious diseases".[7] Predictions are that, unchecked, by 2050 AMR will cause 10 million deaths globally each year.[8]

Systematic review evidence[20] indicates that AMR can result in increased need for second line antibiotics in the community. It can also result in patients needing to spend increased time in hospital, exposing them to further risk of healthcare-acquired infections. In addition, this problem drives up the cost of running taxpayer-funded health systems and imposes financial costs on patients themselves.

Levels of antibiotic consumption are clearly associated with the emergence of resistance, evident in a systematic review of 243 studies by Bell et al.[21] Further evidence, which includes data from Europe, indicates a strong correlation between the level of antibiotic use and the prevalence of resistance.[22] These findings highlight the need to avoid inappropriate use of antimicrobials.

New Zealand (NZ) has traditionally had low rates of AMR compared with many overseas countries, but a progressive increase has occurred recently.[1] Reviews of the growing burden of AMR have noted that resistance to many common antimicrobials is now endemic in NZ, in both community and healthcare settings. Factors contributing to the emergence and spread of antimicrobial-resistant pathogens in NZ include:

- the inappropriate use and overuse of antimicrobials (including over-reliance on broad spectrum antibiotics and excessive use of topical antibiotics[23]);
- transmission of resistant organisms in both community and healthcare settings;
- importation of resistant pathogens from areas where multi-drug resistant organisms are endemic;[24] and
- environmental and genetic factors that alter the viability of resistant bacteria.[25,26]

Other NZ researchers have also highlighted the problems around AMR,[27] reporting on the relative success of interventions, eg. the antimicrobial stewardship programmes at hospitals such as Auckland City Hospital,[28] said to be standard practice in all United Kingdom (UK) hospitals.

The optimal use of antimicrobials is one of the Government's medicines strategy's objectives, ie. to minimise the risk of AMR through targeted and appropriate human, veterinary and agricultural use of antimicrobials.[29] Jointly, the MoH and MPI are developing a national AMR action plan for a coordinated national response to AMR across the human, animal and agricultural sectors; NZ has made a commitment to the WHO to have a national AMR action plan in place by May 2017.[9] This national action plan aligns with the WHO's 'One Heath' initiative – the integration of human medicine, veterinary medicine and environmental science.[3]

The NZCPHM recommends and supports activities in the following areas:

**1. Preventing infections in community settings**

Infections need to be prevented in the first place. This reduces the requirement for the use of antimicrobials and hence the risk that resistance will develop during therapy. Key ways to prevent transmission include the promotion of basic hygiene (eg. hand[30,31] and respiratory[32] hygiene), safe food preparation and handling, good nutrition,[33] breastfeeding,[34] and high immunisation coverage.

Household overcrowding and other hazardous housing conditions are also avoidable causes of hospitalisations in NZ,[35,36] alongside other 'upstream' drivers of infectious complications such as smoking, obesity/diabetes and socioeconomic deprivation[37]. NZ has already achieved considerable success in reducing the burden of foodborne campylobacteriosis by effective regulation of contaminated poultry meat[38] (albeit there is now alarming emerging resistance in *C. jejuni*[39]).

**2. Travel, border control and prevention at source**
Strategies are needed to reduce the transfer of antimicrobial resistant organisms to NZ across international borders.

The role of travel in AMR has been a concern for some time amongst New Zealand's infectious diseases community, including the Australasian Society for Infectious Diseases.[40,41] Control of AMR is an international issue, given strong epidemiological evidence of resistant strains starting elsewhere then spreading rapidly with travel.[42,43] There are appreciable health risks from overseas arrivals/returns acquiring resistant organisms in other countries, some with less effective approaches to infection control than in NZ. Such infections may occur in surgical and other specialist health settings, but mere travel to some countries is a risk factor where there is a high prevalence of multi-drug resistant organisms (MDROs) in the community and environment. These latent infections can be imported into NZ hospitals with serious consequences. Controlling such infections has implications for border control, migration, and refugee services.

**3. Preventing infections in healthcare settings**
Preventing transmission and infection in healthcare settings is essential to controlling the spread of AMR. This is where most of the important resistant pathogens and the mobile genetic elements they contain have disseminated internationally. The main driver of spread is *transmission* rather than the novel development of resistance within an individual patient exposed to antibiotics. While antibiotic exposure in the community almost certainly facilitates transmission and acquisition of resistant clones, community exposure to antibiotics can also generate *de novo* new resistant genes or clones.[23,44,45]

Arguably, once mobile resistance elements and successful resistant clones have emerged and spread internationally, the important strategic response remaining is to contain spread and prevent infections in vulnerable and compromised patients. Thus, although border control, travel and prevention at source is important (section 2 above), currently the only realistic policy lever is the screening of high risk patients for colonisation in healthcare settings (to then implement special infection control precautions). This includes isolation and screening for multi-drug resistant organisms in patients who have been in contact with a health care system or admitted to hospital whilst traveling overseas.

In-hospital infection prevention and control guidelines are crucial, eg. the US CDC guidelines for carbapenemase-producing *Enterobacteriaceae*[46] (arguably the near-term biggest AMR threat to NZ). This is in effect to create an infection control 'fire break' around vulnerable patients in healthcare settings. The practice of 'active surveillance' to detect carriage of resistant organisms in healthcare settings is another important tool.

The NZCPHM notes the health care facility- and DHB-level surveillance of The Institute of Environmental Science and Research (ESR)[47,48] and the infection prevention and control programmes of the Health Quality & Safety Commission (HSQC).[49]

**4. Improving antimicrobial prescribing and stewardship in the community**
Community dispensing of antibiotics in NZ currently accounts for most human use.[50] Preventing over-use of antimicrobials in the community[i] is important in slowing the development and spread of antibiotic resistant bacteria.[51] Preventing antimicrobial over-use needs commitment by health professionals[i] to antimicrobial stewardship; collaboration and coordination; and supporting infrastructure and governance. This includes prescriber and PHO information systems, targets for community consumption of antimicrobials, and feedback, incentives and performance programmes.

A systematic review on reducing primary care antibiotic prescribing for children with respiratory tract infections, reported the most effective interventions target both parents and clinicians during consultations, provide automatic prescribing prompts, and promote clinician leadership in the intervention design.[52]

Strategies using active clinician education and targeting management of all acute respiratory infections may be of particular value in reducing community-level antibiotic use, according to another systematic review.[53] Similarly, another systematic review also indicates how educational interventions can improve prescription and dispensing of antibiotics by clinicians.[54] More specifically, a systematic review by NZ researchers reported that a delayed prescription is an effective means of reducing antibiotic usage for acute respiratory infections.[55] The joint Best Practice Advocacy Centre (BPAC)/ UK National Institute for Health Care Excellence (NICE) NZ-contextualised NICE guideline on antibiotics in self-limited respiratory tract infections emphasises not prescribing antibiotics for most patients with colds, sinusitis, coughs and fevers, and otitis media.[56]

**5. Antimicrobial use in hospitals**
The NZCPHM notes current standards that require NZ hospitals to have a documented policy on antimicrobial use and for the auditing against the relevant NZ Standard (NZS 8134.3:2008).[57] There is also published relative success reported for the antimicrobial stewardship programme at Auckland City Hospital,[28] alongside programmes in other District Health Boards (DHBs).[58] Recommendations include better monitoring/reporting of antimicrobial consumption in hospitals and regional antimicrobial prescribing guidelines for hospital use.[12,1]

**6. Public education**
In addition to what doctors can do, regular multi-media campaigns are important to educate the public about the need for wise use of antibiotics.[60] Such campaigns have been supported by numerous organisations, including the RNZCGP, the Pharmaceutical Society of New Zealand, New Zealand's Pharmaceutical Management Agency (PHARMAC), and Plunket. The effectiveness and cost-effectiveness of such campaigns should ideally be evaluated to inform their optimal design. Of note is the forthcoming work by NICE in the UK (due in 2016[61]) on 'antimicrobial resistance – changing risk-related behaviours in the general population'.

**7. National monitoring and surveillance activities for AMR**
Effective surveillance of AMR includes:

- screening of patients for certain MDROs (depending on local policy), eg. carbapenemase-producing *Enterobacteriaceae* (CPE);
- effective IT systems;

[i] Community prescribing includes inpatient Ward discharges to the community, ED and Outpatient prescribing (by specialists, RMOs), private specialist practice (physicians, surgeons etc), primary care GPs, practice nurses, dentists, and midwives.

- testing isolates from a wide range of patients for susceptibility to a range of relevant antimicrobials;
- reporting results to clinicians;
- integrating and including private microbiology laboratories;
- supplementing the data from local laboratories with national data; and
- developing methods to monitor adaptive resistance occurring below clinical thresholds.[59]

Nationally harmonised and coordinated surveillance is essential to understand the magnitude, distribution and impact of resistant organisms and antimicrobial usage, identify emerging resistance and trends, and determine associations between usage and resistance.[62] Surveillance is needed at local and national levels, and globally,[62] to formulate local antimicrobial guidelines, inform policy decisions, identify high-priority areas for interventions, monitor the impact of interventions designed to prevent or reduce AMR, and identify long-term trends and emerging threats globally.[24,63]

The NZCPHM notes the involvement of key NZ agencies in monitoring AMR, particularly ESR.[47,48,64,65] It also notes MoH surveillance activities such as the use of the Healthcare Associated Infections Governance Group (HAIGG).[66]

Effective surveillance programmes are also needed to monitor for the development of AMR in food-producing animals[67] in NZ. Such surveillance should occur parallel with systematic monitoring and reporting of antimicrobial use in food-producing animals[68], and could be modelled on successful programmes[69,70,71,72,73] like Denmark's DANMAP etc.

**8. DHB-level monitoring**
Beyond DHBs monitoring of AMR, activities supporting DHB-level monitoring of antimicrobial use are important.[27,64,74] This is where reporting, eg. per capita antimicrobial usage within each DHB[48] relative to targets for reductions from present levels of consumption, helps provide impetus for DHBs to address this health threat to their populations.[27]

**9. The need for new antimicrobial development, yet reserving access to those most in need**
Research and development of new antimicrobials is needed, prioritising those areas where AMR is increasing.[8,75,76,77,78] Strategies to minimise the use of new antimicrobials (including vaccines and rapid diagnostic testing[8]) need to be established simultaneously to maintain effectiveness for as long as possible. The corresponding dwindling of the antimicrobial development pipeline, particularly for gram negative organisms, mounts a further hurdle. There is too a need to identify the most effective methods to revive and sustain the effectiveness of existing antimicrobial agents.[79,80] The challenge is to incentivise new antimicrobial development[8,75], without also inadvertently encouraging inappropriate use or reducing access to those most in need. This is no easy task with current research funding models.[76,78]

**10. Agricultural and veterinary use of antimicrobials**
The NZCPHM remains concerned over the potential risks of AMR associated with NZ's agricultural and veterinary antimicrobial use,[67,82] and threats to our ability to regulate their use.[85] A 'One Health'[3] approach is needed, linking the health, veterinary and agriculture sectors.[78]

Veterinary use of antimicrobials (relative to biomass consumption[ii]) is perhaps 8% that of human use in NZ[88] and our use of antimicrobials in animals is likely to be low compared with other developed

[ii] crude antimicrobial usage measured by population correction unit (PCU) viz mg active ingredient per kg biomass[86,87], not total tonnage volume of usage. Neither measure assesses the risk of veterinary use to AMR in humans.

countries, at least in terms of crude antimicrobial tonnage compared with crude livestock biomass.[8,88,90] However, there is little comparative information on how NZ versus other countries' use relates by classes of antimicrobial (including critically important antimicrobials (CIAs) for human health[89] eg. fluoroquinolones) and the types of livestock, intensification[94], their trends over time, and parallel incidence of/trends in AMR in animals.[67,iii] In addition, animals can spread resistance and antibiotics in ways that people generally do not[91,92] – meaning that it is not only about how much antibiotics are used, but how effectively that use causes the spread of resistant organisms.[iv]

Although increasing resistance is driven by complex and interconnected factors, growing evidence suggests that large volumes of antibiotics used in agriculture are in themselves an important contributing factor to AMR[93,94,97] (alongside mode of use and choice of antimicrobial). There is also good evidence from Europe that total usage for any given class is important, correlating closely with resistance rates in animals.[95] Because most countries have poorly regulated prescribing and dispensing expectations alongside minimal requirements for monitoring and reporting agricultural antibiotic use, it is difficult to obtain accurate data on total volumes[iii], but they are known to be very large. In countries like the USA and Australia, approximately 70% of all antibiotic use is consumed by livestock.[15]

There is increasing use in NZ of 3rd-generation cephalosporins and other CIAs in the veterinary sector.[68] This usage increases the risks of developing significant AMR in bacteria infecting both food-producing and companion animals.[24,68] Also concerning is the veterinary use of polymixins,[68] given recent plasmid-mediated resistance in food-producing animals[96] (polymixins being now absolutely last-line). Likewise there are concerns with the inappropriate or over-use of some antimicrobials, and emerging risks, in the plant sector.[98,99]

With the use of some antibiotics in food producing animals in NZ (eg. broiler chickens, pigs, dairy cows)[94] and with intensification,[94] transparent monitoring of usage is an important start. Such monitoring should be not just in terms of volumes[68,88,90] but also antimicrobial class and type of livestock.[v]

Reducing, refining and replacing[105] antibiotic consumption in agriculture is essential, if insufficient[25], to slow the rise in AMR over the long term. Recent[vi] suggested regulatory approaches have included mandatory food labelling (stating whether antibiotics were used during production)[95] and zero tolerance rulings on certain types of resistant organisms in retail food, accompanied by regular monitoring programmes.[103,104] Such approaches, although largely untested to date, accord with informed choice and could potentially help curb AMR worldwide.

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[iii] In NZ, MPI analyses and reports periodically on antibiotic sales for veterinary use, the last being its report for 2009-2011 published in 2013.[68]

[iv] For example, research in the US indicates that, downwind of CAFOs (concentrated animal feeding operations), resistance genes are detected in the air at many times the concentration as upwind.[91,92]

[v] Just as such transparency is being proposed to monitor therapeutic human use in NZ DHBs, there is a strong argument for similar monitoring of routine non-therapeutic prophylactic/metaphylactic use[105] in food-producing animals; in this regard, the NZVA currently leads a programme to better monitor antimicrobial usage in animals.[100]

[vi] The WHO recommends that the routine use of certain antimicrobial agents as growth promoters in agriculture be rapidly phased out or terminated.[101] Evidence from Denmark supports this policy, with AMR substantially reduced following a reduction in antibiotic use for growth promotion.[102] This outcome was achieved through a government ban on the use of particular antibiotics as growth promoters. No antibiotics in NZ are labelled or prescribed for the purposes of growth promotion.[100]

Hence, in order to preserve remaining antimicrobials for patients in whom they are absolutely vital – such as the immune-compromised and critically ill[78] – the capacity to introduce regulations to reduce harmful antibiotic use in the agricultural sector remains important.[82,105] But also important is the ability to reduce the use of non-clinical agents that cause resistance to clinical agents in both agricultural and urban environments.[25,99] Such regulation needs to be protected, alongside a strong human health and animal health approach to preventing the emergence of AMR.[85] This includes ending the non-therapeutic prophylactic/metaphylactic use[105] of antibiotics in animals in NZ as soon as possible[4,105] (and well ahead of the NZVA's goal of NZ by 2030 not needing antibiotics for the maintenance of animal health and wellness[106]).

More generally beyond NZ, and for some countries in particular, stricter regulation of agricultural use is likely to be an important measure to dampen emergence of new resistance mechanisms. In future years, agricultural antibiotic consumption in North America,[107] India and China has the potential to affect antibiotic resistance rates in NZ healthcare settings. This problem is similar in many ways to other international problems in sustainability that involve the 'tragedy of the commons'[108,109,110] like climate change.[4] Such problems highlight the need for international cooperation[78,96] with governance structures, rules and targets[4] to address these challenges.[4,122]

**11. A national strategy that links with international efforts, with NZ complementary high-level review**

The NZCPHM supports the cross government work by multi-agency groups to develop a national strategy, led jointly by the MoH and MPI, committed for May 2017.[9] This accords with calls in NZ for national strategy, coordination and leadership,[2,12,114] similar to other OECD countries[62,63,115,116] and the need for countries to have comprehensive, financed national plans for AMR.[5,6,18]

The NZCPHM notes the recommendations of the recent UK National Institute for Health Care Excellence (NICE) guidelines on antimicrobial stewardship (August 2015),[117] and supports national leadership and efforts at least similar to those of Australia.[118,119]

The 'One Health'[3] approach, combining the efforts of a broad range of sectors and stakeholders eg. health, veterinary and agriculture, should be applied when developing strategic frameworks to reduce AMR.

To enhance various levels of action underway in NZ in 2016, the NZCPHM recommends complementing these with a comprehensive high-level review encompassing both the human and animal health sectors in NZ. This could be led by the Royal Society and the Prime Ministers Chief Science Advisor (similar to the 2014 review of water fluoridation[120]).

**12. International governance**

International coordination and collaboration is needed,[77] with countries individually having comprehensive, financed national plans for AMR,[5,7] but also international governance.[4,122] AMR is a global problem, beset by the 'tragedy of the commons',[4,108,109,110] and needing international governance structures to address it, including rules and targets.[4] This is similar to world-threatening complex health issues like climate change.[112,113,121] Global efforts might eventually include a new UN-level coordinating body and an international treaty with strong implementation mechanisms.[121,122]

***Other organisations***

The NZCPHM supports, in general, the positions on antimicrobial resistance/stewardship of the following organisations:

- The NZ Veterinary Association's 2015 Policy on the judicious use of antimicrobials[10]

- The Royal New Zealand College of General Practitioners' 2015 Policy Brief: Antibiotics and antimicrobial resistance: avoiding the post-antibiotic era[11]
- The Royal Australasian College of Physicians' 2016 policy on antimicrobial resistance[12]
- The UK National Institute for Health Care Excellence's guidelines on antimicrobial stewardship[117]
- The UK Department of Health, Department for Environment Food & Rural Affairs UK 5 Year Antimicrobial Resistance Strategy 2013 to 2018.[63]
- The WHO Western Pacific Regional Office action agenda[6] and WHO Global action plan[7] on antimicrobial resistance.

## Links with other NZCPHM policies

- Pandemics and Emerging Infectious Diseases (forthcoming)
- Sustainability
- Immunisation
- Health Equity
- Housing
- Trans-Pacific Partnership Agreement
- Climate change

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