



# Antimicrobial resistance – 2019 update-provisos

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## to the New Zealand College of Public Health Medicine Policy Statement on Antimicrobial Stewardship and Infection Control

This update-provisos document updates sources and key messages for the NZCPHM's 2016 policy statement on antimicrobial resistance.<sup>1</sup>

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

The NZCPHM continues to support antimicrobial stewardship (AMS) being a national priority, requiring widespread commitment and leadership from all sectors in New Zealand,<sup>1</sup> and supports the 2017 New Zealand AMR Action Plan<sup>2</sup> and the 2018 national guidelines on carbapenemase-producing *Enterobacteriaceae* (CPE).<sup>3</sup>

The NZCPHM continues to call for international governance structures, treaties and targets,<sup>4</sup> and calls for governments to evaluate AMR policies/interventions, ensure such AMR policies/interventions help achieve health equity, explore the full range of possible AMR policy options, and link AMR policies to the United Nations (UN) Sustainable Development Goals.

### Key messages

- Antimicrobial resistance (AMR) is a major public health issue.
- New Zealand needs effective stewardship of antimicrobials, with widespread commitment and leadership from human, animal and agricultural sectors in New Zealand, working together.
- The NZCPHM supports the 2017 New Zealand AMR Action Plan, with its objectives and priority areas.
- Carbapenemase-producing *Enterobacteriaceae* (CPE) are an emerging risk; the NZCPHM supports the national guidelines on CPE and their inclusion of residential care facilities. The NZCPHM recognises the importance of national guidelines specific to long term residential care.
- The NZCPHM continues to call for international governance structures, treaties and targets.
- The NZCPHM calls for governments to evaluate AMR policies/ interventions, ensure such AMR policies/ interventions help achieve health equity, explore the full range of possible AMR policy options, and link AMR policies to the UN Sustainable Development Goals.

## Background/context

This update-provisos document updates sources and key messages for the NZCPHM's 2016 policy statement on antimicrobial resistance.<sup>1</sup>

Public health is the art and science of preventing disease, prolonging life, and promoting health through the organised efforts of society.<sup>5</sup> Public health has historically been the biggest driver of improved health for people.<sup>6</sup> Advancements in public health in the last 100 years, such as control of infectious diseases through clean water and improved sanitation, vaccination, and the recognition of tobacco use as a health hazard, have led to improvements in health and wellbeing, and a substantial increase in life expectancy.<sup>7</sup>

The NZCPHM represents the medical speciality of public health medicine in New Zealand. Public health medicine is defined as the branch of medicine concerned with the epidemiological analysis of the health and health care of populations and population groups. It involves the assessment of population health and health care needs, the development of policy and strategy, health promotion, the control and prevention of disease, and the organisation of services. Public health is focussed on achieving health equity across ethnic, socioeconomic, age, ability, and cultural groups, and promoting environments in which everyone can be healthy.<sup>8</sup>

Public health medicine specialists have a professional responsibility to act as advocates for health for everyone in society.<sup>8-10</sup> This means the NZCPHM advocates for and supports evidence-informed<sup>11</sup> equity-enhancing<sup>12</sup> policies for health and wellbeing that accords with te Tiriti o Waitangi, the UN Sustainable Development Goals, and health promotion and Health in All Policies approaches, each grounded in the societal<sup>i</sup>, economic and environmental determinants of health.<sup>9-19</sup> In relation to AMR and the need for antimicrobial stewardship and infection control, the NZCPHM is therefore continuing to call for widespread leadership and rapid action<sup>1</sup> to meet the objectives and priority areas of the AMR national action plan<sup>2</sup>.

Further information on the context of public health and NZCPHM policy statements is available on the [NZCPHM website](#).

## Update/provisos

The 2016 policy statement on antimicrobial resistance<sup>1</sup> was developed in 2016, with review scheduled for 2018. In this, the NZCPHM supported antimicrobial stewardship (AMS) being a national priority, requiring widespread commitment and leadership from all sectors in New Zealand – using a 'One Health'<sup>20</sup> approach recognising the inextricable links between ecosystems and the development of AMR in humans and in other species.<sup>21</sup>

Developments since the NZCPHM's 2016 policy statement have included:

- the joint NZCPHM/NZMA editorial in the NZMJ 2016,<sup>4</sup> on the RACP's AMR policy statement,<sup>22,23</sup> with the NZCPHM/NZMA calling for international action to complement and coordinate national AMR efforts, including global governance structures, rules and targets;<sup>4,23</sup>
- finalising and publishing the New Zealand AMR Action Plan;<sup>2</sup>
- the Royal Society of New Zealand 2017 report on AMR and its implications for New Zealanders;<sup>26</sup>

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<sup>i</sup> Societal determinants of health include commercial, political, governance, economic, cultural, even religious determinants — being the societal structures that are the conditions for health and disease. Each of the structural determinants eventually impact on health in a positive or negative way.

- development of national guidelines on carbapenemase-producing *Enterobacteriaceae* (CPE);<sup>3,27,28</sup>
- the World Health Organization (WHO) naming antimicrobial resistance as one of the 10 global health threats in 2019 (alongside air pollution and climate change, noncommunicable diseases, global influenza pandemic, vaccine hesitancy, fragile and vulnerable settings, Ebola and other high-threat pathogens, weak primary health care, Dengue, and HIV);<sup>29</sup>
- the 2019 report by the UN Interagency Coordination Group (IACG) on Antimicrobial Resistance;<sup>30</sup>
- increasing recognition of the need for AMR policies/ interventions to help achieve health equity, given the higher burden of infectious diseases in Māori and Pacific Peoples;<sup>31,32</sup>
- systematic evidence of specific government policy interventions addressing AMR, suggesting often a lack of rigorous evaluation of policy options and over-reliance on public awareness and individual prescriber behaviours;<sup>34</sup>
- calls internationally to link AMR policies to the UN Sustainable Development Goals.<sup>35-39</sup>

#### *New Zealand AMR Action Plan*

The New Zealand AMR Action Plan<sup>2</sup> was preceded/informed by WHO recommendations<sup>40-42</sup> and supporting evidence in the joint MoH/MPI situation analysis.<sup>25</sup> The plan is a national, cross government, multi-agency, multi-sector strategic framework and implementation plan that integrates preventing infections, improving antimicrobial prescribing and stewardship in community and healthcare settings, public education, national/DHB-level monitoring/surveillance, regulation of agricultural and veterinary use (and improving stewardship) of antimicrobials, international collaboration and engagement, and research.<sup>1,2</sup>

The national action plan covers the following general objectives and consequent priority action areas (PAAs):<sup>2</sup>

- Objective 1: Awareness and understanding – Improve awareness/understanding of AMR (viz communication, education and training)
  - Priority action area (PAA) 1: consumer awareness (understanding of AMR, importance appropriate use).
  - PAA 2: awareness and education (AMR, antimicrobial stewardship) in all prescribers and the human health, animal health and agricultural sectors.
- Objective 2: Surveillance and research – Knowledge/evidence
  - PAA 3: Coordinated national surveillance programme of AMR/antimicrobial use in humans/animals/agriculture.
  - PAA 4: List priority organisms, key resistance genes and antimicrobials for national reporting.
  - PAA 5: Implement national minimum standard for laboratory testing and reporting of antimicrobial susceptibility.
  - PAA 6: Support national priorities for research on AMR, antimicrobial consumption and stewardship in human health/animal health/agriculture.
- Objective 3: Infection prevention and control – Improve prevention and control measures across human health and animal care settings (to prevent infection and transmission of micro-organisms)

- PAA 7: Develop/update national guidelines/standards for IPC (national consistency), enhance accreditation and quality assurance programmes (for best-practice) across human health/animal health/agriculture.
- PAA 8: 'One Team' approach to IPC in all human health care facilities.
- PAA 9: Immunisation to prevent infections.
- PAA 10: Prevent/control zoonoses.
- PAA 11: Alternative approaches to reduce infection/antimicrobial need in animals.
- Objective 4: Antimicrobial stewardship – Optimise antimicrobial use in human health/animal health/agriculture, including their regulation
  - PAA 12: develop national programme/standard for AMS in all sectors of human health, including resources/targets.
  - PAA 13: national programme/standard for AMS in animal health.
  - PAA 14: programme of regular monitoring/controls for veterinary antimicrobials.
  - PAA 15: Review controls (conditions of registration)/labelling/advertising of antimicrobial-based trade name products.
- Objective 5: Governance, collaboration and investment
  - PAA 16: a sustainable coordinating national governance structure.
  - PAA 17: sustainable investment in ongoing surveillance, communication, stewardship and infection prevention and control, etc.
  - PAA 18: national and international links/collaboration.

The full specific objectives, priority action areas and activities are detailed in the national action plan at <https://www.health.govt.nz/publication/new-zealand-antimicrobial-resistance-action-plan>.<sup>2</sup> The NZCPHM supports the national action plan, and notes progress made to date.<sup>43</sup>

#### *Carbapenemase-producing Enterobacteriaceae*

Carbapenemase-producing *Enterobacteriaceae* (CPE) have been identified as an emerging AMR threat to New Zealand.

In response, national guidelines on CPE were published in 2018 (<https://www.health.govt.nz/publication/infection-prevention-control-and-management-carbapenemase-producing-enterobacteriaceae-cpe>).<sup>3</sup> These guidelines set recommendations, requirements and response actions for the prevention, management, and control of health care-associated CPE infections in New Zealand health care facilities, including acute care facilities (tertiary and secondary-level hospitals, including public and private surgical hospitals) and residential care facilities (including dementia units, rest homes and hospitals and others providing long-term care for people with disabilities).

The guidelines were preceded by calls for CPE to be specifically addressed in the national AMR strategy, and a coordinated systems-based national response plan to CPE (similar to those for pandemic influenza and Ebola) beyond guidelines<sup>27</sup> that will prime for future AMR threats.<sup>27,28</sup> Calls emphasised the risk of CPE spread into aged-related long-term residential care facilities, and had the national plan having both general measures and measures specifically targeting CPE, with number of minimum specifications that included:

- minimum laboratory standards to detect CPE;
- minimum targeted IPC policies and procedures within all healthcare and residential care facilities to identify and manage CPE-colonised patients and reduce transmission;

- public health surveillance for CPE, with systems for prompt response to suspected or confirmed CPE transmission cases and epidemics;
- a broader national antimicrobial stewardship strategy, with sector-wide AMS programmes, including better control in residential care facilities and lessening the use of antibiotics for travellers' diarrhoea (especially ciprofloxacin);
- resourcing the CPE response plan; and
- access to colistin and other essential antimicrobials, including national emergency stockpiles).<sup>27,28</sup>

The NZCPHM generally supports the national guidelines on CPE,<sup>3</sup> in particular the emphasis on systems and extending beyond acute care facilities to residential care facilities.<sup>27,28</sup> The NZCPHM also recognises the importance of national guidelines specific to long term residential care.

### *Health equity*

AMR policies/ interventions need to include and account for health equity, including the higher burden of infectious diseases in Māori and Pacific Peoples.

Balance is needed between appropriate antimicrobial use and the risks of antimicrobial resistance that can arise from overuse. Nuance is necessary, so that programmes and practices to reduce antimicrobial consumption do not inadvertently lead to reduced treatment for those infections where antimicrobials are clearly indicated. This is where, unless designed carefully, programmes aiming to reduce the general rates of antimicrobial treatments could worsen already existing inequity gaps in access and contribute to inequitable health outcomes for Māori and Pacific Peoples.<sup>31,32</sup>

Upstream interventions remain important to reduce health inequities from infections in the first place, by addressing drivers such as immunisation, breastfeeding, nutrition, socioeconomic deprivation, household overcrowding and hazardous housing, smoking, and obesity/diabetes.<sup>1</sup>

The NZCPHM calls for policies and programmes to evaluate equity and monitor for unintended impacts,<sup>32</sup> to achieve health equity.<sup>12,33</sup>

### *General*

The systematic review of specific government policy interventions<sup>34</sup> identified 17 distinct policy options that have been evaluated for their ability to reduce antimicrobial use. Public awareness campaigns and guidelines were those most commonly evaluated, and overall the focus of policies and programmes was more on changing the practice of individual prescribers rather than targeting other healthcare professionals or altering healthcare structures to reduce overuse and misuse of antibiotics. The review highlighted how different governments have different policy levers, including complex regulatory, legislative, fiscal, and service provision levers, which may potentially be more effective than policies focused on individual prescriber behaviour change. The review called for governments to ensure AMR policies and interventions are evaluated and results disseminated, and for governments to explore the full range of possible AMR policy options beyond public awareness campaigns and guidelines.<sup>34</sup>

The NZCPHM continues its call for strengthened international governance structures, treaties and targets.<sup>1,4,24</sup>

The NZCPHM repeats the calls for governments to evaluate AMR policies and interventions and disseminate results,<sup>34</sup> and for governments to explore the full range of possible AMR policy options beyond public awareness campaigns and guidelines,<sup>34</sup> including in and for New Zealand.

The NZCPHM also calls for AMR policies to link with the UN Sustainable Development Goals,<sup>14,35-39</sup> which New Zealand is a signatory to. This would increase the visibility of AMR at international governance forums, highlighting the relationship of AMR to other sustainability issues and goals.<sup>39</sup>

The NZCPHM acknowledges and notes its continued support in general the AMR policies of other New Zealand human and animal health organisations.<sup>22,23,44,45</sup>

The NZCPHM 2016 policy statement on antimicrobial resistance<sup>1</sup> should be read with all of these above provisos.

## Acknowledgement

The original policy statement and these update-provisos were developed by the NZCPHM Policy Committee, NZCPHM members and staff. Authorship or review is recorded in the list of policy statement main authors on the College's Policy Statements webpage at <https://nzcphm.org.nz/Policy-Statements/10944/>.

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# Combating antimicrobial resistance demands nation-wide action and global governance

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Antimicrobial resistance is a growing threat to global health and health systems everywhere. Curbing this threat demands both nation-wide action and strong international governance. The Royal Australasian College of Physicians, New Zealand College of Public Health Medicine and New Zealand Medical Association call for comprehensive, well-funded measures across New Zealand's veterinary medicine, agriculture, human community and healthcare settings. International action is needed in parallel—with effective governance structures, rules and targets.

Antimicrobial resistance (AMR) increasingly threatens New Zealanders' health and our health system. International recognition is growing; in recent weeks we have seen:

- The United Nations (UN) convening a special one-day meeting (only the fourth time the General Assembly has ever held a high-level meeting on a health issue), with global leaders committing to fighting antimicrobial resistance together.<sup>1,2,3</sup>
- The UN's Food and Agriculture Organization (FAO) releasing its action plan on AMR and the food chain.<sup>4</sup>
- The UN Secretary-General's High-Level Panel on Access to Medicines highlighting antimicrobials and AMR in particular.<sup>5</sup>
- In New Zealand, the New Zealand College of Public Health Medicine (NZCPHM) releasing the NZCPHM policy statement on AMR,<sup>6</sup> endorsed by the New Zealand Medical Association (NZMA), calling for national planning to be comprehensive, well-funded and monitored in the face of New Zealand's looming crisis.<sup>6,7,11</sup>
- And in today's issue of the *Journal*,<sup>8</sup> Humphrey Pullon and colleagues for The Royal Australasian College of Physicians (RACP) are strongly reiterating

the RACP's explicit call<sup>9,10</sup> (supported by the NZMA<sup>11</sup>) for measures based on the World Health Organization (WHO)'s 2011 six-point plan.<sup>12,13</sup>

AMR is described as a leading global health issue that "threatens the very core of modern medicine".<sup>14</sup> Some common infections may become very difficult to manage and some forms of surgery and chemotherapy could become untenable or unsafe.<sup>15</sup> As the RACP cites,<sup>8,9</sup> left unchecked, AMR could cause 10 million deaths globally each year (more than from cancer) by 2050 and cost \$US100 trillion in lost economic output (as context, the world's current annual GDP being \$US107–113 trillion, see endnote \*)—although fuller modelling of underlying cumulative incidence/future prevalence is needed (endnote †).<sup>15–18</sup>

The genie of AMR is already well and truly out of the bottle, with AMR impacts now widespread. Pan-resistant (or very close to pan-resistant) gram-negative organisms are found already in many countries, with drug-resistant infections thought responsible now for at least 700,000 deaths each year.<sup>15,16</sup> Given our increasingly interconnected world, these organisms are now being introduced and detected in New Zealand. The scale and extent are described by the RACP, NZCPHM, WHO and the O'Neill Review.<sup>6,8,9,12–16</sup>



Tackling AMR is both national and global. In response to a commitment to the WHO, New Zealand (co-led by the Ministry of Health and Ministry for Primary Industries) is developing a comprehensive national strategic plan for AMR, due by the end of May 2017.<sup>19,20</sup> Directions called for by the WHO, NZCPHM and RACP include:<sup>6,8,9,12-14</sup>

- financed national AMR plans and guidelines
- national quality improvement programmes<sup>8,9</sup>
- clinical governance
- enhanced AMR surveillance
- new antimicrobials and vaccines
- optimising existing antimicrobials
- preventing infections in community and healthcare settings (eg, immunisation; infection prevention and control (IPC)—including isolation and screening for multi-drug resistant organisms in patients previously hospitalised overseas<sup>6</sup>)
- wise use of antimicrobials in human health and animal health/horticulture—with education and governance; a single national antimicrobial prescribing guideline<sup>8,9</sup>
- education/governance/regulation of antimicrobial used in veterinary medicine, agriculture and horticulture.<sup>6</sup>

Successful implementation will need widespread leadership and commitment across the healthcare, veterinary and agricultural sectors—using a ‘One Health’ approach.<sup>6,21</sup> This ‘One Health’ approach recognises that ecosystems and AMR development in humans and other species are inextricably linked, as are the solutions.<sup>6</sup>

## Global efforts are needed beyond national action

National action is important but remains largely confined within countries. International action is essential to complement and coordinate local and national AMR efforts.<sup>22</sup> Globally, countries’ AMR impacts, access to antimicrobials and abilities to address AMR

vary widely,<sup>22-25</sup> yet all our health and health systems will depend on strong consistent action. The unwise and injudicious use of antimicrobials across and within nations has effectively ‘depleted’ them as a common resource for humankind (endnote ‡)—we are all affected and vulnerable. Like climate change,<sup>26</sup> with AMR the practices of some affect many others.<sup>27-31</sup>

Decisive AMR action is also justified from a health equity perspective.<sup>23,32-34</sup> Low- and middle-income countries suffer disproportionately from AMR-related disease, while also lacking resources and capabilities to mitigate this growing problem.<sup>23-25,34-37</sup> Unchecked, AMR is likely to significantly worsen the health of future generations in ways that are not yet conceivable.<sup>23,32</sup> Lack of effective action now has potentially serious implications for intergenerational equity.<sup>23</sup>

The high level UN Panel report<sup>5</sup> highlights the failure of the conventional market model to adequately stimulate the antimicrobial research and development (R&D) pipeline<sup>5,15,38</sup>—which is another reason for international cooperation and governance. To address this market failure, the UN Panel recommends countries negotiate a binding global Health R&D convention that delinks the costs of research and development from end prices, so that access can be universal. In particular, the UN Panel calls for such a global treaty focussing on public health needs, including neglected diseases and AMR.<sup>5</sup>

Equitable access to appropriate antimicrobial treatment is also essential in any international governance framework. Concerns about excess human antimicrobial consumption globally must balance against absent, or delayed, antimicrobial access—which is currently killing more children than AMR does.<sup>34,39,40</sup> Ironically, while children are dying because of lack of access, the same antimicrobials are used liberally to maximise commercial productivity in high intensity agriculture.<sup>34</sup>

But most importantly, resistant strains spread rapidly across borders,<sup>41-44</sup> and international cooperation and governance structures (eg, rules and targets) will be critical to tackling AMR.<sup>22,27,34</sup> These measures include:

- Improved and standardised international integrated systems of surveillance of antimicrobial use (both human and animal), AMR patterns and disease burden (and infectious diseases generally)—including data consistency and sharing.<sup>15,45</sup>
- Addressing the supply of poor-quality and falsified antimicrobial drugs<sup>46,47</sup> (endnote §) and the online sale of antimicrobials without prescription—which transcend borders.<sup>47</sup>
- Stricter regulation of antimicrobial use in agriculture,<sup>6,48</sup> in line with internationally agreed principles and including the revision of international standards.<sup>4</sup>
- Perhaps most crucially, global efforts might eventually include a new supra-national UN-level coordinating body and an international treaty with strong implementation mechanisms<sup>15,31,22</sup> that include rules, setting targets and holding nations to account.<sup>22,27,34</sup>

New Zealand can and should take leadership within this global response—with action both by government agencies and professional organisations. By being a relatively respected country internationally with good governance, and with our large agricultural export sector to future-proof with ‘One Health’,<sup>6,21</sup> we could be a key player. In particular we could help broker larger nations putting their weight into international action<sup>22</sup>—including governance structures, rules and targets<sup>6,22,27,34</sup>—to address the AMR threat.

Pullon et al<sup>8</sup> are absolutely right; we need to do much more in New Zealand now, to establish and follow best practice for control of AMR. Yet at the same time, we must not forget the wider picture. AMR is a big, tough, worldwide problem—and demands both nation-wide action and global governance.

## Endnotes

\* Purchasing parity power (PPP) gross domestic (US\$–PPP) calculations by IMF, World Bank, CIA World Factbook, compiled at [http://en.wikipedia.org/wiki/List\\_of\\_countries\\_by\\_GDP\\_\(PPP\)](http://en.wikipedia.org/wiki/List_of_countries_by_GDP_(PPP))

† The Review on Antimicrobial Resistance<sup>15,16</sup> estimates of AMR burden (year 2050 10 million AMR deaths and US \$100 trillion cost) are broad-brush,<sup>16</sup> being notional scenarios of underlying cumulative incidence/future prevalence that need fuller modelling. The estimates were derived from commissioned reports by Rand Europe ([http://www.rand.org/pubs/research\\_reports/RR911.html](http://www.rand.org/pubs/research_reports/RR911.html))<sup>17</sup> and KPMG (<http://www.kpmg.com/UK/en/IssuesAndInsights/ArticlesPublications/Documents/PDF/Issues%20and%20Insights/amr-report-final.pdf>),<sup>18</sup> which were high-level assessments of future impacts of AMR, based on notional scenarios for rising resistance and economic growth to 2050 (undiscounted). Costs were confined to labour force effects (but not including social or health sector costs), and deaths and costs confined to a subset of resistance (being just three (*K. pneumoniae*, *E. coli*, *S. aureus*) of seven priority drug-resistant bacteria highlighted by WHO as key concerns, and three public health issues (HIV, TB, malaria)), using notional 40% to 100% resistance scenarios, estimating by 2050 world productivity being between 2% and 3.5% less than projected if AMR kept at 2014 levels.<sup>16,17,18</sup> Costs were not discounted.

‡ Addressing the challenge of AMR is complicated by the ‘tragedy of the commons’. This form of market failure is where, within any shared-resource system, no person, organisation or nation state is (or has incentive to be) responsible,<sup>27,28,29,30</sup> to the detriment of the global common good.<sup>49</sup>

§ According to The Review on Antimicrobial Resistance, poor quality and falsified antimicrobials fuel the development of AMR by delivering sub-therapeutic antimicrobial doses, providing sufficient exposure to start to develop resistance without adequately treating the infection. Growing numbers of online pharmacies also exploit gaps in the global regulatory mechanisms to offer antimicrobials for sale around the world, often without prescription or clinical guidance—which fuels self-medication and encourages the development of drug-resistant strains of infection by increasing unnecessary and excessive antimicrobials use.<sup>47</sup>

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SM is an observer on the joint Ministry of Health/Ministry for Primary Industries AMR action plan development group.<sup>20</sup> SM and PM are employed by PHARMAC; the views expressed do not necessarily represent those of PHARMAC.

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<http://www.nzma.org.nz/journal/read-the-journal/all-issues/2010-2019/2016/vol-129-no-1444-28-october-2016/7042>

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# Antimicrobial Stewardship and Infection Control: Limiting the burden of antimicrobial resistance in New Zealand

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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<sup>1,2</sup> – using a ‘One Health’<sup>3</sup> approach that recognises ecosystems and the development of AMR in humans and AMR in other species are linked inextricably.<sup>4</sup>

In line with World Health Organization (WHO) recommendations,<sup>5,6,7</sup> 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.<sup>4,8</sup>

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.<sup>9</sup>

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).<sup>10,11,12</sup>

## Background

The increasing emergence and spread of antimicrobial resistance (AMR) is an international health concern and burden on individual countries.<sup>7,13,14,15,16,17,18</sup> 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.<sup>19</sup> 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”.<sup>7</sup> Predictions are that, unchecked, by 2050 AMR will cause 10 million deaths globally each year.<sup>8</sup>

Systematic review evidence<sup>20</sup> 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.<sup>21</sup> Further evidence, which includes data from Europe, indicates a strong correlation between the level of antibiotic use and the prevalence of resistance.<sup>22</sup> 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.<sup>1</sup> 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<sup>23</sup>);
- transmission of resistant organisms in both community and healthcare settings;
- importation of resistant pathogens from areas where multi-drug resistant organisms are endemic;<sup>24</sup> and
- environmental and genetic factors that alter the viability of resistant bacteria.<sup>25,26</sup>

Other NZ researchers have also highlighted the problems around AMR,<sup>27</sup> reporting on the relative success of interventions, eg. the antimicrobial stewardship programmes at hospitals such as Auckland City Hospital,<sup>28</sup> 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.<sup>29</sup> 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.<sup>9</sup> This national action plan aligns with the WHO’s ‘One Health’ initiative – the integration of human medicine, veterinary medicine and environmental science.<sup>3</sup>

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<sup>30,31</sup> and respiratory<sup>32</sup> hygiene), safe food preparation and handling, good nutrition,<sup>33</sup> breastfeeding,<sup>34</sup> and high immunisation coverage.

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

## **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.<sup>40,41</sup> Control of AMR is an international issue, given strong epidemiological evidence of resistant strains starting elsewhere then spreading rapidly with travel.<sup>42,43</sup> 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.<sup>23,44,45</sup>

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*<sup>46</sup> (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)<sup>47,48</sup> and the infection prevention and control programmes of the Health Quality & Safety Commission (HSQC).<sup>49</sup>

#### **4. Improving antimicrobial prescribing and stewardship in the community**

Community dispensing of antibiotics in NZ currently accounts for most human use.<sup>50</sup> Preventing over-use of antimicrobials in the community<sup>i</sup> is important in slowing the development and spread of antibiotic resistant bacteria.<sup>51</sup> Preventing antimicrobial over-use needs commitment by health professionals<sup>i</sup> 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.<sup>52</sup>

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.<sup>53</sup> Similarly, another systematic review also indicates how educational interventions can improve prescription and dispensing of antibiotics by clinicians.<sup>54</sup> 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.<sup>55</sup> 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.<sup>56</sup>

#### **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).<sup>57</sup> There is also published relative success reported for the antimicrobial stewardship programme at Auckland City Hospital,<sup>28</sup> alongside programmes in other District Health Boards (DHBs).<sup>58</sup> Recommendations include better monitoring/reporting of antimicrobial consumption in hospitals and regional antimicrobial prescribing guidelines for hospital use.<sup>12,1</sup>

#### **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.<sup>60</sup> 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<sup>61</sup>) 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;
- testing isolates from a wide range of patients for susceptibility to a range of relevant antimicrobials;
- reporting results to clinicians;

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<sup>i</sup> 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.

- 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.<sup>59</sup>

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.<sup>62</sup> Surveillance is needed at local and national levels, and globally,<sup>62</sup> 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.<sup>24,63</sup>

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

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

### **8. DHB-level monitoring**

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

### **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.<sup>8,75,76,77,78</sup> Strategies to minimise the use of new antimicrobials (including vaccines and rapid diagnostic testing<sup>8</sup>) 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.<sup>79,80</sup> The challenge is to incentivise new antimicrobial development<sup>8,75</sup>, without also inadvertently encouraging inappropriate use or reducing access to those most in need. This is no easy task with current research funding models.<sup>76,78</sup>

### **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,<sup>57,82</sup> and threats to our ability to regulate their use.<sup>85</sup> A 'One Health'<sup>3</sup> approach is needed, linking the health, veterinary and agriculture sectors.<sup>78</sup>

Veterinary use of antimicrobials (relative to biomass consumption<sup>ii</sup>) is perhaps 8% that of human use in NZ<sup>88</sup> and our use of antimicrobials in animals is likely to be low compared with other developed countries, at least in terms of crude antimicrobial tonnage compared with crude livestock biomass.<sup>8,88,90</sup> 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<sup>89</sup> eg. fluoroquinolones) and the types of livestock, intensification<sup>94</sup>, their trends over time,

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

and parallel incidence of/trends in AMR in animals.<sup>67,iii</sup> In addition, animals can spread resistance and antibiotics in ways that people generally do not<sup>91,92</sup> – meaning that it is not only about how much antibiotics are used, but how effectively that use causes the spread of resistant organisms.<sup>iv</sup>

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<sup>93,94,97</sup> (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.<sup>95</sup> 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<sup>iii</sup>, 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.<sup>15</sup>

There is increasing use in NZ of 3rd-generation cephalosporins and other CIAs in the veterinary sector.<sup>68</sup> This usage increases the risks of developing significant AMR in bacteria infecting both food-producing and companion animals.<sup>24,68</sup> Also concerning is the veterinary use of polymyxins,<sup>68</sup> given recent plasmid-mediated resistance in food-producing animals<sup>96</sup> (polymyxins 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.<sup>98,99</sup>

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

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

Hence, in order to preserve remaining antimicrobials for patients in whom they are absolutely vital – such as the immune-compromised and critically ill<sup>78</sup> – the capacity to introduce regulations to reduce harmful antibiotic use in the agricultural sector remains important.<sup>82,105</sup> 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.<sup>25,99</sup> Such regulation needs to be protected, alongside a strong human health and animal health approach to preventing the emergence of AMR.<sup>85</sup> This includes

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

<sup>iv</sup> 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.<sup>91,92</sup>

<sup>v</sup> 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<sup>105</sup> in food-producing animals; in this regard, the NZVA currently leads a programme to better monitor antimicrobial usage in animals.<sup>100</sup>

<sup>vi</sup> The WHO recommends that the routine use of certain antimicrobial agents as growth promoters in agriculture be rapidly phased out or terminated.<sup>101</sup> Evidence from Denmark supports this policy, with AMR substantially reduced following a reduction in antibiotic use for growth promotion.<sup>102</sup> 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.<sup>100</sup>

ending the non-therapeutic prophylactic/metaphylactic use<sup>105</sup> of antibiotics in animals in NZ as soon as possible<sup>4,105</sup> (and well ahead of the NZVA's goal of NZ by 2030 not needing antibiotics for the maintenance of animal health and wellness<sup>106</sup>).

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,<sup>107</sup> 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'<sup>108,109,110</sup> like climate change.<sup>4</sup> Such problems highlight the need for international cooperation<sup>78,96</sup> with governance structures, rules and targets<sup>4</sup> to address these challenges.<sup>4,122</sup>

### **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.<sup>9</sup> This accords with calls in NZ for national strategy, coordination and leadership,<sup>2,12,114</sup> similar to other OECD countries<sup>62,63,115,116</sup> and the need for countries to have comprehensive, financed national plans for AMR.<sup>5,6,18</sup>

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

The 'One Health'<sup>3</sup> 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<sup>120</sup>).

### **12. International governance**

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

#### ***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<sup>10</sup>
- The Royal New Zealand College of General Practitioners' 2015 Policy Brief: Antibiotics and antimicrobial resistance: avoiding the post-antibiotic era<sup>11</sup>
- The Royal Australasian College of Physicians' 2016 policy on antimicrobial resistance<sup>12</sup>
- The UK National Institute for Health Care Excellence's guidelines on antimicrobial stewardship<sup>117</sup>
- The UK Department of Health, Department for Environment Food & Rural Affairs UK 5 Year Antimicrobial Resistance Strategy 2013 to 2018.<sup>63</sup>



- The WHO Western Pacific Regional Office action agenda<sup>6</sup> and WHO Global action plan<sup>7</sup> 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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