Antimicrobial Stewardship in New Zealand

Scoping Research

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CONTENTS

EXECUTIVE SUMMARY

Interviews involving experts from across the health sector were conducted in April and May 2013 to investigate the context and recommendations for antimicrobial stewardship (AMS) in New Zealand. Participants agreed that antimicrobial resistance (AMR) is an important and growing public health concern, based in both hospital and community settings. Further action to combat AMR was called for, in particular an overarching national approach for AMS including the development of National Antibiotic Guidelines. Rationalising antibiotic use was also seen as a necessary medication safety and cost-efficiency measure. Some activity relating to the stewardship of antibiotics is occurring across multiple agencies, but broader and more joined-up action was recommended. Leadership and coordination of AMS should sit centrally, within the Ministry of Health (MOH) or the Health Quality and Safety Commission (HQSC). Quality improvement methodology should be utilised to enhance the appropriate use of antimicrobials.

RECOMMENDATIONS

There was strongest consensus from interview participants for the following actions to take place:

1. National leadership and coordination of AMS activities should occur
    - Central management of AMS is required, involving HQSC and /or MOH as leaders, in conjunction with system-wide partnerships and clinician buy-in

2. National Antimicrobial Guidelines should be developed as a necessary part of AMS
    - To be facilitated via the MOH, PHARMAC, BPAC, ASID and clinicians

3. Quality improvement tools and measures in relation to appropriate antibiotic use should be established.

1. BACKGROUND

An effective approach to antimicrobial stewardship (AMS) is a key strategy for infection prevention and control. This paper discusses the context and recommendations for AMS in New Zealand. Antimicrobial resistance (AMR) is a growing health threat worldwide, with increasing rates of bacteria resistant to antibiotics and a shortage of new antibiotics becoming available (WHO x2, 2012). Inappropriate antibiotic consumption among humans and animals contributes to the problem. International recommendations to address AMR include the implementation of AMS programs across all healthcare settings and the "stewardship by government" of prudent antibiotic use (WHO, 2011; WHO 2012).

DEFINITIONS

Antibiotic or antimicrobial resistance (AMR): *Resistance of a microorganism to an antibiotic or antimicrobial medicine to which it was previously sensitive. Infections caused by resistant micro-organisms often fail to respond to conventional treatment, resulting in prolonged illness and an increased risk of death (WHO 2012)*

Antibiotic or antimicrobial stewardship (AMS): *Coordinated interventions designed to improve and measure the appropriate use of antimicrobials by promoting the selection of the optimal antimicrobial drug regimen, dose, duration of therapy, and route of administration (IDSA 2012)*

2. PURPOSE AND METHODOLOGY OF THIS PAPER

To investigate the context and recommendations for AMS in New Zealand, Dr Imogen Thompson conducted fifteen semi-structured interviews with 22 participants during April and May 2013. Experts from across the health sector were interviewed, involving infectious diseases (ID) specialists, clinical microbiologists, senior advisors, pharmacists, a sexual health physician, a senior scientist, general practitioners and public health physicians including an epidemiologist and a medical officer of health (see Appendix below for Participant List). Interviews consisted of face-to-face meetings in Auckland and Wellington and phone interviews or teleconferences with South Island contributors.

This paper reports on and summarises the qualitative findings from the interviews, reflecting expert opinion. The paper cites key references to which participants referred, but does not provide an appraisal or review of other evidence and research on AMR and AMS. The research aims to present an initial high-level scoping of opinion throughout the sector.

3. CONTEXT: ANTIMICROBIAL RESISTANCE IN NEW ZEALAND

Interview participants agreed that AMR is a significant health concern in New Zealand, all acknowledging its importance as a public health issue. One described it as "the major infectious disease issue of our time". As has been seen worldwide, the prevalence of resistant microorganisms in New Zealand has increased during the past two decades. Organisms of concern that were most frequently mentioned, with associated comments, are shown in the Table 1 below:

Table 1. Antibiotic-resistant organisms of concern in New Zealand

Organism	Comments from interview participants
Methicillin-resistant *Staphylococcus aureus* (MRSA)	A recent ESR study showed a doubling of MRSA rates across the NZ population from 2005 to 2011 (from 8.6 to 18/ 100,000 people) with MRSA more commonly associated with infections in people in the community than in hospital settings (Williamson DA 2013).
Extended-spectrum β-lactamase-producing enterobacteriaceae (ESBL-E)	ID clinicians stated the problem of multi-drug resistant ESBLs and their insidious spread in hospitals and communities was more threatening than the apparently "more manageable" MRSA situation. Increasing rates of ESBLs are reportedly strongly driven by quinolone and cephalosporin use.
Vancomycin-resistant enterococci (VRE)	Increasing rates of VREs are driven by vancomycin use (vancomycin is increasingly required to treat MRSAs).
Multi-drug resistant tuberculosis (Tb)	Extensively multi-drug resistant cases of Tb have emerged, posing new challenges for public health and ID teams.
Neisseria gonorrhoeae	The increasing resistance of *N gonorrhoeae* to standard and "last line" antibiotics has generated worries that the sexually-transmitted infection (STI) gonorrhoea is becoming progressively untreatable. *N gonorrhoeae* in New Zealand is currently 50% resistant to oral ciprofloxacin and first-line treatment is now with injected ceftriaxone.

Most participants reported that the overall burden of disease from resistant pathogens is not currently as problematic in New Zealand as in other countries, but research on resistance patterns shows the situation is likely to worsen over time. They predicted that AMR will become a bigger concern and expense in the future unless action is taken to maintain effective antimicrobial therapeutic options. For example, there will be increasing resistance to second and third-line treatments, more patients requiring hospitalisation, more invasive or toxic therapies required for infections that were previously straightforward to treat in the community and more deaths due to untreatable bacterial infections. Interviews showed that the threat of a lack of treatment options for common infections was a real worry for clinicians. The additional cost to the health system of increasing AMR is causing concern particularly for DHB employees.

There was some consensus about the factors contributing to AMR in New Zealand but informants differed in their views about the relative contribution of various causes. Academic and clinical experts agreed that resistance among microbes is significantly correlated with antibiotic overuse and inappropriate use internationally. This is also the case in New Zealand, according to some specialists and (currently unpublished) research. Other participants thought globalisation involving increasing travel and migration from parts of the world incubating higher resistance rates was a more important cause of AMR in New Zealand, rather than the overuse of antibiotics here. Local prescribing patterns may contribute to the establishment of resistance after an importation event, rather than *de novo* mutations leading to emerging resistance. Other factors reported to be contributing to AMR in New Zealand were:

- community spread such as among household contacts, particularly in overcrowded settings

- environmental contamination eg in hospital or rest home settings
- poor hygiene
- misuse of antibiotics (eg non-compliance or inappropriate prescribing).

AMR in New Zealand was variably seen as predominantly a community or hospital-based problem, or both. In 11 out of 15 interviews, participants believed the problem was established in both settings and was intrinsically linked. In six interviews, AMR related to community prescribing was reported to be a more concerning – and growing – problem, particularly as about 90% of prescribing takes place in community settings. In four interviews, mainly with hospital specialists, the burden of AMR was seen as more serious for hospitals – as that is where "worst-case scenarios" would end up. It was said during these interviews that resistant microorganisms in secondary or higher care settings were of greatest severity, cost and importance.

The role of antimicrobial over-consumption in agricultural or horticultural settings has been linked to AMR in humans internationally, with transmission thought to occur via the food chain. Most participants agreed that the use of antibiotics in animals and plants was not as significant a causal factor in human AMR in NZ as elsewhere. Surveys have found antimicrobial resistance patterns in animals and food have not matched those of concern for humans in NZ. Some interviewees were concerned that the use of streptomycin, a "top-shelf" human antibiotic, in kiwifruit orchards in NZ could impact on human resistance to the antibiotic. One informant believed there was no causal link between the use of streptomycin in kiwifruit orchards and risk to humans.

4. RATIONALE FOR ANTIMICROBIAL STEWARDSHIP IN NEW ZEALAND

Interview participants reported that New Zealand was in a relatively favourable position on the world stage with a comparatively small AMR problem and conservative antibiotic usage, and so there was strong sentiment that "we now have a wonderful opportunity to stop or delay the emergence of further resistance". Among interviewees, it was unanimously agreed that more could and should be done to rationalise and reduce antibiotic consumption. AMS was described by one informant as the "sensitive use of antibiotics" and defined by another as "ensuring antibiotic selection, dose and duration is appropriate for the indication". Rationale for AMS involved reducing the incidence of resistant bacteria. Reducing unnecessary or inappropriate antibiotic use was also warranted in order to:

- Reduce adverse events such as side effects to antibiotic use (eg diarrhoea, rash, nausea, allergy, *Clostridium difficile* infection)
- Avoid the need for emergency department stays or hospitalisation
- Reduce the length and complexity of hospital stay
- Save money within the health system.

Three participants referred to the 2011 World Health Organization (WHO) policy package to combat AMR as basis for further commitment and action by NZ, as a WHO member state. They cited the WHO six-part policy package, as follows:

1. Commit to a comprehensive, financed national plan with accountability and civil society engagement
2. Strengthen surveillance and laboratory capacity
3. Ensure uninterrupted access to essential medicines of assured quality
4. Regulate and promote rational use of medicines, including in animal husbandry, and ensure proper patient care
5. Enhance infection prevention and control
6. Foster innovations and research and development for new tools (Leung et al, 2011).

Participants indicated were there were gaps in the NZ commitment to the six-part framework, most notably relating to parts 1 and 4: for example, a lack of national stewardship and coordination, limited government commitment, variable AMS programmes across the health sector and a lack of standard treatment guidelines.

Several further interviewees cited the recent warning of the United Kingdom's Chief Medical Officer (CMO) to respond to the "catastrophic threat" of AMR as timely justification for further AMS in NZ (Department of Health, 2013).

5. CURRENT ACTIVITIES RELATING TO AMR AND AMS IN NEW ZEALAND

All participants described recent and current work undertaken in NZ around the surveillance of antibiotic resistance or consumption, and this information is summarised below by organisation.

The Ministry of Health (MOH)

The MOH's Antimicrobial Resistance Advisory Group (ARAG) previously provided advice and oversight concerning all aspects of AMR relating to human health. This group was disbanded in 2010. According to several informants, there has since been little AMR policy development and review by the MOH, surveillance of resistant organisms has continued but data is not formally being used to manage the emergence and spread of AMR and various "control" points have languished.

The MOH's Healthcare-Acquired Infection Governance Group (HAIGG) is focused on hospital and other healthcare settings and includes AMR within its scope. The group has had discussions with PHARMAC, ESR (see below) and MPI (see below) regarding some AMR-related issues, such as matching up Pharmac claims data with antimicrobial resistance patterns identified by ESR.

District Health Boards (DHBs)

Responsibility for AMS in New Zealand primarily sits with DHBs through the IPC standards[1] but a recent MOH survey found "patchy" activity across DHBs. Various larger DHBs have comprehensive stewardship programs while systems in many DHBs are not robust. DHBs with well-developed AMS programs in place include:

- Auckland. ADHB has a long history of conservative antibiotic usage, applying through its AMS Committee the tools of selective antibiotic restriction, education, staff buy-in and some outcome measurements to rationalise and contain antibiotic use
- Counties Manukau. CMDHB is currently piloting a comprehensive programme for AMS, focusing actively on reducing antibiotic consumption by antibiotic awareness, the use of guidelines, restricted formulary, increased pharmacy and clinician engagement.

In 2010-2011, ID doctors at Auckland, Capital & Coast and Taranaki DHBs conducted antimicrobial consumption surveys, determining the defined daily doses (DDDs) of antibiotics dispensed (Ticehurst and Thomas 2011) (Beardsley and Blackmore, Antibiotic prescribing: time for national surveillance 2011) (Beardsley, Morar and Blackmore, Antimicrobial consumption data from New Zealand hospitals 2011) (Hopkins 2012). This enabled comparison of consumption between the DHBs and with other developed countries, suggesting areas for targeted interventions and benchmarking.

[1] See New Zealand Standard Health and Disability Services (Infection Prevention and Control) Standards NZ8134.3: 2008 (available at http://www.health.govt.nz/our-work/regulation-health-and-disability-system/certification-healthcare-services/health-and-disability-services-standards)

ESR (Institute of Environmental Science and Research)

Through its Antibiotic Reference Laboratory, ESR monitors AMR in several areas:

- surveillance of MRSA, ESBLs, VREs, Tb, invasive pathogens (such as meningococcal), salmonellas, and selected emerging resistant organisms
- analysis of all clinical laboratories' susceptibility testing

Surveys tend to be snapshot rather than continuous surveillance, and limited patient data is included with laboratory analyses.

BPAC (Best Practice Advocacy Centre)

BPAC is an independent not-for-profit organisation that disseminates best practice healthcare information and provides Continuing Professional Development resources to medical practitioners throughout New Zealand. Its five shareholders are Procare Health, South Link Health, General Practice NZ, University of Otago and Pegasus Health. Specific work relating to AMR has included:

- A four-part series on Antimicrobials and resistance in the New Zealand community setting published in 2010-2011 (Ikram x3, 2010, 2011)
- Publication of several guides on the appropriate use of antibiotics.

BPAC also has access to multiple sources of healthcare information including prescribing reports, patient (anonymised) demographic details and laboratory ordering. BPAC provides practice feedback to GPs via regular prescriber audits.

PHARMAC

PHARMAC, the New Zealand Crown agency for Pharmaceutical Management, has a mandate for promoting the wise use of medication in New Zealand, as well as ensuring cost-effective access to medicines is provided. PHARMAC has recently been involved in discussions with the MOH regarding the development of National Antimicrobial Guidelines. PHARMAC's antimicrobial subcommittee, which includes ID and microbiology specialist input, provides advice on antimicrobial restrictions based on best clinical practice for specific indications. Restrictions are based on broader concern about resistance not solely pharmaco-economics.

NZ Formulary

The NZ Formulary (www.nzformulary.org) is an independent resource providing electronic point-of-care information for prescribers as well as supplementary guidance on best practice prescribing for practitioners across the New Zealand health-care sector. For example, the Formulary links to the current BPAC Antibiotics Guide for primary care, enabling prescribers to select "an effective agent at the correct dose with the narrowest spectrum, fewest adverse effects and lowest cost"[2].The NZ Formulary has capacity to incorporate further treatment guidelines into its online repository of NZ prescribing information.

Ministry for Primary Industries (MPI)

In accordance with the Agricultural Compounds and Veterinary Medicines **(**ACVM) Act, the MPI registers veterinary medicines for appropriate use in animals, namely for therapeutic purposes. "Critical use antibiotics" – i.e. those with public health significance – are more tightly restricted for non-human use. MPI periodically

[2] http://www.bpac.org.nz/Supplement/2013/March/antibiotics-guide.aspx

monitors AMR in food conducted 2009-2010 and antibiotic sales volumes and is currently scoping further research on *C difficile* infection and its risk profile relating to NZ animal and food sources.

Auckland and Otago Universities and clinical or reference laboratories
Various collaborative pieces of research have been undertaken in recent years including study of *S aureus* resistance to mupirocin ointment, thought to be due to overuse relating to the over-the-counter availability of the antibiotic.

6. SUGGESTED IMPROVEMENTS TO ANTIMICROBIAL STEWARDSHIP IN NEW ZEALAND

Improvements to AMS in New Zealand were proposed by all those interviewed. These were based on the following frequently mentioned limitations of the status quo:

- Costs and harms relating to inappropriate antibiotic use are rising
- No current national coordination of stewardship of antimicrobial use
- Lack of community focus at high level
    - At MOH level, AMR work sits within the HAIGG and needs a broader focus as it is not only a healthcare related issue
- DHB activities currently variable, and not mandated or systematised
- No national trends or comparisons available for antibiotic usage
- ESR surveillance reflects “just the tip of the iceberg” of resistant microbial isolates and data quality is currently limited
- Inadequate clinical engagement.

There was total consensus among participants that a nationally cohesive approach to AMS in New Zealand would be beneficial, in order to reduce inconsistencies and unnecessary duplications occurring across DHBs. During five interviews, contributors proposed that HQSC was very well suited and supported by the sector to lead AMS work, while an equal number felt leadership and co-ordination of AMS should sit with the MOH. There was strong sentiment expressed that AMS is a multidisciplinary pursuit – involving the MOH, HQSC, Pharmac, BPAC, ESR, ID and microbiology specialists and others – and that buy-in across the sector including from clinicians was crucial.

A national approach to AMS should be part of an overarching ID strategy and include sexual health and public health perspectives. Several participants recommended that AMS within hospitals be mandated, suggesting it should be part of mandatory requirements for accreditation.

The majority of participants felt that antibiotic consumption should be measured nationally, with targets to be set, because “feedback on consumption is what is required to reduce rates of resistance”. It was recommended that benchmarking be linked to financial incentives within DHBs and a quality improvement framework be utilised. Determining the right tool, methodology and benchmark for AMS in NZ was more controversial however and further consultation was recommended to determine specific approaches in hospitals and primary care. There were robust endorsements for the use of the standardised Defined Daily Dose (DDD) measurement unit in hospitals, as utilised by the WHO, Australia and European centres focused on consumption and resistance. Several participants felt this measure was best used for comparisons within units not between DHBs. Others thought the DDD measure was prone to misinterpretation. Measures for primary care could readily involve PHARMAC’s Pharmhouse and BPAC data – said to be of excellent quality and readily useable.

AMS was seen first and foremost as an IPC activity, which should involve partnership with the Medication Safety sector, according to most interviewees. As well as prudent antimicrobial use, good basic IPC measures such as hand hygiene and environmental cleanliness were identified as crucial to AMS. About a third of participants were unsure about the role of Quality and Safety (Q&S) in AMS, while others saw it strongly as a Q&S issue, concerning reducing harm to patients and community. Several specialists suggested New Zealand learn from the example of the Australian Commission on Safety and Quality in Health Care, which published the book *Antimicrobial Stewardship in Australian Hospitals* (Duguid and Cruickshank 2010), but that focus should go beyond the hospital setting alone. Other jurisdictions with successful approaches to AMS include Sweden (the STRAMA programme), France, and the European Union (EARS-Net).

There was clear agreement that national Antibiotic Treatment Guidelines are needed as part of AMS, incorporating some local and regional variations. Agencies who should be involved are PHARMAC, the MOH, and BPAC with clinical specialist input (such as ASID – the **Australasian Society for Infectious Diseases).** Compliance with Formulary recommendations could then be audited and used for quality improvement and DHB/ prescriber feedback.

Finally, several contributors recommended that a national forum on AMS in New Zealand be held, to further progress consensus and action in this area. The need to involve key experts particularly clinicians with a long history of working in this field was reinforced. New Zealand should not ignore the call to action made by the WHO and more recently the UK's CMO.

7. DISCUSSION

The main findings from interviews across the New Zealand health sector were that AMR is an important and growing public health issue and that a national approach to manage the health risk is required. Nationally, enhanced AMS including Antimicrobial Guidelines with some regional variation were called for. Problems to address include how to measure antibiotic consumption in hospital and community settings, respond to variation in use and better understand and manage other factors contributing to AMS.

Several opportunities currently exist for enhancing AMS in New Zealand.

- First, there was a high degree of motivation and dedication among those interviewed to support improvements and work together.
- Second, collaborative work is already underway involving, for example, the MOH and PHARMAC, MOH and MPI, and BPAC and the NZ Formulary.
- Third, the profile of AMR has recently been raised both nationally and internationally due to various research and expert statements, and so now is seen as an excellent time to act.

Challenges include

- gaining consensus across the wider group of experts particularly around the following points where disagreements in participant opinion were noted:
    - The relative importance of antimicrobial consumption in New Zealand as a driver of AMR.
    - The measurement of consumption in hospitals – using the world standard DDD measure or another tool.
- workforce capacity, in particular a shortage of ID specialists and pharmacists in some centres.

This scoping research has provided an introductory overview of opinions and activity across the health sector, rather than a comprehensive review of evidence and best practice relating to AMS in New Zealand and overseas. Limitations of the research methodology include interviewee and interviewer biases and incompletely available objective data. The most frequently represented discipline among those interviewed was ID specialists, and further research could include more practitioners from the primary sector as well as consumer perspectives.

In conclusion, this report has found that enhanced national stewardship of antibiotics is recommended to combat increasing AMR. Further consultation is required to determine how best to measure and rationalise antibiotic consumption in hospitals and community settings.

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APPENDIX.

INTERVIEW PARTICIPANTS

Name	Role	Organisation
Anne Hutley	Infection Prevention and Control Nurse Specialist	Counties Manukau DHB
Cheryl Brunton	Medical Officer of Health	Community Public Health, Canterbury DHB
Craig Thornley	Public health physician	Ministry for Primary Industries (MPI)
David Holland	ID Physician and Clinical Microbiologist	Counties Manukau DHB
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Sunita Azariah	Sexual Health Physician	ADHB
Tanya Duplessis	ID pharmacist	Counties Manukau DHB

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