Antimicrobial Resistance Meeting Abstracts

AR1: Prioritising AMR in an ever-changing and increasingly pressured health system.

Old, A.[1]

[1]Public Health Agency - Te Pou Hauora Tūmatanui

In 2017 the Ministry for Primary Industries and Ministry of Health jointly published the New Zealand Antimicrobial Resistance (AMR) Action Plan. The Plan's vision is that New Zealand manages antimicrobials as a valuable shared resource and maintains their efficacy so they can be used to treat infections in humans and manage diseases in animals and plants.

In the 8 years since, there has been a global pandemic and significant reform of the New Zealand health system. Meanwhile, the global health threat posed by AMR remains, New Zealand continues to have high rates of antibiotic use and there have been outbreaks of antimicrobial organisms, such as Vancomycin-resistant enterococci (VRE).

COVID-19 demonstrated how interconnected we are across the world and the impact global public health threats can have on us here in New Zealand. But in an environment of limited resourcing, difficult decisions are a constant, and action on AMR will continue to be prioritised alongside the other needs of the health system.

This plenary speech will give an overview of the role of the Public Health Agency, note the need for a continued One Health approach, and talk about how agencies are working together to continue to champion action on AMR.

AR2: Antimicrobial resistance – a case study in connecting research to government policy.

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In this talk, I will explore the tricky interface between research and policy, using antimicrobial resistance as a case study. In particular, I will focus on the work I led while the Prime Minister's Chief Science Advisor in New Zealand, when we delivered a detailed report from an expert panel[1] to PM Ardern, and what happened (and didn't happen) next.

What can we learn from this case study to better connect evidence with government policies?

1. Infectious disease and antimicrobial resistance | Office of the Prime Minister's Chief Science Advisor. https://www.pmcsa.ac.nz/topics/antimicrobial-resistance-and-infectious-disease/

AR3: The roles of surveillance and public health laboratories in addressing antimicrobial resistance.

Murdoch, D.[1]

[1]Public Health and Forensic Science

Antimicrobial resistance is a critical and growing public health challenge requiring coordinated action across sectors. Surveillance provides the foundation for detecting emerging threats, tracking trends and guiding interventions. Public health laboratories play a pivotal role by delivering reference services, ensuring quality assurance and applying advanced analytical methods to generate reliable, actionable data. Together, these capabilities strengthen national and international responses, enable effective One Health strategies, and support evidence-based policies to contain and mitigate resistance.

AR4: Launch of the New Zealand Antimicrobial Resistance Network (NZAMRNet)

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Antimicrobial resistance (AMR) is a global crisis that complicates treatment of infections and significantly burdens healthcare systems. The Aotearoa New Zealand AMR Network (NZAMRNet) brings together an expert community to contribute to the global fight against the threat of drug-resistant infections. This multi-stakeholder network aims to inspire and support enablers of the fight against AMR, aligning with both regional and global initiatives and drive real impact for Aotearoa New Zealand and beyond.

AR5: Update on cross-government national activity on AMR

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[1]Public Health Agency, Ministry of Health, [2]Ministry for Primary Industries

The Ministry of Health, Health New Zealand, Ministry for Primary Industries and Ministry for the Environment continue to collaborate and promote a One Health approach to addressing the growing threat of AMR. This presentation will provide an update on key joint activities, including:

- The Antimicrobial Resistance Coordination and Oversight Group (AMRCOG), which provides leadership, strategic direction, accountability, and decision-making support to cross agency activity on AMR
- Work underway to replace the New Zealand AMR Action Plan published in 2017.

Agencies are working together to develop a new plan which will be a high-level strategic document, providing an overarching road map for managing AMR across human, animal, plant and environmental sectors. It will set out the national vision and objectives, high-level key priorities, and seek to align stakeholders to support coordinated action and accountability.

By articulating clear priorities and actions, the strategic document will enable stakeholders to align their efforts, monitor progress, and adapt to emerging challenges. Importantly, this will reinforce and redirect New Zealand's commitment to global health security and its responsibilities under the WHO Global Action Plan on AMR.

Overall, the AMR strategic document will act not only as a roadmap for action but also a tool for accountability, innovation, and resilience in safeguarding the effectiveness of antimicrobials for future generations. The framework for action will set expectations for sector-specific action plans, noting that MPI has already published *The New Zealand Animal and Plant Sectors' Antimicrobial Resistance Action Plan 2024-2028*.

AR6: A Stocktake of Surveillance Activities in Aotearoa (including Animal, Plant and Human health)

Williams, E.[1], Melville, V.[2]

[1]Public Health Agency, Ministry of Health, [2]Ministry for Primary Industries

Antimicrobial resistance (AMR) is a complex and growing threat that spans human, animal, and environmental health. In Aotearoa New Zealand, surveillance activities related to AMR are conducted across a range of sectors and systems. Opportunities remain to build a more comprehensive, cross-sectoral view of these activities. This presentation will explore the findings of a stocktake of current AMR surveillance activities, encompassing human, animal, and plant health domains.

Understanding the full landscape of surveillance is critical for identifying strengths, gaps, and opportunities for greater integration. In human health, national public health surveillance is largely led by the New Zealand Institute for Public Health and Forensic Science, while animal and plant health surveillance are conducted through a variety of sector-specific programmes. These efforts provide a strong foundation, with growing opportunities to enhance the coordination and communication between systems and realise the full potential of a One Health approach.

This presentation aims to clearly map existing activities, assess their alignment with national and international strategies, and highlight areas where collaboration and data sharing could be strengthened. By bringing together insights from across sectors, this presentation will inform future planning and investment in AMR surveillance. It will also support the development of a more integrated, resilient, and future-ready surveillance system that can better protect public, animal, and environmental health in New Zealand.

AR7: Antimicrobial Resistance Surveillance in Aotearoa New Zealand: Reflections from clinical practice.

Roberts, S.[1]

[1]Health New Zealand - Te Toka Tumai

WHO states that antimicrobial resistance (AMR) is one of the top global public health and development threats and the main drivers for AMR are the misuse and overuse of antimicrobials across humans, animals and plants health. This global challenge resonates in Aotearoa New Zealand (Aotearoa NZ), where our unique context presents strengthens and gaps.

Antimicrobial medicines are the cornerstone of modern medicine. The emergence and spread of drug-resistant pathogens threaten our ability to treat common infections and to perform life-saving procedures including cancer treatment (chemotherapy, stem cell transplantation and the use of biologics) and prosthetic joint and cardiac valve replacements, solid organ transplantation and other surgeries.

From a human health perspective, Aotearoa New Zealand, with its small population and relative remoteness, has a well-controlled process for approval and use of newer broad-spectrum antimicrobials. However, local data would suggest that the use of existing antimicrobials within the community is higher than it should be.

Since the 1980's we have tracked the shifting landscape of AMR, starting with MRSA, followed by the arrival of extended spectrum beta-lactamase (ESBL) producing Enterobacterales in the 1990's, vancomycin-resistant enterococci (VRE) in the early 2000's and more recently, carbapenemase-producing Enterobacterales (CPE) and *Candidozyma auris*.

The NZ Institute for Public Health and Forensic Science (PHF Science) currently performs surveillance on CPE, carbapenem-resistant *Pseudomonas* spp. and *Acinetobacter baumannii*, colistin-resistant *Escherichia coli* and *Klebsiella pneumoniae,* VRE, vancomycin, linezolid and daptomycin non-susceptible *Staphylococcus aureus,* penicillin non-susceptible *Streptococcus pyogenes* and *Neisseria gonorrhoeae* with reduced susceptibility to ceftriaxone or high-level resistance to azithromycin. They are also interested in organisms with other critical or emerging resistance, such as *C. auris,* and multidrug-resistant organisms associated with outbreaks.

The WHO Global Antimicrobial Resistance Surveillance System GLASS) launched in 2015 requires the standardise collection, analysis and interpretation of data at a regional and country level. There are six objectives; the first and last are key for improving outcomes for patients. They are to generate data to inform AMR prevention and control strategies and to assess the impact of interventions and inform research and development of new tools for the prevention, diagnosis and treatment of human infections caused by common bacterial pathogens.

An integrated AMR strategy is crucial to reduce the impact of AMR across human, animal and plant health in Aotearoa NZ.

AR8: A clinical update on the antimicrobial resistance landscape in New Zealand and the Pacific.

Ussher, J.[1]

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Antimicrobial resistance (AMR) is steadily increasing in New Zealand. With high rates of AMR in neighbouring countries, including the Pacific Islands, importation of WHO critical and high priority AMR pathogens continues to increase. Whole genome sequencing has identified cross-border outbreaks and local transmission clusters, highlighting the growing threat and the urgent need for action. The current situation will be reviewed and the need for a multi-pronged intervention strategy discussed.

AR9: Managing AMR: justice, inclusivity and sustainability

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AMR is driven by a stress response to decades of mass antimicrobial exposures, and is both influenced by, and contributes to planetary environmental crises associated with climate change, pollution and biodiversity loss. Characterised as a global and multifaceted 'superwicked' problem, AMR requires international, multi-sectoral coordination to effectively and sustainably secure human, animal and environmental health.

At present, approaches to addressing AMR often focus on innovation efforts aimed at replacing or better targeting of antimicrobials, and antimicrobial stewardship efforts to curb 'unnecessary' and 'irrational' uses of antibiotics. As a minimum, our responses to AMR must alleviate rather than exacerbate the antimicrobial resistance burden for the people for whom it is heaviest. The lives-and-livelihoods dimension of the antibiotic access–excess trade-off is underscored by structural inequities which leave socioeconomically disadvantaged populations more vulnerable, including to AMR and regulatory responses. The uneven burden of drug-resistant infections, exposure to antimicrobial pollution and AMR in the environment additionally highlights the importance of considering how to jointly address health, inequality, and environmental implications of antimicrobial resistance. [1]

This presentation discusses the importance of interdisciplinary frameworks which make more visible the uneven impacts of antimicrobial resistance action and inaction, and explore approaches to inform systemic changes to reduce reliance on antimicrobials while also responding to structural inequities in the distribution of the AMR burdens now and in coming decade.[1] It prompts consideration of moving beyond the immediacy of averting drug-resistance and conceptualisations of 'silent pandemics' and 'the war against microbes' to think more deliberatively about a future in which humanity seeks to live more sustainably with microbial ecosystems within planetary boundaries.

1. Just Transitions for AMR Working Group.(2023) *A just transition for antimicrobial resistance: planning for an equitable and sustainable future with antimicrobial resistance*. The Lancet, 403:10446, 2766-7

AR10: Droplet Digital PCR-based Detection of Clarithromycin Resistance on Rapid Urease Test Samples Predicts *Helicobacter pylori* Eradication Success: A New Zealand Cohort Study.

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Background:
Helicobacter pylori (*H. pylori*) infection is a major cause of peptic ulcer disease and gastric cancer. Rising clarithromycin resistance has significantly reduced the efficacy of standard triple therapy (clarithromcyin, amoxicillin or metronidazole, and proton pump inhibitor). In New Zealand, the prevalence and impact of antibiotic resistance remain incompletely defined, limiting the development of effective treatment strategies.

Methods and Aims:
This study evaluated the feasibility and clinical utility of detecting clarithromycin resistance genes using droplet digital polymerase chain reaction (ddPCR) on stored Rapid Urease Test (RUT) samples—a relatively novel application of molecular diagnostics. We also assessed the association between resistance status and treatment outcomes. Patients with positive RUTs during gastroscopy were treated with triple therapy and followed up with *H. pylori* stool antigen testing to confirm eradication.

Results:
Among 84 patients, clarithromycin resistance genes were detected in 13 (15.5%). Overall eradication was achieved in 74 (88.1%) patients. However, eradication success was significantly lower in those with resistance (38.5%) compared to those without (97.2%, $p < 0.001$). Treatment regimen and duration were not associated with eradication rates, supporting resistance status as the primary determinant of treatment outcome. Resistance rates were similar between Māori and Pacific patients (18.2%) and other ethnic groups (14.8%), although sample sizes limited definitive conclusions.

Conclusions:
ddPCR testing on stored RUT samples is a feasible and effective method for detecting clarithromycin resistance. This study demonstrates that clarithromycin resistance, rather than treatment regimen or duration, drives *H. pylori* eradication failure in New Zealand. Tailored therapy based on molecular resistance testing may enhance treatment success and support antibiotic stewardship. These findings justify the development of PCR-guided pathways to treat *H. pylori*, and provide a strong rationale for extending this approach to non-invasive stool-based testing suitable for use in primary care and screening programmes.

AR11: AMR after diagnostics: incident management of three laboratory-confirmed CPE cases in three nursing homes in Canterbury and West Coast.

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The emergence and increasing number of carbapenemase-producers among the *Enterobacteriaceae* family pose a major threat to healthcare systems and patient safety. In the 2024 updated *World Health Organisation Bacterial Priority Pathogens list*[1], these gram-negative bacteria resistant to last-resort antibiotics i.e. carbapenems were prioritised as 'critical' informing on-going public health intervention efforts. While prevalence of laboratory-confirmed carbapenemase-producing *Enterobacteriaceae* (CPE) cases in Canterbury and West Coast regions remains currently low, CPE poses a particular threat to vulnerable older persons living communally in nursing homes.

This report provides insights into the regional incident management health response to three separate laboratory-confirmed CPE cases in different nursing homes in Canterbury and West Coast in the past year. This response was led by the transalpine Infection Prevention and Control Service and underpinned by the national *Infection Prevention and Control and Management of CPE Guidelines.*[2] Until very recently nearly all CPE have been imported from overseas, however, in these three nursing home cases there was a high comorbidity burden but no clear overseas source or usual risk factors for acquisition identified. This suggests an increasing trend of colonisation in the community.

On-going coordinated efforts are required to strengthen New Zealand's capacity, governance and infrastructure in response to the threat of antimicrobial resistance. One key measure for tackling this growing burden and minimising transmission risk in the human health sector is robust infection prevention and control practices enforceable through up-to-date national regulatory frameworks.

1. World Health Organisation. 2024. *WHO Bacterial Priority Pathogens List 2024: bacterial pathogens of public health importance to guide research, development and strategies to prevent and control antimicrobial resistance.* Geneva: World Health Organisation.
2. Ministry of Health. 2018. Infec*tion Prevention & Control and Management of Carbapenemase-producing Enterobacteriaceae (CPE) Guidelines for Healthcare Providers in New Zealand Acute and Residential Care Facilities*. Wellington: Ministry of Health.

AR12: Carbapenemase-producing organisms in New Zealand.

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Carbapenemase-producing organisms (CPOs) are a major global health concern. These multidrug-resistant bacteria have steadily increased in prevalence in New Zealand over the past decade, particularly carbapenemase-producing Enterobacterales (CPE).

The most frequently detected carbapenemase genes are NDM and OXA-48-like. Resistome data from CPO suggests that isolates are frequently highly multidrug resistant, across multiple antimicrobial classes, with limited treatment options available. Genomic analyses reveal substantial diversity among isolates, including the presence of several globally recognised 'high-risk' clones.

Most CPOs in New Zealand are identified through screening during hospital admissions or prior to medical procedures, enabling early detection and prevention of further spread. In the early 2010's, cases were predominantly linked to overseas healthcare exposure, however recent data show that not all individuals with CPOs report travel or hospitalisation abroad. This trend, along with increasing detections in patients without travel history, suggests a shift toward local transmission. Data from genomic and epidemiological investigations support the presence of a number of small clusters resulting from local transmission.

Continuous surveillance is needed to promptly identify future transmission events, to initiate timely interventions to prevent CPO becoming endemic in NZ hospitals.

AR13: Mobile Shields: Plasmid-Encoded Barriers to Phage Therapy and Their Role in the Antibiotic Crisis.

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The global rise of multi-drug-resistant bacterial isolates poses a significant threat to public health. In 2024, the World Health Organization emphasized the urgency of this crisis, with models projecting over 10 million annual deaths caused by antimicrobial-resistance (AMR) bacteria by 2050. This crisis is driven by plasmids which facilitate acquisition and spread of AMR. As the antibiotic efficacy continues to decline, phage therapy has regained attention as a potential solution. Recent insights demonstrated that plasmids not only encode a variety of AMR but also phage defense systems. The presence of these systems (both known and currently unknown) on plasmids may dictate phage therapy successes and failures. Additionally, our hypothesis that AMR and phage defense could be co-selected for on plasmids may be consequential for both therapies, forcing us to reconsider treatment applications. By understanding how plasmids spread and select for phage defense systems, we could ensure these therapies do not encounter the same resistance challenges as antibiotic treatments.

AR14: Antimicrobial tolerance will no longer be tolerated

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Bacterial two-component systems (TCS) are signaling proteins involved in antibiotic tolerance. Recent studies in *E. faecalis* showed that deleting the CroRS TCS histidine kinase (HK) gene overcomes tolerance[1]. Here, we aimed to identify small-molecule inhibitors to test whether pharmacological inhibition of CroRS TCS could overcome antimicrobial tolerance. A virtual screening campaign was performed using GOLD molecular-docking and CroS homology models based on PhoQ HK from *T. maritima*.

Multiple conformations were explored using an iterative, ligand-steered procedure. Structures were ranked by their ability to replicate ATP-substrate analogue binding mode and distinguish actives from computer-generated decoys, based on property complementarity with the binding site. The best model was used for virtual screening of a 6-million compound library. Top-ranking compounds were tested using Differential Scanning Fluorimetry (DSF) and ADP-Glo enzyme assays. Structure-activity relationships studies were performed based on catalogue searches.

Data showed docking constraints were essential for accurately predicting AMP-PNP binding mode. The final model also distinguished known HK inhibitors from decoy molecules. A set of 96 compounds combining lead-like and fragment-like properties were purchased after visual inspection and tested in DSF experiments. Of these, 20 increased thermal stability and 9 inhibited enzyme activity. Binding models of actives were then refined through additional modelling rounds, guiding selection of further analogues. We found 4 compounds demonstrated concentration-dependent response IC_{50} curves.

In the absence of a CroS crystal structure, iterative ligand-steered homology modelling proved effective in identifying structures capable of binding ATP analogues and facilitated prospective discovery of HK inhibitors. Furthermore, the CroS kinase domain in *E. coli* was suitable for purification, producing enzyme suitable for biophysical and biochemical assays.

1. Darnell RL, Knottenbelt MK, Todd-Rose FO, Monk IR, Stinear TP, Cook GM (2019). *Genomewide Profiling of the Enterococcus faecalis Transcriptional Response to Teixobactin Reveals CroRS as an Essential Regulator of Antimicrobial Tolerance.* mSphere. 2019;4(3).

AR15: Using Mammals to Map Antimicrobial Resistance Across Aotearoa

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Proactive control of antimicrobial resistance (AMR) in potential pathogen microbes requires identifying and breaking its pathways of emergence and spread. We focus on cycles between environmental reservoirs, people, domestic animals, and agriculture.

Ours is a One Health approach and contributes to both objectives 1 (awareness and understanding) and 2 (surveillance and research) of the Ministry of Health's New Zealand Antimicrobial Resistance Action Plan.

We will use *Escherichia coli* as a bioindicator for AMR, and mammalian pest species (such as rats, mice, stoats, wild pigs, etc.) as sentinels because of their ability to accumulate *E. coli* in their excrement. The use of animal species with varying home ranges will provide a combination of large and fine scale resolution for constructing resistome maps.

Using these maps, we will pinpoint AMR hotspots and derive hypotheses of causation from geographic information on land use or other factors, such as geothermal activity. In addition, we will consider that the sentinel animals are also potential vectors for cycling AMR pathogens to humans and animals in close contact with people.

We will discuss the establishment and work necessary to enable a citizen scientist "wild poo collection network". Phenotyping of AMR frequency and type from the contributions already made by them will be described. Resistances so far are to ciprofloxacin, ampicillin, tetracycline, and cefotaxime. The implications of ciprofloxacin resistance, an antibiotic limited to human medicine, will be discussed. Where possible, links between resistome and dominant environmental impacts will also be discussed.

AR16: Cell Membrane-Mimicking Liposomes as an Anti-Virulence Therapy for *Acinetobacter baumannii* and *Staphylococcus aureus.*

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Acinetobacter baumannii and *Staphylococcus aureus* are two important causes of antibiotic-resistant infections. *A. baumannii* and *S. aureus* secrete toxic virulence factors that disrupt host cell membranes to release nutrients, combat immune cells, and enhance invasion through tissues. Neutralisation of their toxins would diminish the ability of these bacteria to persist in the host and reduce the severity of infection. Sphingomyelin-containing liposomes mimic the eukaryotic cell membrane to bind pore-forming and lipid-degrading toxins. We determined their efficacy against *A. baumannii* under mono- and polymicrobial conditions alongside *S. aureus*. Cultures of A549 (lung epithelial) cells were infected with these bacteria and treated with liposomes composed of sphingomyelin, a combination of sphingomyelin and cholesterol, or both types. LDH cytotoxicity assays were performed to determine the extent of cell death caused by the bacteria. Mass spectrometry was conducted to identify toxins bound by the liposomes. To determine the *in vivo* efficacy of liposome treatment, mice were injected with *A. baumannii* and *S. aureus* subcutaneously to form an abscess, and bacterial counts obtained. Treatment with both types of liposomes reduced the cell death caused by infection by approximately 50% following infection with *A. baumannii* alone or in a polymicrobial infection with *S. aureus*. Mass spectrometry identified membrane-targeting toxins such as hemolysins from *S. aureus* and phospholipase D from *A. baumannii* bound to the liposomes. Liposome-treated abscesses had significantly fewer *A. baumannii* cells than those treated with PBS. These results indicate that liposomes have promise as adjunct therapy to enhance the treatment of infections caused by *A. baumannii* and *S. aureus*. The binding of secreted toxins could protect host tissues and immune cells from damage, restrict the spread of infection and improve the clearance of invading bacteria. Such anti-virulence therapy may become an important tool to combat antimicrobial-resistant pathogens that urgently require new treatment strategies.

AR17: Gels vs Germs

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Chronic rhinosinusitis (CRS) affects up to 10% of the population, with sinus-related symptoms contributing to loss of quality of life comparable to sufferers of chronic heart or lung diseases. CRS recurrence can be due to bacteria like *Pseudomonas aeruginosa* and *Staphylococcus aureus* forming biofilms in the sinonasal mucosa. Biofilms are comprised of bacterial cells that group together and secrete a protective matrix over themselves, which reduces antibiotic sensitivity and makes them treatment difficult. The aim of this project was to develop an antibiofilm agent for CRS patients. A sprayable hydrogel that is liquid at room temperature but gels at nasal temperature (~ 34°C) has been developed, using a 3D-printed perspex model of CRS sinuses to simulate application. Povidone-iodine (PVP-I) was assessed as an antibiofilm agent against planktonic and biofilm-bound *P. aeruginosa* and *S. aureus*. The hydrogel successfully formed a gel within the 3D sinus model at 34°C, which was easily removable with room temperature rinses. PVP-I eradicated planktonic and biofilms of *S. aureus* at concentrations of 0.13% and 0.25%, respectively. Planktonic and biofilms of *P. aeruginosa* were eradicated at PVP-I concentrations of 0.63% and 1.25%, respectively. This study establishes the foundation for a novel antibiofilm treatment using PVP-I in a temperature-responsive hydrogel. The formulation demonstrates effective biofilm eradication and practical application in a sinus model. Once safety and tolerability have been established, this new topical agent can potentially progress to studies in CRS patients.

AR18: RNase HI as a Drug Target in *Neisseria gonorrhoeae*

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Neisseria gonorrhoeae is a significant global pathogen, estimated to cause over 80 million new infections annually, with high rates of antibiotic resistance. The emergence of strains resistant to all available treatments means that finding new targets for the development of antibiotic compounds is essential in retaining the ability to treat infection. RNase HI is an enzyme responsible for the resolution of R-loops (RNA:DNA hybrids that can form during transcription) through the degradation of the RNA strand. R-loops are associated with genome instability and are lethal if not effectively resolved. RNase HI has been shown to be essential in *N. gonorrhoeae*, making it an attractive target for new antibiotics. This work aims to validate RNase HI as a potential drug target in *N. gonorrhoeae* and identify RNase HI inhibitors through a combination of enzyme activity and cell viability assays. A library of compounds was designed for screening, based on previous work identifying viral RNase H inhibitors. A FRET-based enzyme assay was used to identify compounds that inhibit *N. gonorrhoeae* RNase HI activity. A live-dead assay was used to determine bacterial viability in the presence of the identified inhibitors. Several hits have been identified that inhibit both enzyme activity and bacterial growth. These include FDA-approved antiviral compounds designed against enzymes with an RNase H-like structure, and compounds containing a metal chelating motif consisting of three oxygens, designed to bind within the enzymes active site. These results provide evidence that RNase HI is a viable target for the development of new antibiotics against *N. gonorrhoeae*. Future work will include determination of the *N. gonorrhoeae* RNase HI structure using X-ray crystallography to map the interactions of the inhibitory compounds with their target, enabling the structure-guided design of improved inhibitors.

AR19: Acetohydroxyacid Synthase: A target for the discovery of new antimicrobial agents and herbicides.

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Acetohydroxyacid synthase is the first enzyme in the biosynthetic pathway for the synthesis of leucine, isoleucine and valine. This pathway is essential for the growth and viability of many organisms including bacterial, fungal and weed species. Inhibition of this enzyme therefore represents a gifted opportunity for the discovery and development of new biocides. The advantage of acetohydroxyacid synthase as a biocide target is that this enzyme is not present in humans and other animals, so highly specific and potent inhibitors of this enzyme represent a low risk of toxicity. We have used X-ray crystallography and cryo-EM to solve the 3-D structures of this enzyme from plant (*Arabidopsis thaliana*) and from fungi (*Candida alibcans*, *Saccharomyces cerevisiae* and *Cryptococcus neoformans*) as the apo enzyme (1) and in complex with inhibitors that already act as effective herbicides (2), and are promising leads as antimicrobial agents (3, 4). One of the most active antimicrobial agents, is the compound, chlorimuron ethyl, with K_i of 24 nM for *C. albicans* enzyme and is effective in reducing growth in mice infected with this pathogen. The potential for acetohydroxyacid synthase inhibitors as therapeutic drug leads, along with our knowledge of known resistance mechanisms (5, 6) to these compounds will be discussed.

References

1. Lonhienne, T., Low, Y. S., Garcia, M. D., Croll, T., Gao, Y., Wang, Q., Brillault, L., Williams, C. M., Fraser, J. A., McGeary, R. P., West, N. P., Landsberg, M. J., Rao, Z., Schenk, G., and Guddat, L. W. (2020) *Structures of fungal and plant acetohydroxyacid synthases*. *Nature* 586, 317-321
2. Garcia, M. D., Nouwens, A., Lonhienne, T. G., and Guddat, L. W. (2017) *Comprehensive understanding of acetohydroxyacid synthase inhibition by different herbicide families. Proc Natl Acad Sci U S A* 114, E1091-E1100
3. Garcia, M. D., Chua, S. M. H., Low, Y. S., Lee, Y. T., Agnew-Francis, K., Wang, J. G., Nouwens, A., Lonhienne, T., Williams, C. M., Fraser, J. A., and Guddat, L. W. (2018) *Commercial AHAS-inhibiting herbicides are promising drug leads for the treatment of human fungal pathogenic infections*. *Proc Natl Acad Sci U S A* 115, E9649-E9658
4. Low, Y. S., Garcia, M. D., Lonhienne, T., Fraser, J. A., Schenk, G., and Guddat, L. W. (2021) T*riazolopyrimidine herbicides are potent inhibitors of Aspergillus fumigatus acetohydroxyacid synthase and potential antifungal drug leads. Sci Rep* 11, 21055
5. Lonhienne, T., Cheng, Y., Garcia, M. D., Hu, S. H., Low, Y. S., Schenk, G., Williams, C. M., and Guddat, L. W. (2022) *Structural basis of resistance to herbicides that target acetohydroxyacid synthase. Nat Commun* 13, 3368
6. Cheng, Y., Lonhienne, T., Garcia, M. D., Williams, C. M., Schenk, G., and Guddat, L. W. (2023) *Crystal Structure of the commercial herbicide, amidosulfuron, in complex with Arabidopsis thaliana acetohydroxyacid synthase. J Agric Food Chem* 71, 5117-5126

AR20: Ionophore-mediated metal stress to combat antimicrobial-resistant *Staphylococcus aureus.*

Macbeth, E.K.[1], Todd Rose, F.[1], Cheung C-Y.[1], Harbison-Price, N.[1,2], De Oliveira, D.M.P.[2], Whyte, H.G.[2], Walker, M.J.[2], Hussein, M.[3], Velkov, T.[3], Neville, S.L.[4], McDevitt, C.A.[4] , Monk, I.R.[4], Ferguson, S.A.[1], Cook, G.M.[1,5]

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Methicillin-resistant *Staphylococcus aureus* (MRSA) is a significant public health threat due to both extensive antimicrobial resistance and immune evasion capabilities, necessitating alternative therapeutic strategies. Disruption of bacterial metal ion homeostasis, a process already leveraged by host nutritional immunity, represents a promising therapeutic approach. The zinc (Zn) ionophore PBT2 exhibits antibacterial activity and can rescue the efficacy of conventional antibiotics. Here, we use PBT2 and Zn (PZ) to study the cellular response to metal dysregulation in MRSA strain USA300, identifying new metal-dependent molecular vulnerabilities. Integrated transcriptomics, metabolomics and molecular analyses revealed that PZ's antibacterial and oxacillin-resensitisation action is driven by dual metal stress: intracellular Zn accumulation and manganese (Mn) depletion, which excess Mn mitigated. PZ disrupted central carbon metabolism at multiple key nodes, impairing glycolysis, the TCA cycle and respiration, leading to NADH and ATP depletion and compromised peptidoglycan biosynthesis. PZ also altered the metal-dependent oxidative stress response, causing superoxide accumulation. This system presents a targetable interplay between bacterial metal ion homeostasis, central metabolism, and β-lactam resistance. Uncovering how PBT2 subverts MRSA's adaptive responses to host-imposed stresses contributes to our understanding of host-pathogen interactions and offers a foundation for developing novel antimicrobials based on metal homeostasis disruption.

AR21: New Strategies to Target Hard to Treat Gram-Positive Infections

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Bacteria have evolved numerous strategies to evade the immune system and modern antimicrobial treatments to thrive in their given niche. Along with classical antibiotic resistance mechanisms such as efflux pumps, point mutations and inactivating enzymes etc, a number of larger scale phenotypic strategies are also employed that are not based on single molecular level changes. Biofilm formation is the prime example of this, and has been proposed to the culprit of many difficult-to-treat scenarios. Perhaps lesser well-known but equally sinister is the ability of certain bacteria to invade host cells by internalisation, where the seek shelter from both host immunity and antibiotic treatment. In Aotearoa New Zealand, infections caused by Gram-positive pathogens such as *S. pyogenes* and *S. aureus* remain major causes of diseases and are responsible for severe health inequities. These cunning pathogens are known to exhibit both biofilm formation and cellular internalisation. Our research has focused on new strategies to target these difficult-to-treat phenotypes, each of which are associated with treatment failure. In the case of *S. pyogenes* relapsing infection due to failed treatment often leads to the development of acute rhematic fever (ARF) and rheumatic heart disease (RHD) and is a major cause of morbidity and mortality in Aotearoa. Inspired by the similarities of host defence peptides (antimicrobial peptides) and cell-penetrating peptides, we have developed a series of cell-permeable ‘stapled ’antimicrobial peptides. These peptides have demonstrated low cytotoxicity but high efficacy at eliminating intracellular *S. pyogenes* in an *in vitro* assay where amoxicillin, the preferred clinical treatment, fails. Furthermore, these promising treatment candidates demonstrate dramatically improved survival in an *in vivo* invertebrate infection model and are under continued development.

AR22: Nucleoside analogs containing an imino-ribitol sugar exhibit a unique and characteristic pattern of interference with RNA synthesis by the Dengue virus polymerase.

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Iminovirs are antiviral nucleoside analogs in which the naturally occurring ribose sugar is replaced by an imino-ribotol group, linked to the base by a non-native carbon-carbon bond. The prototypical Iminovir is Galidesivir, an adenosine analog that inhibits a wide range of RNA viruses in cell-based studies and in animal models. Initial investigation of the effects of Galidesivir triphosphate on RNA synthesis by the Dengue virus serotype 2 (DENV-2) polymerase[1] showed the enzyme had a primary difficulty incorporating the analog and was also effectively blocked from incorporating the analog at consecutive sites in the nascent RNA. To better understand the origin of these effects on RNA synthesis, we have extended this work, studying both Galidesivir triphosphate and three closely related compounds with variations in both the base and sugar groups. We investigated the effects of these compounds on RNA synthesis using primer extension assays with varying template sequences. Included were experiments where the kinetics of single nucleotide incorporation could be reliably estimated. The single nucleotide incorporation experiments show that the DENV2 polymerase is highly selective for adenosine triphosphate (ATP) relative to ATP analogs carrying an imino-ribotol sugar. Galidesivir triphosphate, for example, is incorporated into the nascent RNA chain around forty times less efficiently than ATP at the same concentration, a difference that is fully ascribable to the presence of the imino-ribotol group. Furthermore, primer extension assays with varying templates show consecutive incorporation of nucleoside triphosphates carrying an imino-ribotol group is strongly disfavored. Consequently, Iminovir triphosphates will slow the overall rate of RNA chain extension when present at high concentrations, with this effect modulated by the sequence of the template, because of the difficulties of consecutive incorporation.

[1]Deshpande, S. *et al.* (2023) *Galidesivir Triphosphate Promotes Stalling of Dengue-2 Virus Polymerase Immediately Prior to Incorporation*. ACS Infect Dis 9, 1658–1673.

AR23: How a dormant, but essential, enzyme in *Pseudomonas aeruginosa* is activated 20,000-fold by a cell-wall precursor

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Glutamate racemase is an essential protein in the important pathogenic bacterium, *Pseudomonas aeruginosa*. Widespread antibiotic resistance in *Pseudomonas* has put this bacterium on the World Health Organization's top list for new antibiotic development.

Highly effective antibiotics, *e.g.* penicillins and cephalosporins, are often found to be inhibitors of enzymes involved in cell wall synthesis. In this vein we targeted *Pseudomonas* glutamate racemase as part of a drug discovery project. However, we found that the enzyme, when purified *in vitro,* is essentially "dead" in its natural or "unliganded" state. But, when complexed with a cell wall precursor, UDP-N-acetylmuramate-L-Ala, enzyme activity accelerates by four orders of magnitude and substrate affinity improves more than 10-fold.

High-resolution structural studies in the presence and absence of this allosteric activator, the first for this enzyme, detail extensive electrostatic remodelling of the enzyme's surface to accommodate activator binding. These changes propagate through the enzyme into the active site and have provided clear hypotheses concerning enzyme activation. In addition, analysis of the molecular details of activator binding have allowed us to develop a sequence based predictive binding model. These details should enhance drug target development for this enzyme and accelerate drug discovery research.

AR24: Bringing environment into the One Health AMR frame: experience from South Asia.

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The environment is a critical component of a one health approach to address AMR given its role in the complex antimicrobial resistance (AMR) ecosystem both as a source and transmission pathway of resistant bacteria and antimicrobial resistance genes. To date the allocation of resources for one health AMR programmes has focused on the human and animal health sectors. While there is an awareness that the environment plays an important role in AMR, the nature of this role and the tools to investigate it are still under research and in early pilot phases with limited inclusion of the environment in national AMR programmes. This situation is beginning to change with increasing engagement of the environment sector, particularly in AMR surveillance.

This situation was reflected in the UK AID-funded Fleming Fund programme to strengthen AMR surveillance in low-and-middle-income countries in Asia and Africa, with inclusion of environmental AMR surveillance several years following surveillance in humans and animals. The Fleming Fund's One Health AMR (AMROH) South Asia Regional Grant team, led by Massey University, has undertaken landscape analyses and provided technical support to develop strategies and protocols for environmental AMR surveillance in five South Asian countries. Key challenges included a lack of clarity regarding the role of environmental AMR surveillance and appropriate leadership. Identifying priority surveillance objectives and targets was challenging and influenced by the limited availability of standardised cost-effective diagnostic methods. Key strategic elements were starting small and tailoring a programme to each country, building on existing laboratory capability and sampling opportunities; for example, public health laboratories conducting drinking water testing and polio surveillance in wastewater and environmental departments testing river water quality. It was important to facilitate the understanding that environmental AMR surveillance is inherently part of a one health approach as it informs aspects of AMR in humans and animals.

AR25: Linking land-use to the likely origins of extended-spectrum beta-lactamase producing *Enterobacterales* (ESBL-E) in freshwater.

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Antimicrobial resistance is a major public health threat, as resistant infections are harder to treat and carry greater risks. Using a One Health approach, this study examined how local land-use influences the presence of extended-spectrum beta-lactamase producing *Enterobacterales* (ESBL-E) in freshwater.

A cross-sectional survey of 340 freshwater samples collected from 49 sites across New Zealand during February–March 2020 and October 2022–July 2023 was undertaken encompassing catchments with urban, dairy, avian, sheep and beef, mixed (sheep, beef, and dairy) and low-impact (exotic/native forest) land-use. ESBL-E (including *E. coli*, *Citrobacter* spp. and *Klebsiella* spp.) were isolated from 35 water samples where urban (32), dairy (1), avian (1), and sheep and beef (1) were identified as the dominant land-use. Faecal source tracking data indicated that human was the dominant faecal source for 30 of 35 ESBL-E positive samples.

Genome assemblies from ESBL-E (n=43) were compared with assemblies from human ESBL-*E. coli* (n=467). Freshwater ESBL-*E. coli* were phylogenetically diverse represented by seven different phylotypes and 20 different sequence types, including ST131 (n=13), ST38, ST68 and ST219. These sequence types are commonly associated with human urinary tract infections, suggesting contamination with urban wastewater. Assembly of closed genomes with long-read sequencing data (Oxford Nanopore Technologies) indicated that two freshwater *E. coli* (ST-410 and ST-617) harboured the plasmid-associated carbapenemase-encoding $bla_{\text{NDM-5}}$ ble_{MBL} gene cassette, but no corresponding genes were identified from the human isolates. Two other freshwater *E. coli* (ST131 and ST8131) carried pAA plasmids containing *agg* genes encoding for enteroaggregative *E. coli* adherence factors. Four human *E. coli* isolates (ST127, ST8131 and two ST394) were also pAA-positive. By linking local land-use at a national scale with the occurrence of freshwater ESBL-E, this study demonstrates the value of a One Health framework for understanding impact of human activities on dispersion of resistance genes in the environment.

AR26: AMR in the environment and the impact of climate change.

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Antimicrobial resistance is a public health crisis that has consequences beyond the simple inability to treat infections. The drivers of resistance too are not simply the excessive and inappropriate use of antimicrobials in medicine and farming that select for resistant bacteria. A One Health approach now recognises the environment as an important venue for the development of resistance, where chemical challenges beyond antimicrobial residues drive the selection of resistant organisms. On top of this, environmental stress in the form of climate warming can further drive the development of resistance, and the combination of AMR and climate change, primarily as warming and flooding, means the consequences of developing AMR in our environment will have more severe consequences for us in the future. Using metagenome, metatranscriptome and metaproteome approaches, with our data and database submissions, we identify reactive oxygen species as a driver of resistance development and antimicrobial resistance gene emergence in freshwater and wastewater and show that this can be exacerbated by climate warming.

AR27: Antibiotic resistant superbugs: it's all about the clones.

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Combatting increasing antimicrobial resistance (AMR) is one of the grand challenges facing human health. Globally, bacterial AMR was directly attributable to 1.27M deaths in 2019, with the combined impact of increasing rates of AMR in all bacterial pathogens and a paucity in the development of new antibiotics predicted to dramatically expand the magnitude of this problem. Increasing AMR threatens to make our current antibiotics ineffective, leading to a lack of treatments, even for infections that have been treatable for decades. A primary example is increasing rates of AMR in uropathogenic *E. coli* (UPEC), the primary cause of urinary tract infections and sepsis. This presentation will discuss our recent discoveries describing the genetics, genomics, virulence and pathogenesis of antibiotic resistant UPEC clones – superbugs that are driving the global AMR problem.

(*Sponsored by Te Niwha Infectious Disease Research Platform*)

AR28: High throughput genetic interaction screens to guide combination drug design for *Mycobacterium tuberculosis*.

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Mycobacterium tuberculosis is the primary causative agent of Tuberculosis (TB) and a leading cause of infectious disease morbidity and mortality. Drug susceptible strains of *M. tuberculosis* are curable, yet this requires the use of four drug regimens for six months. Treatment options for drug-resistant strains of *M. tuberculosis* are woefully inadequate with long treatment times and significant toxicities.

Combination therapies are necessary for the treatment of *M. tuberculosis* to target cells in different physiological states. Combination therapies are favoured for their ability to increase efficacy, delay the development of resistance and reduce toxic side effects. Yet, identifying the most synergistic drug interactions using conventional experimental procedures is an extremely resource intensive process. We hypothesized that high-throughput genetic interaction screens would allow for thousands of potential drug combinations to be screened in a single experiment.

To achieve this we have combined pooled multiplexed CRISRP-interference (CRISPRi) transcriptional repression with deep sequencing. Using this platform we screened >3000 interactions in a single pooled experiment, with each gene being the target of an existing antibiotic or having been previously identified as a high-priority drug target. This presentation will provide updates on our the development of our this experimental platform, results from pooled interaction screens, and our current work validating high value generalists target that have synergistic interactions with a large number of functionally diverse antibiotics.

AR29: Developing phage therapies to tackle antimicrobial resistance.

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With the rise of antimicrobial resistance (AMR) in bacterial pathogens, we urgently need to develop new therapies. Bacteriophages—or phages—are viruses that specifically infect and kill bacteria and have been used treat bacterial infections for over a century. However, several challenges need to be addressed to enable widespread, routine, and equitable use of phage therapies. Our research focuses understanding why some bacterial strains are susceptible to specific phages and not others, with a long-term view to develop a genomics-led approach to phage therapy development. Our mahi includes studying the immune systems that bacteria use to protect themselves from phage infections, developing a phage therapy cocktail for an *Acinetobacter baumannii* outbreak in Fiji, and exploring how to develop and implement phage therapies to address health inequities in Aotearoa-NZ.

AR30: Peptidomimetic strategies to tackle drug-resistant co-infections.

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Antibiotics have long been a cornerstone of infectious disease treatment, but their efficacy is increasingly compromised by the rise of antimicrobial resistance, leaving clinicians with limited therapeutic options. This challenge is further exacerbated by the prevalence of polymicrobial infections, where multiple microbial species co-exist and interact within host environments, mostly in biofilms, which complicates treatment outcomes. In this study, we examined the potential of peptidomimetics, synthetic molecules that mimic the structure and function of peptides, as adjunctive therapies to enhance the efficacy of antibiotics against two clinically significant, drug-resistant pathogens: *Pseudomonas aeruginosa* and *Staphylococcus aureus*. Biofilms formed by these organisms are recalcitrant, conferring antibiotic tolerance and protecting bacteria from host immune responses. Using both *in vitro* dual-species biofilm assays and an *in vivo* murine skin abscess co-infection model, we demonstrated that peptidomimetics significantly reduced both the bacterial burden and the severity of infection. The D-enantiomeric peptide DJK-5 effectively disrupted biofilm architecture and synergized with last-line antibiotics colistin and daptomycin, enhancing their efficacy against both Gram-negative and Gram-positive pathogens in co-biofilms. In parallel, the lipo-peptoid TM18, designed for improved stability and host compatibility, exhibited potent antimicrobial and anti-biofilm activity. TM18 self-assembled into ellipsoidal micelles, retained efficacy under physiologically relevant conditions, and modulated key resistance and virulence pathways in both pathogens, as revealed by transcriptomic profiling. *In vivo* studies demonstrated significant bacterial clearance and synergy with meropenem against co-infections. Together, these findings highlight the therapeutic potential of peptidomimetics, offering structural resilience, protease resistance, and cost-effective synthesis as powerful adjuncts in combating biofilm-associated, drug-resistant co-infections. Our work supports their further development as part of a combination strategy to expand the treatment landscape for complex infectious diseases.

AR31: Tackling biofilm-associated infections in upper respiratory diseases

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Rhinosinusitis, characterised by inflammation and obstruction of the sinuses and nasal cavity, is a significant cause of morbidity affecting millions worldwide. Although antibiotics are commonly prescribed for both acute and chronic rhinosinusitis, many patients do not respond to this treatment. Bacterial biofilms of *Staphylococcus aureus* and *Pseudomonas aeruginosa* are believed to contribute to the disease's pathogenesis and may play a key role in resistance to oral antimicrobial therapy. In light of this unmet clinical need and the growing threat of antimicrobial resistance, there is a demand for novel topical antibiofilm agents.

This study investigates the antibiofilm activity and ciliotoxicity of novel small molecules, as a potential treatment for rhinosinusitis. Minimum biofilm eradication concentrations (MBECs), determined using the Calgary Biofilm Device, and minimum inhibitory concentrations (MICs) were assessed for a range of antimicrobial compounds against *P. aeruginosa* ATCC 25783, *S. aureus* ATCC 6538, and methicillin-resistant *S. aureus* (MRSA) ATCC 33593. An *ex vivo* nasal turbinate model was developed to evaluate ciliotoxicity, with ciliary beat frequency measured using Cilialyzer software after 30 minutes of exposure.

Compared to current treatments, novel small molecules exhibited equivalent MICs against *S. aureus* and MRSA, but a significantly higher MIC against *P. aeruginosa*. However, the novels did demonstrate superior activity against *S. aureus* biofilms. At 128 times the MBEC concentrations the novels did not significantly affect ciliary beat frequency compared to the negative media control.

These findings, along with additional benefits conferred by the chemical modification, suggest that the tested novel small molecules are a promising topical agent for addressing the challenges of antimicrobial resistance and biofilm-associated infections in rhinosinusitis and potentially other diseases.

AR32: CARB-X – Accelerating the Development of Novel Products to Tackle AMR.

Alm, R. A.[1]

[1]CARB-X, Boston University

CARB-X, founded in 2016, is a non-profit public-private partnership focused on accelerating antibacterial products to address drug-resistant bacterial infections, a leading cause of death around the world, and one that disproportionately impacts patients in low- and middle-income countries. Funded by governments and leading philanthropic foundations, CARB-X is the only global partnership that integrates solutions for the prevention, diagnosis, and treatment of life-threatening bacterial infections, translating scientific innovation from basic research to first-in-human clinical trials.

The CARB-X portfolio is the world's most scientifically diverse, early development pipeline of new antibiotics, vaccines, rapid diagnostics, and other products. CARB-X supports the best early development projects from anywhere in the world, and since inception have received over 1,700 expressions of interest from companies or institutions and has successfully supported a number of scientifically diverse programs into initial clinical development since its inception in 2016. The clinical programs include traditional small molecule therapeutics as well as anti-virulence and anti-biofilm products, microbiome-modifying products, engineered peptides and bacteriophages, vaccines, and diagnostic products that address a wide variety of clinical indications.

This presentation will look at the evolution of CARB-X from inception, discuss the important trends that have been observed, and describe the acceleration of a diverse portfolio of novel antibacterial products towards clinical development and regulatory approval with non-dilutive funding, expert technical support and portfolio acceleration tools.

AR33: Fighting Superbugs: The Australian Antimicrobial Resistance Network (AAMRNet)

Bowskill, A.[1]

[1]Australian Antimicrobial Resistance Network (AAMRNet)

Despite a demonstrated unmet need, high income countries with smaller populations such as Australia and New Zealand experience limited access to antimicrobials. The pharmaceutical industry and research community has historically had limited government engagement on AMR, particularly around describing the challenges in ensuring equitable access and research and development into new antibiotics. This was due to a complex AMR stakeholder landscape and lack of a co-ordinated voice prioritising the importance of addressing these issues.
In 2020, MTPConnect, Australia's life-sciences innovation accelerator, established the Australian Antimicrobial Resistance Network – AAMRNet, a public-private, inclusive, multi-stakeholder network comprising and engaging with clinicians, researchers, industry, patients, not-for-profits and government to help address the impact of AMR on human health. AAMRNet works to improve equity of access to and re-invigorate the pipeline of antimicrobials in development by strengthening the evidence base and advocating for action, building consensus amongst stakeholders and establishing connections and partnerships with leading Australian and global AMR-focused organisations.

AAMRNet's contributions to Australian Government consultations have led to specific recommendations aligned with AAMRNet's priorities. AAMRNet has also created an integrated network of researchers and industry that provides an ideal environment for collaboration and scientific exchange that is helping reinvigorate AMR research and development in Australia.

AAMRNet is a good example of how an independent, non-profit, multi-stakeholder network can provide significant value to governments, by playing an important role in progressing national AMR policy to improve access to antimicrobials and assist them to deliver on the overall goals and objectives of national AMR strategies and action plans.

Australia and New Zealand's close relationship, position as leading economies in the South Pacific region, shared values, and challenges around equitable access to antimicrobials presents a strong opportunity for the two countries to collaborate closely on driving action on AMR.

AR34: An Industry Perspective on AMR: Challenges & Opportunities

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The World Health Organization considers antimicrobial resistance (AMR) to be among the top ten health threats facing the globe[1]. AMR threatens the very core of modern medicine and the sustainability of an effective, global public health response to the enduring threat from infectious diseases. Medicines New Zealand acknowledges the urgent global threat posed by AMR, supports a ONE health approach and the development of innovative solutions to address this critical public health issue.

AMR is associated with close to 5 million deaths globally per year and directly responsible for nearly 1.3 million deaths. The number of new antimicrobial drugs that make it to market – and particularly drugs exploiting novel antimicrobial mechanisms of action – has been diminishing. The innovative pharmaceutical industry has long played its part in fighting the threat of AMR, but more needs to be done. Critically, the clinical antibiotic pipeline needs to be replenished, and more antibiotics brought to market.

Research, development and commercialisation of new classes of antimicrobials to address AMR is challenging due to multiple factors, including market failure. Antibiotics in new classes are rightly, sparingly used with strong stewardship. While this is appropriate from an AMR mitigation perspective, this makes them very expensive using the traditional cost-per-dose pricing reimbursement model to recover development, approval, manufacturing, and distribution costs. As a result, market failure has affected not only small specialist biotechnology companies but also large biopharmaceuticals in their quest for suitable solutions to AMR.

Opportunities exist for partnership to address antibiotic development market failure through both ‘push’ and ‘pull’ incentives, explore different methods of funding antimicrobials to enable access, and enhanced use of vaccines to meet the needs of New Zealand patients of today and tomorrow to help mitigate the threat of AMR.

1. *WHO AMR* amr-factsheet.pdf (who.int)