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In this issue:

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FROM THE ASA TEAM

Welcome to Issue 47 of the ASA Newsletter.

Our editors have put together an exciting issue, featuring a summary of Philip Selby's PhD thesis, a review of the 2025 EUCAST and CLSI breakpoints and for those who were unable to attend the 24th Annual Scientific Meeting, a summary of the Plenary presentations by Erin McCreary, Christian Giske and Rachel Thomson. In addition, we hear from our Travel and Poster Award winners.

Many of us have returned from ESCMID Global 2025. The meeting was preceded by a joint high-level AMR event focusing on the key targets in the 2024 United National Global Assembly declaration on AMR, and harnessing data to guide policy actions.

Australian researchers featured prominently on the ESCMID programme. Particular mention goes to Josh Davis and Steven Tong, who presented the eagerly awaited initial results from the SNAP trial at a packed afternoon session. Their results were not only clinically relevant, but practice changing, and there is no doubt the SNAP trial will continue to feature in ESCMID and ASA highlights for many years to come.

This week the ASA Executive met to finalise the program for our 25th ASM in Adelaide, 26th - 28th February 2026. Our international speakers include Mark Gilchrist from the United Kingdom and Angela Huttner from Switzerland. The 2026 Howard Florey Orator will be Christopher (Kit) Fairley. A change in meeting format now provides the opportunity for researchers to present their work in symposiums alongside highly recognised national and international speakers. I would encourage members take advantage of this unique opportunity and to submit abstracts when due later this year.

The 2026 meeting website and registration will be available soon - www.antimicrobials.com.au

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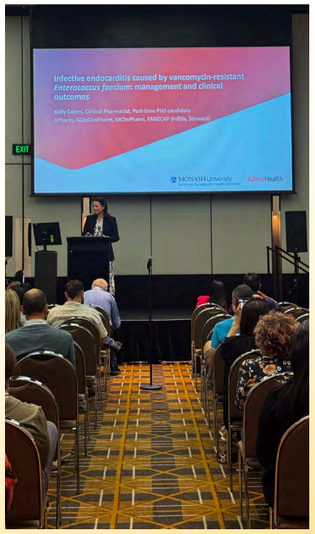
PHOTOS OF ANTIMICROBIAL '25



IN THE SPOTLIGHT

Optimisation of Anti-Infective Medications in Patients Undergoing Allogeneic Haematopoietic Stem Cell Transplantation

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Introduction

Allogeneic haematopoietic stem cell transplantation (alloHCT) is a potentially curative treatment for many high-risk haematological malignancies. However, significant treatment- related mortality complicates its undertaking, comprising a considerable contribution from infection-related mortality. Cytomegalovirus (CMV) and invasive fungal disease (IFD) are prominent examples of these complications, and optimising prevention and management of these infections have the potential to improve the outcomes of alloHCT patients.

Aims of thesis

The aim of this research was to improve the use of ganciclovir in the prevention and treatment of CMV infection and the use of antifungal agents in the prevention and treatment of IFD in patients who have undergone alloHCT. A particular focus was how to best optimise dosing regimens of these agents to maximise efficacy while reducing the probability of toxicity.

Studies and findings

Study 1: A systematic review of ganciclovir PK/PD/TD in alloHCT

By virtue of the treatment procedure and their underlying disease, alloHCT patients are particularly vulnerable to the haematological adverse effects of ganciclovir, while inadequate treatment can lead to resistant and refractory infections resulting in worse outcomes[1]. Being a drug with a narrow therapeutic index and potential for significant consequences with either under- or over-exposure, precision dosing of ganciclovir has potential to improve patient outcomes.

A systematic review was undertaken to describe available data for the clinical pharmacokinetics, pharmacodynamics and toxicodynamics of ganciclovir and valganciclovir in the alloHCT population. While a limited number of studies were identified, we determined there was a high degree of pharmacokinetic variability of ganciclovir and valganciclovir in alloHCT patients. There was also limited evidence for pharmacokinetic-pharmacodynamic (PK-PD) and pharmacokinetic- toxicodynamic (PK-TD) relationships for ganciclovir in this setting. Ganciclovir and valganciclovir pharmacokinetics differed in the alloHCT patient population compared to other populations and there were no pharmacokinetic studies done exclusively with alloHCT patients. This was thought to be problematic as the current dosing recommendations are extrapolated for this high-risk group from other populations where pharmacokinetics, treatment intent and consequences of toxicity can differ. Overall, the review indicated there were likely significant limitations with the current dosing recommendations for ganciclovir in the alloHCT setting[2].

Study 2: Population PK of Ganciclovir in AlloHCT

We subsequently performed a prospective observational single-centre pharmacokinetic study in adult alloHCT patients requiring treatment with intravenous ganciclovir for CMV viremia or disease. A total of 119 measured plasma ganciclovir concentrations from 20 recruited alloHCT patients were obtained specifically for the purposes of this study and were used to develop a ganciclovir population pharmacokinetic model. Observed-versus-predicted goodness-of-fit plots for the model are shown in Figure 1. Considering ganciclovir clearance occurs predominately via renal elimination, different methods of renal function estimation and their correlation to ganciclovir clearance was a focus in development of the model. Monte-Carlo simulations with this model were also performed, testing current dosing guidelines for their effectiveness in achieving accepted therapeutic exposures which were extrapolated from the solid organ transplant literature. The key findings were that loading doses of ganciclovir are required for timely achievement of current suggested target exposures, CKD-EPI[3] was the renal function estimate best correlated with ganciclovir clearance, and increased dose individualization is required compared to current product information dosing recommendations[4]. Figure 2 illustrates the significant effect of small changes in both ganciclovir dose and renal function

on exposure supporting the argument for increased dose individualisation.

Study 3: Optimisation of antifungal prophylaxis in AlloHCT

Our focus then shifted to the prevention and management of another major infective complication of alloHCT; invasive fungal disease (IFD). The significant contribution of IFD to morbidity and mortality in this setting means antifungal prophylaxis and treatment strategies are common, yet randomized controlled trial evidence is lacking for a superior approach and guidelines are heterogenous[5]. Many challenges are encountered with the use of antifungal agents in this patient group including administration difficulties, significant pharmacokinetic variability, adverse effects, and high costs. While these are described in the literature, there was also significant historical anecdotal experience with these issues in the bone marrow transplant unit at our institution. To address these issues, a retrospective observational study was performed to investigate the extent of these problems related to antifungal use in our alloHCT patients. Significant issues were identified relating to large numbers of antifungal changes occurring due to administration difficulties, need to escalate to treatment from prophylaxis, and adverse effects with particularly high rates of voriconazole-associated neuropsychiatric toxicity observed. The results of this observational study were then presented to the relevant stakeholders and changes to the hospital antifungal prophylaxis guidelines were proposed and accepted. The major change involved intravenous voriconazole being replaced by intravenous posaconazole as the preferred option for patients unable to tolerate oral antifungal administration. A subsequent observational study was performed to evaluate the effect of the change in guidelines. Significant advantages of the prophylactic strategy utilizing intravenous posaconazole in these patients was demonstrated with a marked reduction in antifungal associated adverse effects, antifungal drug costs and requirement for escalation to treatment antifungals[6].

Study 4: Population PK of Posaconazole in AlloHCT

With the success of the antifungal strategy utilising oral modified release (MR) posaconazole and intravenous posaconazole as the preferred options for antifungal prophylaxis, our subsequent objective was to improve the understanding of the pharmacokinetics of these two formulations of this agent in allogeneic haematopoietic stem cell transplant (alloHCT) patients. There is limited dosing guidance for clinicians when switching between the oral MR

Figure 1: Observed-versus-predicted goodness-of-fit plots for total ganciclovir concentration

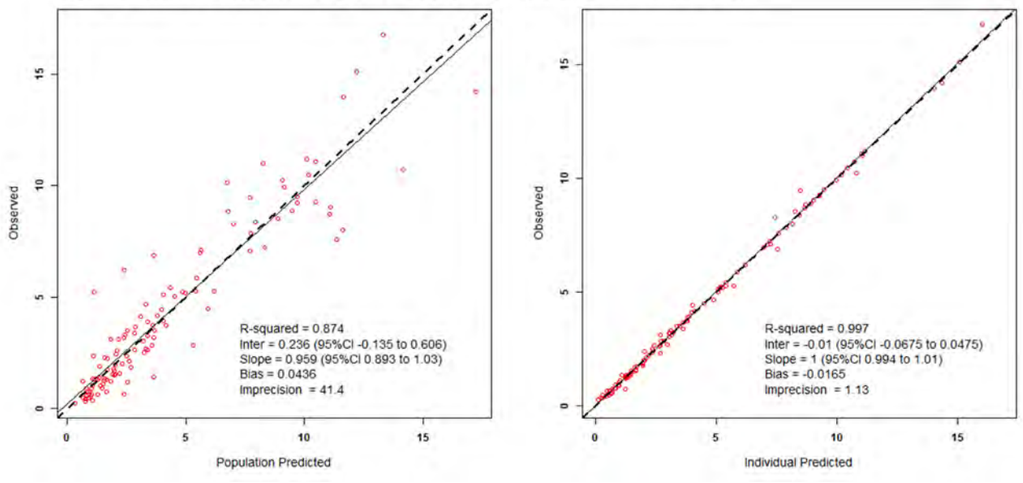
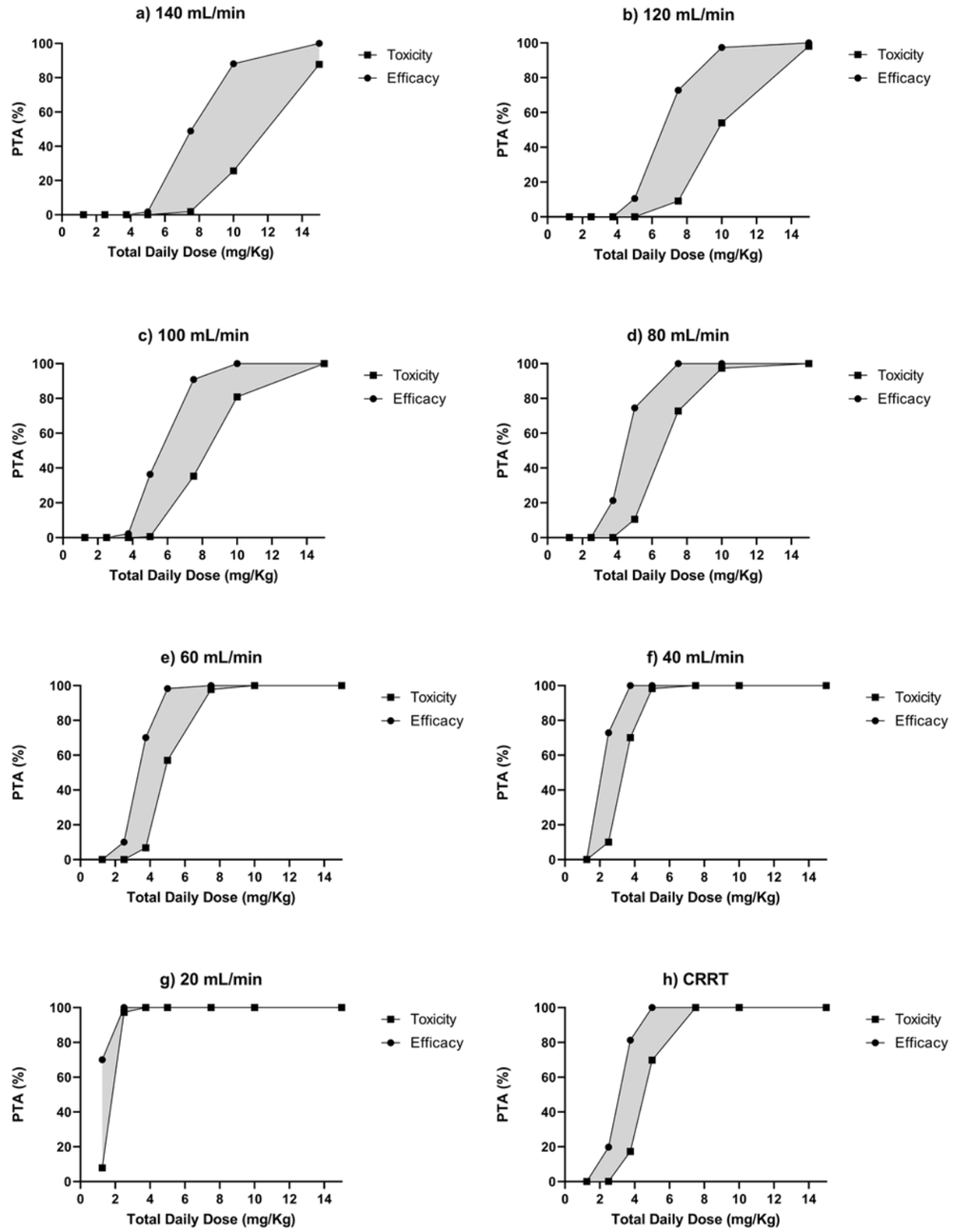
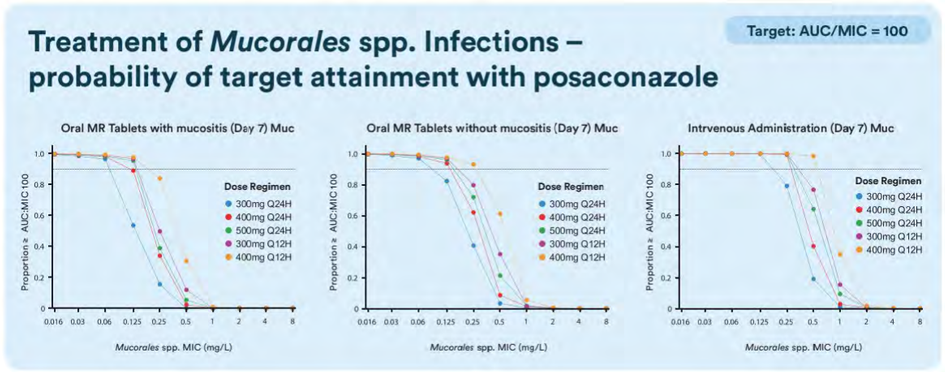
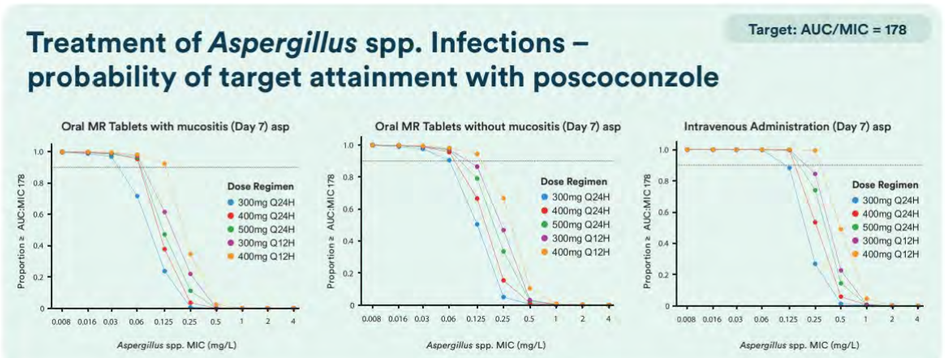


FIGURE 2 (a-h): *Probability of target attainment of efficacy (AUC24 >80) and toxicity (AUC24 <120) on day 7 of ganciclovir induction therapy in patients with different creatinine clearances estimated by the BSA-adjusted CKD-EPI equation and on CRRT (continuous renal replacement therapy). The shaded area indicates the difference between the efficacy and the toxicity probability.*







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and intravenous products and this is a common occurrence in the alloHCT setting due to the high incidence of gastrointestinal adverse effects related to chemotherapy conditioning regimens. It is also known that posaconazole displays highly variable pharmacokinetics. While therapeutic drug monitoring (TDM) is performed at many institutions, guidelines still differ in their recommendations on the requirement for this. Therefore, a prospective observational pharmacokinetic study was performed in adult alloHCT patients requiring a change from oral to intravenous posaconazole for the prophylaxis or treatment of IFD. A 2-compartment pharmacokinetic model incorporating mucositis/diarrhoea to modify the bioavailability of the oral MR formulation best described posaconazole disposition. The mean bioavailability of oral MR posaconazole differed in patients with mucositis/diarrhoea (47%) compared to those without (71%). Simulations indicated higher than currently recommended doses of posaconazole are likely required to increase the proportion of alloHCT patients achieving target exposures, particularly for the oral MR formulation in patients with mucositis/diarrhoea. Probability of target attainment of intravenous and oral MR tablet formulation of posaconazole in patients with or without mucositis for the treatment of Mucorales spp. and *Aspergillus* spp. are shown in Figures 3 and 4. Furthermore, the low probability of target attainment with currently recommended posaconazole doses and the degree of interpatient pharmacokinetic variability showed TDM should be used to optimise posaconazole dosing in the alloHCT setting[7].

Future Perspectives

With the broad range of infective pathogens in alloHCT patients and variety of anti-infective agents therefore utilised, improvements in this area are ongoing. Optimisation of these drugs will continue to be an important research area and is clinically relevant in this setting.

Determining the right drug at the right dose as early as possible in the course of infective illnesses in this highly vulnerable patient group will enable the improvement of patient outcomes. Findings from our studies performed in this thesis provide a foundation to further optimise the management of infections in alloHCT. A new frontier in the dose optimisation of anti-infectives is the use of machine learning and artificial intelligence. This area is still in its relative infancy, but it is likely that the use of population pharmacokinetic models and TDM will be complimentary to these methods[8,9].

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AUSCAST
AUSTRALIAN COMMITTEE ON ANTIMICROBIAL SUSCEPTIBILITY TESTING
Australian Society for Antimicrobials

Overview of most important changes to the 2025 EUCAST and CLSI breakpoint tables

Sanchia Warren
Michael Leung
Iain Abbott
and John Turnidge

Introduction

The annual update to clinical breakpoint tables is an important opportunity for each laboratory to review their antimicrobial susceptibility testing (AST) and reporting practices. Herein, we discuss the most significant or key changes relevant to Australian and New Zealand laboratories. Specific details summarising the EUCAST changes will be made available on the AUSCAST page of the ASA website.

EUCAST Updates Version 15.0

Enterobacterales

Previous changes to aminopenicillin reporting have been challenging to implement in many laboratories. These included providing breakpoints for intravenous (IV) and oral administration, with oral breakpoints further differentiating between infections originating from the urinary tract, uncomplicated UTI and other indications designated breakpoints in brackets. This is particularly relevant to reporting amoxicillin-clavulanic acid susceptibility. A laboratory AST report should consider different breakpoints according to the formulation administered and the clinical scenario. This year's update adds the subtle change to highlights the requirement for "susceptible, increased exposure" dosing for oral therapy when used in combination with active therapy in other indications. For example, oral amoxicillin 750 mg – 1g three-times-daily and amoxicillin-clavulanic acid 875/125 mg three-times-daily.

Ceftriaxone zone diameter breakpoints have shifted to reflect larger zones required for susceptibility. For indications other than meningitis, the zones have changed from S ≥ 25 mm / R < 22 mm to S ≥ 27 mm and R < 24 mm. Similarly for meningitis, breakpoints have moved from S ≥ 25mm and R < 25 mm to S ≥ 27 mm and R < 27 mm.

Implementation of the varying breakpoints, particularly in urine AST is complex and will be dependent on availability of relevant clinical notes to allow interpretation of whether the isolate is an uncomplicated UTI or and infection arising from the urinary tract. Associated interpretive comments would allow clarification for the clinician as to what break point has been used for interpretation.
This complexity also means the ability of the laboratory information system to allow for multiple breakpoints (4 different categories) may be a limiting factor on implementation. AUSCAST is actively working in the area to provide practical guidance to clinical laboratories.

Stenotrophomonas maltophilia

Until 2025 only breakpoints for trimethoprim-sulfamethoxazole were provided. In version 15.0 additional entries have been added for cephalosporins, fluroquinolones, monobactams and tetracyclines. Although no breakpoints have been provided for fluoroquinolones (ciprofloxacin and levofloxacin) or tetracyclines (minocycline and tigecycline), the note highlights their use in combination therapy, where an ECOFF can be used to assess for acquired resistance mechanisms. Cefiderocol has insufficient clinical evidence to support the setting of breakpoint, although MIC values (albeit currently technically difficult to perform) and zone sizes are provided to assess for the likelihood of resistance mechanisms and upper limits provided intimating likely treatment failure with this agent.

Beta-haemolytic Streptococci: Groups A, B, C and G

Benzylpenicillin breakpoints have been split into 2 groups: Group A, C, and G, distinct from *S. agalactiae* (Group B streptococcus) based on the ECOFFs. Susceptibility for all penicillins are inferred from this benzylpenicillin breakpoint, except for *S. agalactiae* where there is insufficient clinical evidence of efficacy for phenoxymethylpenicillin and the isoxazolylpenicillins (flucloxacillin, dicloxacillin, cloxacillin and oxacillin). Laboratories should be aware that they must be able to differentiate these 2 groups of beta haemolytic streptococci to allow implementation of the different breakpoints.

Enterococcus spp.

Penicillin breakpoints for *Enterococcus* species have undergone significant revision. Firstly, breakpoints for oral amoxicillin and oral amoxicillin-clavulanic acid can only be applied to *E. faecalis* with the exception of uncomplicated UTI isolates. Similarly, piperacillin-tazobactam breakpoints only apply to *E. faecalis*.

Where piperacillin tazobactam is tested against *E. faecalis* it will result in either a "susceptible, increase exposure" or "resistant" categorisation, highlighting that depending on the site of infection, that high dosage should be considered (4.5 g IV 6-hourly, infused over 3 hours).

Similar to the approach with *Enterobacterales*, breakpoints exist for three scenarios: IV, oral in uncomplicated UTI, and oral when used for other indications. Note, that the susceptibility to amoxicillin-clavulanic acid is inferred from ampicillin, with the addition of the beta-lactamase inhibitor not adding clinical benefit.

Endocarditis Breakpoints

Breakpoints specifically for endocarditis have been added, when previous versions referred the user to International or National Guidelines. The most relevant are the endocarditis breakpoints for relevant antimicrobials for the Viridans group streptococci, which now has breakpoints for endocarditis and for indications other than endocarditis. Furthermore, for benzylpenicillin, breakpoints differ if using in combination therapy with other antimicrobial treatment.

Implementation of these breakpoints will need understanding of clinical syndrome and if treatment is with or without combination therapy, likely requiring relevant comments added to the final report. Please refer to the EUCAST guidance document: Guidance Document on the reporting of susceptibility in Endocarditis, which provides further information on how to review and consider these changes.

CLSI Updates M100 version 35

Information provided below as a courtesy to laboratories still using CLSI methods. AUSCAST, as a part of the international EUCAST network, promotes the EUCAST system of susceptibility testing and interpretation in Australia.

Some of the notable changes were as follows:

- *Methodology*: Disk diffusion no longer termed as "reference method" but a "standard method". Disk diffusion directly from positive blood cultures has various changes with early reading timeframes and additional/revised breakpoints.
- *Enterobacterales*: Suggest that cefepime results should be suppressed or reported as resistant for carbapenemase-producing isolates. This may occur after AST report has been released, depending on laboratory workflow, and may require a change in the report.
- *Acinetobacter* spp.: Tetracycline and doxycycline breakpoints have been removed and minocycline breakpoints revised. It is expected that more isolates will test non-susceptible to minocycline
- *Burkholderia cepacia* complex: All breakpoints have been removed. There is a lack of correlation between BMD and agar dilution MIC methods, the epidemiological cut off values (in appendix F) are higher than would allow for target attainment with routine antimicrobial dosing. Additionally, correlation of MIC values with clinical outcome is not known. The suggested comment is "AST is not routinely performed for *B. cepacia* complex due to the lack of accurate test methods. MICs for ceftazidime, levofloxacin, meropenem, minocycline or trimethoprim-sulfamethoxazole with wild-type isolates are high and might be above the MICs typically achievable by routine antimicrobial dosing".
- *Staphylococcus* spp.: Introduction of a new term "SOSA", referring to Staphylococci other than *Staphylococcus aureus*. There is also specific recommendation for *S. coagulans* and *S. schleiferi* requiring oxacillin testing for detecting methicillin resistance.

Acknowledgement to Clare Stewart, from Fiona Stanley Hospital site, PathWest Laboratory Medicine, for assisting in compiling the CLSI updates.

PHOTO QUIZ

An 82-year-old female presents with a five weeks' history of progressive dry cough, dyspnoea, night sweats, generalised lethargy and rash. She was recently diagnosed with a medium vessel vasculitis and was immunosuppressed on high dose weaning prednisone and azathioprine. She was taking co-trimoxazole prophylaxis. This occurred on the background of mixed respiratory disease including COPD/Bronchiectasis and 'Bird Fancier's Lung' from childhood. She lived in a rural Australia, previously worked on a poultry and fruit farm, and her hobbies included pigeon racing and gardening.

Clinical examination revealed mottled violaceous patches on bilateral lower limbs extending from ankles to upper thighs with no ulceration, no nodules, no retiform purpura. Computed tomography imaging of the chest revealed bronchiectasis with areas of mucous plugging and tree-in bud nodularity which were long-standing, seen on prior imaging. There was new central parabronchial ground glass opacifications and nodular changes bilaterally.

A bronchoscopy was arranged. Gram stain revealed few polymorphs and no organisms seen. Standard culture only grew a light growth of oral flora. Culture was also set up for Mycobacteria, Fungal and BCYE (buffered charcoal yeast extract) agar. After 6-days, growth on the BCYE agar was identified and investigated further.

Question

What is the most likely causative organism implicated based on the gram stain, modified ZN stain, culture appearance and clinical syndrome?

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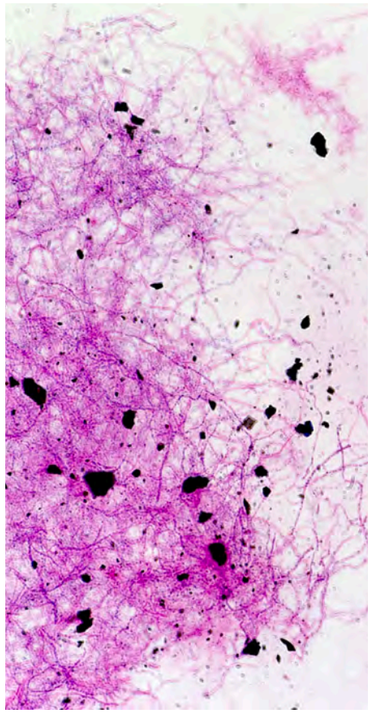

Figure 1 Gram stain from colonies growing on BCYE

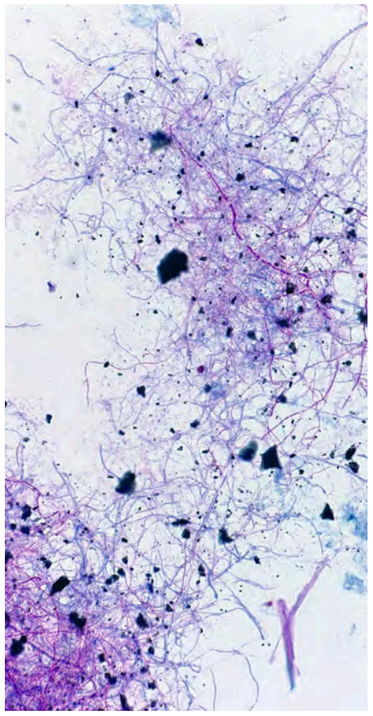

Figure 2 Modified Zeil Neilsen (ZN) stain from colonies growing on BCYE

Figure 3 Subculture of growth on BCYE

PLENARY 1

Precision dosing in complex & critically ill

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Precision dosing can improve clinical and microbiological outcomes in complex, critically ill, and chronically ill patient populations who exhibit vast interindividual variabilities in exposures and responses(1). The artificial intelligence platform OpenEvidence responds to the query 'define precision dosing' as such (Box 1).

In simpler terms, precision dosing tailors drug doses to maximize benefits and minimize risks based on individual patient factors like genetics, biomarkers, and pharmacokinetic/pharmacodynamic (PK/PD) parameters. Model-informed precision dosing (MIPD) enhances this approach by using mathematical models, machine learning, and real-time monitoring to optimize drug regimens.

Notable scenarios where precision dosing of antimicrobials may be particularly valuable include situations where drug exposure and response may be unpredictable or require careful optimization. These include the initiation or discontinuation of interacting medications, which can significantly alter drug metabolism and clearance. Breakthrough infections may indicate suboptimal drug levels and/or multidrug-resistant pathogens, necessitating dose adjustments to enhance efficacy and improve efficacy. Similarly, in cases of resistant or refractory infections, achieving and maintaining effective drug concentrations is essential for treatment success. Patients with questionable gastrointestinal absorption or those receiving enteral nutrition may experience inconsistent drug bioavailability, requiring close monitoring. Precision dosing is also important in critically ill patients, where altered physiology or deranged pharmacokinetics can impact drug distribution and elimination. Special populations, such as patients with obesity or paediatric patients, often require individualized dosing strategies due to variations in drug handling. Additionally, severe hepatic or renal dysfunction can impair drug metabolism and excretion, necessitating careful dose modifications.

Back to basics with pharmacokinetics

Consider what happens when a patient takes an oral pill to break down the basics of pharmacokinetics. That drug must cross the gastrointestinal tract into the bloodstream – absorption. Drug concentrations will rise slowly until it reaches a maximum concentration based on the dose given, and that concentration will distribute to its site of action and exert an effect. Then, the body will clear and eliminate that drug until it is completely gone. When the drug is almost gone, that's the time to take the next dose; in the simplest terms – this is the dosing interval for that drug.
All drugs have a therapeutic window meaning that too much of the drug is going to cause the patient harm, and not enough of the drug is going to lead to a lack of desired effect. Some drugs have a wide therapeutic window which means they're reasonably safe and that one can be a little more forgiving with dosing, because there is a wider margin of error. On the other hand, there are drugs that have a narrow therapeutic window, which means the dosing regimen is very important to prevent toxicity and ensure efficacy.

Dosing regimens in antibiotic package inserts are designed based on empiric targets and adjustments at a population level (historically, in patients who weren't sick from early phase trials) are made according to surrogate markers of drug clearance (e.g., creatinine clearance). Increasingly, we know clinical trial populations and real-world patients are different. There are many ways deranged pharmacokinetics can impact drug exposures, particularly in the critically ill, patients with obesity, patients with third spacing, or patients requiring machines to support them in some way such as extracorporeal membrane oxygenation or continuous renal replacement therapy. For example, hydrophilic antibiotics like beta-lactam antibiotics will demonstrate an increased volume of distribution and dramatic changes in clearance in patients with excessive fluid weight. For lipophilic drugs, variables like extracorporeal membrane oxygenation (ECMO) may increase clearance, and therefore the dose of such agents may need increased. Critically ill patients with augmented renal clearance have increased clearance of renally eliminated drugs, and therefore beta-lactam antibiotics may be dosed aggressively.

"Precision dosing" is defined as the tailoring of drug doses to optimize therapeutic benefits and minimize risks for each individual patient. This approach is particularly crucial for drugs with narrow therapeutic windows and significant adverse effects. Precision dosing involves adjusting doses based on individual patient characteristics, such as genetic factors, biomarkers, and pharmacokinetic/pharmacodynamic (PK/PD) parameters, to achieve the most effective and safest drug exposure.[1-3]

Model-informed precision dosing (MIPD) is a key component of this approach, utilizing mathematical and statistical models to predict the optimal dose for a patient by integrating individual demographic and clinical data.[3-4] This method moves beyond traditional therapeutic drug monitoring by considering multiple sources of variability and employing advanced tools like machine learning and biosensors for real-time monitoring.[3]

Overall, precision dosing aims to enhance therapeutic outcomes by personalizing drug regimens, thereby moving away from the "one-size-fits-all" approach to a more individualized treatment strategy.[1-3]

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Box 1

A greater understanding of PK and PD principles has started to influence how drugs are developed. For example, cefiderocol was the first gram-negative agent to come to market with increased dosing every 6 hours, specifically for augmented renal clearance.
Ultimately, clinicians want to get the optimal exposure right away in patients who are really sick, which poses a problem when trying to engage in precision dosing in clinical practice.
If drug samples are sent on day 1 and results are not available till the next day, the physiological state of the patient could have completed changed and the results may no longer be clinically relevant. MIPD potentially overcomes this by allowing samples taken at any time as that patient's data is superimposed on a PK data set. If the chosen model doesn't match the patient though, these could vary tremendously.

Math only does so much to make patients similar and our patients humble us every day.

However, PK PD principles are not just theoretical, the current literature supports the notion that pharmacokinetic principles genuinely impact patient care. Zusman et al(2) evaluated patients receiving ertapenem versus other carbapenems and noticing an increased risk of death amongst patients treated with ertapenem who were also hypoalbuminemic. Meropenem is 2% protein bound whereas ertapenem is 85-95% protein bound. Meropenem free drug concentrations don't fluctuate with albumin, however ertapenem does significantly. Therefore, low albumin leads to greater free drug concentration of ertapenem, greater clearance, suboptimal exposures and subsequently greater rates of mortality(2).

Pharmacodynamics and the effect of drugs on the body or the bug

PK-PD interplay is a balancing act. You want to have the right amount of drug at the site of the infection in order to kill the bug. For example, underdosing will lead to failed treatment and the patient remaining infected. However, we also can't have too much drug in the patient or else the antibiotic will cause toxicity and it will start to cause damage to human cells in addition to bacterial cells, thus overdosing isn't an ideal option either (Figure 1).

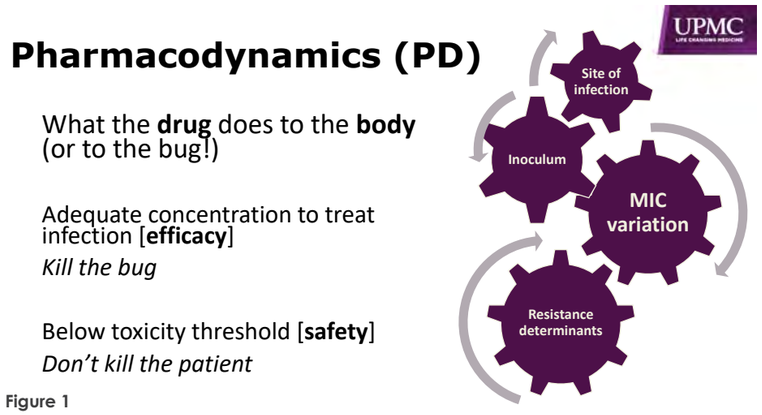

Figure 1

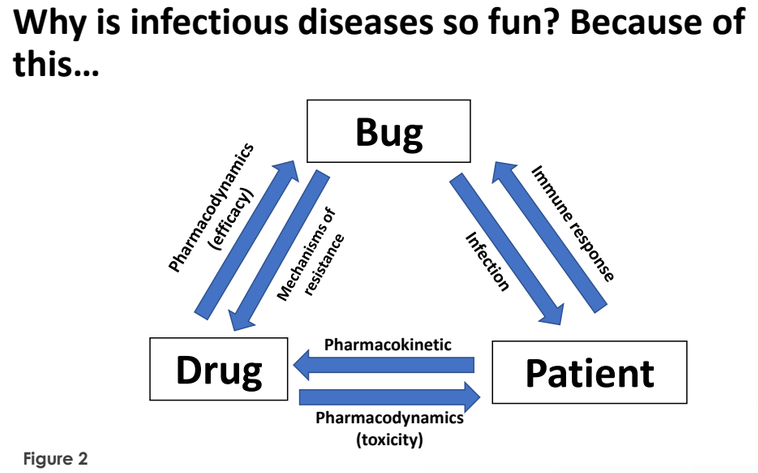

Figure 2

Pharmacodynamic measures such as the time above MIC (T > MIC), the peak concentration to MIC ratio (Cmax/MIC), and the area under the concentration-time curve to MIC ratio (AUC/MIC) are used to predict the efficacy of antibiotics. (3). William Craigs' classic "Pharmacokinetic/ Pharmacodynamic Parameters: Rationale for Antibacterial Dosing of Mice and Men" in 1998, reviewed the interrelationship between PK and PD in determining dosing regimens for different antibacterial classes and the basis for precision dosing targets(4).

Pharmacokinetics (PK) determines how a drug's concentration changes over time, while pharmacodynamics (PD) describes the drug's effects at those concentrations. Together, PK-PD principles establish the relationship between dose, drug exposure, and clinical response, guiding how we should optimize dosing for each patient. These measures support the development of dosing regimens that maximize bacterial killing while minimizing toxicity and resistance development (5).

Treating infectious diseases presents unique challenges because the effects of antimicrobial therapy are not always immediately visible. In many cases, infections occur deep within the body, making it difficult to assess treatment success in real time. Additionally, antimicrobial therapy involves a complex PK-PD interplay between two living organisms—the pathogen and the patient (Figure 2). The goal is to eliminate the infection while minimizing harm to the patient, underscoring the critical need for precise and individualized dosing strategies.

Implementing Precision Dosing Programs

The successful development and implementation of precision dosing programs such as beta-lactam individualization programs, require a multidisciplinary team of stakeholders. Key participants include institutional leadership, healthcare professionals, operational partners, regulatory authorities, and patients or their representatives. Engaging these stakeholders at every stage of program development is crucial, though the level of involvement may vary depending on specific needs at different phases. Precision dosing services are often described as consultative programs primarily led by pharmacists, with antimicrobial stewardship programs providing an ideal framework for implementation. These programs, ideally co-led by at least one pharmacist and one physician, oversee critical functions such as tracking, reporting, education, and the implementation of optimal and judicious medication use. The specific regulatory requirements of an institution's geographic location will determine which team members can engage in various aspects of the program.

For successful implementation, embedding precision dosing workflows into the electronic health record (EHR) is highly beneficial (6, 7). Assays should be electronically orderable and designed for ease of use by providers, with standardized reference ranges, critical values, and clearly defined reporting structures. Results should be seamlessly integrated into the EHR and acted upon in accordance with institutional guidelines and the precision dosing service. Additionally, an important consideration is whether to incorporate a pharmacokinetics calculator or specialized software within the EHR to enhance real-time decision-making and dosing optimization.

Ultimately, the patient experience must remain at the heart of every healthcare initiative, guided by the principle of doing 'for' the patient rather than 'to' the patient. It is essential to remember the fundamental purpose of our work: improving patient outcomes

and well-being. During the design phase of a precision dosing program, patient perspectives should be actively considered, with feedback incorporated to ensure the approach is both acceptable and practical. Engaging patients in this process can enhance adherence to individualized regimens and foster trust in precision dosing as a personalized, patient-centred strategy.

Challenges in Precision Dosing

Several obstacles hinder the effective implementation of precision dosing in clinical practice. One major challenge is the limited availability of individualized pharmacokinetic/pharmacodynamic (PK/PD) data, making it difficult to tailor drug therapy to a patient's specific needs. Additionally, variability in response to therapies among critically ill patients complicates dosing decisions, as factors such as organ dysfunction, altered drug metabolism, and disease severity can significantly impact drug exposure and effectiveness.

Resource constraints also play a role, including delays in laboratory turnaround times, limited staffing, and competing clinical priorities, which can impede timely dose adjustments. Furthermore, expertise is required to interpret drug concentration data, utilize dosing software, and translate findings from bench to bedside, yet not all institutions have access to specialists with this skill set. The logistics of compounding or administering alternative doses add another layer of complexity, particularly for medications requiring precise adjustments. Finally, transitions of care—such as shifts between hospital and outpatient settings—pose a risk for suboptimal dosing continuity, potentially affecting patient outcomes.

Future Directions in Precision Dosing

The future of precision dosing is poised for significant advancements, driven by innovations in technology and personalized medicine. Artificial intelligence (AI) is expected to play a key role by integrating vast amounts of patient data to optimize dosing recommendations in real time. Similarly, advances in pharmacogenomics will enhance personalized medicine by identifying genetic factors that influence drug metabolism and response, allowing for more tailored therapy. Emerging real-time dosing adjustment technologies will further refine treatment by continuously monitoring drug levels and patient-specific variables. Additionally, the development of non-invasive sampling techniques holds promise for simplifying drug monitoring, reducing patient discomfort, and improving accessibility to precision dosing in various healthcare settings. Finally, ongoing research, including randomized controlled trials (RCTs), are essential to establish evidence-based strategies for optimizing drug therapy in critically ill patients.

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PLENARY 2

Novel Antimicrobial Therapies & Laboratory Testing Challenges for Drug-Resistant Gram-Negative Bacteria

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The global burden of antimicrobial resistance continues to grow, with Gram-negative bacteria presenting particularly challenging treatment scenarios. During my recent presentations at the Antimicrobials 2025 Conference in Melbourne, I discussed both the emerging therapeutic options for extensively drug-resistant Gram-negative pathogens and the laboratory challenges we face when performing susceptibility testing on these organisms.

The Current Landscape of Resistance

The prevalence of carbapenem-resistant Enterobacterales varies significantly worldwide, with concerning rates in many regions as shown in recent EARS-Net, CAESAR, and AURA data. At Karolinska University Hospital in 2023, we observed a significant shift toward NDM carbapenemases, partly due to influx from Ukraine. This reflects a broader European pattern. Similarly, in the United States, data from 44 medical centres showed a gradual shift from KPC toward metallo-β-lactamases (MBLs) and OXA-48-like enzymes.

In *Pseudomonas aeruginosa*, carbapenem resistance often stems from chromosomal mechanisms, primarily porin loss, though MBLs, KPCs, and other class A carbapenemases are increasingly common in certain regions. For *Acinetobacter baumannii*, class D carbapenemases predominate globally, with MBLs common in some areas and KPCs emerging recently.

The Therapeutic Armamentarium

Our antimicrobial options can be categorized as "not-so-new" (ceftolozane-tazobactam, ceftazidime-avibactam), "fairly recent" (meropenem-vaborbactam, imipenem-relebactam, cefiderocol), "brand new" (aztreonam-avibactam, cefepime-enmetazobactam, sulbactam-durlobactam), and those "in the pipeline" (cefepime-zidebactam, cefepime-taniborbactam). The efficacy of these agents varies considerably depending on the resistance mechanisms present.

Table 1: *Enterobacterales*

Antimicrobials	KPC-producers	OXA-48 producers	MBL-producers
Ceftolozane-tazobactam	❌	❌	❌
Ceftazidime-avibactam	✅	✅	❌
Meropenem-vaborbactam	✅	❌	❌
Imipenem-relebactam	✅	❌	❌
Cefiderocol	✅	✅	✅
Aztreonam-avibactam	✅	✅	✅
Cefepime-enmetazobactam	❌	❌	❌
	Development of resistance can occur to all agents. MER-VAB has fairly high stability.	*MER-VAB and FEP-ENM can have activity, but not due to the inhibitor*	*Given as CAZ+ATM-AVI, but now ATM-AVI is approved in Europe.*
IDSA guidelines	CAZ-AVI, MER-VAB, IMI-REL. Alternative: FDC	CAZ-AVI. Alternative: FDC	(CAZ)-AVI+AZT, FDC

Assumes an absence of additional acquired resistance.

Enterobacterales

KPC producers: Ceftazidime-avibactam, meropenem-vaborbactam, imipenem-relebactam, cefiderocol, and aztreonam-avibactam show good activity, while ceftolozane-tazobactam and cefepime-enmetazobactam are ineffective.

OXA-48 producers: Ceftazidime-avibactam, cefiderocol, and aztreonam-avibactam are active, while the others generally lack efficacy. Meropenem-vaborbactam and cefepime-enmetazobactam may occasionally show activity, but not due to their inhibitor components.

MBL producers: Only cefiderocol and aztreonam-avibactam maintain reliable activity. Cefiderocol is protected through various side chains, while aztreonam is not a substrate for MBLs but requires avibactam to protect against other enzymes that these strains typically harbor.

Pseudomonas

P. aeruginosa isolates with chromosomal resistance mechanisms, most newer combinations show activity, but MBL-producing strains remain challenging with only cefiderocol demonstrating consistent efficacy. KPC-producing strains show variable responses.

Acinetobacter

For *A. baumannii*, cefiderocol stands alone in demonstrating consistent activity against both OXA-carbapenemase and MBL-producing strains. Sulbactam-durlobactam offers some promise specifically for *Acinetobacter* infections.

Table 2: *Pseudomonas*

Antimicrobials	Chromosomal	MBL-producers	KPC-producers
Ceftolozane-tazobactam	✅	❌	❌
Ceftazidime-avibactam	✅	❌	Weak
Meropenem-vaborbactam*	✅	❌	Weak
Imipenem-relebactam	✅	❌	Weak
Cefiderocol	✅	✅	✅
Aztreonam-avibactam	Weak	Weak	Weak
Cefepime-enmetazobactam*	✅	❌	❌

* No increased activity compared to the parent beta-lactam.

TOL-TAZ and CAZ-AVI resistance through mutations in PDC. Single step mutation occurring in vivo in chromosomal AmpC (PDC) confers resistance to ceftazidime-avibactam and ceftolozane-tazobactam. Associated with too low dose or off-label use? Also shown in hollow-fiber models (Boulant et al. AAC 2019; 63:e01637).

Table 3: *Acinetobacter*

Antimicrobials	OXA-carbapenemase	MBL-producers
Ceftolozane-tazobactam	❌	❌
Ceftazidime-avibactam	❌	❌
Meropenem-vaborbactam*	❌	❌
Imipenem-relebactam*	❌	❌
Cefiderocol	✅	✅
Aztreonam-avibactam	❌	❌
Cefepime-enmetazobactam*	❌	❌

* No increased activity compared to the parent.

Sulbactam: has some activity vs Acinetobacter in high exposure, but largely needs protection from a beta-lactamase inhibitor (e.g. durlobactam).

Stenotrophomonas maltophilia

S. maltophilia remains problematic with limited treatment options. While trimethoprim-sulfamethoxazole is the standard therapy, cefiderocol has shown promising *in vitro* and *in vivo* activity in animal models, with emerging clinical data supporting its use. Aztreonam-avibactam has some *in vitro* activity, but lower than against Enterobacterales. Fluoroquinolones and tetracycline-derivatives have some activity (can be considered in combination therapy). Interestingly, in a murine pneumonia model in neutropenic mice, trimethoprim-sulfamethoxazole was probably not active because of high concentration of thymidine in the mice (Nakamura R, et al. 2021. AAC 65:e01436-2).

Resistance to Novel Agents

Concerningly, we are already observing resistance to these newer agents. Among carbapenemase-producing *E. coli* at Karolinska, resistance to aztreonam-avibactam, cefiderocol, and cefepime-zidebactam is emerging.

Resistance mechanisms typically involve two critical factors that drug development has often neglected:

1. *Cell entry* - Porin loss (OmpF) affects aztreonam-avibactam susceptibility, while iron uptake mutations (CirA) impact cefiderocol.
2. *Receptor binding* - PBP-3 insertions reduce susceptibility to aztreonam-avibactam, cefepime, and cefiderocol, while PBP-2 mutations specifically decrease susceptibility to zidebactam.

Single-step mutations in chromosomal AmpC (PDC) can confer resistance to both ceftazidime-avibactam and ceftolozane-tazobactam in *P. aeruginosa*, particularly with suboptimal dosing or off-label use.

Optimizing Treatment: Infusion Strategies and TDM

Extended and continuous infusion strategies have become increasingly common, particularly for beta-lactams. While these approaches can improve outcomes in ICU patients with altered pharmacokinetics, there is less evidence supporting their role in combating multi-drug resistance. Most novel agents are already developed with extended infusion protocols, limiting further strategies when increased exposure is needed.

When balancing efficacy and toxicity, it's crucial to consider potential beta-lactam neurotoxicity, which manifests as confusion, reduced consciousness, hallucinations, myoclonia, hand tremor, asterixis, and seizures. Risk factors include underlying neurological disease, reduced renal function, and age extremes.

Considering the selection of target MIC for therapeutic drug monitoring is important. A “worst-case scenario” approaches drive aggressive dosing, potentially increasing toxicity. Alternatively, a more balanced approach using realistic MIC targets may be preferable.

Laboratory Testing Challenges

In the laboratory, several issues complicate accurate susceptibility testing of newer agents:

Media considerations: E.g., Cefiderocol testing is particularly challenging due to iron depletion requirements, with specific media recommendations from EUCAST.

Uncertain results: E.g., With cefiderocol, the area of technical uncertainty (ATU) of 21-23 mm for disk diffusion creates interpretation challenges, particularly for NDM-producing organisms where we observe discrepancies between disk diffusion and broth microdilution methods. Generally, disk diffusion overestimates resistance. This can mean that the results in quite a large fraction of NDM-producers will be inconclusive, just when you need the antimicrobial (figure 1).

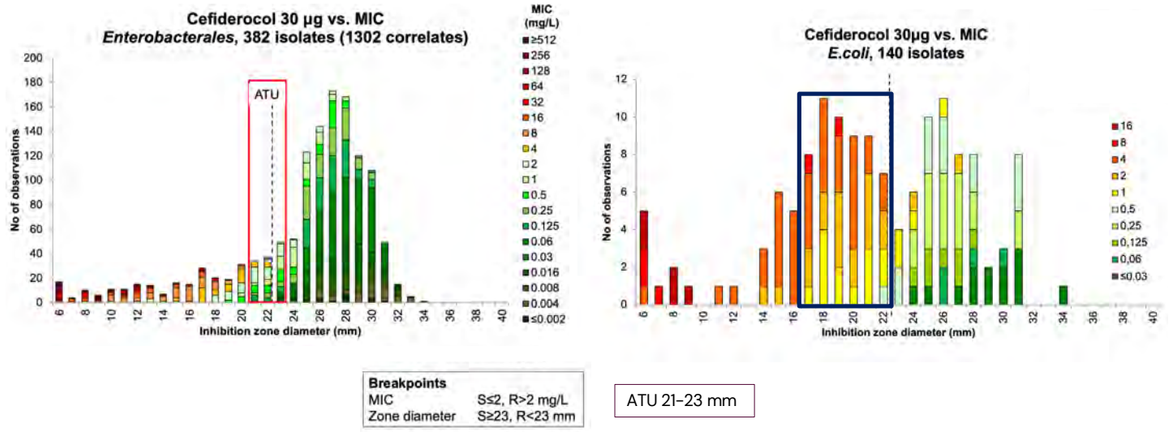

Figure 1: Cefiderocol ATU. A larger issue among NDM-producing *E. coli* isolates.

Fixed concentration vs. ratio testing for beta-lactam/ beta-lactamase inhibitor combinations

EUCAST generally prefers fixed concentrations unless compelling evidence exists for using ratios. Zidebactam represents an exception where ratio testing is justified due to its clinically relevant antimicrobial activity at achievable concentrations.

Historical breakpoints

Many older antimicrobials have breakpoints established before current knowledge about ECOFFs, PK-PD cut-offs, and high-quality clinical trials. EUCAST has taken a cautious approach by maintaining the integrity of its breakpoint-setting process, sometimes refraining from setting breakpoints when insufficient evidence exists.

Method robustness

In some cases, disk diffusion proves more robust than MIC methods for detecting clinically important resistance mechanisms, as demonstrated with the new ‘MIC-free’ algorithm for determining benzylpenicillin susceptibility with *Streptococcus pneumoniae* (figure 2), and in a recent Nordic trial detecting linezolid-resistant enterococci.

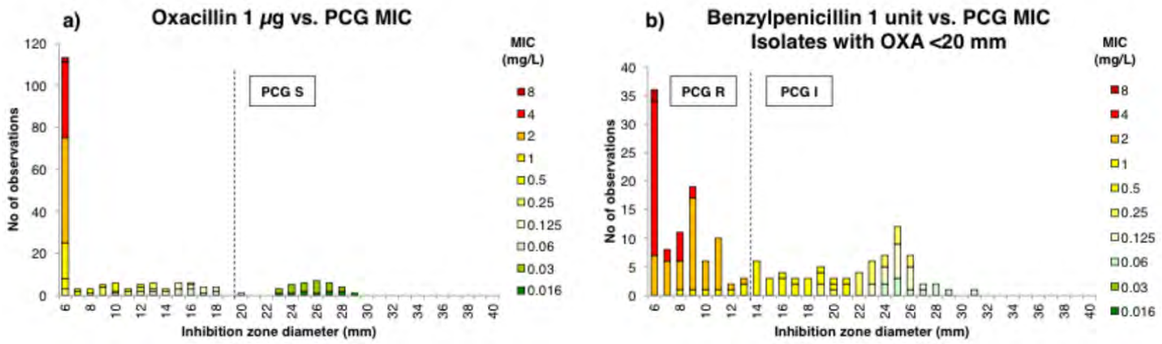

Figure 2: Inhibition zone diameter distribution with corresponding MIC values as coloured bars for *Streptococcus pneumoniae*. (a) The standard screening test for beta-lactam resistance with oxacillin 1 pg, which can be used to report benzylpenicillin as S (100 isolates). (b) The proposed follow-up test with benzylpenicillin 1 unit to distinguish between I and R for *benzylpenicillin in S. pneumoniae* with oxacillin 1 μg zones <20 mm (84 isolates).

Conclusions

While the development of novel antimicrobials offers hope in our battle against multidrug-resistant Gram-negative infections, significant challenges remain. Drug development has focused primarily on evading inactivating enzymes, often neglecting the equally important aspects of cellular entry and receptor binding. This oversight has likely contributed to the rapid emergence of resistance to newer agents.

When novel agents reach clinical practice, we need comprehensive preparedness plans addressing their place in therapy, immediate implementation of susceptibility testing, and strategies to prevent resistance emergence. Pharmaceutical companies must consider more complex drug development approaches; targeting beta-lactamases alone is insufficient.

For clinical laboratories, media modifications should be minimized, with clear justification when necessary. Fixed concentrations generally remain the preferred approach for beta-lactam/beta-lactamase inhibitor testing, with exceptions for agents like zidebactam where the inhibitor's antimicrobial activity is clinically relevant.

As we continue refining our approaches to both therapy and laboratory diagnosis, balance remains crucial - whether balancing efficacy against toxicity in extended infusion strategies or balancing pragmatic clinical needs against rigorous scientific standards in susceptibility testing. Only through such balanced, evidence-based approaches can we hope to maintain our progress against these challenging pathogens.

PLENARY 3

| Epidemiology |

Clinical features & natural history of Nontuberculous Mycobacterial infections

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Epidemiology

There are many areas of uncertainty in the epidemiology of NTM disease, as pathogenicity varies between species, contamination of human samples from environmental sources is common (e.g. dust particles and fomites that contain NTM may contaminate samples and the laboratory process), and clinical reporting is not standardised. In most countries, NTM disease is not a notifiable condition and high-quality data are often not available. Queensland has maintained a mandatory reporting scheme for NTM infections since the introduction of TB control around 1950. All NTM isolates are recorded in QLD Health's Notifiable Conditions Database (NoCS). Three analyses have been published utilising this data (1, 2, 3) that demonstrate a rising incidence of NTM pulmonary disease between 1985 and 2016 (14.8 to 25.88 per 100,000 population). This rise continued through to 2020, but decreased during the COVID pandemic, potentially due to reduced testing. There were 63 different species reported, dominated by *M. intracellulare*, accounting for 35% of notifications, followed by *M. abscessus, M. avium*. The MAC complex, which now comprises 12 slow growing species, made up 47% of notifications. There has been a shift from predominantly cavitary upper lobe disease in males, to the nodular bronchiectatic phenotype more commonly seen in middle aged to elderly females.

NTM are ubiquitous in the environment; >200 species are now described. Household and hospital tap water, bathrooms, potting soil, garden soil and household dust are all potential sources of infection, and transmission routes include aerosols from water, soil, dust and patients coughing. Human interaction with the environment may result in more exposure, along with human activity that affects the environment such as water disinfection, soil disruption, mining and industry. These activities may also influence the evolution of the organisms, including their virulence and hydrophobicity, which in turn influences transmission. Climate change and natural disasters may also impact the environmental prevalence of NTM and their dispersal through aerosolization.

A spatial epidemiological study (4) in QLD identified four NTM species – *M. abscessus, M. avium, M. intracellulare* and *M. kansasii* where the risk of infection was related to geospatial factors. A number of socio-ecological, economic and environmental factors associated with NTM infection risk. e.g. For *M. intracellulare*, risk correlated with a shallower soil depth. In shallow soil, there is poor rooting of vegetation and decreased uptake of soil nutrients, leaving a nutrient rich topsoil environment in which mycobacteria may thrive. Dust particles are also commonly suspended in the air. Of 120 strains NTM isolated from vacuum cleaner dust collected in Queensland, 44% of 50 strains of *M. intracellulare* belonged to serotypes that were recognized as disease associated strains.(5)

A US Study demonstrated an increased NTM risk associated with living in areas of high evapotranspiration,(6) a measure of the atmosphere's ability to remove water from the surface through the processes of evaporation and transpiration. Mycobacteria are naturally hydrophobic and can be aerosolized from natural waters and transferred from seawater to air by natural processes resulting in 1000 fold increase in the numbers of viable mycobacterial cells per ml of water. Mycobacteria have been found in natural aerosols of a respirable size (ie <5µm). The first clinical examples of this mode of transmission came with reports of "Hot tub lung", a form of hypersensitivity pneumonitis, not only associated with use of hot tubs (*M. avium),* also reported in lifeguards/pool attendants, who worked in an indoor swimming pool that featured waterfalls and sprays, and in metalworkers, following disinfection of metalworking fluid (*M. immunogenum).*

There are a wide variety of NTM species identified in water samples back to mid 1900s, but not all have been associated with disease. Accurate speciation, and genotyping to match patient and water isolates is needed to demonstrate possible transmission. This evidence has been published for household/municipal water systems (*M. avium, M. abscessus, M. kansasii, M. lentiflavum*), hospital water (*M. porcinum, M. avium, M. abscessus, M. fortuitum, M. chimaera)* but importantly not for *M. intracellulare*. (7, 8) In 2013 we published the first study to match *M. abscessus* isolates from drinking water with patient isolates using rep-PCR.(9) More recently we provided more definitive evidence for the role of drinking water in *M. abscessus* transmission using whole genome sequencing. (10)

Shower heads also provide a vehicle for transmission. Culture-independent technology (rRNA gene sequences) has identified sequences representative of NTM enriched to high levels in showerhead biofilms, >100-fold above background water contents.(11) Higher relative abundance of MAC and *M. abscessus* in showerheads correlated with higher NTM disease prevalence.(12) NTM have also been grown from shower aerosols (*M. avium, M. abscessus, M. kansasii).(13)*

Once disease is diagnosed, not all patients necessarily need immediate treatment. Predictors of spontaneous culture conversion include lower age, increased BMI, fewer involved lobes, and smear negativity. In four large natural history studies, the rate of spontaneous culture conversion after 12 months of observation was 11-19%. However new culture positive rate after spontaneous conversion was ≈ 17-21% after a median of 18.2 -38.2 months. Eventually the majority of patients will have progressive disease, at varying rates (Figure 1).

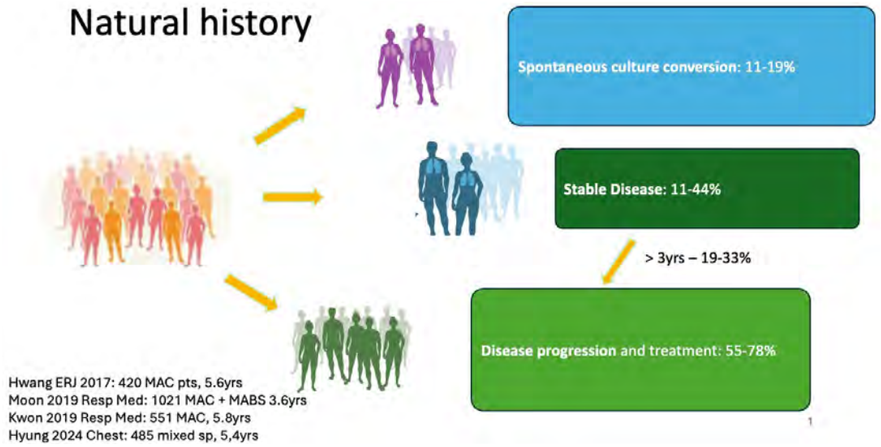

Figure 1

Natural history

As NTM are environmental organisms we are exposed to them regularly in our day to day activities. The impact of that exposure depends on a variety of factors, related to both the organism and the host. Essentially for any NTM species, if you have a big enough dose in a competent host or a minimal dose in weak enough host, you can get disease. And because not all people who culture NTM from their sputum have disease, diagnostic criteria (clinical, microbiological and radiological) have been developed.(14)

Predictors of disease progression reported in cohort studies include younger age (?), lower BMI (<18.5), more involved segments and cavitation on CT, elevated ESR/CRP, Hb<10g/dL, male sex (?), smear status (?), and immunosuppression. Using these predictors of disease progression, the South Korean team came up with a clinical prediction score called the BACES score, which assigns one point each to **B**MI, **A**ge, presence of **C**avitation, elevated **E**SR, and male **S**ex. There have been 4 papers now of reports using this score, and 1 conference abstract. (15, 16, 17, 18, 19) One of the more recent papers reports the validity of

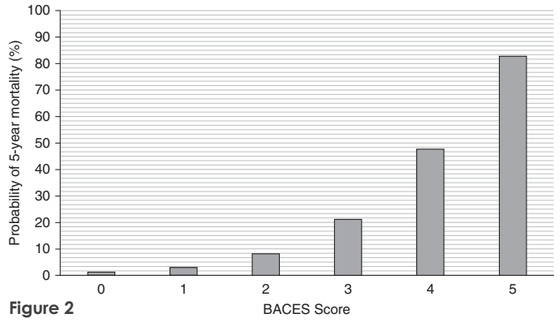

Figure 2

predicting progression and demonstrated a clear separation between the scores. The original study however was designed to predict mortality, with significant mortality associated with a BACES score of 4-5 – both all cause and respiratory mortality (Figure 2). In the Australian and Canadian studies, the performance of the scores was similar, though ours only had 5 patients in the high risk group with a score of 4-5, and the majority were managed in specialized clinics, so this may over-estimate survival.

Clinical features

In order to influence the natural history we need to understand the host. Fibrocavitary (FC) disease predominantly affects the upper lobes of the lung, traditionally described in middle aged, smoking males with COPD. Organisms are easily identified from sputum, and are usually monoclonal. The nodular bronchiectatic phenotype (NB) in contrast is far more common in women >40yrs, especially >65yrs, with no underlying lung disease, and trivial/no smoking history. In these patients NTM is recognized as a cause of bronchiectasis, and they are often polyclonal. As disease progresses, cavitation can occur. Due to the distinct physical features of these patients, an astute clinician labelled them as "Lady Windermere" (and Lord Windermere)(20) and postulated that voluntary cough suppression and sputum retention led to airway inflammation, allowing NTM to attach. In a case-control study they are described as being

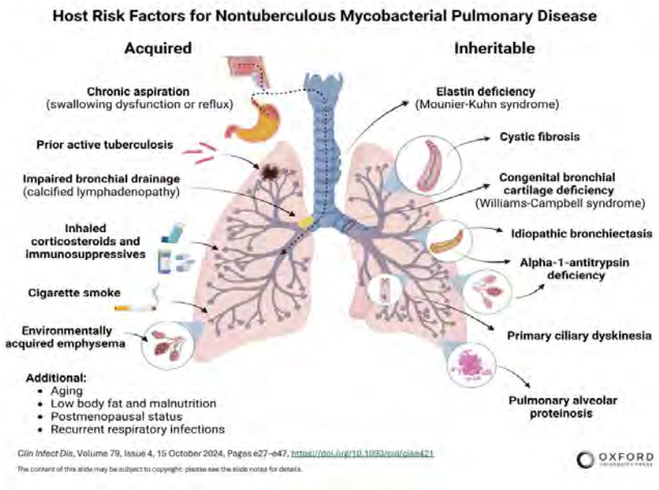

Figure 3

of above average height, slender, more commonly have a pectus excavatum, thoracic scoliosis, and hypermobile joints, raising the possibility of a connective tissue disease. 36.5% (23/63) had ≥ 1 cystic fibrosis transmembrane conductance regulator (CFTR) mutations, and an additional 7 had an abnormal sweat Cl^- >40. Whole exome sequencing revealed patients with NTM-PD have more low-frequency, protein-affecting variants in immune, CFTR, cilia, and connective tissue genes than their unaffected family members and control subjects.(21) Other host factors for NTM susceptibility are highlighted in Figure 3.

In considering immunologic susceptibility, dissecting out specific defects has not been overly successful, but certainly worth considering, in light of the potential benefits of host directed therapies. We do know that the macrophage is a key effector cell in the clearance of NTM, and a range of cytokines play an important role, however no consistent defects have been demonstrated across cohorts.

Mucociliary aspects of host defense that occur locally within the lung can be broadly divided into congenital defects, such as primary ciliary dyskinesia and cystic fibrosis, or acquired defects caused by cigarette smoke, viral infections, and aspiration of gastric acid. The net effect is that of mucous accumulation, attracting polymicrobial infections, epithelial injury and denudation, and the vicious cycle of bronchiectasis (Figure 4).

If we learn from our observations of NTM patients, we frequently see this radiological appearance of small nodules and tree in bud change, that represents mucous plugging in small peripheral airways (Figure 5) In conjunction with this- when we perform bronchoalveolar lavage on such segments, it is common to see these very small mucous plugs that look like casts from these small airways. This raises the question of whether the

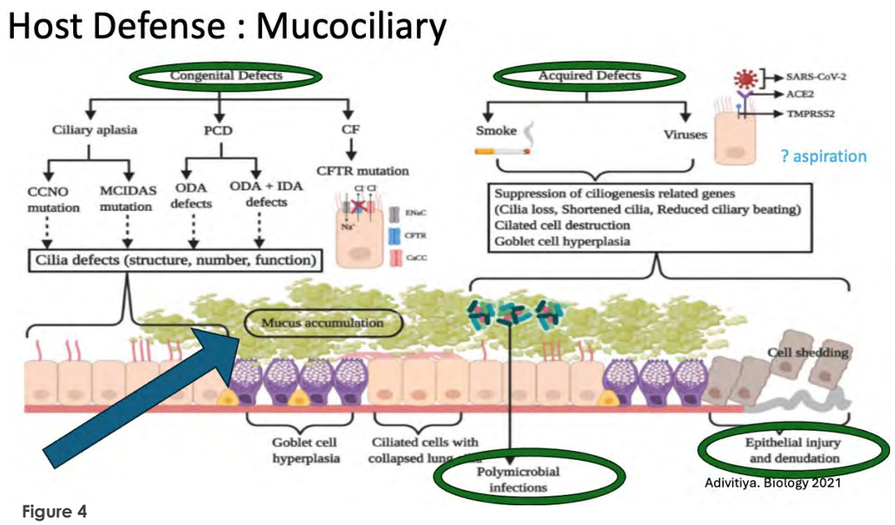

Figure 4

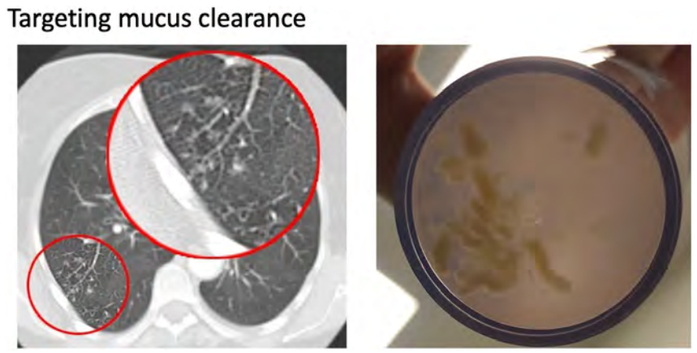

Figure 5

actual secretions in these patients are abnormal, leading to such plugging, and subsequent infection, or is it merely a secondary effect of NTM infection. And could this be a potential avenue for therapeutic intervention.

The critical role of ion transport in pulmonary NTM susceptibility is exemplified by the robust association of mutations in CFTR with active disease. Importantly, this association is true even for heterozygous CFTR mutation carriers, suggesting that even relatively modest changes in normal CFTR function have important late-onset effects on pulmonary NTM disease. The benefits of CFTR modulator therapy reducing the risk of NTM infection have been well described. Further support for ion transport defects contributing to impaired mucociliary clearance comes from a Japanese genome wide association study for pulmonary MAC validated in a separate Japanese, Korean and European cohorts. The strongest association identified came from chromosome 16p21, particularly rs109592, an intronic region of the calcineurin like EF-hand protein 2 (*CHP2*). Expression quantitative trait loci analysis demonstrated an association with lung CHP2 expression. CHP2 was expressed in the lung tissue in pulmonary MAC disease, and this SNP was associated with the nodular bronchiectasis subtype. (22, 23, 24)

Ciliary beat frequency in NTM patients versus healthy controls has been evaluated in vitro. This was restored with the application of nitric oxide donors and PDE5 inhibitors, which had no effect on healthy cells. A pilot study using sildenafil in 9 patients, demonstrated a significant improvement in ciliary beat frequency over 30 days and increased nasal NO production, but no change in sputum clearance.(25) Mucociliary dysfunction can also be acquired and it's important to address factors, such as cigarette smoking, and gastrooesophageal reflux that have been associated with NTM disease in several studies.(26, 27)

Conclusions

NTM pulmonary disease is increasing worldwide, and it is not just an infection. To improve patient outcomes, we need to understand the environmental factors associated with exposure risk, and evolutionary pressure on the organism. It is important to understand the natural history of disease in order to know how we can potentially influence it favorably, by treating the right patients at the right time. To improve treatment success and reduce the risk of reinfection and relapse, a more thorough understanding of the host is required, so that we can ultimately strive towards more personalized medicine.

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TRAVEL AWARDEES

Reflections on Antimicrobials 2025

Reports from Travel Awardees

Auriane Form

Held on the banks of the Yarra River at Crown Promenade, Antimicrobials 2025 showcased the latest developments in antimicrobial research. As a third-year PhD candidate, I was honoured to receive the Antimicrobials 2024 Poster Travel Award, allowing me to attend this event in Melbourne. It was a great opportunity to engage with such a knowledgeable platform.

The conference brought together experts from the clinical, research, and industrial sectors worldwide. This mix of leaders highlighted the importance and impact of antimicrobials from different perspectives.

The event started with a plenary talk on precision dosing across a hospital network by Dr. Erin McCreary from the University of Pittsburgh. Her presentation highlighted the complexities of infections and patient care, considering various comorbidities. Following this, Professor Christian Giske from Karolinska University Hospital and Karolinska Institutet discussed new therapies for extensively drug-resistant gram-negative bacilli. The third plenary talk, delivered by Professor Rachel Thomson from the University of Queensland, focused on nontuberculous mycobacteria pulmonary disease, covering its natural history, clinical manifestations, and epidemiology.

The symposium sessions were equally impressive, covering a wide range of topics such as complex AMR infections in vulnerable populations, mycobacteria, mycology, ongoing public health challenges, and gram-negative bacteria. The session on complex AMR infections in vulnerable populations was particularly insightful, with inspiring contributions from Dr. Lucy Attwood (Alfred Health, Monash Health, and Monash University), Anita Williams (The Kids Research Institute Australia), and Professor Asha Bowen (Perth Children's Hospital).

The proffered paper sessions featured a variety of engaging talks. I was particularly interested in Kelly Cairns' presentation on infective endocarditis caused by vancomycin-resistant *Enterococcus faecium* (VREfm). Her talk highlighted the clinical challenges posed by VREfm and emphasized the importance of using a daptomycin backbone for treatment.

The poster session showcased a wide range of research. Two posters by Chin-Yen Yeo, "Escaping the Burnout" and "The Tortured Antimicrobial Department," stood out for their unique approach to raising awareness about antimicrobials through pop culture references.

Overall, Antimicrobials 2025 was a great success. The conference's ability to bring together experts from various fields was invaluable, and attending was a privilege. I look forward to participating in many more such events in the future.

Xing Li

Attending Antimicrobials 2025, the 24th Annual Scientific Meeting held at Crown Promenade, Melbourne, Victoria, as a travel award recipient was an invaluable experience that broadened my understanding of antimicrobial resistance (AMR) research and its clinical implications.

As a PhD candidate from Murdoch University, my research focuses on AMR in clinically significant bacteria from Australian wildlife using a One Health approach. I am honoured to present my research and share my findings in a talk entitled "Antimicrobial Resistance in *Staphylococcus aureus* Isolated from Australian Wildlife." My study provides a baseline investigation into AMR in *S. aureus* from Australian wildlife, aiming to better understand the resistance profiles of *S. aureus* isolates and the potential role of wildlife in the spread of AMR. Sharing my findings with an audience of experts and peers was an exciting experience, allowing me to contribute to the broader discussion on AMR in both clinical and environmental settings.

The conference featured an impressive lineup of keynote speakers and international experts, including Erin McCreary, Lars Westblade (United States) and Christian Giske (Sweden), who shared global perspectives on antimicrobial use and resistance mechanisms. This year's program placed a strong emphasis on Gram-negative bacteria and mycology, reflecting the ongoing challenges in clinical microbiology and infectious disease management. One particularly engaging aspect of the conference was the in-depth discussion around clinical antibiotic breakpoints, including updates and revisions to established standards such as EUCAST, CLSI, and the establishment of AUSCAST. These discussions are critical for ensuring that diagnostic and therapeutic strategies evolve alongside emerging resistance patterns.

Dedicated workshops, including those focused on pharmacy and antimicrobial stewardship, provided valuable opportunities for professional development. Additionally, expert-led literature reviews summarized recent breakthroughs in microbiology and antimicrobial resistance research, offering key insights for both clinicians and researchers. The poster sessions were a highlight of the conference, providing a dynamic platform to engage with researchers across various disciplines. Discussing my work with scientists from different backgrounds led to insightful exchanges of ideas, helping me see my research from new perspectives. It was particularly inspiring to learn how different methodologies - from genomics to clinical microbiology - are being applied to tackle AMR. These interactions not only deepened my understanding of AMR but also sparked potential collaborations that could enrich my future research.

Receiving the travel award was not only a financial support but also an encouragement to continue pursuing research that contributes to the global fight against AMR. I am deeply grateful for the opportunity to participate in Antimicrobials 2025 and look forward to applying the knowledge gained to my ongoing research.

POSTER AWARD

Novel Sepsis guideline adherence & useability

Impact of a WISCA-derived local sepsis guideline for Queensland

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2 University of Queensland
3 Clinical Excellence Queensland

Background

Inadequate empirical therapy for sepsis patients is associated with increased mortality, morbidity, and length of hospital stay. Administering the best antimicrobials for empiric treatment in a timely manner can be facilitated by appropriate, easy to use, and trustful guidelines.

Methods

The Queensland Sepsis Program was responsible for embedding sepsis pathways with treatment bundles and antimicrobial guidelines in 14 hospitals in Queensland, Australia, between 2018-2020. Local antimicrobial guidelines were developed in 2018 using Queensland antibiogram data and local epidemiological patterns and the Weighted Incidence Syndromic Combination Antibiogram (WISCA) methodology with consensus across 14 hospital Infectious Disease Physicians. Retrospective, multicentre study of adult patients presenting to three tertiary EDs in Queensland, Australia, with symptoms and signs suggestive of sepsis who had blood cultures collected. These participants were stratified as having septic shock, sepsis or infection alone, using Sepsis-3 definitions. Antimicrobial prescriptions were assessed as adherent to antimicrobial guidelines and assessed for 'appropriateness' based on National Antimicrobial Prescribing Survey criteria. An online survey (Microsoft Forms®) was distributed to ED physicians to assess the useability of the guidelines 5 years after embedding of the guidelines.

Results

Of 2591 eligible patients, 721 were randomly selected: 241 in the baseline phase and 480 in the post-intervention phase. The rates of guideline adherence were 54.0% and 59.5%, respectively (adjusted OR (aOR) 1.41 (95% CI 1.00, 1.98)). As compared with baseline, there was an increase in the rates of appropriate antibiotic prescription after bundle implementation (69.9% vs 57.1%, aOR 1.92 (95% CI 1.37, 2.68)). The majority of 29 ED SMO survey respondents agreed with the format of the guidelines, including having a separate septic shock section (83%, 24/29). Just over 50% reported using the guidelines often and 90% were in favour of having 'multiple sources of infection' choices for empiric antimicrobials.

Conclusions

An increase in guideline adherence was noted with introduction of the WISCA-derived local guidelines, but the rates remained low. This was despite favourable feedback and general acceptance of the guidelines by senior Emergency Department Physicians. This discrepancy highlights the complexity in prescribing for sepsis, which goes beyond provision of well-accepted, peer-reviewed guidelines.

Herding Cats* with WISCAs:
Using Weighted-Incidence Syndromic Combination Antibiograms to inform adult sepsis guideline development.

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2. Department of Infectious Diseases, Sunshine Coast Hospital and Health Service, Queensland, Australia
3. Clinical Excellence Queensland, Queensland Health, Brisbane, Australia

AIM

To describe the process of developing novel sepsis guidelines for use in Queensland, Australia

BACKGROUND

Inadequate empirical therapy for sepsis patients is associated with increased mortality, morbidity, and length of hospital stay (1).
Administering the best antimicrobials for empiric treatment in a timely manner can be facilitated by appropriate, easy to use, and trustful guidelines.
Gaining consensus on the best choice of empiric guidelines, whilst recognising epidemiological differences in microbiological spectra and avoiding the use of overly broad-spectrum antimicrobials, can be challenging.

METHODS

The Queensland Sepsis Collaborative was responsible for embedding sepsis pathways with treatment bundles and antimicrobial guidelines in 14 hospitals in Queensland, Australia, between 2018-2020 (1).
The first antimicrobial guidelines were developed in 2017-2018 using Queensland antibiogram data to ensure the empiric regimens selected by a panel of 12 Infectious Diseases Physicians (IDP) would provide adequate spectrum of activity (agreed to be >90% cumulative susceptibility for sepsis and >95% for septic shock).
The WISCAs (2) utilised the epidemiology of respective organisms for each syndrome derived from local data or a review of the literature, including the annual Antimicrobial Use and Resistance in Australia (AURA) report (3).
In addition, mortality-weighted data, using bacteraemia crude fatality rates for Queensland (4), was used to account for the difference in virulence of organisms.

GETTING TO AN AGREEMENT

Expert Group
- 12 Infectious Diseases physicians, representing 8 Hospital and Health Services
- 2 AMS specialist pharmacists

Key Requirements
- Syndromic guidelines rather than broad-spectrum antimicrobial empiric guidelines
- Separate shock section with options for source not apparent
- Tolerance of risk – threshold of 95% antimicrobial spectrum coverage for septic shock and 90% for sepsis

Antibiogram

Figure 1: Frequency of organisms isolated from blood cultures for one region

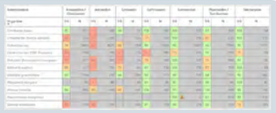

Figure 2: Example of antibiogram for gram negative organisms from one site

Findings:
- Marked differences in MRSA prevalence across Queensland
- Tropical infections *(Burkholderia pseudomallei*)in Northern Queensland

WISCA Key Requirements
- Expert group decided on
  - susceptibility profiles for non-culturable organisms or those without breakpoints
  - Sources of epidemiological data for each syndrome
  - A core antibiotic for septic shock with the addition of other antibiotics depending on risk factors
    - Avoid use of single broad-spectrum antimicrobial agent (eg. meropenem)
  - Syndromes to include:
    - meningitis, community acquired pneumonia, skin and soft tissue infections, intra-abdominal infections, urinary, febrile neutropenia

WISCA

Figure 3: Results of WISCA analysis for bacteraemias from one region.
WISCA incorporates combination antimicrobials and is weighted for organism isolation rates

- Amoxiclav chosen as core antimicrobial for septic shock with addition of gentamicin/vancomycin as a single dose
- Antimicrobial selections based on achieving minimum spectrum threshold

Draft guidelines

Human Factors testing
- 23 ED Medical officers, 21 Nursing staff
- Case vignettes
- Two versions of guidelines - with and without septic shock/'multiple possible sources'
- Testing for ease of use - antibiotic and administration guidelines

Findings:
- 68.3% of prescriptions were adherent to the guidelines for septic shock and 91% for sepsis without shock.
- Medication dosing errors were the cause of most errors and were related to aminoglycosides.
- Guidelines with the separated shock and multiple sources of infection were more satisfactory to participants (median result 8.8/10 vs 7.2/10)

Publish

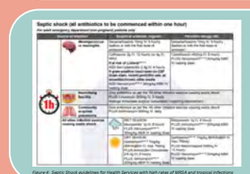

Figure 4: Septic Shock guidelines for Health Services with high rates of MRSA and tropical infections

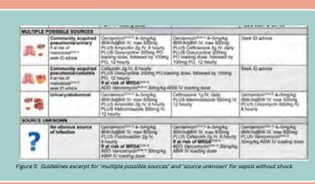

Figure 5: Guidelines excerpt for 'multiple possible sources' and 'source unknown' for sepsis without shock

RESULTS

Using the results of the WISCAs, three epidemiologically distinct areas were identified in Queensland requiring three different guidelines:
- low MRSA (<20% MRSA bacteraemia rate),
- high MRSA (>20% MRSA bacteraemia rate) and
- tropical (with higher *Burkholderia pseudomallei* rates).

By use of the WISCA data, bespoke guidelines to cover a range of potential sources of infection (eg. urinary tract and/or respiratory source) were developed to facilitate timely treatment when the source of infection is not obvious.

CONCLUSIONS

The use of the WISCAs provided assurance that the empiric regimens agreed upon by the IDP panel were not only sufficient in antimicrobial spectrum, but also the most appropriate from an AMS/AMR perspective, leading to safe and trustworthy sepsis guidelines

Limitations and Future work:
- Assumptions on susceptibility patterns can be challenging. For example, the efficacy of ceftriaxone for MSSA.
- Specific syndromes had limited numbers of microbiological culture samples to draw conclusions
  - Future WISCA development with stratification for age and other patient characteristics may be possible by using Bayesian techniques to account for lower specimen numbers.
- Fungi and anaerobes were not included

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- Dr Sonali Coulter, Pathology Queensland

*Spotted-tail quoll, are sometimes erroneously called "native cats" in Australia due to their cat-like appearance and carnivorous habits, but they are marsupials. Quolls are generally solitary, nocturnal predators , Quolls are some of Australasia's feistiest carnivorous mammals. They would not be amenable to herding.

Could it be SEPSIS?

TRAVEL AWARD

Systemic antibiotic treatment after cancer diagnosis among First Nations Peoples in Queensland

Findings from a population based analysis

Sewunet Belachew[1] Shafkat Jahan[1] Abbey Diaz[2] Ming Li[1] Jennifer Ong[3] Gail Garvey[1]

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3 Sydney Pharmacy School, University of Sydney

Background

Cancer poses a significant health concern in Australia, with First Nations Peoples facing disparities in care and outcomes. Infections present a substantial burden for immunocompromised cancer patients, making appropriate antibiotic use a critical aspect of care. However, limited research exists on antibiotic use following cancer diagnosis, particularly among First Nations peoples.

Aim

This study aimed to examine systemic antibiotic treatment utilisation post-cancer diagnosis among First Nations peoples in Queensland.

Methods

First Nations Queenslanders (N=1884) and other Queenslanders (N=104,204) diagnosed with any cancer between 1st July 2011 and 30th June 2015, along with their systemic antibiotic treatment details between 1st July 2011 and 30th June 2018, were identified using the Cancer CostMod project, comprising Queensland Cancer Registry data linked with Pharmaceutical Benefits Scheme (PBS). Of the 106,088 cancer cases with documented ethnicity, 105,079 had corresponding PBS records. Logistic regression was employed to examine differences in antibiotic treatments post-cancer diagnosis.

Results

Among 105,079 cancer patients diagnosed in Queensland, 86.4% received systemic antibiotics following diagnosis. A lower proportion of First Nations cancer patients (n=1,467, 80%) had antibiotics compared to other Queensland cancer patients (n=89,358, 86.6%), $p<0.001$. First Nations cancer patients were less likely to receive antibiotics after a cancer diagnosis than other Queenslanders (adjusted odds ratio (aOR): 0.62, 95% CI: 0.55–0.69), particularly those in remote areas (aOR: 0.49, 95% CI: 0.35-0.69). In total, just over 1 million antibiotic claims were made, with 1,467 First Nations cancer patients making 16,482 claims. The most commonly claimed antibiotics for both groups were amoxicillin, amoxicillin-clavulanic acid, and cephalexin, with penicillins, cephalosporins, and sulfonamides being the most frequently prescribed classes. Melanoma patients had the most antibiotic claims among other Queenslanders (152,183, 15%), while breast cancer patients led among First Nations (2,631, 16%).

Conclusions

The high volume and diversity of antibiotics utilised underscore the need to evaluate the appropriateness of these prescriptions and ensure responsible use to prevent antibiotic resistance. It is also crucial to further explore the drivers of the observed disparities in antibiotic use. Inappropriate antibiotic use or lack of access when needed negatively impacts cancer outcomes, highlighting the importance of addressing underuse and misuse.

Investigating antibiotic use among First Nations Queenslanders

THE UNIVERSITY OF QUEENSLAND AUSTRALIA

Systemic antibiotic treatment after cancer diagnosis among First Nations Peoples in Queensland: Findings from a population-based analysis

Sewunet Admasu Belachew[1], Shafkat Jahan[1], Abbey Diaz[2], Ming Li[1], Jennifer Ong[3], Gail Garvey[1]

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[2]Yardhura Walanit National Centre for Aboriginal and Torres Strait Islander Wellbeing Research, National Centre for Epidemiology & Population Health, Australian National University, Canberra, Australia | [3]Sydney Pharmacy School, University of Sydney NSW Australia.

BACKGROUND

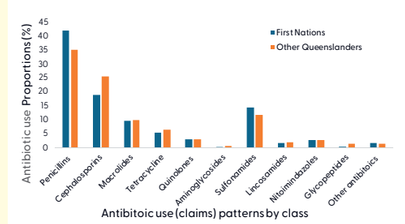
- Cancer poses a significant health concern in Australia, with First Nations Peoples facing disparities in care and outcomes, making appropriate antibiotic use a critical aspect of care.
- Infections impose a substantial burden on immunocompromised patients, such as those with cancer, due to both the disease itself and the effects of treatment, making timely and judicious antibiotic use essential.
- If infections are not effectively prevented and treated with appropriate medications, they can lead to severe complications, increase morbidity and hospital stays, and ultimately negatively impact cancer outcomes, including reduced survival.
- However, limited research exists on antibiotic use and patterns following cancer diagnosis and the associated factors, particularly among First Nations Peoples.

STUDY AIM

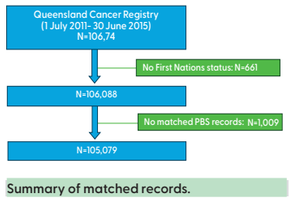
This study aimed to examine systemic antibiotic treatment utilisation and the associated factors among First Nations Peoples post-cancer diagnosis in Queensland, Australia.

RESULTS

- Among 105,079 cancer patients diagnosed in Queensland, 86.4% received systemic antibiotics following diagnosis
- A lower proportion of First Nations cancer patients (n=1,467, 80%) had antibiotics compared to other Queensland cancer patients (n=89,358, 86.6%), p<0.001.
- First Nations cancer patients were less likely to receive antibiotics after a cancer diagnosis than other Queenslanders (adjusted odds ratio (aOR): 0.62, 95% CI: 0.55–0.69), particularly those in remote areas (aOR: 0.49, 95% CI: 0.35-0.69)
- In total, just over 1 million antibiotic claims were made, with 1,467 First Nations cancer patients making 16,482 claims.
- The most commonly claimed antibiotics for both groups were amoxicillin, amoxicillin-clavulanic acid, and cephalexin, with penicillins, cephalosporins, and sulfonamides being the most frequently prescribed classes.
- Melanoma patients had the most antibiotic claims among other Queenslanders (152,183, 15%), while breast cancer patients led among First Nations (2,631, 16%).



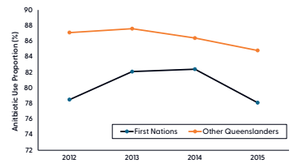
Antibitoic use (claims) patterns by class



Summary of matched records.

Residential remoteness

The Index of Relative Socio-economic Disadvantage



Year of cancer diagnosis

METHODS

First Nations Queenslanders (N=1884) and other Queenslanders (N=104,204) diagnosed with any cancer between 1st July 2011 and 30th June 2015.

Systemic antibiotic treatment details between 1st July 2011 and 30th June 2018, were identified using the Cancer CostMod project, comprising Queensland Cancer Registry data linked with Pharmaceutical Benefits Scheme (PBS).

Systemic antibiotic use was examined by Indigenous status, with further stratification by year of diagnosis, age, sex, and area-level residential remoteness and socioeconomic disadvantage.

The proportion, pattern, and number of claims of systemic antibiotic use were compared by Indigenous status.

Disparity by Indigenous status, individual, area-level socioeconomic, and residential remoteness factors were investigated with logistic regression analysis.

CONCLUSION

The high volume and diversity of antibiotics utilised underscore the need to evaluate the appropriateness of these prescriptions and ensure responsible use to prevent antibiotic resistance. It is also crucial to further explore the drivers of the observed disparities in antibiotic use, such as by-Indigenous status, area-level residential remoteness, and Socio-economic advantage. Inappropriate antibiotic use or lack of access when needed negatively impacts cancer outcomes, highlighting the importance of addressing underuse and misuse.

THE UNIVERSITY OF QUEENSLAND AUSTRALIA
FIRST NATIONS CANCER & WELLBEING RESEARCH PROGRAM

ANTIMICROBIALS 2025
24th Annual Scientific meeting Melbourne 20th-22nd February 2025

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The study is funded by The Australian Society for Antimicrobials (ASA)

TRAVEL AWARD

Antimicrobial Resistance in *Staphylococcus aureus* Isolated from Australian Wildlife

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Aim

This study aims to characterize the prevalence of antimicrobial resistance (AMR) genes and genetic diversity of *S. aureus* from Australian wildlife by performing a baseline investigation at the urban human-animal interface.

Background

AMR is a One Health concern which recognizes wildlife as a potential reservoir of antimicrobial-resistant bacteria. *S. aureus*, including methicillin-resistant *S. aureus* (MRSA) have been reported in European mammals and birds, but rarely investigated in Australian wildlife.

Methods

Six Australian wildlife species (kangaroo, quenda, galah, pelican, bobtail lizard, and longnecked turtle) were included in this study. Skin swabs were collected from 30 members of each wildlife species on admission to the WA Wildlife Hospital and one-week post-admission if the animal was still in rehabilitation. A nasal swab was additionally collected from the kangaroos and quendas. *S. aureus* and MRSA screening was performed using CHROMagar™ selective culture media. Species identification was confirmed by MALDI-TOF. Whole genome sequencing was performed on the Illumina NovaSeq platform and bioinformatics analyses were performed to identify multi-locus sequence types (STs), AMR genes and phylogenetic relationships.

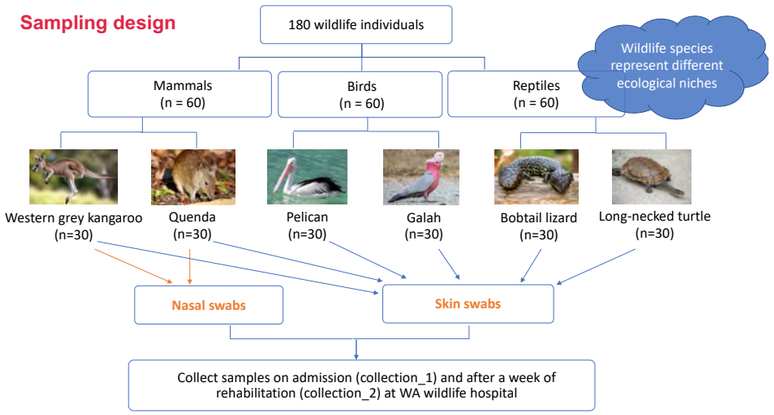
Results

S. aureus was isolated from 18 pelicans, five quendas, five kangaroos, one bobtail lizard and one long-necked turtle. The skin (38/277) and nasal (11/81) carriage rates were 14%. The 49 isolates were genetically diverse and represented by 21 different STs, including four novel STs. The dominant STs were ST5, ST692, ST953, and ST8813. The *blaZ*, *fosB*, *erm*(T), *aph(2")Ib,* and *tet*(L) AMR genes were identified in 63%, 53%, 16%, 4%, and 2% of the isolates, respectively. Additionally, two *mecA*-positive MRSA isolates (ST1-IV and ST93-IV) were identified from two pelicans during rehabilitation. Phylogenetically close relationships were identified between the isolates from Australian wildlife and human suggesting human-animal transmission risks.

Conclusion

A genetically diverse collection of *S. aureus* harbouring multiple AMR genes were identified from Australian wildlife. The detection of MRSA in two post-rehabilitation pelicans indicates a potential pathway for MRSA introduction into Australian wildlife, which may function as a reservoir, thereby posing potential risks to public health.

Sampling design



The number of collections from Australian wildlife

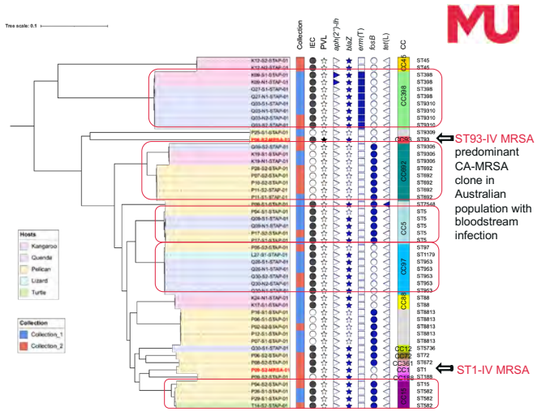
Wildlife species	Sample site	No. of animals swabbed in # collection_1	No. of animals swabbed in # collection_2
Western grey kangaroo	Skin, nose	30	7
Quenda	Skin, nose	30	14
Pelican	Skin	30	21
Galah	Skin	30	14
Bobtail lizard	Skin	30	25
Long-necked turtle	Skin	30	16
Total		180	97

collection_1: When animals on admission

collection_2: After a week of rehabilitation

Phylogenetic relationship

- Multiple clades
- Potential transmission risks within wildlife hosts:
  - ✓ Quenda and kangaroo (CC398)
  - ✓ Quenda, kangaroo and pelican (CC692)
  - ✓ Pelican and quenda (CC5)
  - ✓ Quenda, pelican and lizard (CC97)
  - ✓ Pelican and turtle (CC15)
- Potential risks for human at urban human-wildlife interface



Conclusion

- Australian wildlife may be reservoirs of *S. aureus*
  - ✓ Genetically diverse
  - ✓ Multiple AMR and virulence genes
- The first identification of MRSA in Australian wildlife: in two post-rehabilitation pelicans
- Biosecurity measures remain key to limiting the risk of bidirectional AMR transmission between wildlife and humans at the human-wildlife interface
- Continuous AMR surveillance in wildlife is needed within the One Health framework

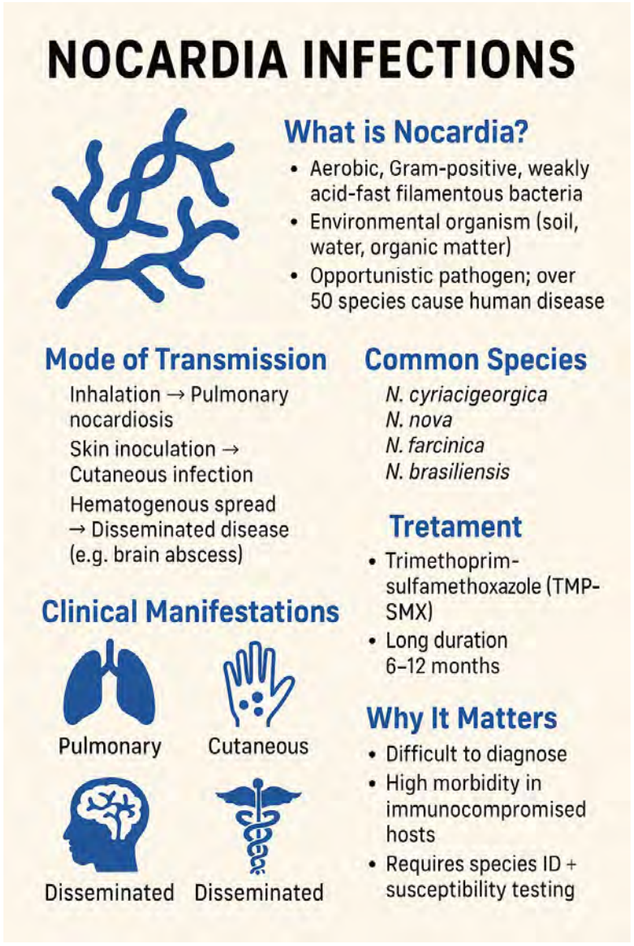
QUIZ ANSWER

A | Pulmonary *Nocardia* infection

The gram stain demonstrates gram positive rods which are beading/branching in appearance. The modified ZN stain reveals red/purple weakly 'acid fast' bacilli. The culture media reveals slow growing small colonies that are 'chalky white' in appearance on horse blood agar and dedicated BCYE (buffered charcoal yeast) agar. Given the above microbiological findings, coupled with the history of immunosuppression, ground glass nodular change, the most likely causative organism is *Nocardia* species. The clinical vignette describes a case of pulmonary nocardiosis. The skin manifestations may also represent cutaneous nocardia but more likely represent the underlying vasculitis.

Identification of the organism by matrix-assisted laser desorption ionization time-of-flight mass spectrometry (MALDI-TOF) confirmed a presumptive diagnosis of *Nocardia abscessus*. The specimen was referred for 16S RNA sequencing for species level identification, however same percentage identification for *N. asiatica*, *N. abscessus* and *N. beijingensis* was found. Susceptibility testing was performed at the reference laboratory:

Ciprofloxacin	R
Clarithromycin	R
Amikacin	S
Doxycycline	S
Imipenem	R
Cotrimoxazole	S
Linezolid	S
Amoxicillin-clavulanate	S
Ceftriaxone	S
Tobramycin	S
Tigecycline	MIC = 0.25 mg/L



Nocardia is a genus of aerobic, Gram-positive, weakly acid-fast, filamentous bacteria found in soil, decaying organic matter, and water. It's considered an opportunistic pathogen, meaning it typically affects people with weakened immune systems but can also infect healthy individuals. Nocardia spp. are widely distributed in nature and geographic trends suggest environmental factors influence species distribution. *N. brasiliensis* more common in Queensland (likely climate-related), while *N. nova* and *N. cyriacigeorgica* have a wider distribution. In the laboratory, they are slow-growing and colonies may take several days to weeks to appear in culture. Over 50 species are known to cause human disease, including *N. asteroides*, *N. brasiliensis*, *N. cyriacigeorgica*, and *N. farcinica*. Infection can be life-threatening, especially in immunocompromised hosts. Early diagnosis is challenging due to nonspecific symptoms and slow growth, requiring species identification and susceptibility testing for effective treatment.

Nocardia can cause different illnesses depending on the mode of entry:

- Inhalation | Pulmonary nocardiosis. Mimics tuberculosis or fungal infections. Symptoms: chronic cough, fever, weight loss, chest pain. Common in people with chronic lung disease or immunosuppression.
- Direct skin inoculation (e.g., through trauma) | Cutaneous infections. Localized abscesses or cellulitis. *N. brasiliensis* is a common cause. Can follow injury or exposure to contaminated soil/water.
- Hematogenous spread | Disseminated disease, including brain abscesses. High morbidity and requires prolonged antibiotic treatment. Infection may spread to multiple organs. Often seen in immunocompromised patients.

In a 2023 publication ("Nocardia species distribution and antimicrobial susceptibility within Australia" from the Internal Medicine Journal, 2023), data were collected from isolates referred to the Australian Nocardia Reference Laboratory (ANRL) between 2011 and 2022. Identification was done using 16S rRNA and secA1 gene sequencing. Broth microdilution was used to test antimicrobial susceptibility. Fifty-two different species identified from 1520 isolates. Most common were: *N. cyriacigeorgica* (16.1%), *N. nova* complex (12.4%), *N. farcinica* (10.7%), and *N. brasiliensis* (9.6%). Antimicrobial susceptibility showed: trimethoprim-sulfamethoxazole (TMP-SMX) was highly effective (91% susceptible overall), linezolid and amikacin also showed high activity. Ceftriaxone and minocycline susceptibility varied widely across species. Imipenem and ceftriaxone less effective against *N. farcinica*. Emerging resistance trends noted in some species to TMP-SMX and imipenem.

Treatment considerations include: Trimethoprim-sulfamethoxazole (TMP-SMX) is the first-line therapy. Other options: linezolid, amikacin, imipenem, depending on the species and susceptibility. Treatment duration is typically long (6–12 months) due to relapse risk

Recent review paper

Zachary A Yetmar, Paige K Marty, Josh Clement, Cyndee Miranda, Nancy L Wengenack, Elena Beam, **State-of-the-Art Review: Modern Approach to Nocardiosis—Diagnosis, Management, and Uncertainties**, Clinical Infectious Diseases, Volume 80, Issue 4, 15 April 2025, Pages e53–e64
https://doi.org/10.1093/cid/ciae643

SHORTLISTED POSTERS

Antimicrobial Stewardship
Improving general medicine antibiotic prescribing quality of the Sunshine Coast

Clinical case study
Ink Invaders | Battling *Mycobacterium* abscessus infections

Pharmacology
Population pharmacokinetics of posaconazole in allogeneic haematopoietic stem call transplant patients

Laboratory techniques
Evaluations and challenges in adoption of EUCAST anaerobic disk diffusion antibiotic susceptibility testing in an Australian hospital microbiology laboratory

Honourable mention
The Tortured Antimicrobial Department
Poetry as an effective health promotion strategy

Improving General Medicine Antibiotic Prescribing Quality on the Sunshine Coast, Queensland, Australia.

Kathryn Wilks[1,2], Patricia Kilfoyle[2], Sarah Kingscote[2], Lisa Course[2]

AIM

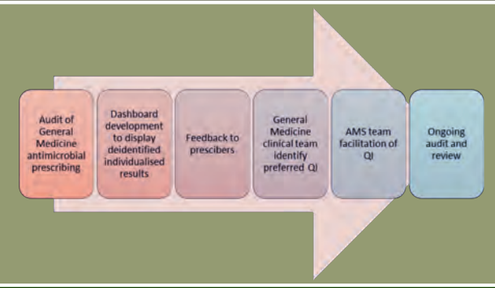
To improve guideline adherence in the management of infections at Sunshine Coast University Hospital (SCUH) and Nambour Hospital.
To implement an innovative model of self-reflective prescriber audit and feedback

BACKGROUND

The appropriateness of antibiotic prescribing in Australian hospitals has remained static over an eight-year period from 2013-2021. Locally, such trends have been mirrored during National Antimicrobial Prescribing Survey audits.
This study aimed at identifying areas of inappropriate antibiotic prescribing in the General Medicine directorate by developing local dashboards to provide individual feedback to prescribers. A participatory approach was then used to develop quality improvement (QI) interventions facilitated by the Antimicrobial Stewardship (AMS) team.

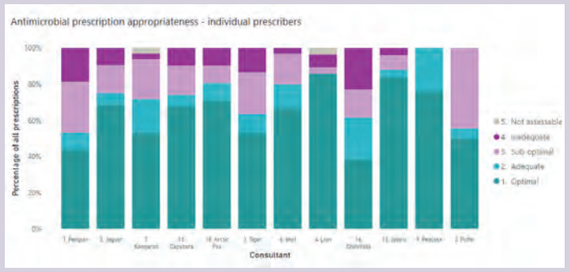
METHOD

This prospective, participatory intervention study aimed to improve antimicrobial prescribing at SCUH and Nambour hospital. A data visualisation dashboard using Microsoft PowerBI® was developed to feedback antibiotic prescribing data to individual prescribers. Whilst individual prescriber results were deidentified using an alias, individual prescribers were unblinded to their own results allowing for self-reflection, collegial comparison, and detection of outliers in prescribing practice. The service director was provided access to the unblinded results, enabling shared ownership, and recognising the importance of medical hierarchies in prescribing practice. The clinical team selected their preferred QI for facilitation by the AMS team.



RESULTS

The study dataset addressed many of the gaps in standardised AMS audits. Specifically, length of stay, duration of intravenous antimicrobials, total combined duration of antimicrobials (all routes), Multi-Resistant Organism risk and colonisation, number of regimens per indication and whether the prescription was Senior Medical Officer (SMO) initiated or reviewed. The Range of guideline adherence between individual General Medicine SMOs was 41-88%. This range reflects discordance and variation in antimicrobial use across the directorate.
The general medicine team elected to commence a consensus building project for urinary tract infection treatment guidelines, facilitated by the AMS team.



CONCLUSION

Improving uniformity in practice with oversight of General Medicine leadership, was the key driver for individualised benchmarking. Less focus is placed on scrutiny of the data as is the 'norm' for AMS programs, and more emphasis is placed upon the process of engagement and departmentally designed interventions.

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Ink Invaders: Battling *Mycobacterium abscessus* infections

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[4]*Microbiology and Infectious Diseases, SA Pathology*

Background

Mycobacterium abscessus is an environmental non-tuberculous mycobacterium (NTM) detected in water, soil, and biofilms in drinking water systems.

NTM rarely causes disease in immunocompetent patients but if introduced via penetrating skin trauma, such as contaminated ink used in tattooing, skin and soft tissue infection can result.

Treatment is challenging due to baseline and acquired drug resistance necessitating prolonged courses of combination therapy to prevent relapse. Access to therapy and cost are important considerations when deciding on a treatment course, as is the availability of close monitoring for toxicity.

Mycobacterium abscessus Cluster

A cluster of 17 linked cases presented with tattoo associated mild to moderate cutaneous *Mycobacterium abscessus* subspecies abscessus infections. All 17 individuals developed skin complaints 1 to 3 weeks after receiving tattoos. They had been clients of the same tattoo artist, who used a specific batch of grey ink.

Each case was managed individually, considering the patient's clinical course and preferences.

- 15 patients experienced mild infections that gradually resolved without the need for antimicrobial therapy and were closely monitored.
- None of the cases progressed to severe disease or displayed systemic features necessitating inpatient care or intravenous treatment.
- In 2 patients, the infection failed to improve spontaneously and treatment was required.

Case Reports

We present the antimicrobial therapy prescribed for the two patients requiring treatment for cutaneous *Mycobacterium abscessus* subspecies abscessus infections.

Treatment Considerations

A multidisciplinary team including the SA Tuberculosis Service, Infectious Diseases and pharmacy decided on a combined regimen of linezolid, azithromycin, clofazimine and rifabutin based on susceptibilities (Table 1 and 2), and cost, availability and ease of administration in the outpatient setting (Table 3).

TABLE 1: ANTIBIOTIC SENSITIVITIES

ANTIBIOTIC	BROTH MIC (mg/L)	INTERPRETATION
AMIKACIN	16	S
CEFEPIME	> 32	NI
CEFOXITIN	32	I
CIPROFLOXACIN	4	R
CLARITHROMYCIN (14 DAYS)	> 16	R
*CLOFAZIMINE	0.25	
IMIPENEM	16	I
LINEZOLID	16	I
MOXIFLOXACIN	8	R
*RIFABUTIN	> 4	
*RIFAMPIN	> 4	
TIGECYCLINE	0.12	NI
TOBRAMYCIN	16	R

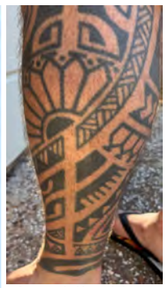

Image used with permission

*Tested by Sensititre™ SLOMYCO V2 broth microdilution

- The antimicrobial sensitivities presented in Table 1 are a compilation of 6 isolates tested by Sensititre™ RAPMYCOI broth microdilution.
- The isolates were genetically identical but there was variability with the MIC testing. Most MICs either had categorical agreement or were within 1 dilution of each other.
- For amikacin there was discordance in sensitivity testing: 2 patients had MIC=16 (sensitive), 3 patients had MIC=32 (intermediate) and 1 patient had MIC=64 (resistant).

Despite the reported resistance to clarithromycin and rifabutin individually, the combination of rifabutin with azithromycin was chosen based on *in vitro* synergism reported in the literature. Aziz et al demonstrated that rifabutin can suppress inducible macrolide resistance by blocking the induction of *whiB7* and therefore *erm41* expression, which is the gene responsible for inducible macrolide resistance. Local lab E-test synergy analysis on one isolate also supported the additive effects on the MICs of this combination (Table 2).

TABLE 2: ANTIBIOTIC SYNERGY TESTING *

ANTIBIOTIC COMBINATION	FRACTIONAL INHIBITORY CONCENTRATION	INTERPRETATION
AZITHROMYCIN + IMIPENEM	0.115	SYNERGY
CEFOXITIN + IMIPENEM	0.053	SYNERGY
RIFAMPICIN + AZITHROMYCIN	0.688	ADDITIVITY
CEFTAROLINE + IMIPENEM	2	INDIFFERENCE
RIFAMPIN + IMIPENEM	2	INDIFFERENCE
AMOXICILLIN + CEFUROXIME	4	ANTAGONISM

* E-test is not a validated nor recommended testing method for synergy testing for mycobacteria and was done in these cases for research purposes

TABLE 3: ANTIBIOTIC TREATMENT CHOICES – DOSE, COST AND AVAILABILITY

	STANDARD DOSE	COST PER PATIENT PER 30 DAYS	STOCK AVAILABILITY
OMADACYCLINE (SAS)	300mg PO daily	$30,000-35,000	Nil stock Lead time 7-15 business days
TIGECYCLINE	100mg IV load then 50mg IV BD	$3500 (plus HITH cost)	Small supply on hand
CLOFAZIMINE (SAS)	100mg PO daily	$100	Small supply on hand
BEDAQUILINE (SAS)	400mg PO daily for 2 weeks then 200mg 3 x week	$1441	Small supply on hand
AZITHROMYCIN	500mg PO daily	$25	Kept on hand
LINEZOLID	600mg PO twice daily	$720 (plus TDM)	Kept on hand
RIFABUTIN	300mg PO daily	$270	Small supply on hand
IMIPENEM-CILASTIN	1g IV BD	$10,000 (plus HITH cost)	Stock shortage
CEFOXITIN	2g IV 6-hourly	$5,000 (plus HITH cost)	Small supply on hand

Outcomes

Treatment for both patients continued for 3 to 4 months with clinical improvement in their cutaneous disease. Side effects reported included diarrhoea, orange coloured urine, intermittent stomach pains, fatigue, transient creatinine rise and generalised myalgias. These improved and did not require a change in therapy.

Conclusion

The growing popularity of tattoos has led to more tattoo-related complications, including challenging-to-treat NTM skin infections that often require complex, costly therapies with high risks of adverse reactions and toxicity.

References

1. Aziz D, Go ML, Dick T, Rifabutin Suppresses Inducible Clarithromycin Resistance in *Mycobacterium abscessus* by Blocking Induction of *whiB7* and *erm41*, Antibiotics; 2020,9,72 doi:10.3390/antibiotics9020072

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Population pharmacokinetics of posaconazole in allogeneic haematopoietic stem cell transplant patients

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Posaconazole in alloHCT

- Commonly used for prevention and treatment of invasive fungal disease (IFD) in alloHCT patients (First option in Australian Guidelines)
- MR tablets preferred formulation
- Mucositis and diarrhoea likely affect oral absorption and may result in subtherapeutic exposures
- Change to IV therapy often required

Purpose of our study

- Describe population pharmacokinetics of posaconazole oral MR tablet and IV formulations in patients in the early post – alloHCT period
- Determine dosing regimens likely to achieve therapeutic exposures
- Note only one other study describing posaconazole pharmacokinetics when changing from oral to IV posaconazole

Methods

Recruitment of 20 patients requiring change from oral to IV posaconazole during initial alloHCT admission

219 samples analysed using LC-MS/MS

Population pharmacokinetic model developed using Pmetrics version 1.9.7 software package for R

Monte Carlo Simulations (n=1000) performed for probability of both prophylaxis and treatment target attainment

Patient Characteristics

Data presented as summary (%) or Median (range)

Gender (M/F)	Age (y)	Height (cm)	Weight (kg)	Baseline Serum Creatinine (μmol/L)	Baseline Bilirubin (μmol/L)	Baseline Albumin (g/L)	Haematological Diagnosis	Stem Cell Donor Type	Conditioning Chemotherapy Intensity
M: 50% F: 50%	49 (21 – 70)	169 (142 – 192)	82 (55 – 114)	64 (29 – 96)	11 (3 – 34)	28 (18 – 34)	AML: 55% ALL: 40% CMML: 5%	MUD: 55% HAPLO: 20% CORD: 5% SIB(M): 20%	RIC: 70% MIDI: 5% MAC: 25%

Details of posaconazole sampling and dosing

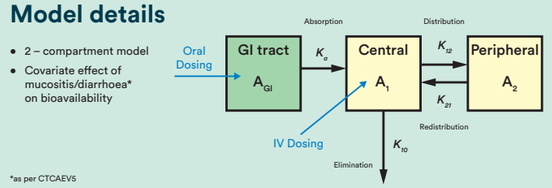
Data presented as Median (range)

No. of samples while on intravenous posaconazole (n)	No. of samples while on oral posaconazole (n)	Doses of oral posaconazole (n)	Transplant day changed to intravenous posaconazole (n)	Doses of intravenous posaconazole (n)	Transplant day changed back to oral posaconazole (n)	Days of mucositis/ diarrhoea (n)	Posaconazole Cmin prior to change to intravenous posaconazole (mg/L)
7 (4 – 11)	4 (1 – 6)	16 (5 – 50)	9 (3 – 20)	17 (8 – 53)	22 (15 – 40)	19.5 (13 – 29)	0.7 (0.2 – 1.6)

• Doses of both oral and intravenous posaconazole were between 300mg – 600mg* total daily dose
*Doses > 500mg given as split doses BD

Pharmacokinetic Model details

- 2 – compartment model
- Covariate effect of mucositis/diarrhoea* on bioavailability



*as per CTCAEV5

Effect of mucositis/diarrhoea on bioavailability

Bioavailability without mucositis/diarrhoea = 71%

Bioavailability with ≥ grade 1 mucositis and/or diarrhoea = 47%

TROUGH

Probability (%) of C_{min} ≥0.5, 0.7 and 1 mg/L on Day 7 of posaconazole administration

Dose Regimen^ ↓	Oral MR Tablets with muc/diar			Oral MR Tablets without muc/diar			Intravenous Administration		
	≥0.5	≥0.7	≥1	≥0.5	≥0.7	≥1	≥0.5	≥0.7	≥1
300mg Q24H	39.1	21.9	4.2	64.5	44.7	17.3	95.1	77.2	55.6
400mg Q24H	57.6	38.4	19.5	81.7	58.9	41.6	98.3	93.1	70.8
500mg Q24H	78.2	48.6	29.7	91.2	76.8	51.8	99.0	97.3	87.2
300mg Q12H	93.3	72.2	44.2	95.4	91.2	72.3	99.7	99.4	97.9
400mg Q12H	96.8	91.1	66.0	97.0	94.9	89.6	99.9	99.6	99.3

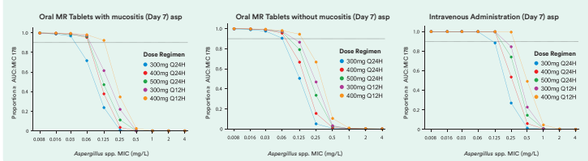
AUC

Probability (%) of AUC_{24} ≥16.1, 21.4 and 29.3 mg.h/L on Day 7 and of posaconazole administration

Dose Regimen^ ↓	Oral MR Tablets with muc/diar			Oral MR Tablets without muc/diar			Intravenous Administration^		
	≥16.1	≥21.4	≥29.3	≥16.1	≥21.4	≥29.3	≥16.1	≥21.4	≥29.3
300mg Q24H	36.1	25.5	7.0	68.5	53.1	23.6	99.7	93.2	66.3
400mg Q24H	58.7	39.6	28.5	85.9	68.7	52.6	99.9	99.7	89.5
500mg Q24H	82.7	50.5	33.3	93.2	80.7	65.0	99.9	99.8	99.5
300mg Q12H	94.0	66.6	39.4	94.8	89.2	70.9	100	99.9	99.9
400mg Q12H	96.8	94.0	62.7	97.0	94.8	87.3	100	100	99.9

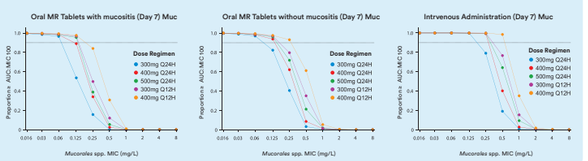
Treatment of *Aspergillus* spp. Infections – probability of target attainment with poscoconzole

Target: AUC/MIC = 178



Treatment of *Mucorales* spp. Infections – probability of target attainment with posaconazole

Target: AUC/MIC = 100



Key Points

1. Many alloHCT patients will require higher doses than the standard 300mg daily with the oral formulation to achieve target exposures. The presence of mucositis and/or diarrhoea makes it more difficult to achieve these exposures.
2. Increased posconazole doses are likely needed for treatment of aspergillus spp. and mucorales spp. Infections.
3. Therapeutic drug monitoring should be done for all alloHCT patients on posaconazole.

Evaluation and Challenges in Adoption of EUCAST Anaerobic Disk Diffusion Antibiotic Susceptibility Testing in an Australian Hospital Microbiology Laboratory

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Aims

To evaluate EUCAST anaerobic disk diffusion antibiotic susceptibility testing (AST) methodology for significant isolates and audit anaerobic susceptibility profiles.

Background

AST is uncommonly performed for anaerobes in clinical microbiology laboratories due to challenges in methodology and perceived predictable susceptibility patterns.(1) Antimicrobial resistance (AMR) in anaerobic bacteria is increasing and routine testing with a standardised method is indicated.(2-3) We evaluated our experience in introducing EUCAST anaerobic susceptibility testing in our laboratory as a cost-effective alternative to reference methods.

Methods

QC methods were applied as defined in the EUCAST v12.0 breakpoint table to *Clostridium perfringens* ATCC 13124, *C. perfringens* DSM 25589 anaerobiosis control, and *Bacteroides fragilis* ATCC 13124 isolates with stock laboratory organisms and newly ordered controls. Repeated testing was performed with sequential Fastidious Anaerobe Agar (FAA) with 5% defibrinated horse blood batches (Edwards Group, Queensland) and antibiotic disks (Thermo Fisher Scientific, Victoria). After incubation in an anaerobic atmosphere maintained with an Axonomat Workstation (Don Whitely Scientific, West Yorkshire, UK) at 37 degrees for 18± 2 hours incubation plates were read by 2 independent observers. Cumulative data were assessed against defined EUCAST quality control (QC) ranges for antibiotics and target mean zone diameters. Included antimicrobial disks were benzylpenicillin 1 unit, piperacillin/tazobactam 30/6µg, meropenem 10µg, vancomycin 5µg, clindamycin 2µg and metronidazole 5µg.

A review of all isolate susceptibility tests from significant sites (sterile tissue and blood cultures) between January 2023 and December 2024 was performed with the addition of amoxicillin/clavulanate AST with the advent of EUCAST v13.1 breakpoints.

Results

QC verification with 66 observations of B. fragilis ATCC 25285 demonstrated clindamycin consistently outside of acceptable QC ranges (mean 28mm, SD 1.86, Target 26±1mm) with manufacturer discussions prompting media production modification. 19.7% of clindamycin and 4.54% of meropenem individual observations fell outside the acceptable ranges for individual results. Observations (n=26) with the new FAA formulation testing yielded acceptable clindamycin QC results (mean 26.23mm, p= <0.0001) with no individual antibiotic observations falling outside the acceptable QC range for a single test.

Laboratory stock *C. perfringens* ATCC 13124 QC metrics on 74 observations with the original FAA demonstrated mean diameter deviations of >1mm for meropenem (35.94mm, target 37mm), metronidazole (24.04mm, target 23mm) and clindamycin (19.12mm, target 23).

28 observations with the stock organism and revised FAA demonstrated appropriate individual and mean QC metrics for all antibiotics except clindamycin. This remained outside of acceptable range (mean 18.46mm, SD 0.79, target 23±1mm) with 96% of individual observations falling outside the acceptable range of 20-26mm. Repeated testing with newly ordered control organism on the revised FAA media demonstrated acceptable clindamycin QC results (mean 23.21mm, p=<0.0001).

Sufficient anaerobiosis was maintained for each experiment with *C. perfringens* DSM 25589 observations (n=56) meeting the defined cut off of ≥25mm.

Audit of AST results for 287 isolates after implementation demonstrated a predominance of *Cutibacterium acnes* (n=161), *Bacteroides* spp. (n=61) and *C. perfringens* (n=38) (Table 1). Low rates of penicillin (8.3%) and amoxicillin/clavulanate (16.7%) susceptibility were seen in *Prevotella* spp. Low rates of meropenem susceptibility were seen in *Bacteroides* spp. (75%) and *Fusobacterium necrophorum* (66.7%). Subjective reports from observers found determination of large zone diameters challenging particularly for meropenem and piperacillin/tazobactam with fine growth of some isolates.

Discussion

Revised FAA media and new QC organisms confirmed EUCAST anaerobic AST QC criteria could be met with minimal observations falling outside acceptable ranges for individual test quality assurance.

The changes seen when comparing a preexisting laboratory stock of *C. perfringens* ATCC 13124 with a fresh control are concerning for an acquired resistance mechanism. This highlights the importance of storage, traceability and training of staff using QC organisms.

Results highlight the role that media production plays in accurate and reproducible disk diffusion methods with changes in mean antibiotic zone diameters, particularly with clindamycin, when changing to the revised FAA formulation. The nature of this change remains undisclosed but changes in agar density, preservatives, pH, additives and thickness may affect antibiotic diffusion and microbial growth. (4)

Other studies performed by EUCAST found similar concerns with interpretation of meropenem and piperacillin/tazobactam with recommendations for second opinions when unclear. (4,5)

FIGURE 1: EUCAST disk diffusion *C. perfringens 13124*

Figure 1: Disk diffusion with ECUAST methods performed on ATCC control strain C. perfringens 13124. Note the large zone diameters surrounding MEM (meropenem) and TZP (piperacillin/tazobactam) that can be challenging to interpret.

Audit of AST results showed unexpectedly high numbers of isolates resistant to meropenem and piperacillin/tazobactam. For *Prevotella* and F*usobacterium* species, low included numbers included make it challenging to draw conclusions.

Global carbapenem resistance in *Bacteroides* spp. varies between 1% and 30% globally. Carbapenem resistance in *B. fragilis* may be associated with *cfi*A metallo-β-lactamase genes and may be able to be detected with hydrolysis based carbapenemase testing, for example the Carba NP test. (6,7) This may be a simple method to determine the mechanism of carbapenem resistance. In Carba NP negative isolates, reference method confirmation of resistance or molecular analysis for *cfi*A or other molecular mechanisms, including efflux pumps, may prove useful to ensure result accuracy.

Prevotella spp. had low susceptibility to amoxicillin/clavulanate with all isolates remaining susceptible to piperacillin/tazobactam. Rising MICs to amoxicillin/clavulanate have been demonstrated in other studies despite the majority of isolates remaining susceptible, our data warrants further evaluation. (8)

Conclusions

EUCAST disk diffusion anaerobic AST needs careful attention to QC including media and controls. Variable susceptibility results, especially in infrequently isolated organisms suggests a benefit for establishing an external quality assurance program. Development of an antibiogram may help rationalise testing for reliably susceptible antimicrobials in select organisms and inform clinical practice.

Table 1. Isolate susceptibilities by EUCAST anaerobic disk diffusion method in sterile specimens 2023-2024

Organism (n)	Penicillin		Amoxicillin/Clavulanate		Clindamycin		Meropenem		Metronidazole		Piperacillin/Tazobactam		Vancomycin	
	Sensitive (%)	Count	Sensitive (%)	Count	Sensitive (%)	Count	Sensitive (%)	Count	Sensitive (%)	Count	Sensitive (%)	Count	Sensitive (%)	Count
Bacteroides spp. (61)			**75.4**	57	**73.8**	61	**75**	60	**98.4**	61	**85.7**	21		
Prevotella spp. (12)	**8.3**	12	**16.7**	12	**50**	12	**91.70**	12	**91.70%**	12	**100**	3		
F. necrophorum (5)	**80**	5	**100**	4	**80**	5	**66.70**	6	**100%**	4	**66.70**	3		
C. perfringens (38)	**100**	10	**97.4**	38	**48.60**	37	**100**	38	**100%**	38	**100%**	38	**100**	38
C. acnes (171)	**97.70**	171	**95.20%**	168	**93.50**	170	**93.50**	170					**97.1**	171

Count: number of isolates tested against antibiotic

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PUB-0293 v3

To use POETRY as a health promotion strategy to engage hospital staff in learning and reflecting on the threat of antimicrobial resistance in a fun and innovative way!

BACKGROUND

Creative words, both bold and grand,
Help messages take a strong stand.
For health they convey,
In a poetic way,
To raise awareness throughout the land!

ACTION

In November '23, a contest took flight,
At Concord, for poems to write.
On resistance's harm,
And stewardship's charm,
Staff rhymed with all of their might!

To boost antimicrobial awareness this year,
A limerick challenge brought cheer.
With posters galore,
And word spreading more,
Staff penned verses both witty and clear!

THE TORTURED ANTIMICROBIAL DEPARTMENT

POETRY AS AN EFFECTIVE HEALTH PROMOTION STRATEGY

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OUTCOMES

Forty limericks penned with zest,
Anaesthetists wrote up the best.
Then residents came,
Consultants by name,
While pharmacists joined with the rest.

Through verses, important themes came to light,
As staff shared their thoughts and insights.
Hands don't stay clean,
Bugs reign supreme,
Infections become much harder to fight

Broad-spectrums prescribed out of fear,
By physicians who hold them too dear.
Anxiety high,
They reach for supply,
When narrower choices are clear.

READ OUR LIMERICK ENTRIES HERE!

DISCUSSION

The limerick contest brought delight,
Proving poetry's power to ignite.
With staff engaged,
Creative minds staged,
Our health promotion took artistic heights

The contest brought themes into view,
Helping stewards find focus anew.
For AMS goals clear,
They'll plan for next year,
To guide AMS efforts right through!

ChinYen.Yeo@health.nsw.gov.au @chinyenyeo

NSW Health Sydney Local Health District | CASI

AGAR POSTERS

The Australian Group on Antimicrobial Resistance (AGAR)

Australian *Staphylococcus aureus* Surveillance Outcome Program (ASSOP) 2023

Australian Enterococcus Surveillance Outcome Program (AESOP) 2023

Report from the Gram-negative Surveillance Outcome Program (GnSOP) 2014 – 2023

Report from the Gram-negative Surveillance Outcome Program (GnSOP) 2023 Susceptibility Data

Report from the Gram-negative Surveillance Outcome Program (GnSOP) 2023 Clinical Outcomes

National Alert System for Critical Antimicrobial Resistances | What is happening in Australia?

Australian Passive AMR Surveillance | Trends in multidrug-resistant organisms in Australia

The Australian Group on Antimicrobial Resistance (AGAR) Australian *Staphylococcus aureus* Surveillance Outcome Program (ASSOP) 2023

D. A. Daley[1,2], G. W. Coombs[1,2,3] P. Shoby[3], S. Mamoottil Sudeep[3], and S. Mowlaboccus[1,2,3]
on behalf of the Australian Group on Antimicrobial Resistance
[1]The Australian Group on Antimicrobial Resistance, Fiona Stanley Hospital, WA, [2]Department of Microbiology, PathWest Laboratory Medicine, Fiona Stanley Hospital, WA, [3]Antimicrobial Resistance and Infectious Diseases Laboratory (AMRID), Murdoch University, WA

INTRODUCTION

In 2023, 33 institutions across Australia servicing 57 hospitals participated in the AGAR Australian *Staphylococcus aureus* Surveillance Outcome Program (ASSOP). The primary objective of ASSOP 2023 was to determine the proportion of *S. aureus* bacteraemia (SAB) isolates in Australia that exhibited antimicrobial resistance, with particular emphasis on susceptibility to methicillin, and to characterize the molecular epidemiology of the methicillin-resistant *S. aureus* (MRSA).

METHODS

Isolates

From 1 January to 31 December 2023 the 33 participating laboratories collected all *S. aureus* isolated from blood cultures (excluding duplicates within a 14-day period). Data were collected on age, sex, date of admission and discharge and mortality at 7 and 30 days post blood culture collection.

Susceptibility testing

Isolates were identified by the participating laboratories and antimicrobial susceptibility testing was performed using the Vitek® 2 (bioMérieux, France) or the BD Phoenix™ (Becton Dickinson, USA) automated microbiology systems. European Committee on Antimicrobial Susceptibility Testing (EUCAST) breakpoints (2024) were utilised for interpretation.

Whole genome sequencing

Whole genome sequencing (WGS) was performed on MRSA isolates at the AMRID laboratory, Murdoch University, WA.

RESULTS

- 3,422 unique episodes of SAB were identified.
- The mean patient age was 58 years. 66.0% of patients were male.
- 77.0% of episodes were community-onset.
- All-cause mortality at 30 days was 16.2% (95%CI 14.7-17.8). There were no significant differences in mortality between hospital-onset and community-onset SAB (17.4% and 15.9% respectively) (P = 0.36) or between MRSA and methicillin-susceptible *S. aureus* (MSSA) bacteraemia (14.8% and 16.5% respectively) (P = 0.44).
- Osteomyelitis/septic arthritis (20.6%) and skin/skin structure infection (19.2%) were the most common principal clinical manifestations.

MSSA

- With the exception of the β-lactams and erythromycin, antimicrobial resistance in MSSA was rare (Table 1).
- Three MSSA were resistant to teicoplanin.
- Three MSSA were resistant to daptomycin. One from Tasmania with a daptomycin MIC of 1.5 mg/L was ST9295 and carried the L341I MprF mutation, one from NSW with a daptomycin MIC of 3.0 mg/L was ST97 and carried the L776S MprF mutation and one from WA with a daptomycin MIC of 2.0 mg/L was ST5. No mutations in known loci were detected in the WA isolate.
- Resistance was not detected for linezolid or vancomycin.

MRSA

- 16.1% (550) *S. aureus* were methicillin resistant. Comparison with EARS-Net and WHO CAESAR data is shown in Figure 1.
- Two MRSA were resistant to teicoplanin (Table 1). Two MRSA were resistant to daptomycin, both from NSW with daptomycin MICs of 3 and 4 mg/L. One was ST22-IV carrying the V351E MprF mutation and the other ST45-V carrying the T345I MprF mutation. Resistance was not detected for linezolid or vancomycin.
- 491 (89.3%) MRSA were available for typing by WGS. Overall 15.1% and 84.9% were classified as healthcare-associated (HA) and community-associated (CA) clones respectively (Figure 2). 67.6% and 76.5% of HA-MRSA and CA-MRSA respectively were community-onset.
- Three HA-MRSA clones were identified, ST22-IV [2B] (EMRSA-15), ST239-III [3A] (Aus-2/3 EMRSA) and ST9276-III (Figure 3).
- Although polyclonal (84 clones), 70.3% of CA-MRSA clones were classified into nine major sequence types (ST) each with >10 isolates: ST93-IV, ST5-IV, ST1-IV, ST45-V, ST30-IV, ST8-IV, ST6-IV, ST97-IV and ST953-IV (Figure 4).
- Overall 191 (45.8%) of MRSA were PVL positive, all of which were CA-MRSA.

RESULTS (continued)

Table 1. *Staphylococcus aureus* susceptibility data, EUCAST, 2023

	Methicillin-susceptible			Methicillin-resistant		
Antimicrobial	No.	% S-IE	% R	No.	% S-IE	% R
Benzylpenicillin*	2,819	–†	76.8	549	–†	100.0
Ciprofloxacin	2,855	97.1	2.9	546	67.2	32.8
Clindamycin§	2,854	0.0	12.8	546	0.0	24.9
Daptomycin	2,862		0.3	550	0.0	0.4
Erythromycin	2,828	–†	15.6	539	–†	30.2
Fusidic acid	2,828		2.5	538		4.1
Gentamicin	2,841	–†	4.5	542	–†	13.3
Mupirocin (high-level)	2,018	–†	1.7	354	–†	3.4
Rifampicin	2,851	–#	0.4	545	–#	1.1
Teicoplanin	2,861		0.1	550		0.2
Tetra/doxycycline	2,851	–†	3.2	546	–†	13.5
Trimethoprim–sulfa	2,839	0.1	0.4	540	0.2	3.1

No. = number of isolates; R = resistant; S-IE = susceptible, increased exposure
* = β-lactamase adjusted; † = no category defined; § = constitutive + inducible; # = rifampicin concentration range on some cards restricts category interpretation

Figure 1. Methicillin-resistant *Staphylococcus aureus*, international comparisons, WHO European region and Australia, 2023

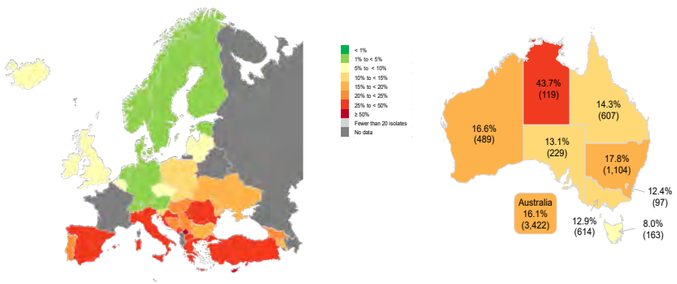


Figure 2. HA- and CA-associated MRSA clones, by state and territory, 2023

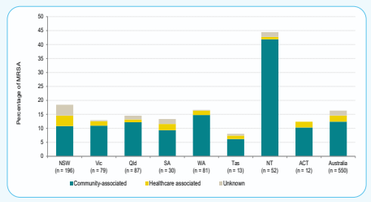


Figure 3. HA-associated MRSA, by state and territory, 2023

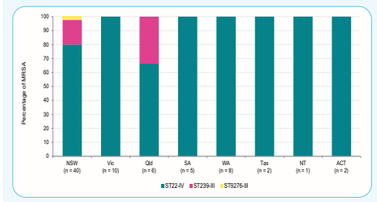
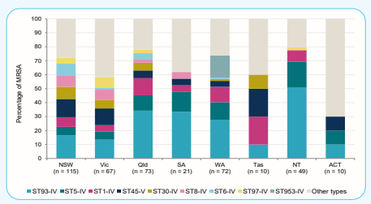


Figure 4. CA-associated MRSA, by state and territory, 20223



CONCLUSIONS

- ASSOP 2023 has demonstrated antimicrobial resistance in SAB in Australia remains a significant problem and is associated with a high mortality. This may be due, in part, to the high prevalence of methicillin-resistant SAB in Australia.
- MRSA must remain a public health priority and continuous surveillance of SAB and its outcomes and the implementation of comprehensive MRSA strategies targeting hospitals and long-term care facilities are essential.

Acknowledgements

We wish to thank the staff of the AGAR laboratories for the collection of data and isolates.

The AGAR Surveillance Outcome Programs are funded by the Australian Government Department of Health and Aged Care.

AUSTRALIAN GROUP on ANTIMICROBIAL RESISTANCE

Murdoch University

The Australian Group on Antimicrobial Resistance (AGAR) Australian *Enterococcus* Surveillance Outcome Program (AESOP) 2023

D. A. Daley[1,2], G. W. Coombs[1,2,3] P. Shoby[3], A. Form[3], and S. Mowlaboccus[1,2,3] on behalf of the Australian Group on Antimicrobial Resistance

[1]The Australian Group on Antimicrobial Resistance, Fiona Stanley Hospital, WA, [2]Department of Microbiology, PathWest Laboratory Medicine, Fiona Stanley Hospital, WA, [3]Antimicrobial Resistance and Infectious Diseases Laboratory (AMRID), Murdoch University, WA

INTRODUCTION

In 2023, 32 institutions servicing 56 hospitals across Australia participated in the AGAR Australian *Enterococcus* Surveillance Outcome Program (AESOP). The objective of AESOP 2023 was to determine the proportion of enterococcal bacteraemia isolates in Australia that exhibited antimicrobial resistance in particular to ampicillin and glycopeptides, and to characterize the molecular epidemiology of the *E. faecium* isolates.

METHODS

Isolates

From 1 January to 31 December 2023 participating laboratories collected all enterococci isolated from blood cultures (excluding duplicates within a 14-day period). Data were collected on age, sex, date of admission and discharge, clinical manifestation and mortality at 7 and 30 days post blood culture collection.

Susceptibility testing

Isolates were identified by the participating laboratories and antimicrobial susceptibility testing was performed using the Vitek® 2 (bioMérieux, France) or the BD Phoenix™ (Becton Dickinson, USA) automated microbiology systems. EUCAST breakpoints (2024) were utilised for interpretation.

Whole genome sequencing

Whole genome sequencing (WGS) was performed on *E. faecium* isolates by the AMRID laboratory at Murdoch University, WA. The multilocus sequence type (ST) was determined using the PubMLST website and *van* genes were identified using nucleotide sequences from the NCBI database and a BLAST interface.

RESULTS

- 1,599 episodes of enterococcal bacteraemia were identified with 92.9% of episodes caused by *E. faecalis* (828, 51.8%) or *E. faecium* (657, 41.1%).
- Other enterococcal species included *E. lactis* (*n* = 35), *E. gallinarum* (28), *E. casseliflavus* (25), *E. avium* (10), *E. raffinosus* (6), *E. durans* (5) *E. hirae* (2), and one each of *E. cecorum, E. gilvus* and *E. mundtii* (Figure 1).
- The mean patient age was 63 years, 65.0% of patients were male.
- 67.3% of *E. faecalis* and 26.6% of *E. faecium* were community-onset. The most common principal clinical manifestation was urinary tract infection in *E. faecalis* (21.8%) and intra-abdominal infection (other than biliary tract) in *E. faecium* (17.7%).
- All-cause mortality at 30 days was 20.4% (95% CI 18.1-23.0). There was a significant difference in mortality between *E. faecalis* and *E. faecium* episodes (17.0% vs 26.3%, p<0.01). There was no significant difference between vancomycin susceptible and vancomycin resistant *E. faecium* episodes (23.6% vs 28.7%, *P* = 0.18) respectively.

E. faecalis

- No ampicillin, daptomycin, vancomycin or teicoplanin resistance was seen.
- 12.2% of *E. faecalis* were high-level gentamicin resistant.
- Two *E. faecalis* were resistant to linezolid. Both isolates from Victoria harboured the *optrA* gene, had linezolid MICs of 6 mg/L and were vancomycin susceptible. One isolate was identified as ST16, the other ST86.

RESULTS (continued)

Figure 1. Enterococcal species, 2023

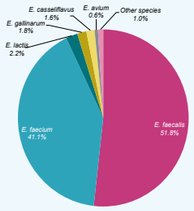


Figure 3. *Enterococcus faecium* sequence types, 2023

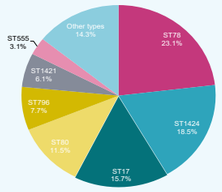


Figure 2. Vancomycin-resistant *Enterococcus faecium*, WHO European region and Australia, 2023

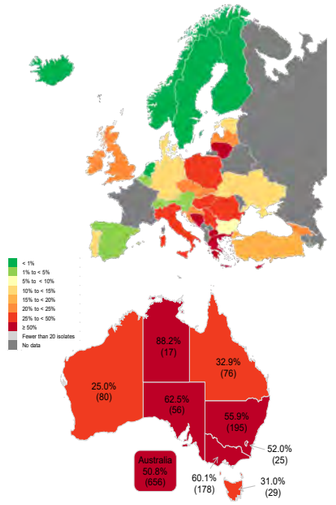


Figure 4. *Enterococcus faecium* sequence types, by state and territory, 2023

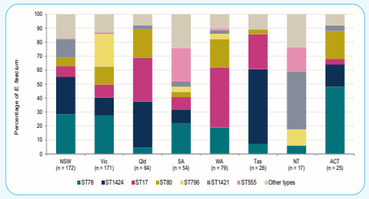
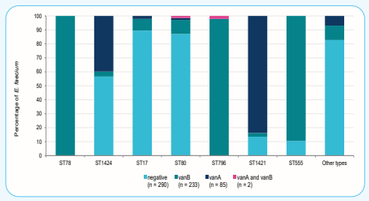


Figure 5. *van* genes in *Enteroccus faecium* sequence types, 2023



E. faecium

- In 2023, 94.2% of *E. faecium* were ampicillin resistant, 12.7% teicoplanin resistant and 50.8% vancomycin resistant. No significant changes in resistance were observed between 2022 and 2023, however trends for past five years (2019–2023) show increases in vancomycin but decreases in teicoplanin.
- Australia's rate of vancomycin resistance ranks in the top quarter when compared to the EARS-Net program and the WHO CAESAR network (Figure 2).
- No daptomycin or linezolid resistance was seen.
- 610/657 (92.8%) of *E. faecium* were available for typing by WGS.
- 58 STs were identified with 85.7% characterised into seven major STs (>10 isolates): ST78, ST1424, ST17, ST80, ST796, ST1421 and ST555 (Figures 3 and 4). There were 37 STs with a single isolate.
- 53.2% of *E. faecium* harboured *van* genes; 38.3% *vanB*, 14.6% *vanA* and 0.3% *vanA* and *vanB*. Distribution of *van* genes by sequence type are seen in Figure 5.

CONCLUSIONS

- The AESOP 2023 study has shown although predominately caused by *E. faecalis*, enterococcal bacteraemia in Australia is frequently caused by ampicillin-resistant high-level gentamicin-resistant *E. faecium*.
- The *vanB* operon was historically the dominant genotype, although there was a steady increase in *vanA* from 2013 to 2018 when *vanA* predominated. In AESOP 2023 the *vanB* genotype was the most dominant.
- In addition to being a significant cause of healthcare-associated bacteraemia, the emergence of multiple multi-resistant hospital-adapted *E. faecium* strains has become a major infection control issue in Australian hospitals.
- Further studies of the enterococcal genome will contribute to our understanding of the rapid and ongoing evolution of enterococci in the hospital environment and assist in preventing their nosocomial transmission.

Acknowledgements

We wish to thank the staff of the AGAR laboratories for the collection of data and isolates.

The AGAR Surveillance Outcome Programs are funded by the Australian Government Department of Health and Aged Care.

AUSTRALIAN GROUP on ANTIMICROBIAL RESISTANCE

Murdoch University

The Australian Group on Antimicrobial Resistance Report from the Gram-negative Surveillance Outcome Program (GnSOP) 2014–2023

Jan Bell[1], Thomas Gottlieb[2,3] and Jonathan Iredell[3,4,5] for the Australian Group on Antimicrobial Resistance

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INTRODUCTION

In 2013, AGAR began the ongoing *Enterobacterales* Sepsis Outcome Program. In 2015, *Pseudomonas aeruginosa* and *Acinetobacter* species were added, and the program evolved into the Gram-negative Surveillance Outcome Program (GnSOP).

The aim of GnSOP is to monitor antimicrobial resistance (AMR), and to detect critical emerging AMR in Gram-negative isolates from patients with documented bacteraemia.

METHODS

- Participating laboratories servicing hospitals from all States and mainland Territories of Australia, collected either all or up to 200 isolates from different patient bacteraemia episodes. Species were identified using the routine method for each laboratory. MICs were determined using commercial systems Vitek® 2 (BioMérieux) or Phoenix™ (BD). The results were analysed using EUCAST breakpoints (January 2024).
- The number of institutions included increased from 27 in 2013 to 45 in 2015 and 57 in 2023. In addition, the relative distribution of sites has changed. Paediatric and/or facilities providing specialist obstetric services increased from three (2013), to six (2017), and eight since 2022. Hospitals from north-west regional Western Australia were included from 2015.

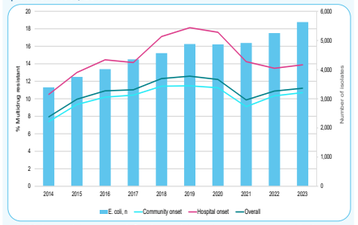
RESULTS

- Since 2013, 80,947 *Enterobacterales* have been studied, along with 6,753 *P. aeruginosa* and 995 *Acinetobacter* spp. since 2015.
- Overall rates of resistance to key antimicrobial agents over the period 2014-2023 are shown in Figure 1 for *Escherichia coli* and in Figure 2 for *Klebsiella pneumoniae* complex.
- The frequency of multidrug resistant (MDR) *E. coli* varied from 7.9% (2014), 12.6% (2019), 9.9% (2021), to 11.2% in 2023 (Figure 3). For *E. coli* isolates that were hospital-onset (collected > 48-h after admission), the rate of MDR remained steady at 14% since 2021.
- For the *K. pneumoniae* complex, the frequency of MDR decreased from 5.6% in 2019 to 2.5% in 2023.
- Between 2014-2021, 50.0%-70.6% of all CPE carried a bla_{IMP-4} gene, and 14.3%-33.3% carried a bla_{NDM} and/or bla_{OXA-48}-like gene(s). In 2023, three-quarters (22/30, 73.3%) of CPE carried a bla_{NDM} and/or bla_{OXA-48}-like gene(s) and 26.7% (n = 8) carried a bla_{IMP-4} gene (Figure 4).

RESULTS (continued)

- From 2019–2023, in Victoria, there were significantly decreasing trends (*P* < 0.01) in resistance to ciprofloxacin, third generation cephalosporins and aminoglycosides in *E. coli* and *K. pneumoniae* complex isolates (Figure 5).
- There were increasing trends in resistance to third generation cephalosporins in *E. coli* in the Northern Territory and Queensland, and decreasing trends in resistance to aminoglycosides in Tasmania. In *K. pneumoniae* complex isolates, there were decreasing trends in resistance to ciprofloxacin in South Australia and aminoglycosides in New South Wales and Tasmania.

Figure 3. 10-year trend in mutlidrug-resistant *Escherichia coli*, by place of onset, 2014–2023



1. Multi-drug resistance was defined as resistance to one or more agent in three or more antimicrobial categories.
2. Antimicrobial categories (agents) were aminoglycosides (gentamicin and/or tobramycin), carbapenems (meropenem), extended-spectrum cephalosporins (ceftriaxone and/or ceftazidime), fluoroquinolones (ciprofloxacin), and penicillins (ampicillin).

Figure 4. Carbapenemase genes detected among *Enterobacterales*, 2014–2023

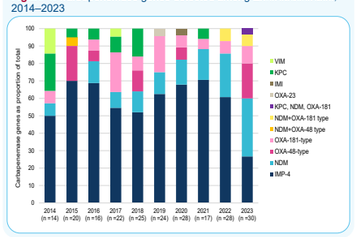


Figure 1. *Escherichia coli*, resistance to key antimicrobials, 2014–2023

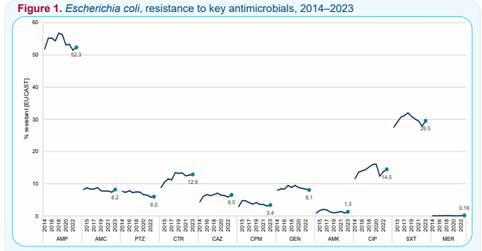
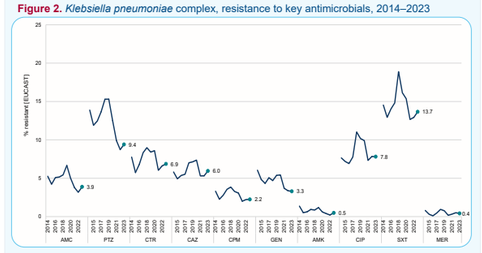


Figure 2. *Klebsiella pneumoniae* complex, resistance to key antimicrobials, 2014–2023

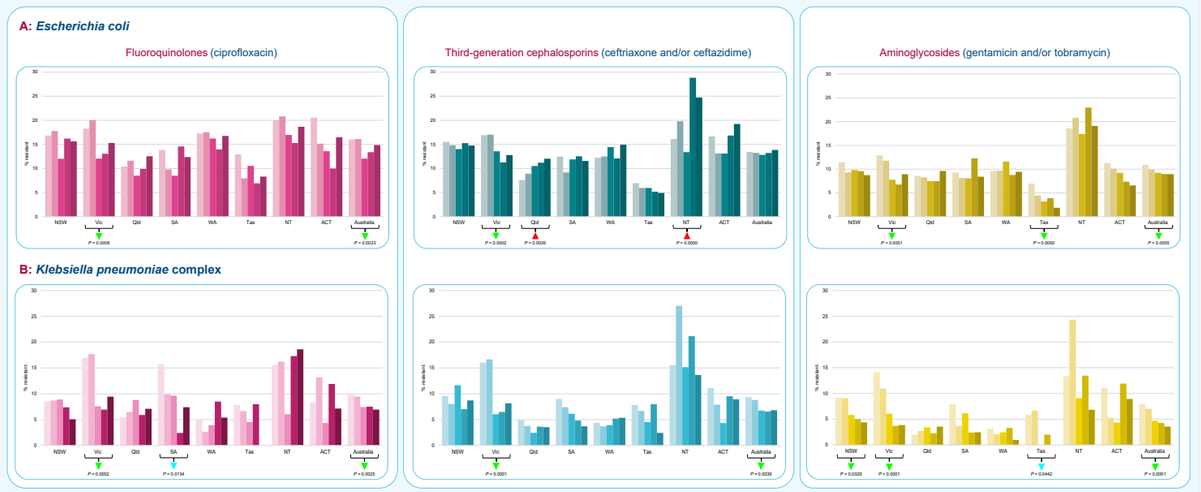


AMC = amoxicillin–clavulanate (2:1 ratio); AMK = amikacin; AMP = ampicillin; CAZ = ceftazidime; CIP = ciprofloxacin; CPM = cefepime; CTR = ceftriaxone; GEN = gentamicin; MER = meropenem; PTZ = piperacillin–tazobactam; SXT = trimethoprim-sulfamethoxazole

CONCLUSIONS

- AGAR data show different longitudinal trends in *E. coli* resistance to key anti-gram-negative antimicrobial agents, such as ceftriaxone and ciprofloxacin, by state and territory.
- There has been a notable change in the proportion of carbapenemase gene types, likely reflecting increases in international travel from 2022
- AGAR surveillance remains core to Australia's response to informing the national response to AMR.

Figure 5. Resistance (%) to fluoroquinolones, third-generation cephalosporins and aminoglycosides, *Escherichia coli* (A) and *Klebsiella pneumoniae* complex (B), by state and territory, 2019–2023



Chi-square test for trend for past five years (2019-2023); significant decrease ▼ *P* <0.01, ▼ 0.01 < *P* <0.05
Notes: 1. Percentage resistance determined using EUCAST 2024 breakpoints for all years. 2. Data only from hospitals consistently reporting for all five years were included.

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Acknowledgements

We wish to thank the staff of the AGAR laboratories throughout Australia for the collection of data and isolates.

The AGAR Surveillance Outcome Programs are funded by the Australian Government Department of Health and Aged Care.

The Australian Group on Antimicrobial Resistance Report from the Gram-negative Surveillance Outcome Program (GnSOP) 2023 – Susceptibility Data

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INTRODUCTION

The Australian Group on Antimicrobial Resistance (AGAR) Gram-negative Surveillance Outcome Programme (GnSOP) focuses on the collection of resistance and demographic data on *Enterobacterales*, *Pseudomonas aeruginosa* and *Acinetobacter* species isolated from patients with bacteraemia.

METHODS

Isolates

From 1 January to 31 December 2023, 33 laboratories servicing 57 participating hospitals across Australia collected either all or up to 200 isolates (*Enterobacterales*, *P. aeruginosa* or *Acinetobacter* spp.) from different patient episodes of bacteraemia. Isolates were identified using the routine method for each laboratory.

Susceptibility testing

MICs were determined using Vitek® 2 (BioMérieux) or Phoenix™ (BD). The results were analysed using EUCAST breakpoints (January 2024). *E. coli*, *Klebsiella* spp., *Proteus* spp. and *Salmonella* spp. with ceftazidime or ceftriaxone MIC > 1 mg/L, or cefoxitin MIC > 8 mg/L, any other *Enterobacterales* with cefepime MIC > 1 mg/L, *Salmonella* spp. with ciprofloxacin MIC > 0.25 mg/L, all isolates with meropenem MIC > 0.125 mg/L, all isolates with amikacin MIC > 32 mg/L, and all isolates with colistin MIC > 4 mg/L were referred for whole genome sequencing (WGS).

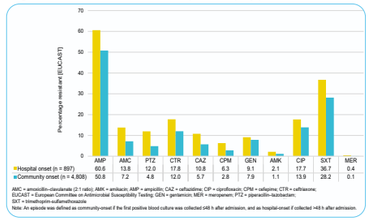
Whole genome sequencing

WGS was performed on all referred isolates using Illumina platforms. Data were analysed using a modified version of the Nullarbor bioinformatic pipeline.

RESULTS

- In 2023, of 10,453 gram-negative isolates, four genera (*Escherichia,* 54.6%; *Klebsiella,* 18.4%; *Pseudomonas,* 7.7%; *Enterobacter*, 5.4%), accounted for 86.1%.
- For *E. coli*, there was a slight increase in resistance to trimethoprim-sulfamethoxazole (1.7 percentage points [pp]) and ciprofloxacin (0.8 pp) compared to 2022.
- Ciprofloxacin resistance rates in 2023 were 14.5% overall for *E. coli*, 17.7% for hospital-onset (HO) and 13.9% for community-onset (CO), and for *K. pneumoniae* complex 7.8% overall, 10.3% HO and 6.9% CO (Figure 1).

Figure 1. *Escherichia coli* resistance (EUCAST), by place of onset, 2023



- In 2023, 15.2% (HO, 21.6%; CO, 14.1%) of *E. coli* isolates and 8.5% (HO, 12.4%; CO, 7.1%) of *K. pneumoniae* complex isolates had an extended-spectrum β-lactamase (ESBL) phenotype. The proportion of ESBLs by state and territory and place of onset is shown in Figure 2.
- Among these *E. coli* isolates, there was an increase in the proportion of $bla_{\text{CTX-M-27}}$ and a decrease in $bla_{\text{CTX-M-14}}$ compared to 2022.
- Of 753 *E. coli* isolates with confirmed β-lactamase gene(s), 609 (80.9%) had $bla_{\text{CTX-M}}$ gene(s), mostly $bla_{\text{CTX-M-27}}$ (*n* = 271), or $bla_{\text{CTX-M-15}}$ (*n* = 268). $bla_{\text{CTX-M-15}}$ genes were dominant in SA, WA, and the ACT. $bla_{\text{CTX-M-27}}$ genes were more prevalent in NSW, Qld, and the NT.
- Among *K. pneumoniae* complex isolates with confirmed β-lactamase gene(s), 78 of 97 (80.4%) contained a $bla_{\text{CTX-M}}$ gene, predominantly $bla_{\text{CTX-M-15}}$ (*n* = 65, 82.1%).
- The β-lactamase genes detected in *Enterobacterales* with an ESBL phenotype are shown in Figure 3.
- Comparison of *E. coli* and *K. pneumoniae* resistance rates to key antimicrobial groups in Australia and the WHO European region countries are shown in Figure 4.
- Overall, 33 (0.3%) isolates from 33 patients harboured a carbapenemase gene (Table 1). The prevalence of carbapenemase genes among *Enterobacterales* was 0.3% (29/8,773).
- Three-quarters (19/30, 63.3%) of *Enterobacterales* with MIC > 2 mg/L harboured carbapenemase gene(s). Two *Enterobacterales* with a $bla_{\text{OXA-48}}$-like gene had meropenem MICs of ≤ 0.125 and ≤ 0.25 mg/L.

RESULTS (continued)

Figure 2. Proportion of *Escherichia coli* and *Klebsiella pneumoniae* with extended-spectrum β-lactamase phenotype, by state and territory, 2023

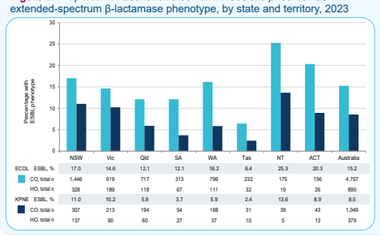


Figure 3. β-lactamase genes detected in *Enterobacterales* with extended-spectrum β-lactamase phenotype, 2023

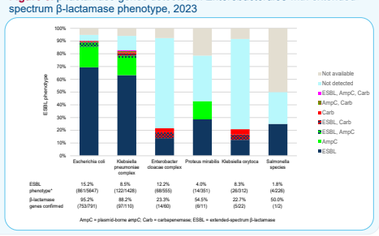
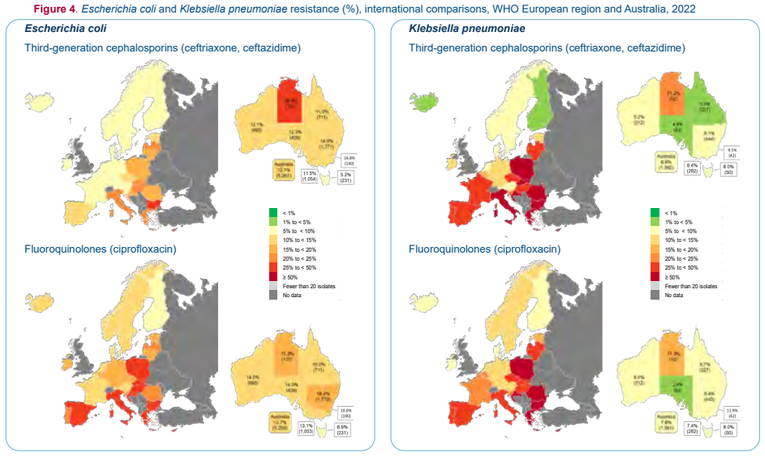


Figure 4. *Escherichia coli* and *Klebsiella pneumoniae* resistance (%), international comparisons, WHO European region and Australia, 2022



- A carbapenemase gene was found in 1/16 (6.3%) meropenem-resistant (MIC > 8 mg/L) *P. aeruginosa* and in the only meropenem-resistant (0.8%) *Acinetobacter* isolate.

Acknowledgements

We wish to thank the staff of the AGAR laboratories for the collection of data and isolates.

The AGAR Surveillance Outcome Programs are funded by the Australian Government Department of Health and Aged Care.

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CONCLUSIONS

- Compared with European countries, Australia ranks towards the middle in rates of resistance to third-generation cephalosporins in *E. coli*, but in the bottom quarter in rates of resistance to fluoroquinolones. In *K. pneumoniae* complex isolates, resistance to both fluoroquinolones and third-generation cephalosporins is low (<10.0%).
- Carbapenem resistance attributable to acquired carbapenemase genes is still uncommon in patients with bacteraemia in Australia.

Table 1. Number of carbapenemase and associated resistance genes, by species, and state and territory, 2023

Gene	S/T	Species	ST	MIC	ESBL/pAmpC	PMQR gene†	RMT	MCR
$bla_{\text{IMP-4}}$ (*n* = 8)	NSW	*E. hormaechei*	168	≥ 16	–§	–§	–§	–§
	NSW	*E. hormaechei*	78	≥ 16	$bla_{\text{VEB-3}}$	*aac(6')-Ib-cr, qnrS1*	–§	–§
	NSW	*E. hormaechei*	133	-	$bla_{\text{VEB-3}}$, $bla_{\text{CTX-M-15}}$	*aac(6')-Ib-cr*	–§	–§
	NSW	*C. braakii*	356	≥ 16	$bla_{\text{CTX-M-15}}$	*qnrB2*	–§	–§
	NSW	*E. coli*	6958	≥ 16	–§	–§	–§	–§
	NSW	*S. marcescens*	–§	> 8	–§	*qnrB2*	–§	–§
	Qld	*E. coli*	58	≥ 16	–§	–§	–§	–§
	ACT	*K. oxytoca*	323	≥ 16	–§	*qnrB2*	–§	–§
$bla_{\text{OXA-48}}$ (*n* = 2)	NSW	*E. coli*	224	0.5	–§	*qepA4*	–§	–§
	NSW	*E. coli*	131	≤ 0.125	$bla_{\text{CTX-M-27}}$	*qnrB4*	–§	–§
$bla_{\text{OXA-244}}$ (*n* = 4)	NSW	*E. coli*	–§	0.25	–§	–§	–§	–§
	NSW	*E. coli*	131	0.5	$bla_{\text{CTX-M-15}}$	–§	–§	–§
	Vic	*E. coli*	38	≤ 0.125	$bla_{\text{CTX-M-27}}$	–§	–§	–§
	WA	*E. coli*	38	2	$bla_{\text{CTX-M-27}}$	–§	–§	–§
$bla_{\text{OXA-181}}$ (*n* = 1)	ACT	*K. aerogenes*	4	≥ 16	$bla_{\text{CTX-M-15}}$	*aac(6')-Ib-cr, qnrS1*	–§	–§
$bla_{\text{OXA-232}}$ (*n* = 1)	ACT	*K. pneumoniae*	6092	1	$bla_{\text{CTX-M-14}}$	*qnrB4, qnrS1*	–§	–§
$bla_{\text{OXA-484}}$ (*n* = 1)	ACT	*E. coli*	410	0.5	–§	*qnrS1*	–§	–§
$bla_{\text{NDM-1}}$ (*n* = 4)	Vic	*E. hormaechei*	1015	≥ 16	$bla_{\text{SHV-12}}$	*aac(6')-Ib-cr, qnrA1*	–§	*mcr-9.1*
	Vic	*E. hormaechei*	269	≥ 16	–§	*qnrS1*	–§	–§
	Old	*K. variicola*	1563	≥ 16	–§	*aac(6')-Ib-cr, qnrB4*	–§	–§
	WA	*K. pneumoniae*	307	≥ 16	$bla_{\text{CTX-M-15}}$	*qnrB1, qnrS1*	–§	–§
$bla_{\text{NDM-5}}$ (*n* = 4)	NSW	*E. coli*	167	0.5	$bla_{\text{CTX-M-15}}$	*aac(6')-Ib-cr*	–§	–§
	NSW	*E. coli*	167	≥ 16	$bla_{\text{CMY-42}}$	–§	–§	–§
	Vic	*E. coli*	361	≥ 16	–§	–§	–§	–§
	WA	*E. coli*	410	≥ 16	$bla_{\text{CTX-M-15}}$	–§	–§	–§
$bla_{\text{NDM-7}}$ (*n* = 2)	NSW	*K. oxytoca*	178	≥ 16	$bla_{\text{CTX-M-15}}$	*aac(6')-Ib-cr, qnrS1*	–§	*mcr-9.1*
	NSW	*E. coli*	1716	≥ 16	–§	–§	–§	–§
$bla_{\text{NDM-5, OXA-181}}$ (*n* = 1)	NSW	*K. pneumoniae*	147	≥ 16	$bla_{\text{CTX-M-15}}$	*qnrB1*	*rmtB1, rmtF1*	–§
$bla_{\text{NDM-5, OXA-484}}$ (*n* = 1)	NSW	*E. coli*	410	8	–§	*aac(6')-Ib-cr, qnrS1*	*rmtB1*	–§
$bla_{\text{KPC-2, NDM-5, OXA-181}}$ (*n* = 1)	NSW	*K. pneumoniae*	656	≥ 16	–§	*aac(6')-Ib-cr, qnrS1*	*rmtB1*	–§
$bla_{\text{OXA-23}}$ (*n* = 1)	SA	*A. baumannii complex*	1794	0.25	–§	–§	–§	–§
$bla_{\text{IMP-4, OXA-23, OXA-58}}$ (*n* = 1)	Vic	*A. radioresistens*	1972	≥ 16	–§	–§	–§	–§
$bla_{\text{IMP-4}}$ (*n* = 1)	NSW	*P. aeruginosa*	2136	≥ 16	–§	–§	–§	–§

ESBL = extended-spectrum β-lactamase; pAmpC = plasmid-bourne *ampC*; MCR = mobile colistin resistance; MIC = meropenem (mg/L); ST = sequence type; S/T = state or territory

† Plasmid-mediated quinolone resistance: *aac(6')-Ib-cr, qnr,* efflux (*qepA*).

§ Not detected

‡ *mcr-9* is not associated with a colistin resistant phenotype but is typically found on HI2 plasmids which may carry $bla_{\text{IMP-4}}$

The Australian Group on Antimicrobial Resistance Report from the Gram-negative Surveillance Outcome Program (GnSOP) 2023 – Clinical Outcomes

J.M. Bell[1], T. Gottlieb[2,3] and J. Iredell[3,4,5] for the Australian Group on Antimicrobial Resistance

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INTRODUCTION

The Australian Group on Antimicrobial Resistance (AGAR) Gram-negative Surveillance Outcome Programme (GnSOP) 2023 survey focused on resistance and demographic data on *Enterobacterales*, *Pseudomonas aeruginosa* and *Acinetobacter* species. Survey objectives were to monitor resistance (including co-resistance and multi-resistance), and to detect critical emerging resistance.

This report documents the available clinical features and bacteraemia outcomes.

METHODS

Thirty-three laboratories servicing 57 hospitals from all States and mainland Territories of Australia participated in the 2023 survey. Each hospital collected either all or up to 200 isolates from different patient bacteraemia episodes. In patients with more than one isolate, a new episode was defined if another positive blood culture was collected ≥ 2 weeks after the initial positive culture.

RESULTS

- Of 10,453 gram-negative episodes, *Enterobacterales* accounted for 90.9%, along with *P. aeruginosa* (7.7%) and *Acinetobacter* species (1.4%).
- Four genera made up 86.1% of all isolates (*Escherichia* 54.6%, *Klebsiella* 18.4%, *Pseudomonas* 7.7%, and *Enterobacter* 5.4%) (Figure 1).
- For gram-negative bacteraemia, the proportion from males was 53.5% (Figure 2), and 5.8% were from children (<18 y).

Figure 1. Top ten species causing bacteraemia, 2023

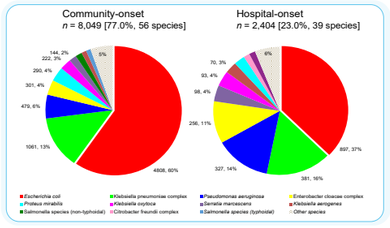
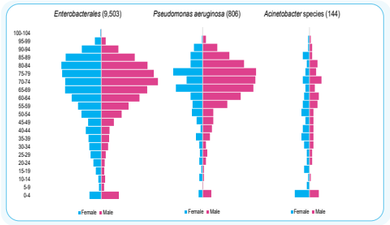


Figure 2. Patient age group and sex, 2023



- Overall, 77.0% of episodes were designated community-onset (CO), first positive blood culture collected ≤ 48 h after admission. Only 15.7% of *E. coli* bacteraemia was hospital-onset (HO); whereas 46.0% of *Enterobacter cloacae* complex, and 40.6% of *P. aeruginosa* bacteraemias were HO (Table 1).
- Urinary tract infection was the most frequent principal manifestation for episodes caused by *Enterobacterales* (43.3%; CO, 49.0%; HO, 23.2%) and *P. aeruginosa* (27.4%; CO, 29.6%; HO, 24.2%) (Table 2).
- Almost one-half (47.0%) of patients with an *Enterobacterales* bacteraemia stayed in hospital for < 7 days post bacteraemia (CO, 54.9%; HO, 20.2%).

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RESULTS (continued)

A little over one-third (38.3%) of patients with HO bacteraemia caused by *Acinetobacter* species, and over one-quarter (28.5%) with bacteraemia caused by *P. aeruginosa* remained in hospital for more than 30 days.

- The 30–day all-cause mortality for patients with *Enterobacterales* was 11.5%, 17.3% for *P. aeruginosa*, and 8.4% for *Acinetobacter* species) (Table 3). *E. coli* had a significantly higher 30-day all-cause mortality for HO than CO bacteraemia (HO 95/695, 13.7%; CO 280/3,064, 9.1%, *P* < 0.01).
- There was a significant difference in 30-day all-cause mortality between children (4.5%, 17/379) and adults (12.0%, 725/6,054) with an *Enterobacterales* bactaeramia (*P* < 0.0001).
- For *P. aeruginosa*, there was a significant association between multidrug-resistance (MDR) (resistant to at least one agent in three or more antimicrobial groups) and 30-day all-cause mortality for HO bacteraemia (MDR: 6/13, 13.2%; non-MDR: 45/247, 18.2%, *P* = 0.0242).
- Nationally, 54.4% of all *E. coli* isolates were resistant to at least one of five key antimicrobial groups (aminopenicillins, fluoroquinolones, third-generation cephalosporins, aminoglycosides and carbapenems); 3.3% were resistant to four groups.
- For *K. pneumoniae* complex, 11.5% were resistant to at least one antimicrobial group (fluoroquinolones, third-generation cephalosporins, aminoglycosides and carbapenems).
- Almost 1 in 5 (19.6%) of *P. aeruginosa* were resistant to at least one antimicrobial group (piperacillin–tazobactam, fluoroquinolones, ceftazidime, aminoglycosides or carbapenems).

CONCLUSIONS

- Gram-negative sepsis is common in Australia and continues to be a significant cause of morbidity and mortality.
- There was little change in the demographic and clinical features of gram-negative bacteraemia in Australia in the GnSOP 2023 survey.

Table 1. Species recovered, by place of onset, 2023

Organism	Community % (*n*)	Hospital % (*n*)	Total
Gram-negative species*	*77.0 (8,049)*	*23.0 (2,404)*	*10,453*
Acinetobacter species	63.9 (92)	36.1 (52)	144
Enterobacterales	78.7 (7,478)	21.3 (2,025)	9,503
Escherichia coli	84.3 (4,808)	15.7 (897)	5,705
Klebsiella pneumoniae complex	73.6 (1,061)	26.4 (381)	1,442
Enterobacter cloacae complex	54.0 (301)	46.0 (256)	557
Proteus mirabilis	81.9 (290)	18.1 (64)	354
Klebsiella oxytoca	70.5 (222)	29.5 (93)	315
Serratia marcescens	59.5 (144)	40.5 (98)	242
Klebsiella aerogenes	57.8 (96)	42.2 (70)	166
Salmonella species (non-typhoidal)	91.4 (128)	8.6 (12)	140
Citrobacter freundii complex	67.9 (76)	32.1 (36)	112
Morganella morganii	67.9 (72)	32.1 (34)	106
Other *Enterobacterales* (*n* = 38)	76.9 (280)	23.1 (84)	364
Pseudomonas aeruginosa	59.4 (479)	40.6 (327)	806

* *Enterobacterales*, *Acinetobacter* and *Pseudomonas aeruginosa*

Table 2. Principal clinical manifestation, organism group, 2023

Principal clinical manifestation	Organism group, % (n)			Total
	Acinetobacter species	*Enterobacterales*	*Pseudomonas aeruginosa*	
Urinary tract infection	5.6 (7)	43.3 (3,447)	27.4 (186)	41.5 (3,640)
Biliary tract infection (including cholangitis)	4.0 (5)	16.2 (1,294)	5.7 (39)	15.3 (1,338)
Intra-abdominal infection other than biliary tract	2.4 (3)	10.1 (808)	8.0 (54)	9.9 (865)
Other clinical syndrome	17.7 (22)	8.2 (654)	13.5 (92)	8.8 (768)
Febrile neutropenia	5.6 (7)	7.9 (631)	17.4 (118)	8.6 (756)
No identifiable focus	21.8 (27)	8.0 (641)	9.7 (66)	8.4 (734)
Device-related infection without metastatic focus	23.4 (29)	2.9 (230)	9.1 (62)	3.7 (321)
Skin and skin structure infection	14.5 (18)	2.1 (169)	7.2 (49)	2.7 (236)
Osteomyelitis/septic arthritis	2.4 (3)	0.9 (69)	0.7 (5)	0.9 (77)
Device-related infection with metastatic focus	2.4 (3)	0.3 (25)	1.2 (8)	0.4 (36)
Total	124	7,968	679	8,771

Table 3. Place of onset setting and 30-day all-cause mortality, 2023

Organism	Community-onset		Hospital-onset		Total	
	Number	Deaths % (*n*)	Number	Deaths % (*n*)	Number	Deaths % (*n*)
Gram-negative species*	*5,270*	*10.8 (568)*	*1,883*	*15.3 (289)*	*7,153*	*12.0 (857)*
Acinetobacter species	69	10.1 (7)	38	5.3 (2)	107	8.4 (9)
Enterobacterales	4,853	10.4 (506)	1,580	14.9 (236)	6,433	11.5 (742)
Escherichia coli	3,064	9.1 (280)	695	13.7 (95)	3,759	10.0 (375)
Klebsiella pneumoniae complex	711	12.7 (90)	310	14.8 (46)	1,021	13.3 (136)
Enterobacter cloacae complex	197	14.2 (28)	197	16.2 (32)	394	15.2 (60)
Proteus mirabilis	217	15.7 (34)	42	23.8 (10)	259	17.0 (44)
Klebsiella oxytoca	172	14.0 (24)	74	13.5 (10)	246	13.8 (34)
Serratia marcescens	94	9.6 (9)	74	18.9 (14)	168	13.7 (23)
Klebsiella aerogenes	63	12.7 (8)	57	10.5 (6)	120	11.7 (14)
Citrobacter freundii complex	54	20.4 (11)	29	24.1 (7)	83	21.7 (18)
Salmonella species (non-typhoidal)	64	6.3 (4)	9	0.0 (0)	73	5.5 (4)
Other *Enterobacterales* (*n* = 34)	169	8.3 (14)	69	14.5 (10)	238	10.1 (24)
Pseudomonas aeruginosa	348	15.8 (55)	265	19.2 (51)	613	17.3 (106)

* *Enterobacterales*, *Acinetobacter* and *Pseudomonas aeruginosa*

Acknowledgements

We wish to thank all of the contributing laboratories throughout Australia who provided isolates and or information for this study.
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National Alert System for Critical Antimicrobial Resistances: What is happening in Australia?

J. M. Bell, B. Carey, and K. Stewart

BACKGROUND

The National Alert System for Critical Antimicrobial Resistances (CARAlert) was established in March 2016 by the Australian Commission on Safety and Quality in Health Care for the Antimicrobial Use and Resistance in Australia (AURA) surveillance program. CARAlert provides timely communication on critical antimicrobial resistances (CARs) to health departments in each state and territory to inform infection prevention and control strategies.

METHODS

CARAlert uses existing laboratory testing and confirmation systems to capture data on CARs – resistances to last-line antimicrobials that are uncommon or rare, but with the capacity to become established in Australia. Laboratories that confirm CARs enter results into a national database at the time of confirmation. Data were extracted on 2 February 2025.

RESULTS

- From 1 April 2016 to 31 December 2024, a total of 16,087 CARs were reported (Table 1).
- Carbapenemase-producing *Enterobacterales* (CPE) was the most prevalent CAR reported yearly (37.9% in 2017 to 58.0% in 2022), except in 2017 when azithromycin-nonsusceptible *Neisseria gonorrhoeae* (ANSNG) dominated (47.5%).
- CPE reports declined nationally in 2020 and 2021, following a peak in 2019, but increased rapidly in 2022 and 2023. There was a 26.2% increase in CPE reports in 2024 compared to 2023 (Figure 1).
- IMP-types historically have been the dominant gene reported except in South Australia, where NDM-types are dominant (Figure 2). Nationally, the proportion of NDM-types (either alone or co-produced with other types) has doubled from 20.1% in 2016 to 44.3% in 2024.
- In Victoria, NDM-types accounted for over 56% of all CPE reported in both 2022 and 2023, rising to 63.0% in 2024. Reports of IMP-types declined to 10% of reports in 2023 and 12% in 2024.
- Despite multidrug-resistant (MDR) *Shigella* species decreasing in 2021, there was an 11-fold increase in reports in 2023 (Figure 3). Reports from WA doubled from 30 in 2023 to 62 in 2024. The number of reports from New South Wales, Victoria and South Australia declined in 2024.
- ANSNG declined annually after it peaked in 2017 (Figure 4). In 2022, the number of reports fell to the lowest number since CARAlert commenced, but increased nearly 9-fold in 2024.
- In 2022, of all *N. gonorrhoeae* CARAlert reports, 23.3% (37/159) were ceftriaxone-nonsusceptible (MIC ≥ 0.125 mg/L), 5.0% (8/159) were azithromycin-nonsusceptible (high-level, MIC > 256 mg/L); the remaining reports were azithromycin-nonsusceptible (low-level, MIC ≤ 256mg/L). In 2024, 3.6% (39/1,077) were ceftriaxone-nonsusceptible.
- Carbapenemase-producing *Pseudomonas aeruginosa* (*n* = 367) have been reported to CARAlert since July 2019. The dominant types were GES (175, 47.7%), VIM (75, 20.4%), NDM (72, 19.6%), and IMP (27, 7.4%); KPC-, AIM-, and DIM-types were also reported reported.
- The majority (151/181, 83.4%) of carbapenemase-producing *Acinetobacter baumannii* complex isolates reported since July 2019 produced OXA 23-like types either alone (*n* = 128) or co-produced with other types (*n* = 23).
- There were nine reports of *Enterobacterales* with transmissible resistance to colistin (*mcr-1.1*) since July 2019; seven *Escherichia coli* (2019 [3], 2020 [1], 2023 [2], 2024 [1]), and two *Klebsiella pneumoniae* (2022). Four isolates were also carbapenemase-producing.
- Both linezolid-nonsusceptible (*n* = 9) and, and vancomycin-nonsusceptible (*n* = 5) *Staphylococcus aureus* have been reported.
- There were 54 reports of *Candida auris* since July 2019, from all states and territories except Tasmania.
- Linezolid-resistant *Enterococcus faecium* (*n* = 111) and *E. faecalis* (*n* = 152) have been reported from all states and territories since 2016. In Victoria, reports have increased 3.6-fold from 20 in 2023 to 72 in 2024.
- In 2024, almost all *E. faecalis* (36/37, 97.3%) and over 60% (49/81) *E. faecium* contained *optrA*.
- Nine ciprofloxacin-nonsusceptible *N. meningitidis* were reported since 2023.

Table 1. Critical antimicrobial resistances reported to CARAlert, by year, 1 April 2016 to 31 December 2024

Species	Critical resistance	Year									Relative change (%)*
		2016	2017	2018	2019	2020	2021	2022	2023	2024	
Acinetobacter baumannii	Carbapenemase-producing†	–	–	–	32	25	17	23	37	47	▲ 27.0
Candida auris	–†	–	–	–	6	5	1	9	17	16	▼ 5.9
Enterobacterales	Carbapenemase- and/or ribosomal methyltransferase-producing	324	585	647	886	649§	609	839§	1,220§	1,540	▲ 26.2
	Transmissible resistance to colistin†	–	–	–	3	0	0	1	1	0	–
Enterococcus species	Linezolid-resistant	5	4	14	22	19	13	17	51	118	▲ 131
Mycobacterium tuberculosis	Multidrug-resistant – resistant to at least rifampicin and isoniazid	18	21	27	24	18	13	16	21	14	▼ 33.3
Neisseria gonorrhoeae	Azithromycin-nonsusceptible (low-level)	211	730	518	424	267	250	114	669	1,008	▲ 50.7
	Azithromycin-nonsusceptible (high-level)	4	4	7	7	1	0	8	22	30	▲ 36.4
	Ceftriaxone-nonsusceptible	4	0	3	4	3	0	33	14	28	▲ 100
	Ceftriaxone- and azithromycin-nonsusceptible	0	0	3	0	0	1	4	9	11	▲ 22.2
Neisseria meningitidis	Ciprofloxacin-nonsusceptible#	–	–	–	–	–	–	–	4	5	▲ 25.0
Pseudomonas aeruginosa	Carbapenemase-producing†	–	–	–	27	44	67	57	75	97	▲ 29.3
Salmonella species	Ceftriaxone-nonsusceptible	17	38	52	45	33	24	51	96	104	▲ 8.3
Shigella species	Multidrug-resistant	14	41	104	331	299	42	99	469	364	▼ 22.4
Staphylococcus aureus	Daptomycin-nonsusceptible	57	121	122	161	213	265	170	–	–	–
	Vancomycin- and daptomycin-nonsusceptible	0	0	1	0	1	0	2	1	0	–
	Linezolid-nonsusceptible	0	1	2	0	2	1	3	0	0	–
Streptococcus pyogenes	Penicillin-reduced susceptibility	0	0	0	0	0	0	0	0	0	–
	Total	654	1,545	1,500	1,972	1,579	1,303	1,446	2,706	3,382	▲ 25.0

– = not applicable; ▲ = increase; ▼ = decrease
* Relative change = absolute change between 2023 and 2024, for each CAR, expressed as a percentage of 2023 base
† New CAR reported from July 2019
§ Includes one isolate with transmissible resistance to colistin
# New CAR reported from January 2023. In 2023 gentamicin-resistant *N. gonorrhoeae* was added (no reports) and reporting of daptomycin-nonsusceptible *S. aureus* was suspended.

Figure 1. Carbapenemase-producing *Enterobacterales*, by month of collection, setting (3-month moving averages), April 2016 to 2024

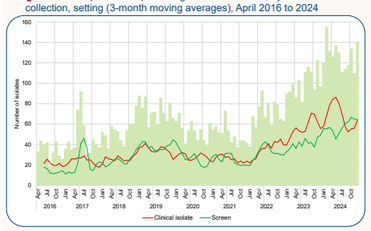


Figure 2. *Enterobacterales*, top five carbapenemase types, by state and territory, April 2016 to 2024

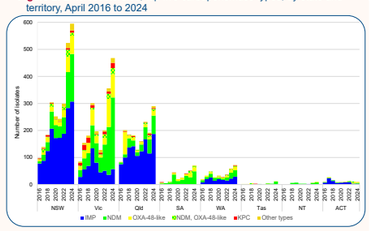


Figure 3. Multidrug-resistant *Shigella* species, by month of collection and state and territory, April 2016 to 2024

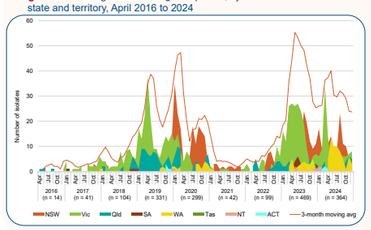
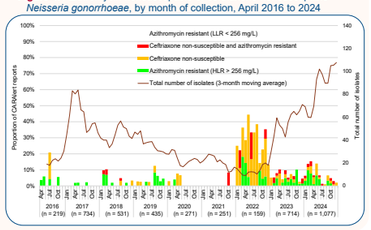


Figure 4. Azithromycin-nonsusceptible or ceftriaxone-nonsusceptible *Neisseria gonorrhoeae*, by month of collection, April 2016 to 2024



CONCLUSIONS

- Several CARs are detected in Australia on a regular basis. In 2024, higher numbers were reported for most CARs, compared with the previous year; there was notable variation between jurisdictions, and evidence of local outbreaks of carbapenemase-producing organisms.
- The return of international travel after the COVID-19 pandemic has coincided with an increase in reports of CPE, ANSNG and MDR *Shigella* species from 2023.

National Alert System for Critical Antimicrobial Resistances (CARAlert) | Australian Commission on Safety and Quality in Health Care

The Commission's AURA Project is funded by the Australian Government Department of Health and Aged Care with contributions from the states and terriories.

Australian Passive AMR Surveillance: Trends in multidrug-resistant organisms in Australia

J. M. Bell, B. Carey, K. Stewart, and J. Turnidge

BACKGROUND

APAS was established in 2015 by the Australian Commission on Safety and Quality in Health Care in collaboration with Queensland Health for the Antimicrobial Use and Resistance in Australia surveillance program.

APAS captures data on multidrug-resistant organisms (MROs) including vancomycin-resistant *Enterococcus faecium* (VRE), fluoroquinolone-resistant *Escherichia coli* and methicillin-resistant *Staphylococcus aureus* (MRSA). MROs pose significant risks to patient safety and APAS data informs actions to address the prevention, control and treatment of these antimicrobial-resistant infections.

VRE and MRSA are in the high priority group in the World Health Organization Bacterial Priority Pathogen List.

METHODS

APAS collects routine categorical susceptibility testing data from participating laboratory information systems via OrgTRx. Data were extracted 1 May 2024. APAS contributor pathology services are listed in the Table.

State/Territory	Pathology service
New South Wales	NSW Health Pathology*†
Victoria	Alfred Health
	Monash Health
Queensland	Mater Pathology Brisbane*
	Pathology Queensland*
South Australia	SA Pathology*
Western Australia	PathWest Laboratory Medicine
Tasmania	Launceston General Hospital§
	Royal Hobart Hospital
Australian Capital Territory	ACT Pathology#

* NSW Health Pathology (South Western Sydney and Sydney Local Health Districts), Mater Pathology Brisbane, Pathology Queensland and SA Pathology since 2006
† NSW Health Pathology West since 2010
§ Launceston General Hospital since 2021
# No data from ACT Pathology for 2023

RESULTS

Enterococcus faecium

- There was a sharp increase in the proportion of VRE isolates from 5.3% in 2006 to 51.9% in 2015. There was a steady decreasing trend until 2020 (33.2%) before increasing to over 42% in 2022 and 2023 (Figure 1).
- The proportion of VRE was lower in children (aged < 18 years) than adults in each year over this period. The resistance trends were similar across all age groups.
- A little over two-thirds (70.1%) of *E. faecium* isolates reported by APAS contributors for 2015 to 2023 were from patients residing in major cities of Australia.
- The 2023 VRE data mapped to Australian Statistical Area Level 4 (SA4) are shown in Figure 2.

Escherichia coli

- Fluoroquinolone resistance (FQ-R) in *E. coli* has increased from 1.9% in 2006 to 13.4% in 2023 (Figure 3).
- Of *E. coli* isolates from APAS contributors for 2015 to 2023, 90.7% were from adults and 9.3% from children.
- The highest proportion of FQ-R was seen in tissue/fluid/pus/prosthesis isolates from adults. The proportion of FQ-R *E. coli* was slightly lower among children with urinary tract infections.
- FQ-R was similar in hospitals and the community (both 13.4% in 2023).
- Despite low numbers of isolates, the proportion of FQ-R *E. coli* was highest in very remote Australia (19.4% in 2023).
- The 2023 FQ-R *E. coli* data mapped to SA3 are shown in (Figure 4).

Staphylococcus aureus

- The proportion of *S. aureus* that were methicillin resistant remained steady from 2006 to 2023 (range: 19.8-22.8%) (Figure 5).
- MRSA was lowest among children with respiratory infections. A decreasing trend in the MRSA rate was observed in patients aged 65 years and over across all specimen types. There was little difference in the proportion of MRSA observed in the three age groups for *S. aureus* isolated from blood. However, in 2023, the MRSA rate was 1.6-fold lower in paediatric patients (9.1%) compared to adults (14.9%).
- The prevalence of MRSA was highest in remote and very remote Australia (2023: 31.5% and 33.5%, respectively); this was compared to major cities (19.4% in 2023) where the greatest number of *S. aureus* isolates were collected.
- In 2023, the highest rates of MRSA were observed in WA and the NT: Kimberly (44.1%), Alice Springs (39.3%), West Pilbara (39.0%), Gascoyne (38.4%), and East Pilbara (37.5%). The lowest rate was observed in Tasmania in Hobart Inner (4.9%) (Figure 6).

CONCLUSIONS

- Ongoing surveillance of antimicrobial resistance, compliance with *Australian Guidelines for the Prevention and Control of Infection in Healthcare* and implementation of antimicrobial stewardship are critical to control the upward trend in MROs across healthcare and community settings.
- This is particularly important for vulnerable populations in aged care and where resistance rates are highest such as remote and very remote regions and northern Australia.

Figure 1. Vancomycin resistance in *Enterococcus faecium*, 2006 to 2023

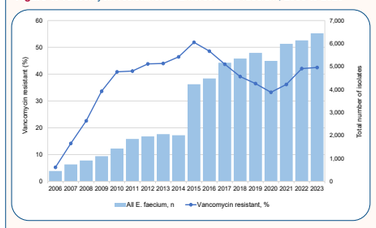


Figure 3. Fluoroquinolone resistance in *Escherichia coli*, 2006 to 2023

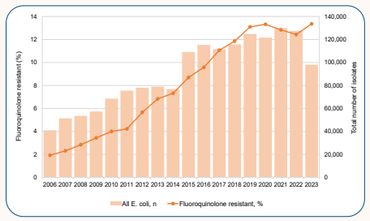


Figure 5. Methicillin resistance in *Staphylococcus aureus*, 2006 to 2023

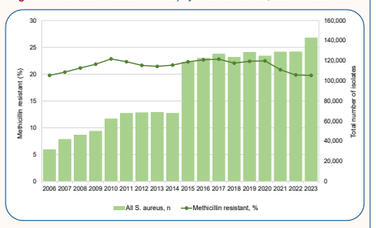


Figure 2. Vancomycin resistance in *Enterococcus faecium*, mapped to Australian SA4 areas, 2023

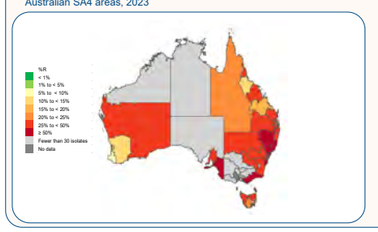


Figure 4. Fluoroquinolone resistance in *Escherichia coli* mapped to Australian SA3 areas, 2023

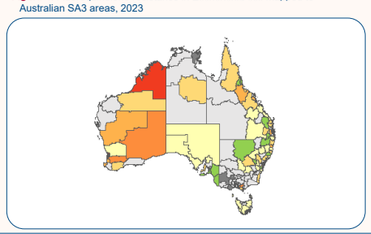
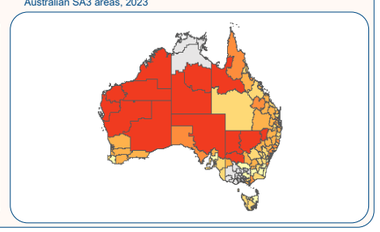


Figure 6. Methicillin resistance in *Staphylococcus aureus* mapped to Australian SA3 areas, 2023



Notes:
1. SA3 and SA4 areas are based on postcode of residence (where known). Data available from the NT were from NT residents who received pathology services interstate.
2. Data from ACT pathology services were not available for 2023, except where ACT residents received pathology services interstate.
3. The map colour key shown in Figure 2 also applies to Figures 4 and 5.

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