# A S A

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# In this issue:



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# FROM THE ASA TEAM

Welcome to Issue 48 of Breakpoint as we navigate the evolving landscape of antimicrobial resistance and stewardship in 2025.

This issue showcases expertise in combating one of medicine's greatest challenges. **Chris Robson's** PhD research on infective endocarditis demonstrates how rigorous investigation can transform our approach to this life-threatening condition. From optimizing prophylaxis during TAVI procedures to establishing multidisciplinary care models that save lives.

**AUSCAST** brings crucial updates on aminopenicillin breakpoints that will directly impact laboratory reporting and clinical practice. While these changes present implementation challenges, the detailed guidance provided ensures we maintain both scientific accuracy and practical utility in our susceptibility reporting.

**Angela Huttner's** viewpoint article challenges us to critically evaluate combination antimicrobial therapy. *In vitro* promise must be balanced with clinical evidence and the fundamental principle of "first, do no harm."

The 2024 **AGAR** surveillance data reveals concerning trends, including rising ESBL rates and fluoroquinolone resistance among Gram negatives, while highlighting Australia's relatively favourable position globally. These insights are essential for guiding both local stewardship efforts and national policy.

Our **photo quiz** presents a diagnostic challenge that underscores the importance of considering vaccine-preventable diseases in our differential diagnoses.

Looking ahead, mark your calendars for Antimicrobials 2026 in Adelaide, an opportunity to engage with leading experts and shape the future of antimicrobial practice in our region.

I hope this issue informs your practice and inspires continued dedication to antimicrobial stewardship.

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**Front Cover** *Clostridium difficile*. David Goulding, Wellcome Trust Sanger Institute. Source: Wellcome Collection.

*Clostridium difficile* is a major cause of antibiotic-associated diarrheal disease. Part of the reason for it's persistence in the hospital environment has been ineffective disinfection regimes which have enabled the highly resistant spores to accelerate host transmission. This image illustrates how effectively the vegetative core is protected by three clearly defined coats 100nm thick and an exosporium.

IN THE SPOTLIGHT

# Optimising the prevention diagnosis & management of infective endocarditis

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## Introduction

Infective endocarditis (IE) is a serious infection of the heart's inner lining, valves, or implanted devices, with a high mortality rate of around 25% despite modern treatment. Survivors often face long-term complications, and diagnosis and management remain complex due to its subtle presentation and need for coordinated multidisciplinary care. Changing epidemiology, driven by increased injection drug use and cardiac device implants, demands evolving strategies. This research program focused on improving outcomes through three key areas: understanding antimicrobial pharmacology in IE, particularly beta-lactam therapy; identifying risk factors and improving diagnostics, including the role of blood culture time-to-positivity; and developing effective multidisciplinary care models in Australia. It aimed to enhance understanding of IE pathogenesis, improve therapeutic strategies, and establish structured, collaborative care frameworks tailored to the Australian healthcare system.

## Studies and findings

**Study 1** A systematic review of optimal PK/PD parameters for beta-lactam therapy in IE

The requirement for prolonged treatment with active antimicrobials has been well established in IE. However, optimal drug selection and dosing is constrained by a limited understanding of antimicrobial PK/PD in this condition. Beta-lactam antibiotics represent the backbone of many treatment regimens for IE and have generally been considered agents with a wide therapeutic index, although evidence has suggested that standard dosing may leave critically ill patients with subtherapeutic or toxic concentrations. Evidence-based, disease-specific PK/PD targets are lacking for beta-lactam therapy.

A systematic review was performed to synthesise the diverse experimental evidence from both animal models and human studies detailing beta-lactam PK/PD in IE. From 3043 abstracts, 62 articles were included for synthesis, addressing antibiotic-vegetation dynamics, PK/PD targets, organism factors and combination antimicrobial therapy. Many studies were from animal models, with only a small number of human case series and cohort studies included. The findings suggested that, as with other conditions, time-dependent killing was important for beta-lactam efficacy, but substantial variability likely exists in how different antimicrobials penetrate vegetations and maintain effective concentrations. Furthermore, specific PK/PD targets are likely specific to drug-bug combinations, and current evidence lacks the detail to adequately define these targets for clinical practice[1].

**Study 2** Population PK and optimised dosing of cefazolin during transcatheter aortic valve implantation (TAVI)

TAVI is a less-invasive alternative to surgical valve replacement in patients with aortic stenosis. Whilst initially utilised in high-risk surgical candidates, indications for TAVI have been broadened to include lower-risk patients, and its use is increasing exponentially. As with other prosthetic valves, IE following TAVI can occur and is a significant complication. Its microbiology is unique in that there is a predominance of enterococci[2]. Optimisation of procedural antimicrobial prophylaxis is a key component of preventing TAVI-IE. The objective of this study was to establish a population PK profile for cefazolin prophylaxis in TAVI recipients to inform optimal prophylaxis regimens and dosing.

Adult patients receiving cefazolin prophylaxis for TAVI were prospectively enrolled at a specialty referral hospital between 2022 and 2023. Four periprocedural blood samples were collected for determination of total and unbound cefazolin concentrations by a validated UHPLC-MS/MS method. 188 total and 171 unbound plasma concentrations were obtained from 50 participants and were utilised to inform model development. The unbound concentrations were best described by a two-compartment model with first-order elimination. Monte Carlo simulation was performed and corresponding probability

of target attainment (PTA) profiles were generated based on 100%$fT_{>MIC}$ (Figure 1). Using the simulated PTAs, fractional target attainment (FTA) was also calculated for common TAVI-IE organisms.

Modelling suggested prophylactic cefazolin at a dose of 2g performed well for procedures of 2 hours duration. The median procedure duration for our cohort was 72.5 minutes. FTA calculations suggested good performance against MSSA but less reliable activity against *S. epidermidis*. Timing of cefazolin administration prior to procedure was variable as it was frequently administered on the ward rather than in the procedural laboratory[3].

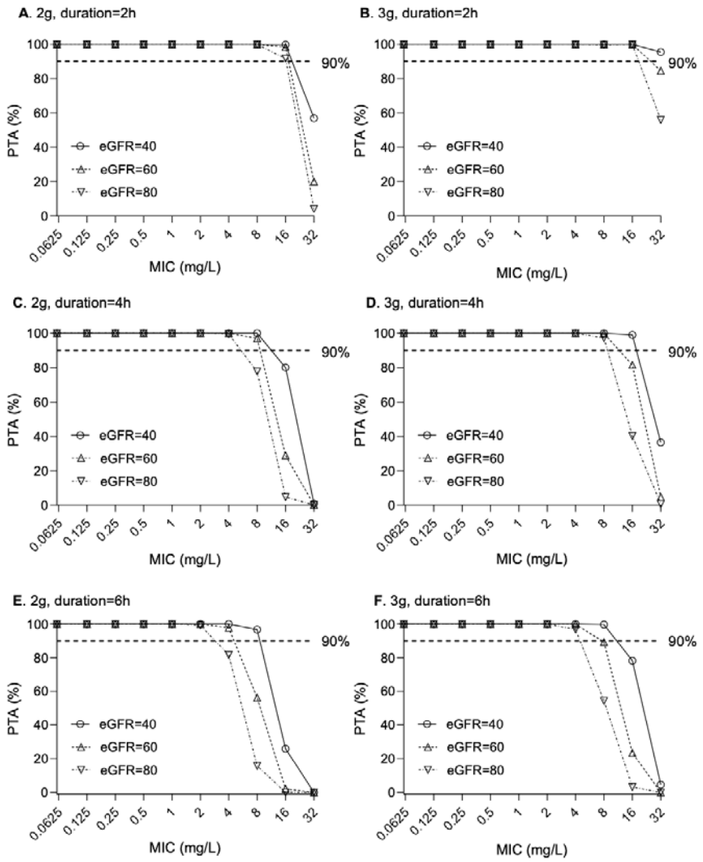


**Figure 1** PTA for unbound cefazolin concentrations in plasma with the target of 100%fT>MIC for duration of 2h (A,B) 4h (C,D) and 6h (E,F) for dose of 2g (A,C,E) and 3g (B,D,F). The horizontal dash line represents a PTA of 90%

**Study 3** Incidence of periprocedural bacteraemia during TAVI implantation

As mentioned, the most frequently reported pathogen in TAVI-IE is *E. faecalis*. The proposed mechanism for this has been periprocedural bacteraemia and valve seeding due to the transfemoral approach which is often utilised. However, the population that have been the main recipients of TAVI in the past decade, being the elderly and co-morbid, also reflect those at highest risk of *E. faecalis* bacteraemia[4].

This study, performed in conjunction with Study 2, aimed to define the incidence and microbiology of periprocedural bacteraemia in TAVI recipients to further understanding of the pathogenesis or TAVI-IE. 75 TAVI recipients were prospectively enrolled and had blood cultures collected at three time points periprocedurally. Participants received cefazolin for procedural prophylaxis or, in the case of antibiotic allergy, vancomycin. 12-month follow up was performed to identify any cases of TAVI-IE.

Of 221 blood cultures, 4 returned positive results (3 with *Corynebacterium spp.* and 1 with *P. mirabilis*). No episodes of enterococcal bacteraemia were identified. A single episode of TAVI-IE due to *S. mitis* was identified in the follow up period, in a participant who had no positive study blood cultures.

Whilst there are several limitations to this study, the findings challenge the hypothesis that periprocedural bacteraemia is responsible for the microbiology of TAVI-IE.

**Study 4** Blood culture time-to-positivity in IE

Blood culture time-to-positivity (TTP), the time from blood culture incubation to detection of bacterial growth, has been studied as a diagnostic tool for several conditions including IE. TTP is inversely related to bacterial load, with shorter TTP suggesting higher bacterial inoculum. Several studies have investigated the relationship between TTP and IE in *S. aureus* bacteraemia, generally finding shorter TTP correlating with an IE diagnosis. Research for other IE-prone organisms, including *E. faecalis* is limited. This study aimed to define the relationship between TTP and IE in *E. faecalis* bacteraemia.

We performed a retrospective study of blood cultures at a metropolitan healthcare network between 2017-2021, identifying individuals with *E. faecalis* bacteraemia. Incomplete blood culture sets, polymicrobial growth, receipt of systemic antimicrobials within 7 days of blood culture collection and repeat *E. faecalis* bacteraemia were exclusion criteria. Individuals were defined as having 'definite' IE by the 2023 Duke-ISCVID criteria, but cases of 'clinical' IE, where the Duke criteria were not fulfilled but the patient received IE treatment, were also recorded. TTP and demographic data were collected.

114 episodes of *E. faecalis* bacteraemia were included for analysis, including 27 cases of 'definite' IE. When 'clinical' cases of IE were considered, the number of IE cases grew to 42. TTP was not

**"Despite guideline recommendations fewer than one-third of Australian centres currently utilise an MDET [multidisciplinary endocarditis team] model"**

significantly different between IE cases, either 'definite' or 'clinical', and bacteraemia of other sources (Figure 2). This contrasts with the small number of previous studies showing shorter TTP in *E. faecalis* IE. Differences in echocardiography rates, disease stage at presentation, and microbial activity in vegetations may explain the variation. TTP's utility remains uncertain due to inconsistent findings, methodological limitations, and inter-laboratory variation. Compared to *Staphylococcus aureus*, where TTP is a more reliable IE marker, *E. faecalis* presents greater diagnostic challenges[5].

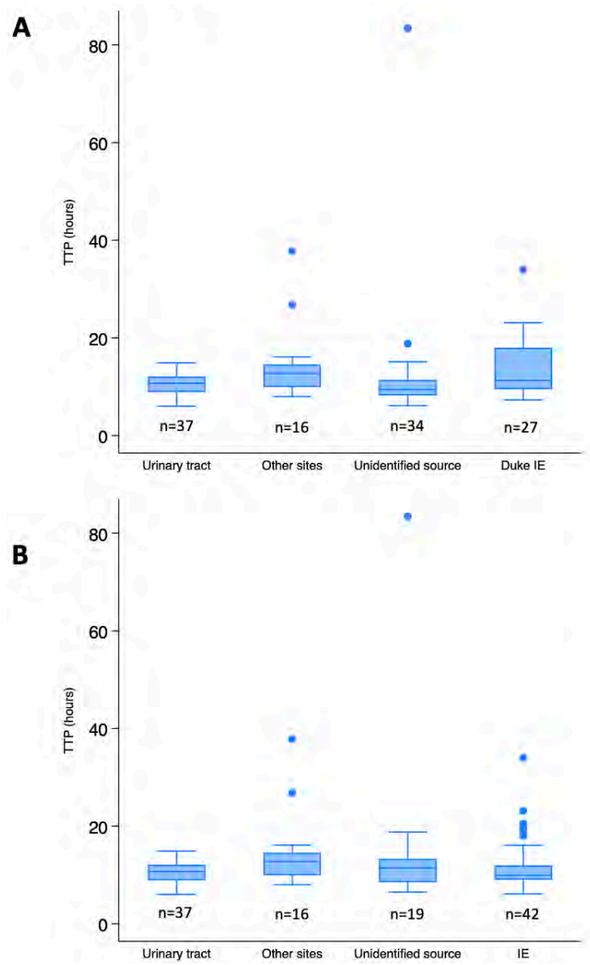


**Figure 2** Box and whisker plot of TTP stratified by site of infection with Duke IE cohort (A) and clinical IE cohort (B)

**Study 5** IE models of care in Australia

Multidisciplinary endocarditis team (MDET) management is supported by current evidence and recommended in international guidelines[6]. However, the extent of its implementation in Australian specialist centres, along with the associated attitudes, barriers, and facilitators, remains unclear.

This study aimed to describe current models of care for IE in Australian specialist referral centres and evaluate perceptions of, and obstacles to, MDET implementation. Two online surveys were used: Survey 1, distributed to infectious diseases physicians at cardiac surgery centres, audited existing IE care models; Survey 2, distributed via professional society email lists, assessed attitudes, barriers, and facilitators toward MDET implementation from key stakeholders.

Of 56 identified cardiac surgery centres, Survey 1 received 47 responses (84%), revealing that only 28% (13/47) had established MDETs. Most of these were based in public hospitals (85%) and high-volume IE centres (85%). Survey 2 received 109 responses, with participants expressing generally favourable attitudes toward MDET implementation. Reported barriers included insufficient funding, limited resources, lack of time, expertise, and interdepartmental collaboration. Key facilitators were strong leadership, engagement of relevant stakeholders, and clear clinical benefits.

Despite guideline recommendations, fewer than one-third of Australian centres currently utilise an MDET model. Broader adoption will require targeted financial and administrative support, along with committed leadership to overcome current systemic barriers[7].

## Future directions

Future research in IE must address key gaps across prevention, diagnosis, and treatment. Antimicrobial prophylaxis guidelines, especially for procedures like dental work and cardiac interventions (e.g. TAVI), require further evidence to clarify optimal agents, timing, and duration. The pathogenesis of TAVI-associated IE remains poorly understood and warrants investigation through *in vitro* studies and clinical risk factor analysis.

Diagnostic advancements should focus on refining tools like blood culture time-to-positivity, incorporating emerging methods such as metagenomics and microbial cell-free DNA sequencing, and improving risk stratification across bacterial species. Imaging research should explore the role of advanced echocardiography, PET, and CT, while evaluating vegetation characteristics that may impact treatment outcomes. Artificial intelligence could enhance diagnostic accuracy and imaging interpretation but needs validation in IE-specific settings.

Personalised therapy remains an unmet need. Future studies should define PK/PD targets to support tailored treatment and explore oral therapy further, particularly in comparison to outpatient IV antibiotic programs. Large platform trials will be crucial in addressing these questions.

Additionally, more inclusive research involving regional and lower-acuity centres is essential. Efforts like the Australasian Collaboration in Endocarditis and its planned national registry offer a foundation for collaborative, multidisciplinary research that reflects real-world practice and supports improved IE care across diverse healthcare settings.

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# ANTIMICROBIALS 2026

25th Annual Scientific Meeting

**26TH - 28TH FEBRUARY 2026**

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ADELAIDE, SOUTH AUSTRALIA

# ABSTRACTS SUBMISSION

**Abstract Submission Deadline** **Friday | 12th December 2025 11:59 PM AEDT**

## The ASA Travel Award

ASA has made funds available to assist Members wanting to attend the Society's Annual Scientific Meeting.

- Travel awards are avaialble to ASA financial members who present a proffered paper (oral or poster) at the meeting.
- Applicants must have current ASA membership and must have been ASA members for at least the last 12 months.
- Recipients are required to write a report on the meeting for the ASA Newsletter.

The awards consist of return economy airfare, accommodation, and meeting registration for Antimicrobials 2026, valued up to AUD 2,500.

ASA members who wish to apply for this award are invited to submit their application to the ASA Secretary at **info@asainc.net.au** by **Friday 12th December 2025**. The application should include a copy of the abstract, and for abstracts with more than one author, a letter stating the relative contribution of the applicant towards the research.

## ASA Poster Travel Award

The ASA Poster Travel Award is presented to an individual based on a flash poster presented during the ASA's Annual Scientific Meeting.

- The awardee must have been a financial member of the ASA for at least the last twelve months.
- The award committee will consist of three ASA committee members or their nominees and will take into account the quality and originality of the flash poster presentation and the poster.

The award comprises return economy airfare, accommodation, and meeting registration, valued at up to AUD 2,500, for the recipient(s) to attend Antimicrobials 2027.

## ASA bioMérieux Identifying Resistance Travel Awards

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- The award committee will consist of three ASA members.
- The award committee will take into account the quality and originality of the paper.

The award consists of an AUD 1,000 cash prize, a commemorative plaque, and the provisions of flights, accommodation, and registration for the recipient to attend Antimicrobials 2027.

# Register Now!


# ASA Keryn Christiansen Research Grant

The 2026 Australian Society for Antimicrobials (ASA) Keryn Christiansen Research Grant of up to $25,000 to support original research is now available.

The following conditions apply:

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- The Principal Investigator (PI) must have been an ASA member for at least twelve months
- Preference will be given to stand-alone projects that align with the Society's aims
- Preference will be given to early-career researchers
- The successful applicant will present their work at an ASA annual scientific meeting
- ASA will be acknowledged in all resulting publications and presentations
- 12 and 24 months progress reports must be submitted to the ASA committee and an article for the ASA newsletter

The research funds are to be used for the project, as per the budget application only. ASA does not support an institution's infrastructure or overhead costs.

The application must be performed online via the ASA website using the ASA Keryn Christiansen Research Grant Application Form and must include:

- A copy of the PI's CV.
- Head of Department confirmation of the application and the Department has the resources required to undertake the project.

The grant application and CV will be assessed by a panel of at least six independent reviewers using a standardised scoring system. Applicants will be informed of the decision one week before the ASA annual scientific meeting "Antimicrobials 2026".

Applications will be accepted online up to 30th October 2025.

Click here for the Research Grant Application Form.
For further enquiries please contact the ASA secretary on info@asainc.net.au.

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# Aminopenicillins | EUCAST revised breakpoints & reporting considerations

Robert Stevens
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## Introduction

Over recent years EUCAST has revised aminopenicillin breakpoints. The rationale for these revisions includes the differences in exposure between intravenous and oral formulations of all aminopenicillins, the notably lower oral bioavailability of ampicillin compared to amoxicillin, and the fact that amoxicillin bioavailability is saturable. The maximal achievable serum levels of amoxicillin with oral administration only covers pathogens with MICs up to 2 mg/L which is below the ECOFF of most common Enterobacterales (8 mg/L) and the cut off for resistance for the enterococci (> 4 mg/L).

Aminopenicillins have high urinary excretion and hence are suitable for uncomplicated urinary tract infection or localised infections (i.e. cystitis). Infections originating from the urinary tract, such as pyelonephritis, with or without bacteraemia, have better outcomes than other systemic infections and hence follow-on therapy with oral amoxicillin (± clavulanate) may be reasonable in this setting.

The European Association of Urology proposed classification of UTIs no longer uses the terms 'uncomplicated' and 'complicated'; instead, it emphasises the difference between localised and systemic UTIs identified by clinical signs and symptoms. The definitions are as follows (Figure 1):

- Localised UTI: A cystitis without any signs and symptoms of systemic infection in either sex.
- Systemic UTI: An infection with signs and symptoms of systemic infection with or without localised symptoms originating from any site in the urinary tract in either sex.

Both localised and systemic UTIs may be accompanied by risk factors that increase the likelihood of a challenging clinical course and jeopardise treatment success. An overview of risk factors to identify and address early in the treatment process is outlined (Table 1).

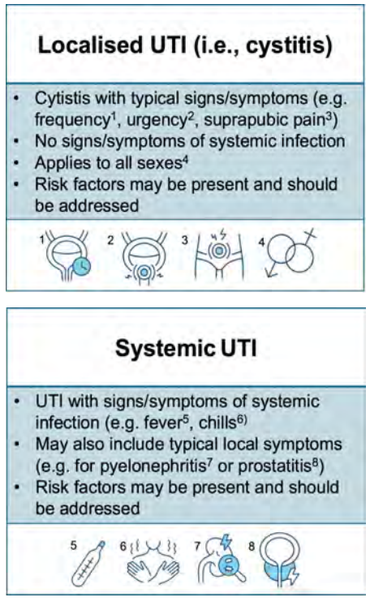



**Figure 1** EAU Guidelines. Edn. presented at the EAU Annual Congress Madrid, Spain 2025. ISBN 978-94-92671-29-5.

## Enterobacterales

Apart from oral amoxicillin-clavulanate for uncomplicated UTI only, the resistant breakpoints are the same, regardless of formulation or indication. However, for oral amoxicillin-clavulanate, the uncomplicated UTI only breakpoint is R > 32 mg/L, compared with R > 8 mg/L for all other formulations and indications. Therefore, differentiating between localised and systemic urinary tract infections will impact upon the reported susceptibility category. For other forms of systemic infection outside of the urinary tract caused by Enterobacterales, maximum exposure with oral amoxicillin (± clavulanate) is inadequate. Clinical evidence is lacking, but these agents may still be considered for specific indications in combination with another active agent or other measure (e.g. surgical intervention). These recommendations do not apply to Enterobacterales with an expected resistance phenotype to amoxicillin (± clavulanate). Further details are available here.

## *Enterococcus* spp.

Susceptibility to amoxicillin for enterococci is inferred from ampicillin, demonstrating the lack of phenotypically detectable resistance mechanisms. Again, the high urinary excretion of aminopenicillins renders them suitable for the treatment of uUTI. However, for other indications, oral amoxicillin should be used only with high exposure, in combination therapy, and for *Enterococcus faecalis* only. As such, for non-urinary *E. faecalis* isolates with ampicillin MICs ≤ 4 mg/L (zone diameter ≥ 10 mm), EUCAST provide for oral amoxicillin, a susceptible increased exposure category in brackets. The addition of a beta-lactamase inhibitor does not add clinical benefit as beta-lactamase production in the enterococci is extremely rare. Please consult the EUCAST breakpoint tables for more information.

## Breakpoints in brackets

These are used to warn against the use of oral aminopenicillins without the use of additional therapeutic measures. The breakpoints in brackets are in essence ECOFFs that distinguish between isolates with and without acquired resistance. Isolates with resistance can be reported as R (resistant). For wildtype strains, the report can indicate an absence of resistance, the need for high dose and adjunctive therapy. Categorical reporting of "susceptible, increased exposure" should be avoided where possible.

**UTI Risk Factors**

Patient factors
- Infants
- Geriatric or frail patients

Anatomical or functional abnormalities
- Neurourological patients
- Urinary tract stones / obstruction
- Increase post void residual volume

Underlying health conditions
- Immunocompromised state
- Diabetes
- Renal impairment

Medical interventions
- Indwelling urinary catheters
- Recent instrumentation

Males with
- Prostate involvement

Females with
- Pregnancy
- Pelvic organ prolapse

**Table 1** Adapted from EAU Guidelines. Edn. presented at the EAU Annual Congress Madrid, Spain 2025. ISBN 978-94-92671-29-5.

## Implementation

These revised EUCAST aminopenicillin breakpoints although scientifically valid, raise significant challenges for implementation. These include but are not limited to:

**1 The need for clinical information to inform appropriate break point adoption for urinary isolates.**

To be fully compliant with reporting guidelines requires clinical details to correlate with a clinical syndrome such as uncomplicated UTI, or infections originating from the urinary tract. This relies on the ordering clinician. Such details may not be provided nor be feasible to actively seek this information prior to reporting.
Community-based laboratories will often process large urine volumes (up to 3000 daily) and report that clinical notes are rarely given and that most samples come from GPs, therefore, to differentiate cystitis from systemic UTI at a bench level would be unworkable. It is also reported that standard urine positivity rate is approximately 30%, from which two-thirds are finalised using direct susceptibility testing. Without automated methods to record, report and interpret different zones diameters for different clinical scenarios, reporting multiple interpretations for the same aminopenicillin agent may be onerous. Those laboratories relying solely of automated AST methods (such as Vitek2) may more readily able to interpret and report for cystitis and systemic UTI breakpoints.

When a mid-stream urine sample cultures Enterobacterales or *E. faecalis*, some laboratories may find it acceptable to assume that the clinical syndrome is compatible with an uncomplicated UTI (i.e. cystitis only). Other details that could be considered include clinical information suggesting a complicated (or systemic) infection (e.g. flank pain, fever, hypotension) and concurrent blood cultures or other specimens collected.

Without clinical information, it remains uncertain the extent of the infections. For urine specimens, if the decision is made to only report interpretations applying the uncomplicated UTI breakpoints, a comment should be added to the report, such as:

*"Oral amoxicillin or amoxicillin-clavulanate susceptibility assumes treatment of cystitis only. Different breakpoints are applied for systemic urinary tract infections, and increased dosing is required."*

For infections from non-urinary source, reporting is not reliant to the same degree on provided clinical details. A comment may also be added to these reports, such as:

*"Treatment alone with oral amoxicillin or amoxicillin-clavulanate is not recommended for infections outside of those originating from the urinary tract."*

Alternatively, laboratories may elect to report aminopenicillin susceptibility results across several rows, such as:

For a urine culture:
- Amoxicillin-clavulanate (oral, cystitis only)
- Amoxicillin-clavulanate (oral, urinary source)
- Amoxicillin-clavulanate (iv)

For blood and other non-urine sites:
- Amoxicillin-clavulanate (oral, urinary source)
- Amoxicillin-clavulanate (oral, non-urinary source)
- Amoxicillin-clavulanate (iv)

**2 Consideration of amendments to reporting cascades to include additional second- or third-line agents.**

Traditionally, where susceptibility has been demonstrated, oral amoxicillin therapy has been recommended as a first line agent given the narrow spectrum of activity and good tolerability. The reporting of broader-spectrum agents may be withheld from the final report. However, where the clinical context is uncertain, microbiologist may choose to recommend and report alternate agents. This may necessitate review of laboratory reporting cascades to ensure adequate and appropriate release of susceptibility for second- or third-line agents in line with local and national reporting guidelines.

**3 Adaptability of laboratory information systems to accommodate reporting multiple breakpoints or incorporating additional interpretive comments.**

Separate reporting rules for different agents and routes of administration may require modifications to the Laboratory Information System (LIS). Although deviations from EUCAST guidelines are not encouraged, in circumstances where a laboratory cannot strictly adhere to these revised guidelines, pragmatically they may be required to find short-term work arounds until LIS modifications can be implemented. These temporary solutions will be dictated by the flexibility inherent in the system used, the ability to include interpretive comments, and capacity of reporting microbiologist and/or scientists to amend or comment upon reports.

Depending upon LIS limitations, the following may be considered:

- Specification of IV aminopenicillin ± clavulanic acid breakpoints only for non-urinary isolates with an additional comment specifying concerns about monotherapy and that therapeutic target attainment with oral therapy is not assured.
- Specification of PO amoxicillin ± clavulanic acid susceptibility only in the context of mid-stream urine isolates consistent with uUTI and with an appropriate comment (see point 1).
- Reporting of MIC's or Zone sizes only, with referral to EUCAST breakpoint tables for interpretation, unless Resistance is demonstrated and can be reported. The difficulty for clinicians in result interpretation with this approach makes it least favoured.

### 4 Education and additional training for laboratory staff, microbiologists and clinicians regarding which breakpoints to apply in which circumstance.

Any change in testing or reporting should be accompanied by appropriate education. Scientists and microbiologists need to be educated regarding the revised testing and reporting criteria and training records updated to reflect this. Clinicians also need to be advised (ideally in advance) of any change to reporting and what the implications are for their therapeutic choices and clinical practise. Reference to EUCAST resources in this context may be of benefit.

### 5 Adaptability of automated instruments to accommodate multiple reporting breakpoints.

Proprietary instruments for susceptibility testing such as BD Phoenix, Vitek 2, or BiomicV3 may also experience the same limitations as LIS systems with regards to adaptability for reporting multiple breakpoint interpretations from a single AST result. Additionally, they may not be equipped for adequate bidirectional data flow, making recognition of mid-stream urine isolates and adoption of cystitis-only breakpoints impossible. The use of middleware may assist in this process but is likely to have limitations similar to LIS modifications (see point 3 above).

### 6 Comparison to historical data for hospital antibiograms and resistance surveillance

Altered breakpoints may impact direct comparability of cumulative antimicrobial susceptibility test data across time. Breakpoints indicative of resistance, however, have not been impacted. Hence this issue can be overcome by only comparing rates of resistance to aminopenicillins. There can also be implications for National AMR Surveillance Programs (e.g. AGAR and APAS). Changes in the antimicrobial codes used in the LIS, and their corresponding reference to a specific breakpoint interpretation, requires careful consideration and consistent application and reporting. Regardless of what is reported on the clinician-facing report, it is preferential if the categorical interpretation for all versions of the aminopenicillins are retained in the background of the LIS, thereby enabling transfer of all AST data into surveillance systems.

### 7 Impacts on Antimicrobial Stewardship (AMS) initiatives and clinician confidence.

Minimising the use of broad-spectrum agents, an early switch from IV to oral therapy, correct dosing schedule, and the use of monotherapy where possible, are key AMS program goals. The revised EUCAST reporting for aminopenicillins has the potential to impact these. Liaison with the AMS services with advanced warning of any intended amendments to susceptibility reporting is recommended. Such efforts can negate the concerns that clinicians who are uncertain with "susceptible, increased exposure" reporting, or resistance mechanism implications, may elect to treat with broader spectrum agents or be reluctant to adopt oral follow-on therapy if there is differential reporting of IV and oral formulations. Furthermore, the co-design of report comments can be a helpful approach, especially in situations when breakpoints in brackets are applied. Reference to EUCAST dosing regimens may improve appropriateness of antimicrobial prescribing.



# Aminopenicillins Reporting Recommendations

## Enterobacterales

**Urine cultures**

*Option 1* Interpret and report for localised infection (i.e. cystitis only)

- Apply breakpoints for uncomplicated UTI only
- Report: S or R (oral, cystitis only)
- Comment: "*Oral amoxicillin or amoxicillin-clavulanate susceptibility assumes treatment of cystitis only. Different breakpoints applied for systemic infections, and increased dosing is required.*"

*Option 2* Interpret and report for both localised and systemic UTIs (i.e., cystitis or pyelonephritis)

- Apply both breakpoints for uncomplicated UTI and infections originating from the urinary tract
- Report: S or R (oral, cystitis only), I or R (oral, urinary source), S or R (iv)
- Comment: "*Oral amoxicillin or amoxicillin-clavulanate should be used with increased dosing for systemic or complicated urinary tract infections.*"

**Blood cultures**

May represent systemic UTI or an infection from a non-urinary source

- Apply breakpoints infections originating from the urinary tract
- Report: I or R (oral, urinary source), S or R (iv)
- Comment: "*Oral amoxicillin or amoxicillin-clavulanate should be used with increased dosing for systemic or complicated urinary tract infection. For other indications, only consider at high dose and in combination with another active agent or intervention (e.g. surgery).*"

**All other samples**

- Apply breakpoints-in-brackets for other non-urinary infections
- Report: (I) or R (oral, non-urinary source), S or R (iv)
- Comment: "*Treatment alone with oral amoxicillin or amoxicillin-clavulanate is not recommended for infections outside of those originating from the urinary tract. Consider only for specific indications, at high dose, and in combination with another active agent or intervention (e.g. surgery).*"

# Aminopenicillins Reporting Recommendations

## *Enterococcus* spp.

**Urine samples**

*Option 1* Do not test and report with a comment only

- Comment: "*Enterococci and group B streptococci only rarely cause acute uncomplicated cystitis. Routine susceptibility is not performed. Oral amoxicillin can be used if treatment is clinically indicated. Addition of a beta-lactamase inhibitor (clavulanate) does not add clinical benefit.*"

*Option 2* Interpret and report for localised infection (i.e. cystitis only)

- Apply breakpoints for uncomplicated UTI only (for all enterococci)
- Report: S or R (oral, cystitis only)
- Comment: "*Oral amoxicillin susceptibility assumes treatment of cystitis only. Addition of beta-lactamase inhibitor (clavulanate) does not add clinical benefit.*"

*Option 3* Interpret and report for both localised and systemic UTIs (i.e., cystitis or pyelonephritis)

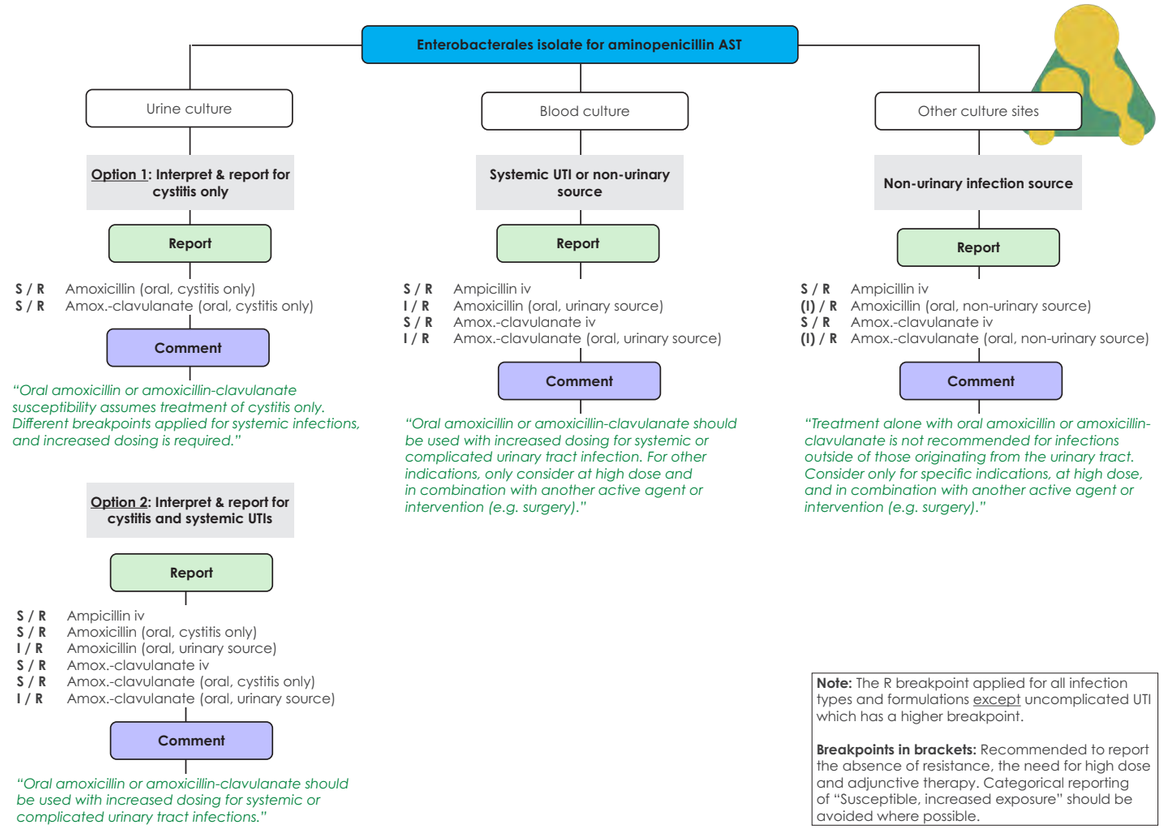
- Apply both breakpoints for uncomplicated UTI and infections originating from the urinary tract (*E. faecalis* only)
- Report: S or R (oral, cystitis only), I or R (oral, other indication), S or R (iv)
- Comment: "*Oral amoxicillin susceptibility assumes treatment of cystitis only. Systemic urinary tract infections caused by E. faecalis requires high dose and in combination with another active agent or other measure (e.g. surgical intervention). Addition of beta-lactamase inhibitor (clavulanate) does not add clinical benefit.*"

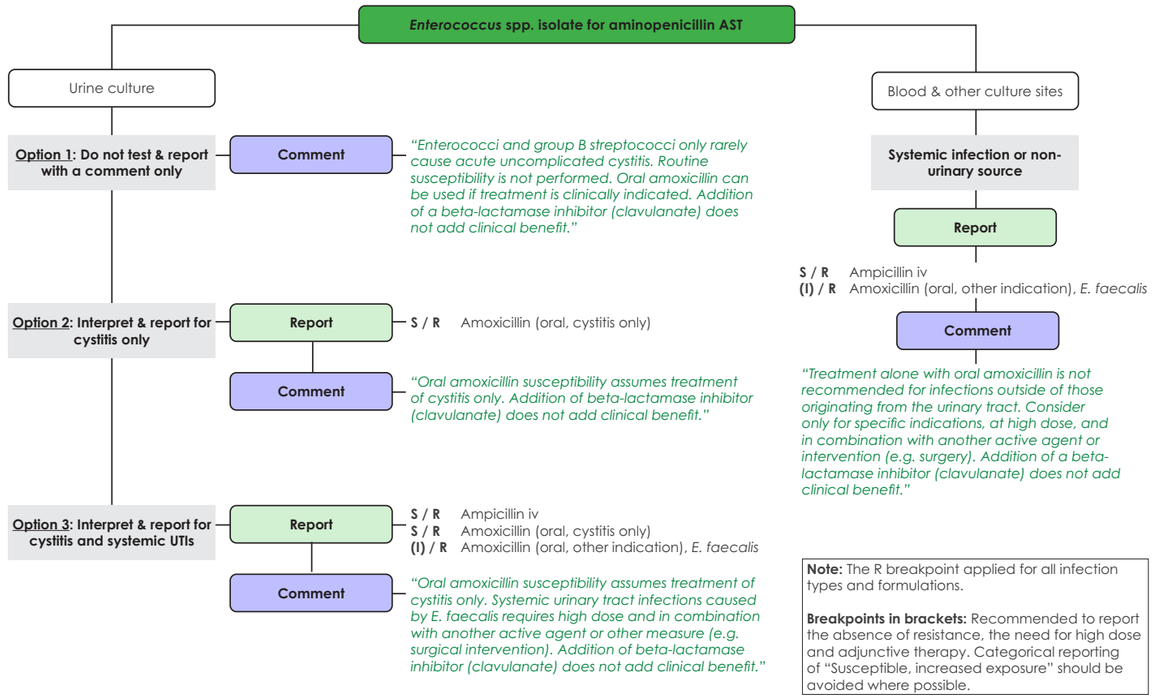
**All other samples**

- Apply breakpoints-in-brackets for other non-urinary infections (*E. faecalis* only)
- Report: (I) or R (oral, other indication), S or R (iv)
- Comment: "*Treatment alone with oral amoxicillin is not recommended for infections outside of those originating from the urinary tract. Consider only for specific indications, at high dose, and in combination with another active agent or intervention (e.g. surgery). Addition of a beta-lactamase inhibitor (clavulanate) does not add clinical benefit.*"

NB: Applies to reporting oral amoxicillin and not oral ampicillin despite that susceptibility is inferred from ampicillin. *E. faecalis* that test resistant to ampicillin with disk diffusion should be confirmed with an MIC test. The addition of a beta-lactamase inhibitor does not add clinical benefit as beta-lactamase production in the enterococci is extremely rare.





# PHOTO QUIZ

A 4-month-old unvaccinated infant was brought to hospital with a 3-day history of prolonged coughing episodes, associated vomiting, and intermittent pauses in breathing. This occurred in the context of concurrent upper respiratory tract symptoms in two older siblings. The mother expressed growing concern, noting a lack of improvement despite several days of illness.

On examination, the infant was afebrile with normal oxygen saturation and no signs of increased work of breathing. Auscultation revealed wheeze and fine crackles, raising initial concern for bronchiolitis.

As part of the diagnostic workup, two nasopharyngeal flocked swabs were collected, one in viral transport medium (VTM) for BioFire FilmArray Respiratory panel (BioMerieux, France) testing, and the other in liquid Amies transport medium for bacterial culture. The BioFire FilmArray Respiratory panel (BioMerieux, France) only detected rhinovirus/enterovirus. The bacterial swab was plated onto charcoal-cephalexin blood agar and incubated at 35°C in ambient air with high humidity for seven days.

On day four of incubation, small pearly colonies appeared as per **Figure 1.** Fine Gram negative rods were appreciated from the Gram stain of the colony shown in **Figure 2**. Identification by matrix-assisted laser desorption ionization time-of-flight mass spectrometry (MALDI-TOF MS) was inconclusive. Additional phenotypic testing demonstrated an oxidase-positive, non-motile organism that failed to grow on MacConkey agar. An azithromycin MIC was determined for the organism using a 0.5 McFarland concentration of the organism on charcoal-cefalexin blood agar incubated at 35 °C in ambient air with high humidity for 48 hours as shown in **Figure 3**.

***Based on the clinical presentation and laboratory findings, what is the most likely causative organism?***

***What is the purpose of cefalexin in the selective culture medium used?***

***What antimicrobial susceptibility testing would be appropriate for this organism, and what methodology would you use?***

**Dr Andrew Walczak**
**Dr I-Ly Joanna Chua**
**Brittany Brennan**
**Sir Charles Gairdner Hospital**
**Pathwest Laboratory | Perth WA**

**Figure 1** Colonies observed on charcoal-cefalexin blood agar at 5 days

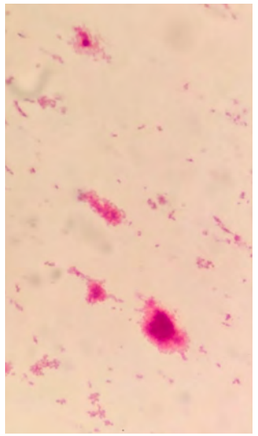


**Figure 2** Microscopic appearance (×1000) of Gram-stain from cultured colony

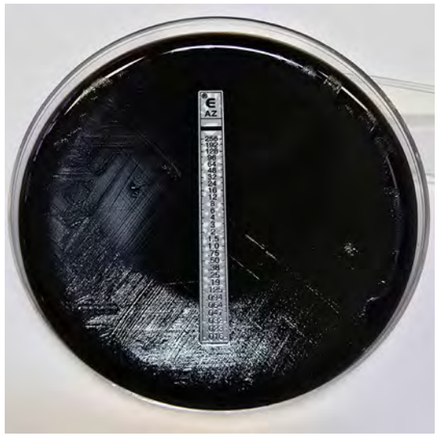


**Figure 3** Azithromycin Etest (BioMérieux, France) on charcoal-cefalexin blood showing organism MIC of 0.125 mg/L.

## ANTIMICROBIAL VIEWPOINTS

# Do antibiotic combinations proposed from *in vitro* studies lead to changes in treatments?

REVIVE by GARDP

**Angela Huttner** is an associate professor of medicine at the University of Geneva, Switzerland, and an attending physician in the Infectious Disease Division of Geneva University Hospitals, Switzerland where she is Head of the outpatient clinic for urinary tract infections. She is editor-in-chief of CMI Communications, the open-access journal of the European Society of Clinical Microbiology and Infectious Diseases (ESCMID). She conducts clinical trials and other studies with a focus on UTI as well as other gram-negative infections and antibiotic optimization, including therapeutic drug monitoring of the beta-lactams, and infection and resistance control.

**We look forward to hosting Angela Huttner as a Plenary Speaker at Antimicrobials 2026, 26th - 28th February 2026, Adelaide Convention Centre, SA.**

This Viewpoint was originally published on the REVIVE website revive.gardp.org, an activity of the Global Antibiotic Research & Development Partnership (GARDP).



## YES, THEY DO.

That is the simple answer to the question I will be focusing on in this viewpoint. The next question is more difficult: Should they? Should an antibiotic combination be given to a patient because it was seen to be effective in *in vitro* experiments? The answer there is neither simple nor satisfying, but it is clear.

*In vitro* studies remove the complexity and nuance of a messy world to provide simple but important mechanistic information. In the reductive world of bacterium versus antibacterial, we gain valuable insights into which antibiotics work to kill or inhibit the growth of bacteria, which do not, and which work even better when applied in combination.

## THE URGE TO ADD A SECOND ANTIBIOTIC

In the clinic, when your previously healthy patient enters septic shock, those insights make it hugely tempting to add a second antibiotic. There is evidence that combination therapy is more effective at bacterial destruction than your single antibiotic alone. Meanwhile, the additional agent is likely to be market-approved with a known safety profile, making risks to your patient seem minimal. In those challenging moments when you watch your patient deteriorate and fall out of your control, it may feel almost unethical to deny her this one last chance. So you add the antibiotic. A few hours later, your patient's blood pressure begins to stabilize. A few hours more, and she no longer requires supplemental oxygen. Still later, she has left the intensive-care unit and will make a full recovery.

That is a story whose simplicity matches that of the stories told by *in vitro* experiments. All of them tell a truth, one truth, but none of them tell the whole truth. In *in vitro* experiments, important variables are left out of the equation. In clinical anecdotes such as this one, important biases are left in.

The whole truth is that combination therapy certainly puts patients under higher selection pressure for resistant bacterial strains and increased risk for side effects, and that we do not yet know how or whether most antibiotic combinations improve clinical outcomes. The part of the Hippocratic oath, which instructs to 'first do no harm', should push us clinicians to produce that missing clinical evidence. This applies especially to those of us in teaching hospitals, where clinical research can be integrated into daily clinical activity.

## WHAT *IN VITRO* STUDIES CAN MISS

By definition, *in vitro* observations leave out important elements of the story, a chief one being host factors. Immune responses are not assessed. The dynamic conditions of the anatomic site of infection are also typically omitted: environmental pH, which influences antibiotic activity, the abundance or

dearth of iron, necessary for bacterial survival, and so on.[1,2] While host factors are not accounted for, many bacterial factors cannot be fully captured either. The development of biofilms and their subsequent effects may take more time than that allotted for the *in vitro* experiment. Bacterial escape mechanisms, such as persistence and tolerance, may not be picked up in *in vitro* experiments.[3] Finally, antibiotic properties are also not fully accounted for.[4] How well does the antibiotic penetrate the tissue where the infection is occurring? How protein-bound will the antibiotic be *in vivo*? Indeed, well-powered randomized clinical trials to date have not returned positive results for combination therapy. The AIDA trial could not show a benefit in adding meropenem to colistin for severe infections due to carbapenem-resistant Gram-negative organisms.[5] The CAMERA2 trial could not show a benefit in adding an anti-staphylococcal beta-lactam antibiotic to vancomycin or daptomycin for staphylococcal bloodstream infections; indeed, the trial had to be stopped early because of increased kidney injury in the combination group.[6] The SAFO[7] and ARREST[8] trials could not show a benefit in adding fosfomycin to cloxacillin or rifampicin to standard antibiotic therapy, respectively, for these infections either.

**"Should an antibiotic combination be given to a patient because it was seen to be effective in *in vitro* experiments? The answer there is neither simple nor satisfying, but it is clear"**

Clinical efficacy is not the only uncertainty. The safety profile of two antibiotics in combination is not simply the sum of their individual safety profiles, as demonstrated by the CAMERA2 trial. As another example, combining intravenous fosfomycin with, say, flucloxacillin would subject patients to higher levels of fluid overload that could much more easily tip them into pulmonary edema than either antibiotic alone.[9]

## WHAT WE REALLY NEED

The truest answer to this question is that we need more clinical data. We should not be fooled by our anecdotal experiences, and we should not let them stand in for clinical evidence. Our biases—and our wishful thinking—may lead us to think that our one-off clinical interventions are safe and effective. In the particular scenario described above, the patient was not responding to antibiotic monotherapy because she had not yet entered steady state. She began to improve once she was in steady state and the single antibiotic had reached therapeutic levels in tissue. The second antibiotic was not going to, and did not, change her trajectory.

We need more clinical evidence from randomized trials with sufficient statistical power to confirm (or refute) any clinical synergy with combination therapy. In Geneva, we will soon launch a randomized trial comparing ceftazidime alone to ceftazidime with fosfomycin in patients with severe bacterial infections.[10] We hope for superior clinical outcomes which is why we will include a placebo and blind both ourselves and participants. We also know, however, that we may not see them— and may well see increased side effects instead.

Yet no matter the outcome, at the end of the trial we will know the answer to “Should they?” That is, we will know it for that particular antibiotic combination. The answer is not simple or satisfying—or ‘one size fits all’. The answer is that we need good-quality clinical data for each combination proposed by those *in vitro* studies before we can know what should, or should not, be done for our patients.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# QUIZ ANSWER

***Bordetella pertussis***

*Bordetella pertussis* is a fastidious, gram-negative coccobacillus and the causative agent of pertussis, also known as “whooping cough.” It is a highly contagious pathogen, classically presenting in three clinical phases:

1. **Catarrhal phase** – non-specific upper respiratory symptoms such as cough and rhinorrhoea.
2. **Paroxysmal phase** – severe coughing fits, often with a characteristic inspiratory “whoop,” cyanosis, and post-tussive vomiting.
3. **Convalescent phase** – gradual resolution of symptoms over week.

Mass immunisation programs introduced in the 1950s in Australia significantly reduced the morbidity and mortality burden, particularly in infants. While, adolescents and adults tend to have relatively mild symptoms, they can contribute to ongoing transmission. Despite widespread vaccination, pertussis continues to circulate, with a global resurgence in 2024, compounded by the emergence of pertactin-deficient and macrolide resistant *B. pertussis* strains that challenge both vaccine efficacy and treatment.

Laboratory diagnosis of *B. pertussis* is challenging due to the organism's fastidious nature and the need for well collected upper respiratory tract specimens. Given the organism’s tropism for ciliated respiratory epithelial cells, nasopharyngeal aspirates or flocked swabs that reach the posterior nasopharynx and are placed in appropriate transport media are recommended. In contrast, throat swabs are less sensitive, and anterior nasal swabs or sputum are unsuitable for culture.

Amies transport medium (with or without charcoal) is appropriate if plating is rapid. For delayed plating (up to 72 hours), specialised media such as Regan-Lowe are recommended.

**What is the purpose of cefalexin in the selective culture medium used?**

Cefalexin acts as a selective agent to inhibit the growth of normal nasopharyngeal flora, allowing for the selective isolation of *B. pertussis*.

The diagnostic yield of culture is low (30–50%) and influenced by multiple factors, including illness stage, antibiotic exposure, specimen type, and time to plating. Sensitivity is highest in the catarrhal and early paroxysmal stages. Historically, *B. pertussis* was cultured on Bordet-Gengou agar which contains blood, potato extract, and glycerine. In contemporary practice, variations of horse blood agar with charcoal and cefalexin are preferred for primary isolation. Colonies typically appear after 3–4 days and have a "half-pearl" appearance. The organism is a small, gram-negative, catalase-positive coccobacillus. While MALDI-TOF MS (Bruker, Germany) can assist with identification, it may not reliably distinguish *B. pertussis* from other *Bordetella* species. It is oxidase-positive, urease-negative, non-motile, and does not grow on MacConkey agar.

Due to the complexity of culturing *B. pertussis*, relatively few laboratories perform this routinely. Molecular methods such as PCR, performed on nasopharyngeal swabs or aspirates, have become the primary diagnostic tool in acute settings. Multiple PCR targets may be used, with IS481 insertion sequence one of the most common targets due to its high copy number and sensitivity (present in up to 238 copies per genome). However, cross-reactivity with *B. holmesii* and *B. bronchiseptica* may result in false-positives without confirmatory testing. The BioFire® FilmArray® Respiratory Panel (Biomerieux, France) uses the pertussis toxin (*ptxP*) promoter region as its target, which is more specific but less sensitive than IS481, potentially leading to missed infection such as may have occured in this case.

**What antimicrobial susceptibility testing would be appropriate for this organism, and what methodology would you use?**

Azithromycin is the first-line agent for both treatment and prophylaxis of *B. pertussis*. Macrolide-resistant B.pertussis (MRBP) strains have been reported globally including Australia, with particularly high prevalence in parts of China, where resistance rates have reached 100%. This resistance presents a significant challenge to the treatment and is under-recognised using traditional diagnostic and surveillance methods.

While no clinical breakpoints have been established by the Clinical and Laboratory Standards Institute (CLSI) or the European Committee on Antimicrobial Susceptibility Testing (EUCAST) for *B. pertussis,* phenotypic susceptibility testing is possible, provided a cultured isolate is available.

- **Agar dilution MIC testing** on Bordet-Gengou agar can be used, with an erythromycin MIC < 0.12 mg/L considered indicative of *in vitro* susceptibility.
- **Gradient strip testing (e.g. Etest, bioMérieux, France)** on charcoal-cefalexin agar has been used for both erythromycin and azithromycin. Resistant strains typically have MICs >256 mg/L.

Molecular detection of resistance adds value in characterising macrolide resistance mutations and supporting public health laboratory surveillance. In an Australian study, whole genome sequencing identified the A2037G mutation in the 23S rRNA gene as the most common mechanism of macrolide resistance.

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# ANTIMICROBIALS 2026

25th Annual Scientific Meeting

**26TH - 28TH FEBRUARY 2026**

**ADELAIDE CONVENTION CENTRE**
**ADELAIDE, SOUTH AUSTRALIA**

## Plenary Speakers

**Angel Huttner**
Switzerland

**Christopher Blyth**
Western Australia

**Mark Gilchrist**
United Kingdom

## Howard Florey Oration

**Christopher Fairley**
Victoria

## ASA President Welcome

On behalf of the Australian Society for Antimicrobials, I would like to invite you to the Society's 25th Annual Scientific Meeting "Antimicrobials 2026", to be held at the Adelaide Convention Centre on Thursday 26th - Saturday 28th February 2026. I am pleased to announce Mark Gilchrist from the UK, Angela Huttner from Switzerland, and Chris Blyth from Western Australia will be joining the Meeting.

Mark will present the plenary "Antimicrobial Stewardship in the Home", Angela will present "Management of Urinary Tract Infections: An Exciting New Frontier?", and Chris will present "Antimicrobial Resistance in Kids".

The 2026 Howard Florey Oration will be delivered by Christopher (Kit) Fairley AO, Director of the Melbourne Sexual Health Centre and Professor of Public Health at Monash University.

The programme's symposia cover many different aspects of antimicrobials and sessions including:

- *Staphylococcus aureus*
- Complex AMR Infections in Vulnerable Populations
- Better Diagnostics, Optimal Treatment
- Molecular Diagnostics
- Emerging Threats and Novel Solutions
- Optimising Antimicrobials in Different Settings – Be Proactive!

We have scheduled Pharmacy and AusCAST workshops for the Saturday afternoon. The agenda includes two literature review sessions featuring Tony Korman's presentation "The Year in Clinical Microbiology" and Elaine Cheong's presentation on "The Year in Infectious Diseases." Additionally, the meeting will consist of oral proffered paper sessions, two poster sessions, and the introduction of a fast-paced Flash Poster Presentation session.

To encourage engagement between delegates and invited speakers, the meeting's registration includes lunches, as well as morning and afternoon teas, and admission to the Howard Florey Dinner.

I am confident you will find the meeting's program both scientifically stimulating and informative. We look forward to meeting you in Adelaide!

Associate Professor Louise Cooley
ASA President

**Register Now!**

www.antimicrobials.com.au #antimicrobials2025

APCCMI2025 BANGKOK

Join us in Bangkok, Thailand for the 20th Asia Pacific Congress of Clinical Microbiology and Infection (APCCMI 2025) & the 51st Annual Meeting of the Infectious Disease Association of Thailand (IDAT) between 2-4 November 2025 at ICONSIAM, Thailand's iconic national landmark.

Group registrations of 10 persons or more will be eligible for a 10% discount. Please contact the APCCMI 2025 Secretariat at email: info@apccmi2025.com for more information.

## Featured Speakers & Sessions

- Prof. Arunaloke Chakrabarti - Current Trends in Management of Invasive Fungal Infections in Critically Ill Patients
- Prof. David L. Paterson - Novel Antobiotics to Combat with Asia AMR Hot Zone
- Prof. Yong Poovorawan - Emerging Viral Pathogens in Asia: The Next Armageddon
- Prof. Robin Patel - Diagnostic Microbiology: How It Can Help Clinicians Fight AMR in the Real World
- Prof. Raymund R. Razonable - Transforming New Evidences in Transplant Infectious Diseases into Clinical Guideline
- Prof. Kim Mulholland - Back to the Future on Vaccination
- Prof. Nicholas Day - Ground Breaking Malaria Research: From Human Challenges to Vaccine Development
- Prof. Eng Eong Ooi - Dengue: Infinity War or Endgame

## Important Dates

| | |
|---|---|
| Sponsorship Application Period | 1 January - 31 March 2025 |
| Abstract Submission | 1 April - 30 June 2025 |
| Early Bird Registration | 2 May - 2 July 2025 |
| Regular Registration | 3 July - 15 October 2025 |

View Full Program

Organized by APSCMI

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AGAR

# AGAR Key Findings 2024

Geoffrey Coombs[1,2], Jan Bell[3], Denise Daley[2], Jon Iredell[4], Shakeel Mowlaboccus[1] on behalf of AGAR

**1** Australian Group on Antimicrobial Resistance, Murdoch University, Murdoch, WA
**2** Australian Group on Antimicrobial Resistance, Fiona Stanley Hospital, Murdoch, WA
**3** Australian Group on Antimicrobial Resistance, Canberra, ACT
**4** Westmead Institute for Medical Research, Westmead, NSW

## Key Findings of the 2024 Australian Group on Antimicrobial Resistance Surveillance Outcome Programs

Using standardised methods, the Australian Group on Antimicrobial Resistance (AGAR) has collected ongoing data on the prevalence of antimicrobial resistance (AMR) in Australia since 1986[1]. Since 2013 AGAR has focused on bloodstream infections and performs three ongoing surveillance programs:

- The Australian *Staphylococcus aureus* Surveillance Outcome Program (ASSOP)
- The Australian Enterococcal Surveillance Outcome Program (AESOP)
- The Gram-negative Surveillance Outcome Program (GnSOP)

In 2024, 55 hospitals, including six private institutions, located across Australia contributed to AGAR (Table 1)

AGAR's focus on bacteraemia allows examination of laboratory-confirmed, invasive infections and comparison of rates over time for hospitals, states and territories. AGAR compares Australian data with the European surveillance program known as EARs-Net, enabling benchmarking and trend projections.

AGAR contributes to the Antimicrobial Use and Resistance in Australia (AURA) surveillance program funded and coordinated by the Australian Government Department of Health, Disability and Ageing, and to the WHO Global Antimicrobial Resistance and Use Surveillance System (GLASS)[2].

Many of the organisms reported by the AGAR surveillance programs are included in the WHO bacterial priority pathogens list, 2024[3].

### The Australian *Staphylococcus aureus* Surveillance Outcome Program (ASSOP)

- A total of 3,358 *Staphylococcus aureus* bacteraemia (SAB) episodes were reported from 1 January to 31 December 2024, 78.6% of which were community-onset. Of all episodes, 15.0% were due to methicillin-resistant *S. aureus* (MRSA) (Figure 1).
- The 30-day all-cause mortality for SAB was 14.0%. In 2024 there was a significant difference in mortality between healthcare-associated MRSA (HA-MRSA) and community-associated MRSA (CA-MRSA) (25.6% and 9.8% respectively, P=0.01) There was no significant difference in mortality between place of onset or methicillin susceptibility.
- The 30-day all-cause mortality for SAB was significantly lower amongst children (<18 years) (1.3%, 3/237) compared to adults (15.3%, 354/2,313) (P < 0.01).
- Osteomyelitis/septic arthritis (21.1%) and skin and skin structure infections (21.0%) were the most common principal clinical manifestations.
- The hospital length of stay following SAB was more than 30 days in 25.7% of patients (30.5% in MRSA, 24.9% in methicillin-susceptible *S. aureus* (MSSA) which was significantly different P = 0.01).
- Resistance to the non-β-lactams in MRSA continued to decline overall, largely due to the substantial decline in the multi-resistant ST239-III clone.
- Two MRSA isolates were confirmed as daptomycin-resistant. Both were isolated in New South Wales (NSW). One, identified as

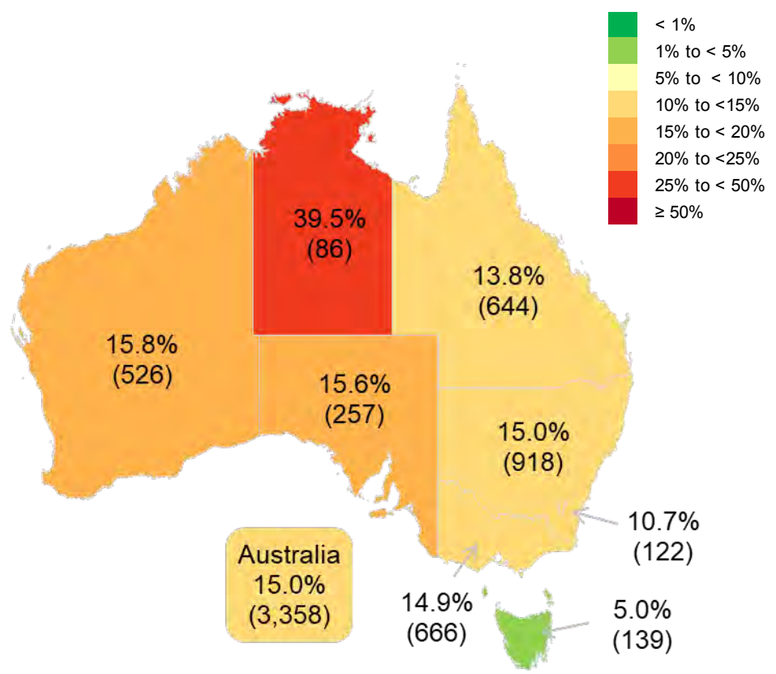



**Figure 1** Percentage of *Staphylococcus aureus* bacteraemia episodes resistant to methicillin defined by EUCAST, Australia, AGAR, 2024

| State or territory | Hospital |
|---|---|
| New South Wales | Children's Hospital Westmead |
| | Concord Repatriation General Hospital |
| | Gosford Hospital |
| | Liverpool Hospital |
| | Nepean Hospital |
| | Prince of Wales Hospital |
| | Royal North Shore Hospital |
| | Royal Prince Alfred Hospital |
| | St Vincent's Hospital, Sydney* |
| | Sydney Children's Hospital |
| | Westmead Hospital |
| | Wollongong Hospital |
| Victoria | Alfred Hospital |
| | Austin Hospital (Austin Health) |
| | Monash Children's Hospital† |
| | Monash Medical Centre (Dandenong Hospital)† |
| | Monash Medical Centre (Monash Health) |
| | Royal Melbourne Hospital |
| | Royal Women's and Children's Hospital |
| | St Vincent's Hospital* |
| Queensland | Cairns Base Hospital |
| | Gold Coast Hospital |
| | Mater Private Hospital Townsville§, # |
| | Prince Charles Hospital** |
| | Princess Alexandra Hospital** |
| | Queensland Children's Hospital** |
| | Royal Brisbane and Women's Hospital |
| | Greenslopes Private Hospital§, # |
| South Australia | Flinders Medical Centre |
| | Royal Adelaide Hospital |
| | Women's and Children's Hospital†† |
| Western Australia | Fiona Stanley Hospital |
| | Joondalup Hospital* |
| | North-west regional WA (Broome, Derby, Fitzroy Crossing, Halls Creek, Karratha, Kununurra, Newman, Onslow, Paraburdoo, Port Hedland, Roebourne, Tom Price, Wyndham) §§ |
| | Perth Children's Hospital§§ |
| | Royal Perth Hospital## |
| | Sir Charles Gairdner Hospital |
| | St John of God Hospital, Murdoch# |
| Tasmania | Launceston General Hospital |
| | Royal Hobart Hospital |
| Northern Territory | Alice Springs Hospital |
| | Royal Darwin Hospital |
| ACT | Canberra Hospital |



ST88-IV, had a daptomycin MIC of 1.5 mg/L with no known daptomycin mutations detected. The second, identified as ST5-V, had a daptomycin MIC of 6.0 mg/L and harboured the S337L MprF mutation.

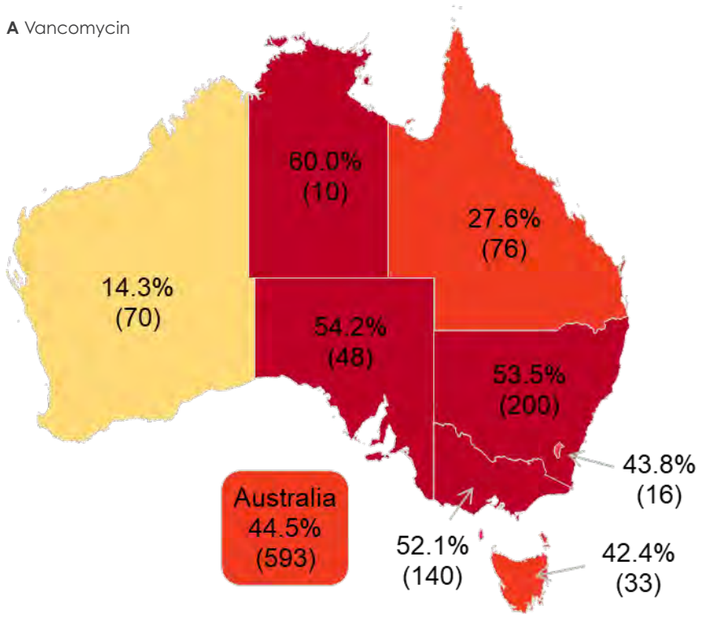
- Approximately 50% of the MRSA harboured the Panton-Valentine leucocidin (PVL) associated genes.
- CA-MRSA were the dominant cause of MRSA bacteraemia. Fifty-one CA-MRSA clones were identified. Apart from Tasmania, the PVL-positive Queensland CA-MRSA clone (ST93-IV) was seen in all states and territories and was the most common CA-MRSA clone in all other regions.
- Two HA-MRSA clones were identified; ST22-IV (EMRSA-15) and ST239-III (Aus 2/3 EMRSA). ST22-IV (EMRSA-15), the dominant HA-MRSA clone, was found in all states and territories except Queensland and the Australian Capital Territory. Neither of the HA-MRSA clones harboured the PVL-associated genes.
- Australia ranks towards the middle in rates of resistance to methicillin in *S. aureus* compared to European countries reporting to EARs-Net.

## The Australian Enterococcal Surveillance Outcome Program (AESOP)

- Between 1 January to 31 December 2024 a total of 1,461 enterococcal bacteraemia episodes were reported. The majority (92.5%) of episodes were caused by *Enterococcus faecalis* (51.5%) or *E. faecium* (41.0%).
- Forty-two *E. lactis* were identified. Prior to 2022 *E. lactis* was classified as *E. faecium*.
- Approximately two thirds (70.6%) of the *E. faecalis* bacteraemia were community-onset, whilst 70.6% of the *E. faecium* bacteraemia were hospital-onset.
- The most frequent source or clinical manifestation of *E. faecalis* bacteraemia was urinary tract infection (23.7%); whilst for *E. faecium* bacteraemia, it was biliary tract infection (19.3%).
- The combined 30-day all-cause mortality for *E. faecalis* and *E. faecium* was 23.6%.
- There was a significant difference in 30-day all-cause mortality between *E. faecalis* (15.5%) and *E. faecium* (34.0%) ($P$ <0.01).

* Public/Private hospital
† Microbiology services provided by Monash Medical Centre (Monash Health)
§ Microbiology services provided by Sullivan Nicolaides Pathology
# Private hospital
** Microbiology services provided by Pathology Queensland Central Laboratory
†† Microbiology services provided by SA Pathology, Royal Adelaide Hospital
§§ Microbiology services provided by PathWest Laboratory Medicine WA, Queen Elizabeth II Medical Centre
## Microbiology services provided by PathWest Laboratory Medicine WA, Fiona Stanley Hospital

Note: In 2024, one hospital from NSW was not able to contribute for Quarter Four.



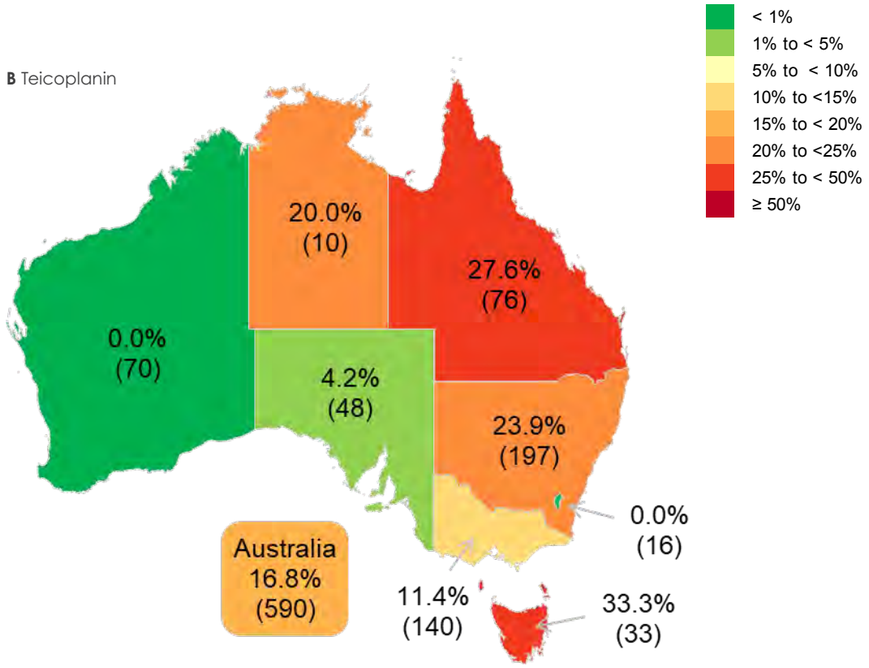




**Figure 2** Percentage of *Enterococcus faecium* bacteraemia episodes resistant to vancomycin (A) and teicoplanin (B)



However, there was no significant difference between vancomycin-resistant and vancomycin-susceptible *E. faecium* episodes (33.3% and 34.2% respectively) ($P = 0.85$).

- The length of stay in hospital following enterococcal bacteraemia was more than 30 days for 20.9% of patients.
- Overall, 44.5% of *E. faecium* bacteraemia were phenotypically vancomycin resistant (Figure 2). However, in 2024, 48.8% of *E. faecium* harboured *vanA* and/or *vanB* genes (*vanA* 19.4%, *vanB* 28.9%, *vanA* and *vanB* 0.5%). In 2023, 53.2% of *E. faecium* harboured *vanA* or *vanB* genes (*vanA* 14.6%, *vanB* 38.3%).
- For the vancomycin-resistant *E. faecium* bacteraemia, 37.5% were *vanA* positive. *vanA* was the dominant genotype in NSW, Queensland and Tasmania.
- Fifty-six *E. faecium* multi-locus sequence types (STs) were identified, of which ST78, ST1424, ST17, ST80, ST1421, ST117, ST796 and ST555 were the most frequent.
- *vanA* genes were detected in ten STs, *vanB* genes were detected in 15 STs and both *vanA* and *vanB* in two STs. The clonal diversity of *E. faecium* harbouring *van* genes varied across Australia.
- Five linezolid-resistant *E. faecalis*, four from Victoria and one from NSW, were confirmed in 2024. MICs ranged from 6.0 to 8.0 mg/L and all harboured the *optrA* linezolid resistant gene.
- One linezolid-resistant *E. faecium* from Victoria was confirmed. The linezolid MIC was 6.0 mg/L and the isolate harboured the *optrA* gene.
- The percentage of *E. faecium* bacteraemia isolates that are resistant to vancomycin in Australia is significantly higher than that seen in almost all European countries reporting to EARs-Net

## The Gram-negative Surveillance Outcome Program (GnSOP)

- From 1 January 2024 to 31 December 2024, a total of 10,340 episodes of gram-negative bacteraemia were reported, including *Enterobacterales* (90.7%), *Pseudomonas aeruginosa* (7.8%) and *Acinetobacter* (1.5%). Three genera – *Escherichia* (59.8%), *Klebsiella* (21.3%) and *Enterobacter* (5.7%) – contributed 86.8% of all *Enterobacterales* bacteraemias.
- The 30-day all-cause mortality rate for gram-negative bacteraemia was 13.5% (12.9% for *Enterobacterales*, 19.7% for *P. aeruginosa*, and 12.9% for *Acinetobacter* species).
- Urinary tract infections were the most frequent source of bacteraemia or clinical manifestation (*Enterobacterales* 43.7%; *P. aeruginosa* 25.8%). For *Enterobacterales*, device-related urinary tract infections were more common in hospital-onset than community-onset episodes (20.5% versus 7.8%, $P < 0.0001$).
- There was a significant difference in 30-day all-cause mortality between children and adults (4.9% versus 13.4%, respectively, $P < 0.01$) for *Enterobacterales* bacteraemia episodes. For adults aged 18-64 years, the rate was 8.1%, increasing to 13.0% for those in the 65-74 age group, and 18.7% in those aged greater than 74 years.
- For *E. coli* isolates, 83.4% were from community-onset episodes and 14.1% of community-onset *E. coli* isolates were ceftriaxone resistant.
- In 2024, 17.5% of *E. coli* (community-onset 16.2%; hospital-onset 23.9%) exhibited an extended-spectrum β-lactamase (ESBL) phenotype, up from 15.2% in 2023 (CO 14.1%; HO 21.6%). Similarly, 12.9% of *K. pneumoniae* complex isolates (CO 10.1%; HO 20.4%) had an ESBL phenotype, an increase from 8.5%.
- Third-generation cephalosporin resistance in *E. coli* isolates increased to 15.8% in 2024 (up from 13.5% in 2023), the most notable rises were in NSW (18.0%, up from 14.6% in 2023), and Tasmania (12.3%, up from 4.9% in 2023). In *K. pneumoniae* complex isolates, resistance increased in South Australia (23.4%, up from 3.7% in 2023), and Queensland (12.8%, up from 4.7% in 2023) (Figures 3 and 4).

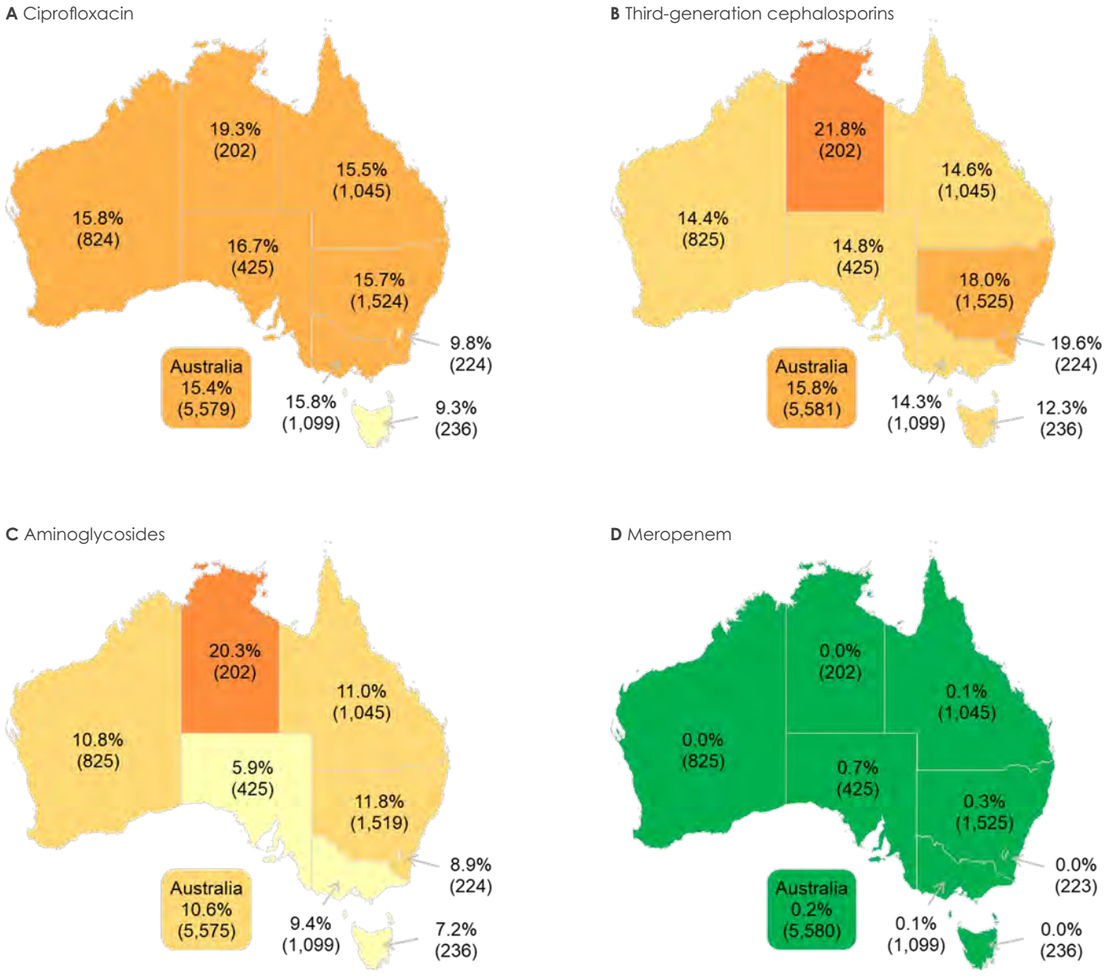



**Figure 3** Percentage of *Escherichia coli* from patients with bacteraemia with resistance, as defined by EUCAST, to ciprofloxacin (A), third-generation cephalosporins (B), aminoglycosides (C) or meropenem (D), Australia, AGAR, 2024

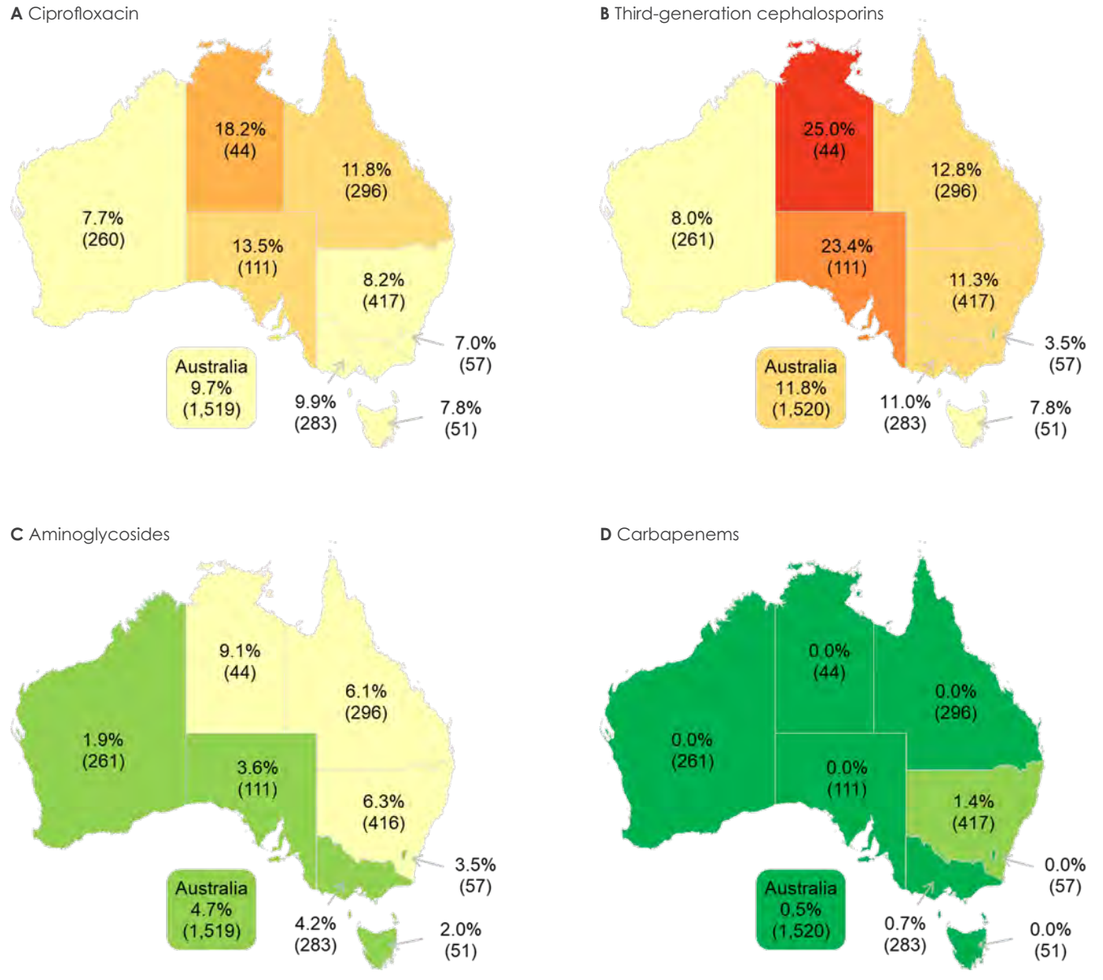



**Figure 4** Percentage of *Klebsiella pneumoniae* complex isolates from patients with bacteraemia with resistance, as defined by EUCAST, to ciprofloxacin (A), third-generation cephalosporins (B), aminoglycosides (C) or meropenem (D), Australia, AGAR, 2024

- Fluoroquinolone resistance in *E. coli* increased to 15.4% in 2024 (up from 14.5% in 2023), most notably in Queensland (15.5%, up from 11.4% in 2023).
- Just over a quarter (26.6%) of *E. coli* and 11.4% of *K. pneumoniae* complex isolates were classified as multidrug-resistant, no change from the 2023 survey.
- Rates of carbapenemase-producing *Enterobacterales* (CPE) remained low among bacteraemic isolates (0.4%). In 2024, over three-quarters (28/36, 77.8%) of CPE carried a $bla_{NDM}$ and/or $bla_{OXA-48}$-like gene, only 19.4% ($n$ = 7) carried a $bla_{IMP-4}$ gene.
- Compared to European countries reporting to EARs-Net, Australia ranks in the bottom quarter for rates of resistance to fluoroquinolones in *E. coli* and *K. pneumoniae* complex isolates, and to third-generation cephalosporins in *K. pneumoniae* complex isolates. It ranks towards the middle in rates of resistance to third-generation cephalosporins in *E. coli*

**AGAR publishes detailed annual reports on each program on its website, and also in the Communicable Diseases Intelligence (CDI) journal.**


## ASSOP and AESOP Reference laboratories

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## GnSOP Reference laboratories

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The 30-day all-cause mortality for SAB was 14.0%

The combined 30-day all-cause mortality for *E. faecalis* and *E. faecium* was 23.6%

The 30-day all-cause mortality rate for gram-negative bacteraemia was 13.5%


**References**

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