Penicillin Allergy Delabelling:
An antimicrobial stewardship strategy

National Medicines Symposium 2026

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Centre for Antibiotic Allergy and Research

What are the **five things** we need to know about *penicillin allergy delabelling?*

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1. What is **penicillin allergy** *delabelling?*

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Penicillin Allergy *Delabelling*



CURRENT OPINION

Antimicrobial stewardship's new weapon? A review of antibiotic allergy and pathways to 'de-labeling'

Jason Trubiano[a] *and Elizabeth Phillips*[b,c]

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2. **Penicillin allergy** is a *public health crisis*?

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Penicillin Allergy *Impact*

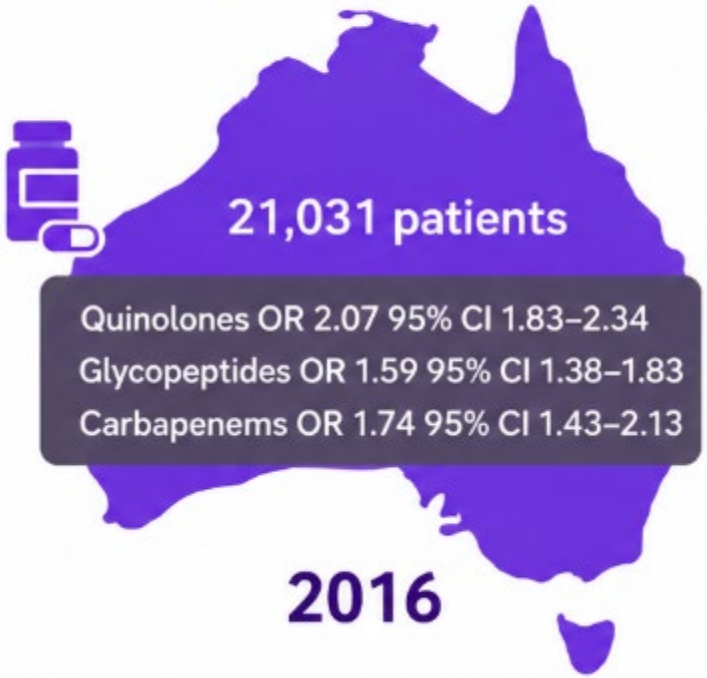
BURDEN

1 / 10



Report a penicillin allergy

IMPACT



IMPACT

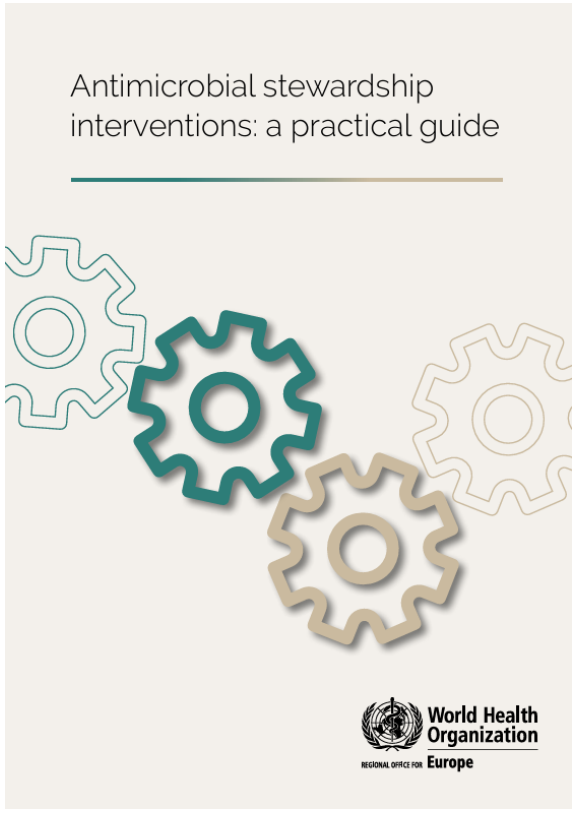
- **Increased AMR** (inc. *C. difficile*)
- **Inferior Patient outcomes** (inc. mortality)
- **Inferior Hospital outcomes** (inc. $, readmission, LOS)

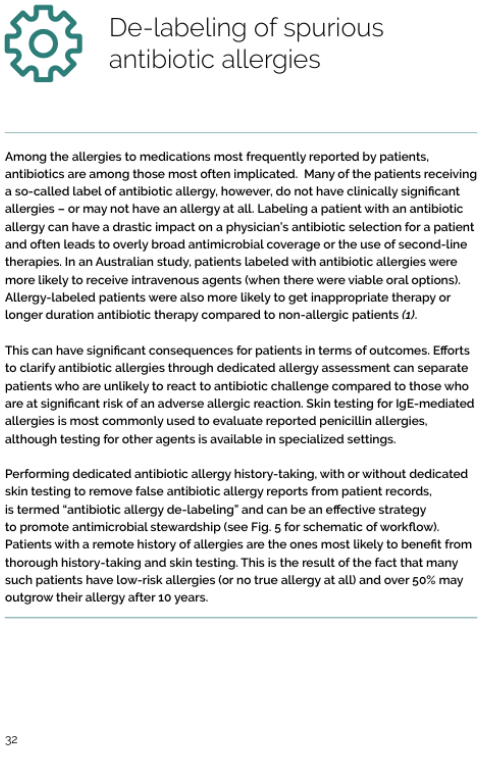
Trubiano *et al.* JAC 2016; 71(6): 1715
Arnold *et al*. JACI-IP 2023; 11(10): 3133
Blumenthal *et al* Lancet 2019; 393 (10167): 183
Waldron *et al*. Transplant Infect Dis 2022; 24: E13955
Fu *et al.* Lancet Infectious Diseases 2024

SAME GLOBAL BURDEN AND IMPACT CONCERNS

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Penicillin Allergy *Global Health Response*





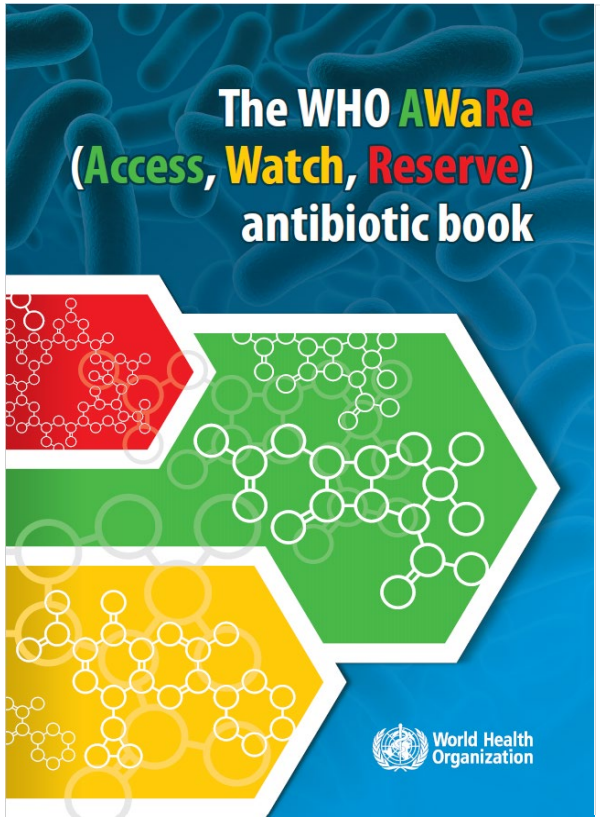
De-labeling of spurious antibiotic allergies

Among the allergies to medications most frequently reported by patients, antibiotics are among those most often implicated. Many of the patients receiving a so-called label of antibiotic allergy, however, do not have clinically significant allergies – or may not have an allergy at all. Labeling a patient with an antibiotic allergy can have a drastic impact on a physician's antibiotic selection for a patient and often leads to overly broad antimicrobial coverage or the use of second-line therapies. In an Australian study, patients labeled with antibiotic allergies were more likely to receive intravenous agents (when there were viable oral options). Allergy-labeled patients were also more likely to get inappropriate therapy or longer duration antibiotic therapy compared to non-allergic patients *(1)*.

This can have significant consequences for patients in terms of outcomes. Efforts to clarify antibiotic allergies through dedicated allergy assessment can separate patients who are unlikely to react to antibiotic challenge compared to those who are at significant risk of an adverse allergic reaction. Skin testing for IgE-mediated allergies is most commonly used to evaluate reported penicillin allergies, although testing for other agents is available in specialized settings.

Performing dedicated antibiotic allergy history-taking, with or without dedicated skin testing to remove false antibiotic allergy reports from patient records, is termed "antibiotic allergy de-labeling" and can be an effective strategy to promote antimicrobial stewardship (see Fig. 5 for schematic of workflow). Patients with a remote history of allergies are the ones most likely to benefit from thorough history-taking and skin testing. This is the result of the fact that many such patients have low-risk allergies (or no true allergy at all) and over 50% may outgrow their allergy after 10 years.

“ antibiotic allergy de-labelling can be an effective strategy to promote antimicrobial stewardship” [2021]



3. Allergy to antibiotics

Key messages

- True severe allergy to antibiotics is rare and allergies are often over-reported
- Beta-lactam antibiotics (penicillins and cephalosporins) of the Access group are among the most effective and safe medicines for many infections, and they should only be avoided when there is a high suspicion of true allergy.
- Cephalosporins and carbapenems can be safely used in most cases of non-severe penicillin allergy.
- All patients who are labelled as allergic should be carefully evaluated and their antibiotic allergy risk level should be determined.
- Routine skin testing before prescribing a beta-lactam antibiotic (e.g. penicillin or amoxicillin) is not needed, and direct oral challenge can be performed in carefully selected low-risk phenotypes.

The AWaRe book does not include alternative antibiotic options in cases of allergy to first-choice antibiotics. The reason for this is that a true allergy to antibiotics (true meaning an allergic reaction that is immune-mediated) is rare and the AWaRe book focuses on the empiric treatment options for most patients. Beta-lactam antibiotics of the Access group are among the most effective and safe medicines for many infections. Avoiding the use of this class, unless clearly justified because of severe allergy, exposes the patient to the risk of receiving suboptimal treatment for their infection.

This chapter on allergy describes general principles of the mechanisms of allergies to antibiotics and the implications for treatment. From the perspective of antibiotic stewardship, it is important to avoid over-diagnosing antibiotic allergies. Such over-diagnosis often occurs with antibiotics in the Access category (e.g. with penicillins) and can lead to the subsequent prescription of antibiotics in the Watch category, for example, macrolides that may be less effective and less safe. The detailed management of allergic reactions is beyond the scope of this chapter.

Definitions

- An **allergy** is a reaction of the immune system to a "non-self" substance.
- An **adverse reaction** is a response to a medicine which is harmful and unintended, and which occurs at the doses normally used *(23)*. Most adverse

“ direct oral challenge can be performed in carefully selected low risk phenotypes” [2022]

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3. *Non-allergists* can safely assess **penicillin allergy**

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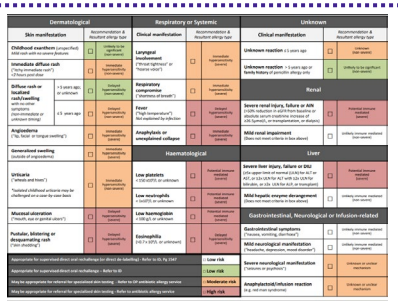
Penicillin Allergy *Assessment* via Non-Allergists

Our Risk Assessment Tools

PEN-FAST PENICILLINS

3-point clinical decision rule

96.3% NPV Score < 3



Phenotyping Tool

Adult & Paediatric Validated

Trubiano *et al.* JAMA Intern Med 2020; 180 (5): 745
Devchand *et al.* JACI In Pract 2019
Rischin *et al.* J Paediatr Child Health 2022

PEN-FAST PENICILLINS

CRITERIA			POINTS
PEN	Penicillin allergy	History of penicillin allergy	(Prerequisite)
F	Five or fewer years ago	Allergy event occurred ≤ 5 years ago	2 points
A	Anaphylaxis/Angioedema OR SCAR*	History of anaphylaxis, angioedema OR severe cutaneous adverse reaction*	2 points
S	Treatment required†	Treatment was required for the allergy episode†	1 point
	(Total score)	Sum of points (range 0–5)	

INTERPRETATION:

PEN-FAST score < 3 = Low risk of penicillin allergy

In the validation cohort, only 3.7% had a positive allergy test

Negative predictive value 96.3% (95% CI, 94.1%–97.8%)

AUC 0.81 (0.75, 0.86)

THE 4 RISK GROUPS

- Very low risk (0 points): 0.6%
- Low risk (1 or 2 points): 5%
- Moderate risk (3 points): 20%
- High risk (4 or 5 points): 50%

Risk of positive penicillin test result

FOR LOW-RISK PATIENTS:

Penicillin skin testing may not be required

Consider direct oral challenge or delabelling strategies

* Severe cutaneous adverse reaction (SCAR): For phenotypes that are consistent with DRESS, AGEP, SJS/TEN or any blistering eruption OR eruption that involves mucous membranes.

† Treatment required: For systemic treatments or if unknown.

Note: Does not apply to AIN, serum sickness, DILI or isolated drug fever.

Trubiano JA, et al. *JAMA Intern Med.* 2020;180(5):745–752.

PEN-FAST PRIMARY AND SECONDARY VALIDATIONS

Australia	(2)
USA	(6)
Canada	(1)
France	(2)
Germany	(2)
Singapore	(1)
Ireland	(1)

PUBLISHED EXPERIENCES (IMPLEMENTATION / USE)

USA	Emergency department, Inpatient (ID/AMS pharmacists), Pregnancy, STI clinic
Canada	Pregnancy
Australia	Inpatient (ID/AMS pharmacists), LMIC, Multiple countries
Germany	Primary care, Critical illness (ICU), Beta-lactams, LMIC
Turkey	Paediatrics
France	Primary validation (anaphylaxis), Maxillofacial surgery
Ireland	Primary validation (anaphylaxis)
UK	LMIC, Multiple countries
New Zealand	LMIC, Multiple countries
South Africa	LMIC
Multiple countries (UK, Australia, New Zealand)	LMIC

= Population in

Validation studies: Trubiano *et al.* JAMA IM 2020; Copaescu *et al.* JAMA IM 2023; Piotin *et al.* Ann Allergy Asthma Immunol. 2022; Su *et al.* JAMA IM 2023; Gocebe *et al.* J Dtsch Dermatol Ges 2026; Lim *et al.* Clin Exp Allergy 2025; Su *et al.* JACI Global 2026; Dugan *et al.* Clin Ther 2026; Gocebe *et al.* Clin Transl Allergy 2026

Risk Assessment Tools: 1-1-1 Urticaria (Sabato *et al.* JACI Pract 2024); EAACI/EDNA (Romano *et al.* Allergy 2020); Chiriac Score (Chiriac *et al.* JACI Pract 2018); Beta-lactam predictor (Labella *et al.* Allergy 2026); Blumenthal Pathway (Blumenthal *et al.* Ann Allergy Asthma Immunol 2015)

Non-allergist vs. allergist

(PEN-FAST < 3 use by either group)
aOR 0.99 (95% CI -.65-1.51)*
No associated increase in AEs

Powell *et al.* Clin Micro Infect 2026 May 16

4. **Penicillin allergy** *delabelling* is **safe** with a significant resultant **AMS impact**

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Penicillin Allergy *Delabelling* via Direct Oral Challenge (DOC)

Direct Oral Challenge (DOC)

PALACE Study

DOC non-inferior to skin testing then oral challenge

95.3% low-risk negative on DOC at Day 5

Meta-analysis of > 9500 patients 96.5% negative

Copaescu *et al.* JAMA Intern Med 2023; 152 (1): 39

Research

JAMA Internal Medicine | Original Investigation

Reaction Risk to Direct Penicillin Challenges
A Systematic Review and Meta-Analysis

Kimberly G. Blumenthal, MD, MSc; Liam R. Smith, BS; Jushin Teg S. Mann, BS; Ingrid Salciccioli, MBBS; John J. O. Accarino, MD; Ruchi J. Shah, MD; Fatima I. Alvi, MD; António Cardoso-Fernandes, MD; Renato Ferreira-da-Silva, MPharm; Holger J. Schunemann, MD, PhD; Bernardo Sousa-Pinto, MD, PhD



IS IT ENOUGH EVIDENCE?

Table 1. Results of Univariable Meta-Regression and Subgroup Analyses for Frequency of Reactions Following Direct Penicillin Challenges

Variable	No. of studies	No. of participants (No. of reactions)	Frequency of reactions (95% CrI), %	I^2, %	OR (95% CrI)
All studies	56[14-69]	9225 (438)	3.5 (2.5-4.6)	99.7	NA
Study characteristics					
Location					
North America	25[14, 15, 17, 22, 25-28, 31, 34, 36, 37, 39, 40, 43, 44, 48, 49, 56, 57, 59, 65, 67-69]	4861 (167)	2.3 (1.5-3.1)	97.7	0.36 (0.20-0.61)[a]
Europe	18[18, 19, 30, 32, 35, 45-47, 50, 52-55, 58, 60-62, 66]	3051 (213)	5.9 (3.4-9.0)	99.1	NA
Asia or Oceania	12[16,20,23,24,29,33,38,41,42,51,63,64]	1276 (56)	4.6 (2.0-10.4)	98.7	NA
Age group					
Children (<18 y)	21[15, 16, 19-21, 25, 29, 30, 38, 40, 45-47, 49, 50, 53-55, 58, 61, 66]	5005 (315)	6.6 (4.6-9.5)	99.2	3.37 (1.98-5.98)
Adults (≥18 y)	21[17, 18, 22-24, 26, 31, 32, 35, 37, 39, 42, 44, 56, 57, 60, 62, 64, 65, 67, 69]	2053 (53)	2.2 (1.2-3.2)	93.0	1 [Reference]
Patient setting					
Outpatient	30[14-16, 19, 22, 26-30, 33-35, 38-40, 44-46, 48-50, 52, 53, 55, 58, 60, 61, 65, 68]	4585 (254)	4.2 (2.8-6.0)	99.4	2.19 (1.08-4.75)
Inpatient	14[17, 18, 23, 24, 31, 32, 37, 42, 51, 57, 62, 64, 67, 69]	1356 (37)	2.3 (1.1-3.6)	92.0	1 [Reference]
No specific participant population	50[14-36,38-43,45-55,57-59,61-64,67-69]	8405 (426)	3.9 (2.8-5.2)	99.6	NA

Blumenthal *et al.* JAMA Intern Med 2025; 1;184 (11): 1375

5 more RCTs

Mustafa *et al.* JACI IP 2019;
Rose *et al.* ICM 2024;
Lillis *et al.* CID 2024;
De Luca *et al.* JAMA Surg 2025;
Patrawala *et al.* JACI IP 2025

Yes!
(Level 1A)

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Penicillin Allergy *Delabelling* AMS Impact & Implementation

iNAAN
International Network of Antibiotic Allergy Nations

Hybrid Type 2 Implementation Trial

P Inpatient adult PEN* allergy

I DOC + Audit & Feedback

C No DOC

PRIMARY

Implementation Outcomes
Adoption of penicillin allergy toolkit

Effectiveness Outcomes

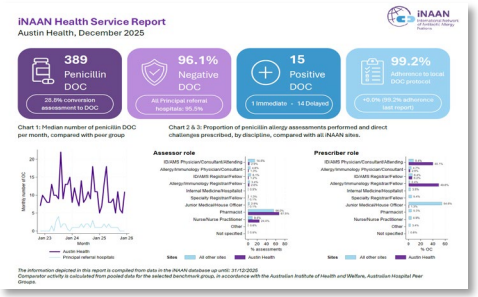
No. delabelled (n, %)

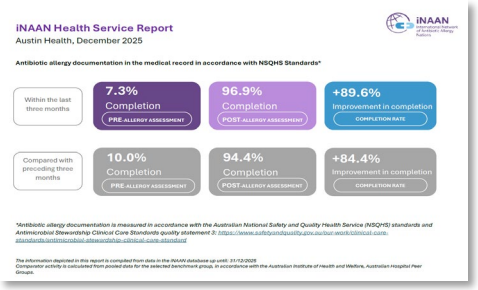
* Penicillin

Implementation Strategy: Digital Audit and Feedback (bimonthly)

Implementation Strategy

A&F: iNAAN HSR





Mitri *et al.* PLOS One 2025

8 Countries in 40 Hospitals

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Penicillin Allergy *Delabelling* AMS Impact

Global Implementation

iNAAN
International Network of Antibiotic Allergy Nations

40 Hospitals & 8 countries

95.5% low-risk negative on DOC at Day 5 (0.4% SAE)

Safe irrespective of **"low-risk" criteria**

No difference in DOC safety when performed **by allergist OR non-allergist**

Mitri *et al.* Clin Infect Dis 2026; April 1:ciag083/082
Mitri *et al.* Allergy 2026 Jun 12
Powell *et al.* Clin Micro Infect 2026 May 16

Prescribing Impacts



13.25 RR Any penicillin
(95% CI 7.82, 22.46)

0.69 RR WHO HPCIA
(95% CI 0.52, 0.91)

0.73 RR WHO Watch & Reserve
(95% CI 0.60, 0.89)

Target Trial Emulation (TTE) analysis (892 DOC; 960 control)

AMR Impacts



0.57 RR MDGRN
(95% CI 0.33, 0.99)

0.58 RR *C. difficile*
(95% CI 0.17, 2.03)

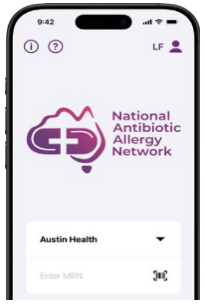
No impact on mortality or hospital stay

MDGRN, Multi-drug-resistant gram negative

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Penicillin Allergy *Delabelling* AMS Implementation

ADOPTION

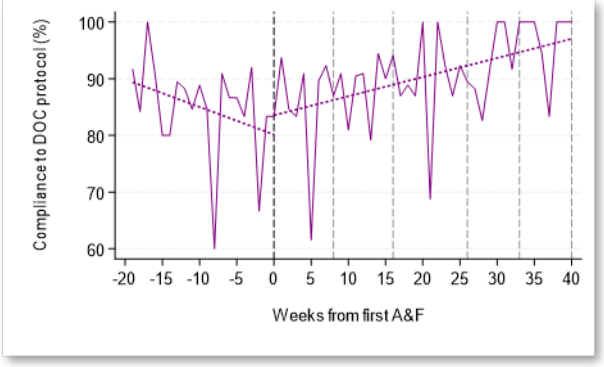


77 clinicians adopted within 6-months

Median **1.5 users**
IQR 1,3 / hospital

FIDELITY

Protocol Compliance Over Time

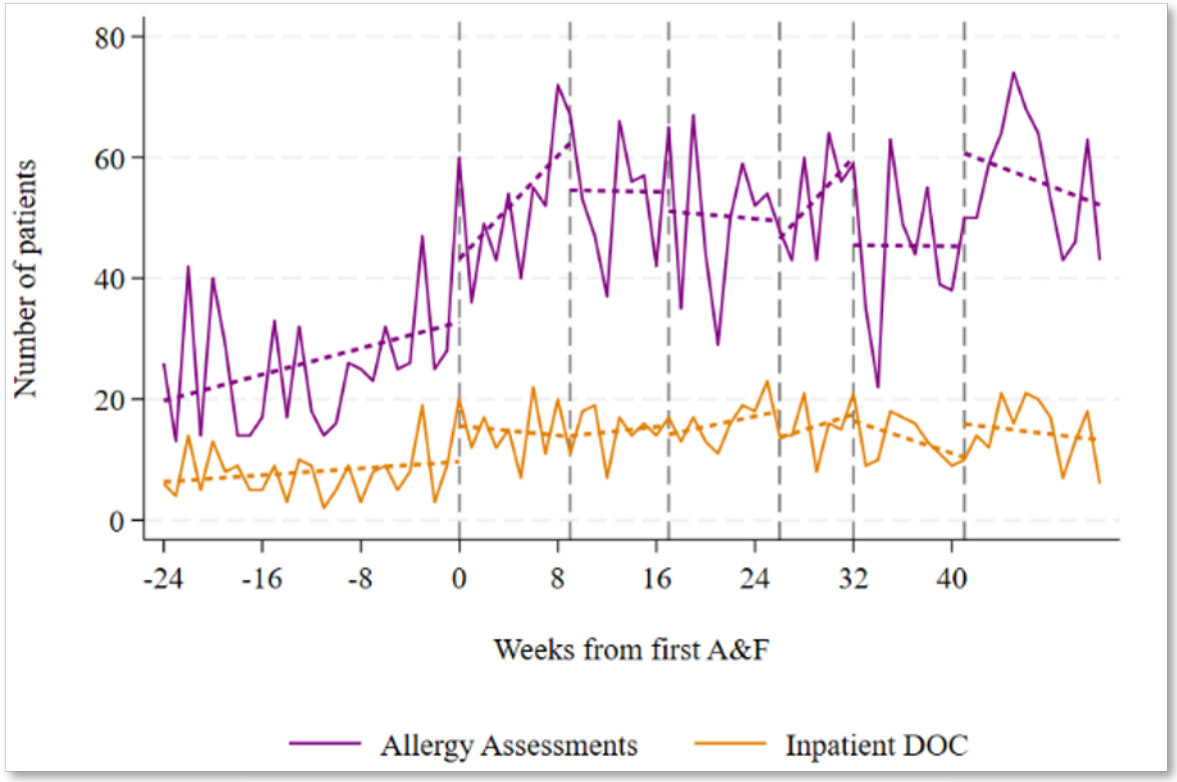


90%

Local site protocol adherence

Improved following Audit & Feedback

SUSTAINABILITY



Immediate increase 1st episode
DOC (10/week, 95%CI 3.18-16.2)
Stable over next 6 episodes (n=18)

Mitri *et al.* CID 2026. doi.org/10.1093/cid/ciag083

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5. **Penicillin allergy** *delabelling* should be the standard of care in Australian Hospitals

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Penicillin Allergy *Delabelling* Meeting National Standards

Quality statement 3

3

Quality statement 3 – Adverse reactions to antimicrobials

When an adverse reaction (including an allergy) to an antimicrobial is reported by a patient or recorded in their healthcare record, the active ingredient(s), date, nature and severity of the reaction are assessed and documented. This enables the most appropriate antimicrobial to be used when required.

Purpose

To ensure the accurate assessment and documentation of patient adverse reaction information to allow for optimal antimicrobial prescribing. This means using the most appropriate and narrow-spectrum antimicrobial possible, while ensuring that potential harms (such as anaphylaxis) are avoided.

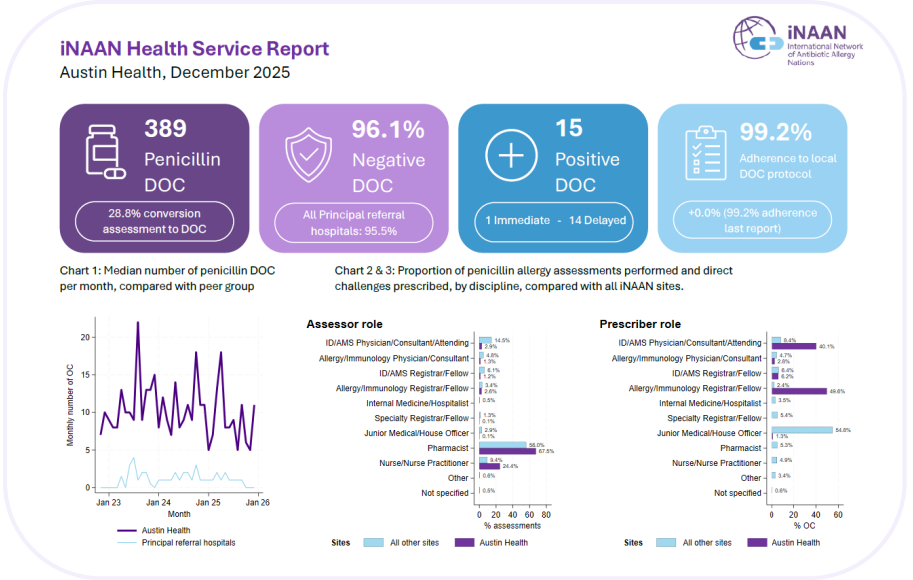
What the quality statement means

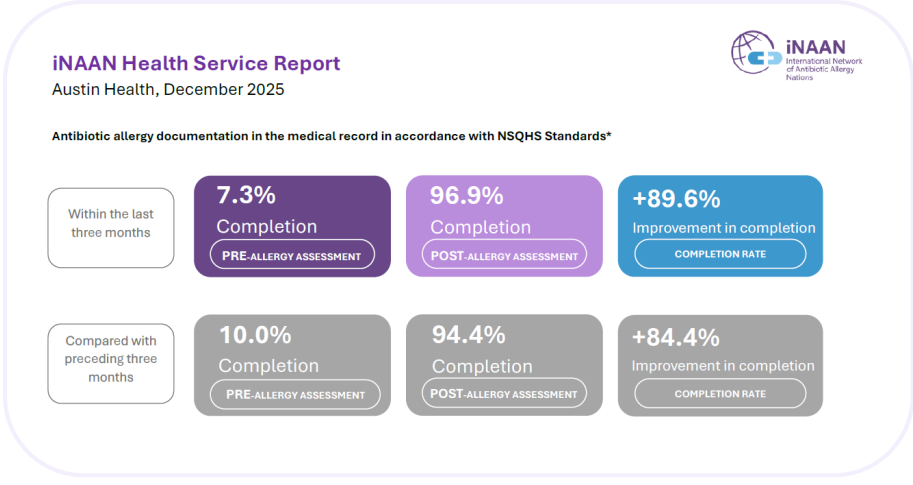
For patients

Adverse reactions are any unwanted effects of a medicine. Many adverse reactions are expected side effects of medicines, and can range from mild to severe. An 'allergic reaction' is one type of adverse reaction.

If you have ever had an unwanted response to a medicine used to treat an infection, even if it was many years ago, talk to your clinician. They will ask you about what happened to find out whether it was because of the medicine, how severe it was and what it means for your care. As a result, your treatment may change and your healthcare record will be updated. Important changes will be communicated to you and your regular doctor.

If you have had an adverse reaction to a medicine, it is important that this information is added to your healthcare record. You can also review and update your information in your My Health Record. Carry a list of your medicines with you, and make sure that it includes the most up-to-date information about your previous adverse reactions to medicines, including allergies.





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43
Sites eligible

403
Health Service Reports

7
AIHW Hospital Peer Groups

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Penicillin Allergy *Delabelling* Impacting Policy

Impacts on medical record documentation

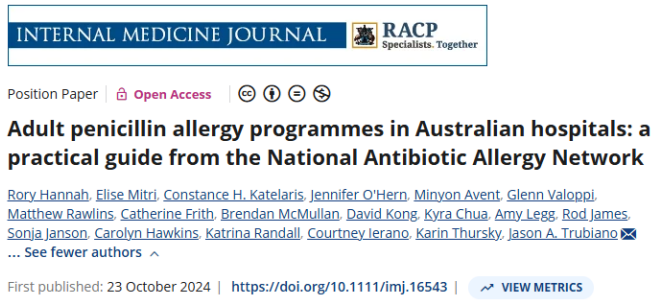
Aligned with Standard 3

Discipline	Adherence PRE-allergy assessment No. (%)		Adherence POST-allergy assessment No. (%)	No.
Overall Assessments	5419	591 (10.9)	4244 (78.3)	690
Assessments, by discipline	360	42 (11.7)	290 (80.6)	71
Allergist/Immunologist	1037	85 (8.2)	753 (72.6)	211
Non-allergist medical practitioner	3340	385 (11.5)	2694 (80.7)	321
Pharmacist	582	79 (11.6)	507 (74.3)	87
Nurse/Nurse practitioner	582	79 (11.6)	507 (74.3)	87

Mitri *et al.* CID 2026

NAAN Guideline - Adults

- ✓ Evidence-based national consensus
- ✓ Supports safe prescribing & implementation of delabelling programs
- ✓ Aligned with global best practice



INTERNAL MEDICINE JOURNAL | RACP Specialists. Together

Position Paper | Open Access

Adult penicillin allergy programmes in Australian hospitals: a practical guide from the National Antibiotic Allergy Network

Rory Hannah, Elise Mitri, Constance H. Katelaris, Jennifer O'Hern, Minyon Avent, Glenn Valoppi, Matthew Rawlins, Catherine Frith, Brendan McMullan, David Kong, Kyra Chua, Amy Legg, Rod James, Sonja Janson, Carolyn Hawkins, Katrina Randall, Courtney Ierano, Karin Thursky, Jason A. Trubiano

... See fewer authors

First published: 23 October 2024 | https://doi.org/10.1111/imj.16543 | VIEW METRICS

*** NAAN Guideline – 'Kids' under development**

Data informing national & international guidelines

EAACI EUROPEAN ACADEMY OF ALLERGY AND CLINICAL IMMUNOLOGY

THERAPEUTIC GUIDELINES®

Future 'Big Data' Potential

NAUSP National Antimicrobial Utilisation Surveillance Program



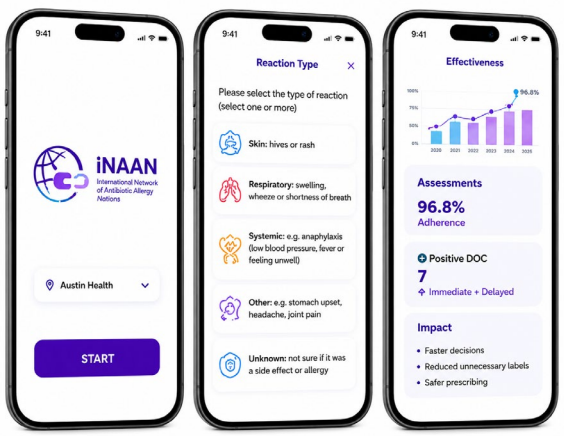
Penicillin Allergy *Delabelling* Next Steps

2026 Status

- **60** iNAAN Hospitals
- **46** Australian Hospitals
- **>360** Clinicians
- **>8800** Patients
- **>2700** DOC

REDCap Research Electronic Data Capture

BioGrid Connecting health information



iNAAN Health Service Report

Austin Health, September 2024

- **227** Penicillin DOC — 27.3% conversion to DOC
- **96.8%** Negative DOC — All Principal Referral Hospitals 96.1%
- **98.6%** Adherence to local protocol — ↑ 0.2% (last report)
- **7** Positive DOC — 1 Immediate, 6 Delayed

A&F Implementation Strategy
Driving better outcomes through point-of-care intervention and data capture

Next Steps

Community
General Practice, First Nations & Sexual Health Practice

Non-penicillins
Sulfa & Cephalosporin antibiotic allergy labels

Children
Hospitalised
iNAAN KID2

Data Linkage
NAUSP, AGAR

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Join our *Penicillin Allergy* Community of Practice

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National Antibiotic Allergy Network (NAAN) Collaborative

The Check Again Program is a statewide antibiotic allergy quality improvement initiative. It improves access to penicillin allergy assessment and testing across Victorian health services.

National Antibiotic Allergy Network

iNAAN International Network of Antibiotic Allergy Nations

Centre for Antibiotic Allergy and Research

Acknowledgements & Questions

Australian and International Partners

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iNAAN and AUS-SCAR Steering Committees
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St George Hospital – Dr Richard Sullivan
Royal North Shore Hospital – Prof Suran Fernando
Fiona Stanley Hospital – Mr Matt Rawlins
Royal Brisbane and Women's – Dr Michael Lane
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Alfred Health – Prof Peel/ Dr Zubrich/ Prof Kerns
Alfred Hospital – Dr Ar Kar Aung
Royal Darwin Hospital – Dr Jane Davies
Vanderbilt University – Prof Elizabeth Phillips (USA)
Groote Schuur Hospital, Cape Town – Prof Jonny Peter (S.Africa)
McGill University Health Centre – Dr Ana Copaescu (Canada)
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- Dr Samantha Chan
- Dr Gemma Reynolds

BioGrid Australia

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- Ms Rebecca Hall
- Ms Kerryn McIness
- Ms Sharon Hankinson
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Austin Health Department of Infectious Diseases and Immunology

- All staff and registrars
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- Prof Sharon Lewin
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Further resources:
antibioticallergy.org.au/

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