

# Time to re-examine penicillin allergy in Australian general practice

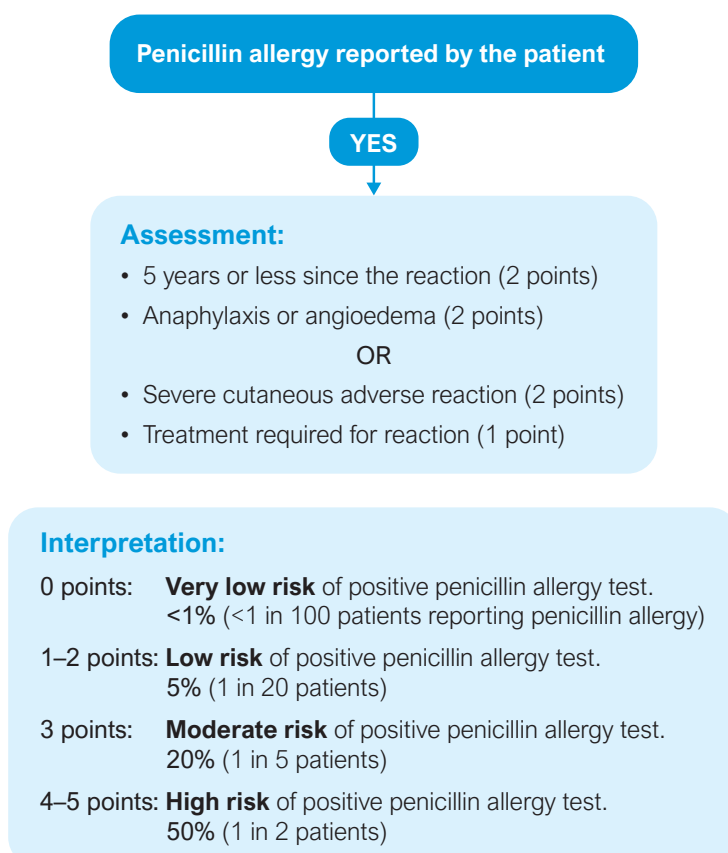
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**PENICILLIN ALLERGY 'LABELS'** are both common and consequential — affecting up to 25% of hospitalised patients and nearly 10% of the general population in Australia and internationally<sup>1,2</sup> — yet up to 90% of these 'labels' are inaccurate or outdated.<sup>3</sup> These labels result in the unnecessary avoidance of first-line, beta-lactam antibiotics, leading to increased use of broader-spectrum, inappropriate and often less-effective alternatives.<sup>1,4</sup> This contributes to higher rates of antimicrobial resistance (AMR), *Clostridioides difficile* infection, longer hospital stays, re-admissions, surgical site infections and even intensive care unit (ICU) admissions.<sup>3</sup> In the community setting, they are associated with elevated mortality and methicillin-resistant *Staphylococcus aureus* (MRSA) colonisation.<sup>5,6</sup> The process of removing these inaccurate penicillin allergy labels via drug provocation (with or without prior skin testing) or medical reconciliation is defined as 'delabelling'.<sup>7</sup> Thus, addressing penicillin allergy labels through accurate assessment and delabelling is critical, not only to improve individual patient outcomes but also to enhance antimicrobial stewardship (AMS).

Addressing penicillin allergy does not have to require complex interventions. Hospital evidence has demonstrated that direct delabelling, the removal of a patient's penicillin allergy via medical reconciliation without testing, is effective at both removing the 'label' and subsequently increasing narrow-spectrum penicillin use.<sup>8</sup> This could

be achieved in the primary care setting with a targeted penicillin allergy assessment. There has been increased use of point-of-care antibiotic allergy assessment tools, which have been extensively validated in the

Australian healthcare setting, including rural and remote areas, and by non-allergists.<sup>9,10</sup> With a maximum score of five points, the Penicillin Allergy Clinical Decision Rule (PEN-FAST; Figure 1) considers a reaction



**Figure 1.** Penicillin Allergy Clinical Decision Rule (PEN-FAST).

Adapted from Trubiano JA et al. Development and validation of a penicillin allergy clinical decision rule. JAMA Intern Med 2020, with permission from the authors.

history within the previous 5 years (2 points), anaphylaxis, angioedema or severe cutaneous adverse reactions (SCAR) (2 points) and whether treatment was required or unknown for the reaction (1 point) as the predominant criteria to predict a positive direct oral challenge (DOC). A PEN-FAST score  $<3$  is considered low risk (Negative predictive value [NPV] 96.3%).<sup>11</sup> PEN-FAST is included in our national therapeutic guidelines,<sup>12</sup> and paves a way for penicillin allergy assessment in primary care to support safer prescribing.

One of the most impactful developments has been the increasing safety and feasibility of single-step DOC, in those assessed with a low-risk phenotype (eg PEN-FAST score  $<3$ ). A systematic review and meta-analysis by Powell et al examined interventions involving non-allergy specialists and confirmed that pharmacist-, nurse- and general practitioner-led delabelling protocols could be delivered safely and effectively, with low rates of adverse events and improved antibiotic prescribing outcomes.<sup>13</sup> The ALABAMA trial — the first randomised controlled trial in this space — evaluated a penicillin allergy assessment pathway initiated in 51 UK general practices.<sup>14</sup> It demonstrated that delabelling patients via structured non-allergist pathways improved beta-lactam prescribing, reduced overall antibiotic use and had a favourable safety profile.

However, as highlighted in the accompanying editorial, key barriers remain.<sup>15</sup> These include logistical complexity in scaling general practice delabelling pathways, variation in clinician confidence, limited access to training and practicalities of delivering DOC in the general practice setting. However, recent Australian data demonstrate that DOC can indeed be implemented safely in general practice. In a study by Waldron et al, patients assessed using a streamlined, protocolised pathway were successfully delabelled via DOC within a primary care setting, with no serious adverse events reported.<sup>16</sup> This builds on robust international evidence of DOC in primary care,<sup>17,18</sup> including a meta-analysis by Blumenthal et al, which found that the risk of a serious reaction during DOC in low-risk patients is less than 1%, with most adverse events being mild, self-limiting skin rashes.<sup>19</sup> Further, international evidence has demonstrated both the negative impacts

of a penicillin allergy 'label' on antibiotic utilisation in primary care and positive prescribing benefits post delabelling.<sup>20</sup>

The future of penicillin allergy delabelling lies in embedding DOC into primary care infrastructure. Priority should be given to contexts where the burden of inaccurate allergy labels is highest and the benefits most tangible — such as sexual health services, First Nations health, and rural and remote practice. Trials conducted in community sexual health clinics 30 years apart in Baltimore (US) have already demonstrated that targeted delabelling pathways significantly improve antibiotic selection and patient care in this priority population.<sup>21,22</sup> These findings align with the broader international consensus that sustainable and scalable allergy delabelling requires integration into everyday clinical workflows, supported by tailored tools, digital aids and accessible training for frontline clinicians.

Collectively, this large evidence base confirms that penicillin allergy delabelling is not only safe when led by non-allergists but forms an essential part of antimicrobial stewardship and protects patients from avoidable harm across both hospital and community settings. Although selected uptake of DOC in general practice is likely to proceed more easily in metropolitan practices where there is an immediate benefit (eg syphilis, splenectomy prophylaxis), there will be additional benefit to remote or regional practices where different drivers exist (eg group A streptococcus, MRSA, rheumatic heart disease). Either way, widespread utilisation requires a detailed roadmap including targeted education with continuing professional development (CPD) education, implementation strategy and appropriate remuneration for clinicians. Partnerships between allergists, infectious diseases physicians, pharmacists and general practitioners will aid in delivering this roadmap, to ensure penicillin allergy delabelling has the desired impact on the patient (ie infection outcomes), community (ie infection transmission) and public health (ie antimicrobial resistance) level. In particular, addressing penicillin allergy in First Nations rural and remote communities is likely to have significant infection gains, but requires engagement with Aboriginal Community Controlled

Health Organisations and co-design and consultation with consumers. Beyond the efficacy of penicillin allergy programs, we must co-design, implement and evaluate tailored penicillin allergy interventions that enable safe, effective delabelling in primary care—ensuring this critical aspect of antimicrobial stewardship is accessible where it is needed most.

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