External validation of beta-lactam antibiotic allergy assessment tools: implications for clinical practice and workforce capacity

To the Editor:

In their recent paper, Devchand et al[1] propose a point-of-care β-lactam allergy assessment tool for health care workers to assess antibiotic allergy labels and enable risk stratification to determine further evaluation pathways to facilitate appropriate delabeling or confirmation. Almost concurrently, a similar tool for penicillin allergy was published by Shenoy et al in *JAMA*[2] that included risk stratification after completion of an accurate allergy history assessment, coupled with recommendations for clinical evaluation on the basis of risk. In this increasingly critical era of antimicrobial stewardship, strategies to facilitate evaluation of penicillin allergy (which should allow delabeling in the majority of cases) are essential to reduce the use of broad-spectrum antibiotics, associated with the increased risk of antimicrobial resistance and poor patient health outcomes.[3,4]

Although approximately 10% of the population have reported penicillin allergy, the majority (95%) are able to tolerate penicillins.[5] We recently examined 43,011 adverse drug reports (ADRs) from electronic health records from 3 tertiary referral hospitals in South Australia, identifying 5023 ADRs to penicillin.[6] Using these data (August 2013 to January 2015), we applied the criteria for these recently published β-lactam/penicillin allergy assessment tools[1,2] to assess their applicability to real-world clinical practice (Table I).

TABLE I. Application of β-lactam[1]/penicillin[2] allergy assessment tools to electronic health record ADRs

Total penicillin ADRs (n = 5,023)	ADRs meeting criteria, N (%)
Devchand et al, 2019[1]	
(1) Appropriate for direct delabeling (unlikely to be immune mediated, nonsevere, low risk)	509 (10.1)
(2) Appropriate for supervised direct oral rechallenge (unlikely to be significant/delayed hypersensitivity, nonsevere, low risk)	67 (1.3)
(3) Appropriate for skin testing followed by oral rechallenge (immediate hypersensitivity, severe)	1,980 (55.4)
(4) Appropriate for outpatient antibiotic allergy assessment ± testing (delayed/immediate hypersensitivity/immune mediated, severe)	1,613 (32.1)
Shenoy et al, 2019[2]	
(1) Intolerance histories	494 (9.8)
(2) Low-risk allergy histories	1,135 (22.6%)
(3) Moderate-high risk allergy histories (potential IgE reaction)	3,304 (65.8%)
(4) High risk: contraindicated penicillin skin testing/challenge (potential severe nonimmune reaction)	88 (1.8)

ADR, Adverse drug report.

Approximately 10% of penicillin ADRs using both tools were categorized as intolerance, unlikely to be immune mediated. Although the Shenoy assessment does not include a pathway for immediate delabeling,[2] we postulate that on appropriate review of the patient electronic health record, these patients could be directly delabeled. Whether this strategy is acceptable to both patients and clinicians remains to be determined. Only 1% of patient penicillin ADRs met the criteria for oral challenge according to the Devchand assessment tool, whereas almost a fifth were deemed suitable for an oral challenge using the Shenoy criteria; the discrepancy was attributable to almost 2000 ADRs of "rash with no other information." For both tools, the majority of patient penicillin ADRs (55.4% to 65.8%) would be classified as requiring skin testing followed by an oral challenge. High-risk patients where penicillin skin test/oral challenge is contraindicated comprised only 1.8% of all ADRs, and this group would likely contain a high proportion who are truly allergic.[5] By comparison, almost a third of the ADRs would require outpatient antibiotic allergy assessment according to Devchand criteria. However, 63.1% of these ADRs (n = 1017/1613) were reported as "unknown/uncertain timing" (Table I).

Despite the lack of concordance between the 2 tools in terms of numbers of patients within risk stratification categories, the results highlight significant implications for health care resource use and clinical workforce requirements in conducting appropriate allergy testing and the large number of patients with inadequate documented history. We recommend that research evaluate the resource implications of conducting a detailed and dedicated allergy medication history, and its utility in categorizing these unknown reactions into lower-risk categories. Although this assessment would ideally be done by a pharmacist, research could evaluate the role of other health care professionals, including specifically trained nursing staff, as part of the antimicrobial stewardship role. Furthermore, prioritization of patients based on the use of high-cost antibiotics, specific comorbidities, or local microbial resistances may facilitate streamlining of resources.[7] Ultimately, investment in systemic evaluation together with the provision of appropriate resources for formal evaluation will improve appropriate antibiotic prescribing and efficiencies within the health care system.

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Reply

To the Editor:

We read with the interest the correspondence by Caughey et al[1] regarding the recently published antibiotic allergy assessment tool (AAAT).[2] We agree that external validation is required for widespread implementation and strongly encourage the practice undertaken by the authors. Caughey et al have demonstrated the efficacy of the AAAT to detect intolerances, which arguably should not be reported in the "allergy" electronic medical record (EMR), when matched against the EMR allergy documentation alone. The application of the tool to a database that only includes the EMR of the adverse drug reaction (ADR) and without active reconciliation of the patients' ADRs by a trained professional is not how the AAAT was initially designed or internally validated. This is important considering that 25% to 30% of allergies in the EMR are incorrect and a significant proportion incomplete or "unknown."[3,4] This tool was designed and validated to enable health care providers obtain an accurate and prospective β-lactam allergy assessment after patient interview/case scenario, subsequently improving the accuracy of the EMR. The authors highlighted the large proportion (n = 1980) of EMRs stating "rash with no other information" and "unknown/uncertain timing" (n = 1017). However, we suspect that the vast majority of these reactions, after correct application of the AAAT at the bedside, could have been more appropriately classified as "low risk." The collective low-risk phenotypes of (1) unknown reaction, (2) rash >10 years previously, and (3) childhood rash account for greater than 50% of reported antibiotic allergies, extrapolating from an interviewed inpatient population with antibiotic allergies.[3] The AAAT was recently applied to a real-world scenario, in an Antimicrobial Stewardship (AMS)-led penicillin allergy ward round, resulting in 40% of inpatients with a penicillin allergy being considered "low risk."[5] Although point-of-care "delabeling" is the optimal way of reducing the burden of penicillin allergies, tools such as the AAAT are most likely to be used by nonallergists; therefore, they need to ensure safety.

The discussion around health care utilization and avoiding costly and labor-intensive skin testing, which in the most part is currently unavailable to most stakeholders,[6] is timely. Clearly, this is not feasible with a projected 2 million Australians and over 30 million North Americans reporting a penicillin allergy.[7] However, assessment tools should endeavor to enable a larger skilled health care proportion to directly delabel and/or oral challenge patients with validated "low-risk" allergies. As authors correctly suggest, patients identified with a "moderate-risk" allergy are likely to be referred to testing services. We suggest that testing services should specifically prioritize patients with immediate and/or ongoing antibiotic needs, which reflects our practice as demonstrated in a previously published outpatient-tested cohort where 48% were immunocompromised.[8] The development of multidisciplinary models of care,[9] engagement of a pharmacist workforce,[10] and improvement of the exposure of fellows in training to drug allergy,[11] is likely to help offset the increased demand for testing services. Published antibiotic allergy tools, in addition to aiding assessment, hopefully will provide clinicians with direction around the safety of alternative β-lactam utilization. We hope that the uptake of alternative β-lactams, in particular cephalosporins, occurs in patients with reported low- and moderate-risk allergies, considering the under 2% rate of cross-reactivity.[9] We look forward to further work to validate a range of β-lactam allergy tools that will improve EMR accuracy, β-lactam utilization, and point-of-care delabeling.

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