Supplementary Online Content


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This supplementary material has been provided by the authors to give readers additional information about their work.
**eMethods 1. Data Collection and Case Report Form (CRF)**

The standardized case report form utilized for inpatient and outpatient data collection for the prospective cohorts in Melbourne (Austin Health and Peter MacCallum Cancer Centre) are provided in the following.

In brief, this standardized case report form was completed by the treating clinician (including trained infectious diseases physicians) during inpatient or outpatient consultation. Allergy phenotypic assessment was at clinician discretion utilizing patient-reported phenotypes and standard definitions for anaphylaxis\(^8\) and potential severe cutaneous adverse reactions (SCAR - DRESS\(^9\); SJS/TEN\(^10\); AGEP\(^11\)), as performed in previous publications utilizing this dataset.\(^1,12\)

In brief, anaphylaxis was adjudged by the clinician if the history was consistent with a cutaneous manifestation plus one of respiratory, cardiovascular or gastrointestinal symptoms or acute onset hypotension or bronchospasm/airway obstruction alone. SJS/TEN also included potentially compatible syndromes of rash with mucosal ulceration.

Every attempt was made to reconcile the patient-reported label (e.g. “anaphylaxis”) with a detailed history of the allergy event from the patient supplemented with hospital medical records but where this was not available, the patient-reported label was used.
FORM 01

ANTIBIOTIC ALLERGY CLINIC
DATA COLLECTION FORM

1- Baseline Demographic:

UR number: __________________________ Cohort ID: ____________________ (office use)

Site: □ Austin □ PMCC □ Vanderbilt

Age: __________ Sex: □ male □ female □ transsexual

Ethnicity: □ African □ Asian □ Caucasian

COB: ____________________________

Referrer: □ LMO □ ADR committee □ community specialist □ allergist
(multiple choices) □ pharmacist □ ID physician □ respiratory physician □ other doctor

First Clinical Review Date: _______/______/20_______ (1st antibiotic allergy clinic appointment)

First Allergy Test Date: _______/______/20_______ or □ not done

Psychiatric history: □ no □ unk □ anxiety □ bipolar □ depression
□ personality disorder □ psychosis

Age adjust CCI (refer to Charlson comorbidity index): __________________

Antibiotics previously tolerated (list them all): __________________________

2- Immunosuppression history:

Immunosuppressed: □ no → go to section 3, “Family History”

□ Autoimmune □ Connective tissue disorder

□ Haematological Malignancy □ Oncological Malignancy

□ Diabetes (insulin requiring) □ Inflammatory Bowel Disease

□ Prednisolone > 10mg/day for month □ Rheumatological disorder

□ Allogeneic transplant □ Autologous transplant

□ Lung transplant □ Liver transplant

□ Renal transplant □ Renal/pancreas transplant

□ Other

Transplant: □ no □ yes → days post last transplant: ____________
FORM 01

Transplant rejection:  □ no
□ yes → episode/s requiring treatment: ____________

Immunosuppressed at first clinical review:  □ no
□ yes → tick as many as apply

☐ AML induct/consol  ☐ azacitidine  ☐ azathioprine  ☐ chemotherapy
☐ cyclosporin  ☐ everolimus  ☐ ibritinib  ☐ MMF
☐ myeloma  ☐ methotrexate  ☐ rituximab  ☐ sirolimus
☐ small molecule inhibitor (solid tumours)  ☐ tacrolimus  ☐ TNF inhibitor
☐ other

Prednisolone:  □ no  □ yes → Daily dose (mg): ____________

3- Family Allergy History:

Allergy history:  □ no → go to section 4
□ yes

Antibiotic allergy history:  □ no  □ yes

Drug allergy history:  □ no  □ yes

Food allergy history:  □ no  □ yes

Environmental allergy history:  □ no  □ yes

4- Radioallergosorbent test

RAST performed:  □ no  □ yes → □ neg
□ pos—against:  ☐ amoxicillin (circle) no / yes
              ☐ cefaclor (circle) no / yes
              ☐ penicillin (circle) no / yes

Neutropenia:  □ no  □ yes

Neutropenia < 0.5:  □ no  □ yes

Anaemia <10:  □ no  □ yes

Total lymphocyte count: ________________ Date: _______/ _______/ 20______

CD4 count: ___________ Date: _______/ _______/ 20______

CD4 %: ___________ Date: _______/ _______/ 20______

IgG total: ___________ Date: _______/ _______/ 20______

IgA total: ___________ Date: _______/ _______/ 20______

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FORM 01

5- Antibiotic Allergy History:

☐ no → END of study

☐ yes → Time since last antibiotic allergy or Adverse drug event: ________ days

Number of allergy labels: ________ → list All (refer to FORM 02 section 6 Antibiotic Allergy Label)

Previous SPT/IDT test:  ☐ no  ☐ yes → ☐ neg

☐ pos → tick all agents that apply

Agent:  ○ ampicillin  ○ aztreonam  ○ azithromycin  ○ bactrim  ○ cefepime  ○ ceftazadim  ○ ceftriaxone  ○ cephalizin  ○ ciprofloxacin  ○ clavulanic acid  ○ clindamycin  ○ DAP major  ○ DAP minor  ○ flucloxacillin  ○ histamine  ○ meropenem  ○ moxifloxacin  ○ penicillin  ○ penicillin G 1000  ○ penicillin G 10000  ○ tazocin  ○ timentin  ○ vancomycin

Would you be happy to be re-challenged with the offending antibiotic if negative on SPT/IDT testing?

☐ no → go to section 7  ☐ yes

If the oral challenge allergy testing was negative, would you be willing to take that antibiotic in the future?

☐ no  ☐ yes

7- Allergy Test Results:

Skin prick test performed:  ☐ no  ☐ yes → ☐ neg

☐ pos → tick as many as apply

Agent:  ○ ampicillin  ○ aztreonam  ○ azithromycin  ○ bactrim  ○ cefepime  ○ ceftazadim  ○ ceftriaxone  ○ cephalizin  ○ ciprofloxacin  ○ clavulanic acid  ○ clindamycin  ○ DAP major  ○ DAP minor  ○ flucloxacillin  ○ histamine  ○ meropenem  ○ moxifloxacin  ○ penicillin  ○ penicillin G 1000  ○ penicillin G 10000  ○ tazocin  ○ timentin  ○ vancomycin

Intradermal test:  ☐ no  ☐ yes → ☐ neg

☐ pos → tick as many as apply

Agent:  ○ ampicillin  ○ aztreonam  ○ azithromycin  ○ bactrim  ○ cefepime  ○ ceftazadim  ○ ceftriaxone  ○ cephalizin

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FORM 01

☐ ciprofloxacin ☐ clavulanic acid ☐ clindamycin ☐ DAP major
☐ DAP minor ☐ flucloxacinil ☐ histamine ☐ meropenem
☐ moxifloxacin ☐ penicillin ☐ penicillin G 1000 ☐ penicillin G 10000
☐ tazocin ☐ timentin ☐ vancomycin

Patch test: ☐ no ☐ yes → ☐ pos → tick as many as apply

Agent: ☐ Antiretroviral (other) ☐ Beta-lactam (other) ☐ Sulfamethoxazole
☐ Teicoplanin ☐ Trimethoprim ☐ Vancomycin

Direct oral challenge: ☐ no ☐ yes → tick as many as apply

☐ amoxycillin(S) ☐ amoxycillin (L) ☐ augmentin(S) ☐ augmentin(L)
☐ ciprofloxacin(S) ☐ ciprofloxacin(L) ☐ cephalexin(S) ☐ cephalexin(L)
☐ flucloxacinil ☐ penicillin(S) ☐ penicillin(L) ☐ tazocin

→post testing oral challenge: ☐ neg ☐ pos → tick as many as apply

☐ amoxycillin(S) ☐ amoxycillin(L) ☐ augmentin(S) ☐ augmentin(L)
☐ ciprofloxacin(S) ☐ ciprofloxacin(L) ☐ cephalexin(S) ☐ cephalexin(L)
☐ flucloxacinil ☐ penicillin(S) ☐ penicillin(L) ☐ tazocin

8- Antibiotic Allergy Label Post Testing:

De-labelled: ☐ no

☐ yes → how many _______________

Revised label: ☐ no ☐ yes

Antibiotic label/s:

________________________________________

________________________________________

Antibiotic label/s_30 days: _____________________________

Antibiotic label/s_90 days: _____________________________

Antibiotic label/s_365 days: _____________________________
FORM 01

9- Antibiotic Usage and Admission (refer to FORM 03, section 9)

Antibiotic usage and admission with infective diagnosis 60 days prior to testing:

☐ no  ☐ yes → go to FORM 03 - section 9, page 1

Antibiotic usage and admission with infective diagnosis 12 months prior to testing:

☐ no  ☐ yes → go to FORM 03 - section 9, page 2

Antibiotic usage and admission with infective diagnosis 60 days post to testing:

☐ no  ☐ yes → go to FORM 03 - section 9, page 3

Antibiotic usage and admission with infective diagnosis 12 months post to testing:

☐ no  ☐ yes → go to FORM 03 - section 9, page 4

10- T-cell ELISpot

Referred for T-cell ELISpot:  ☐ no

☐ yes → Blood taken ______________ mLs

Date _______ / ____ / 20_____

PBMC count ______________

Result:  ☐ neg

☐ pos → list antibiotics

________________________

________________________

________________________

Referred for TCK analysis:  ☐ no  ☐ yes

Referred for HLA typing:  ☐ no  ☐ yes
FORM 02: Antibiotic Allergy Label

Section 6: (make copy of this page for more allergy labels if necessary)

Label number: _______  Antibiotic name: ______________________

Date started: _______/_____/20____  Date stopped: _______/_____/20____

Number of allergy episodes: _______  Date of reaction: _______/_____/20____

Description: tick all that apply

- Acute interstitial nephritis (urinalysis or Bx proven)
- Anaphylaxis
- Collapse (unspecified)
- Diffuse non-itchy rash (nil other)
- Drug fever (nil other)
- FDE
- Headache or dizziness
- Itch (unspecified)
- Linear IgA
- Liver function derangement
- Psychiatric
- Rash with skin ulceration or blisters (unspecified)
- Respiratory distress
- Seizures
- SJS/TENS overlap
- Urticaria

Type:  □ A  □ B1  □ B2  □ B3  □ B4  □ unk

Biopsy proven:  □ no  □ yes

Re-challenge:  □ no

□ yes → Adverse Event:  □ no  □ yes

Concurrent viral infection:  □ no

□ yes → tick all that apply  □ CMV  □ EBV  □ HHV6  □ HHV8  □ mycoplasma  □ other respiratory virus

Concurrent neuroleptic agents:  □ no  □ yes
FORM 02: Antibiotic Allergy Label

☐ unk

Concurrent anti-inflammatory agents  ☐ no
☐ yes
☐ unk

Concurrent antibiotics:
☐ no
☐ yes

Treatment:
☐ no
☐ yes  → tick all that apply:

☐ prednisolone (including dose) _____ mg

☐ antihistamine  ☐ adrenaline

☐ intragam  ☐ surgery

Hospitalisation:  ☐ no  ☐ yes

ICU:  ☐ no  ☐ yes

Review by ID physician:  ☐ no  ☐ yes

Review by Allergist/Immunologist:  ☐ no  ☐ yes
**eMethods 2. Antibiotic Allergy Testing (AAT) Procedures From Derivation and Validation Cohorts**

**Derivation and Internal Validation Cohorts – Melbourne (Australia)**

AAT was performed for out- and in-patients as previously described for immediate and delayed hypersensitivities. In brief, in all patients reporting a penicillin allergy, skin testing using the validated Diater (DAP; Madrid, Spain) was used for the major (benzylpenicilloyl-poyl-L-lysine [PPL]) and minor determinant mixtures (MDM) in patients with a penicillin hypersensitivity, in addition to penicillin G (SPT 10,000 U/mL; IDT 1000 IU/mL and 10,000 IU/mL), ampicillin (25 mg/mL), flucloxacillin (2 mg/mL), cefazolin (1 mg/mL) and ceftriaxone (2.5 mg/mL) as per previously published protocols. Following AAT, an observed oral penicillin challenge was undertaken (immediate hypersensitivity - single or two-step penicillin VK 250 mg or amoxicillin 250 mg); delayed hypersensitivity - prolonged 5-day). For patients with a potential SCAR phenotype, testing was performed as per previously published methods, using the same panel of IDT reagents/concentrations as above –(isolated PT only performed in SJS/TEN). From April 2017, patients identified as having a pre-defined low risk criteria (i.e. childhood exanthema, delayed rash > 10 years previously, or Type A adverse drug reaction) as per a validated antibiotic allergy assessment tool were offered a direct oral penicillin VK 250 mg or amoxicillin 250 mg challenge without preceding skin testing.

**External Validation Cohorts – Sydney (Australia), Perth (Australia), Nashville (USA)**

**Perth** – A standard testing protocol for all patients reporting a penicillin allergy of Diater-DAP PPL (benzylpenicilloyl poly-L-lysine; 0.04 mg/mL) and MDM (sodium benzylpenicillin, benzylpenicilloic acid, sodium benzylpenicilloate; 1.5 mg/mL), penicillin G (SPT 10,000 IU/mL; IDT 1000 IU/mL and 10,000 IU/mL), amoxicillin (20 mg/mL), cefazolin (1 mg/mL), and ceftriaxone (1 mg/mL).

**Sydney** - Standard testing protocol of penicillin G (10,000 IU/mL) and amoxicillin (20 mg/mL). In moderate to high risk patients, Diater-DAP PPL (benzylpenicilloyl poly-L-lysine; 0.04 mg/mL), MDM (sodium benzylpenicillin, benzylpenicilloic acid, sodium benzylpenicilloate; 1.5 mg/mL), cefazolin (20mg/mL), and ceftriaxone (10mg/mL) were also tested.
Nashville - A standard protocol similar to that employed in the validation cohort from Melbourne (Australia), consisting of Pre Pen, minor determinant mix (consisting of the alkalinization of Penicillin G), ampicillin (25 mg/mL), penicillin G (1000 IU/mL and 10,000 IU/mL), cefazolin (1 mg/mL), and ceftriaxone (2.5 mg/mL).

Definitions of positive AAT results

In all cohorts (internal derivation/validation and external validation) a SPT considered positive in the setting of a wheal 3 mm more than control wheal and flare 5 mm more than control flare, read after 15 minutes. An IDT was considered positive if there was a 3 mm or greater increase in inoculation site (0.02 mL) with >5 mm flare, read after 15 minutes. A positive oral challenge excluded non-immune mediated reactions and only included patients reporting an immune-mediated reaction (e.g. rash), including those that reported delayed reactions captured by study centre.
LASSO Logistic Regression With Cross-Validation

Logistic LASSO regression was also fitted using the same variables as stepwise logistic regression (main Table 3). Cross validation was used to select lambda (10-fold cross validation with 100 lambdas).

Final model consisted of 4 non-zero coefficient with lambda 0.016, and out-of-sample deviance ratio of 0.161. Variables with non-zero coefficients were the same as with the stepwise logistic regression with an additional variable of previous hospitalizations due to allergy. Penalized coefficients and coefficients from the logit model are presented in table.

<table>
<thead>
<tr>
<th></th>
<th>LASSO logistic regression</th>
<th>Logit model</th>
<th>Stepwise logit model used in PEN-FAST</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;5 years since last allergy or unknown</td>
<td>1.38</td>
<td>1.73</td>
<td>1.79</td>
</tr>
<tr>
<td>Anaphylaxis, angioedema, SJS, TENS, DRESS or AGEP</td>
<td>1.24</td>
<td>1.45</td>
<td>1.56</td>
</tr>
<tr>
<td>Treatment required†</td>
<td>0.33</td>
<td>0.88</td>
<td>1.02</td>
</tr>
<tr>
<td>Hospitalisation required</td>
<td>0.22</td>
<td>0.41</td>
<td>Not included</td>
</tr>
<tr>
<td>AUC of the model</td>
<td>0.817</td>
<td>0.817</td>
<td>0.808</td>
</tr>
</tbody>
</table>

† Any systemic treated as outlined in case report form (i.e. antihistamine, adrenaline, steroids, intragam)
**eFigure 1.** Patient-Reported Antibiotic Allergy Labels in Antibiotic Allergy–Tested Cohort

**A)** Antibiotic allergy labels recorded for all patients (n = 773) reporting an antibiotic allergy; (B) Penicillin allergy labels recorded for all patients (n = 679) reporting any penicillin allergy; (C) Non-penicillin allergy labels recorded for all patients (n = 679) reporting a penicillin allergy

**eFigure 1 Legend:** (A) Antibiotic allergy labels recorded for all patients (n = 773) reporting an antibiotic allergy; (B) Penicillin allergy labels recorded for all patients (n = 679) reporting any penicillin allergy; (C) Non-penicillin allergy labels recorded for all patients (n = 679) reporting a penicillin allergy
**eFigure 2.** Area Under the Receiver Operating Characteristic Curve (AUC) Analysis

The graph shows the Receiver Operating Characteristic (ROC) curves for PEN-FAST in different cohorts. The legend explains the AUC values for each cohort:

- **Melbourne:** AUC 0.81 (0.75, 0.86)
- **NSW:** AUC 0.81 (0.71, 0.91)
- **Perth:** AUC 0.73 (0.66, 0.80)
- **Nashville:** AUC 0.85 (0.74, 0.96)

**eFigure 2 Legend:** AUC for PEN-FAST in the derivation/validation (Melbourne, Australia) and external validation cohorts (Sydney, Perth, Nashville).
**eFigure 3.** Calibration of the PEN-FAST Rule in Derivation/Validation Cohort (Melbourne, Australia)

**eFigure 3 Legend:** Numbers above the bars represent the PEN-FAST score
### Table 1. Baseline Demographics of External Validation Cohorts of Patients Reporting Any Oral Penicillin Allergy Who Underwent Testing as per Specified Methods

<table>
<thead>
<tr>
<th>Patient characteristics</th>
<th>Perth (n = 334) No. (%)</th>
<th>Sydney (n = 80) No. (%)</th>
<th>Vanderbilt (n = 531) No. (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age (years), median (IQR)</strong></td>
<td>47 (31, 63)</td>
<td>52 (37, 63.5)</td>
<td>60 (44, 70)</td>
</tr>
<tr>
<td><strong>Sex (female)</strong></td>
<td>216 (64.7)</td>
<td>53 (66)</td>
<td>393 (74)</td>
</tr>
<tr>
<td><strong>Allergy phenotypes</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Immune mediated</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SCAR</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>8 (1.6)</td>
</tr>
<tr>
<td>Angioedema/Anaphylaxis</td>
<td>130 (38.9)</td>
<td>17 (21.3)</td>
<td>112 (21.1)</td>
</tr>
<tr>
<td>Other†</td>
<td>201 (60.0)</td>
<td>45 (56.3)</td>
<td>399 (75)</td>
</tr>
<tr>
<td>Non-immune mediated</td>
<td>0 (0)</td>
<td>11 (13.8)</td>
<td>6 (1)</td>
</tr>
<tr>
<td>Unknown</td>
<td>3 (1)</td>
<td>7 (8.8)</td>
<td>6 (1)</td>
</tr>
<tr>
<td><strong>Treatment for allergy‡</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>0 (0)</td>
<td>26 (32.5)</td>
<td>161 (30.3)</td>
</tr>
<tr>
<td>No</td>
<td>0 (0)</td>
<td>43 (53.8)</td>
<td>220 (41.4)</td>
</tr>
<tr>
<td>Unknown</td>
<td>334 (100)</td>
<td>11 (13.8)</td>
<td>150 (28.2)</td>
</tr>
<tr>
<td><strong>Time from reaction</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt; 5 years</td>
<td>63 (19)</td>
<td>24 (30.0)</td>
<td>292 (55)</td>
</tr>
<tr>
<td><strong>Skin prick and intradermal testing</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Oral challenge</td>
<td>332 (99.4)</td>
<td>78 (97.5)</td>
<td>531 (100)</td>
</tr>
<tr>
<td></td>
<td>297 (88.9)</td>
<td>64 (80.0)</td>
<td>525 (98.9)</td>
</tr>
<tr>
<td><strong>Any penicillin allergy test positive</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>IDT</td>
<td>48 (14)</td>
<td>27 (33.8)</td>
<td>19 (3.6)</td>
</tr>
<tr>
<td>Oral challenge</td>
<td>42 (13)</td>
<td>17 (21.3)</td>
<td>15 (2.8)</td>
</tr>
<tr>
<td></td>
<td>6 (3)</td>
<td>11 (13.8)</td>
<td>4 (1.7)</td>
</tr>
</tbody>
</table>

**Abbreviations:** SCAR, severe cutaneous adverse reaction; IQR, interquartile range; IDT, intradermal testing.

† Immune mediated reactions including rash (immediate or delayed), pruritis, respiratory or airway involvement.

‡ Any systemic therapy (i.e. antihistamine, adrenaline, steroids, intragam
eTable 2. Percentage of PEN-FAST Risk Scores for All Datasets Utilized

<table>
<thead>
<tr>
<th>Clinical characteristics</th>
<th>Melbourne (AUS)</th>
<th>Sydney (AUS)</th>
<th>Perth (AUS)</th>
<th>Nashville (USA)</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of patients</td>
<td>622</td>
<td>80</td>
<td>334</td>
<td>531</td>
</tr>
<tr>
<td>No. (%) of PEN-FAST risk scores</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Very low risk (0)</td>
<td>164 (26)</td>
<td>9 (11.3)</td>
<td>0 (0)</td>
<td>79 (14.9)</td>
</tr>
<tr>
<td>Low risk (1-2)</td>
<td>296 (48)</td>
<td>44 (55.0)</td>
<td>120 (35.9)</td>
<td>232 (43.7)</td>
</tr>
<tr>
<td>Moderate risk (3)</td>
<td>132 (21)</td>
<td>15 (18.8)</td>
<td>140 (41.9)</td>
<td>147 (27.7)</td>
</tr>
<tr>
<td>High risk (4-5)</td>
<td>30 (5)</td>
<td>12 (15)</td>
<td>74 (22.2)</td>
<td>73 (13.8)</td>
</tr>
<tr>
<td>No. (%) of allergy within PEN-FAST categories – observed risk</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Very low risk (0)</td>
<td>1 (0.6)</td>
<td>1 (11.1)</td>
<td>n/a</td>
<td>1 (1.3)</td>
</tr>
<tr>
<td>Low risk (1-2)</td>
<td>16 (5.4)</td>
<td>7 (15.9)</td>
<td>6 (5.0)</td>
<td>4 (1.7)</td>
</tr>
<tr>
<td>Moderate risk (3)</td>
<td>25 (18.9)</td>
<td>9 (60.0)</td>
<td>15 (10.7)</td>
<td>5 (3.4)</td>
</tr>
<tr>
<td>High risk (4-5)</td>
<td>16 (53.3)</td>
<td>10 (83.3)</td>
<td>27 (36.5)</td>
<td>9 (12.3)</td>
</tr>
</tbody>
</table>

Abbreviations: No., number
**eTable 3. Derivation of Cutoff Scores for Clinical Decision Rule, PEN-FAST**

<table>
<thead>
<tr>
<th>Score</th>
<th>Negative CDR</th>
<th>False negative score†</th>
<th>Positive CDR</th>
<th>False positive score‡</th>
<th>Sensitivity (95% CI)</th>
<th>Specificity (95% CI)</th>
<th>PPV (95% CI)</th>
<th>NPV (95% CI)</th>
<th>AUC (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥1</td>
<td>164 (26.4%)</td>
<td>1 (0.6%)</td>
<td>458 (26.4%)</td>
<td>401 (87.6%)</td>
<td>98.3 (90.8,100.0)</td>
<td>28.9 (25.2,32.8)</td>
<td>12.4 (9.6,15.8)</td>
<td>99.4 (96.6,100.0)</td>
<td>0.64 (0.61,0.66)</td>
</tr>
<tr>
<td>≥2</td>
<td>417 (67.0%)</td>
<td>14 (3.4%)</td>
<td>205 (33.0%)</td>
<td>161 (78.5%)</td>
<td>75.9 (62.8, 86.1)</td>
<td>71.5 (67.5,75.1)</td>
<td>21.5 (16.0,27.7)</td>
<td>96.6 (94.4,98.2)</td>
<td>0.74 (0.68,0.80)</td>
</tr>
<tr>
<td>≥3</td>
<td>460 (74.0%)</td>
<td>17 (3.7%)</td>
<td>162 (26.0%)</td>
<td>121 (74.7%)</td>
<td>70.7 (57.3, 81.9)</td>
<td>78.5 (74.9,81.9)</td>
<td>25.3 (18.8,32.7)</td>
<td>96.3 (94.1,97.8)</td>
<td>0.75 (0.68,0.81)</td>
</tr>
<tr>
<td>≥4</td>
<td>592 (95.2%)</td>
<td>42 (7.1%)</td>
<td>30 (4.8%)</td>
<td>14 (46.7%)</td>
<td>27.6 (16.7,40.9)</td>
<td>97.5 (95.9,98.6)</td>
<td>53.3 (34.3,71.7)</td>
<td>92.9 (90.5, 94.8)</td>
<td>0.63 (0.57,0.68)</td>
</tr>
</tbody>
</table>

**Abbreviations:** CDR, clinical decision rule; CI, confidence interval; PPV, positive predictive value; NPV, negative predictive value; AUC, area under receiver-operator curve.

† Positive penicillin allergy test (any)
‡ Negative penicillin allergy test (any)
eReferences