JOURNAL OF MICROBIOLOGY AND INFECTION
Jul - Dec 2026, VOL. 4, ISSUE 2, pp. 1-6
https://doi.org/10.61577/jmi.2026.100006

RESEAPRO JOURNALS

MINI REVIEW

OPEN ACCESS

Penicillin allergy delabeling in hospitals: A review of prescribing, safety, and implementation

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ABSTRACT

A penicillin allergy label can steer prescribers away from preferred β-lactam antibiotics and toward alternatives. This review examines how hospital allergy assessment and delabeling relate to antibiotic prescribing, patient safety, implementation, and cost. It draws on twelve publications from 2017–2026, including seven primary hospital studies, four systematic reviews or meta-analyses, and one economic evaluation. Findings were grouped by topic without statistical pooling or formal risk-of-bias assessment. Several hospital studies reported more use of preferred β-lactams and less use of selected restricted or alternative antibiotics. Few findings directly addressed whether inappropriate broad-spectrum prescribing declined, and the evidence on this outcome was inconsistent. Serious reactions during testing were uncommon in the populations studied. Programs led by pharmacists or other nonallergists appeared feasible when staff had appropriate training and followed defined protocols. The economic findings came from modeling. Selective inclusion, differences in outcomes, and possible overlap between the primary studies and reviews limit confidence in the synthesis. Structured allergy review may help hospitals improve antibiotic selection. Its effect on inappropriate broad-spectrum use requires more direct evaluation.

KEYWORDS

Penicillin allergy; Delabeling; Antimicrobial stewardship; Antimicrobial resistance; Broad-spectrum antibiotics; β-lactam antibiotics; Restricted antibiotics

ARTICLE HISTORY

Received 06 July 2026;
Accepted 22 July 2026;
Published 29 July 2026

Introduction

Antimicrobial stewardship aims to help clinicians choose the right antibiotic, dose, route, and duration. When a medical record lists a penicillin allergy, clinicians may avoid the preferred antibiotic and prescribe an alternative. The implications depend on the infection being treated, the alternative chosen, and the reliability of the documented allergy history.

Approximately 10% of patients report a penicillin allergy, although evaluation finds that most labels do not reflect a clinically significant allergy [1]. Labels may persist after a childhood reaction, a nonallergic adverse effect, or an event that was poorly documented. A structured review can help clinicians decide whether to correct the record, offer testing, or refer the patient to a specialist.

The allergy history helps determine which assessment is appropriate. Depending on the patient's risk, clinicians may use skin testing, an observed oral challenge, or direct removal of the label if the history supports it. Chua et al., for example, combined history-based delabeling with oral challenge in selected low-risk adult inpatients [2].

The choice of prescribing measure affects how study findings should be interpreted. β-Lactams include both narrow- and broad-spectrum agents, so an increase in total β-lactam use leaves open what happened to broad-spectrum exposure. Hospitals define restricted antibiotics through local policy. An alternative antibiotic is defined relative to the preferred treatment, and whether its use is appropriate depends on the clinical indication. These categories can overlap, but each measures a different aspect of prescribing.

Hospital programs differ in which patients they assess, who delivers the service, how testing is done, and what they measure. Some track narrow-spectrum or restricted-antibiotic use. Others focus on feasibility or label removal. Nürnberg et al., identified resource constraints and other barriers to implementation, making it important to consider how many patients a program reaches as well as what happens to those who complete testing [3].

How do hospital penicillin allergy assessment and delabeling relate to antibiotic prescribing, and what is known about its safety, implementation, and cost?

The review focuses on antibiotic selection and uses evidence on safety, implementation, and cost to put the prescribing findings in context. It considers reductions in inappropriate broad-spectrum use only when the outcomes measured support that interpretation. The synthesis is narrative and draws on selected publications.

Methods

This narrative review examined published evidence on hospital penicillin allergy assessment and delabeling. It involved no original patient data or meta-analysis. The methods were those of a focused literature review, with no systematic or umbrella review protocol.

The reported search used PubMed and Google Scholar, with additional searches or article retrieval through publisher platforms and journal websites, including Oxford Academic, JAMA Network Open, Springer, ScienceDirect, and the International Journal of Infectious Diseases. Reported search terms included "penicillin allergy," "penicillin allergy delabeling," "hospital penicillin allergy review," "antimicrobial stewardship," "broad-spectrum antibiotics," and "β-lactam antibiotics." The review considered publications from 2017–2026.

Study selection

Twelve publications addressed allergy assessment or delabeling and reported findings on prescribing, safety, implementation, or cost. They included six primary hospital intervention or pilot studies, one retrospective parallel-cohort

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study, four systematic reviews or meta-analyses, and one economic evaluation. Reports outside the review's scope were excluded. Detailed eligibility rules for age, language, and setting were not recorded, nor were reasons for excluding individual reports. Reviews of pediatric, outpatient, or mixed populations provided context, with limited direct applicability to adult hospital practice.

An evidence matrix captured each publication's design, population or setting, intervention, main findings, and reported limitations. The synthesis grouped findings by prescribing, safety, implementation, and cost. Primary studies provided direct evidence from hospitals, and systematic reviews supplied broader context. A primary study and a review that includes it may draw on the same evidence.

Table 1 describes the 12 publications. Study limitations were assessed descriptively. The review used neither a formal quality appraisal tool nor a framework for grading certainty.

The interpretation accounted for differences in how studies defined outcomes, which denominators they used, how they tested patients, and how long they followed them. The review calculated neither a combined patient total nor a pooled effect. Because overlap between the primary studies and the four reviews was not formally mapped, agreement across publications may partly reflect shared data. The synthesis treated prescribing, label removal, negative tests, and clinical outcomes as separate findings.

Table 1. Characteristics of Studies Included in the Literature Review.

Design	Setting and pathway	Evidence contribution	Main limitation	Source
Primary hospital intervention	625 hospitalized patients; skin testing or computerized guidance	Preferred β-lactam use; uptake; no clear overall reduction in alternatives	Single center; incomplete testing uptake	[4]
Primary multicenter intervention	Two Australian hospitals; history review and low-risk oral challenge	Narrow-spectrum use, appropriate prescribing, restricted use, safety	Observational; selected eligible patients	[2]
Primary ward-round intervention	106 adult inpatients; multidisciplinary pharmacist-led review	Restricted use; recommendation acceptance; feasibility	Small single-center study; no separate control	[5]
Systematic review	284 publications; 98,316 participants; β-lactam testing	Delabeling, safety, subsequent use	Low overall quality; heterogeneous populations; possible overlap	[6]
Retrospective parallel cohort	368 patients at two Canadian campuses; direct oral challenge program	β-lactam use within six months of the index admission	Retrospective; setting and selection effects	[7]
Systematic review	42 studies; hospitalized adults; varied pathways	Effectiveness, barriers, facilitators	Heterogeneous strategies; possible overlap	[3]
Systematic review and meta-analysis	Adult/pediatric and mixed settings; nonallergist delivery	Delabeling, harm, reach of pathways	Heterogeneity; indirectness for hospital adults; possible overlap	[8]
Systematic review	Penicillin testing; five studies in pathway comparison	Direct challenge versus skin-test-plus-drug safety	Low-certainty comparison; selected populations	[9]
Primary before-and-after intervention	Hospital; education and risk-based test-dose algorithm	Relative changes in antibiotic use	Small, nonrandomized; concurrent practice changes	[10]
Primary pilot program	66 adults; pharmacist-led history review	18% delabeled; approximately five minutes per assessment	Small pilot; no control; limited prescribing inference	[11]
Economic evaluation	24 base-case inpatient/outpatient models	Modeled cost savings and uncertainty	Assumption-dependent; not observed hospital savings	[12]
Primary observational program evaluation	US tertiary hospital; pharmacist assessment and skin testing	Antibiotic use; testing; clinical outcomes	Single center; residual confounding	[1]

Results

Impact on Antibiotic Prescribing

The hospital studies measured several aspects of prescribing, including use of preferred β-lactams, narrow-spectrum penicillins, restricted antibiotics, and alternatives to penicillin. These measures differ in how directly they address inappropriate broad-spectrum exposure.

Table 2 summarizes prescribing findings from the seven primary hospital studies. The four reviews and the economic evaluation are discussed separately because they provide different types of evidence.

Table 2. Prescribing Findings in Primary Hospital Studies.

Outcome	Reported finding	Interpretation	Source
Preferred β-lactam and alternative use	Preferred use increased with some approaches; no clear overall fall in alternatives	Does not establish consistent broad-spectrum reduction	[4]

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Table 2 (continued)

Outcome	Reported finding	Interpretation	Source
Distinct prescribing outcomes	Narrow-spectrum penicillin aOR 10.51 (95% CI 5.39–20.48); appropriate use aOR 2.13 (1.45–3.13); restricted use aOR 0.38 (0.27–0.54)	Observational associations; endpoints should remain separate	[2]
Restricted-antibiotic use	42.5% before versus 17.9% after; −24.6 percentage points	Local restriction category; no separate control	[5]
Subsequent β-lactam use	Greater β-lactam use in the intervention group within six months of the index admission	Total β-lactam use does not identify spectrum or appropriateness	[7]
Antibiotic-specific relative use	Penicillins +256% (P=.04); cephalosporins +121.2% (P=.03); reduced vancomycin use	Relative changes; broad-spectrum inference requires agent-level data	[10]
History-based delabeling feasibility	18% of assessed patients delabeled	Does not provide a robust comparative broad-spectrum effect	[11]
β-lactams and selected alternatives	Favorable associations with β-lactam use and reduced selected alternative/high-CDI-risk use	Different endpoints; observational program evaluation	[1]

Chua et al., found that delabeling was associated with more narrow-spectrum penicillin use (adjusted odds ratio (aOR), 10.51, 95% confidence interval (CI), (5.39–20.48), more appropriate prescribing (aOR, 2.13, 95% CI, 1.45–3.13), and less restricted-antibiotic use (aOR, 0.38, 95% CI, 0.27–0.54) [2]. The study assessed these as separate outcomes within a framework that covered the index admission and 90-day follow-up. Its observational design leaves open how much of the change was attributable to delabeling alone.

After an intervention that combined education with risk stratification, Sacco et al. (2019) reported relative increases of 256% in penicillin use (P = .04) and 121.2% in cephalosporin use (P = .03) [4]. The percentages describe changes relative to baseline. The spectrum of the additional β-lactam prescriptions cannot be inferred from these changes alone.

Turner et al., found associations between pharmacist-led assessment or testing and changes in antibiotic use [1]. Mir et al., reported that β-lactam use within six months of the index admission was higher in the intervention group [5]. These findings suggest improved access to β-lactam treatment. They leave open whether inappropriate broad-spectrum use declined and by how much.

Restricted-antibiotic use fell from 42.5% to 17.9% in Devchand et al., a decrease of 24.6 percentage points [6]. Sacco et al., reported less vancomycin use, and Chua et al., reported less use of restricted antibiotics [2,4]. Turner et al., examined alternatives to penicillin and antibiotics associated with a higher risk of Clostridioides difficile infection [1]. Each measure addresses a different prescribing concern, so they cannot be combined into a single measure of broad-spectrum exposure.

The programs produced different results. Blumenthal et al., reported more use of preferred β-lactams with some intervention approaches, with no clear overall decline in use of alternative antibiotics [7]. Song et al., primarily examined whether history-based delabeling was feasible and offered limited comparative evidence on broad-spectrum prescribing [8].

The primary studies suggest that structured allergy review can change which antibiotics patients receive. Direct evidence on inappropriate broad-spectrum use was limited and inconsistent. Differences in who underwent assessment, concurrent stewardship activities, and patient case mix may explain some of the observed changes.

Safety of Penicillin Allergy Label Review

The interpretation of safety findings depends on the type of allergy reaction, eligibility for testing, the testing method, and the observation period. Table 3 distinguishes negative skin tests, negative oral challenges, formal label removal, and tolerance during subsequent treatment where data are available. Patients on different pathways may have different baseline risks, which limits direct comparison of percentages.

Powell et al., reported a pooled delabeling proportion of 98% (95% CI, 97–99%) among 1,373 patients who underwent direct challenge [9]. Nonserious harm was reported in 1% (95% CI, 0–2%). Among the 4,207 patients assessed for the direct-challenge pathway, the pooled proportion delabeled was 27% (95% CI, 18–37%). The two estimates describe different groups and show why the number assessed matters when judging a program's reach.

Powell et al., also examined skin testing followed by drug provocation [9]. Among 1,294 patients tested, 95% were delabeled (95% CI, 90–99%). Reported harm was 0% (95% CI, 0–1%). Loprete et al., reviewed 284 publications covering 98,316 participants and found that 95.6% of those who underwent provocation testing were delabeled [10]. Testing-related anaphylaxis occurred in 95 of the 31,667 participants with relevant data (0.3%). The denominator for this estimate was the subset with relevant data. The included studies varied widely, and the overall quality of the evidence was low.

Table 3. Safety Outcomes of Penicillin Allergy Testing and Delabeling Across Included Studies.

Endpoint or pathway	Result	Interpretive limitation	Source
Direct drug provocation	98% delabeled among 1,373 tested (95% CI 97–99%); 1% nonserious harm (0–2%)	27% pooled delabeling among 4,207 assessed; selected completers	[9]

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Table 3 (continued)

Endpoint or pathway	Result	Interpretive limitation	Source
Skin test followed by provocation	95% delabeled among 1,294 tested (95% CI 90–99%); reported harm 0% (0–1%)	Testing success differs from pathway reach	[9]
Provocation; heterogeneous pathways	95.6% delabeled after provocation; anaphylaxis 95/31,667 (0.3%)	98,316 total review participants are not the anaphylaxis denominator	[10]
Direct challenge vs skin-test-plus-drug pathway	Minor immediate reactions 2.3% vs 11.5%; RR 0.25 (95% CI 0.15–0.45); no anaphylaxis/deaths reported	Five comparative studies; low certainty; pathway-specific risks	[11]
Selected low-risk oral challenge	194/200 negative challenges (97%); 355 total delabeled including 161 by history	Challenge negativity is not population-wide delabeling	[2]
Skin testing	187/193 skin tests negative (96.9%)	Not equivalent to completed delabeling or long-term tolerance	[1]
Ward-round review and selected testing	One delayed rash reported; no serious immediate reaction reported	Small selected population; precision limited	[6]

Providencia et al., identified five studies that compared direct oral challenge with skin testing followed by drug administration [11]. Minor immediate reactions occurred in 2.3% of patients in the direct-challenge group and 11.5% of patients in the skin-testing-plus-challenge group (risk ratio, 0.25, 95% CI, 0.15–0.45). The latter rate covers the full pathway, including subsequent drug administration. None of the comparative studies reported anaphylaxis or deaths. The low certainty of the evidence limits how far these findings can be generalized.

In Chua et al., 194 of 200 oral challenges were negative (97%) [2]. The program delabeled 355 patients altogether, including 161 whose labels were removed based on their histories. The 97% figure applies only to selected patients who underwent oral challenge.

Turner et al., reported 187 negative results among 193 skin tests (96.9%) [1]. A negative result leaves open whether the label was removed and whether the patient later tolerated treatment. The safety findings support protocol-based assessment in appropriately selected patients. There is less evidence on longer-term outcomes and patients who would fall outside the studies' selection criteria.

Implementation and Hospital Stewardship

Hospitals used pharmacist-led history review, multidisciplinary ward rounds, computerized prescribing guidance, skin testing, and observed oral challenge. These approaches serve different clinical purposes and require different staff and resources. Feasibility assessments should distinguish between correcting a label based on the history and using a challenge to confirm tolerance.

Devchand et al., described a weekly multidisciplinary ward round involving a pharmacist, an infectious diseases physician, and an allergy nurse [6]. The median round lasted 75 minutes, and medical teams accepted 81.5% of the recommendations. In Turner et al., pharmacists took allergy histories, identified patients eligible for testing, and helped coordinate testing through the stewardship program [1].

In Song et al., pharmacist-led history review took about five minutes per patient [8]. Of the 66 patients assessed, 18% were delabeled without routine skin testing or oral challenge. Powell et al., also found that trained nonallergy professionals could conduct assessments under defined protocols [9]. The need for specialist support still depends on the patient and the assessment pathway.

Across 42 studies, Nürnberg et al., reported 5,017 successful delabelings among 6,269 patients who underwent assessment or a delabeling pathway (80%) [3]. Limited resources, reluctance among patients or staff, training, and workflow all affected implementation. As a synthesis of existing studies, this review provides context for the primary hospital findings and may overlap with them.

A program's reach depends on how many eligible patients complete assessment or testing. In Blumenthal et al., 43 of the 179 patients eligible for proactive skin testing completed it [7]. A high success rate among those tested can therefore coexist with limited uptake. Reporting both figures gives a fuller picture of program performance.

Cost and feasibility

A brief history review has different staffing and observation needs from skin testing or an observed challenge. Whether a pathway is feasible at another hospital depends on the resources available and the patients it serves.

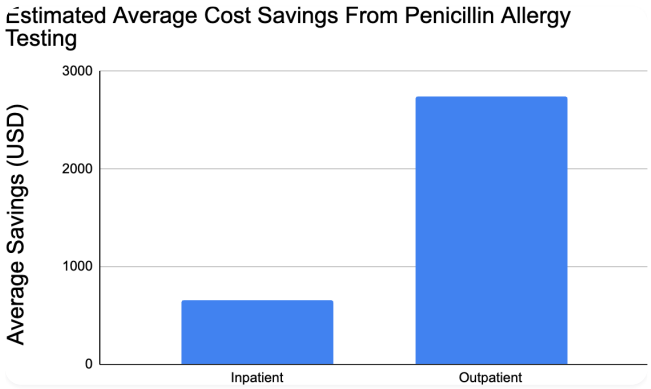

Figure 1. Modeled Average Cost Savings From Penicillin Allergy Testing.

Note. Values are model-based averages in US dollars, not observed trial savings. Source: Sousa-Pinto et al. [12]. Approximately 75% of probabilistic sensitivity-analysis simulations favored testing; regional estimates varied.

All 24 base-case models in Sousa-Pinto et al., estimated that testing would save money [12]. The models of skin testing followed by drug challenge estimated average savings of US$657 per inpatient and US$2,746 per outpatient. Approximately 75% of simulations in the probabilistic sensitivity analysis identified testing as the less costly option. Figure 1 shows the modeled averages for the two settings. The

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estimates represent projected savings rather than costs observed in a clinical trial.

The outpatient estimate offers context for the economic analysis and has limited applicability to inpatient programs. Local treatment costs, staffing, testing performance, and regional assumptions all affect whether the estimates apply elsewhere. Song et al., reported five minutes per history assessment, whereas Devchand et al., reported 75 minutes for a weekly ward round [6,8]. These are different units of activity and cannot be compared as per-patient costs.

Hospitals weighing different pathways need to consider which patients are eligible, what expertise is available, how many patients complete testing, and what the service costs locally. The evidence leaves open which approach is most feasible or least costly for a particular hospital.

Discussion

Hospital penicillin allergy review may help eligible patients receive preferred β-lactams. Several programs also reported lower use of selected restricted or alternative antibiotics. Because studies measured different prescribing outcomes, there is less direct evidence that allergy review reduces inappropriate broad-spectrum prescribing.

The primary studies are most relevant to hospital practice. Many used observational or before-and-after designs, however, so the reported changes may reflect who was selected for assessment, other stewardship initiatives, or changes in prescribing over time.

Chua et al., Devchand et al., Sacco et al., and Turner et al., reported favorable changes or associations in prescribing [1,2,4,6]. Blumenthal et al., found that use of preferred β-lactams could increase without a clear corresponding decline in alternative-antibiotic use [7]. Differences in the interventions, baseline prescribing, patient populations, and follow-up may help explain why findings varied.

Future studies could address inappropriate broad-spectrum use more directly by measuring exposure to individual antibiotics, defining what counts as broad-spectrum or restricted use, and judging appropriateness against explicit clinical criteria. Comparable denominators, such as patient-days for reporting days of therapy, would help readers compare findings across hospitals.

Serious reactions were uncommon in the selected populations studied under defined testing protocols. Risk remains, and findings from low-risk oral challenge candidates have limited applicability to patients with a history of severe immediate or delayed reactions. Studies should report negative tests, label removal, and sustained tolerance separately.

Pharmacists and other trained professionals can help assess patients and coordinate testing. How well a program works depends on who takes part as well as the results among those who complete testing. Training, clear protocols, access to specialist advice, and fit with existing hospital workflows all matter. The studies provide limited evidence for comparing delivery models directly.

Models suggest that testing can save money, although the estimates depend on assumptions and vary by region. Existing systematic reviews cover delabeling effectiveness, safety, and barriers. This narrative review focuses on what the selected evidence means for hospital prescribing and distinguishes changes in antibiotic use from testing success and program reach. It provides a qualitative interpretation of effectiveness.

Limitations

This selective narrative review included 12 publications. Search dates, full search strategies, screening counts, and detailed eligibility decisions were not documented, making the search difficult to reproduce and its coverage uncertain. The review included no formal appraisal of risk of bias or grading of evidence certainty.

Some of the primary studies may also appear in the included systematic reviews. Because the overlap was not formally mapped, apparently consistent findings may reflect the same data. Reviews covering different age groups and care settings also have limited direct applicability to adult hospital care.

Confounding and selection bias are possible in the observational and before-and-after studies. The studies also differed in what the interventions involved, how outcomes were defined, which denominators were used, and how long patients were followed. Some studies did not directly measure broad-spectrum use or prescribing appropriateness, which prevented a unified estimate for those outcomes.

Most safety findings came from selected testing populations. Longer-term follow-up is needed to establish whether patients with negative tests remain delabeled and tolerate treatment. Publication bias is possible and was not formally assessed. Modeled economic findings may have limited applicability to local costs and workflows.

Conclusion and Recommendations

Hospital penicillin allergy review may help eligible patients receive preferred β-lactams and improve antibiotic selection. Several studies reported less use of selected restricted or alternative antibiotics. Evidence that allergy review reduces inappropriate broad-spectrum prescribing was limited and inconsistent.

Serious reactions during testing and delabeling were uncommon among appropriately selected patients. Trained pharmacists and other healthcare professionals helped deliver these services, although the proportion of patients reached and the resources required varied by program.

Hospitals considering structured allergy review as part of stewardship can use local protocols and available expertise to decide how to assess risk, correct labels based on history, arrange testing, and refer patients to specialists.

Comparative studies should specify how prescribing appropriateness is judged, measure use of individual antibiotics, and report how many patients complete each pathway and whether they remain delabeled over time. Longer-term safety follow-up and local economic evaluations would help clarify which approaches can reduce inappropriate broad-spectrum use across hospital settings.

Author Contributions

Research planning and study design: R.S., A.B.; Literature synthesis: R.S., A.B.; Manuscript development: R.S., A.B.; Critical revision and technical assistance: R.S., A.B.; Project leadership & supervision: A.B. All authors have reviewed, approved the final manuscript, and agree to be accountable for the work.

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https://doi.org/10.61577/jmi.2026.100006

Funding

The authors received no specific external grants from any funding agency in the public, commercial, or not-for-profit sectors for this review.

Conflict of Interest

The authors declare no competing financial, personal, or professional interests.

Ethics Declaration

Not Applicable

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