

Original Article

Antibiotic use and financial impact of a comprehensive beta-lactam allergy management program

Karan Raja PharmD, BCPS, BCIDP, AAHIVP^{1,2} , Lakhini Vyas PharmD, BCPS, BCCCP¹ , Susan Morrison MD³, Donald Beggs MD³, Mitesh Patel PharmD, BCCCP¹ and Mona Philips RPh, MAS¹

¹Pharmacy Department, Clara Maass Medical Center, Belleville, NJ, USA, ²Rutgers, The State University of New Jersey, New Brunswick, NJ, USA and ³Medicine Department, Clara Maass Medical Center, Belleville, NJ, USA

Abstract

Objective: A multidisciplinary beta-lactam allergy management program was implemented at our community medical center to facilitate allergy documentation, conduct penicillin skin testing (PST), and decrease non-beta-lactam (NBL) use. This study measures PST-associated antibiotic use and financial outcomes.

Design: Cohort study.

Setting: Non-teaching, urban, community medical center within a multi-hospital health system.

Patients: Adult inpatients who underwent PST and received antibiotic therapy during a 5-year period at our facility.

Methods: Demographics, allergies, laboratory results, PST outcome, and antimicrobial regimens were assessed. Actual NBL days of therapy (DOT) were collected from the electronic medical record. NBL DOT that patients would have received without PST were modeled by forecasting the original regimen to end of inpatient treatment. Difference between actual and forecasted DOT was deemed DOT avoided (DOT-A) for each consecutively enrolled patient. The financial analysis evaluated cumulative NBL cost avoided. PST outcomes and average time from antibiotic initiation to PST were assessed.

Results: The study included 600 patients who underwent PST an average of 3.7 days into treatment. The most common indication was acute bacterial skin and skin structure infections (23.9%). PST results were negative in 98% of patients. NBL DOT-A was 944.8/1000DT (8.8 DOT-A per intervention) accounting for an estimated cost savings of \$206,500 (\$344.10 per intervention), driven primarily by aztreonam avoidance.

Conclusions: This study highlights significant avoidance of NBL DOT in one of the largest identified cohort of inpatients undergoing PST. Associated cost avoidance contributes to the sustainability and longevity of the allergy management program.

(Received 31 October 2024; accepted 17 January 2025)

Introduction

Beta-lactam class antibiotics are among the safest and most efficacious agents used in treating various bacterial infections.^{1–4} However, beta-lactams account for the majority of inpatients' self-reported medication allergies in the United States.¹ Published literature confirms that a majority of patients do not have an IgE-mediated reaction upon skin testing and can be safely transitioned to an appropriate, targeted beta-lactam.^{1,2} Additionally, a significant number of patients with reported anaphylaxis to penicillins may lose their sensitivity over time.²

Allergy misclassification increases use of broad-spectrum, alternative antibiotics, potentiates antimicrobial resistance, and increases cost of care.^{1–3,5–8} This can heighten the risk of

suboptimal infection-related outcomes, prolonged hospital stays, and readmission.^{1,6,9–11} NBL prescribing likely stems from allergy documentation rather than microbiologic criteria in patients with a documented beta-lactam allergy.^{1,6} Therefore, clarifying antibiotic allergy status is beneficial in both immediate and long-term antimicrobial stewardship efforts. Previous studies have also described an increase in direct antimicrobial treatment cost in patients with a documented penicillin allergy.^{12,13} Trubiano and colleagues compared oncology patients with and without an antimicrobial allergy label (primarily beta-lactams, 65%).¹¹ Those with an allergy label experienced increased overall antibiotic use per admission, increased fluoroquinolone use, longer antibiotic courses, and higher readmission rates.

The Infectious Diseases Society of America and American Academy of Allergy, Asthma, and Immunology advocate for avoiding non-beta-lactam (NBL) antibiotic overuse without thorough allergy evaluations.^{14,15} Comprehensive allergy management programs should include detailed allergy history-taking, risk

Corresponding author: Karan Raja; Email: karan.raja@rwjbh.org

Cite this article: Raja K, Vyas L, Morrison S, Beggs D, Patel M, Philips M. Antibiotic use and financial impact of a comprehensive beta-lactam allergy management program. *Antimicrob Steward Healthc Epidemiol* 2025. doi: 10.1017/ash.2025.36

© The Author(s), 2025. Published by Cambridge University Press on behalf of The Society for Healthcare Epidemiology of America. This is an Open Access article, distributed under the terms of the Creative Commons Attribution licence (<https://creativecommons.org/licenses/by/4.0/>), which permits unrestricted re-use, distribution and reproduction, provided the original article is properly cited.

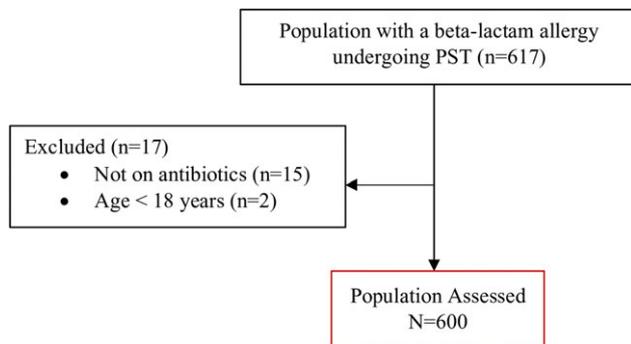


Figure 1. Patient CONSORT diagram.

Table 1. Baseline characteristics

Characteristic	
Age – year, mean (SD)	67.4 (16.8)
Female sex – no (%)	414 (69)
Length of stay – days, mean (SD)	11.2 (8.5)
Duration of antibiotic therapy – days, mean (SD)	9.2 (7.0)
Antibiotic Allergen Class – no (%)	Total Allergens = 613
Penicillin	554 (90.4)
Cephalosporin	54 (8.8)
Carbapenem	5 (0.8)
Antibiotic Indication – no (%)	Total Infections = 669
Skin and soft tissue	160 (23.9)
Urinary tract	156 (23.3)
Pulmonary	144 (21.5)
Intra-abdominal	93 (13.9)
Other	116 (17.4)

Note. Some patients had multiple allergens documented and were treated for multiple infections; therefore, the total number of allergens and infections is greater than the total number of patients.

stratification, and penicillin skin testing (PST) or direct drug challenge if needed.^{3,5} A thorough allergy history is often sufficient to rule out significant allergy and allows for beta-lactam use.⁵ PST additionally offers a >95% negative predictive value for ruling out IgE-mediated hypersensitivities and is an instrumental component of antimicrobial stewardship programs.^{2,3,16–20}

Studies evaluating PST programs have demonstrated a reduction in NBL antibiotic days of therapy (DOT), length of hospital stay (LOS), hospital readmissions, and cost of care, by avoiding costly alternatives or combination therapy.^{1,2,5,7,8,21} Heil and colleagues found a reduction in aztreonam use from 3.4 to 1.9 DOT/1000 PD after PST implementation.²² This corresponded to approximately \$26,000 in savings per year. However, there are limited studies assessing the financial and NBL use impact of a comprehensive allergy management program in such a large patient population, particularly in non-teaching, community medical centers without medical residents or ID fellows.

A multidisciplinary beta-lactam allergy management program was implemented at our institution to facilitate complete allergy documentation and increase use of targeted beta-lactams. The objective of the current study is to evaluate NBL utilization and financial outcomes associated with this program. To our

knowledge, this study presents outcomes in one of the largest published inpatient PST cohorts.

Methods

This study was conducted at a non-teaching, urban, community medical center with a multidisciplinary allergy management program established in April 2019. As part of this existing program, pharmacists, infectious disease physicians, and an allergy and immunology physician identified inpatients with a beta-lactam allergy and collected detailed medication allergy histories. Patients were risk stratified as high, moderate, or low risk of IgE-mediated allergy based on the reaction history. Direct beta-lactam drug challenge was recommended for patients with low-risk histories. Moderate-risk patients were recommended to be further evaluated with PST. Beta-lactam avoidance was recommended in high-risk patients. For de-labeled patients, the pharmacist and allergist collaborated with hospitalists or ID consultants to optimize antimicrobial therapy and increase use of beta-lactams, as appropriate. We previously published details of this program.²³

The electronic medical record (EMR) was queried for all inpatients who underwent PST at our institution from program initiation (April 11, 2019). Patients were excluded if not on inpatient antibiotic therapy or were under 18 years old. Patients were consecutively screened and enrolled. Patient demographics, allergy information, antimicrobial indications, laboratory and culture results, PST results, and antimicrobial therapy regimens were retrieved from the EMR. Patient's actual antibiotic DOT was collected from the EMR. "Actual NBL DOT" included total NBL DOT that the patients received throughout the treatment course, before and after undergoing PST. We assumed that if no PST had been conducted, patients' antibiotic therapy before PST would have remained unchanged for the remainder of the treatment course, termed "forecasted NBL DOT." Treatment course was defined as antibiotic therapy for the current indication(s) and was censored at hospital discharge if needed. The difference between actual and forecasted DOT was deemed DOT avoided (DOT-A) for each patient. Although all antibiotic regimens were evaluated, this study focused on decreasing NBL use. Outcomes evaluated include total NBL DOT-A normalized per PST intervention and per 1000 days of inpatient antibiotic treatment (1000DT). The financial analysis evaluated the cumulative NBL cost avoided normalized per PST intervention and per 1000DT. The cost per day was calculated by multiplying the defined daily dose (DDD) of each antibiotic by the wholesale acquisition cost (WAC), as of April 2024, in USD. The DDD and WAC were used to allow for greater generalizability in various practice settings. Additional endpoints evaluated were PST outcomes and the average time into antimicrobial therapy that PST was conducted to uniquely frame the impact on our results. Outcomes were assessed with descriptive statistics, including measures of central tendency and dispersion.

Results

Between April 1, 2019 and July 8, 2024, there were 617 inpatients with a beta-lactam allergy who underwent PST at our institution. After excluding those without inpatient antimicrobial therapy or under 18 years old, 600 patients were included for study analysis (see Figure 1). Patients were an average of 67.4 ± 16.8 years old and a majority were female (69%). The average hospital length of stay was 11.2 ± 8.5 days and average duration of antibiotic therapy was 9.2 ± 7 days. Patients underwent PST an average of 3.7 ± 3.6 days into antimicrobial treatment.

Table 2. Cost of NBL therapy

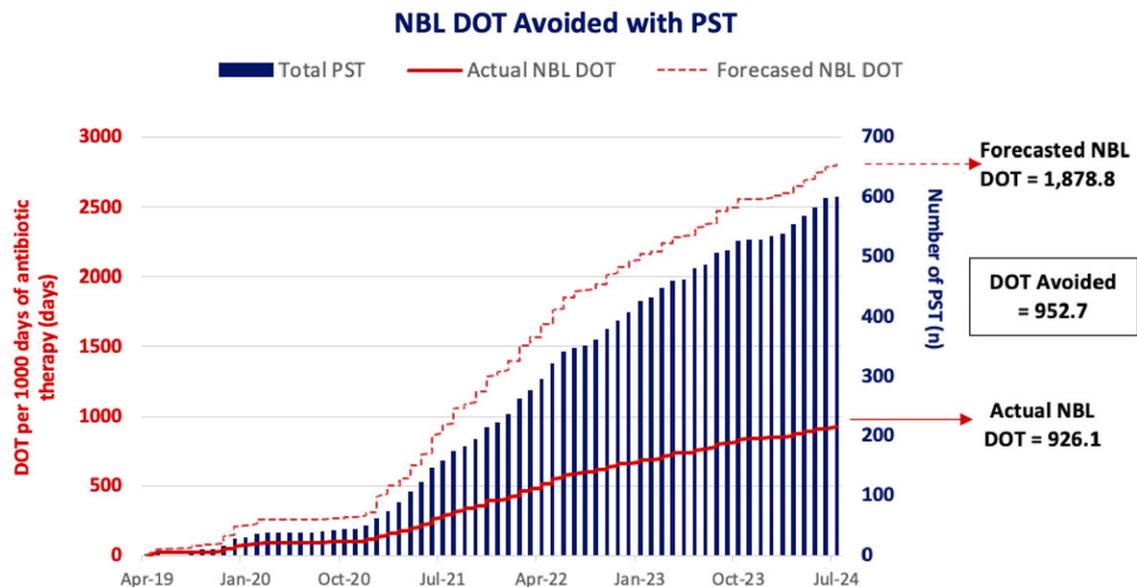
	Forecasted	Actual	Avoided
NBL DOT (days)	10,352	5,103	5,249
NBL DOT per 1000DT	1,878.8 ± 3.24	926.1 ± 1.65	952.7 ± 2.2
NBL DOT per intervention	17.3 ± 0.03	8.50 ± 0.02	8.8 ± 0.02
Total NBL Cost	\$380,609	\$174,151	\$206,458
NBL cost per 1000DT	\$69,076.04 ± \$173.30	\$31,606.35 ± \$106.09	\$37,469.69 ± \$100.56
NBL cost per intervention	\$634.35 ± \$1.59	\$290.25 ± \$0.97	\$344.10 ± \$554.38

Abbreviations: NBL, non-beta-lactam; DOT, days of therapy; 1000DT, 1000 days of antibiotic therapy.

Table 3. Non-beta-lactam cost avoided

	Total DOT Avoided	Cost per day ^a	Cost Avoided (\$)
Aztreonam	1,735	\$92.00	\$159,620
Vancomycin	893	\$16.00	\$14,288
Clindamycin	387	\$33.00	\$12,771
Linezolid	223	\$24.00	\$5,352
Doxycycline	240	\$16.00	\$3,840
OTHER	1,771		\$10,587
Total	5,249		\$206,458

^aCost per day is calculated based on WHO DDD × WAC cost in USD (as of April 2024).

**Figure 2.** Non-beta-lactam days of therapy per 1000 days of antibiotic therapy. Abbreviations: NBL, non-beta-lactam; DOT, days of therapy.

There were 613 distinct beta-lactam allergies and 669 antimicrobial indications in the study population, as some patients had more than one drug allergen or infection source documented. There were 554 patients with a penicillin class allergy (90.4%), 54 patients with a cephalosporin class allergy (8.8%), and 5 patients with a carbapenem class allergy (0.8%). Antimicrobial indications included acute bacterial skin and skin structure infections (23.9%), urinary tract infection (23.3%), pulmonary infection (21.5%), intra-abdominal infection (13.9%), and other infections (17.4%). Upon PST, 588 patients (98%) tested negative, 8 (1.3%) tested positive, and 4 (0.7%) were indeterminate due to recent antihistamine administration. There were two instances of antimicrobial intolerance after administration of optimized therapy after negative PST. All baseline characteristics are shown in Table 1.

Amongst the 600 patients evaluated, total NBL DOT-A was 5,249 days and total associated cost savings were \$206,458. This equated to NBL DOT-A of 952.7 per 1000DT or an average of 8.8 ± 12.3 DOT-A per PST intervention (see Figure 2). Total cost savings was \$37,469.69 per 1000DT or an average of \$344.10 ± \$554.38 per PST intervention, driven primarily by aztreonam

avoidance. NBL DOT and cost outcomes are shown in Table 2. Cost savings for each NBL agent is shown in Table 3.

Discussion

This study evaluated a large inpatient PST cohort that demonstrated significant NBL DOT and cost avoidance per PST intervention, supporting program financial viability and sustainability. PST benefits likely extend beyond these study outcomes, contributing to reduced morbidity, mortality, and hospital LOS with targeted antimicrobial therapy²⁵, likely secondary to greater effectiveness and/or lower adverse event rates.^{24,25} Additionally, optimal inpatient management and stewardship positively impact outpatient antibiotic use and costs.^{25,26}

There were 8.8 ± 12.3 NBL DOT-A per PST intervention or an average of 952.7 NBL DOT-A per 1000DT. Chen and colleagues evaluated 228 patients who underwent PST in a pharmacist-allergist collaboratively managed program, where 504 inpatient days (2.2 DOT-A per PST intervention) and 648 outpatient days of alternative antibiotic therapy were avoided.²⁶ Ramsey and

colleagues described an PST program that avoided 982 days of combined inpatient and outpatient second-line antibiotic therapy.²⁵ Differences in DOT-A rate may be attributable to time into therapy PST was conducted, evaluation of inpatient-only compared to combined inpatient and outpatient data and baseline NBL prescribing rates. The significant avoidance of NBL DOT after PST intervention contributed to the total cost savings of \$206,458 amongst the 600 patients in the 5-year study period. This equates to \$37,469.69 per 1000DT and an average of \$344.10 ± \$554.38 per PST intervention. Other studies have identified similar results with an estimated cost savings of \$225 to \$350 per patient undergoing PST.^{1,19,27,28}

In our study, the expected NBL cost decreased by 54.2% after PST, from forecasted \$380,609 to actual cost of \$174,151 (see Table 2). Macy and colleagues evaluated 236 patients and found the average antibiotic cost per patient fell 30.6% from \$71.17 to \$49.63 if the subject had a negative PST.⁹ A PST program in North Carolina demonstrated an estimated cost savings of \$82,000 in patients receiving antibiotic therapy changes as a result of PST.²

The cost savings in this study are largely driven by aztreonam avoidance. Staicu and colleagues evaluated aztreonam use after PST program implementation in 178 patients.²⁹ They found a significant reduction in aztreonam DOT from 9.5 to 4.4 DOT/1000 patient days with an associated \$60,000–\$100,000 annualized projected cost avoidance compared to other first-line agents. Heil and colleagues evaluated 90 patients and conducted PST on 76. They found a reduction in aztreonam use from 3.4 to 1.9 DOT/1000PD after PST implementation, corresponding to approximately \$26,000 in savings per year.²² In our study of 600 patients undergoing PST, a total of 1,735 days of aztreonam therapy were avoided, which accounted for a cost savings of \$159,620 for aztreonam alone during the study period. The total cost avoided for NBL agents was \$206,458, making aztreonam responsible for over 75% of total cost savings.

A strength of the study is its strong internal validity, ensured by a consistent team managing the program, which limited practice variability. Furthermore, the study reflects a pragmatic view of program outcomes, as earlier identification, assessment, and intervention of candidates could magnify study results. Treatment durations were measured observationally, reflecting true clinical practice and thereby enhancing the external validity of findings. The rate of negative PST in previous studies has ranged from 94 to 100 percent, similar to the 98% of patients who tested negative upon PST in our study.^{25,30–34} Patients underwent PST on average 3.7 days into antibiotic treatment. Some patients had antibiotics discontinued or were discharged on the day of PST. The study period also includes the peak of the COVID-19 pandemic, which likely limited program workflow due to strict infection control measures. Additionally, some patients did not have changes to their NBL antimicrobial if it was considered drug of choice.

Cost savings were derived from NBL DOT-A during the acute treatment course, not including beta-lactam therapy costs or program implementation expenses. However, while not directly measured in this study, PST programs are likely cost-effective overall as previous studies estimate a cost of \$256 [2020 USD] per PST, though variability exists.^{35,36} Additionally, patients with antimicrobial allergy labels face higher healthcare burdens, including increased risk of hospital-acquired infections (eg *Clostridioides difficile* infection), adverse drug reactions, and hospital readmissions.^{12,37,38} Therefore, cost-effectiveness of PST encompasses factors beyond direct drug costs, demonstrates sustainability, and offers enduring value. Larger studies are needed to assess long-term clinical and economic outcomes and

the impact of allergy re-labeling after PST. Cost evaluation was based on WAC of each drug as of April 2024 and DDD as per the World Health Organization. Actual cost savings may vary as per institutional contracted prices and daily dose as per indication or dose adjustment for hepatic or renal dysfunction.

Conclusion

This study presents the NBL use and financial impact in the largest identified cohort of inpatients undergoing PST in an urban, community, and non-teaching medical center. Results highlight significant avoidance of NBL DOT. Associated cost avoidance contributes to the sustainability and longevity of an allergy management program.

Financial support. None reported.

Competing interests. Dr. Donald Beggs was a former physician speaker for AbbVie Inc. The remaining authors report no conflicts of interest relevant to this article.

References

- Jones BM, Avramovski N, Concepcion AM, Crosby J, Bland CM. Clinical and economic outcomes of penicillin skin testing as an antimicrobial stewardship initiative in a community health system. *Open Forum Infect Dis* 2019;6:1–7.
- Bland CM, Bookstaver PB, Griffith NC, et al. A practical guide for pharmacists to successfully implement penicillin allergy skin testing. *Am J Health-System Pharm* 2019;76:136–147.
- Justo JA, Kufel WD, Avery L, Bookstaver PB. Penicillin allergy skin testing in the inpatient setting. *Pharm* 2019;7:120.
- Kufel WD, Justo JA, Bookstaver PB, Avery LM. Penicillin allergy assessment and skin testing in the outpatient setting. *Pharm* 2019;7:136.
- Griffith NC, Justo JA, Winders HR, Al-Hasan MN, Mediwala KN, Bookstaver PB. Regulatory approval, implementation, and brief assessment of a pharmacist- and pharmacy trainee-administered penicillin allergy assessment and skin testing program. *J Am Coll Clin Pharm* 2020;3:1269–1279.
- Taremi M, Artau A, Foolad F, et al. Safety, efficacy, and clinical impact of penicillin skin testing in immunocompromised cancer patients. *J Allergy Clin Immunol Pract* 2019;7:2185–2191.
- Macy E, Shu YH. The effect of penicillin allergy testing on future health care utilization: a matched cohort study. *J Allergy Clin Immunol Pract* 2017;5:705–710.
- Irawati L, Hughes JD, Keen N, et al. Influence of penicillin allergy on antibiotic prescribing patterns and costs. *J Pharm Pract Res* 2006;36:286–290.
- Macy E. Elective penicillin skin testing and amoxicillin challenge: effect on outpatient antibiotic use, cost, and clinical outcomes. *J Allergy Clin Immunol* 1998;102:281–285.
- Huang KG, Cluzet V, Hamilton K, Fadugba O. The impact of reported betalactam allergy in hospitalized patients with hematologic malignancies requiring antibiotics. *Clin Infect Dis* 2018;67:27–33.
- Trubiano JA, Chen C, Cheng AC, et al. Antimicrobial allergy 'labels' drive inappropriate antimicrobial prescribing: lessons for stewardship. *J Antimicrob Chemother* 2016;71:1715–1722.
- Macy E, Contreras R. Health care use and serious infection prevalence associated with penicillin "allergy" in hospitalized patients: a cohort study. *J Allergy Clin Immunol* 2014;133:790–796.
- Mattingly TJ. The economics of drug allergy. *Curr Opin Allergy Clin Immunol* 2020;20:395–400.
- Barlam TF, Cosgrove SE, Abbo LM, et al. Implementing an antibiotic stewardship program: guidelines by the Infectious Diseases Society of America and the Society for Healthcare Epidemiology of America. *Clin Infect Dis* 2016;62:e51–77.
- American Academy of Allergy, Asthma & Immunology. Choosing Wisely: Five Things Physicians and Patients Should Question. Available at: www.choosingwisely.org/wp-content/uploads/2015/02/AAAAI-Choosing-Wisely-List.pdf. Published 2015. Accessed August 2024.

16. Cook DJ, Barbara DW, Singh KE, *et al.* Penicillin skin testing in cardiac surgery. *J Thoracic Cardiovasc Surg* 2014;147:1931–1935.
17. Shenoy E.S., Macy E., Rowe T., Blumenthal K.G. Evaluation and management of penicillin allergy: a review. *JAMA* 2019;321:188–199.
18. Package Insert PRE-PEN®. Available online: <https://www.penallergytest.com/implementation-2/package-inserts/>. Published n.d. Accessed May 25, 2019.
19. Rimawi RH, Cook PP, Gooch M, *et al.* The impact of penicillin skin testing on clinical practice and antimicrobial stewardship. *J Hosp Med* 2013;8:341–345.
20. Gadde J, Spence M, Wheeler B, *et al.* Clinical experience with penicillin skin testing in a large inner-city STD clinic. *JAMA* 1993;270:2456–2463.
21. Forrest DM, Schellenberg RR, Thien VS, *et al.* Introduction of a practice guideline for penicillin skin testing improves the appropriateness of antibiotic therapy. *Clin Infect Dis* 2001;32:1685–1690.
22. Heil EL, Bork JT, Schmalzle SA, *et al.* Implementation of an infectious disease fellow-managed penicillin allergy skin testing service. *Open Forum Infect Dis* 2016;3:1–7.
23. Vyas L, Raja K, Morrison S, *et al.* Beta-lactam comprehensive allergy management program in a community medical center. *Antimicrob Steward Health Epidemiol* 2023;3:e189.
24. Mattingly JT, Fulton A, Lumish RA, *et al.* The cost of self reported penicillin allergy: a systematic review. *J Allergy Clin Immunol Pract* 2018;6:1649–1654.
25. Ramsey A, Staicu ML. Use of a penicillin allergy screening algorithm and penicillin skin testing for transitioning hospitalized patients to first-line antibiotic therapy. *J Allergy Clin Immunol Pract* 2018;6:1349–1355.
26. Chen JR, Tarver SA, Alvarez KS, *et al.* A proactive approach to penicillin allergy testing in hospitalized patients. *J Allergy Clin Immunol Pract* 2017;5:686–693.
27. King EA, Challa S, Curtin P, *et al.* Penicillin skin testing in hospitalized patients with β -lactam allergies: effect on antibiotic selection and cost. *Ann Allergy Asthma Immunol* 2016;117:67–71.
28. Jones BM, Bland CM. Penicillin skin testing as an antimicrobial stewardship initiative. *Am J Health-Syst Pharm* 2017;74:232–237.
29. Staicu ML, Brundige ML, Ramsey A, *et al.* Implementation of a penicillin allergy screening tool to optimize aztreonam use. *Am J Health Syst Pharm* 2016;73:298–306.
30. Gugkaeva Z, Crago JS, Yasnogorodsky M. Next step in antibiotic stewardship: Pharmacist-provided penicillin allergy testing. *J Clin Pharm Ther* 2017;42:509–512.
31. Wall GC, Peters L, Leaders CB, Willie JA. Pharmacist-managed service providing penicillin allergy skin tests. *Am J Health Syst Pharm* 2004;61:1271–1375.
32. Leis JA, Palmay L, Raybardhan S, *et al.* Point-of-care B-lactam allergy skin testing by antimicrobial stewardship programs: a pragmatic multicenter prospective evaluation. *CID* 2017;65:1059–1065.
33. Torney N, Tiberg M. Implementation of a pharmacist-managed penicillin skin testing (PST) service at a community teaching hospital. *Open Forum Infect Dis* 2016;3:1857.
34. Englert E, Weeks A. Pharmacist-driven penicillin skin testing service for adults prescribed nonpreferred antibiotics in a community hospital. *Am J Health-Syst Pharm* 2019;76:2060–2069.
35. Thao V, Sharpe EE, Dholakia R, *et al.* Evaluating the cost-effectiveness of testing pregnant women for penicillin allergy. *PLoS One* 2023;18:e0280151.
36. Blumenthal KG, Li Y, Banerji A, *et al.* The cost of penicillin allergy evaluation. *J Allergy Clin Immunol Pract* 2019;6:1019–1027.
37. Trubiano JA, Leung VK, Chu MY, *et al.* The impact of antimicrobial allergy labels on antimicrobial usage in cancer patients. *Antimicrob Resist Infect Control* 2015;4:1–4.
38. MacFadden DR, LaDelfa A, Leen J, *et al.* Impact of reported beta-lactam allergy on inpatient outcomes: a multicenter prospective cohort study. *Clin Infect* 2016;63:904–910.