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Research Article

Development and Pilot Testing of a Pharmacist-Led β-Lactam Allergy Risk Assessment Tool for Chinese Patients

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Abstract

Background: β-lactam allergy labels (BALs) are commonly found in patient records but are often inaccurate. This can lead to suboptimal antibiotic selection, increased healthcare costs, and antimicrobial resistance. Most existing risk assessment tools were developed in Western settings and are not applicable in Chinese clinical contexts. This study developed and pilot-tested a pharmacist-led BAL risk assessment tool tailored to the Chinese healthcare environment. **Methods**: The study was conducted in three phases: (1) A systematic review of 90 studies to identify key β-lactam allergy risk factors; (2) Grounded theory and text co-occurrence analysis to extract high-risk features and construct the assessment framework; and (3) A pilot implementation in a tertiary hospital to evaluate the tool's feasibility, clinical impact, and patient outcomes using a quasi-experimental design. **Results**: The final tool comprised eight dimensions, 35 subdimensions, and over 1328 distinct coded nodes. Of the 289 patients involved in the pilot, 18.7% were classified as high risk. Compared with patients with BALs but without high-risk features, those at lower risk had significantly shorter hospital stays (8.5 $\pm$ 4.3 vs. 10.6 $\pm$ 5.5 days; $p < 0.001$), reduced hospitalization costs (17,800 $\pm$ 6200 vs. 21,000 $\pm$ 7500; $p = 0.0011$), and lower allergy event rates (0% vs. 6.5%; $p = 0.002$). β-lactam use increased (75.3% vs. 40.3%; $p < 0.001$), whereas second-line antibiotic use decreased (24.7% vs. 59.7%; $p < 0.001$). The tool also demonstrated high feasibility, achieving a 100% completion rate and strong adherence among pharmacists. **Conclusion**: This pharmacist-led risk assessment tool has strong potential for accurately identifying high-risk β-lactam allergy patients and optimising antimicrobial stewardship in Chinese hospitals. Further large-scale validation is warranted.

Keywords: beta-lactam; allergy and immunology; risk assessment; antimicrobial stewardship

1. Introduction

β-lactam allergy labels (BALs) refer to information recorded in patients' medical histories or allergy sections indicating intolerance or allergic reactions to β-lactam antibiotics, such as penicillins and cephalosporins [1]. In clinical practice, most BALs originate from self-reports by patients, family history, or undocumented adverse events, without any standardised diagnostic confirmation. It is estimated that between 6% and 25% of hospitalised patients have a BAL [2]; however, a meta-analysis published in JAMA revealed that over 95% of patients with a BAL test negative for Immunoglobulin E (IgE)-mediated allergy upon standardised skin or drug provocation testing [3], indicating a substantial mislabelling rate.

β-lactam antibiotics are considered the first-line treatment for bacterial infections due to their broad-spectrum efficacy, low toxicity, and favourable safety profile. They account for over 60% of global antibiotic use [4]. Nevertheless, patients are often denied these optimal agents and instead prescribed alternative, broader-spectrum antibiotics that are more costly and pose a greater risk of adverse effects. Studies, including a systematic review by The Lancet Infectious Diseases journal [5] and a large US cohort study [6], have demonstrated that unverified BALs are associated with an increased risk of surgical site infections, Clostridium difficile infections, colonisation with multidrug-resistant organisms, and long-term mortality [7–9]. Notably, over 50% of patients allergic to penicillin may tolerate the drug after five years, with this figure rising to 80% after ten years [4]. These findings highlight the critical need for accurate allergy assessment to avoid missed therapeutic opportunities and ensure optimal antimicrobial stewardship.

Several international tools have been developed in recent years to help clinicians identify low-risk patients who are eligible for de-labeling. These include the PEN-FAST score in Australia [10], Shenoy's multidimensional algorithm in the US [11], the Antibiotic Allergy Assessment Tool [12], and electronic screening tools tailored for paediatric populations [13]. In 2022, the American Academy of Allergy, Asthma & Immunology and the American College of Allergy, Asthma & Immunology jointly updated their clinical practice parameters, further reinforcing the importance of risk stratification based on the nature and severity of prior reactions [14]. Through the use of structured symptom checklists and risk-scoring algorithms, these tools have demonstrated success in reducing the unnecessary use of broad-spectrum antibiotics, shortening hospital stays, and lowering healthcare costs.

However, most existing tools were developed in Western settings, focusing on specific populations or use-case scenarios. Their heterogeneous assessment criteria and limited indicator coverage have hindered their adoption in clinical practice. Key variables, such as the timing of the initial reaction, reaction type and severity, organ system involvement, and comorbidities, are inconsistently defined across tools, which reduces the comparability and generalisability of results. Furthermore, cultural and systemic differences pose additional challenges to their application in non-Western healthcare environments.

The clinical use of allergy risk assessment tools remains limited in China. Despite a prevalence of 4–5.8% of BAL among hospitalised patients [15–17], there is no standardised, validated tool tailored to the Chinese population. Risk evaluation often relies heavily on clinician experience rather than objective criteria, which contributes to a persistently high false-positive rate. This issue is compounded by vague symptom descriptions, incomplete or fragmented medical records, and a lack of systematic follow-up for allergy re-evaluation. Existing international tools cannot be directly adopted by the Chinese healthcare system due to differences in language, symptom expression, phenotype, and healthcare infrastructure.

Furthermore, pharmacists in China are frequently underutilised in the allergy assessment process and are primarily responsible for dispensing medication rather than making active clinical decisions. However, given their expertise in taking medication histories and evaluating cross-reactivity, pharmacists are well-positioned to lead allergy risk assessments if they are supported by the appropriate tools and frameworks.

Therefore, there is an urgent need to develop a pharmacist-led, evidence-based, China-specific BAL risk assessment tool to address this critical issue. This would improve diagnostic accuracy, optimise the use of antimicrobials, and support national initiatives that promote the rational use of drugs and antimicrobial stewardship.

2. Materials and Methods

2.1 Study Overview

This study used a three-phase, mixed-methods approach to develop and trial a pharmacist-led β-lactam allergy risk assessment tool adapted for the Chinese clinical context. Specifically, Phase 1 involved conducting a systematic literature review to identify existing β-lactam allergy risk assessment tools, scoring criteria, and clinical indicators; Phase 2 focused on constructing the risk assessment tool using grounded theory coding and co-occurrence analysis; and Phase 3 involved evaluating the tool's feasibility and preliminary clinical outcomes through a prospective pilot implementation in a real-world hospital setting. The overall research process is summarized in Fig. 1. The study was approved by our hospital's Ethics Committee (Ethics No. KYLL-2025-293).

2.2 Phase 1: Systematic Review to Identify Risk Assessment Indicators (April 2024–August 2024)

To identify commonly used domains, indicators, and scoring methodologies in existing β-lactam allergy risk assessment tools and guidelines, which would inform the conceptual framework and content of the new tool.

2.2.1 Search Strategy

This systematic review was conducted in accordance with Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 guidelines. Four electronic databases were searched: PubMed, Embase, Web of Science, and the Cochrane Library. The search strategy included combinations of Medical Subject Headings (MeSH) and keywords such as: 'β-lactam antibiotics', 'penicillin allergy', 'cephalosporin allergy', 'drug hypersensitivity', 'risk factor', 'risk assessment', 'clinical predictor', 'allergy label'.

The search covered articles published between January 2000 and July 2024. Additionally, the reference lists of relevant articles and guidelines were manually screened to identify further eligible studies. The search strategy is provided in **Supplementary Table 1**.

2.2.2 Inclusion and Exclusion Criteria

Studies were included if they met the following criteria: reported the development, validation, or implementation of β-lactam or penicillin allergy risk assessment tools; described structured assessment frameworks, scoring systems, or symptom checklists; provided relevant outcome data (e.g., risk stratification, antibiotic use, de-labelling rates, or accuracy); and published in English. Studies were excluded if they: focused exclusively on laboratory-based or *in vitro* testing (e.g., IgE assays or skin prick tests without clinical scoring); were editorials, letters, or conference abstracts without full data; or lacked sufficient methodological detail.

2.2.3 Data Extraction and Synthesis

Two independent reviewers screened the titles, abstracts, and full texts. Any discrepancies were resolved through discussion or by a third reviewer. A standardised data extraction form was used to collect the following information: (1) Study characteristics (year, country, setting, and population); (2) Tool type (score-based, algorithmic, or checklist); (3) Assessment domains (e.g., reaction type, timing, severity, treatment, and comorbidities); (4) Risk stratification methods (e.g., numerical score or tiered categories); (5) Validation metrics (e.g., sensitivity, specificity, and predictive values); and (6) Clinical implementation outcomes (e.g., antibiotic prescribing, delabelling, and infection rates).

The extracted indicators and domains were categorised and mapped using a narrative synthesis approach. Dimensions that recurred across multiple tools were iden-

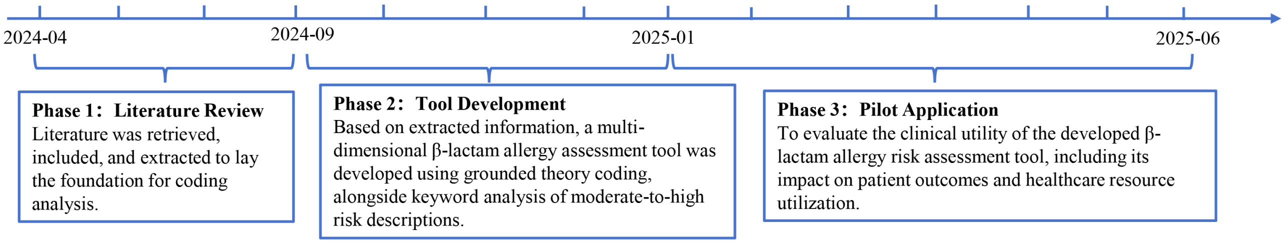

Fig. 1. Flowchart of the research process.

tified and grouped thematically to form the preliminary framework for tool development in Phase 2.

2.3 Phase 2: Tool Development (September 2024–December 2024)

The aim was to develop a structured, pharmacist-administered β-lactam allergy risk assessment tool tailored to Chinese clinical practice. This tool is intended to reflect the key domains identified in the international literature, while ensuring semantic clarity, linguistic relevance, and clinical applicability for Chinese patients and healthcare providers.

2.3.1 Literature-Based Coding and Domain Extraction

A three-stage, grounded theory-inspired coding framework was applied to publications, guidelines, and reviews on β-lactam allergy assessment.

Two trained researchers performed open coding independently, identifying meaningful semantic units related to allergy risk. These included symptom descriptors (e.g., urticaria, rash, wheezing, and anaphylaxis), temporal markers (e.g., immediate and within 1 hour), and exposure indicators (e.g., multiple doses and cross-reactivity). Diagnostic terms were also included (e.g., IgE, skin tests, and drug provocation test).

During axial coding, these concepts were categorised based on their shared clinical meaning. For instance:

• Symptom-related terms were categorised by organ system (e.g., skin/mucosa, respiratory, cardiovascular).

• Timing-related expressions were grouped under reaction latency and reaction duration.

• Exposure and outcome data were integrated into drug history, tolerance, and recurrence domains.

During selective coding, a draft framework comprising eight primary sections was constructed:

(1) Basic patient demographics, (2) Allergy history, (3) Suspected drug characteristics, (4) Reaction characteristics, (5) Management measures, (6) Clinical outcomes, (7) Diagnostic indicators, and (8) Data sources and patient concerns.

The tool's structure emphasised terminology and question logic that is suitable for use in Chinese clinical environments. This includes specific local risk factors, such as the use of traditional Chinese medicine and hospital insurance classification, as well as symptom expressions that are common in Chinese medical documentation.

Theoretical saturation was reached when five consecutive articles yielded no new codes. Coding consistency was monitored through iterative consensus discussions.

2.3.2 Semantic Risk Feature Extraction via Text Co-Occurrence Analysis

To complement and validate the results of the literature-based coding analysis, a text co-occurrence analysis [18] was performed on the complete texts of the 90 articles included in the study. Term frequencies were calculated, and the Term Frequency-Inverse Document Frequency (TF-IDF) algorithm was applied to identify important terms across the literature. A network analysis of co-occurrence with clinical descriptors such as 'high-risk', 'severe', 'immediate', and 'contraindicated' was then conducted using Python's NetworkX tool to extract keywords semantically related to severe or high-risk allergic events. These keywords were then mapped to the relevant domains of the assessment framework, such as reaction characteristics (symptom descriptors and temporal patterns), auxiliary diagnostics (immunological or laboratory markers), and drug history. This supports the data-driven construction of preliminary risk stratification logic, whereby the presence of certain semantic features could trigger a high-risk classification.

2.3.3 Risk Stratification Logic and Tool Assembly

A structured draft tool was created based on the coded domains and text-derived semantic indicators. Patients were classified as high risk if they met one or more of the following conditions:

- Presence of one or more of the 50 high-risk terms in historical or reported symptoms.

- Onset of symptoms within 1 hour of β-lactam administration.

- History of allergy to multiple β-lactam subclasses (e.g., penicillin and cephalosporin, or carbapenem).

The tool embedded management recommendations for both high- and lower-risk groups.

- High-risk patients: Referral to an allergy specialist or use of β-lactams only under close medical supervision.

Research Subjects	Inclusion/Exclusion Criteria	Usage Format	Staff Training	Usage Procedure	Effect Evaluation
Objective: Clarify the target population for tool validation to ensure sample representativeness.	**Objective:** Ensure that selected subjects meet the research goals and tool application scenarios.	**Objective:** Guarantee the standardized application of the assessment tool.	**Objective:** Improve staff understanding and operational ability of the tool to ensure accurate and standardized data collection.	**Objective:** Ensure systematic, comprehensive, and accurate patient information collection, avoiding data bias or omissions caused by improper operation.	**Objective:** Evaluate the clinical value of the tool from multiple dimensions, including risk identification ability, potential impact on patient safety, and resource optimization.
Steps: Patients hospitalized at our hospital between January 1 and June 30, 2025, with self-reported or medically documented β-lactam antibiotic allergy (e.g., penicillin, cephalosporins).	**Steps:** **Inclusion:** Age ≥18 years; capable of autonomous decision-making or with legal guardian consent; signed informed consent to participate and allow data collection. **Exclusion:** 1) Allergy to antibiotics other than β-lactams (e.g., vancomycin, quinolones); 2) Incomplete medical records or inability to obtain full allergy/clinical history; 3) Non-hospitalized patients (e.g., outpatient or emergency without admission); 4) Terminal illness or life expectancy under 3 months to avoid confounding from severe underlying diseases.	**Steps:** 1) The assessment tool is presented as a paper questionnaire, completed by pharmacists during patients' admission interviews, based on medical records and patient statements. 2) Questionnaires are collected centrally and entered into a database by the research team to ensure data integrity and accuracy.	**Steps:** Training covers: basic knowledge of β-lactam antibiotic allergy; purpose and significance of the tool; detailed explanation of dimensions and items; instructions for questionnaire completion; case demonstrations and Q&A. Delivered via PPT presentation and handbook distribution; training duration approximately 30 minutes.	**Steps:** 1) Identify patients with β-lactam allergy history at admission. 2) Pharmacists complete the assessment tool based on patient information. 3) Collect basic demographics, allergy history, clinical manifestations, reaction timing, and management measures. 4) Provide preliminary risk stratification results and management suggestions to clinicians to assist decision-making.	**Steps:** 1) Risk assessment results: number and distribution of high- and low-risk patients identified. 2) Patient prognosis: incidence of allergic reactions during hospitalization, length of stay. 3) Healthcare resource utilization: changes in usage rates of β-lactam antibiotics and alternative antibiotics, and antibiotic-related hospitalization costs before and after tool implementation.

Fig. 2. Research steps of phase 3.

- Lower-risk patients: Considered eligible for β-lactam use with informed consent and careful monitoring, contributing to future evidence accumulation for delabeling.

Each item in the tool was formatted as a closed or semi-structured question with standardised response options, making it suitable for both paper-based and electronic implementation. This structure enables pharmacists to use the tool in inpatient, outpatient, and emergency care settings.

2.4 Phase 3: Pilot Testing in Clinical Settings (January 2025–June 2025)

2.4.1 Study Design and Setting

A single-centre, quasi-experimental pilot study was conducted at a tertiary general hospital in northern China. The tool was implemented across multiple internal medicine and surgical wards as part of routine, pharmacist-led medication reconciliation at the time of patient admission. A pre-post design was employed, supplemented by interrupted time series (ITS) analysis and propensity score matching (PSM) to evaluate changes in outcomes and control for confounding factors. The detailed steps of phase 3 are illustrated in Fig. 2.

2.4.2 Participants and Implementation

Eligible participants were adult inpatients (aged $\geq$18 years) who had self-reported or had a documented history of a β-lactam antibiotic allergy upon admission. Trained clinical pharmacists administered the finalised paper-based risk assessment tool within 24 hours of hospital admission. Prior to this, a brief training programme was delivered to the pharmacists to ensure consistent interpretation and usage of the tool. Each completed form recorded patient demographics, allergy history, clinical presentation, antibiotic prescriptions, and hospitalisation outcomes. All data were recorded on structured case report forms for analysis.

For patients classified as lower-risk and considered eligible for β-lactam rechallenge, informed consent was obtained prior to drug administration. Patients were provided with detailed explanations regarding the purpose of the rechallenge, potential risks, possible adverse reactions, and monitoring procedures. Depending on the clinical setting, consent was obtained either verbally, with documentation in the medical record, or in writing. This approach ensured that all rechallenges were conducted in accordance with ethical standards and patient safety protocols.

2.4.3 Outcome Measures

The outcome evaluation focused on the feasibility of implementing the tool and its preliminary clinical impact. Feasibility indicators included pharmacist adherence, completion rate of the tool, and the time required for each assessment. To assess clinical utility, several outcome variables were collected and compared before and after implementation, including length of hospital stay, total hospitalisation cost, utilisation rate of β-lactam antibiotics, use of alternative antimicrobial agents, and incidence of in-hospital allergic reactions. These metrics were selected to capture the tool's potential influence on prescribing behaviour, resource consumption, and patient safety in routine inpatient care.

2.5 Statistical Analyses

The data were managed using Microsoft Excel 2021 (Microsoft Corp., Redmond, WA, USA) and analysed using IBM SPSS Statistics (version 25.0; IBM Corp., Armonk, NY, USA), R (version 4.4.0; R Foundation for Statistical

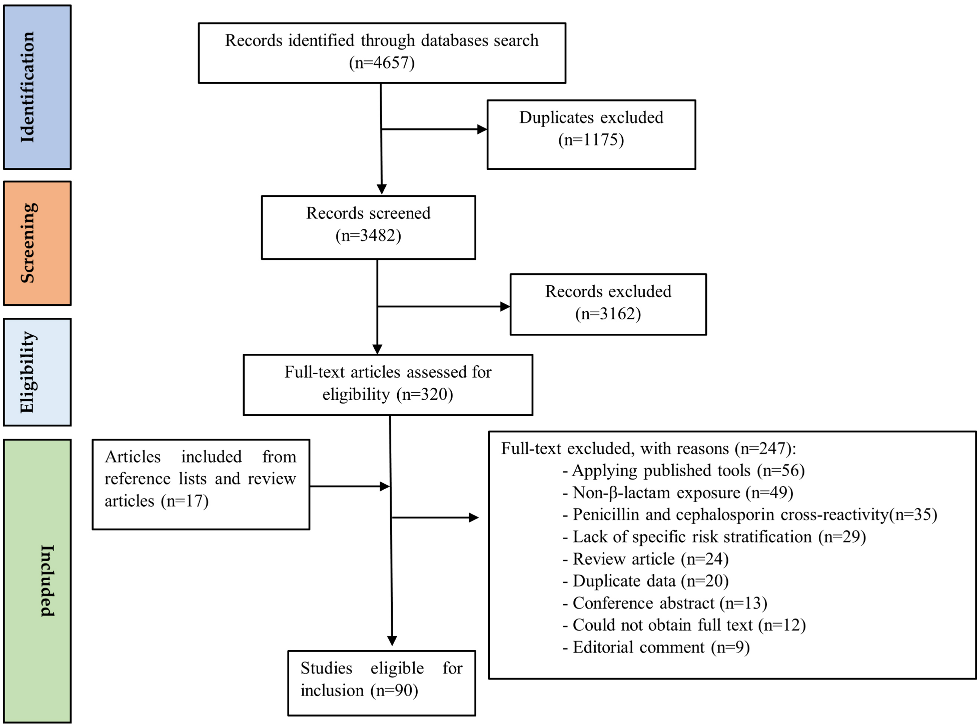

Fig. 3. PRISMA flowchart. PRISMA, Preferred Reporting Items for Systematic Reviews and Meta-Analyses.

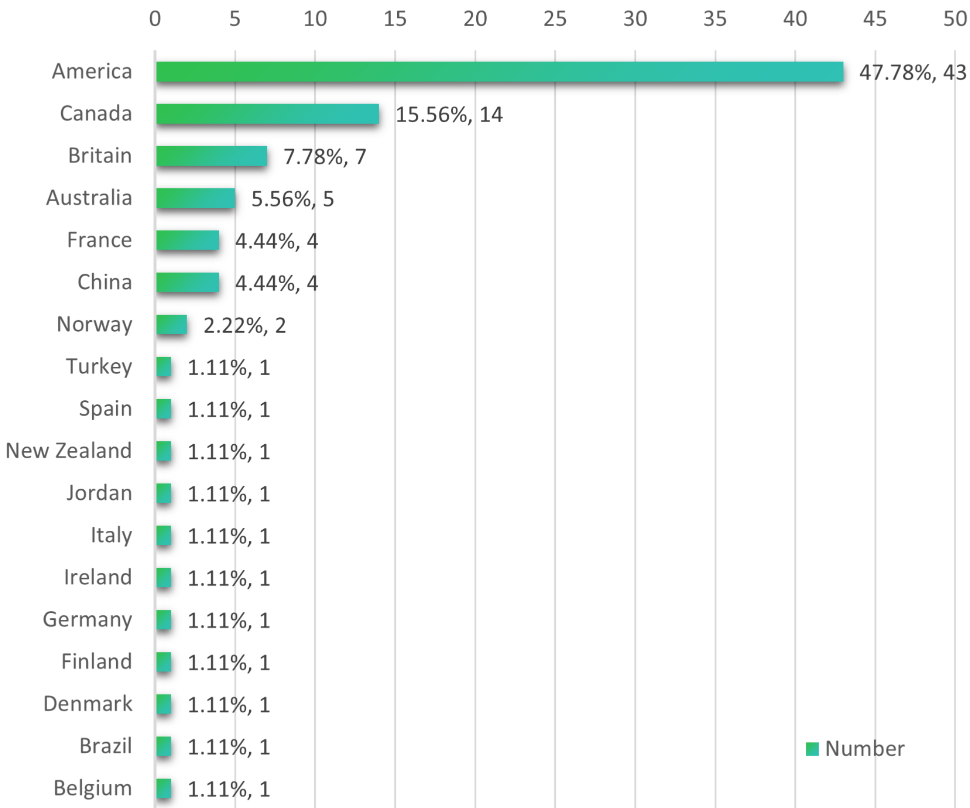

Fig. 4. Country distribution of included studies.

Computing, Vienna, Austria), and Python (Spyder, Py3; Python Software Foundation, Wilmington, DE, USA). Descriptive statistics summarised patient characteristics and implementation metrics. Between-group comparisons were conducted using chi-square or Fisher's exact tests for categorical variables and *t*-tests or Mann–Whitney U tests

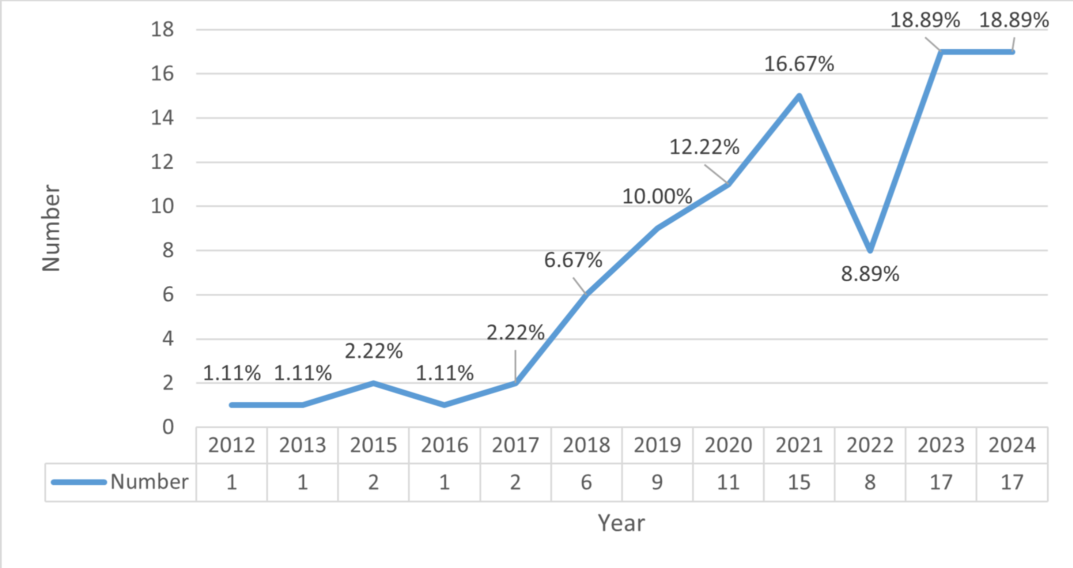

Fig. 5. Publication years of included studies.

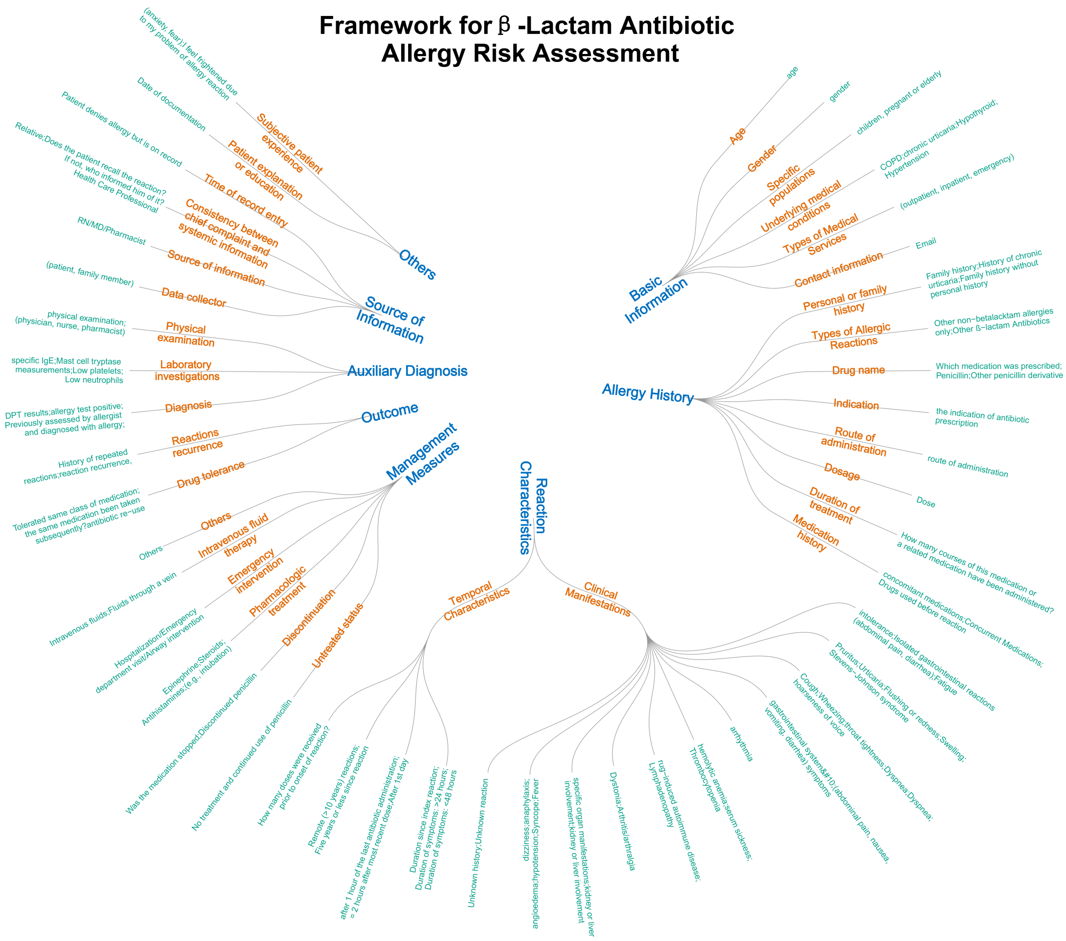

Fig. 6. Tree diagram of the β-lactam allergy risk assessment dimension framework.

for continuous variables. PSM was employed to balance baseline differences between the pre- and post-intervention groups with respect to age, sex, comorbidities, and prior antibiotic use. Additionally, an ITS analysis was performed to evaluate changes in the level and trend of outcome indicators following the implementation of the tool. A two-tailed p-value of less than 0.05 was considered statistically significant.

3. Results

3.1 Literature Screening Results

A total of 4657 records were identified through systematic database searches. Following the removal of 1175 duplicates, 3482 titles and abstracts were screened. Of these, 3162 were excluded due to irrelevance or a lack of methodological clarity. The remaining 320 full-text articles were reviewed in detail.

Subsequently, a further 247 articles were excluded for the following reasons: use of previously published tools without a methodological explanation (n = 56); non-β-lactam exposure (n = 49); focus solely on cross-reactivity between penicillins and cephalosporins (n = 35); absence of specific risk stratification criteria (n = 29); review article format (n = 24); duplicate data (n = 20); conference abstracts (n = 13); unavailable full text (n = 12); and editorial or commentary nature (n = 9).

An additional 17 eligible articles were identified by screening the reference lists of the included reviews and clinical practice guidelines. In total, 90 studies were included in the final synthesis. The selection process is illustrated in Fig. 3 (PRISMA flowchart).

3.2 Characteristics of the Included Studies

Supplementary Table 2 summarises the characteristics of the included studies. These studies were conducted in multiple countries (including the United States, Canada, China, and the United Kingdom) and employed various designs (such as observational studies, randomised controlled trials, and quality improvement studies). The study populations mainly consist of adult and paediatric patients with penicillin antibiotic allergy labels (PALs) and BALs. Sample sizes range from a few individuals to over a million, and risk stratification approaches include qualitative classification, screening questionnaires, decision algorithms, and scoring systems. These studies reflect the diverse practices involved in the global management of penicillin and β-lactam antibiotic allergies.

Fig. 4 shows the geographical distribution of the studies, and Fig. 5 presents their publication years, revealing geographical and temporal trends in this research area.

3.3 Structured Dimension System Construction

A total of 1328 distinct open codes related to the assessment of risk of β-lactam allergy were extracted from the 90 articles included in the study. These codes represented a variety of clinically relevant descriptors, such as symptoms, drug attributes, diagnostic markers, and historical information.

During axial coding, these codes were clustered into multiple hierarchical levels. The final framework, which was constructed using selective coding, comprised 35 secondary-level categories and over 150 specific data elements. This formed the basis of a multidimensional assessment tool. Fig. 6 (tree diagram) visualises this structure, and **Supplementary Table 3** presents representative concepts, citation frequencies, and document coverage per subcategory.

The most frequently coded elements were: skin and mucous symptoms (e.g., urticaria, rash and angioedema), which were presented in 74 studies totalling 446 citations; multisystem involvement (e.g., anaphylaxis, hypotension and fever), which was observed in 75 studies totalling 201 citations; and respiratory features (e.g., wheezing and dyspnoea), which were cited in 46 studies totalling 128 instances. Temporal patterns (e.g., onset time after administration or symptom duration) were covered by 13–20 studies, depending on the indicator. Drug reuse/tolerance and reaction recurrence were cited in seven and two studies, respectively.

Inter-coder agreement analysis indicated a raw agreement rate of 89.7% and a Cohen's kappa coefficient of 0.82, suggesting substantial reliability in the coding process. To confirm theoretical saturation, five additional studies were sequentially reviewed after code stabilisation. None produced new categories, which supports the sufficiency and comprehensiveness of the framework.

3.4 Semantic Risk Feature Extraction

To validate and enhance the findings from the qualitative coding analysis, a text mining analysis was conducted on the full text of the 90 included studies. A total of 220 unique keywords that frequently co-occurred with "high-risk" or "severe" β-lactam allergy reaction descriptors in clinical narratives were identified.

The top 20 high-frequency co-occurring terms such as 'anaphylaxis', 'urticaria', 'angioedema', 'systemic', 'immediate', 'eosinophilia', 'epinephrine', 'DRESS', and 'Stevens–Johnson syndrome', were then quantitatively ranked based on normalised term frequency and visualised using a word cloud and a tree map (Figs. 7,8). The three most frequently occurring terms were anaphylaxis (n = 97, 6.06%), urticaria (n = 92, 5.75%), and angioedema (n = 84, 5.25%) (Table 1). The full version is shown in **Supplementary Table 4**.

3.5 Risk Stratification and Tool Assembly

Based on the structured coding framework and keyword frequency analysis, the final β-lactam allergy risk assessment tool was assembled, incorporating eight core information domains. The top 50 high-risk terms identified through text mining were embedded within relevant sections (e.g., reaction characteristics, auxiliary diagnostics) to support semantic precision in risk identification.

Among the 150+ extracted elements, three indicators were empirically selected as primary stratification triggers: (1) High-risk term presence (e.g., anaphylaxis, DRESS, epinephrine); (2) Immediate reaction onset ($<$1 hour post-administration); (3) Reported allergies to multiple β-lactam subclasses.

Table 1. Top 20 word frequency and percentage of 'high-risk' co-occurring keywords.

Keyword	Count	Percentage (%)
Anaphylaxis	97	6.06%
Urticaria	92	5.75%
Angioedema	84	5.25%
Systemic	67	4.18%
Immediate	62	3.87%
Positive	53	3.31%
Swelling	51	3.19%
Eosinophilia	49	3.06%
Dress	47	2.94%
Serum	42	2.62%
Sickness	41	2.56
Hives	40	2.50%
Johnson	40	2.50%
Stevens	40	2.50%
Epidermal	38	2.37%
Necrolysis	38	2.37%
Toxic	38	2.37%
Wheezing	33	2.06%
Shortness	26	1.62%
Epinephrine	24	1.50%

Patients meeting any of these criteria were preliminarily classified as high risk. Risk tiering was directly linked to tailored clinical recommendations (e.g., specialist referral, desensitization, pharmacist-supervised use) and informed the tool's final logic (Risk Assessment Tool for β-Lactam Antibiotic Allergy is provided in the **Supplementary Material**).

3.6 Pilot Testing Outcomes

A total of 289 patients were included in the pilot phase, with 139 assessed before tool implementation and 150 afterwards. There were no statistically significant differences in baseline characteristics between the groups, confirming the effectiveness of propensity score matching. No differences were observed in sex ($p = 0.65$), age ($p = 0.15$), major diagnoses, or comorbidities such as diabetes ($p = 0.51$) and hypertension ($p = 0.33$) (Table 2).

Further feasibility indicators supported clinical integration. The tool achieved a completion rate of over 95%, with each assessment taking an average of 5–7 minutes. Pharmacists consistently adhered to assessment protocols at a rate above 90% throughout the study period, demonstrating the tool's high acceptability and ease of integration into routine clinical workflows.

Of those assessed post-intervention, 18.7% were categorised as high risk based on predefined semantic and clinical criteria. Patients without identified high-risk features demonstrated significantly better clinical and economic outcomes. Specifically, their average length of hospital stay decreased from 10.6 $\pm$ 5.5 days to 8.5 $\pm$ 4.3 days ($p < 0.001$), and their mean hospitalisation costs decreased from 21,000 $\pm$ 7500 CNY (Chinese Yuan) to 17,800 $\pm$ 6200 CNY (Chinese Yuan) ($p = 0.0011$). Furthermore, the incidence of allergic reactions declined from 6.5% in the pre-intervention group to 0% in the post-intervention group ($p = 0.002$). Regarding antimicrobial usage, the proportion of patients receiving first-line β-lactam antibiotics increased significantly from 40.3% to 75.3% ($p < 0.001$), while the use of second-line carbapenems decreased markedly from 59.7% to 24.7% ($p < 0.001$). This indicates that the tool effectively minimised inappropriate β-lactam avoidance while maintaining safety (see Figs. 9,10).

4. Discussion

This study developed and piloted a multidimensional, pharmacist-led β-lactam antibiotic allergy risk assessment tool. The tool combines systematic literature integration, theory-based qualitative coding, and text co-occurrence analysis methods, and is specifically designed for the Chinese clinical environment. Practical results show that the tool is feasible and clinically valuable in supporting antimicrobial drug decisions.

One of the most notable findings was the significant improvement in antimicrobial stewardship outcomes following its implementation. Among patients without high-risk allergy features, the tool enabled the safe reintroduction of β-lactams, as evidenced by a reduced hospital stay and lower costs, with no allergic events occurring post-intervention. Furthermore, the use of first-line β-lactams increased by over 35%, whereas the use of carbapenems was almost halved. Compared with previous reports in the literature, which reported increases in first-line β-lactam use ranging from 10% to 25% following allergy delabelling

Table 2. Baseline characteristics of patients after propensity score matching.

Variable	Pre-intervention group (n = 139)	Post-intervention group (n = 150)	χ^2/t	*p*-value
Sex (Male)	85 (61.2%)	88 (58.7%)	0.19	0.67
Age (years)	47.3 ± 13.0	45.1 ± 12.8	1.45	0.15
Primary diagnosis				
Pneumonia	42 (30.2%)	40 (26.7%)	0.43	0.51
Urinary tract infection	30 (21.6%)	32 (21.3%)	0.00	0.96
Oral infection	14 (10.1%)	18 (12.0%)	0.27	0.60
Osteomyelitis	20 (14.4%)	27 (18.0%)	0.69	0.41
Neurological infection	17 (12.2%)	20 (13.3%)	0.08	0.78
Others	16 (11.5%)	13 (8.7%)	0.65	0.42
Department				
Department of Infectious Diseases	56 (40.3%)	70 (46.7%)	1.19	0.28
Department of Urology	30 (21.6%)	35 (23.3%)	0.13	0.72
Department of Stomatology	14 (10.1%)	18 (12.0%)	0.27	0.60
Department of Orthopedics	22 (15.8%)	22 (14.7%)	0.08	0.78
Department of Neurosurgery	17 (12.2%)	5 (3.3%)	8.12	<0.01
Type of allergic drugs				
Penicillins	30 (21.6%)	32 (21.3%)	0.00	0.96
Cephalosporins	15 (10.8%)	17 (11.3%)	0.02	0.88
Comorbidities				
Diabetes	50 (36.0%)	48 (32.0%)	0.51	0.47
Hypertension	55 (39.6%)	50 (33.3%)	0.20	0.27
Length of hospital stay (days)	10.6 ± 5.5	8.5 ± 4.3	3.60	<0.001
Hospitalization cost (CNY, Chinese Yuan)	21,000 ± 7500	17,800 ± 6200	3.94	=0.0011
First-line antibiotic usage rate	56 (40.3%)	113 (75.3%)	36.54	<0.001
Second-line antibiotic usage rate	83 (59.7%)	37 (24.7%)	35.80	<0.001

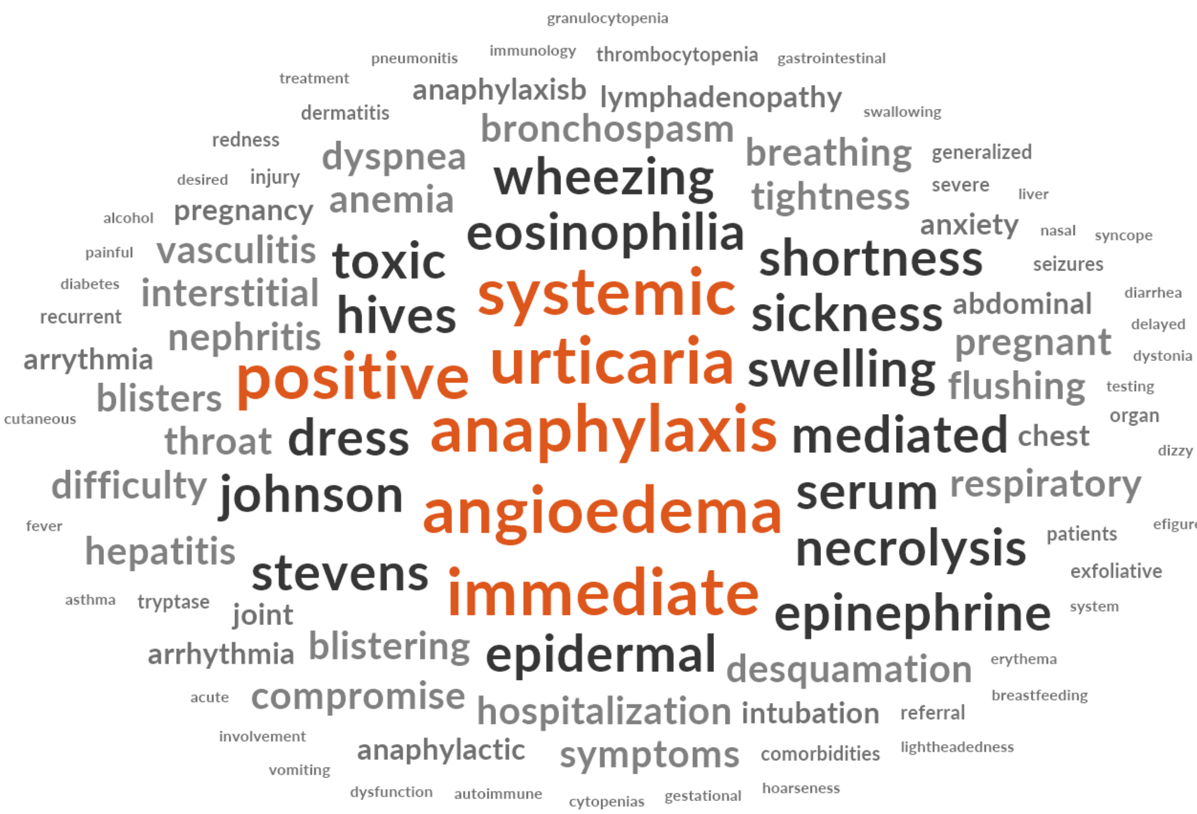

Fig. 7. Word cloud of text co-occurrence analysis for "high-risk" terms.

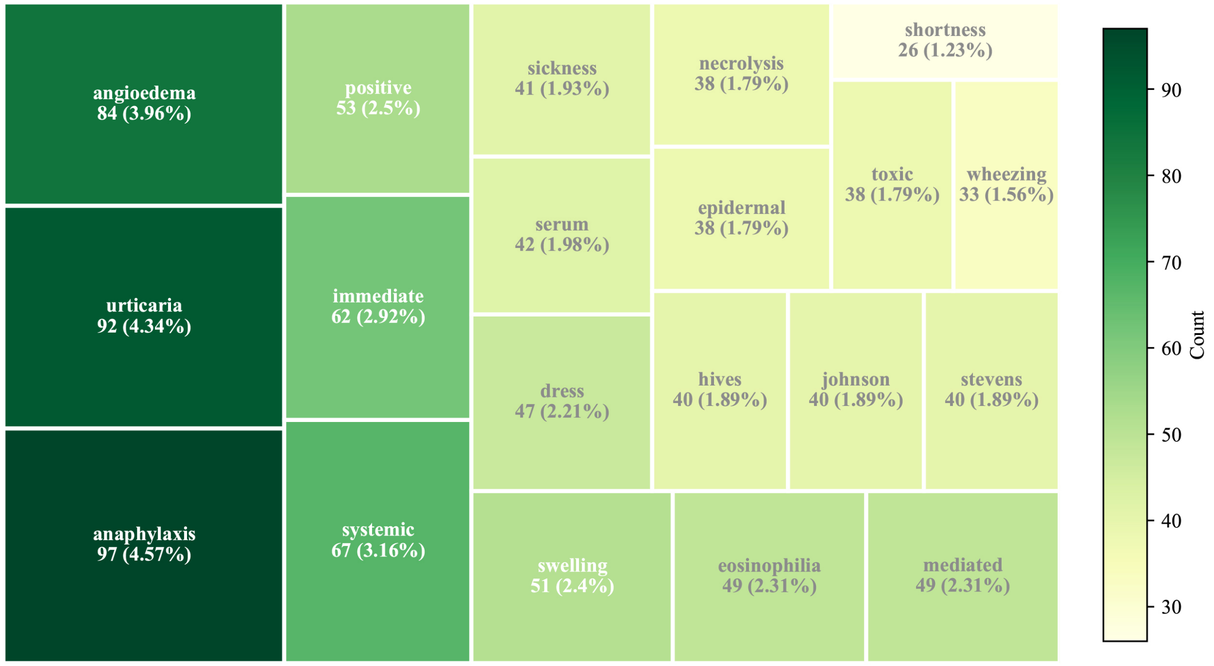

Fig. 8. Tree map of top 20 co-occurring terms associated with "high-risk".

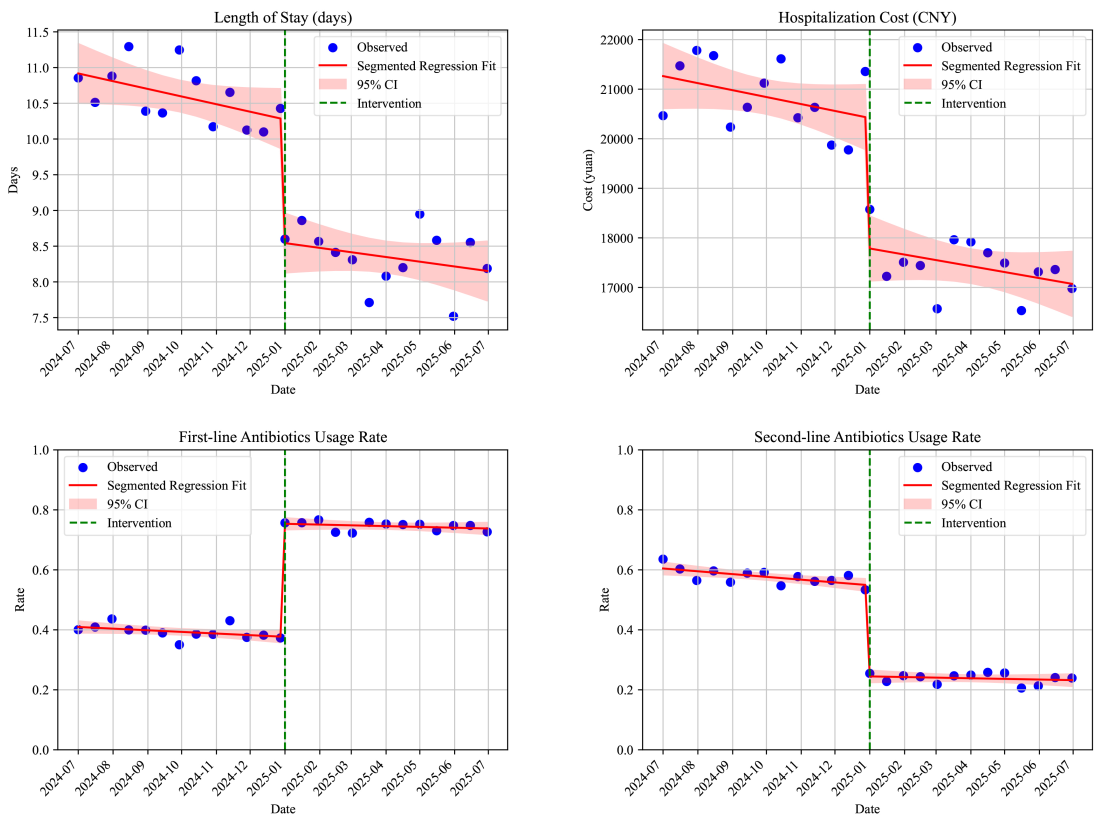

Fig. 9. ITS segmented regression plot. ITS, interrupted time series.

interventions [6,19–24], our results indicate greater efficiency in optimizing antibiotic selection. These results suggest that a structured approach to risk stratification could help to mitigate the over-prescription of β-lactams and the unnecessary use of broad-spectrum antibiotics [4,11].

In this study, 18.7% of patients were classified as high risk using the tool. This is broadly consistent with previous reports, which have ranged from 10% to 20% [25–29]. However, it is still higher than the true prevalence of β-lactam allergy, as suggested by systematic reviews and

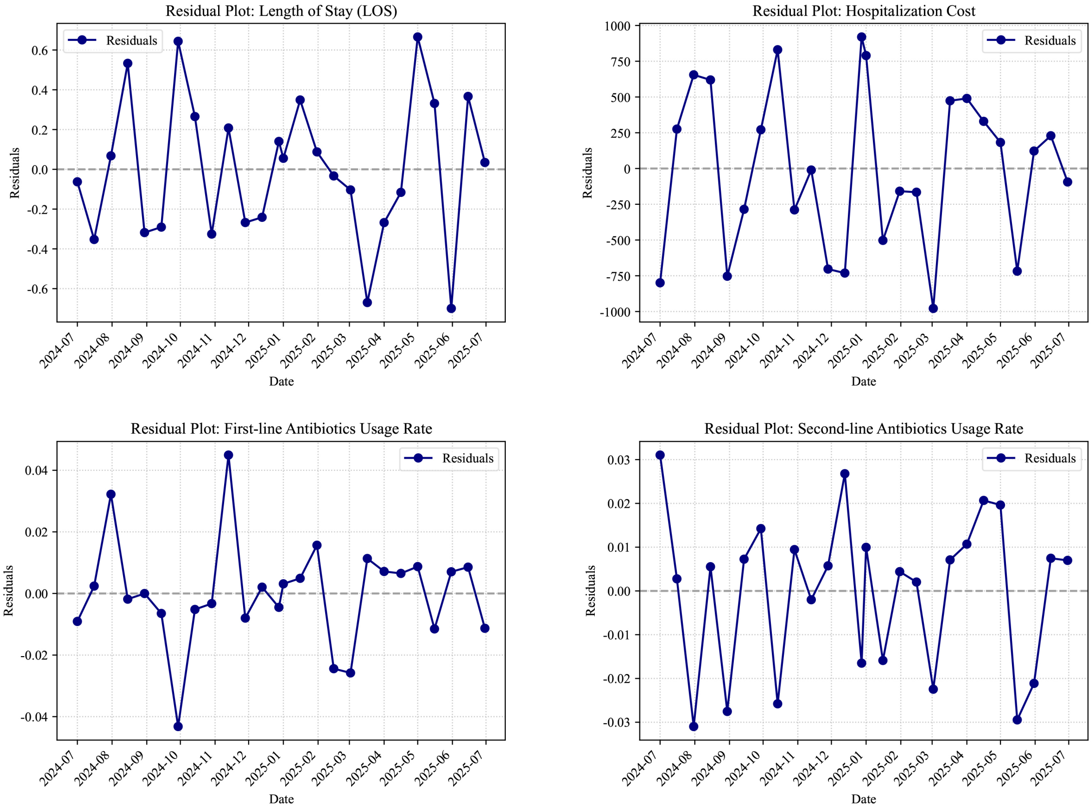

Fig. 10. Residuals of the segmented regression model.

meta-analyses (approximately 5%) [3]. This discrepancy may be due to the fact that the tool was designed to prioritise sensitivity in order to minimise the risk of missing high-risk patients, which leads to a higher proportion of high-risk classifications. While this approach may overestimate the true high-risk population, it helps to ensure patient safety. Subsequent validation studies using skin or drug provocation tests could further optimise risk thresholds and achieve a better balance between sensitivity and specificity.

Future research should aim to validate the tool across multiple hospital levels and regions, and to explore real-time integration into hospital information systems. Further enhancement of natural language processing functions may also enable automatic flagging of high-risk features in narrative documentation. Longitudinal monitoring of allergy-related outcomes and resistance trends would be essential to assess broader public health impacts.

In summary, this study presents a locally adapted, semantically grounded β-lactam allergy risk assessment tool that offers a feasible and scalable strategy to support rational antibiotic use and advance pharmacist-led interventions in China's evolving healthcare landscape.

5. Limitations

Despite the promising results, this study has several limitations.

First, the pilot validation was conducted in a single tertiary hospital, with a relatively small sample size and short follow-up period, which may limit the generalisability of the findings.

Second, although the tool's stratification logic was consistent with keyword analysis and expert consensus, it has not yet been validated through objective diagnostic testing such as skin tests, specific IgE assays, or drug provocation tests. This represents an important limitation. Future research should design prospective validation studies using allergist-confirmed diagnoses as the gold standard to systematically evaluate the tool's predictive performance.

Third, some of the tool's inputs relied on retrospective recall or manual extraction from medical records, which may introduce recall or documentation bias [26].

Finally, the tool has not yet been tested across multiple hospital levels or regions, and real-time integration into hospital information systems remains to be explored.

6. Conclusion

This study developed and preliminarily validated a pharmacist-led, multidimensional β-lactam allergy risk assessment tool tailored for Chinese patients. By integrating evidence from literature synthesis, qualitative coding, and text mining, the tool enables structured and context-sensitive risk stratification of β-lactam allergy histories.

Pilot implementation demonstrated the tool's feasibility and clinical utility, supporting more accurate identification of high-risk patients, reducing unnecessary avoidance of β-lactams, and improving antibiotic utilization patterns.

The results suggest that such tools may play a key role in optimizing antimicrobial stewardship and reducing healthcare costs in real-world hospital settings. Further large-scale validation and integration into electronic health systems are warranted to enhance scalability and long-term impact.

Availability of Data and Materials

The datasets generated and analyzed during the current study are available from the corresponding author upon reasonable request.

Author Contributions

XZ: Supervision, provision of resources, and critical revision of the manuscript; contributed to study design and interpretation of data. XY: Conceptualization, methodology, project administration, and writing—original draft; participated in study design and data interpretation. NS: Data collection, investigation, revision of the manuscript and validation; contributed to analysis and interpretation of results. WC: Formal analysis, visualization, and writing—review & editing; contributed to interpretation of data and preparation of figures and tables. All authors have read and approved the final manuscript, contributed sufficiently to the work, and agree to be accountable for all aspects of the work in accordance with ICMJE authorship criteria.

Ethics Approval and Consent to Participate

The study was reviewed and approved by the Ethics Committee of the First Hospital of Shanxi Medical University (Ethics No. KYLL-2025-293) and was carried out in accordance with the guidelines of the Declaration of Helsinki. Written informed consent was obtained from all participants prior to data collection.

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Conflict of Interest

The authors declare no conflict of interest.

Declaration of AI and AI-Assisted Technologies in the Writing Process

During the preparation of this work the authors used ChatGPT-3.5 in order to check spell and grammar. After using this tool, the authors reviewed and edited the content as needed and take full responsibility for the content of the publication.

Supplementary Material

Supplementary material associated with this article can be found, in the online version, at https://doi.org/10.31083/Pharmazie51744.

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