JIDC | THE JOURNAL OF INFECTION IN DEVELOPING COUNTRIES

Review

Efficacy and safety of Tanreqing Injection combined with conventional antimicrobial therapy in the treatment of multidrug-resistant bacterial pneumonia: a meta-analysis

Bofei Shu[1], Tingting Qiu[1], Keke Li[1], Xiaolin Wang[1], Bangjiang Fang[2]

[1] School of Clinical Medicine, Jiangxi University of Traditional Chinese Medicine, Nanchang, Jiangxi, China, 330000
[2] Institute of Critical Care Medicine, Shanghai University of Traditional Chinese Medicine, Shanghai, China, 201203

Abstract

Background: Multidrug-resistant (MDR) bacterial pneumonia is a growing public health concern with limited treatment options and high mortality rates. Tanreqing injection, a traditional Chinese medicine with anti-inflammatory, antibacterial, and immunomodulatory properties, has shown potential as an adjunctive therapy, but its efficacy and safety remain unclear.

Methods: A systematic search of six English and Chinese databases was conducted to identify randomized controlled trials (RCTs) published before July 2025 evaluating Tanreqing injection for MDR pneumonia. Meta-analysis was performed using RevMan 5.4. Primary outcomes included clinical effectiveness and 28-day all-cause mortality. Secondary outcomes included bacterial clearance, inflammatory markers (WBC, CRP, PCT), healthcare utilization (duration of antibiotic use, mechanical ventilation, hospital stay), and adverse events. Risk of bias was assessed using the RoB 2.0 tool.

Results: Seventeen RCTs involving 1,616 patients were included. All studies were conducted in China. Tanreqing combined with standard therapy significantly improved clinical effectiveness (RR = 1.21) and bacterial clearance (RR = 1.42), and reduced CRP, WBC, PCT, antibiotic duration (MD = – 3.55 days), ventilation time (MD = – 1.57 days), and hospital stay (MD = – 4.98 days). A trend toward lower 28-day mortality was observed (RR = 0.56, $p = 0.15$). No serious adverse events were reported. Publication bias was not significant (Harbord test, $p = 0.639$).

Conclusions: Tanreqing injection may enhance the clinical outcomes of patients with MDR pneumonia when used alongside antibiotics and appears to be safe and well-tolerated. Further high-quality RCTs are needed to confirm these findings.

Key words: Tanreqing injection; multidrug-resistant organisms; drug-resistant pneumonia; systematic review; meta-analysis; anti-infective therapy; integrative medicine.

J Infect Dev Ctries 2026; 20(6):780-791. doi:10.3855/jidc.22151

(Received 28 July 2025 – Accepted 12 October 2025)

Introduction

The advent of antimicrobial agents has greatly improved the clinical outcomes of bacterial pneumonia. However, the widespread and often inappropriate use of broad-spectrum antibiotics has led to escalating antimicrobial resistance. Pneumonia caused by multidrug-resistant (MDR) bacteria has become an increasingly important cause of treatment failure and mortality, particularly among critically ill patients, older adults, and those with chronic comorbidities [1]. These infections are typically prolonged, difficult to treat, and associated with limited therapeutic options.

According to a 2022 report by The Lancet on the global burden of antimicrobial resistance, approximately 1.27 million deaths occur annually due to drug-resistant infections, with pneumonia ranking among the leading causes of mortality [2]. Surveillance data from China have shown a rising prevalence of multidrug-resistant pathogens—particularly carbapenem-resistant *Klebsiella pneumoniae, Acinetobacter baumannii*, and *Pseudomonas aeruginosa*—among ICU patients, with MDR strains responsible for more than 50% of pneumonia cases in certain regions [3,4]. A multicenter case–control study conducted in central China estimated that healthcare-associated infections attributable to multidrug-resistant organisms increased hospitalization costs by an average of US$ 2047 per patient and prolonged the length of stay by approximately 10 days [5]. The additional antimicrobial drug expenditure alone accounted for nearly 60% of these excess costs. These findings highlight the severe clinical and financial consequences of MDR infections in China and reinforce the urgency of exploring integrative therapeutic strategies such as Tanreqing Injection.

Given these challenges, relying solely on antimicrobial therapy is no longer sufficient to address the complex management needs of MDR infections—especially in immunocompromised patients or those with multiple comorbidities who require broader, multidimensional support. Traditional Chinese Medicine (TCM), with its holistic approach of "strengthening vital Qi and eliminating pathogenic

factors," has garnered growing attention for its potential role in combating infections. Among these, Tanreqing Injection — known for its heat-clearing, detoxifying, phlegm-resolving, and lung-diffusing properties — shows promise as an adjunctive therapy for MDR pneumonia [6].

Modern pharmacological studies have demonstrated that Tanreqing Injection may inhibit drug-resistant bacteria through multiple mechanisms, including disruption of biofilm formation, interference with efflux pump function, and modulation of immune-inflammatory responses [7]. In 2022, Li *et al.* [8] conducted a systematic review of randomized controlled trials assessing Tanreqing for drug-resistant pulmonary infections. Their findings indicated improvements in treatment effectiveness and reduced duration of illness, highlighting favorable clinical prospects. However, the review included only nine studies and lacked evaluation of key outcome indicators such as mortality, inflammatory markers, and bacterial clearance. Thus, the scope and quality of the available evidence remain limited.

Against this background, the present study aims to systematically evaluate the clinical efficacy and safety of Tanreqing injection in the treatment of multidrug-resistant bacterial pneumonia through a systematic review and meta-analysis. Particular focus is placed on its effects across multiple outcome dimensions, including treatment effectiveness, mortality, bacterial clearance, inflammatory markers, and length of hospital stay. This study seeks to provide higher-quality evidence to support the integration of traditional Chinese medicine in the management of drug-resistant infections and to further explore its potential role within modern antimicrobial treatment frameworks.

Methods

Study Design

This study was conducted in strict accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA 2020) guidelines. The study protocol was prospectively registered in the International Prospective Register of Systematic Reviews (PROSPERO) under the registration number CRD420251078460. This systematic review and meta-analysis aimed to synthesize evidence from existing randomized controlled trials (RCTs) to evaluate the clinical efficacy and safety of Tanreqing injection in the treatment of multidrug-resistant bacterial pneumonia.

Search Strategy

A comprehensive literature search was conducted across six electronic databases: China National Knowledge Infrastructure (CNKI), VIP Database, Wanfang Data, SinoMed, PubMed, and Embase. The search covered all records from the inception of each database to July 1, 2025. The search strategy was developed using a combination of subject terms (e.g., MeSH) and free-text keywords, focusing on the core concepts of "Tanreqing Injection," "drug-resistant bacteria," and "pneumonia." No restrictions were placed on language or publication status to ensure the broadest possible inclusion of relevant studies. The detailed search strategies are provided in Supplementary Table 1.

Inclusion and Exclusion Criteria

Inclusion Criteria

Studies were included if they met the following criteria: (1) randomized controlled trials (RCTs); (2) participants diagnosed with pneumonia caused by multidrug-resistant (MDR) bacteria, confirmed by clinical symptoms, radiological imaging (e.g., X-ray or CT), sputum culture, and antimicrobial susceptibility testing; (3) the intervention group received Tanreqing injection combined with conventional Western antimicrobial therapy, while the control group received the same conventional therapy alone, with consistent basic treatment across both groups; (4) at least one clinical outcome related to efficacy or safety was reported; (5) the publication was in Chinese or English; and (6) sufficient statistical data were available for effect size calculation.

Exclusion criteria

(1) studies without a confirmed diagnosis of MDR bacterial infection; (2) intervention involving other traditional Chinese medicine (TCM) injections or formulas that could confound treatment effects; (3) unclear or missing outcome data, and inability to retrieve original data; (4) non-original research types, including reviews, case reports, animal or in vitro studies, conference abstracts, or duplicate publications. In cases of duplicate reports, the version with the most complete information or the largest sample size was included.

Outcomes

The primary outcomes were overall clinical effectiveness rate and 28-day all-cause mortality. The former assessed the improvement of clinical symptoms, while the latter reflected the impact of the intervention

on patient prognosis — both are key endpoints in infectious disease research. Secondary outcomes encompassed multiple dimensions: 1) Infection control indicators, including bacterial clearance rate, Clinical Pulmonary Infection Score (CPIS), and procalcitonin (PCT), were used to comprehensively evaluate microbiological outcomes and infection severity; 2) Inflammatory biomarkers, such as white blood cell (WBC) count and C-reactive protein (CRP), reflected systemic inflammatory status; 3) Healthcare resource utilization indicators, including duration of antibiotic use, mechanical ventilation time, and length of hospital stay, were used to evaluate treatment efficiency and healthcare burden; 4) Safety indicators, including incidence of adverse events, were analyzed to assess the safety profile of the combination therapy.

Study Selection and Data Extraction

Two reviewers independently and blindly screened the literature. Initial screening was based on titles and abstracts to exclude studies clearly unrelated to the research topic. Full texts of potentially eligible studies were then reviewed against predefined inclusion and exclusion criteria. Reasons for exclusion and discrepancies in study counts were documented. Any disagreements between the two reviewers were resolved through discussion with a third reviewer. The entire selection process is illustrated using a PRISMA flow diagram.

Data extraction was also performed independently by two reviewers. Extracted information included: (1) General study information: first author, year of publication, study location, sample size; (2) Participant characteristics: age, sex distribution, disease course, ICU admission status, and whether participants were elderly; (3) Intervention details: treatment regimens for the experimental and control groups, including drug names, dosages, and treatment durations; (4) Outcome data: values for clinical effectiveness, mortality, bacterial clearance, WBC, CRP, PCT, CPIS, duration of antibiotic use, mechanical ventilation time, length of hospital stay, and incidence of adverse events; (5) Methodological features: randomization methods, allocation concealment, and blinding procedures. For studies with incomplete or inconsistent data, attempts were made to contact the original authors for clarification. If the missing data could not be obtained, those outcomes were excluded from the meta-analysis and analyzed qualitatively instead.

Risk of Bias Assessment

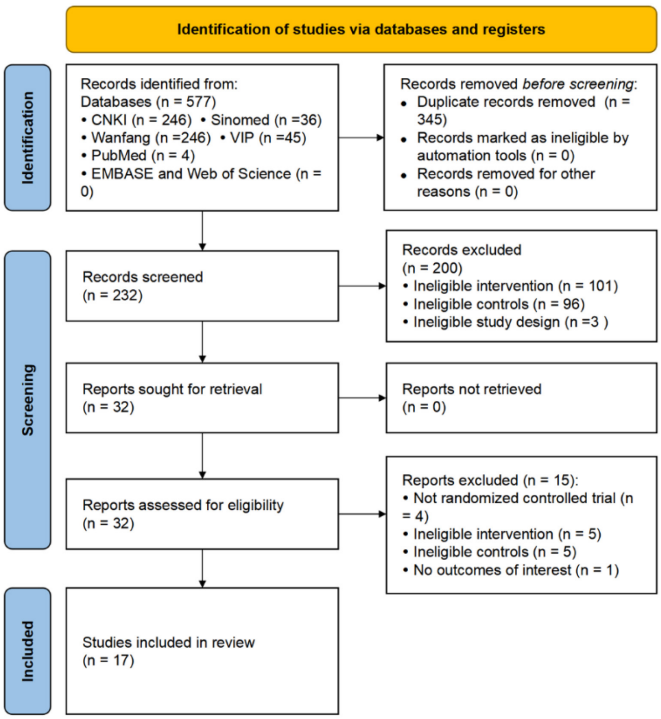
Two reviewers independently assessed the risk of bias for each included study using the Cochrane Risk of Bias tool version 2.0 (RoB 2) [9].This tool evaluates five domains of potential bias: (1) bias arising from the randomization process, (2) bias due to deviations from intended interventions, (3) bias in measurement of the outcome, (4) bias due to missing outcome data, and (5) bias in selection of the reported result.

If all five domains were rated as “low risk” or “some concerns” the study was judged to have an overall low risk of bias. If any domain was rated as “some concerns” or “high risk” the overall risk was considered to be of concern or high risk. After independent assessments, the two reviewers cross-checked their evaluations. Any disagreements were resolved through discussion, and if necessary, adjudicated by a third reviewer.

Statistical Analysis

Meta-analysis was conducted to synthesize the outcome data from the included RCTs. For dichotomous outcomes, relative risk (RR) with 95% confidence intervals (95% CI) was used as the effect measure and pooled using the Mantel − Haenszel method. For continuous outcomes, mean difference (MD) with 95% CI was used, and pooled using the inverse variance method. To assess the robustness of

Figure 1. PRISMA 2020 flow diagram of study selection.



the results and the impact of bias risk, sensitivity analyses were performed by excluding studies deemed to have an overall high risk of bias. All meta-analyses were conducted using a random-effects model. When the number of included studies was ≥ 10, publication bias was assessed using funnel plots along with Egger's or Harbord's test.

Results

Literature Search and Study Selection

A total of 577 records were retrieved from six databases, including CNKI (n = 246), Wanfang (n = 246), VIP (n = 45), SinoMed (n = 36), PubMed (n = 4), and EMBASE (n = 0). After removing 345 duplicates using reference management software, 232 records remained for title and abstract screening. During the initial screening, 200 studies were excluded due to inappropriate interventions (n = 101), inappropriate comparators (n = 96), and non-RCT study design (n = 3). The remaining 32 articles were retrieved for full-text review and further assessed for eligibility. An additional 15 studies were excluded during full-text screening for the following reasons: non-randomized controlled trials (n = 4), inappropriate interventions (n = 5), inappropriate comparators (n = 5), and irrelevant outcome indicators (n = 1). Ultimately, 17 studies [10-

Table 1. Table of Study Characteristics.

Study	Sample size (T/C)	Male ratio (T/C)	Mean age (T/C)	Tanreqing intervention	Basic anti-infective regimen	Treatment duration (days)	Baseline characteristics of the patients	Types of resistant pathogens
Song 2009	50/50	/	/	TRQ 20ml IV drip qd	Vancomycin	10	Pulmonary infection	Methicillin-resistant *Staphylococcus aureus*
Song 2010	50/50	/	/	TRQ 20ml IV drip qd	Vancomycin	10	Pulmonary infection	Methicillin-resistant *Staphylococcus aureus*
Sun 2012	36/32	19/17	65.38/64.92	TRQ 20ml IV drip qd	Selected based on drug susceptibility results	14	Chronic obstructive pulmonary disease, Bronchiectasis, Lung cancer, Diabetes mellitus, Sequelae of cerebrovascular disease	*Pseudomonas aeruginosa*
Liu 2014A	29/40	18/31	58.41/55.78	TRQ 20ml IV drip qd	Selected based on drug susceptibility results	10	Cranial and cerebral disorders, Gastrointestinal malignancies, Spinal cord injury	*Pseudomonas aeruginosa*
Liu 2014B	23/29	16/20	57.52/53.41	TRQ 20ml IV drip qd	Selected based on drug susceptibility results	10	Cranial and cerebral disorders, Gastrointestinal malignancies, Spinal cord injury	*Acinetobacter baumannii*
Hu 2017	31/30	19/18	61.52/62.19	TRQ 30ml IV drip qd	Cefoperazone–sulbactam sodium	14	Hypertension, Diabetes mellitus	*Acinetobacter baumannii*
Shi 2017	39/39	25/27	81.4/82.8	TRQ 20ml IV drip qd	Imipenem–cilastatin sodium	28	Diabetes mellitus, Coronary heart disease, Hypertension, Osteoarticular disorders	*Pseudomonas aeruginosa*
Fang 2019	50/49	28/26	68.32/68.98	TRQ 20ml IV drip qd	Cefoperazone–sulbactam sodium	13	Pulmonary infection	*Acinetobacter baumannii*
Luo 2019	32/32	21/19	67.5/66.4	TRQ 110ml Repeated bronchoalveolar lavage	Imipenem–cilastatin sodium combined with cefoperazone–sulbactam sodium	14	Pulmonary infection	*Acinetobacter baumannii*
Xiao 2020	32/32	17/18	62.41/62.37	TRQ 30ml IV drip qd	Cefoperazone–sulbactam sodium	14	Pulmonary infection	*Acinetobacter baumannii*
Deng 2021	54/51	28/24	65.12/64.31	TRQ 10ml IV drip qd	Selected based on drug susceptibility results	14	Pulmonary infection	*Pseudomonas aeruginosa, Acinetobacter baumannii, Klebsiella pneumoniae, Staphylococcus aureus*
Yuan 2021	30/30	23/20	69.81/67.45	TRQ 10ml IV drip qd	Selected based on drug susceptibility results	14	Pulmonary infection	*Pseudomonas aeruginosa, Acinetobacter baumannii, Klebsiella pneumoniae*
Liu 2021A	70/70	37/36	77.51/75.79	TRQ 20ml IV drip qd	Selected based on drug susceptibility results	7	Pulmonary infection	*Pseudomonas aeruginosa, Acinetobacter baumannii, Klebsiella pneumoniae, Staphylococcus aureus*
Liu 2021B	34/34	23/19	67.19/65.78	TRQ 20ml IV drip qd	Piperacillin–tazobactam sodium	14	Chronic obstructive pulmonary disease, Bronchiectasis	/
Jiang 2022	31/30	15/14	58.01/55.75	TRQ 20ml IV drip qd	Meropenem	14	Pulmonary infection	/
Wang 2023	30/30	20/18	60.17/58.5	TRQ 10ml IV drip qd	Cefoperazone–sulbactam sodium	14	Chronic obstructive pulmonary disease, Bronchiectasis	*Acinetobacter baumannii*
Pan 2024	50/50	29/28	65.68/64.35	TRQ 20ml IV drip qd	Meropenem	10	Diabetes mellitus, Hypertension, Cerebrovascular disease	/

TRQ: Tanreqing Injection, qd: once daily.

26] were included in the final systematic review. The detailed screening process is presented in Figure 1.

Characteristics of Included Studies

A total of 17 randomized controlled trials (RCTs) were included in this review, with publication years ranging from 2009 to 2024. All studies were conducted in mainland China. Sample sizes ranged from 60 to 140 participants, with relatively balanced group allocation between the intervention and control arms.

Participants were primarily patients with pneumonia caused by multidrug-resistant (MDR) bacteria. Several studies further focused on subpopulations such as critically ill patients, elderly individuals, or those with chronic comorbidities, including chronic obstructive pulmonary disease (COPD), diabetes, hypertension, and post-stroke sequelae. Most studies reported the average age of participants, which predominantly ranged from 55 to 82 years. The proportion of male patients was generally higher, although two studies [10,11] did not report age or sex information.

In terms of interventions, all studies administered Tanreqing Injection in combination with conventional Western antimicrobial therapy in the experimental group. The typical dosage of Tanreqing was 20 mL per day via intravenous infusion, although some studies used 10 mL or 30 mL. One study [18] used bronchial lavage as the administration method, with a dosage of 110 mL.

The control groups received the same basic antimicrobial regimens as the experimental groups to ensure comparability. The antibiotics used included vancomycin, cefoperazone-sulbactam, imipenem-cilastatin, meropenem, and piperacillin-tazobactam. In six studies [12-14, 20-22], antibiotics were selected based on drug susceptibility testing (DST), while the remaining eleven studies [10,11,15-19,23-26] specified the antimicrobial agents used. The duration of treatment ranged from 7 to 28 days, with most studies administering therapy for 10 to 14 days.

The most commonly reported pathogens were *Acinetobacter baumannii* and *Pseudomonas aeruginosa*. Some studies involved mixed infections, including *Klebsiella pneumoniae* and methicillin-resistant *Staphylococcus aureus* (MRSA). Three studies [23,24,26] did not specify the causative organisms. Detailed study characteristics are summarized in Table 1.

Risk of Bias Assessment

All 17 randomized controlled trials (RCTs) included in this review were evaluated for methodological quality using the Cochrane Risk of Bias 2.0 (RoB 2) tool. Detailed results of the assessment are presented in Figure 2.

All studies reported the use of randomization. Eight studies [14,18,21-26] explicitly stated the use of a random number table for group allocation and were therefore judged as low risk of bias in the randomization domain. The remaining nine studies [10-13,15-17,19,20] did not provide detailed descriptions of the randomization methods and lacked information on allocation concealment, leading to a high risk of bias in this domain.

Regarding bias due to deviations from intended interventions, none of the included studies reported the use of blinding for participants or personnel. However, given that the primary outcomes (e.g., inflammatory markers, CRP, length of hospital stay) were mainly objective measures, the risk of performance bias was considered limited. As a result, all studies were rated as having "some concerns" in this domain. In terms of bias due to missing outcome data, all studies reported complete outcome data for predefined endpoints, with no obvious loss to follow-up or dropout, and were thus

Figure 2. Risk of bias assessment of included studies using the Cochrane RoB 2.0 tool.

rated as low risk of bias in this domain.

For bias in the measurement of outcomes, there was no evidence of selective detection or measurement bias, and all studies were judged as low risk in this domain. Finally, regarding bias in the selection of the reported results, although none of the included studies had a pre-registered protocol or published statistical analysis plan, no obvious discrepancies were observed between the methods and results sections. Therefore, most studies were rated as having "some concerns" in this domain.

Clinical Effectiveness and 28-Day Mortality

A total of 13 studies [10-12,15-17,20-26] reported clinical effectiveness rates (n = 881). Meta-analysis showed that the Tanreqing group had a significantly higher overall clinical effectiveness compared with the control group (RR = 1.21, 95% CI: 1.14–1.27, $p < 0.00001$), with no significant heterogeneity ($I^2 = 0\%$). Detailed results are presented in Figure 3. Three studies [13,14,19] reported 28-day mortality data, with 8 deaths in the intervention group (n = 84) and 19 deaths in the control group (n = 101). The meta-analysis yielded an RR of 0.56 (95% CI: 0.26–1.23, $p = 0.15$), suggesting a 44% relative reduction in 28-day mortality in the Tanreqing group; however, the difference was not statistically significant. See Figure 4 for details.

Bacterial Clearance Rate, Clinical Pulmonary Infection Score (CPIS) and Procalcitonin

Six studies [12,15,17,18,21,22] reported bacterial clearance rates (n = 492). Meta-analysis showed that the bacterial clearance rate was significantly higher in the Tanreqing group compared to the control group (RR = 1.42, 95% CI: 1.23–1.64, $p < 0.00001$), with no observed heterogeneity ($I^2 = 0\%$). Detailed results are presented in Figure 5. Four studies [21,22,25,26] reported Clinical Pulmonary Infection Score (CPIS) data (n = 360). The results showed that CPIS scores in the Tanreqing group were significantly lower than those in the control group following treatment (MD = –1.92, 95% CI: –2.51 to –1.32, $p < 0.00001$), with moderate heterogeneity ($I^2 = 66\%$). Additionally, four studies [21,23,24,26] reported procalcitonin (PCT) levels (n = 289). Meta-analysis showed that the Tanreqing group had significantly lower PCT levels compared to the control group (MD = –0.06, 95% CI: –0.10 to –0.02, $p = 0.006$), with substantial heterogeneity ($I^2 = 72\%$). See Figure 6 for details.

White Blood Cell Count (WBC) and C-Reactive Protein (CRP)

Seven studies [16-18,21,22,24,26] reported white blood cell (WBC) count data (n = 602). Meta-analysis showed that the WBC level was significantly lower in the Tanreqing group compared to the control group (MD = – 3.10, 95% CI: – 4.67 to – 1.52, $p = 0.0001$), with high heterogeneity ($I^2 = 90\%$). Eight studies [15-18,21,22,24,26] reported changes in C-reactive protein (CRP) levels (n = 666). The CRP level in the Tanreqing group was significantly lower than that in the control group (MD = – 8.60, 95% CI: – 12.33 to – 4.87, $p < 0.00001$), also with substantial heterogeneity ($I^2 = 88\%$). Detailed results are shown in Figure 7.

Duration of Antibiotic Use, Mechanical Ventilation, and Hospital Stay

This study further analyzed the effects of Tanreqing on antibiotic duration, mechanical ventilation time, and length of hospital stay. For antibiotic duration, six studies [12-14,19,21,23] (n = 381) were included. Meta-analysis showed that the duration of antibiotic use in the Tanreqing group was significantly shorter than in the control group (MD = – 3.55, 95% CI: – 4.47 to – 2.63, $p < 0.00001$), with low heterogeneity ($I^2 = 0\%$). Regarding mechanical ventilation time, four studies [13-15,19] (n = 261) showed that the Tanreqing group had significantly shorter ventilation time compared to the control group (MD = – 1.57, 95% CI: – 1.82 to – 1.33, $p < 0.00001$), with low heterogeneity ($I^2 = 20\%$). For hospital stay, four studies [13,14,19,23] (n = 253) reported that the length of hospital stay was significantly reduced in the Tanreqing group (MD = – 4.98, 95% CI: – 6.23 to – 3.74, $p < 0.00001$), with similarly low heterogeneity ($I^2 = 21\%$). Overall, Tanreqing Injection was associated with significant reductions in antibiotic use, ventilation time, and hospitalization duration. Detailed results are presented in Figure 8.

Adverse Events Reporting

Eight studies [15-18,21,23-25] reported on the safety of Tanreqing Injection. The most commonly described adverse events in the Tanreqing group were mild gastrointestinal symptoms (e.g., nausea, abdominal discomfort) and transient skin allergic reactions (e.g., rash, pruritus). A few studies mentioned hematological or cardiovascular symptoms, but without detailed characterization. Both the Tanreqing and control groups experienced mild and reversible adverse events, with no reports of serious or life-threatening reactions. However, only a minority of trials provided quantitative data on the frequency or proportion of

Figure 3. Forest plot of clinical effectiveness rate.

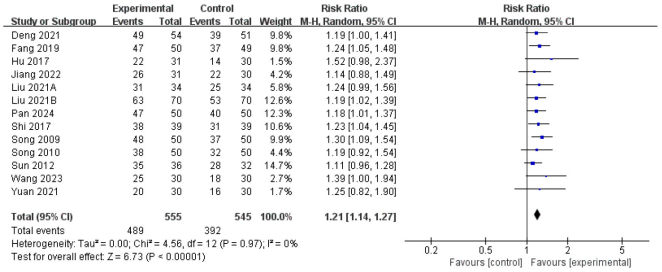


Figure 4. Forest plot of 28-day all-cause mortality.

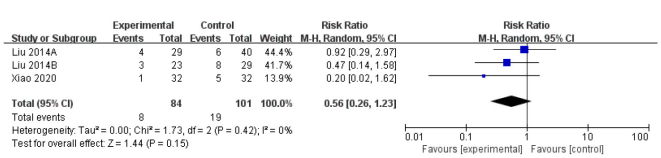


Figure 5. Forest plot of bacterial clearance rate.

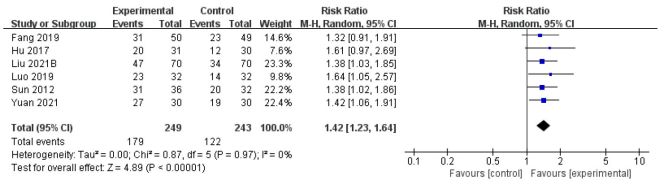


Figure 6. Forest plots of CPIS and procalcitonin (PCT).

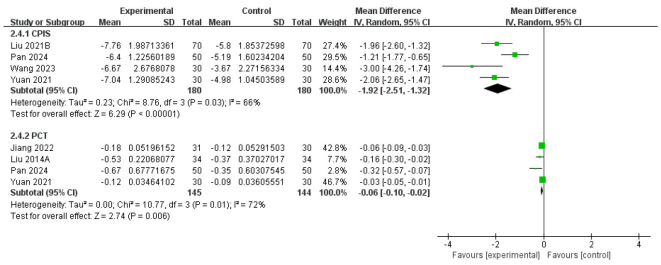


Figure 7. Forest plots of white blood cell (WBC) count and C-reactive protein (CRP).

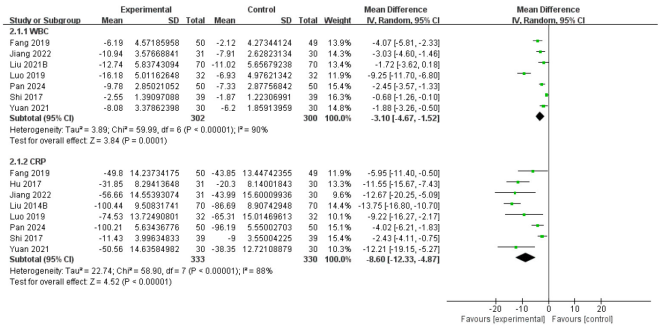


Figure 8. Forest plots of antibiotic duration, mechanical ventilation time, and hospital stay.

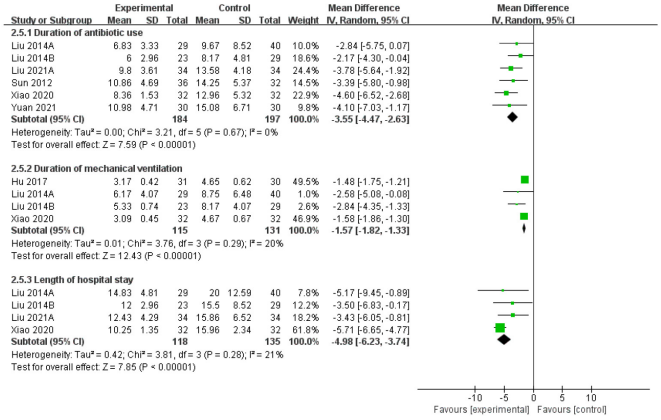


Table 2. Adverse Event Reporting.

Study	Sample size (T/C)	Adverse events in the Tanreqing group	Adverse events in the control group
Hu 2017	31/30	Nausea/vomiting (n = 3), pruritus (n = 2), thrombocytopenia (n = 1), headache/fatigue (n = 1)	Gastrointestinal reactions (n = 2), thrombocytopenia (n = 2)
Shi 2017	39/39	Skin flushing (n = 1), pruritus (n = 2)	Pruritus (n = 1), gastrointestinal reaction (n = 1)
Fang 2019	50/49	Nausea/vomiting (n = 3), diarrhea (n = 1)	Nausea/vomiting (n = 9), diarrhea (n = 5)
Luo 2019	32/32	Sinus tachycardia (n = 3), transient decrease in oxygen saturation (n = 5)	Not reported
Yuan 2021	30/30	Rash (n = 1), nausea (n = 2)	Rash (n = 3), nausea (n = 1)
Liu 2021B	34/34	Rash (n = 2), nausea (n = 1)	Rash (n = 3), nausea (n = 2)
Jiang 2022	31/30	Rash (n = 1), nausea (n = 1)	Rash (n = 1), nausea (n = 1)
Wang 2023	30/30	Rash (n = 1), nausea (n = 1)	Rash (n = 1)

adverse events, and reporting quality was inconsistent. Consequently, the overall incidence of adverse reactions could not be reliably estimated.

Taken together, current evidence suggests that Tanreqing Injection appears to be generally well tolerated when used in combination with antibiotics, but the limited and heterogeneous safety reporting across studies warrants cautious interpretation. Future randomized controlled trials should incorporate standardized definitions and detailed recording of adverse events to allow a more robust assessment of safety. Detailed safety data are summarized in Table 2.

Sensitivity Analysis

Sensitivity analyses were conducted by sequentially removing each included study to assess the robustness of the main outcomes. The results showed no substantial changes in the pooled effect estimates, indicating good overall stability of the findings. Furthermore, studies that did not explicitly describe their randomization methods were considered low quality and excluded for additional sensitivity analysis. After excluding these studies, the direction of the pooled effects remained consistent across all outcome indicators. Although some effect sizes were slightly increased or decreased, statistical significance remained unchanged. These findings suggest that the results of this meta-analysis are robust, with no evidence of directional bias. Detailed results are presented in Table 3.

Table 3. Sensitivity analysis.

Outcomes	results	No. of patients (T/C)	RR/WMD/SMD (95% CI)	Heterogeneity
Response rate	Original results	555/545	1.21 (1.14, 1.27)	$I^2 = 0\%$, $p < 0.00001$
	After removal of studies with high risk of bias	245/244	1.20 (1.10, 1.31)	$I^2 = 0\%$, $p < 0.00001$
28-day mortality rate	Original results	84/101	0.56 (0.26, 1.23)	$I^2 = 0\%$, $p = 0.15$
	After removal of studies with high risk of bias	23/29	0.47 (0.14, 1.58)	$p = 0.22$
Bacterial Clearance Rate	Original results	249/243	1.42 (1.23, 1.64)	$I^2 = 0\%$, $p < 0.00001$
	After removal of studies with high risk of bias	132/132	1.44 (1.19, 1.74)	$I^2 = 0\%$, $p = 0.0001$
Clinical Pulmonary Infection Score	Original results	180/180	-1.92 (-2.51, -1.32)	$I^2 = 66\%$, $p < 0.00001$
	After removal of studies with high risk of bias	NR	NR	NR
Procalcitonin	Original results	145/144	-0.06 (-0.10, -0.02)	$I^2 = 72\%$, $p = 0.006$
	After removal of studies with high risk of bias	NR	NR	NR
White blood cell count	Original results	302/300	-3.10 (-4.67, -1.52)	$I^2 = 90\%$, $p = 0.0001$
	After removal of studies with high risk of bias	213/212	-3.48 (-5.43, -1.53)	$I^2 = 87\%$, $p = 0.0005$
C-reactive protein	Original results	333/330	-8.60 (-12.33, -4.87)	$I^2 = 88\%$, $p< 0.00001$
	After removal of studies with high risk of bias	213/212	-10.13 (-15.48, -4.78)	$I^2 = 86\%$, $p = 0.0002$
Duration of antibiotic use	Original results	184/197	-3.55 (-4.47, -2.63)	$I^2 = 0\%$, $p < 0.00001$
	After removal of studies with high risk of bias	87/93	-3.27 (-4.54, -2.01)	$I^2 = 0\%$, $p < 0.00001$
Duration of mechanical ventilation	Original results	115/131	-1.57 (-1.82, -1.33)	$I^2 = 20\%$, $p < 0.00001$
	After removal of studies with high risk of bias	23/29	-2.84 (-4.35, -1.33)	$p = 0.0002$
Length of hospital stay	Original results	118/135	-4.98 (-6.23, -3.74)	$I^2 = 21\%$, $p < 0.00001$
	After removal of studies with high risk of bias	57/63	-3.46 (-5.52, -1.40)	$I^2 = 0\%$, $p = 0.001$

Publication Bias

For the primary outcome of clinical effectiveness, publication bias was visually assessed using a funnel plot. The distribution of studies appeared approximately symmetrical, with no evident clustering or skewness suggestive of small-study effects.

To further evaluate the potential for publication bias, Harbord's test was performed. The regression coefficient was 0.340 with a p of 0.639, indicating no statistically significant asymmetry and suggesting no apparent publication bias. Detailed results are presented in Figure 9.

Discussion

This study systematically synthesized evidence from 17 randomized controlled trials to evaluate the efficacy and safety of Tanreqing Injection combined with conventional antimicrobial therapy in the treatment of multidrug-resistant (MDR) bacterial pneumonia. The meta-analysis results demonstrated that the combination therapy significantly improved overall clinical effectiveness, promoted microbiological clearance (e.g., bacterial eradication), reduced inflammatory markers (CRP, WBC, PCT), and shortened antibiotic use duration, mechanical ventilation time, and hospital stay. Most of the included outcomes showed low heterogeneity, indicating good stability and consistency of the results. However, substantial heterogeneity was observed for several continuous outcomes, particularly inflammatory markers such as WBC, CRP, and PCT. This variability may be attributable to differences in study populations (e.g., severity of illness, age distribution, or underlying comorbidities), variations in Tanreqing Injection dosage and treatment duration, and inconsistencies in laboratory measurement methods across centers. Sensitivity analyses excluding low-quality or extreme-value studies did not materially change the overall results, suggesting that the findings were robust. Given that only 4−8 studies contributed to these outcomes, formal subgroup analysis or meta-regression was not feasible due to limited statistical power. Future high-quality RCTs with standardized outcome definitions are needed to enable more rigorous quantitative exploration of heterogeneity.

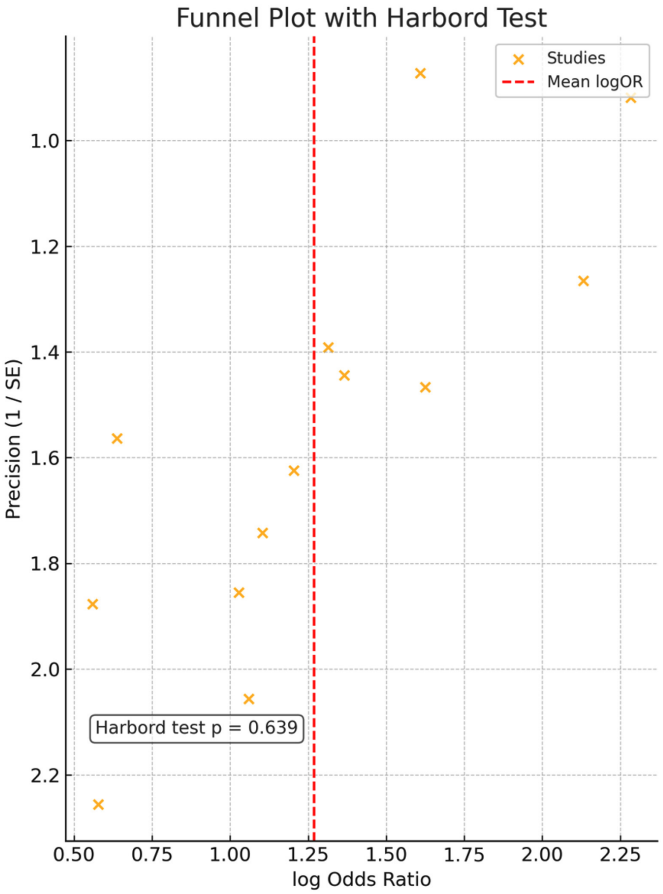
Although the difference in 28-day all-cause mortality was not statistically significant, a downward trend in mortality risk was observed in the Tanreqing group, suggesting a potential protective effect in patients with severe infections. Regarding safety, no serious adverse events were reported. The most common adverse reactions were mild to moderate and reversible, indicating that Tanreqing Injection is generally well tolerated in clinical practice.

The therapeutic effects of Tanreqing Injection against drug-resistant bacteria are reflected in multiple aspects. In terms of bacterial biofilm regulation, Tanreqing has been shown to broadly inhibit the formation and maturation of biofilms produced by various multidrug-resistant pathogens, including *Staphylococcus aureus*, *Klebsiella pneumoniae*, *Acinetobacter baumannii*, and *Pseudomonas aeruginosa*, thereby reducing bacterial adhesion and protecting host tissues [27].

It also interferes with bacterial efflux pump systems, such as the MexAB-OprM system in *P. aeruginosa* and the adeB pump in *A. baumannii*, enhancing antibiotic susceptibility and partially reversing resistance [28,29].

Moreover, Tanreqing modulates quorum-sensing pathways and virulence gene expression in *P. aeruginosa* and S. aureus, resulting in reduced toxin production and attenuated pathogenicity [30]. Beyond its antibacterial effects, Tanreqing exhibits notable anti-

Figure 9. Funnel plot for clinical effectiveness (publication bias assessment).



inflammatory and immunomodulatory properties. It can regulate key signaling pathways, including PI3K–Akt, MAPK, and JNK, thereby suppressing excessive inflammatory responses and downregulating cytokines such as TNF-α, IL-6, and IL-1β. These actions help alleviate alveolar injury and inflammatory exudation, conferring both anti-infective and immunoprotective effects [31].

From the perspective of traditional Chinese medicine (TCM), although multidrug-resistant (MDR) bacterial pneumonia is classified as a modern infectious disease, its underlying pathogenesis is often understood through the lens of complex TCM syndromes, such as "toxic heat obstructing the lungs" and "phlegm-heat accumulation in the lung." These syndromes reflect internal imbalances characterized by external pathogenic invasion, intense heat toxicity, and impaired lung dispersing and descending function.

In TCM theory, prolonged or repeated use of antibiotics may be seen as a cause of "lingering pathogenic factors," which weaken the body's vital Qi (defensive energy), allowing the pathogen to penetrate deeper into the meridians and collaterals. This results in a persistent struggle between upright Qi and pathogenic influences, manifesting as a syndrome of both excess and deficiency. Such interpretations offer a theoretical rationale for integrative approaches that combine antimicrobial agents with herbal interventions aimed at clearing heat, resolving phlegm, and supporting the body's resistance [32].

Tanreqing Injection is derived from traditional Chinese medical principles of "clearing heat and detoxifying, resolving phlegm, and eliminating retained fluids," as outlined in classical texts such as Wenbing Tiaobian. It reflects the TCM treatment philosophy of reinforcing the body's resistance and eliminating pathogenic factors, while addressing both the root cause and the clinical manifestations. In the context of MDR pneumonia, Tanreqing not only provides traditional therapeutic effects such as heat-clearing and phlegm-resolving, but also demonstrates modern pharmacological actions including antibacterial, anti-inflammatory, and immunomodulatory properties. When combined with conventional antimicrobial therapy, it may enhance treatment efficacy, reduce antibiotic load, and lower the risk of adverse effects. This integrative approach highlights the potential of Chinese medicine as a complementary strategy in the comprehensive management of complex infectious diseases.

Limitations of the Study

This study has several limitations. Although all included trials were randomized controlled trials, more than half did not clearly report the randomization methods or allocation concealment procedures, and blinding was generally absent, which may have introduced selection and performance biases. These methodological weaknesses may have led to overestimation of treatment effects, particularly for subjective outcomes such as the clinical effectiveness rate. Although most laboratory and objective indicators (e.g., CRP, WBC, PCT) are less susceptible to observer bias, the absence of blinding could still influence clinical decision-making, co-interventions, and outcome assessment. Therefore, the results should be interpreted with caution, and future trials should adopt more rigorous randomization, allocation concealment, and blinding procedures to enhance the reliability of evidence.

In addition, some outcome indicators were supported by a limited number of studies. For example, only three studies reported 28-day mortality, with few events observed, leading to low statistical power and a potential underestimation of the true effect. This limitation underscores the urgent need for larger, well-designed randomized controlled trials with adequate sample sizes to improve the precision of effect estimates. Future studies should also ensure standardized and transparent reporting of clinically meaningful endpoints — such as mortality, microbiological eradication, and safety outcomes—to enable more reliable evidence synthesis and facilitate international comparability.

While the control groups were uniformly described as receiving "conventional antimicrobial therapy," variations in specific antibiotics, dosages, and treatment durations may have affected the comparability between groups. Lastly, key information such as pathogen classification, antibiotic regimens, and grading of adverse events was inadequately reported in some studies, limiting the ability to conduct detailed subgroup analyses and comprehensive safety evaluations. Moreover, all the included studies were conducted in China, where clinical practices, antibiotic stewardship policies, and pathogen distribution patterns may differ from those in other regions. Therefore, the external generalizability of our findings to other populations and healthcare systems should be interpreted with caution.

Conclusions

This systematic review and meta-analysis suggest that Tanreqing Injection, when used in combination with conventional antimicrobial therapy, may provide potential clinical benefits in the management of multidrug-resistant (MDR) bacterial pneumonia. The combination was associated with a possible improvement in clinical effectiveness, bacterial clearance, and inflammatory marker levels, as well as a trend toward shorter antibiotic use, mechanical ventilation, and hospital stay. No serious safety concerns were identified across the included studies.

Given the methodological limitations and regional concentration of the available evidence, these findings should be interpreted with caution. Tanreqing Injection may represent a promising adjunctive option within an integrative traditional Chinese and Western medicine framework for MDR infections, but further large-scale, rigorously designed randomized trials and real-world studies are needed to confirm its efficacy and clarify its mechanisms of action.

Data Availability Statement

The data supporting this research article are available from the corresponding author upon reasonable request.

Ethics Statement

An ethics statement is not applicable because this study is based exclusively on published literature.

Authors Contributions

Bofei Shu: Conceptualization, Methodology, Data Curation, Formal Analysis, Writing – Original Draft. Tingting Qiu: Literature Search, Data Extraction, Visualization, Writing – Review & Editing. Keke Li: Risk of Bias Assessment, Statistical Analysis, Quality Control. Xiaolin Wang: Validation, Software, Figures and Tables Preparation. Bangjiang Fang: Supervision, Project Administration, Funding Acquisition, Writing – Review & Final Approval.

Corresponding author

Professor Bangjiang Fang
Longhua Hospital, Shanghai University of Traditional Chinese Medicine
Tel: +8618879100228
Email: fangbangj@163.com

Conflict of interest

No conflict of interest is declared.

References

1. Antimicrobial Resistance Collaborators (2022) Global burden of bacterial antimicrobial resistance in 2019: a systematic analysis. Lancet 399: 629-655. doi: 10.1016/S0140-6736(21)02724-0.
2. Ho CS, Wong CTH, Aung TT, Lakshminarayanan R, Mehta JS, Rauz S, McNally A, Kintses B, Peacock SJ, de la Fuente-Nunez C, Hancock REW, Ting DSJ (2025) Antimicrobial resistance: a concise update. Lancet Microbe 6: 100947. doi: 10.1016/j.lanmic.2024.07.010.
3. Li D, Li Y, Wang J, Yang W, Cui K, Su R, Li L, Ren X, Li X, Wang Y (2024) In-depth analysis of the treatment effect and synergistic mechanism of Tanreqing injection on clinical multidrug-resistant *Pseudomonas aeruginosa*. Microbiol Spectr 12: 272623. doi: 10.1128/spectrum.02726-23.
4. Li P, Li Y, Zhang Y, Bao J, Yuan R, Lan H, Sun M (2022) Economic burden attributable to healthcare-associated infections in tertiary public hospitals of Central China: a multicentre case-control study. Epidemiol Infect 150: 155. doi: 10.1017/S0950268822001340.
5. Ma N, Pan B, Ge L, Li M, Zhu H, Deng X, Li D, Wang X, Wu L, Xiao J, Lai H, Tian J, Niu J, Yang K. (2024) Efficacy and safety of Tanreqing injection for cough caused by acute trachea-bronchitis disease: a systematic review and meta-analysis of randomized controlled trials. J Ethnopharmacol 321: 117429. doi: 10.1016/j.jep.2023.117429.
6. Wang W, Xu J, Lai Q, Wang Y, He Q, Liu Q, Lu Y, Mo D, Zou K, Sun X (2025) Effect of Tanreqing injection on multidrug resistance organisms: a test-negative case-control study and network pharmacology analysis. Phytomedicine 136: 156358. doi: 10.1016/j.phymed.2024.156358.
7. Yang W, Cui K, Tong Q, Ma S, Sun Y, He G, Li D, Lin L, Blazekovic B, Chevalier S, Wang Y, Wei Q, Wang Y (2022) Traditional Chinese medicine Tanreqing targets both cell division and virulence in *Staphylococcus aureus*. Front Cell Infect Microbiol 12: 884045. doi: 10.3389/fcimb.2022.884045.
8. Yang ZR, Sun F, Zhan SY (2017) Risk of bias assessment: revised Cochrane risk of bias tool for individually randomized, parallel group trials (RoB 2.0). Zhonghua Liu Xing Bing Xue Za Zhi 38: 1285-1291. doi: 10.3389/fcimb.2022.884045.
9. Bu JH, Sun LH, Chen M, Song JC, Wu QC, Fang BJ (2022) Clinical experience of Professor Bangjiang Fang in the treatment of drug-resistant bacterial infections. Chin J Integr Tradit West Med 42: 363-365.
10. Deng SS, Ren CJ (2021) Effect of Tanreqing injection on reducing the rate of drug-resistant bacterial infection in patients with severe pneumonia. Drug Eval Res 44: 381-384.
11. Ding JR, Li XB, Wang W, Weng YQ (2024) Current status and resistance mechanisms of carbapenem-resistant *Pseudomonas aeruginosa*. Clin Rational Drug Use 17: 170-173. doi: 10.33073/pjm-2025-022.
12. Fang F, Li S, Chen M, Diao LL (2019) Clinical observation of Tanreqing injection combined with cefoperazone−sulbactam in the treatment of severe pulmonary infection caused by drug-resistant *Acinetobacter baumannii* in elderly patients. Mod J Integr Tradit Chin West Med 28: 2791-2793.
13. He S, Qiao J, Chen L (2025) Multidrug-resistant bacterial infections in critically ill ICU patients and associated factors. Pract Prev Med 32: 342-345.
14. Hu YF, Wang CM, Song YF, Wang MX (2017) Efficacy and safety of Tanreqing injection as an adjunctive therapy for severe pneumonia caused by drug-resistant *Acinetobacter*

baumannii. Mod J Integr Tradit Chin West Med 26: 2346-2348.

15. Jiang D, Zhang Z, Yang ZL (2022) Clinical observation of Tanreqing injection combined with step-down antibiotic therapy in the treatment of severe pneumonia caused by drug-resistant bacterial infection. Chin J Tradit Med Emerg 31: 1065-1067.
16. Li ZY, Li ZF, Ren PZ, Chen QY, Cui HS (2022) Efficacy and safety of Tanreqing injection in the treatment of pulmonary infections caused by drug-resistant bacteria: a systematic review. World Chin Med 17: 993-997.
17. Liu H, Qu NN (2021) Clinical efficacy of Tanreqing injection combined with Western medicine in elderly patients with multidrug-resistant bacterial pneumonia. Chin J Exp Tradit Med Formulae 27: 125-130.
18. Liu JF, Shi HP, Xie XW (2021) Clinical efficacy of Tanreqing injection in patients with AECOPD induced by drug-resistant bacteria and its effect on antibiotic resistance. Chin J Tradit Med Emerg 30: 1254-1256.
19. Liu JL, Yang WF, Sun YN, Ma SH, Xing YJ, Wang Y (2017) Effect of Tanreqing injection on the three-dimensional biofilm structure of methicillin-resistant *Staphylococcus aureus*. Chin J Pathog Biol 12: 1152-1156.
20. Liu Y, Ma XY, Chen SP, Xu H, Yu XY (2014) Clinical observation of Tanreqing injection as an adjunctive therapy for pulmonary infection caused by *Acinetobacter baumannii*. Chin J Infect Control 13: 134-137.
21. Liu Y, Ma XY, Xu H, Chen SP, Yu XY (2014) Clinical study of Tanreqing injection for pulmonary infection caused by *Pseudomonas aeruginosa* in ICU patients. Clin Pulm Med J 19: 974-976.
22. Luo WJ, Wang CM, Hu YF, Ye MY (2019) Efficacy analysis of Tanreqing injection administered via bronchoalveolar lavage for the treatment of multidrug-resistant *Acinetobacter baumannii* pneumonia in critically ill patients. J Tradit Chin Med Inform 25: 95-98.
23. Pan JJ, Zheng XG (2024) Effect of Tanreqing injection combined with step-down antibiotic therapy in the treatment of severe pneumonia caused by drug-resistant bacterial infection. Chin J Min Kang Med 36: 103-105.
24. Shi WR, Zhou JY (2017) Clinical efficacy of Tanreqing injection combined with imipenem in elderly patients with drug-resistant *Pseudomonas aeruginosa* pulmonary infection. Pract J Card Cereb Pneum Vasc Dis 25: 103-106.
25. Song ZX, Li LK, Li XG (2010) Clinical observation of Tanreqing injection in the treatment of pneumonia caused by MRSA infection. Chin J Nosocomiol 20: 1596-1598.
26. Song ZX, Lu W, Chen L, Wang S, Li XG (2009) Study on the efficacy and resistance of Tanreqing injection combined with vancomycin in the treatment of pneumonia caused by methicillin-resistant *Staphylococcus aureus*. Chin J Nosocomiol 19: 1861-1863.
27. Sun GX, Chang R, Li S, Zhai JX (2012) Clinical study of Tanreqing injection in the treatment of lower respiratory tract infection caused by multidrug-resistant *Pseudomonas aeruginosa*. Chin J Integr Med 27: 1348-1349.
28. Wang L, Tao YL, Chen WS (2020) Research progress on the chemical constituents, pharmacological actions, and clinical applications of Tanreqing injection. Chin Tradit Herb Drugs 51: 3318-3328.
29. Wang P, He W (2023) Clinical observation of Tanreqing combined with cefoperazone–sulbactam in patients with acute exacerbation of chronic obstructive pulmonary disease complicated by multidrug-resistant *Acinetobacter baumannii* infection and phlegm-heat obstructing the lung syndrome. World J Integr Tradit West Med 18: 2006-2010.
30. Xiao Y, Zhang HH, Liu YL (2020) Effects of Tanreqing injection on cytokine levels in patients with pulmonary infection caused by *Acinetobacter baumannii*. Electron J Clin Med Lit 7: 48-60.
31. Yuan MY, Pei XY, Ma Y (2021) Clinical observation of Tanreqing injection combined with antibiotics in the treatment of drug-resistant bacterial pneumonia in ICU patients. Chin J Tradit Med Emerg 30: 880-882.
32. Zhang WX, He M, Liu SF, Hu XH, Zhang ML, Zhou XH, Zhang FH (2024) Antibacterial effects of Tanreqing injection on drug-resistant bacteria and its mechanisms of action. J Immunoassay Clin 31: 948-952.

Annex – Supplementary Items

Supplementary Table 1. Detailed search strategies for each database.

Database	*Search Strategies*
PubMed	*#1 "Tanreqing Injection"[Title/Abstract] OR "Tan Re Qing"[Title/Abstract]* *#2 "Drug Resistance, Bacterial"[MeSH] OR "drug-resistant bacteria"[Title/Abstract] OR "antibiotic resistance"[Title/Abstract] OR "multidrug resistant"[Title/Abstract] OR "MDR"[Title/Abstract]* *#3 "Pneumonia"[MeSH] OR "pulmonary infection"[Title/Abstract] OR "lung infection"[Title/Abstract] OR "respiratory tract infection"[Title/Abstract]* *#4 "Randomized Controlled Trial"[Publication Type] OR "randomized"[Title/Abstract] OR "randomised"[Title/Abstract] OR "random allocation"[MeSH] OR "RCT"[Title/Abstract]* *#5 #1 AND #2 AND #3 AND #4* *Filters: Humans; Publication date to July 1, 2025*
EMBASE	*#1 'tanreqing injection':ti,ab OR 'tan re qing':ti,ab* *#2 'drug resistance'/exp OR 'multidrug resistance'/exp OR 'drug resistant bacteria':ti,ab OR 'antibiotic resistance':ti,ab OR 'mdr':ti,ab* *#3 'pneumonia'/exp OR 'lung infection':ti,ab OR 'pulmonary infection':ti,ab OR 'respiratory tract infection':ti,ab* *#4 'randomized controlled trial'/exp OR random*:ti,ab OR rct:ti,ab* *#5 #1 AND #2 AND #3 AND #4*
CNKI	*主题 = ("痰热清注射液")* *AND (关键词 = "耐药菌" OR "多重耐药" OR "抗药性" OR "耐药细菌")* *AND (关键词 = "肺炎" OR "肺部感染" OR "呼吸道感染")* *AND (关键词 = "随机" OR "随机对照" OR "RCT")* *时间：不限 – 2025年7月1日* *文献类型：期刊* *语言：中文*
VIP	*全文 = ("痰热清注射液")* *AND ("耐药菌" OR "耐药细菌" OR "多重耐药")* *AND ("肺炎" OR "肺部感染" OR "呼吸道感染")* *AND ("随机" OR "对照" OR "RCT")* *发表时间：无时间限制至2025年7月1日*
Wanfang	*主题 = ("痰热清注射液")* *AND ("耐药菌" OR "抗药性" OR "多重耐药")* *AND ("肺炎" OR "肺部感染" OR "呼吸道感染")* *AND ("随机" OR "对照" OR "随机对照试验" OR "RCT")* *发表时间：≤2025年7月1日*
SinoMed	*主题词 = ("痰热清注射液")* *AND ("耐药菌" OR "耐药性细菌" OR "抗药性")* *AND ("肺炎" OR "呼吸道感染" OR "肺部感染")* *AND ("随机对照试验" OR "随机" OR "RCT")* *文献类型 = 临床试验 OR 随机对照试验*