INPLASY

INPLASY2025110036
doi: 10.37766/inplasy2025.11.0036
Received: 13 November 2025
Published: 13 November 2025

AI-Driven Systematic Review and Meta-Analysis of Traditional Chinese Medicine for Acute Respiratory Distress Syndrome and Acute Lung Injury

Ren, Y; Wang, YJ; Meng, JS; Cui, QS; Yin, JH.

Corresponding author:
Jinghu Yin

yinjh2025jh@163.com

Author Affiliation:
Yanbian University Hospital.

ADMINISTRATIVE INFORMATION

Support - This study did not receive any funding in any form.

Review Stage at time of this submission - Completed but not published.

Conflicts of interest - None declared.

INPLASY registration number: INPLASY2025110036

Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 13 November 2025 and was last updated on 13 November 2025.

INTRODUCTION

Review question / Objective To conduct an AI-driven systematic review and meta-analysis evaluating the effects of Traditional Chinese Medicine (TCM) on clinical outcomes in acute respiratory distress syndrome (ARDS) and acute lung injury (ALI).

Condition being studied Acute respiratory distress syndrome (ARDS) and acute lung injury (ALI) are critical syndromes characterized by severe hypoxemia, diffuse alveolar damage, and high short-term mortality. Despite advances in supportive care such as low tidal volume ventilation and prone positioning, the overall mortality of ARDS remains between 30% and 45% worldwide, posing a substantial public health and economic burden. The COVID-19 pandemic further amplified the incidence of ARDS, especially among severe and critically ill patients, highlighting the urgent need for effective adjunctive therapies.

In recent years, Traditional Chinese Medicine (TCM) has been widely explored as an adjunct in the management of ARDS and related critical conditions. Formulations such as Xuebijing injection, Qingfei Paidu decoction, and Shenhuang granules have shown potential in modulating systemic inflammation, improving oxygenation, and reducing multi-organ dysfunction. Several randomized controlled trials (RCTs) and observational studies have reported improved clinical outcomes—including reduced mortality and shortened mechanical ventilation duration—when TCM was integrated into standard treatment protocols.

Conventional systematic reviews and meta-analyses of TCM interventions in ARDS/ALI have generally supported these potential benefits but also revealed limitations. Many of these reviews were constrained by manual literature searches, selective outcome reporting, and methodological issues such as handling of multiple correlated endpoints within the same study. Traditional bias assessments have relied heavily on funnel plots or

Egger's regression, which are less reliable in small and heterogeneous datasets. These limitations restrict the generalizability and reproducibility of prior findings.

The rapid evolution of artificial intelligence (AI) and machine learning has opened new opportunities for evidence synthesis. AI-driven literature retrieval, powered by semantic expansion, natural language processing, and automated deduplication, has been increasingly applied in systematic reviews to improve coverage, recall, and efficiency. Combined with advanced statistical frameworks that accounts for correlated outcomes, and structured bias assessment tools such as Risk of Bias due to Missing Evidence (ROB-ME)—AI offers a methodological upgrade that can overcome key shortcomings of traditional reviews.

METHODS

Participant or population Population: Adults (Age≥18) diagnosed with acute respiratory distress syndrome (ARDS) or acute lung injury (ALI), including ARDS secondary to COVID-19 or sepsis.

Intervention Any Traditional Chinese Medicine (TCM) formulation (injection, decoction, or granule), used alone or in combination with standard therapy.

Comparator Standard treatment, placebo, or no TCM intervention.

Study designs to be included Randomized controlled trials and comparative observational studies. Case series, reviews, preclinical studies, and articles without sufficient data were excluded.

Eligibility criteria

We included studies meeting the following criteria:

Population: Adults (Age≥18) diagnosed with acute respiratory distress syndrome (ARDS) or acute lung injury (ALI), including ARDS secondary to COVID-19 or sepsis.

Interventions: Any Traditional Chinese Medicine (TCM) formulation (injection, decoction, or granule), used alone or in combination with standard therapy.

Comparators: Standard treatment, placebo, or no TCM intervention.

Outcomes: Primary outcomes were all-cause mortality and oxygenation index (PaO_2/FiO_2 ratio). Secondary outcomes included duration of mechanical ventilation, ICU stay, hospital stay, and changes in inflammatory biomarkers— C-reactive protein (CRP), interleukin-6 (IL-6), interleukin-8 (IL-8), procalcitonin (PCT), and tumor necrosis factor-α (TNF-α). .

Study design: Randomized controlled trials and comparative observational studies. Case series, reviews, preclinical studies, and articles without sufficient data were excluded.

Information sources This study employed an AI-driven intelligent search method, combining natural language processing and semantic expansion technology, to systematically search PubMed, Embase, the Cochrane Library, Web of Science, China National Knowledge Infrastructure (CNKI), Wanfang Database, and clinical trial registries (ClinicalTrials.gov, ChiCTR) from database inception to July 2025, with no language restrictions.

The AI tool performed the following search process: Keyword generation and optimization: Large-scale semantic analysis was used to automatically generate and expand core search terms, including diseases (ARDS/ALI, Sepsis, COVID-19), interventions (Xuebijing, Qingfei Paidu, Shenhuang, etc.), outcomes (Mortality, PaO_2/FiO_2, Ventilation, Biomarkers), and methodology-related terms (RCT, Meta-analysis)(Figure S1A–B). Semantic Expansion Network: This approach enables synonym clustering and cross-concept mapping (e.g., ARDS ↔ ALI, Sepsis ↔ Septic shock, TCM ↔ Traditional Chinese Medicine) to ensure maximum coverage of potential literature.

Main outcome(s) A total of 2,847 records were retrieved through the AI-assisted database search and 156 additional records from other sources. After AI-based deduplication, 2,234 unique records remained for screening. Following title and abstract review (PRISMA flow[22]), 2,156 records were excluded as irrelevant. Seventy-eight (n = 78) full-text articles were then assessed for eligibility. Of these, 66 studies were excluded for the following reasons: wrong intervention (n = 24), wrong outcome (n=18), inappropriate design (n = 12), insufficient data (n = 8), and duplication (n = 4). Finally, 11 studies met the inclusion criteria and were included in both the qualitative synthesis and quantitative meta-analysis.

A total of 11 studies were included (6 randomized controlled trials and 5 observational studies), encompassing patients with ARDS/ALI secondary to COVID-19 or sepsis. Sample sizes ranged from 33 to 6,371 per group. Interventions covered Chinese herbal injections (e.g., Xuebijing), decoctions (e.g., Qingfei Paidu, Xuanbai Chengqi), and granules (e.g., Shenhuang). Control groups received standard care or placebo. Study characteristics are summarized in Table 1. Evidence mapping revealed heterogeneity in outcome selection, with mortality and PaO_2/FiO_2 ratio most frequently reported, while inflammatory

biomarkers were measured inconsistently across time points.

Across nine studies involving 12,046 patients (4,901 in the TCM group and 7,135 in the control group), pooled analysis revealed that TCM treatment was significantly associated with a reduction in mortality compared with conventional therapy (random-effects model: RR = 0.41, 95% CI 0.29–0.58, $p < 0.01$; $I^2 = 73.3\%$). The common-effect model produced a consistent estimate (RR = 0.40, 95% CI 0.33–0.47). When stratified by study design, the mortality benefit remained significant in both randomized controlled trials (RCTs) and observational studies (OBS). Among RCTs (four studies, n = 911), the pooled effect favored TCM with RR = 0.58 (95% CI 0.45–0.74; $I^2 = 4.7\%$), indicating low heterogeneity.

Additional outcome(s) Four studies comprising 399 participants (211 in the TCM group and 188 in the control group) evaluated changes in oxygenation as measured by the PaO_2/FiO_2 ratio .

Pooled analysis demonstrated that TCM treatment significantly improved oxygenation compared with conventional therapy (MD = 25.9 mmHg, 95% CI 20.7–31.1; p 0.05).

When stratified by study design, the pooled mean difference was 24.7 mmHg (95% CI 19.4–30.0; $I^2 = 76.4\%$) across randomized controlled trials (Zhen 2019, Zeng 2023, Yu 2024) and 60.3 mmHg (95% CI 32.6–88.1) in one large observational study (Wang 2025). The subgroup difference was statistically significant ($p = 0.013$ for common-effect model), indicating that study design may explain part of the heterogeneity.

The Baujat plot identified Zhen 2019 and Zeng 2023 as the major contributors to both overall effect and heterogeneity, suggesting that differences in baseline oxygenation and intervention protocols (e.g., timing of TCM initiation) may influence outcomes.

The leave-one-out sensitivity analysis confirmed the robustness of the pooled results; sequential exclusion of any single study did not materially alter the direction or magnitude of the effect.

Pooled analysis demonstrated that TCM significantly shortened mechanical ventilation duration(SMD = –1.50, 95% CI –1.72 to –1.27; $I^2 = 0\%$, $p < 0.0001$) .

For ICU stay, reduction was observed statistical significance (MD = –2.32, 95% CI –3.10 to –1.54; $I^2 = 98.1\%$, $p < 0.0001$).

For hospital stay, the effect was inconsistent; MD = –3.19, 95% CI –3.51 to –2.86; $I^2 = 96.4\%$, $p < 0.0001$), driven by wide variation between Zhen 2019 (–9 days) and Zeng 2023 (–1 day).

Quality assessment / Risk of bias analysis For RCTs, the Cochrane Risk of Bias 2.0 (RoB 2.0) tool was used, evaluating domains of randomization, deviations from intended interventions, missing data, outcome measurement, and selective reporting. For observational studies, the ROBINS-I tool was applied, covering confounding, classification of intervention, deviations, missing data, outcome measurement, and reporting bias. Assessments were performed independently by two reviewers, with disagreements resolved by consensus.

Strategy of data synthesis Search and Duplicate Removal Process: AI automatically generates a Boolean search formula combining MeSH/Emtree and free terms, performs searches across multiple databases, and automatically removes duplicates and dynamically updates candidate articles before outputting them.

Performance Evaluation: As shown in Figure S1D, the Achieved bars represent the actual performance of the AI-assisted search system, while the Target bars correspond to the baseline performance of conventional manual retrieval. Compared with manual searches, the AI system demonstrated markedly higher recall and time efficiency, with comparable performance in duplicate removal.

Finally, two researchers independently conducted manual review, including title/abstract screening and full-text review. Disagreements were resolved by a third researcher.

Two reviewers independently screened titles/abstracts, assessed full texts, and extracted data. Discrepancies were resolved through discussion or adjudication by a third reviewer. Extracted data included: study design, year, country, sample size, patient characteristics, TCM intervention and dosage, comparator, and reported outcomes. When necessary, corresponding authors were contacted for missing or clarifying information.

Effect measures for binary outcomes (e.g., mortality) were expressed as Relative Risk (RR) or Hazard Ratio (HR), while continuous outcomes (e.g., PaO_2/FiO_2, length of stay, biomarker levels) were expressed as mean differences (MDs) or standardized mean differences (SMDs), each with 95% confidence intervals (CIs). Owing to anticipated clinical and methodological heterogeneity across populations, interventions, time points, and outcome definitions, we prespecified a random-effects model as the primary approach. A fixed-effect model was additionally performed as a sensitivity analysis when heterogeneity was negligible (e.g., I^2 0.10, and $\tau^2 \approx 0$) and the common-effect assumption

was clinically plausible; for outcomes with a single study, fixed-effect estimates were presented.
Graphical diagnostics included Baujat plots to identify influential studies and GOSH plots to assess the distribution of effect sizes across all possible study subsets. Leave-one-out analyses were performed to test robustness.
Bias due to missing evidence was assessed using the ROB-ME framework, which distinguishes publication bias, selective non-reporting, and small-study effects. Funnel plots, Egger's regression, and trim-and-fill were also applied for comparison.
All analyses were performed in R (version 4.4.2) using the meta and metafor packages, with $\alpha = 0.05$ considered statistically significant.

Subgroup analysis Bias due to missing evidence was assessed using the ROB-ME framework, which distinguishes publication bias, selective non-reporting, and small-study effects. Funnel plots, Egger's regression, and trim-and-fill were also applied for comparison.

Sensitivity analysis All analyses were performed in R (version 4.4.2) using the meta and metafor packages, with $\alpha = 0.05$ considered statistically significant.

Country(ies) involved China - Yanbian University Hospital.

Keywords Acute Respiratory Distress Syndrome; Acute Lung Injury; Traditional Chinese Medicine; AI-driven systematic reviewAcute Respiratory Distress Syndrome.

Contributions of each author
Author 1 - Ying Ren.
Author 2 - Yanju Wang.
Author 3 - Jisheng Meng.
Author 4 - Qingsong Cui.
Author 5 - Jinghu Yin.