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Traditional Chinese Medicines for Adult Non-Small Cell Lung Cancer: An Umbrella Review

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ADMINISTRATIVE INFORMATION

Support - No.

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Conflicts of interest - None declared.

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Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 30 April 2026 and was last updated on 30 April 2026.

INTRODUCTION

Review question / Objective Traditional Chinese medicines (TCMs) are extensively employed as adjuvant therapy for non-small cell lung cancer (NSCLC). Nevertheless, the existing evidence is dispersed across numerous meta-analyses and lacks large-scale, standardized grading of evidence credibility, which restricts its clinical translation. This study intends to systematically quantify the efficacy, safety, and evidence level of TCMs interventions for NSCLC via an umbrella review.

Condition being studied Lung cancer represents the most prevalent malignant neoplasm worldwide and is the leading cause of cancer-related death. In 2022, an estimated 2,480,675 new cases and 1,817,469 deaths attributable to lung cancer were recorded globally, corresponding to an age-standardized incidence rate (ASIR) of 23.60 per 100,000 persons and an age-standardized mortality rate (ASMR) of 16.80 per 100,000 persons . Non-small cell lung cancer (NSCLC), accounting for 85% of all lung cancers, is mostly diagnosed at locally advanced or metastatic stages [3]. Over the past two decades, the therapeutic landscape of NSCLC has changed dramatically; platinum-based doublet chemotherapy,Epidermal growth factor receptor-tyrosine kinase inhibitor (EGFR-TKIs) , and immune checkpoint inhibitors (ICIs) have significantly improved progression-free survival (PFS) and overall survival (OS) of patients . However, these treatments are limited by severe toxicities, acquired drug resistance, and compromised quality of life . Thus, there is an urgent clinical need for safe and effective adjuvant strategies to enhance efficacy, reduce toxicities, and improve patient outcomes.

METHODS

Participant or population Population: Patients with histologically or cytologically confirmed NSCLC, regardless of stage, age, or gender.

Intervention Intervention: TCMs interventions (including Chinese patent medicines, Chinese herbal medicine, Chinese herbal injections, TCM decoctions, and TCM compound prescriptions) combined with conventional NSCLC therapy (including platinum-based chemotherapy, EGFR-TKIs, ICIs, or radiotherapy).

Comparator Control: Conventional therapy alone, with the same regimen as the intervention group.

Study designs to be included Study type: Systematic reviews or meta-analyses of RCTs, with extractable pooled effect sizes and 95% confidence intervals (CIs).

Eligibility criteria (1) Population: Patients with histologically or cytologically confirmed NSCLC, regardless of stage, age, or gender; (2) Intervention: TCMs interventions (including Chinese patent medicines, Chinese herbal medicine, Chinese herbal injections, TCM decoctions, and TCM compound prescriptions) combined with conventional NSCLC therapy (including platinum-based chemotherapy, EGFR-TKIs, ICIs, or radiotherapy); (3) Control: Conventional therapy alone, with the same regimen as the intervention group; (4) Study type: Systematic reviews or meta-analyses of RCTs, with extractable pooled effect sizes and 95% confidence intervals (CIs); (5) Outcomes: At least one of the core outcomes: objective response rate (ORR), Karnofsky Performance Status (KPS) improvement rate, chemotherapy-induced gastrointestinal toxicity, or chemotherapy-induced myelosuppression; (6) Language: English or Chinese, to cover both international and Chinese literature.

Information sources The following databases were searched from their inception to March 31, 2026: PubMed, MEDLINE, Scopus, Web of Science, Cochrane Library, Embase, China National Knowledge Infrastructure (CNKI), Science and Technology Journal Database (VIP), and Wanfang Data. The search focused on MAs investigating the association between Traditional Chinese Medicine (TCMs) and adult non-small cell lung cancer using Medical Subject Headings terms and keywords such as “non-small cell lung cancer”, “Traditional Chinese Medicines (TCMs)”, and “meta-analysis” or “systematic review”. We also performed manual searches. When necessary, corresponding authors of original studies were contacted via email for additional data or clarifications. If they did not respond, the requests were subsequently closed.

Main outcome(s) The following databases were searched from their inception to March 31, 2026: PubMed, MEDLINE, Scopus, Web of Science, Cochrane Library, Embase, China National Knowledge Infrastructure (CNKI), Science and Technology Journal Database (VIP), and Wanfang Data.

Quality assessment / Risk of bias analysis Two reviewers (MW and SNL) independently reviewed the methodological quality of included MAs using the AMSTAR 2 tool comprising 16 core items . These items assess the following key domains: clarity of research questions and inclusion criteria; comprehensiveness of literature search strategy; reproducibility of study selection and data extraction; risk of bias assessment for included studies; publication bias testing; heterogeneity analysis; and robustness validation of conclusions. Methodological quality was stratified into four levels: “High”, “Moderate”, “Low”, and “Critically Low”.
The Ioannidis criteria were used to grade the evidence strength for TCMs intervention efficacy (Supplementary Table 3). This framework involves five core elements: study design, effect size magnitude, result consistency, sample size adequacy, and risk of publication bias. It categorizes evidence into four grades, from class I (convincing evidence) to class IV (weak evidence). Class I evidence represents the highest level for clinical recommendations.

Strategy of data synthesis The DerSimonian and Laird (D-L) random-effects model was used to re-model all eligible studies, correcting for heteroscedasticity's impact on effect size estimation. This stage had two key steps: (1) Primary effect size extraction: Raw effect sizes were retrieved from included SRs and MAs; pooled OR or RR, corresponding 95% CI and sample sizes were extracted. (2) Handling of overlapping MAs: For the same "TCMs intervention-outcome combination", the study with the largest sample size and latest publication date was prioritized.
In the second stage, a random-effects umbrella meta-analysis model was constructed using the metaumbrella package in R software (Version 4.3.1) [31-32]. The steps were: (1) Outcome calculation: Effect size-corrected pooled eOR and their 95% CI were computed. (2) Heterogeneity and uncertainty assessment: The I^2 statistic was used to quantify inter-study heterogeneity; 95% PIs were calculated. (3) Publication bias assessment: Egger’s linear regression test was used with $P < 0.1$. (4) Estim.

Subgroup analysis Our umbrella analysis revealed distinct efficacy profiles among different categories of traditional Chinese medicines (TCMs) interventions for improving objective response rate (ORR), with Chinese herbal injections (CHI) providing the most robust and consistent high-level evidence.For performance status (KPS) improvement, all TCMs adjuvant interventions exhibited consistent benefits.

Sensitivity analysis No.

Country(ies) involved China.

Keywords Non-small cell lung cancer; Traditional Chinese medicines; Umbrella review; Evidence credibility; Chinese herbal injections.

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