

Comparative Effectiveness of Different Prehabilitation Modalities on Postoperative Outcomes After Lung Cancer Resection: A Systematic Review and Network Meta-Analysis

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ADMINISTRATIVE INFORMATION**Support** - No support.**Review Stage at time of this submission** - Formal screening of search results against eligibility criteria.**Conflicts of interest** - None declared.**INPLASY registration number:** INPLASY2026100058

Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 13 October 2026 and was last updated on 13 October 2026.

INTRODUCTION

Review question / Objective Objective: To systematically compare the comparative effectiveness of different prehabilitation modalities (exercise, inspiratory muscle training, nutritional, psychological, and multimodal) versus usual care and against each other on postoperative outcomes in patients with primary lung cancer undergoing curative-intent lung resection, and to rank these modalities for the primary outcome of postoperative pulmonary complications (PPC).

Review questions:

1. In adults (≥ 18 years) with primary lung cancer scheduled for curative-intent lung resection, what is the comparative effectiveness of different prehabilitation modalities (exercise, inspiratory muscle training, nutritional, psychological, multimodal) versus usual care and against each other on PPC, length of hospital stay, 6-minute

walking distance, postoperative pulmonary function, health-related quality of life, 30-day readmission, 30-day/90-day mortality, and overall complication rates?

2. Which prehabilitation modality or combination of modalities confers the greatest benefit for reducing PPC in this population?

Rationale Postoperative pulmonary complications (PPCs) remain a leading cause of morbidity and prolonged hospital stay after curative-intent lung resection for primary lung cancer. Prehabilitation has been increasingly integrated into enhanced recovery after surgery (ERAS) pathways; however, the current evidence base is dominated by pairwise meta-analyses comparing a single prehabilitation modality (e.g., exercise, inspiratory muscle training, nutrition, or psychological intervention) with usual care. There is a lack of a comprehensive network meta-analysis that simultaneously compares all relevant prehabilitation modalities—including multimodal combinations—and ranks them for postoperative

outcomes in this population. A preliminary PubMed search (27 September 2026) using “prehabilitation + lung cancer + surgery” retrieved 554 records, including 41 systematic reviews/meta-analyses and only 2 network meta-analyses; none covered the full spectrum of exercise, inspiratory muscle training, nutritional, psychological, and multimodal prehabilitation in lung cancer resection. This review will therefore synthesize both direct and indirect evidence to estimate the comparative effectiveness of different prehabilitation modalities, with the primary outcome of PPC, and to provide a ranking that can inform clinical decisions on the optimal prehabilitation strategy.

Condition being studied Primary lung cancer (lung carcinoma) in adults aged ≥ 18 years scheduled for curative-intent lung resection. Histological subtype and surgical approach are unrestricted. Stage IV/metastatic disease, palliative surgery, lung metastases, and benign lesions are excluded.

METHODS

Search strategy 1. PubMed

("Lung Neoplasms"[Mesh] OR "Carcinoma, Non-Small-Cell Lung"[Mesh]
OR "lung cancer"[tiab] OR "lung carcinoma"[tiab]
OR "lung neoplasm"[tiab]
OR "NSCLC"[tiab] OR "non-small cell lung"[tiab]
OR "non small cell lung"[tiab]
OR "pulmonary cancer"[tiab] OR "pulmonary neoplasm"[tiab])
AND
("Pneumonectomy"[Mesh] OR "Thoracic Surgery, Video-Assisted"[Mesh] OR "Thoracotomy"[Mesh]
OR "Thoracic Surgical Procedures"[Mesh]
OR "lung resection"[tiab] OR "pulmonary resection"[tiab] OR "thoracic surgery"[tiab]
OR "lobectomy"[tiab] OR "segmentectomy"[tiab]
OR "pneumonectomy"[tiab]
OR "thoracoscopy"[tiab] OR "thoracotomy"[tiab]
OR "VATS"[tiab]
OR "video-assisted"[tiab] OR "robot-assisted"[tiab]
OR "anatomical resection"[tiab]
OR "radical resection"[tiab] OR "curative resection"[tiab])
AND
("Preoperative Exercise"[Mesh] OR "Preoperative Care"[Mesh:NoExp] OR "Breathing Exercises"[Mesh]
OR "Exercise Therapy"[Mesh] OR "Exercise"[Mesh]
OR "Resistance Training"[Mesh]
OR "Nutrition Therapy"[Mesh] OR "Physical Therapy Modalities"[Mesh]
OR "Rehabilitation"[Mesh] OR "Smoking Cessation"[Mesh]

OR "prehabilitation"[tiab] OR "pre-habilitation"[tiab]
OR "preoperative rehabilitation"[tiab]
OR "preoperative exercise"[tiab] OR "inspiratory muscle training"[tiab] OR "IMT"[tiab]
OR "respiratory muscle training"[tiab] OR "breathing exercise"[tiab]
OR "aerobic exercise"[tiab] OR "resistance training"[tiab]
OR "physical activity"[tiab] OR "exercise training"[tiab] OR "pulmonary rehabilitation"[tiab]
OR "physiotherapy"[tiab] OR "physical therapy"[tiab]
OR "nutritional support"[tiab] OR "nutritional supplementation"[tiab]
OR "dietary intervention"[tiab] OR "psychological intervention"[tiab]
OR "cognitive behavioral"[tiab] OR "cognitive behavioural"[tiab]
OR "smoking cessation"[tiab] OR "multimodal prehabilitation"[tiab]
OR "comprehensive prehabilitation"[tiab] OR "enhanced recovery"[tiab] OR "ERAS"[tiab])
AND
("randomized controlled trial"[pt] OR "controlled clinical trial"[pt]
OR "randomized"[tiab] OR "randomised"[tiab] OR "placebo"[tiab]
OR "randomly"[tiab] OR "trial"[tiab] OR "groups"[tiab])

2. Embase

('lung cancer'/exp OR 'non small cell lung cancer'/exp OR 'lung tumor'/exp OR 'lung carcinoma'/exp
OR 'lung cancer':ti,ab,kw OR 'lung carcinoma':ti,ab,kw OR 'lung neoplasm':ti,ab,kw
OR 'nsccl':ti,ab,kw OR 'non-small cell lung':ti,ab,kw OR 'non small cell lung':ti,ab,kw
OR 'pulmonary cancer':ti,ab,kw OR 'pulmonary neoplasm':ti,ab,kw)
AND
('lung resection'/exp OR 'pneumonectomy'/exp OR 'video assisted thoracoscopic surgery'/exp
OR 'thoracotomy'/exp OR 'thorax surgery'/exp
OR 'lung resection':ti,ab,kw OR 'pulmonary resection':ti,ab,kw OR 'lobectomy':ti,ab,kw
OR 'segmentectomy':ti,ab,kw OR 'pneumonectomy':ti,ab,kw OR 'thoracoscopy':ti,ab,kw
OR 'thoracotomy':ti,ab,kw OR 'vats':ti,ab,kw OR 'video-assisted':ti,ab,kw
OR 'robot-assisted':ti,ab,kw OR 'anatomical resection':ti,ab,kw OR 'radical resection':ti,ab,kw)
AND
('preoperative exercise'/exp OR 'breathing exercise'/exp OR 'kinesiotherapy'/exp
OR 'nutritional support'/exp OR 'smoking cessation'/exp OR 'physiotherapy'/exp

OR 'rehabilitation'/exp OR 'exercise'/exp OR 'resistance training'/exp
 OR 'prehabilitation':ti,ab,kw OR 'prehabilitation':ti,ab,kw OR 'preoperative rehabilitation':ti,ab,kw
 OR 'preoperative exercise':ti,ab,kw OR 'inspiratory muscle training':ti,ab,kw OR 'imt':ti,ab,kw
 OR 'respiratory muscle training':ti,ab,kw OR 'breathing exercise':ti,ab,kw
 OR 'aerobic exercise':ti,ab,kw OR 'resistance training':ti,ab,kw
 OR 'physical activity':ti,ab,kw OR 'exercise training':ti,ab,kw
 OR 'pulmonary rehabilitation':ti,ab,kw OR 'physiotherapy':ti,ab,kw OR 'physical therapy':ti,ab,kw
 OR 'nutritional support':ti,ab,kw OR 'nutritional supplementation':ti,ab,kw
 OR 'psychological intervention':ti,ab,kw OR 'cognitive behavioral':ti,ab,kw
 OR 'multimodal prehabilitation':ti,ab,kw OR 'comprehensive prehabilitation':ti,ab,kw
 OR 'enhanced recovery':ti,ab,kw OR 'eras':ti,ab,kw)
 AND
 ('randomized controlled trial'/exp OR 'controlled clinical trial'/exp
 OR random*:ti,ab,kw OR placebo:ti,ab,kw OR 'double blind':ti,ab,kw OR 'clinical trial':ti,ab,kw)

3.CENTRAL

#1 MeSH descriptor: [Lung Neoplasms] explode all trees
 #2 MeSH descriptor: [Carcinoma, Non-Small-Cell Lung] explode all trees
 #3 (lung cancer* OR lung carcinoma* OR lung neoplasm* OR NSCLC OR "non-small cell lung" OR "non small cell lung" OR pulmonary cancer* OR pulmonary neoplasm*):ti,ab,kw
 #4 #1 OR #2 OR #3

#5 MeSH descriptor: [Pneumonectomy] explode all trees
 #6 MeSH descriptor: [Thoracic Surgery, Video-Assisted] explode all trees
 #7 MeSH descriptor: [Thoracotomy] explode all trees
 #8 MeSH descriptor: [Thoracic Surgical Procedures] explode all trees
 #9 (lung resection* OR pulmonary resection* OR thoracic surgery OR lobectom* OR segmentectom* OR pneumonectom* OR thoracoscop* OR thoracotom* OR VATS OR "video-assisted" OR "robot-assisted" OR "anatomical resection" OR "radical resection"):ti,ab,kw
 #10 #5 OR #6 OR #7 OR #8 OR #9

#11 MeSH descriptor: [Preoperative Exercise] explode all trees
 #12 MeSH descriptor: [Breathing Exercises] explode all trees
 #13 MeSH descriptor: [Exercise Therapy] explode all trees
 #14 MeSH descriptor: [Exercise] explode all trees
 #15 MeSH descriptor: [Resistance Training] explode all trees
 #16 MeSH descriptor: [Nutrition Therapy] explode all trees
 #17 MeSH descriptor: [Physical Therapy Modalities] explode all trees
 #18 MeSH descriptor: [Rehabilitation] explode all trees
 #19 MeSH descriptor: [Smoking Cessation] explode all trees
 #20 (prehabilitation OR "pre-habilitation" OR "preoperative rehabilitation" OR "preoperative exercise"
 OR "inspiratory muscle training" OR IMT OR "respiratory muscle training" OR (breathing NEXT exercise*)
 OR "aerobic exercise" OR "resistance training" OR "physical activity" OR "exercise training"
 OR "pulmonary rehabilitation" OR physiotherapy OR "physical therapy"
 OR "nutritional support" OR "nutritional supplementation" OR "psychological intervention" OR "multimodal prehabilitation" OR "comprehensive prehabilitation" OR "enhanced recovery" OR ERAS):ti,ab,kw
 #21 #11 OR #12 OR #13 OR #14 OR #15 OR #16 OR #17 OR #18 OR #19 OR #20
 #22 #4 AND #10 AND #21

4.Web of Science

TS=(("lung cancer" OR "lung carcinoma" OR "lung neoplasm" OR NSCLC OR "non-small cell lung") AND ("lung resection" OR "pulmonary resection" OR lobectom* OR segmentectom* OR pneumonectom* OR thoracoscop* OR thoracotom* OR VATS OR "video-assisted") AND (prehabilitation OR "pre-habilitation" OR "preoperative rehabilitation" OR "preoperative exercise"
 OR "inspiratory muscle training" OR IMT OR "respiratory muscle training" OR "aerobic exercise" OR "resistance training" OR "nutritional support" OR "psychological intervention" OR "multimodal prehabilitation" OR "comprehensive prehabilitation" OR ERAS))
 AND TS=(random* OR RCT OR trial OR placebo OR groups)

5.CNKI:

SU= (肺肿瘤 + 肺癌 + 非小细胞肺癌 + 支气管肺癌)
AND SU= (肺切除 + 肺叶切除 + 肺段切除 + 全肺切除 + 胸腔镜 + 胸外科手术 + 胸外科 + VATS) AND
SU= (预康复 + 术前康复 + 术前训练 + 运动训练 + 呼吸训练 + 吸气肌训练 + 肺康复 + 呼吸功能训练 + 多模式预康复 + 营养支持 + 心理干预 + ERAS)

6.CINAHL: (To ensure comprehensive retrieval of the relevant literature, the search strategy includes a relatively large number of search terms. Due to the word limit, the complete CINAHL search strategy is provided in the supplementary fil) .

Participant or population Adults aged ≥ 18 years with primary lung cancer scheduled for curative-intent lung resection. Resection types include anatomical segmentectomy, lobectomy, bilobectomy, pneumonectomy, and wedge resection; surgical approach is unrestricted (VATS, robot-assisted, or open thoracotomy). Patients receiving neoadjuvant chemotherapy, immunotherapy, or targeted therapy before curative-intent resection are eligible and will be analyzed as a subgroup. Clinical stage or specific resection type need not be reported in the primary study; eligibility is confirmed when primary lung cancer and curative intent are ascertainable from the full text. Excluded: stage IV/metastatic disease, palliative surgery, lung metastases, benign lesions, or patients not undergoing surgery. Studies with mixed populations will not enter the primary analysis unless outcomes for the target population can be separated.

Intervention Preoperative prehabilitation modalities, categorized into five nodes: (1) aerobic/resistance exercise; (2) inspiratory muscle training (IMT); (3) nutritional intervention; (4) psychological intervention; (5) multimodal prehabilitation, defined as any combination of ≥ 2 non-pharmacological interventions. Smoking cessation, alcohol abstinence, and medical optimization are considered components of multimodal prehabilitation only and are not separate nodes. Pharmacological interventions are not included.

Comparator Usual care/control, including sham intervention, no intervention, or standard perioperative care. Head-to-head comparisons between prehabilitation modalities are also eligible.

Study designs to be included Randomized controlled trials (RCTs) only. Observational studies, conference abstracts without data, and duplicate publications are excluded.

Eligibility criteria Inclusion criteria:

Population: Adults aged ≥ 18 years with primary lung cancer scheduled for curative-intent lung resection. Resection types include anatomical segmentectomy, lobectomy, bilobectomy, pneumonectomy, and wedge resection; surgical approach is unrestricted (VATS, robot-assisted, or open thoracotomy). Clinical stage or specific resection type need not be reported; when primary lung cancer and curative intent are ascertainable from the full text, studies are eligible, and unreported stage/resection type is recorded as NR. Mixed-resection studies and studies with predominantly wedge resection are not excluded based on resection proportion; the previous $>50\%$ anatomical resection threshold is no longer used. Numbers/proportions of each resection type and the source of information will be recorded as study characteristics, and a sensitivity analysis restricted to clearly anatomical resection will be performed. Primary lung cancer and curative intent may be determined by comprehensive judgment based on the study population, inclusion criteria, treatment pathway, and tumor resection intent; positive supporting evidence is required, and unreported items and judgment limitations will be recorded. VATS, the term “lung resection” alone, or absence of contradictory evidence is insufficient to confirm eligibility. Suspected lung cancer with unclear final identity, inconsistent disease terms between text and abstract, or unexplained “Other” pathology/stage potentially affecting eligibility will be kept pending. Patients receiving neoadjuvant chemotherapy, immunotherapy, or targeted therapy followed by curative-intent resection are eligible and will be analyzed as a subgroup.

Intervention: Preoperative prehabilitation modalities, categorized into five nodes: (1) aerobic/resistance exercise; (2) inspiratory muscle training (IMT); (3) nutritional intervention; (4) psychological intervention; (5) multimodal prehabilitation, defined as any combination of ≥ 2 non-pharmacological interventions. Smoking cessation, alcohol abstinence, and medical optimization are considered components of multimodal prehabilitation only and are not separate nodes.

Comparator: Usual care/control, including sham intervention, no intervention, or standard perioperative care; head-to-head comparisons between prehabilitation modalities are also eligible.

Outcomes: Primary outcome: postoperative pulmonary complications (PPC). Secondary outcomes: length of hospital stay (LOS); 6-minute walking distance (6MWD) change; postoperative pulmonary function (FEV1, FVC change or measured values); health-related quality of life

(EORTC QLQ-C30/LC13, SF-36); 30-day readmission; 30-day/90-day mortality; overall complication rate; adherence and safety. Studies must report at least one eligible outcome.

Study design: Randomized controlled trials (RCTs) only.

Language/date: No language restriction; no date restriction.

Exclusion criteria:

Definite stage IV/distant metastasis, palliative surgery, pulmonary metastases, benign lesions, or patients not undergoing surgery.

Observational studies (used only for background and supplementary discussion).

Conference abstracts without data.

Duplicate publications (retain the most complete data set).

Mixed populations where outcomes for the target population cannot be separated; these will not enter the primary analysis, except for pre-specified population sensitivity analyses.

Studies where primary lung cancer identity or curative intent cannot be confirmed after contacting authors once; these will be recorded as pending/unclassified and will not enter the primary analysis. Missing information will not be directly treated as ineligibility.

Information sources PubMed/MEDLINE, Embase, Cochrane Central Register of Controlled Trials (CENTRAL), Web of Science, CINAHL, and CNKI (China National Knowledge Infrastructure). No language or date restrictions.

Main outcome(s) Postoperative pulmonary complications (PPC), as defined by the included studies.

Additional outcome(s) Length of hospital stay (LOS, days); change in 6-minute walking distance (6MWD); postoperative pulmonary function (FEV1 and FVC, change values or measured values); health-related quality of life (EORTC QLQ-C30/LC13, SF-36); 30-day readmission; 30-day and 90-day mortality; overall complication rate; adherence and safety.

Data management Records retrieved from all databases will be imported into Covidence for

deduplication, title/abstract screening, and full-text review. Two reviewers will independently screen studies and extract data using a standardized extraction form; disagreements will be resolved by a third reviewer.

Data to be extracted include: study characteristics (first author, year, country, study design, sample size), population characteristics (age, sex, clinical/pathological stage, diagnostic evidence for primary lung cancer, curative intent judgment and its basis, numbers/proportions of each resection type, surgical approach, neoadjuvant treatment), intervention details (prehabilitation modality, components, duration, frequency, supervision), comparator details, and outcome data for all primary and secondary outcomes. Unreported items will be recorded as NR; when segmentectomy and wedge resection are reported together, the original categories will be retained without calculating separate numbers.

Missing data will be handled by contacting the corresponding author once; if data remain unavailable, the study will be analyzed according to the intention-to-treat principle or the reported method, with the approach clearly noted. All extracted data will be managed in Microsoft Excel and cross-checked independently by a second reviewer.

Quality assessment / Risk of bias analysis Risk of bias for each outcome in included randomized controlled trials will be assessed using the Cochrane Risk of Bias 2 (RoB 2) tool. Two reviewers will independently assess each study, and disagreements will be resolved through discussion or by a third reviewer. The assessment will cover the five RoB 2 domains: randomization process, deviations from intended interventions, missing outcome data, measurement of the outcome, and selection of the reported result. For each outcome, studies will be judged as low risk of bias, some concerns, or high risk of bias. Sensitivity analyses restricted to studies at low risk of bias will be performed when data permit.

Strategy of data synthesis Pairwise random-effects meta-analysis will be performed (RR for binary outcomes; MD/SMD for continuous outcomes; I^2 and τ^2 reported). The primary NMA will be frequentist random-effects using netmeta (inverse variance), with network plots, contribution matrices, league tables, forest plots, and SUCRA/P-score rankings. Bayesian sensitivity analysis will use gemtc + JAGS. Heterogeneity will be assessed by τ^2 ; consistency by node-splitting and design-by-treatment tests if loops exist; transitivity by

comparing effect modifiers. Pre-specified subgroup and sensitivity analyses will be conducted. Publication bias will be assessed by comparison-adjusted funnel plots; certainty of evidence by CINeMA (NMA) and GRADE (pairwise). R (netmeta, meta, dmetar, gemtc) and Stata (mvmeta) will be used.

Subgroup analysis Pre-specified subgroup analyses will include: resection type (anatomical resection / wedge resection / mixed / not reported); surgical approach (minimally invasive vs open thoracotomy); baseline lung function (FEV1 %pred <80 vs ≥80); neoadjuvant treatment (yes vs no); duration of prehabilitation (<4 weeks vs ≥4 weeks); and single-modality vs multimodal prehabilitation. Subgroup analyses will be performed only when the number of studies and the available reported information are sufficient. The pooled effect from mixed populations will not be interpreted as a subgroup effect for resection type.

Sensitivity analysis Sensitivity analyses will include: (1) restriction to studies with clearly anatomical resection (all analyzed patients underwent segmentectomy, lobectomy, bilobectomy, or pneumonectomy, or outcomes for this population were separately extractable); (2) exclusion of studies with mixed wedge/anatomical resection where outcomes cannot be separated, and exclusion of studies not reporting specific resection type; (3) restriction to studies at low risk of bias; (4) exclusion of pilot/feasibility studies; (5) exclusion of high-influence nodes; (6) exclusion of neoadjuvant populations; and (7) exclusion of studies whose population eligibility relied on comprehensive judgment. Eligibility based on comprehensive judgment must first satisfy the eligibility criteria; sensitivity analysis will not replace eligibility verification.

Language restriction No language restriction.

Country(ies) involved China.

Other relevant information This is a secondary study using published data; no ethical approval is required. The results will be reported according to the PRISMA-NMA statement. The protocol and INPLASY registration number will be included in the final manuscript. No funding was received for this work.

Keywords Lung cancer; Prehabilitation; Lung resection; Postoperative pulmonary complications; Network meta-analysis; Systematic review;

Inspiratory muscle training; Multimodal prehabilitation.

Dissemination plans The findings of this systematic review and network meta-analysis will be submitted for publication in a peer-reviewed journal and presented at relevant academic conferences. The final report will be prepared according to the PRISMA-NMA statement. The protocol and the INPLASY registration number will be cited in all publications and presentations. Any important protocol amendments will be updated in the INPLASY record. As this is a secondary study using published data, no ethical approval is required.

Contributions of each author

Author 1 - Pengfei Wang - Conceptualization; Methodology; Investigation (title/abstract and full-text screening; data extraction); Risk of bias assessment (RoB 2); Formal analysis (pairwise and network meta-analysis); Writing – original draft. Email: 373861108@qq.com

Author 2 - Mengchen Liu - Conceptualization; Methodology; Investigation (title/abstract and full-text screening; data extraction); Risk of bias assessment (RoB 2); Validation (independent cross-check of extracted data and analyses); Writing – review & editing. Email: liumc0806@163.com

Author 3 - Ping He - Methodology; Investigation (third-reviewer arbitration of screening and data extraction disagreements); Validation (verification of statistical analyses); Writing – review & editing; Supervision. Email: pinghe@hust.edu.cn