Evidence – based Guidelines for Lung Cancer Treatment

Lung Cancer Treatment: Supplement

Department of Health Research
Directorate General of Health Services

Ministry of Health and Family Welfare
Government of India

In patients planned for lung cancer surgery, does prehabilitation improve perioperative outcomes over standard of care?

PICO

In patients planned for lung cancer surgery, does prehabilitation improve perioperative outcomes over standard of care?

Frame work	Description
Population	Patients planned for lung cancer surgery **Subgroup:** • Surgical approach (Open vs minimally invasive) • Type of surgery (lobectomy vs pneumonectomy) • Pre-existing cardiopulmonary comorbidities / poor performance status
Intervention	Prehabilitation
Comparator	Standard of care
Outcome	• Perioperative outcomes (Critical outcome) • Mortality (Critical outcome) • Quality of life (Critical outcome) • Length of hospital stay (Important outcome) • Surgical complications (Important outcome) • Functional recovery (Important outcome)

Key Question in PICO format

Should Prehabilitation vs. Standard of care be used for patients undergoing surgery for lung cancer?

Search Strategy

Search strings:

a) PubMed: (As on date 01/07/2024)

Search domain	Search strategy	Number of hits
P	("Lung Neoplasms/surgery"[Mesh])	3641
I	(("Preoperative Exercise"[Mesh]) OR "Diet"[Mesh] OR "Yoga"[Mesh] OR "Spirometry"[Mesh] OR "Counseling"[Mesh])	42250
C		
O (if applicable)		
Combined search domain (P AND I	("Lung Neoplasms/surgery"[Mesh]) AND (("Preoperative Exercise"[Mesh]) OR "Diet"[Mesh] OR "Yoga"[Mesh] OR "Spirometry"[Mesh] OR "Counselling"[Mesh])	265

AND C AND O)	("lung cancer patients" OR "lung neoplasms" OR "lung carcinoma" OR "pulmonary neoplasms") AND ("prehabilitation" OR "preoperative rehabilitation" OR "preoperative conditioning" OR "preoperative exercise" OR "preoperative physical therapy" OR "preoperative training" OR "preoperative intervention") AND ("standard care" OR "routine care" OR "usual care" OR "conventional care" OR "standard of care") AND ("perioperative outcomes" OR "surgical outcomes" OR "surgery outcomes" OR "operative outcomes" OR "postoperative outcomes" OR "perioperative complications" OR "perioperative morbidity" OR "perioperative mortality" OR "quality of life" OR "length of hospital stay" OR "hospital length of stay" OR "surgical complications" OR "postoperative complications" OR "functional recovery")	

b) EMBASE: (As on date 01/07/2024)

Search domain	Search strategy	Number of hits
P	("lung cancer patients" OR "lung neoplasms" OR "lung carcinoma" OR "pulmonary neoplasms")	7114
I	("prehabilitation" OR "preoperative rehabilitation" OR "preoperative conditioning" OR "preoperative exercise" OR "preoperative physical therapy" OR "preoperative training" OR "preoperative intervention")	6945
C	("standard care" OR "routine care" OR "usual care" OR "conventional care" OR "standard of care")	7287
O (if applicable)	("perioperative outcomes" OR "surgical outcomes" OR "surgery outcomes" OR "operative outcomes" OR "postoperative outcomes" OR "perioperative complications" OR "perioperative morbidity" OR "perioperative mortality" OR "quality of life" OR "length of hospital stay" OR "hospital length of stay" OR "surgical complications" OR "postoperative complications" OR "functional recovery")	5916
Combined search domain (P AND I AND C AND O)	("lung cancer patients" OR "lung neoplasms" OR "lung carcinoma" OR "pulmonary neoplasms") AND ("prehabilitation" OR "preoperative rehabilitation" OR "preoperative conditioning" OR "preoperative exercise" OR "preoperative physical therapy" OR "preoperative training" OR "preoperative intervention") AND ("standard care" OR "routine care" OR "usual care" OR "conventional care" OR "standard of care") AND ("perioperative outcomes" OR "surgical outcomes" OR "surgery outcomes" OR "operative outcomes"	6433

	OR "postoperative outcomes" OR "perioperative complications" OR "perioperative morbidity" OR "perioperative mortality" OR "quality of life" OR "length of hospital stay" OR "hospital length of stay" OR "surgical complications" OR "postoperative complications" OR "functional recovery")	

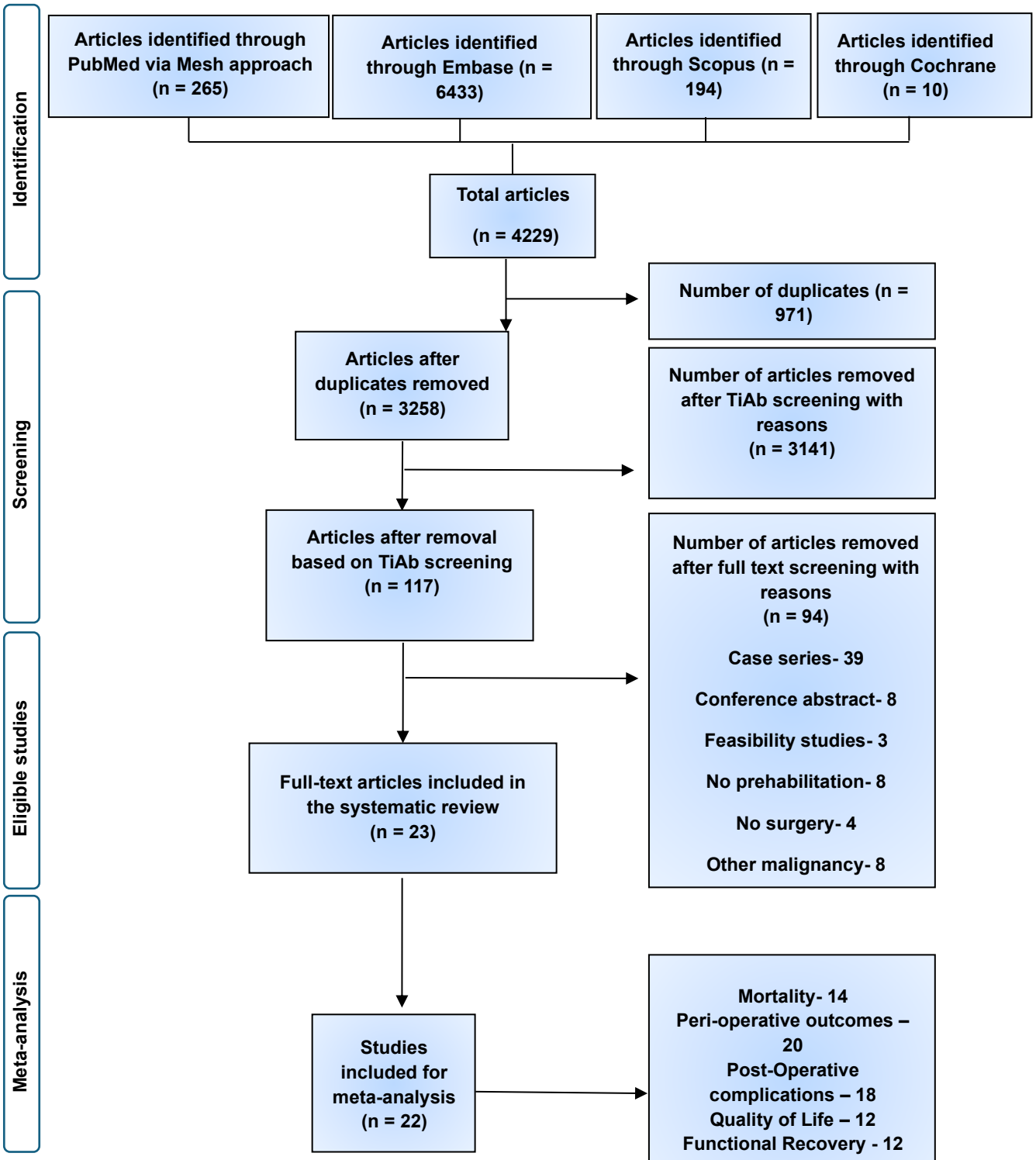
c) SCOPUS: (As on date 01/07/2024)

Search domain	Search strategy	Number of hits
P	("lung cancer patients" OR "lung neoplasms" OR "lung carcinoma" OR "pulmonary neoplasms")	
I	("prehabilitation" OR "preoperative rehabilitation" OR "preoperative conditioning" OR "preoperative exercise" OR "preoperative physical therapy" OR "preoperative training" OR "preoperative intervention")	
C	("standard care" OR "routine care" OR "usual care" OR "conventional care" OR "standard of care")	
O	("perioperative outcomes" OR "surgical outcomes" OR "surgery outcomes" OR "operative outcomes" OR "postoperative outcomes" OR "perioperative complications" OR "perioperative morbidity" OR "perioperative mortality" OR "quality of life" OR "length of hospital stay" OR "hospital length of stay" OR "surgical complications" OR "postoperative complications" OR "functional recovery")	
Combined search domain (P AND I AND C AND O)	("lung cancer patients" OR "lung neoplasms" OR "lung carcinoma" OR "pulmonary neoplasms") AND ("prehabilitation" OR "preoperative rehabilitation" OR "preoperative conditioning" OR "preoperative exercise" OR "preoperative physical therapy" OR "preoperative training" OR "preoperative intervention") AND ("standard care" OR "routine care" OR "usual care" OR "conventional care" OR "standard of care") AND ("perioperative outcomes" OR "surgical outcomes" OR "surgery outcomes" OR "operative outcomes" OR "postoperative outcomes" OR "perioperative complications" OR "perioperative morbidity" OR "perioperative mortality" OR "quality of life" OR "length of hospital stay" OR "hospital length of stay" OR "surgical complications" OR "postoperative complications" OR "functional recovery")	194

d) Cochrane Central: (As on date 01/07/2024)

Search domain	Search strategy	Number of hits
P	("lung cancer patients" OR "lung neoplasms" OR "lung carcinoma" OR "pulmonary neoplasms")	51
I	("prehabilitation" OR "preoperative rehabilitation" OR "preoperative conditioning" OR "preoperative exercise" OR "preoperative physical therapy" OR "preoperative training" OR "preoperative intervention")	1365
C	("standard care" OR "routine care" OR "usual care" OR "conventional care" OR "standard of care")	1178
O	("perioperative outcomes" OR "surgical outcomes" OR "surgery outcomes" OR "operative outcomes" OR "postoperative outcomes" OR "perioperative complications" OR "perioperative morbidity" OR "perioperative mortality" OR "quality of life" OR "length of hospital stay" OR "hospital length of stay" OR "surgical complications" OR "postoperative complications" OR "functional recovery")	3289
Combined search domain (P AND I AND C AND O)	("lung cancer patients" OR "lung neoplasms" OR "lung carcinoma" OR "pulmonary neoplasms") AND ("prehabilitation" OR "preoperative rehabilitation" OR "preoperative conditioning" OR "preoperative exercise" OR "preoperative physical therapy" OR "preoperative training" OR "preoperative intervention") AND ("standard care" OR "routine care" OR "usual care" OR "conventional care" OR "standard of care") AND ("perioperative outcomes" OR "surgical outcomes" OR "surgery outcomes" OR "operative outcomes" OR "postoperative outcomes" OR "perioperative complications" OR "perioperative morbidity" OR "perioperative mortality" OR "quality of life" OR "length of hospital stay" OR "hospital length of stay" OR "surgical complications" OR "postoperative complications" OR "functional recovery")	10

PRISMA flow diagram



Summary of Included studies

S. No	Study id	Population- Inclusion criteria	Population- Exclusion criteria	Intervention	Comparator	Outcome reported with time points
1	Benzo et al	Presence of lung cancer, operated by either open thoracotomy (segment, lobe or pneumonectomy) or by Video Assisted Thoracoscopy (at least lobe), moderate to severe COPD	NA	Preoperative pulmonary rehabilitation	Usual care	Outcomes were hospital length of stay and post operative pulmonary complications (pneumonia (new infiltrate + either fever (>38.5 ◦ C) and white cell count >11,000 or fever and purulent secretions), severe atelectasis (requiring bronchoscopy), prolonged chest tubes (>7 days), and prolonged mechanical ventilation (>24 h)
2	Chen et al	NA	NA	Pulmonary rehabilitation nursing program.	Standard care	Quality of life.
3	Garcia et al	1. Adults (⩾18 years old), 2. Suspected or confirmed diagnosis of NSCLC, 3. At least one of the following: (a) FEV1 ⩽80% of predicted value; (b) BMI ⩾30; (c) age ⩾75 years or (d) two or more co-morbidities identified in the	1. Neoadjuvant therapy with chemo- or radiotherapy in the six months prior to surgery. 2. Inability to perform the exercise training. 3. Not sign the informed consent.	preoperative pulmonary rehabilitation programme (a combination of moderate endurance and resistance	standard care	Exercise capacity.

		Colinet Comorbidity Score, 4. Distance to the facility centre ⩽80km.		training plus breathing exercises three to five times per week)		
4	Han et al	Patients aged 18 -80 years with a history of smoking >20 pack-years)	1. Poor pulmonary function, 2. severe brain, heart, kidney or liver dysfunction. 3. Inability to co-operate. 4. Stage 4 lung cancer with distant metastasis, 5. need for emergency surgery, 6. history of pre-operative chemotherapy, radiotherapy or chemo-radiotherapy for lung cancer. 7. pathologically confirmed benign lesion.	Respiratory and lower limb endurance exercises	regular care	The primary endpoint was the in-hospital incidence of PPCs, including (1) pneumonia; (2) atelectasis; (3) empyema; (4) prolonged air leak; (5) pleural effusion; and (6) respiratory failure.
5	Huang et al-IMT	(I) a definite diagnosis of primary non-small cell lung cancer (NSCLC) based on preoperative pathological examination and following NSCLC diagnosis and treatment guidelines; (II) presence of PPC risk factors, including age >70 years, body mass index (BMI) >30, COPD	patients who had contraindications to the PR regimen or risk of adverse events including myocardial infarction or cerebrovascular accident within one-year, unstable angina pectoris, aneurysm, recent history (<90 days) of hemoptysis,	conventional single-mode IMT (inspiratory muscle training)	routine preoperative preparation	Post-operative pulmonary complications

		with a heavy smoking history (≥20 pack-year or a preoperative smoking control time ≤2 weeks), forced expiratory volume in one second (FEV1) to forced vital capacity (FVC) (FEV1/FVC) ratio ≤70%, or prior history of thoracic surgery; (III) no surgical contraindication and willingness to undergo video-assistant thoracic surgery (VATS) or traditional open thoracotomy (open); and (IV) patient agreement to receive preoperative interventions.	severe arrhythmia, musculoskeletal or mental disorders.			
6	Huang et al-IMT and CRT	(I) a definite diagnosis of primary non-small cell lung cancer (NSCLC) based on preoperative pathological examination and following NSCLC diagnosis and treatment guidelines; (II) presence of PPC risk factors, including age >70 years, body mass index (BMI) >30, COPD with a heavy smoking history (≥20 pack-year or a preoperative smoking control time ≤2 weeks), forced	patients who had contraindications to the PR regimen or risk of adverse events including myocardial infarction or cerebrovascular accident within one-year, unstable angina pectoris, aneurysm, recent history (<90 days) of hemoptysis, severe arrhythmia, musculoskeletal or mental disorders.	high-intensity pulmonary rehabilitation (PR) that combined inspiratory muscle training (IMT) with conventional resistance training (CRT)	routine preoperative preparation	Post-operative pulmonary complications

		expiratory volume in one second (FEV1) to forced vital capacity (FVC) (FEV1/FVC) ratio ≤70%, or prior history of thoracic surgery; (III) no surgical contraindication and willingness to undergo video-assistant thoracic surgery (VATS) or traditional open thoracotomy (open); and (IV) patient agreement to receive preoperative interventions.				
7	Karenovics et al	Adult patients with proven or suspected NSCLC, stage IIIA or less. The criteria of resectability were based on the recommendations of the European Respiratory Society and European Society of Thoracic Surgery	Exclusion criteria were any contraindication to perform CPET (e.g., uncontrolled cardiac disease, severe pulmonary hypertension, limitations impeding cycling) or the inability to adhere to a rehabilitation program.	Pre-operative high-intensity interval training (HIIT)	usual care	Postoperative changes in CPET (Cardiopulmonary exercise testing)- (VO2peak; WRpeak) and in PFTs (pulmonary functional tests)- (FVC, FEV1)
8	Kaya et al	Patients operated due to non-small cell lung carcinoma	Malnourished (BMI less than 18.5), metabolic disorders, pre- operational radiotherapy and/or chemotherapy, patients who were under parenteral nutritional support, chronic renal and hepatic	Preoperative nutrition program with immune modulating formulae	Normal diet	Change in post-operative serum albumin levels and development of post-operative pulmonary complications,

			disorders, patients with history of another operation or major trauma recently or received blood transfusion recently, coagulation disorders, patients with previous history of extended and/or broncho plastic resection			
9	Lai et al	Diagnosis of primary non-small-cell LC (NSCLC), no surgical contraindication to and were willing to 91 undergo video-assisted thoracic surgery (VATS) or traditional thoracotomy (open) lobectomy, willing to receive preoperative PR	history of myocardial infarction, cerebrovascular accident (<1 year), unstable angina pectoris, aneurysm, hemoptysis (<90 days), severe arrhythmia or musculoskeletal or mental disorders, SpO2 <90% during the 6-min walking test; an absence of NSCLC, sub-lobar resection or pneumonectomy	Preoperative PR program - physical intervention focusing on exercise endurance training and inspiratory muscle training (IMT)	Conventional preoperative respiratory management	6-min walking distance (6-MWD), the peak expiratory flow (PEF), and quality-of-life scores before and after the rehabilitation regimen as well as the incidence of postoperative pulmonary complications (PPCs)
10	Lai et al*	>20 pack-year smoking history, age >75 years, body mass index >30, postoperative predicted percentage forced expiratory volume in 1s (ppoFEV1%) <60%,	(i) refusal to participate; (ii) contraindications to the physical rehabilitation including myocardial infarction or cerebrovascular accident	Preoperative, 7-day systematic, integrated, high-intensity pulmonary exercise regimen	Standard preoperative care	PPCs occurring within 30 days were identified and recorded as the primary endpoint

		postoperative predicted diffusing capacity of the lungs for carbon monoxide (ppoDLCO) <60% or chronic obstructive pulmonary disease	within the past year, unstable angina pectoris, aneurysm, recent history (<90 days) of haemoptysis, severe arrhythmia, musculoskeletal or mental disorders; (iii) not undergoing surgery; (iv) undergoing sub-lobar resection or pneumonectomy; or (v) having a diagnosis other than NSCLC			
11	Lai et al**	(I) diagnosis of non-small cell lung cancer (NSCLC) in the thoracic department of our hospital, a regional tertiary center; (II) reception of video-assisted thoracic surgery (VATS) lung cancer lobectomy with ppoFEV1% <60%; (III) and age between 45 to 80 years old; (IV) agreement to participate in the study with a consent	Contraindication to exercise or risk of adverse events, such as unsteady chest pain, uncontrolled high blood pressure or irregular heartbeat, serious aortic stenosis, acute illness or fever, severe arrhythmia, and musculoskeletal or mental disorders	One-week physical training combining aerobic and breathing exercises	Routine preoperative preparation	The primary endpoint was the change in 6-MWD conducted on the first day and one week later to evaluate the exercise capacity of patients
12	Laurent et al	Adult patients who were eligible for NSCLC resection (lobectomy or pneumonectomy	Tracheotomy, myasthenia gravis, recurrent paralysis or unstable coronary	3-week preoperative respiratory	Usual chest physical therapy	The primary outcome was the effect of 3-week preoperative RMET

		with video- assisted thoracic surgery or open thoracotomy), affiliated to the French health insurance and who gave their written consent	artery disease, patients who were unable to perform the isocapnic hyperpnoea endurance test or the RMET after the first habituation sessions	muscle endurance training (RMET) added to usual chest physical therapy		program which was evaluated with the isocapnic hyperpnoea endurance test.
13	Liu et al	Adult patients <70 years old with newly suspected or confirmed NSCLC, clinical stage I–III, who were scheduled for VATS lobectomy	Patients with American Society of Anesthesiologists (ASA) grade >III or patients who received neoadjuvant therapy, declined to participate in the study, or had pre-morbid conditions that contraindicated any items in the program	2-week multimodal intervention program before surgery, including aerobic and resistance exercises, respiratory training, nutrition counseling with whey protein supple-mentation, and psychological guidance	usual clinical care	The primary outcome was perioperative functional capacity measured as the 6-minute walk distance (6MWD), which was assessed at 1 day before and 30 days after surgery.
14	Liu et al*	(1) Patients diagnosed with primary non-small cell lung cancer and scheduled for thoracoscopic surgery; (2) Age ≥18 years old; (3) No mental illness or cognitive impairment; (4) Informed consent and	(1) Patients undergoing thoracotomy surgery; (2) Patients with other malignant tumors; (3) Patients with language communication disorders; (4) Patients engaged in	Mindful breathing group received mindful breathing training in addition to routine care. Patients assigned to the	routine care	Dyspnea. The degree of dyspnea was assessed by the Borg dyspnea scale, which ranges from 0 to 10 points, with higher scores indicating more severe dyspnea

		voluntary participation in the study	continuous rehabilitation training prior to admission	combined intervention group were given mindful breathing training combined with diary-based rehabilitation guidance, in addition to routine care		
15	Macha do et al	Adult candidates for surgery (age ≥ 18 years) to treat confirmed or suspected lung malignancy (clinical stage IIIA or lower) who had medical approval for exercise and surgery scheduled for at least 2 weeks from the baseline assessment	Metastatic tumor, contraindications for exercise training or physical testing, inability to speak or understand Portuguese, and current involvement in regular exercise training (aerobic and resistance training during the past month ≥ 2 days per week, ≥ 30 min per session)	PHET group-preoperative home-based exercise training (PHET)	Usual preoperative care	Quality of life (QoL)

16	Morano et al	(1) Non-small cell lung cancer resection by open thoracotomy or by video-assisted thoracoscopy; and (2) previous pulmonary disease, interstitial lung disease, or obstructive airway disease, with impaired respiratory function by spirometry	Not Available	PR (strength and endurance training)	CPT (breathing exercises for lung expansion)	Phase 1: The functional parameters after the completion of the programs (spirometry, MEP, MIP, 6MWT, and blood gas measurements) Phase 2: Hospital length of stay and PPCs
17	Pehlivan et al	Operable (stage IA to IIIB) lung cancer patients without major cardiac morbidity (ASA II or better)	Not Available	Intensive physical therapy (IPT) (chest physiotherapy and walking exercise)	No intensive physical therapy (IPT)	Reduction in hospital-stay
18	Stefanelli et al	Male or female, Age <75 years, Diagnosis of NSCLC stage I–IIA, Concomitant diagnosis of COPD according to the GOLD guidelines	Diabetes, Cardiovascular disease, Chronic renal failure, Liver failure, Respiratory failure (PaO2 <60 mmHg, breathing room air at rest) SpO2 <90% during the 6-min walking test, BMI>30	3-week preoperative outpatient intensive pulmonary rehabilitation programme (PRP) based on high-intensity training of both	Normal standard preoperative protocol	Respiratory function, by means of FEV1, FVC and DLCO; dyspnoea by means of Borg scale; physical performance by means of CPET peak VO2 measure. All patients had a baseline evaluation at the time of enrolment in the study (T0), an intermediate evaluation (T1) at the end of the PRP for Group R and

				upper- and lower-limb muscles		immediately before surgery for Group S, respectively. The final evaluation (T2) was performed 60 days after lobectomy for both groups
19	Tencon i et al	Patients affected by NSCLC in clinical stage I-II, eligible for lung resection, able to walk independently, with or without medical device, able to give informed consent	Patients known to require adjuvant treatments and patients unfit for the physical exercise re-quired by intervention or affected by sensorial or cognitive deficits with potential severe impact on compliance (deafness, blindness, dementia, etc.)	Standard of care + intensive perioperative pulmonary rehabilitation (sc+pr)	Standard of care (sc)	the primary aim of this study was to investigate the superiority of intensive perioperative pr over sc on exercise capacity six months after surgery, assessed through the change in the distance walked during a Six-Minute Walking Test (6MWT) compared to baseline
20	Wang et al	(i) patients with suspected or con- firmed primary NSCLC based on preoperative pathological and X-ray images; (ii) undergoing video-assisted thoracic surgery; (iii) the age > 18 years old; (v) able to provide informed written consent.	(i) received radiotherapy or chemotherapy before surgery; (ii) required mechanical ventilation after surgery; (iii) patients with contraindications or risk factors for adverse events, such as myocardial infarction, unstable angina pectoris, severe arrhythmia, cerebrovascular accident	Breathing exercises program	Routine care	Dyspnea, Inspiratory capacity, 6- min walk distance, Anxiety, Depression.

			within one year, musculoskeletal or mental dis- orders.			
21	Yao et al	1 According to the 2020 NCCN Guidelines for the Diagnosis and Treatment of Non-small Cell Lung Cancer and the eighth edition of international lung cancer pathological staging criteria, all patients were stage I-II lung cancer patients with feasible surgical resection; 2 Patients who underwent video-assisted thoracoscopic surgery; 3 The patient has no physical activity disorder, is conscious, and can understand and cooperate with medical staff; 4 Age ≤75 years old.	1 Patients with lung cancer in which the tumor has invaded the peripheral organs and extensive adhesion to the pleura; 2 Patients with a previous history of ipsilateral pulmonary surgery; 3 Lung tumors cannot undergo one-lung ventilation; 4 Patients with severe complications before operation, including patients with severe hematological and immune system diseases; 5 Patients with cardiac function ≥Class ≥III; 6 Patients with compact adhesion of thoracic cavity explored during operation and tumor invading thoracic wall; 7 Patients who switched from video-assisted thoracoscopic surgery to thoracotomy due to massive	Trimodal prehabilitation intervention strategy with aerobic and breathing exercises	Routine care	Activity capacity: 6-minute walking test (6 MWT), Psychological status: Hospital Anxiety and Depression Scale (HADS), Nutrition status- Serum albumin (albumi, ALB), prealbumin (PA) and transferrin (TRF), Comparison of the incidence of postoperative complications and the postoperative hospital stay between the two groups, the patient's nursing satisfaction at discharge.

			hemorrhage; 8 Patients who underwent pneumonectomy by changing the operation mode during the operation; 9 Postoperative patients with active bleeding tendency; 10 Patients with incomplete or untrue clinical data			
22	Zhou et al	(1) diagnosis of suspicious malignant lung nodule planned for minimally invasive lung resection; (2) age between 18 and 80 years; (3) preoperative clinical diagnosis stage I or II; (4) approval obtained from relevant surgeons; and (5) provision of informed consent	(1) emergency surgery; (2) contraindications to cardiopulmonary exercise testing (e.g., uncontrolled cardiac disease, severe pulmonary hypertension); (3) unable to perform exercise training due to disease; (4) refusal to participate in exercise training; (5) with other types of tumors; (6) previous thoracic surgery; and (7) malignant tumors in the past 5 years.	Preoperative exercise training	Routine care	Short-term postoperative complications within 30 days after surgery
23	Zou et al	(1) pathologically diagnosed with lung cancer according to the Chinese Medical Association guidelines for	(1) needed pneumonectomy; (2) had other organ diseases that required simultaneous	ABCDEF comprehensive nursing intervention	Routine nursing measures	First second volume (FEV1), forced vital capacity (FVC), FEV1/FVC ratio, 6 min walking distance, Borg

		clinical diagnosis and treatment of lung cancer20; (2) planning to undergo thoracoscopic lobectomy or segmental resection; (3) older than 18 years; and (4) those who voluntarily participated and signed a consent form	treatment; (3) had scoliosis or severe chest wall deformities, such as pectus excavatum, (4) had cognitive dysfunction; and (5) had mobility impairments (such as severe gout or stroke).	measures-(Acapella positive vibration pressure training, breathing exercise, cycling training, dance in the square, education, and follow-up)		score, incidence of postoperative complications, length of indwelling chest tube, and length of postoperative stay

Data Extraction

Name	Preoperative pulmonary rehabilitation before lung cancer resection: Results from two randomized studies
Author	Benzo et al
Study Type	Randomized controlled study
Countries and setting	USA
Number of Participants	19
Duration of study follow up (in months)	NA
Inclusion Criteria	Presence of lung cancer, operated by either open thoracotomy (segment, lobe or pneumonectomy) or by Video Assisted Thoracoscopy (at least lobe), moderate to severe COPD
Exclusion Criteria	NA
Recruitment/Selection of Patients	University of Pittsburgh (IRB#0603002) and Mayo Clinic (IRB# 08- 007135)
Intervention	Preoperative pulmonary rehabilitation
Outcome reported with time points	Outcomes were hospital length of stay and post operative pulmonary complications (pneumonia (new infiltrate + either fever (>38.5 ◦ C) and white cell count >11,000 or fever and purulent secretions), severe atelectasis (requiring bronchoscopy), prolonged chest tubes (>7 days), and prolonged mechanical ventilation (>24 h)
Funding	Grant # K23CA106544-05-06 from the National Cancer Institute
ROB 2 Assessment	Randomisation process - Some concerns Deviations from the intended interventions - Low Missing outcome data - Some concerns Measurement of the outcome - Low Selection of the reported result - Low Overall - Some concerns

Name	Effectiveness of precise and quantitative rapid pulmonary rehabilitation nursing program for elderly patients with lung cancer during the perioperative period: A randomized controlled trial
Author	Chen et al
Study Type	Randomized controlled study
Countries and setting	China
Number of Participants	218
Duration of study follow up (in months)	NA
Inclusion Criteria	NA
Exclusion Criteria	NA
Recruitment/Selection of Patients	Patients with lung cancer aged ≥70 years undergoing the thoracic surgeries during 2021 (at the Outpatient Department of Thoracic Surgery; Shanghai Pulmonary Hospital, China)
Intervention	Pulmonary rehabilitation nursing program.
Outcome reported with time points	Quality of life.
Funding	None
ROB 2 Assessment	Randomisation process - Low Deviations from the intended interventions - Some concerns Missing outcome data - Low Measurement of the outcome - Low Selection of the reported result - Low Overall - Some concerns

Name	Preoperative exercise training prevents functional decline after lung resection surgery: a randomized, single-blind controlled trial
Author	Garcia et al
Study Type	Randomized controlled study
Countries and setting	Spain
Number of Participants	40

Duration of study follow up (in months)	3
Inclusion Criteria	1. Adults (⩾18 years old), 2. Suspected or confirmed diagnosis of NSCLC, 3. At least one of the following: (a) FEV1 ⩽80% of predicted value; (b) BMI ⩾30; (c) age ⩾75 years or (d) two or more co-morbidities identified in the Colinet Comorbidity Score, 4. Distance to the facility centre ⩽80km.
Exclusion Criteria	1. Neoadjuvant therapy with chemo- or radiotherapy in the six months prior to surgery. 2. Inability to perform the exercise training. 3. Not sign the informed consent.
Recruitment/Selection of Patients	Those patients recruited who were considered for lung resection surgery at the Thoracic Surgery Department of the University Hospital of A Coruña were assessed for eligibility. Potentially eligible patients were contacted by phone and then scheduled for an interview with a specialized physiotherapist. Those who agreed to participate gave written informed consent prior to any formal testing.
Intervention	preoperative pulmonary rehabilitation programme (a combination of moderate endurance and resistance training plus breathing exercises three to five times per week)
Outcome reported with time points	Exercise capacity.
Funding	three-year predoctoral research fellowship from the Xunta de Galicia
ROB 2 Assessment	Randomisation process - Low Deviations from the intended interventions - Some Concerns Missing outcome data - High Risk Measurement of the outcome - Low Selection of the reported result - Low Overall - High Risk

Name	Ultra-short-period Perioperative Pulmonary Rehabilitation on Short-term Outcomes after Surgery in Smoking Patients with Lung Cancer: A Randomized Clinical Trial
Author	Han et al
Study Type	randomized controlled study
Countries and setting	China
Number of Participants	194
Duration of study follow up (in months)	NA
Inclusion Criteria	Patients aged 18 -80 years with a history of smoking >20 pack-years)
Exclusion Criteria	1. Poor pulmonary function, 2. severe brain, heart, kidney or liver dysfunction. 3. Inability to co-operate. 4. Stage 4 lung cancer with distant metastasis, 5. need for emergency surgery, 6. history of pre-operative chemotherapy, radiotherapy or chemo-radiotherapy for lung cancer. 7. pathologically confirmed benign lesion.
Recruitment/Selection of Patients	NA
Intervention	Respiratory and lower limb endurance exercises
Outcome reported with time points	The primary endpoint was the in-hospital incidence of PPCs, including (1) pneumonia; (2) atelectasis; (3) empyema; (4) prolonged air leak; (5) pleural effusion; and (6) respiratory failure.
Funding	None
ROB 2 Assessment	Randomisation process - Low Deviations from the intended interventions - Some Concerns Missing outcome data - Some concerns Measurement of the outcome - Some concerns Selection of the reported result - Low Overall - Some concerns

Name	Short-term high-intensity rehabilitation in radically treated lung cancer: a three-armed randomized controlled trial
Author	Huang et al
Study Type	Randomized controlled study (2 Arms - IMT, IMT and CRT)
Countries and setting	China
Number of Participants	45
Duration of study follow up (in months)	1
Inclusion Criteria	(I) a definite diagnosis of primary non-small cell lung cancer (NSCLC) based on preoperative pathological examination and following NSCLC diagnosis and treatment guidelines; (II) presence of PPC risk factors, including age >70 years, body mass index (BMI) >30, COPD with a heavy smoking history (≥20 pack-year or a preoperative smoking control time ≤2 weeks), forced expiratory volume in one second (FEV1) to forced vital capacity (FVC) (FEV1/FVC) ratio ≤70%, or prior history of thoracic surgery; (III) no surgical contraindication and willingness to undergo video-assistant thoracic surgery (VATS) or traditional open thoracotomy (open); and (IV) patient agreement to receive preoperative interventions.
Exclusion Criteria	patients who had contraindications to the PR regimen or risk of adverse events including myocardial infarction or cerebrovascular accident within one-year, unstable angina pectoris, aneurysm, recent history (<90 days) of hemoptysis, severe arrhythmia, musculoskeletal or mental disorders.
Recruitment/Selection of Patients	Preoperative lung cancer volunteers were recruited from the Department of Thoracic Surgery and Department of Rehabilitation Medicine, West China Hospital
Intervention	conventional single-mode IMT (inspiratory muscle training)
Outcome reported with time points	Post-operative pulmonary complications
Funding	(No. 2014SZ0148 and No. 2015SZ0158) from the Foundation of Science and Technology support plan, Department of Sichuan Province, China

ROB 2 Assessment	Randomisation process - Some concerns Deviations from the intended interventions - Some Concerns Missing outcome data - Low Measurement of the outcome - Low Selection of the reported result - Low Overall - Some concerns

Name	Short-term preoperative exercise therapy does not improve long-term outcome after lung cancer surgery: a randomized controlled study
Author	Karenovics et al
Study Type	Randomized controlled study
Countries and setting	Switzerland
Number of Participants	151
Duration of study follow up (in months)	12
Inclusion Criteria	Adult patients with proven or suspected NSCLC, stage IIIA or less. The criteria of resectability were based on the recommendations of the European Respiratory Society and European Society of Thoracic Surgery
Exclusion Criteria	Exclusion criteria were any contraindication to perform CPET (e.g., uncontrolled cardiac disease, severe pulmonary hypertension, limitations impeding cycling) or the inability to adhere to a rehabilitation program.
Recruitment/Selection of Patients	Study was registered at the National Institutes of Health ClinicalTrials.Gov (NCT01258478) and conducted at the University Hospitals of Geneva (UHG) and the Hospital of Valais (HV)
Intervention	Pre-operative high-intensity interval training (HIIT)
Outcome reported with time points	Postoperative changes in CPET (Cardiopulmonary exercise testing)- (VO2peak; WRpeak) and in PFTs (pulmonary functional tests)- (FVC, FEV1)
Funding	Centre de la Recherche Clinique of the University Hospital of Geneva and the Ligue Genevoise contre le Cancer

ROB 2 Assessment	Randomisation process - Low Deviations from the intended interventions - Some Concerns Missing outcome data - Some concerns Measurement of the outcome - Low Selection of the reported result - Low Overall - Some concerns

Name	Is preoperative protein-rich nutrition effective on postoperative outcome in non-small cell lung cancer surgery? A prospective randomized study
Author	Kaya et al
Study Type	Randomized controlled study
Countries and setting	Turkey
Number of Participants	58
Duration of study follow up (in months)	NA
Inclusion Criteria	Patients operated due to non-small cell lung carcinoma
Exclusion Criteria	Malnourished (BMI less than 18.5), metabolic disorders, pre- operational radiotherapy and/or chemotherapy, patients who were under parenteral nutritional support, chronic renal and hepatic disorders, patients with history of another operation or major trauma recently or received blood transfusion recently, coagulation disorders, patients with previous history of extended and/or broncho plastic resection
Recruitment/Selection of Patients	NA
Intervention	Preoperative nutrition program with immune modulating formulae
Outcome reported with time points	Change in post-operative serum albumin levels and development of post-operative pulmonary complications,
Funding	None

ROB 2 Assessment	Randomisation process - Some Concerns Deviations from the intended interventions - Some Concerns Missing outcome data - Some concerns Measurement of the outcome - Some Concerns Selection of the reported result - Low Overall - Some concerns

Name	**Impact of one-week preoperative physical training on clinical outcomes of surgical lung cancer patients with limited lung function: a randomized trial**
Author	Lai et al
Study Type	Randomized controlled study
Countries and setting	China
Number of Participants	68
Duration of study follow up (in months)	NA
Inclusion Criteria	Diagnosis of primary non-small-cell LC (NSCLC), no surgical contraindication to and were willing to 91 undergo video-assisted thoracic surgery (VATS) or traditional thoracotomy (open) lobectomy, willing to receive preoperative PR
Exclusion Criteria	history of myocardial infarction, cerebrovascular accident (<1 year), unstable angina pectoris, aneurysm, hemoptysis (<90 days), severe arrhythmia or musculoskeletal or mental disorders, SpO2 <90% during the 6-min walking test; an absence of NSCLC, sub-lobar resection or pneumonectomy

Recruitment/Selection of Patients	A prospective randomized controlled trial (RCT) with a total of 127 subjects was conducted in the 84 Department of Thoracic Surgery, West China Hospital, between June 2015 and March 2016. During the 85 study, patients were screened according to the inclusion/exclusion criteria (Table 1) and were randomly 86 allocated into the PR or control (non-pulmonary rehabilitation, NPR) group
Intervention	Preoperative PR program - physical intervention focusing on exercise endurance training and inspiratory muscle training (IMT)
Outcome reported with time points	6-min walking distance (6-MWD), the peak expiratory flow (PEF), and quality-of-life scores before and after the rehabilitation regimen as well as the incidence of postoperative pulmonary complications (PPCs)
Funding	None
ROB 2 Assessment	Randomisation process - Some Concerns Deviations from the intended interventions - Some Concerns Missing outcome data - Low Measurement of the outcome - Low Selection of the reported result - Low Overall - Some concerns

Name	**Seven-Day Intensive Preoperative Rehabilitation for Elderly Patients with Lung Cancer: A Randomized Controlled Trial**
Author	Lai et al*
Study Type	Randomized controlled study
Countries and setting	China
Number of Participants	60
Duration of study follow up (in months)	NA

Inclusion Criteria	>20 pack-year smoking history, age >75 years, body mass index >30, postoperative predicted percentage forced expiratory volume in 1s (ppoFEV1%) <60%, postoperative predicted diffusing capacity of the lungs for carbon monoxide (ppoDLCO) <60% or chronic obstructive pulmonary disease
Exclusion Criteria	(i) refusal to participate; (ii) contraindications to the physical rehabilitation including myocardial infarction or cerebrovascular accident within the past year, unstable angina pectoris, aneurysm, recent history (<90 days) of haemoptysis, severe arrhythmia, musculoskeletal or mental disorders; (iii) not undergoing surgery; (iv) undergoing sub lobar resection or pneumonectomy; or (v) having a diagnosis other than NSCLC
Recruitment/Selection of Patients	NA
Intervention	Preoperative, 7-day systematic, integrated, high-intensity pulmonary exercise regimen
Outcome reported with time points	PPCs occurring within 30 days were identified and recorded as the primary endpoint
Funding	Foundation of Science and Technology Support Plan, Department of Sichuan Province (2014SZ0148 and 2015SZ0158)
ROB 2 Assessment	Randomisation process - Some Concerns Deviations from the intended interventions - Some Concerns Missing outcome data - Low Measurement of the outcome - Low Selection of the reported result - Low Overall - Some concerns

Name	**Systematic short-term pulmonary rehabilitation before lung cancer lobectomy: a randomized trial**
Author	Lai et al**
Study Type	randomized controlled study
Countries and setting	China
Number of Participants	101
Duration of study follow up (in months)	NA

Inclusion Criteria	(I) diagnosis of non-small cell lung cancer (NSCLC) in the thoracic department of our hospital, a regional tertiary center; (II) reception of video-assisted thoracic surgery (VATS) lung cancer lobectomy with ppoFEV1% <60%; (III) and age between 45 to 80 years old; (IV) agreement to participate in the study with a consent
Exclusion Criteria	Contraindication to exercise or risk of adverse events, such as unsteady chest pain, uncontrolled high blood pressure or irregular heartbeat, serious aortic stenosis, acute illness or fever, severe arrhythmia, and musculoskeletal or mental disorders
Recruitment/Selection of Patients	NA
Intervention	One-week physical training combining aerobic and breathing exercises
Outcome reported with time points	The primary endpoint was the change in 6-MWD conducted on the first day and one week later to evaluate the exercise capacity of patients
Funding	Department of Sichuan Province (2014SZ0148 and 2015SZ0158)
ROB 2 Assessment	Randomisation process - Low Deviations from the intended interventions - Some Concerns Missing outcome data - Low Measurement of the outcome - Low Selection of the reported result - Low Overall - Some concerns

Name	**Preoperative respiratory muscle endurance training improves ventilatory capacity and prevents pulmonary postoperative complications after lung surgery**
Author	Laurent et al
Study Type	randomized controlled study
Countries and setting	France
Number of Participants	26
Duration of study follow up (in months)	3

Inclusion Criteria	Adult patients who were eligible for NSCLC resection (lobectomy or pneumonectomy with video- assisted thoracic surgery or open thoracotomy), affiliated to the French health insurance and who gave their written consent
Exclusion Criteria	Tracheotomy, myasthenia gravis, recurrent paralysis or unstable coronary artery disease, patients who were unable to perform the isocapnic hyperpnoea endurance test or the RMET after the first habituation sessions
Recruitment/Selection of Patients	patient's selection was performed by the referent surgeon at first medical visit. The randomization was performed electronically after recruitment, by clinical research as- sociate who was independent of the assessors. allocation was transmitted by emails send to assessors and therapists
Intervention	3-week preoperative respiratory muscle endurance training (RMET) added to usual chest physical therapy
Outcome reported with time points	The primary outcome was the effect of 3-week preoperative RMET program which was evaluated with the isocapnic hyperpnoea endurance test.
Funding	None
ROB 2 Assessment	Randomisation process - Some Concerns Deviations from the intended interventions - Some Concerns Missing outcome data - Low Measurement of the outcome - Some Concerns Selection of the reported result - Low Overall - Some concerns

Name	**Two-Week Multimodal Prehabilitation Program Improves Perioperative Functional Capability in Patients Undergoing Thoracoscopic Lobectomy for Lung Cancer: A Randomized Controlled Trial**
Author	Liu et al
Study Type	randomized controlled study
Countries and setting	China

Number of Participants	73
Duration of study follow up (in months)	1
Inclusion Criteria	Adult patients <70 years old with newly suspected or confirmed NSCLC, clinical stage I–III, who were scheduled for VATS lobectomy
Exclusion Criteria	Patients with American Society of Anesthesiologists (ASA) grade >III or patients who received neoadjuvant therapy, declined to participate in the study, or had pre-morbid conditions that contraindicated any items in the program
Recruitment/Selection of Patients	Patients scheduled for VATS lobectomy at PUMCH were recruited from March 2017 to December 2017 according to the inclusion and exclusion criteria
Intervention	2-week multimodal intervention program before surgery, including aerobic and resistance exercises, respiratory training, nutrition counseling with whey protein supple- mentation, and psychological guidance
Outcome reported with time points	The primary outcome was perioperative functional capacity measured as the 6-minute walk distance (6MWD), which was assessed at 1 day before and 30 days after surgery.
Funding	None
ROB 2 Assessment	Randomisation process - Low Deviations from the intended interventions - Some Concerns Missing outcome data - Low Measurement of the outcome - Low Selection of the reported result - Low Overall - Some concerns

Name	Effects of mindful breathing training combined with diary-based rehabilitation guidance in lung cancer patients undergoing surgery: A randomized controlled trial
Author	Liu et al*
Study Type	randomized controlled study
Countries and setting	China
Number of Participants	65
Duration of study follow up (in months)	NA
Inclusion Criteria	(1) Patients diagnosed with primary non-small cell lung cancer and scheduled for thoracoscopic surgery; (2) Age ≥18 years old; (3) No mental illness or cognitive impairment; (4) Informed consent and voluntary participation in the study
Exclusion Criteria	(1) Patients undergoing thoracotomy surgery; (2) Patients with other malignant tumors; (3) Patients with language communication disorders; (4) Patients engaged in continuous rehabilitation training prior to admission
Recruitment/Selection of Patients	Participants were recruited within the department of thoracic surgery at a tertiary hospital in Changchun, China according to the inclusion and exclusion criteria.
Intervention	Mindful breathing group received mindful breathing training in addition to routine care. Patients assigned to the combined intervention group were given mindful breathing training combined with diary-based rehabilitation guidance, in addition to routine care
Outcome reported with time points	Dyspnea. The degree of dyspnea was assessed by the Borg dyspnea scale, which ranges from 0 to 10 points, with higher scores indicating more severe dyspnea
Funding	None
ROB 2 Assessment	Randomisation process - Low Deviations from the intended interventions - Some Concerns Missing outcome data - Low Measurement of the outcome - Low Selection of the reported result - Low Overall - Some concerns

Name	Effect of Preoperative Home-Based Exercise Training on Quality of Life After Lung Cancer Surgery: A Multicenter Randomized Controlled Trial
Author	Machado et al
Study Type	randomized controlled study
Countries and setting	Portugal
Number of Participants	41
Duration of study follow up (in months)	1
Inclusion Criteria	Adult candidates for surgery (age ≥ 18 years) to treat confirmed or suspected lung malignancy (clinical stage IIIA or lower) who had medical approval for exercise and surgery scheduled for at least 2 weeks from the baseline assessment
Exclusion Criteria	Metastatic tumor, contraindications for exercise training or physical testing, inability to speak or understand Portuguese, and current involvement in regular exercise training (aerobic and resistance training during the past month ≥ 2 days per week, ≥ 30 min per session)
Recruitment/Selection of Patients	This multicenter, single-blind, parallel-arm, randomized controlled trial (RCT) recruited patients from the Portuguese Oncology Institute of Coimbra, Leiria Hospital Center, District Hospital of Santarém and District Hospital of Figueira da Foz (Portugal).
Intervention	PHET group- preoperative home-based exercise training (PHET)
Outcome reported with time points	Quality of life (QoL)
Funding	Portuguese Foundation for Science and Technology (UIDB/05704/2020)
ROB 2 Assessment	Randomisation process - Low Deviations from the intended interventions - Some Concerns Missing outcome data - Low Measurement of the outcome - Low Selection of the reported result - Low Overall - Some concerns

Name	Preoperative Pulmonary Rehabilitation Versus Chest Physical Therapy in Patients Undergoing Lung Cancer Resection: A Pilot Randomized Controlled Trial
Author	Morano et al
Study Type	randomized controlled study
Countries and setting	Brazil, Spain
Number of Participants	21
Duration of study follow up (in months)	NA
Inclusion Criteria	(1) Non-small cell lung cancer resection by open thoracotomy or by video-assisted thoracoscopy; and (2) previous pulmonary disease, interstitial lung disease, or obstructive airway disease, with impaired respiratory function by spirometry
Exclusion Criteria	Not Available
Recruitment/Selection of Patients	This randomized trial study recruited 31 patients between the period of March 2008 and March 2011 from a teaching hospital in Ceara´ (northeastern Brazil)
Intervention	PR (strength and endurance training)
Outcome reported with time points	Phase 1: The functional parameters after the completion of the programs (spirometry, MEP, MIP, 6MWT, and blood gas measurements) Phase 2: Hospital length of stay and PPCs
Funding	None
ROB 2 Assessment	Randomisation process - Low Deviations from the intended interventions - Some Concerns Missing outcome data - Low Measurement of the outcome - Low Selection of the reported result - Low Overall - Some concerns

Name	The Effects of Preoperative Short-term Intense Physical Therapy in Lung Cancer Patients: A Randomized Controlled Trial
Author	Pehlivan et al
Study Type	randomized controlled study
Countries and setting	Turkey
Number of Participants	60
Duration of study follow up (in months)	NA
Inclusion Criteria	Operable (stage IA to IIIB) lung cancer patients without major cardiac morbidity (ASA II or better)
Exclusion Criteria	Not Available
Recruitment/Selection of Patients	NA
Intervention	Intensive physical therapy (IPT) (chest physiotherapy and walking exercise)
Outcome reported with time points	Reduction in hospital-stay
Funding	None
ROB 2 Assessment	Randomisation process - High Risk Deviations from the intended interventions - Some Concerns Missing outcome data - Low Measurement of the outcome - Some Concerns Selection of the reported result - Low Overall – High Risk

Name	High-intensity training and cardiopulmonary exercise testing in patients with chronic obstructive pulmonary disease and non-small-cell lung cancer undergoing lobectomy
Author	Stefanelli et al
Study Type	randomized controlled study
Countries and setting	Italy

Number of Participants	40
Duration of study follow up (in months)	2
Inclusion Criteria	Male or female, Age <75 years, Diagnosis of NSCLC stage I–IIA, Concomitant diagnosis of COPD according to the GOLD guidelines
Exclusion Criteria	Diabetes, Cardiovascular disease, Chronic renal failure, Liver failure, Respiratory failure (PaO2 <60 mmHg, breathing room air at rest) SpO2 <90% during the 6-min walking test, BMI>30
Recruitment/Selection of Patients	NA
Intervention	3-week preoperative outpatient intensive pulmonary rehabilitation programme (PRP) based on high-intensity training of both upper- and lower-limb muscles
Outcome reported with time points	Respiratory function, by means of FEV1, FVC and DLCO; dyspnoea by means of Borg scale; physical performance by means of CPET peak VO2 measure. All patients had a baseline evaluation at the time of enrolment in the study (T0), an intermediate evaluation (T1) at the end of the PRP for Group R and immediately before surgery for Group S, respectively. The final evaluation (T2) was performed 60 days after lobectomy for both groups
Funding	None
ROB 2 Assessment	Randomisation process - Some Concerns Deviations from the intended interventions - Some Concerns Missing outcome data - Low Measurement of the outcome - Some Concerns Selection of the reported result - Low Overall - Some concerns

Name	**Rehabilitation for lung cancer patients undergoing surgery: results of the PUREAIR randomized trial**
Author	Tenconi et al
Study Type	Randomized controlled study

Countries and setting	Italy
Number of Participants	140
Duration of study follow up (in months)	6
Inclusion Criteria	Patients affected by NSCLC in clinical stage I-II, eligible for lung resection, able to walk independently, with or without medical device, able to give informed consent
Exclusion Criteria	Patients known to require adjuvant treatments and patients unfit for the physical exercise required by intervention or affected by sensorial or cognitive deficits with potential severe impact on compliance (deafness, blindness, dementia, etc.)
Recruitment/Selection of Patients	NA
Intervention	Standard of care + intensive perioperative pulmonary rehabilitation (sc+pr)
Outcome reported with time points	the primary aim of this study was to investigate the superiority of intensive perioperative pr over sc on exercise capacity six months after surgery, assessed through the change in the distance walked during a Six-Minute Walking Test (6MWT) compared to baseline
Funding	Italian Ministry of health in “bando ricerca finalizzata, Giovani ricercatori 2011/2012”. project code: Gr-2011-02351711
ROB 2 Assessment	Randomisation process - Low Deviations from the intended interventions - Some Concerns Missing outcome data - Some Concerns Measurement of the outcome - Some Concerns Selection of the reported result - Low Overall - Some concerns

Name	**Effect of breathing exercises in patients with non-small cell lung cancer receiving surgical treatment: A randomized controlled trial**
Author	Wang et al
Study Type	Randomized controlled study
Countries and setting	China
Number of Participants	65

Duration of study follow up (in months)	NA
Inclusion Criteria	(i) patients with suspected or con- firmed primary NSCLC based on preoperative pathological and X-ray images; (ii) undergoing video-assisted thoracic surgery; (iii) the age > 18 years old; (v) able to provide informed written consent.
Exclusion Criteria	(i) received radiotherapy or chemotherapy before surgery; (ii) required mechanical ventilation after surgery; (iii) patients with contraindications or risk factors for adverse events, such as myocardial infarction, unstable angina pectoris, severe arrhythmia, cerebrovascular accident within one year, musculoskeletal or mental dis- orders.
Recruitment/Selection of Patients	A researcher evaluated consecutive hospitalized patients in thoracic surgery of the First Hospital of Jilin University. Patients who met the inclusion criteria were invited to participate in the study, and another researcher who was unaware of the group assignment assessed baseline data after obtaining patients informed consent. The patients with NSCLC who agreed to participate in this study were recruited until the required sample size was achieved.
Intervention	Breathing exercises program
Outcome reported with time points	Dyspnea, Inspiratory capacity, 6- min walk distance, Anxiety, Depression.
Funding	None
ROB 2 Assessment	Randomisation process - Low Deviations from the intended interventions - Some Concerns Missing outcome data - Low Measurement of the outcome - Low Selection of the reported result - Low Overall - Some concerns

Name	**Application and practice of trimodal prehabilitation model in preoperative management of patients with lung cancer undergoing video-assisted thoracoscopic surgery**

Author	Yao et al
Study Type	randomized controlled study
Countries and setting	China
Number of Participants	148
Duration of study follow up (in months)	NA
Inclusion Criteria	According to the 2020 NCCN Guidelines for the Diagnosis and Treatment of Non-small Cell Lung Cancer and the eighth edition of international lung cancer pathological staging criteria, all patients were stage I-II lung cancer patients with feasible surgical resection; 2 Patients who underwent video-assisted thoracoscopic surgery; 3 The patient has no physical activity disorder, is conscious, and can understand and cooperate with medical staff; 4 Age ≤75 years old.
Exclusion Criteria	1 Patients with lung cancer in which the tumor has invaded the peripheral organs and extensive adhesion to the pleura; 2 Patients with a previous history of ipsilateral pulmonary surgery; 3 Lung tumors cannot undergo one-lung ventilation; 4 Patients with severe complications before operation, including patients with severe hematological and immune system diseases; 5 Patients with cardiac function ≥Class ≥III; 6 Patients with compact adhesion of thoracic cavity explored during operation and tumor invading thoracic wall; 7 Patients who switched from video-assisted thoracoscopic surgery to thoracotomy due to massive hemorrhage; 8 Patients who underwent pneumonectomy by changing the operation mode during the operation; 9 Postoperative patients with active bleeding tendency; 10 Patients with incomplete or untrue clinical data
Recruitment/Selection of Patients	Patients who received video-assisted thoracoscopic surgery for lung cancer in the inpatient department of Shanghai Chest Hospital from June 2021 to December 2021 were selected according to the inclusion and exclusion criteria.
Intervention	Trimodal prehabilitation intervention strategy with aerobic and breathing exercises

Outcome reported with time points	Activity capacity: 6-minute walking test (6 MWT), Psychological status: Hospital Anxiety and Depression Scale (HADS), Nutrition status- Serum albumin (albumi, ALB), prealbumin (PA) and transferrin (TRF), Comparison of the incidence of postoperative complications and the postoperative hospital stay between the two groups, the patient's nursing satisfaction at discharge.
Funding	General Nursing Research Project of Medical College of Shanghai Jiaotong University (2021 year) (No: Jyh2108)
ROB 2 Assessment	Randomisation process - Some Concerns Deviations from the intended interventions - Some Concerns Missing outcome data - Low Measurement of the outcome - Some Concerns Selection of the reported result - Low Overall - Some concerns

Name	**Preoperative exercise training decreases complications of minimally invasive lung cancer surgery: A randomized controlled trial**
Author	Zhou et al
Study Type	Randomized controlled study
Countries and setting	China
Number of Participants	101
Duration of study follow up (in months)	1
Inclusion Criteria	(1) diagnosis of suspicious malignant lung nodule planned for minimally invasive lung resection; (2) age between 18 and 80 years; (3) preoperative clinical diagnosis stage I or II; (4) approval obtained from relevant surgeons; and (5) provision of informed consent

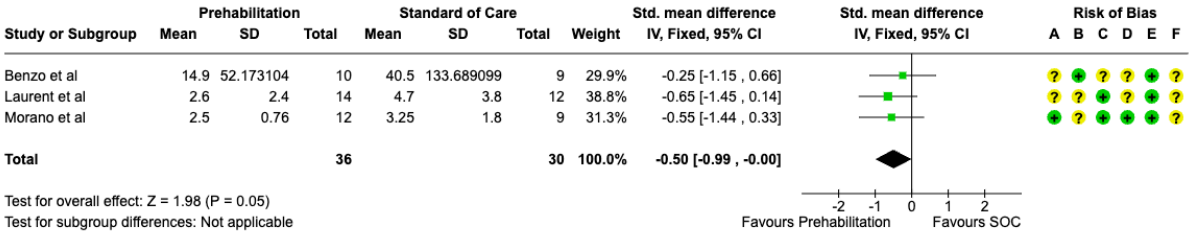
Exclusion Criteria	(1) emergency surgery; (2) contraindications to cardiopulmonary exercise testing (e.g., uncontrolled cardiac disease, severe pulmonary hypertension); (3) unable to perform exercise training due to disease; (4) refusal to participate in exercise training; (5) with other types of tumors; (6) previous thoracic surgery; and (7) malignant tumors in the past 5 years.
Recruitment/Selection of Patients	The intervention and treatments were performed at Xiangya Hospital from September 2020 to February 2022. Patients were consecutively recruited from the department of thoracic surgery based on the inclusion criteria and exclusion criteria.
Intervention	Preoperative exercise training
Outcome reported with time points	Short-term postoperative complications within 30 days after surgery
Funding	National Natural Science Foundation of China (82172549 to S.L. and 82272613 and 82002403 to Y.D.), the Natural Science Foundation of Hunan Province (2021JJ70073 to S.L. and 2021JJ40981 to Y.D.
ROB 2 Assessment	Randomisation process - Low Deviations from the intended interventions - Some Concerns Missing outcome data - Low Measurement of the outcome - Some Concerns Selection of the reported result - Low Overall - Some concerns

Name	**ABCDEF pulmonary rehabilitation program can improve the mid-term lung function of lung cancer patients after thoracoscopic surgery: A randomized controlled study**
Author	Zou et al
Study Type	Randomized controlled study
Countries and setting	China
Number of Participants	90

Duration of study follow up (in months)	3
Inclusion Criteria	(1) pathologically diagnosed with lung cancer according to the Chinese Medical Association guidelines for clinical diagnosis and treatment of lung cancer20; (2) planning to undergo thoracoscopic lobectomy or segmental resection; (3) older than 18 years; and (4) those who voluntarily participated and signed a consent form
Exclusion Criteria	(1) needed pneumonectomy; (2) had other organ diseases that required simultaneous treatment; (3) had scoliosis or severe chest wall deformities, such as pectus excavatum, (4) had cognitive dysfunction; and (5) had mobility impairments (such as severe gout or stroke).
Recruitment/Selection of Patients	The study was conducted between November 2019 and August 2020 at Hunan Provincial People's Hospital, a comprehensive tertiary teaching hospital located in Changsha, south-central China.
Intervention	ABCDEF comprehensive nursing intervention measures- (Acapella positive vibration pressure training, breathing exercise, cycling training, dance in the square, education, and follow-up)
Outcome reported with time points	First second volume (FEV1), forced vital capacity (FVC), FEV1/FVC ratio, 6 min walking distance, Borg score, incidence of postoperative complications, length of indwelling chest tube, and length of postoperative stay
Funding	Research Foundation of the Health Commission of Hunan Province, China (Grant No. 20200517) `
ROB 2 Assessment	Randomisation process - Some Concerns Deviations from the intended interventions - Some Concerns Missing outcome data - Low Measurement of the outcome - Low Selection of the reported result - Low Overall - Some concerns

Forest Plots of Important Outcomes

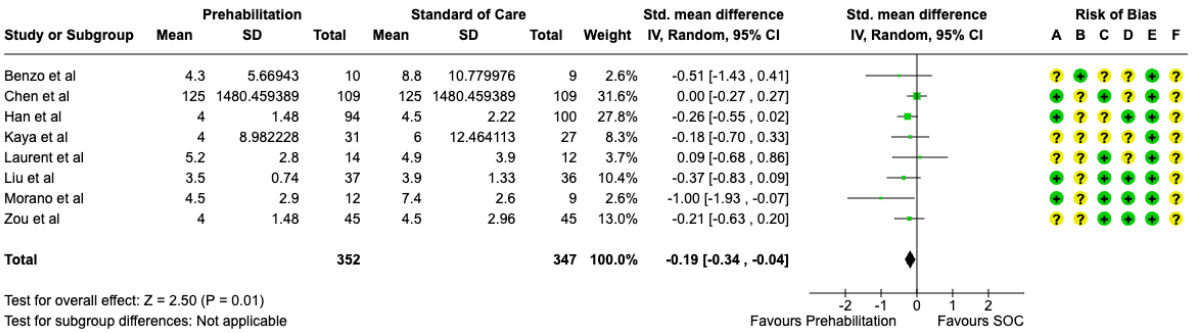
ICU Stay after lung cancer surgery



Test for overall effect: Z = 1.98 (P = 0.05)
Test for subgroup differences: Not applicable
Heterogeneity: Chi² = 0.46, df = 2 (P = 0.80); I² = 0%

Risk of bias legend
(A) Bias arising from the randomization process
(B) Bias due to deviations from intended interventions
(C) Bias due to missing outcome data
(D) Bias in measurement of the outcome
(E) Bias in selection of the reported result
(F) Overall bias

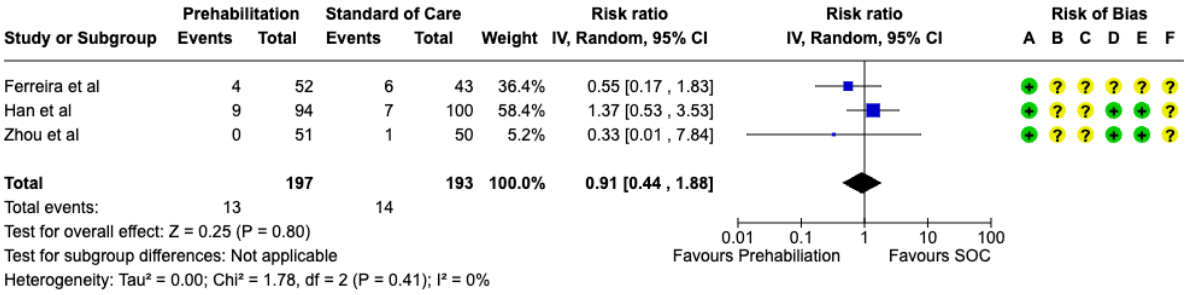
Duration of ICD placement after lung cancer surgery



Test for overall effect: Z = 2.50 (P = 0.01)
Test for subgroup differences: Not applicable
Heterogeneity: Tau² = 0.00; Chi² = 6.71, df = 7 (P = 0.46); I² = 0%

Risk of bias legend
(A) Bias arising from the randomization process
(B) Bias due to deviations from intended interventions
(C) Bias due to missing outcome data
(D) Bias in measurement of the outcome
(E) Bias in selection of the reported result
(F) Overall bias

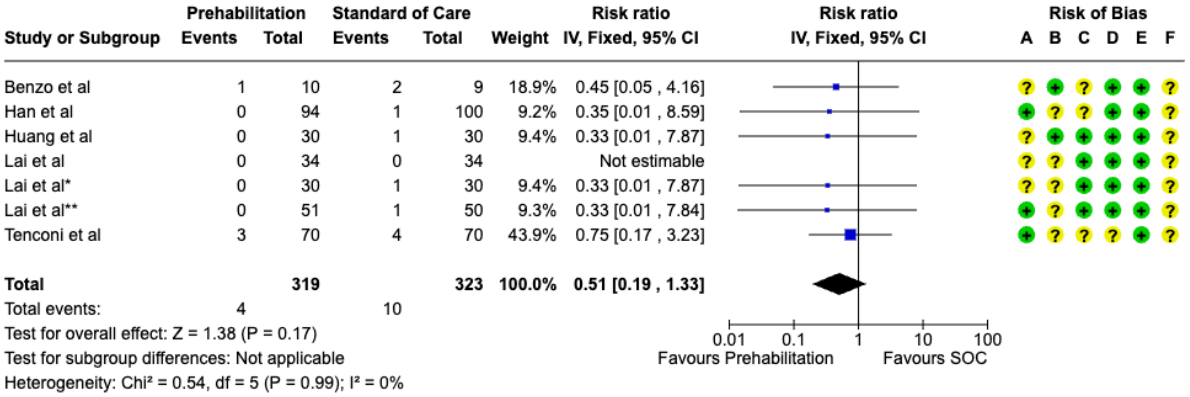
Readmissions



Risk of bias legend
(A) Bias arising from the randomization process
(B) Bias due to deviations from intended interventions
(C) Bias due to missing outcome data
(D) Bias in measurement of the outcome
(E) Bias in selection of the reported result
(F) Overall bias

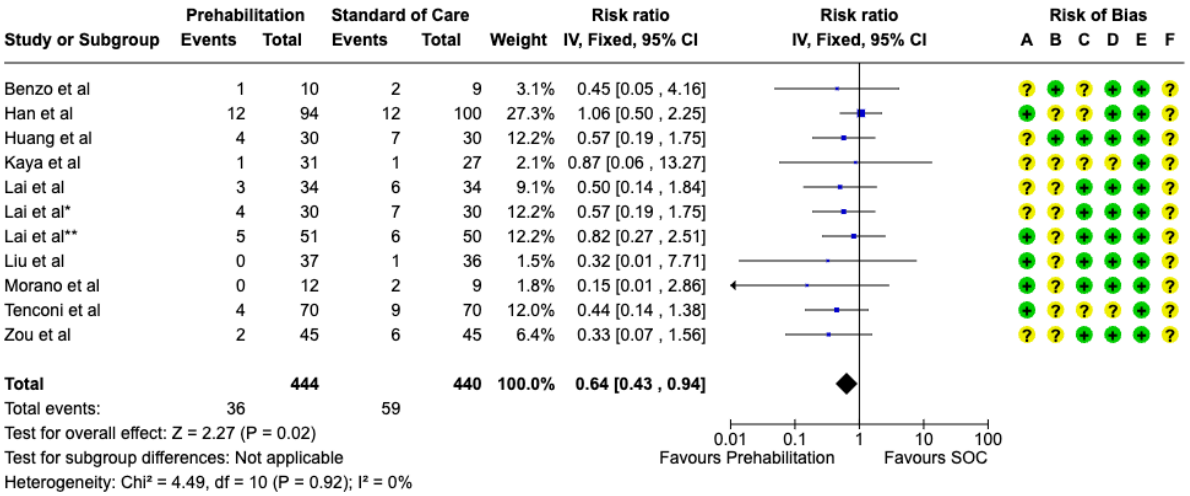
Post-operative Complications

Respiratory failure



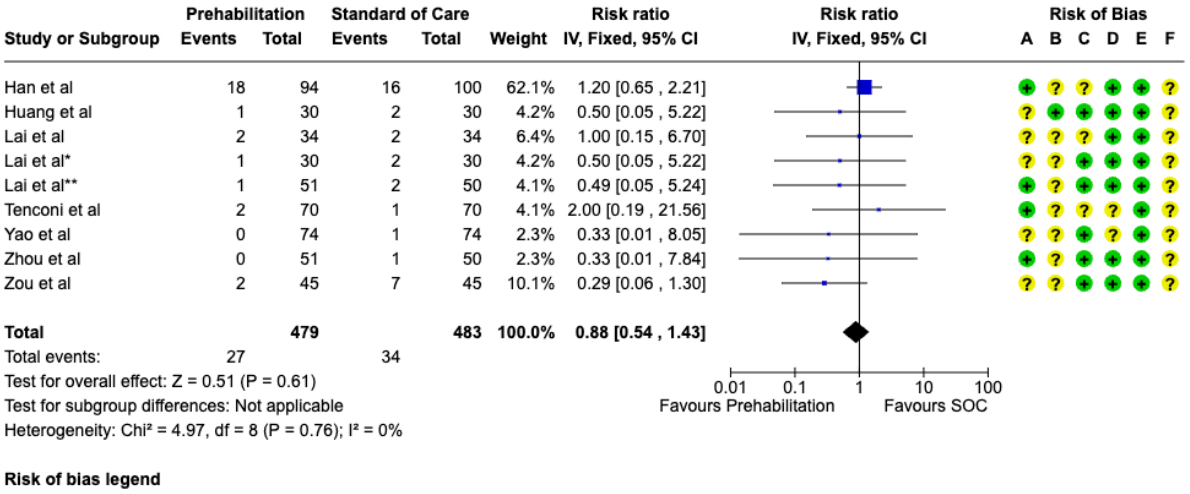
Risk of bias legend
(A) Bias arising from the randomization process
(B) Bias due to deviations from intended interventions
(C) Bias due to missing outcome data
(D) Bias in measurement of the outcome
(E) Bias in selection of the reported result
(F) Overall bias

Pneumonia



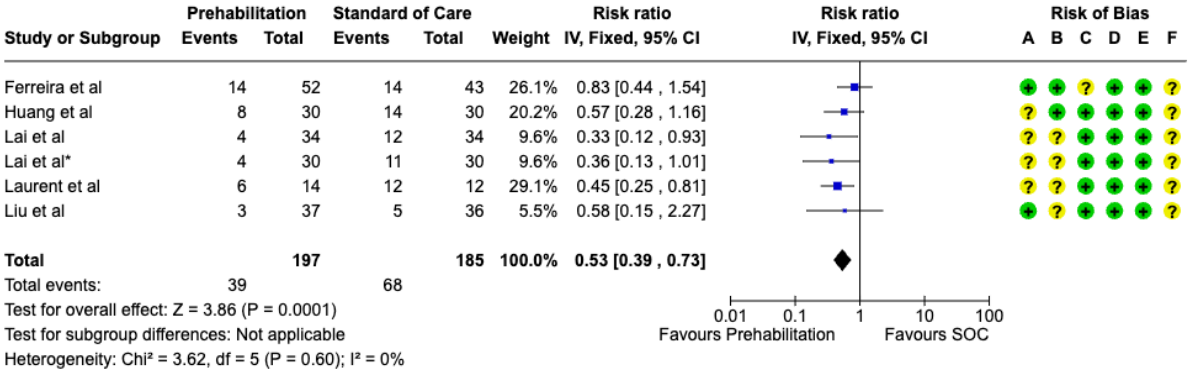
Risk of bias legend
(A) Bias arising from the randomization process
(B) Bias due to deviations from intended interventions
(C) Bias due to missing outcome data
(D) Bias in measurement of the outcome
(E) Bias in selection of the reported result
(F) Overall bias

Pleural effusion



Risk of bias legend
(A) Bias arising from the randomization process
(B) Bias due to deviations from intended interventions
(C) Bias due to missing outcome data
(D) Bias in measurement of the outcome
(E) Bias in selection of the reported result
(F) Overall bias

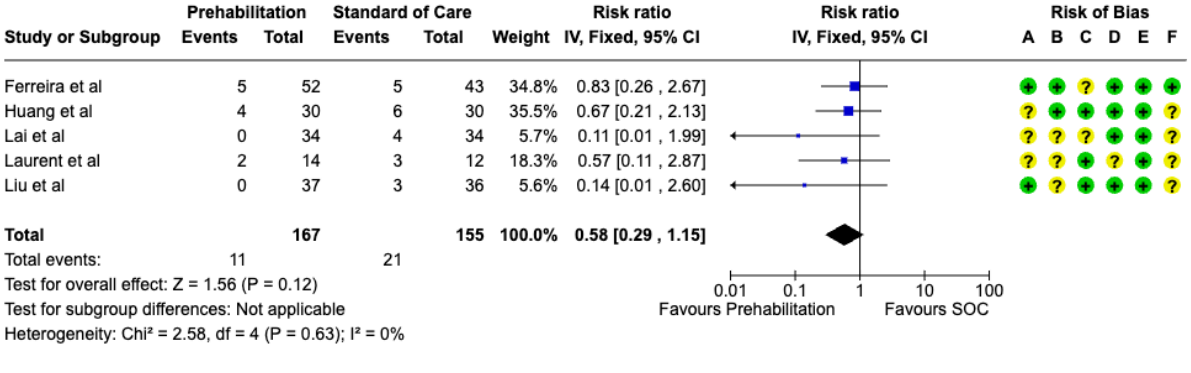
Clavein Dindo grade 2 and above complications



Risk of bias legend

(A) Bias arising from the randomization process
(B) Bias due to deviations from intended interventions
(C) Bias due to missing outcome data
(D) Bias in measurement of the outcome
(E) Bias in selection of the reported result
(F) Overall bias

Clavein Dindo grade 3 and above complications

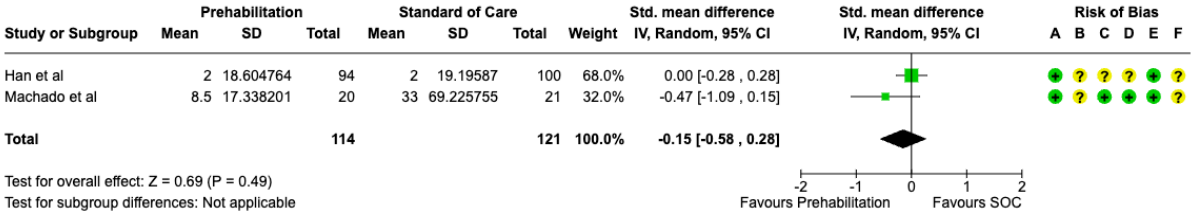


Risk of bias legend

(A) Bias arising from the randomization process
(B) Bias due to deviations from intended interventions
(C) Bias due to missing outcome data
(D) Bias in measurement of the outcome
(E) Bias in selection of the reported result
(F) Overall bias

Functional recovery

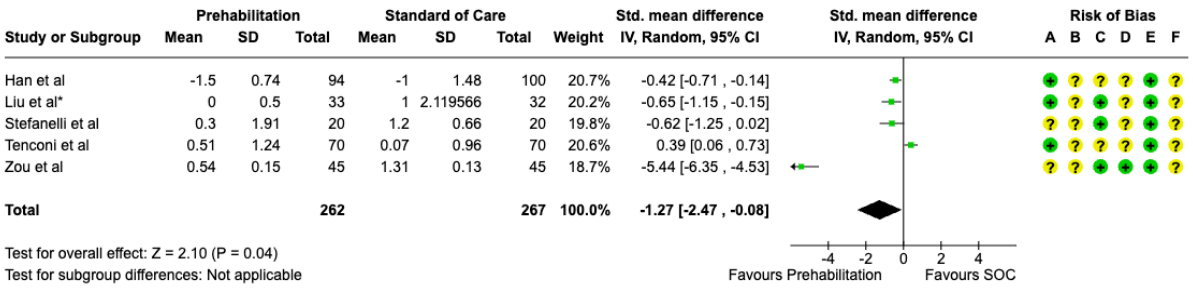
Pain score in patients on day 2 following lung cancer surgery



Test for overall effect: Z = 0.69 (P = 0.49)
Test for subgroup differences: Not applicable
Heterogeneity: Tau² = 0.05; Chi² = 1.83, df = 1 (P = 0.18); I² = 45%

Risk of bias legend
(A) Bias arising from the randomization process
(B) Bias due to deviations from intended interventions
(C) Bias due to missing outcome data
(D) Bias in measurement of the outcome
(E) Bias in selection of the reported result
(F) Overall bias

Change in Borg score from baseline to post surgery

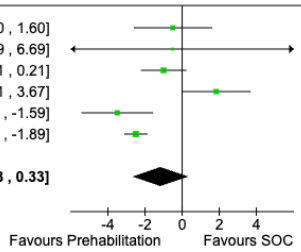


Test for overall effect: Z = 2.10 (P = 0.04)
Test for subgroup differences: Not applicable
Heterogeneity: Tau² = 1.76; Chi² = 140.38, df = 4 (P < 0.00001); I² = 97%

Risk of bias legend
(A) Bias arising from the randomization process
(B) Bias due to deviations from intended interventions
(C) Bias due to missing outcome data
(D) Bias in measurement of the outcome
(E) Bias in selection of the reported result
(F) Overall bias

Change in HADS anxiety score (baseline to post lung cancer surgery)

Study or Subgroup	Prehabilitation Mean	SD	Total	Standard of Care Mean	SD	Total	Weight	Mean difference IV, Random, 95% CI
Ferreira et al	-2.3	4.78	52	-1.8	5.52	43	16.5%	-0.50 [-2.60 , 1.60]
Liu et al	-2	17.854616	37	-1.5	13.204921	36	3.7%	-0.50 [-7.69 , 6.69]
Liu et al*	-2	3.172212	33	-1	1.55688	32	21.0%	-1.00 [-2.21 , 0.21]
Tenconi et al	-1.18	5.47	70	-3.02	5.56	70	17.9%	1.84 [0.01 , 3.67]
Wang et al	-5	5.19	31	-1.5	1.67	34	17.5%	-3.50 [-5.41 , -1.59]
Yao et al	-4.5	2.5	74	-2	1	74	23.4%	-2.50 [-3.11 , -1.89]
Total			**297**			**289**	**100.0%**	**-1.18 [-2.68 , 0.33]**

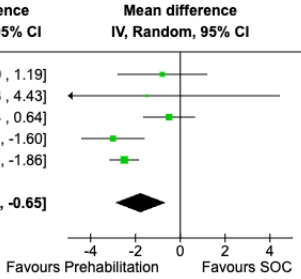


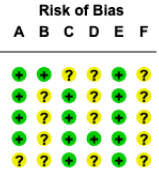
Test for overall effect: Z = 1.53 (P = 0.13)
Test for subgroup differences: Not applicable
Heterogeneity: Tau² = 2.43; Chi² = 26.44, df = 5 (P < 0.0001); I² = 81%

Risk of bias legend
(A) Bias arising from the randomization process
(B) Bias due to deviations from intended interventions
(C) Bias due to missing outcome data
(D) Bias in measurement of the outcome
(E) Bias in selection of the reported result
(F) Overall bias

Change in HADS Depression score (baseline to post lung cancer surgery)

Study or Subgroup	Prehabilitation Mean	SD	Total	Standard of Care Mean	SD	Total	Weight	Mean difference IV, Random, 95% CI
Ferreira et al	-0.9	4.31	52	-0.1	5.39	43	16.7%	-0.80 [-2.79 , 1.19]
Liu et al	-2	17.854616	37	-0.5	4.40164	36	3.3%	-1.50 [-7.43 , 4.43]
Liu et al*	-1	2.994223	33	-0.5	1.472551	32	25.8%	-0.50 [-1.64 , 0.64]
Wang et al	-4	3.71	31	-1	1.48	34	22.8%	-3.00 [-4.40 , -1.60]
Yao et al	-4.5	2	74	-2	2	74	31.4%	-2.50 [-3.14 , -1.86]
Total			**227**			**219**	**100.0%**	**-1.78 [-2.91 , -0.65]**

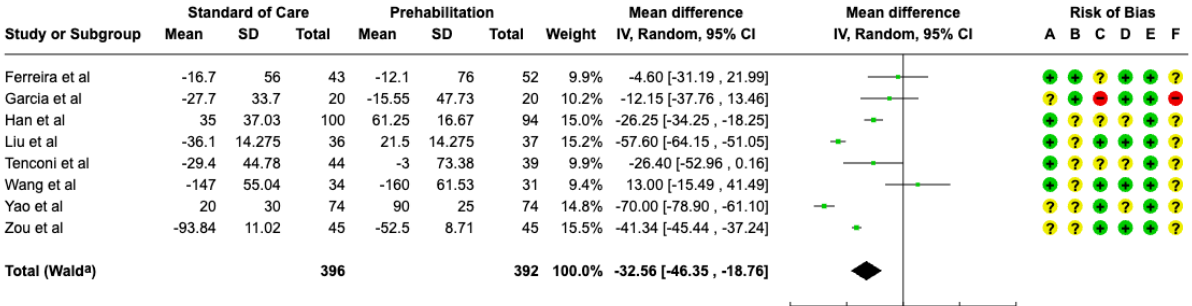




Test for overall effect: Z = 3.09 (P = 0.002)
Test for subgroup differences: Not applicable
Heterogeneity: Tau² = 0.95; Chi² = 12.27, df = 4 (P = 0.02); I² = 67%

Risk of bias legend
(A) Bias arising from the randomization process
(B) Bias due to deviations from intended interventions
(C) Bias due to missing outcome data
(D) Bias in measurement of the outcome
(E) Bias in selection of the reported result
(F) Overall bias

Change in 6MWD (6 minute walking distance) from baseline to post cancer surgery



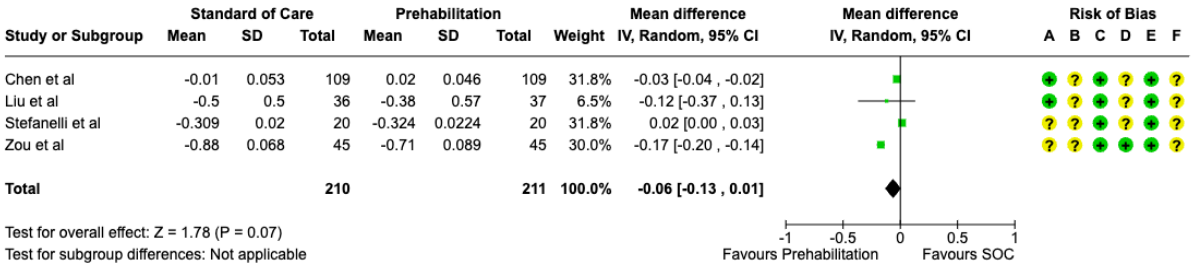
Study or Subgroup	Standard of Care Mean	SD	Total	Prehabilitation Mean	SD	Total	Weight	Mean difference IV, Random, 95% CI	Risk of Bias A	B	C	D	E	F
Ferreira et al	-16.7	56	43	-12.1	76	52	9.9%	-4.60 [-31.19 , 21.99]	+	+	?	+	+	?
Garcia et al	-27.7	33.7	20	-15.55	47.73	20	10.2%	-12.15 [-37.76 , 13.46]	?	+	-	+	+	-
Han et al	35	37.03	100	61.25	16.67	94	15.0%	-26.25 [-34.25 , -18.25]	+	?	?	?	+	?
Liu et al	-36.1	14.275	36	21.5	14.275	37	15.2%	-57.60 [-64.15 , -51.05]	+	?	+	+	+	?
Tenconi et al	-29.4	44.78	44	-3	73.38	39	9.9%	-26.40 [-52.96 , 0.16]	+	?	?	?	+	?
Wang et al	-147	55.04	34	-160	61.53	31	9.4%	13.00 [-15.49 , 41.49]	+	?	+	+	+	?
Yao et al	20	30	74	90	25	74	14.8%	-70.00 [-78.90 , -61.10]	?	?	+	?	+	?
Zou et al	-93.84	11.02	45	-52.5	8.71	45	15.5%	-41.34 [-45.44 , -37.24]	?	?	+	+	+	?
Total (Wald[a])			**396**			**392**	**100.0%**	**-32.56 [-46.35 , -18.76]**						

Test for overall effect: Z = 4.63 (P < 0.00001)
Test for subgroup differences: Not applicable
Heterogeneity: Tau² (DL[b]) = 314.50; Chi² = 101.32, df = 7 (P < 0.00001); I² = 93%

Footnotes
[a]CI calculated by Wald-type method.
[b]Tau² calculated by DerSimonian and Laird method.

Risk of bias legend
(A) Bias arising from the randomization process
(B) Bias due to deviations from intended interventions
(C) Bias due to missing outcome data
(D) Bias in measurement of the outcome
(E) Bias in selection of the reported result
(F) Overall bias

Change in FEV1 from baseline to post lung cancer surgery

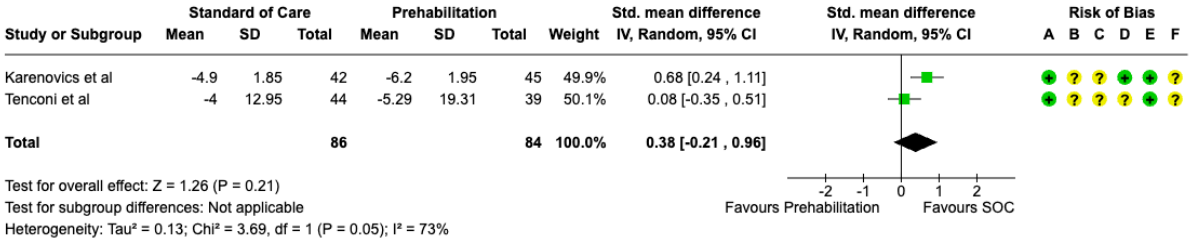


Study or Subgroup	Standard of Care Mean	SD	Total	Prehabilitation Mean	SD	Total	Weight	Mean difference IV, Random, 95% CI	Risk of Bias A	B	C	D	E	F
Chen et al	-0.01	0.053	109	0.02	0.046	109	31.8%	-0.03 [-0.04 , -0.02]	+	?	+	?	+	?
Liu et al	-0.5	0.5	36	-0.38	0.57	37	6.5%	-0.12 [-0.37 , 0.13]	+	?	+	?	+	?
Stefanelli et al	-0.309	0.02	20	-0.324	0.0224	20	31.8%	0.02 [0.00 , 0.03]	?	?	+	?	+	?
Zou et al	-0.88	0.068	45	-0.71	0.089	45	30.0%	-0.17 [-0.20 , -0.14]	?	?	+	+	+	?
Total			**210**			**211**	**100.0%**	**-0.06 [-0.13 , 0.01]**						

Test for overall effect: Z = 1.78 (P = 0.07)
Test for subgroup differences: Not applicable
Heterogeneity: Tau² = 0.00; Chi² = 110.73, df = 3 (P < 0.00001); I² = 97%

Risk of bias legend
(A) Bias arising from the randomization process
(B) Bias due to deviations from intended interventions
(C) Bias due to missing outcome data
(D) Bias in measurement of the outcome
(E) Bias in selection of the reported result
(F) Overall bias

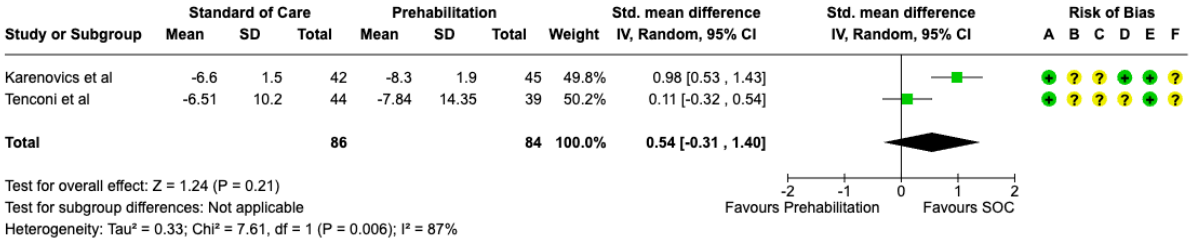
Change in FVC from baseline to post lung cancer surgery (6 months – 1 year following lung cancer surgery)



Test for overall effect: Z = 1.26 (P = 0.21)
Test for subgroup differences: Not applicable
Heterogeneity: Tau² = 0.13; Chi² = 3.69, df = 1 (P = 0.05); I² = 73%

Risk of bias legend
(A) Bias arising from the randomization process
(B) Bias due to deviations from intended interventions
(C) Bias due to missing outcome data
(D) Bias in measurement of the outcome
(E) Bias in selection of the reported result
(F) Overall bias

Change in FEV1 from baseline to post lung cancer surgery (6 months – 1 year post lung cancer surgery)



Test for overall effect: Z = 1.24 (P = 0.21)
Test for subgroup differences: Not applicable
Heterogeneity: Tau² = 0.33; Chi² = 7.61, df = 1 (P = 0.006); I² = 87%

Risk of bias legend
(A) Bias arising from the randomization process
(B) Bias due to deviations from intended interventions
(C) Bias due to missing outcome data
(D) Bias in measurement of the outcome
(E) Bias in selection of the reported result
(F) Overall bias

Evidence to Decision Framework

QUESTION

Should Prehabilitation vs. Standard of care be used for patients undergoing surgery for lung cancer?	
Population:	Patients planned for lung cancer surgery
Intervention:	Prehabilitation
Comparison:	Standard of care
Main outcomes:	Critical outcomes: 1. Perioperative outcomes 2. Mortality 3. Quality of life Important Outcomes 1. Length of hospital stay 2. Surgical complications 3. Functional recovery

ASSESSMENT

Problem
Is the problem a priority?

Judgement	Research evidence	Additional considerations
○ No ○ Probably no ○ Probably yes ● Yes ○ Varies ○ Don't know	Despite advances in surgical techniques, lung cancer surgery is associated with significant perioperative risks, including respiratory complications, reduced functional capacity, prolonged hospital stays, and decreased quality of life. As a result, preoperative optimization strategies have become increasingly important to improve surgical outcomes and recovery. Prehabilitation, a concept that focuses on enhancing a patient's physical and mental health before surgery, has emerged as a potential means to improve postoperative outcomes in lung cancer patients. Prehabilitation interventions can include physical exercise, nutritional support, breathing exercises, and psychological counselling (singly or in combination), aimed at preparing the patient for the physiological stress of surgery. and improving peri-operative outcomes.	No additional considerations.
Desirable Effects How substantial are the desirable anticipated effects?		
Judgement	Research evidence	Additional considerations
○ Trivial ○ Small ● Moderate ○ Large ○ Varies ○ Don't know	There appears to be a beneficial effect of prehabilitation in reducing pulmonary complications, with a risk reduction of approximately 16%, though the certainty of evidence is low. It appears that prehabilitation is associated with a decrease in hospital stay, with a mean reduction of approximately one day, but the clinical relevance of this difference remains uncertain. There is a trend towards a reduction in postoperative mortality following lung cancer surgery with prehabilitation; however, the observed difference is not statistically significant.	The panel acknowledged the moderate beneficial effects of prehabilitation across multiple patient-important outcomes. They specifically noted that while the overall magnitude of benefit may vary the consistent direction of effect toward improved outcomes supports its value as a

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)
	Risk with Standard of Care	Risk with Prehabilitation			
Pulmonary Complications	28.6% (232/812)	13.9% (118/846)	**RD -0.16** (-0.21 to -0.11)	1658 (19 RCTs)	⨁⨁◯◯ Low
Hospital stay after lung cancer surgery	The mean hospital stay 8.27 days	The mean hospital stay 7.41 days	MD **0.86 lower** (1.63 lower to 0.08 lower)	1620 (20 RCTs)	⨁◯◯◯ Very low
Mortality following lung cancer surgery	1.85% (10 per 543)	0.88% (5 per 569)	**RD -0.04** (-0.07 to 0.00)	1112 (14 RCTs)	⨁◯◯◯ Very low

Quality of life: Prehabilitation may lead to improved postoperative quality of life (QoL) outcomes across various measurement tools.

perioperative strategy. The panel discussed the interpretation of effect sizes in relation to minimum important differences (MIDs) and concluded that for the outcomes reported, the effect sizes were either above or approaching the MID for most parameters.

Study	QoL Tool Used	Key Findings	Conclusion
Chen et al.	EQ-5D	Better general health status in Prehab group; significant improvements in mobility (p=0.002), self-care (p<0.001), activity (p=0.002), pain (p<0.001), anxiety (p=0.05), and overall QoL (p=0.01).	Prehabilitation improved overall health across multiple domains, supporting its role in maintaining function post-surgery.
Ferreira et al.	SF-36 & FACT-L	Higher general health (p=0.007) and mental health (p=0.044) scores in Prehab group; FACT-L Total Score (105.6 vs. 101.3, p=0.17) and Lung Cancer Subscale (21 vs. 20.2, p=0.35) were also higher.	Prehabilitation improved general and mental health, though some differences were not statistically significant.
Garcia et al.	SF-36	Better physical function recovery in Prehab group; mean reduction in physical score was smaller (-2.8 vs. -7.4 post-surgery). At 3 months, physical function improved (+4.3 in Prehab) while it declined (-4.8) in SOC (p<0.001).	Prehabilitation enhanced physical function recovery and maintained improvements at 3 months post-surgery.
Machado et al.	EORTC QLQ-C30	Better QLQ-C30 scores at 4 weeks post-surgery (mean difference: 12.4 points, p=0.029). Lower deterioration rates in physical (p=0.004), role (p=0.006), and social function (p=0.043). Improved fatigue (p=0.047), pain (p=0.041), and appetite loss (p=0.024).	Prehabilitation led to lower deterioration in physical, role, and social function, with improved symptom burden.

Undesirable Effects

How substantial are the undesirable anticipated effects?

Judgement	Research evidence	Additional considerations
● Trivial ○ Small ○ Moderate ○ Large ○ Varies ○ Don't know	Prehabilitation was generally safe and well tolerated across included studies. Most trials did not report any adverse events. However, a few studies documented minor, self-limiting effects attributable to the intervention. None of the studies reported serious or life-threatening intervention-related complications. A total of 15 studies (840 participants) reported regarding the adverse events. Among these, 11 studies reported no adverse effects. 4 studies mentioned minor, self-limiting effects. Machado et al. systematically reported Grade 1 adverse events in 30% of participants, primarily leg muscle soreness. Zhou et al. noted fatigue in 6 patients, dizziness in 2, and nausea in 1 during exercise sessions — all resolved with rest and without serious consequences. Han et al. reported dropouts due to acute exacerbation of COPD and knee pain, and Lai et al. (2016) noted withdrawals related to intensity intolerance and musculoskeletal discomfort. Lai et al. (2017) also reported dropouts due to perceived lack of benefit or inability to tolerate the program.	The panel discussed the safety profile of prehabilitation and agreed that the reported adverse events were minor. They concluded that the intervention does not raise safety concerns significant enough to limit its use, particularly given the observed clinical benefits.
Certainty of evidence What is the overall certainty of the evidence of effects?		
Judgement	Research evidence	Additional considerations

● Very low ○ Low ○ Moderate ○ High ○ No included studies	The certainty of the evidence is very low due to high risk of bias, inconsistency and imprecision in the reported studies.	No additional considerations.
Values Is there important uncertainty about or variability in how much people value the main outcomes?		
Judgement	Research evidence	Additional considerations
○ Important uncertainty or variability ○ Possibly important uncertainty or variability ○ Probably no important uncertainty or variability ● No important uncertainty or variability	1. overall survival (36 out of 40) 90%, postoperative complications (92.5%), and Health-related quality of life factors, (77.5%) were highly valued by patients who underwent lung surgery (Wong MSH, Pons A, De Sousa P, Proli C, Jordan S, Begum S, Buderi S, Lim E. Assessing patient perception and preferences for outcomes in lung cancer resection surgery: a cross-sectional study. J Thorac Dis. 2024 Jun 30;16(6):3844-3853) 2. For participants with early-stage lung cancer, maintaining independence and QOL were more highly valued than survival or cancer recurrence. (Sullivan DR, Eden KB, Dieckmann NF, Golden SE, Vranas KC, Nugent SM, Slatore CG. Understanding patients' values and preferences regarding early-stage lung cancer treatment decision-making. Lung Cancer. 2019;131:47-57.)	Critical outcomes: Perioperative outcomes., Mortality and QoL are valued highly by patients undergoing lung cancer surgery. The panel discussed that patient and caregiver preferences may influence how the benefits of prehabilitation are perceived. However, no major uncertainty was identified in the value assigned to critical

		outcomes. The group also discussed the lack of standardized prehabilitation protocols and how this might affect patient expectations, but did not consider it to introduce significant variability in values. An illustrative case discussed patient experience: a patient diagnosed with early-stage lung cancer during routine screening who underwent surgery without prehabilitation but received intensive postoperative rehabilitation. His relapse within a year and subsequent choice of alternate treatment were highlighted to reflect individual patient perspectives and reinforce the importance of preoperative optimization.

Balance of effects Does the balance between desirable and undesirable effects favor the intervention or the comparison?		
Judgement	Research evidence	Additional considerations
○ Favors the comparison ○ Probably favors the comparison ○ Does not favor either the intervention or the comparison ○ Probably favors the intervention ● Favors the intervention ○ Varies ○ Don't know	The balance of effects favours prehabilitation over standard care. The strongest benefits are seen in reducing pulmonary complications (16% absolute reduction in prehabilitation as compared to SOC) and improving postoperative QoL, with a trend towards reducing mortality and hospital stay.	The panel discussed that the benefits clearly outweigh harms: Strong evidence supports a reduction in pulmonary complications and improved QoL. The balance of effects favours prehabilitation over standard care, as the desirable effects outweigh the undesirable effect. However, the magnitude of effect is debatable.
Resources required		
Judgement	Research evidence	Additional considerations

○ Large costs ○ Moderate costs ○ Negligible costs and savings ○ Moderate savings ○ Large savings ● Varies ○ Don't know	As per the systematic review which included 45 studies that evaluated the cost-effectiveness of prehabilitation for patients awaiting elective surgery. Among 45 studies included in the systematic review, 6 articles are on lung cancer patients undergoing surgery. The resource requirements for prehabilitation include multidisciplinary interventions such as physiotherapy, nutritional support, psychological counseling, and respiratory therapy, the cost of prehabilitation programs varies widely, depending on the intensity and setting of the intervention. For example: Exercise-based prehabilitation programs: Costs range from $200 to $1,500 per patient, depending on duration and frequency. Nutritional support: Costs typically range from $50 to $500 per patient, including dietary consultations and supplements. Psychological interventions: Cognitive-behavioral therapy (CBT) or counseling services may add $100 to $800 per patient. Respiratory therapy (e.g., inspiratory muscle training): Costs range from $100 to $600 per patient. These costs can vary significantly based on whether prehabilitation is delivered in-person, remotely, or as a hybrid model. However, the initial investment in these services may be offset by reduced postoperative complications and hospital resource utilization. Ref: Rombey T et al. Cost effectiveness of prehabilitation prior to elective surgery: a systematic review of economic evaluations. BMC Medicine (2023) 21: 265	The resource requirements for prehabilitation appear to be high but vary depending on the type and intensity of the program. While structured prehabilitation programs may require additional costs for physiotherapy, nutritional support, and psychological counselling, these costs may potentially be offset by potential reductions in postoperative complications, ICU admissions, and hospital stay (although there is no data to make firm conclusions). The GDG discussed that resource requirements for prehabilitation would vary substantially across contexts. They emphasized the need to contextualize costs

		based on GDP and healthcare expenditure in low- and middle-income countries (LMICs), including India. Components of cost—such as personnel, program duration, delivery modality (inpatient, outpatient, or home-based), and facility type (public vs. private)—should be carefully considered. The panel noted that introducing prehabilitation universally could entail significant system-wide costs and recommended assessing average costs for each component in local settings before large-scale adoption. Cost components of intervention is required. The average costs of the different components should be considered for decision making.

		GDP comparison for different countries could be helpful for contextualization. Validity of all the components of interventions fitting the Indian context to be considered Setting like Private/Public Sector. How much cost would rehabilitation add if recommended for all/majority of patients. Factors considered for Variation in resources – Level of healthcare facility Private/Government Setting Type of healthcare provider Intervention package.
Certainty of evidence of required resources		

What is the certainty of the evidence of resource requirements (costs)?		
Judgement	Research evidence	Additional considerations
● Very low ○ Low ○ Moderate ○ High ○ No included studies		The certainty of evidence regarding the resource requirements for prehabilitation is low, as cost-effectiveness analyses in lung cancer patients are limited from LMICs and vary across healthcare settings. While prehabilitation may reduce hospital costs by lowering complication rates and shortening ICU stays, the initial costs of implementing structured prehabilitation programs remain uncertain.
Cost effectiveness Does the cost-effectiveness of the intervention favor the intervention or the comparison?		
Judgement	Research evidence	Additional considerations

○ Favors the comparison ○ Probably favors the comparison ○ Does not favor either the intervention or the comparison ○ Probably favors the intervention ● Favors the intervention ○ Varies ○ No included studies	Among 45 studies included in the systematic review, 4 articles are on lung cancer patients undergoing surgery. Three out of 4 studies reported that prehabilitation was cost effective intervention (Lai et al.,2017, Lai et al., 2019 and Zhou et al 2017). One study (Gao et al 2015 reported as unclear, ICER was not applicable for CCA) Ref: Rombey T et al. Cost effectiveness of prehabilitation prior to elective surgery: a systematic review of economic evaluations. BMC Medicine (2023) 21: 265	Incremental cost/unit benefit - Purist Perspective For every unit benefit of rehabilitation, what would be the cost to be added Other perspective – Added cost per unit of benefit is unknown but the benefit is shown effective cost wise as per existing literature. While the intervention appears cost-effective overall, the lack of detailed economic modeling in LMIC settings was noted.
Equity What would be the impact on health equity?		
Judgement	Research evidence	Additional considerations

○ Reduced ○ Probably reduced ○ Probably no impact ● Probably increased ○ Increased ○ Varies ○ Don't know	No direct research evidence was identified	Prehabilitation has the potential to reduce health disparities by improving perioperative outcomes in vulnerable populations, such as older adults, patients with comorbidities, and those with limited access to postoperative rehabilitation. Ensuring access to the prehabilitation services to all patients undergoing lung cancer surgery could enhance its impact on health equity. While acknowledging potential barriers, the GDG concluded that prehabilitation is more likely to increase health equity overall. This judgement is based on the intervention's potential to positively impact vulnerable and disadvantaged groups, particularly:

		Older adults, patients with comorbidities, and those borderline fit for surgery, who often have poorer surgical outcomes and limited postoperative rehabilitation access. By enhancing perioperative fitness and potentially improving recovery, prehabilitation could help these patients access curative surgery more safely, thereby reducing disparities in surgical outcomes.
Acceptability Is the intervention acceptable to key interest-holders?		
Judgement	Research evidence	Additional considerations
○ No ○ Probably no ○ Probably yes ● Yes ○ Varies	There is no direct evidence available in the Indian context. Based on Powell et al. (2023), Patients who engaged in prehabilitation found it beneficial, particularly in enhancing recovery post-surgery, while clinicians largely viewed it as a valuable	The panel discussed that acceptability is a cross-cultural belief. However, it would take a lot of effort to exercise all the components of the

○ Don't know	and appropriate intervention. However, barriers to uptake included feeling overwhelmed at diagnosis, logistical challenges (e.g., transport, time constraints), and lack of awareness of its benefits. A supportive, flexible approach tailored to individual needs was key to acceptability, rather than a directive or mandatory approach. Prehabilitation may be generally acceptable to patients who perceive tangible functional benefits and minimal disruption to their treatment timeline. Ref: Powell, R., Davies, A., Rowlinson-Groves, K. et al. Acceptability of prehabilitation for cancer surgery: a multi-perspective qualitative investigation of patient and 'clinician' experiences. BMC Cancer 23, 744 (2023).	intervention across the nation.
Feasibility Is the intervention feasible to implement?		
Judgement	Research evidence	Additional considerations
○ No ○ Probably no ○ Probably yes ● Yes ○ Varies ○ Don't know	There is no direct evidence from India. In the UK, prehabilitation is feasible as demonstrated by the Prehab4Cancer (P4C) program in Greater Manchester, UK. The program successfully integrated multimodal prehabilitation (exercise, nutrition, and psychological support) into routine lung cancer care across 11 hospitals, with 80% of patients attending the initial assessment and 48% completing the program.	The panel suggested that it would be more feasible to consider prehabilitation over increasing the overall quality of the treatment process (surgery).

	Statistically significant improvements in functional capacity and quality of life were observed preoperatively. (Mean increase in the incremental shuttle walk test of 50 m) Ref: Bradley P, Merchant Z, Rowlinson-Groves K, Taylor M, Moore J, Evison M. Feasibility and outcomes of a real-world regional lung cancer prehabilitation programme in the UK. Br J Anaesth. 2023 Jan;130(1):e47-e55.	

Summary of Judgements	**JUDGEMENT**						
PROBLEM	No	Probably no	Probably yes	**Yes**		Varies	Don't know
DESIRABLE EFFECTS	Trivial	Small	**Moderate**	Large		Varies	Don't know
UNDESIRABLE EFFECTS	**Trivial**	Small	Moderate	Large		Varies	Don't know
CERTAINTY OF EVIDENCE	**Very low**	Low	Moderate	High			No included studies
VALUES	Important uncertainty or variability	Possibly important uncertainty or variability	Probably no important uncertainty or variability	**No important uncertainty or variability**			
BALANCE OF EFFECTS	Favors the comparison	Probably favors the comparison	Does not favor either the intervention or the comparison	Probably favors the intervention	**Favors the intervention**	Varies	Don't know

Summary of Judgements	JUDGEMENT						
RESOURCES REQUIRED	Large costs	Moderate costs	Negligible costs and savings	Moderate savings	Large savings	**Varies**	Don't know
CERTAINTY OF EVIDENCE OF REQUIRED RESOURCES	**Very low**	Low	Moderate	High			No included studies
COST EFFECTIVENESS	Favors the comparison	Probably favors the comparison	Does not favor either the intervention or the comparison	Probably favors the intervention	**Favors the intervention**	Varies	No included studies
EQUITY	Reduced	Probably reduced	Probably no impact	**Probably increased**	Increased	Varies	Don't know
ACCEPTABILITY	No	Probably no	Probably yes	**Yes**		Varies	Don't know
FEASIBILITY	No	Probably no	Probably yes	**Yes**		Varies	Don't know

Type of recommendation

Strong recommendation against the intervention	Conditional recommendation against the intervention	Conditional recommendation for either the intervention or the comparison	Conditional recommendation for the intervention	**Strong recommendation for the intervention**
○	○	○	○	●

Conclusions

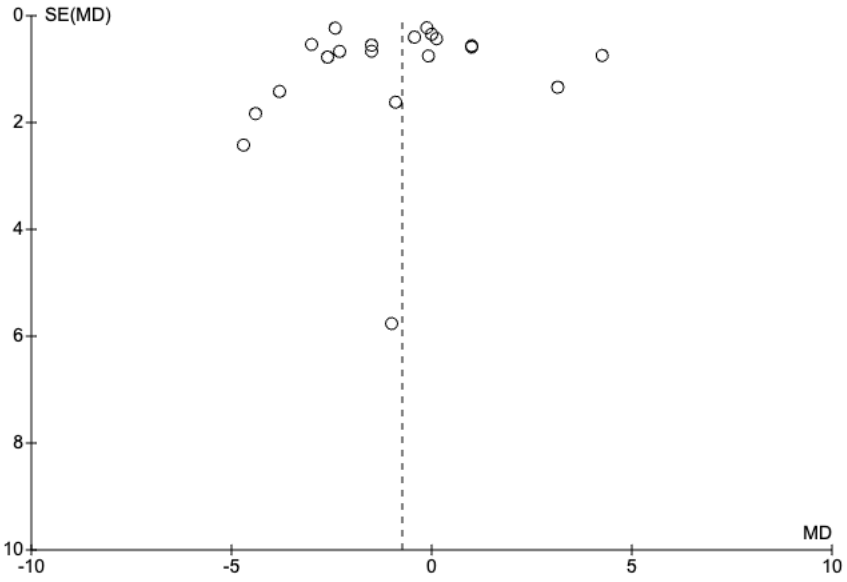
Recommendation
Prehabilitation is ***recommended*** for patients planned to undergo lung cancer surgery. **Strength:** Strong **Certainty of Evidence**: Very low
Justification
The evidence showed moderate desirable effects with trivial harms, alongside cost-effectiveness favouring the prehabilitation, increased equity, acceptability, and feasibility supporting a strong recommendation despite very low certainty of evidence.

Publication Bias

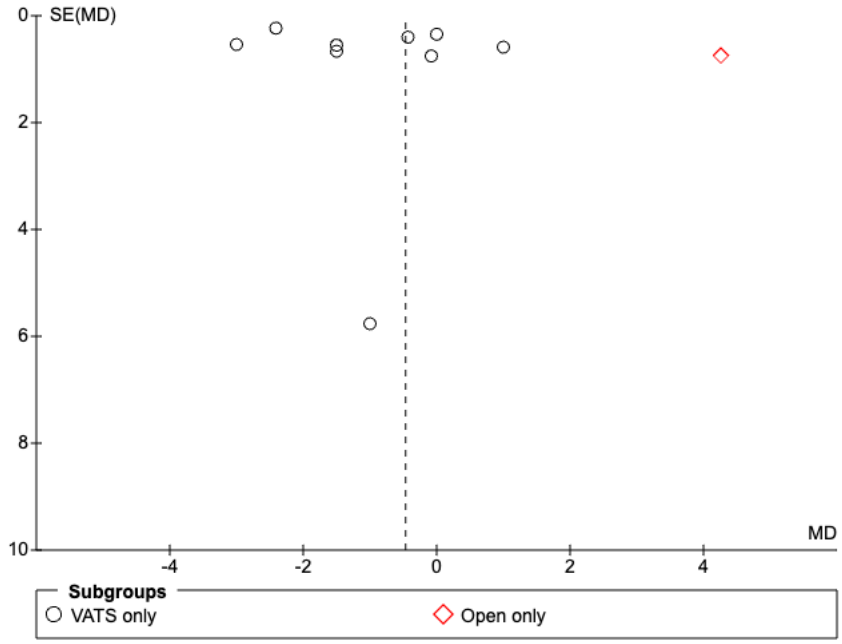
Funnel plots were examined for 26 outcomes, including mortality, hospital stay, ICU stay, pulmonary complications, respiratory failure, quality of life domains, and functional outcomes such as the 6-minute walk distance. In several analyses—such as those for hospital stay, Hospital stay, pneumonia, and pulmonary complication—more than 10 studies contributed data, permitting a reasonably informative visual inspection. In these plots, the distribution of studies appeared broadly symmetric around the pooled effect estimate, without substantial clustering on one side. This suggests a low likelihood of small-study effects or directional publication bias in these key outcomes.

In most other funnel plots, fewer than 10 studies contributed data, limiting the interpretability of asymmetry. Nevertheless, these plots were examined visually and did not display strong patterns of skew or evidence of missing studies. While some scatter and mild asymmetry were observed in a few outcomes, no consistent or directional pattern indicative of publication bias was identified. Taken together, the visual inspection of funnel plots across all outcomes does not suggest any compelling evidence of publication bias, although the limited number of studies in many comparisons warrants cautious interpretation.

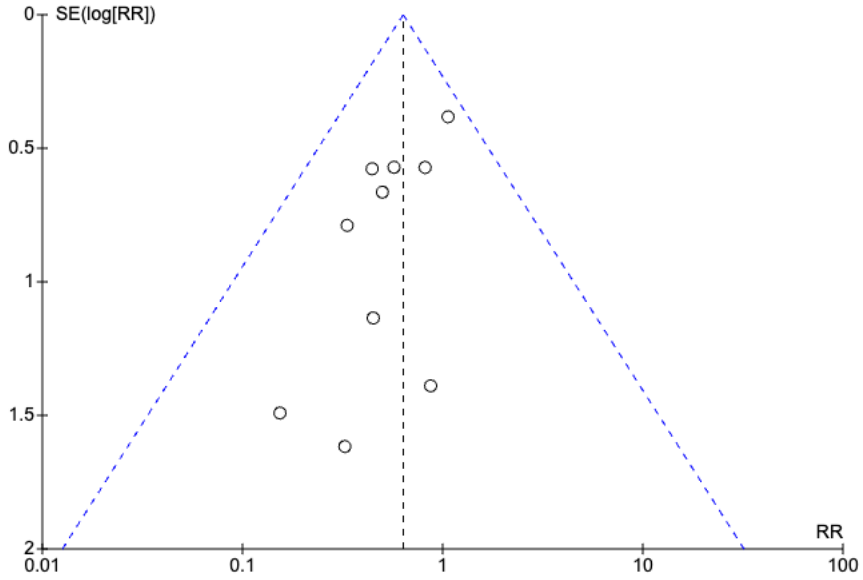
8.1: Funnel plot (Hospital stay after lung cancer surgery)



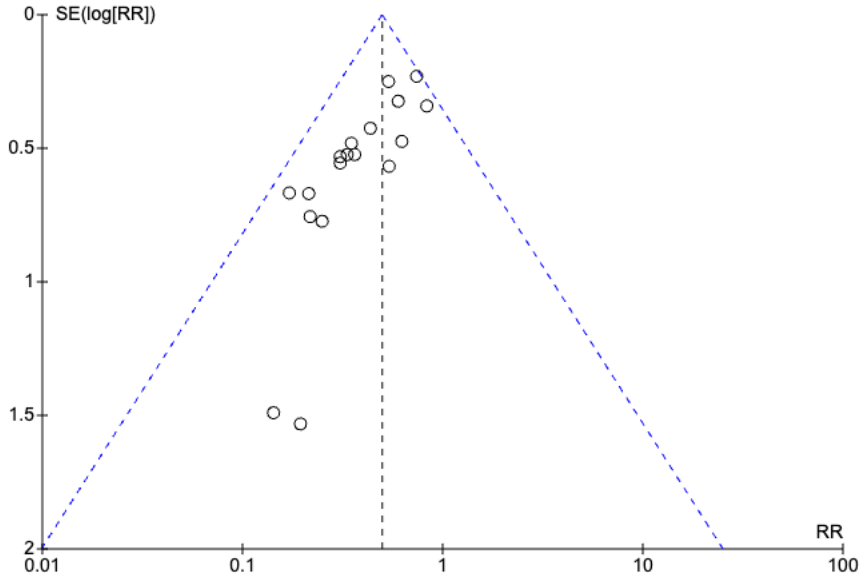
8.2: Funnel plot (Hospital stay after lung cancer surgery in studies that included VATS only and open surgery only)



8.3: Funnel plot (Pneumonia)



8.4: Funnel plot (Pulmonary Complications)



List of Excluded Studies

S.No.	Study	Reason of exclusion
1	Abdelaziz M, Bradley A, Agostini P, Jordan C, Reaper L, Gillies J, Stonehewer L, Naidu B. 77 A multidisciplinary complex perioperative intervention to reduce complications and enhance recovery after lung resection surgery. Lung Cancer. 2011(71):S26.	Case series
2	Abdelaziz M.Z., Bradley A., Agostini P., Bishay E., Steyn R.S., Kalkat M.S., et al. A pre and postoperative rehabilitation programme for lung resection surgery reduces post operative complications and hospital readmission rates. Interact Cardiovasc Thorac Surg. 2011;13(SUPPL. 1):S40.	Case series
3	Aghajaanpour R, Sponholz S, Trainer S. Exercise capacity of cancer patients after thoracic surgery Perioperative factors crucial for rehabilitation. ONKOLOGE. 2022 Mar 1;28(3):193-202.	Case series
4	Andersen AH, Vinther A, Poulsen LL, Mellemgaard A. Do patients with lung cancer benefit from physical exercise?. Acta oncologica. 2011 Feb 1;50(2):307-13.	Case series
5	Bibo L, Goldblatt J, Merry C. Does preoperative pulmonary rehabilitation/physiotherapy improve patient outcomes following lung resection?. Interactive CardioVascular and Thoracic Surgery. 2021 Jun 1;32(6):933-7.	Case series
6	Billé A, Buxton J, Viviano A, Gammon D, Veres L, Routledge T, Harrison-Phipps K, Dixon A, Minetto MA. Preoperative physical activity predicts surgical outcomes following lung cancer resection. Integrative cancer therapies. 2021 Mar;20:1534735420975853.	Case series
7	Bobbio A, Chetta A, Ampollini L, Primomo GL, Internullo E, Carbognani P, Rusca M, Olivieri D. Preoperative pulmonary rehabilitation in patients undergoing lung resection for non-small cell lung cancer. European journal of cardio-thoracic surgery. 2008 Jan 1;33(1):95-8.	Case series
8	Boujibar F, Bonnevie T, Debeaumont D, Bubenheim M, Cuvellier A, Peillon C, Gravier FE, Baste JM. Impact of prehabilitation on morbidity and mortality after pulmonary lobectomy by minimally invasive surgery: a cohort study. Journal of thoracic disease. 2018 Apr;10(4):2240.	Case series
9	Boujibar F, Bonnevie T, Debeaumont D, Bubenheim M, Cuvellier A, Peillon C, Gravier FE, Baste JM. Impact of prehabilitation on morbidity and mortality after pulmonary lobectomy by minimally invasive surgery: a cohort study. Journal of thoracic disease. 2018 Apr;10(4):2240.	Case series

10	Bradley A, Marshall A, Stonehewer L, Reaper L, Parker K, Bevan-Smith E, Jordan C, Gillies J, Agostini P, Bishay E, Kalkat M. Pulmonary rehabilitation programme for patients undergoing curative lung cancer surgery. European Journal of Cardio-Thoracic Surgery. 2013 Oct 1;44(4):e266-71.	Case series
11	Bradley A, Marshall A, Stonehewer L, Reaper L, Parker K, Bevan-Smith E, Jordan C, Gillies J, Agostini P, Bishay E, Kalkat M. Pulmonary rehabilitation programme for patients undergoing curative lung cancer surgery. European Journal of Cardio-Thoracic Surgery. 2013 Oct 1;44(4):e266-71.	Case series
12	Bradley A, Marshall A, Stonehewer L, Reaper L, Parker K, Bevan-Smith E, Jordan C, Gillies J, Agostini P, Bishay E, Kalkat M. Pulmonary rehabilitation programme for patients undergoing curative lung cancer surgery. European Journal of Cardio-Thoracic Surgery. 2013 Oct 1;44(4):e266-71.	Case series
13	Fair S, Taylor M. Personalised prehabilitation improves functional capacity and strength in patients awaiting major surgery. Physiotherapy. 2024 Jun 1;123:e105-6.	Case series
14	Finch A, Assadourian A, Grant D, Redman J, Jalali S, Ricketts W. Impact of prehabilitation on pre-operative function, post-operative complications and length of stay in resectable lung cancers. Lung Cancer. 2023 Apr 1;178:S82-3.	Case series
15	Funatsu K, Matsugaki R, Imamura H, Takenaka M, Tanaka F, Fushimi K, Matsuda S, Saeki S. Association of preoperative rehabilitation with postoperative length of hospital stay for elderly lung cancer patients. Journal of UOEH. 2023 Sep 1;45(3):155-60.	Case series
16	Goldsmith I, Chesterfield-Thomas G, Toghill H. Pre-treatment optimisation with pulmonary rehabilitation of elderly lung cancer patients with frailty for surgery. Journal of Cardiothoracic Surgery. 2023 Dec 8;18(1):356.	Case series
17	Goldsmith I, Chesterfield-Thomas G, Toghill H. Pre-treatment optimization with pulmonary rehabilitation in lung cancer: making the inoperable patients operable. EClinicalMedicine. 2021 Jan 1;31.	Case series
18	Gravier FE, Bonnevie T, Boujibar F, Médrinal C, Prieur G, Combret Y, Muir JF, Cuvelier A, Baste JM, Debeaumont D. Effect of prehabilitation on ventilatory efficiency in non–small cell lung cancer patients: A cohort study. The Journal of thoracic and cardiovascular surgery. 2019 Jun 1;157(6):2504-12.	Case series
19	Gupta P, Deo S, Ray MD, Kumar S, Khan MA, Bhatnagar S, Mishra S. A prospective study evaluating perioperative quality metrics of cancer surgery: Experience from a tertiary care cancer centre in India. Journal of Surgical Oncology. 2023 Aug;128(2):385-92.	Case series

20	Handy Jr JR, Asaph JW, Skokan L, Reed CE, Koh S, Brooks G, Douville EC, Tsen AC, Ott GY, Silvestri GA. What happens to patients undergoing lung cancer surgery?: Outcomes and quality of life before and after surgery. Chest. 2002 Jul 1;122(1):21-30.	Case series
21	Hashmi A, Baciewicz Jr FA, Soubani AO, Gadgeel SM. Preoperative pulmonary rehabilitation for marginal-function lung cancer patients. Asian Cardiovascular and Thoracic Annals. 2017 Jan;25(1):47-51.	Case series
22	He L. The influence of preoperative pulmonary rehabilitation training on the prognosis of lung cancer patients with chronic obstructive pulmonary disease. Chinese Journal of the Frontiers of Medical Science. 2018;10(4):106-9.	Case series
23	Korstjens I, May AM, van Weert E, Mesters I, Tan F, Ros WJ, Hoekstra-Weebers JE, van der Schans CP, van den Borne B. Quality of life after self-management cancer rehabilitation: a randomized controlled trial comparing physical and cognitive-behavioral training versus physical training. Psychosomatic Medicine. 2008 May 1;70(4):422-9.	Case series
24	Li L, Tao LD. EP10. 01-002 The Effect of Group Rehabilitation Training in the Ward on the Psychological Status and Quality of Life of Lung Cancer Patients. Journal of Thoracic Oncology. 2022 Sep 1;17(9):S500-1.	Case series
25	Marhic A, Dakhil B, Plantefeve G, Zaimi R, Oltean V, Bagan P. Long-term survival following lung surgery for cancer in high-risk patients after perioperative pulmonary rehabilitation. Interactive cardiovascular and thoracic surgery. 2019 Feb;28(2):235-9.	Case series
26	Minnella EM, Baldini G, Le Quang AT, Bessissow A, Spicer J, Carli F. Prehabilitation in thoracic cancer surgery: from research to standard of care. Journal of Cardiothoracic and Vascular Anesthesia. 2021 Nov 1;35(11):3255-64.	Case series
27	Misumi K, Harada H, Yamashita Y, Nakano J, Matsutani J, Yamasaki M, Ohakawachi T, Taniyama K. Comprehensive preoperative pulmonary rehabilitation including intensive nutrition support for lung cancer patients. Chest. 2012 Oct 1;142(4):37A.	Case series
28	Nakao J, Harada H, Handa Y, Tsubokawa N, Yamashita Y. Clinical benefit of comprehensive preoperative pulmonary rehabilitation including intensive nutritional support for the elderly, low body weight, lung cancer patients. InRespirology 2015 Dec 1 (Vol. 20, pp. 64-64). 111 RIVER ST, HOBOKEN 07030-5774, NJ USA: WILEY-BLACKWELL.	Case series
29	Palmer E, Brower A, Geytenbeek M, Quirke E. 113 Optimising physical performance and improving treatment tolerance in a lung cancer patient with comorbidities: a case study of allied health	Case series

	intervention across the phases of rehabilitation. Lung Cancer. 2024 Apr 1;190:107674.	
30	Parsons A, Bradley A, Reaper L, Jordan C, Paul A, Dowswell G, Dunn J, Naidu B. 195 Patient's experiences of a pre and post surgery rehabilitation programme for lung cancer (Rehabilitation Of lung Cancer (ROC) programme): a qualitative interview study. Lung Cancer. 2012(75):S64.	Case series
31	Pedziwiatr M, Kisialeuski M, Wierdak M, Stanek M, Natkaniec M, Matlok M, Major P, Malczak P, Budzynski A. Early implementation of Enhanced Recovery After Surgery (ERAS (R)) protocol-Compliance improves outcomes: A prospective cohort study. Int J Surg. 2015 Sep 1;21(7):75-81.	Case series
32	Pengfei LI, Yutian LA, Kun ZH, Jianhua SU, Guowei CH. Can Perioperative Oscillating Positive Expiratory Pressure Practice Enhance Recovery in Lung Cancer Patients Undergoing Thorascopic Lobectomy?. Chinese Journal of Lung Cancer. 2018 Dec 20;21(12).	Case series
33	Qingtong SH, Yali DI, Jun QI. Application of Single-hole Thoracoscopic Surgery Combined with ERAS Concept for Respiratory Function Exercise in Perioperative Period of Lung Cancer. Chinese Journal of Lung Cancer. 2020 Aug 1;23(8).	Case series
34	Risco R, González-Colom R, Montané-Muntané M, Cano I, Vela E, Sebio R, Dana F, Faner J, Coca M, Laxe S, Roca J. Actionable factors fostering health value generation and scalability of prehabilitation: a prospective cohort study. Annals of Surgery. 2023 Aug 1;278(2):e217-25.	Case series
35	Shukla A, Wright G, Denehy L, Granger C. Prehabilitation for Individuals Having Lung Cancer Surgery. Heart, Lung and Circulation. 2019 Jan 1;28:S73-4.	Case series
36	Su XE, Wu SH, He HF, Lin CL, Lin S, Weng PQ. The effect of multimodal care based on Peplau's interpersonal relationship theory on postoperative recovery in lung cancer surgery: a retrospective analysis. BMC Pulmonary Medicine. 2024 Jan 27;24(1):59.	Case series
37	Ten Cate DW, van den Berg R, Scholten-Bakker M, Molenaar CJ, von Meyenfeldt EM, Slooter GD, van den Broek FJ, Marres GM. Multimodal prehabilitation in patients with non-small cell lung cancer: a feasibility study. Journal of Thoracic Disease. 2024 May 5;16(5):2776.	Case series
38	Yusen RD, Lefrak SS, Gierada DS, Davis GE, Meyers BF, Patterson GA, Cooper JD. A prospective evaluation of lung volume reduction surgery in 200 consecutive patients. Chest. 2003 Apr 1;123(4):1026-37.	Case series

39	Zhang H, Zhao Y. Influence of preoperative rehabilitation exercise training on pulmonary rehabilitation of elderly lung cancer patients complicated with moderate COPD. Chinese Nursing Research. 2014;28(5):1625-6.	Case series
40	Agostini P, Lugg S, Adams K, Smith T, Kalkat M, Rajesh P, Steyn R, Naidu B, Rushton A, Bishay E. MA 08.09 Postoperative Mobilization and Rehabilitation Requirements for Lung Cancer Patients Undergoing Minimally Invasive Surgery. Journal of Thoracic Oncology. 2017 Nov 1;12(11):S1833-4.	Conference abstract
41	Fouladbakhsh J., Yarandi H., Davis J. A randomized controlled trial examining the effect of a standardized yoga intervention on breathing, mood, sleep and quality of life of no-small cell lung cancer patients. J Altern Complement Med. 2016;22(6):A75–6.	Conference abstract
42	Hsiao WL. Testing efficacy of a pulmonary rehabilitation program for post lung cancer resection surgery. InJOURNAL OF THORACIC ONCOLOGY 2017 Nov 1 (Vol. 12, No. 11, pp. S2023-S2023). STE 800, 230 PARK AVE, NEW YORK, NY 10169 USA: ELSEVIER SCIENCE INC.	Conference abstract
43	Kerr A, Oswald N, Webb J, Kadiri S, Bancroft H, Taylor J, Rajesh P, Steyn R, Kalkat M, Bishay E, Naidu B. Outcome of Pilot RCT in Lung Cancer Surgery Patients Receiving Either Preop Carbohydrate & Postop Nutritional Drinks or Water. InJOURNAL OF THORACIC ONCOLOGY 2017 Nov 1 (Vol. 12, No. 11, pp. S2022-S2022). STE 800, 230 PARK AVE, NEW YORK, NY 10169 USA: ELSEVIER SCIENCE INC.	Conference abstract
44	Lee L, Chasen M, Carli F, Mayo N, MacDonald N, Mulder DS, Ferri LE. The impact of a pre-operative multidisciplinary program on improving nutritional reserve and exercise capacity in lung cancer patients. InC102. LUNG CANCER: RECENT ADVANCES IN STAGING, DIAGNOSIS, AND SURGICAL INTERVENTION 2011 May (pp. A5392-A5392). American Thoracic Society.	Conference abstract
45	Patel Y, Churchill I, Sullivan K, Beauchamp M, Wald J, Mbuagbaw L, Agzarian J, Shargall Y, Finley C, Fahim C, Hanna W. Move For Surgery, a novel preconditioning program to optimize health before thoracic surgery: a randomized controlled trial. Canadian Journal of Surgery. 2021 Dec 1;64:S107-.	Conference abstract
46	Pereira ED, Morano MT, Araujo A, Nascimento F, Pinheiro G, Mesquita R, Pinto J, Morais Filho O. Preoperative pulmonary rehabilitation versus chest physical therapy in patients undergoing lung cancer resection: a pilot randomized clinical trial. InC107. PULMONARY REHABILITATION: ORGANIZATION AND OUTCOMES 2013 May (pp. A5119-A5119). American Thoracic Society.	Conference abstract

47	Ray AD, Mador MJ, Wendel E, Lane J, Attwood K, Dexter E, Hennon M, Hong CC, Yendamuri S. Respiratory Muscle Training Prior to Lung Resection Surgery Improves Post-Operative Fatigue and Quality of Life. In2024 Combined Sections Meeting (CSM) 2024 Feb 16. APTA.	Conference abstract
48	Ferreira V, Lawson C, Carli F, Scheede-Bergdahl C, Chevalier S. Feasibility of a novel mixed-nutrient supplement in a multimodal prehabilitation intervention for lung cancer patients awaiting surgery: A randomized controlled pilot trial. International Journal of Surgery. 2021 Sep 1;93:106079.	Feasibility study
49	Lawson C, Ferreira V, Carli F, Chevalier S. Effects of multimodal prehabilitation on muscle size, myosteatosis, and dietary intake of surgical patients with lung cancer—a randomized feasibility study. Applied Physiology, Nutrition, and Metabolism. 2021;46(11):1407-16.	Feasibility study
50	Ricketts WM, Bollard K, Streets E, Hutton K, Hornby C, Lau K. Feasibility of setting up a pre-operative optimisation 'pre-hab'service for lung cancer surgery in the UK. Perioperative Medicine. 2020 May 13;9(1):14.	Feasibility study
51	Ansari BM, Hogan MP, Collier TJ, Baddeley RA, Scarci M, Coonar AS, Bottrill FE, Martinez GC, Klein AA. A randomized controlled trial of high-flow nasal oxygen (Optiflow) as part of an enhanced recovery program after lung resection surgery. The Annals of thoracic surgery. 2016 Feb 1;101(2):459-64.	No prehabilitation
52	Barassi G, Bellomo RG, Di Iulio A, Lococo A, Porreca A, Di Felice PA, Saggini R. Preoperative rehabilitation in lung cancer patients: yoga approach. Rehabilitation Science in Context. 2018:19-29.	No surgery
53	Bhatia C, Kayser B. Preoperative high-intensity interval training is effective and safe in deconditioned patients with lung cancer: A randomized clinical trial. Journal of rehabilitation medicine. 2019 Oct 3;51(9):712-8.	No surgery
54	Ferreira V, Lawson C, Carli F, Scheede-Bergdahl C, Chevalier S. Feasibility of a novel mixed-nutrient supplement in a multimodal prehabilitation intervention for lung cancer patients awaiting surgery: A randomized controlled pilot trial. International Journal of Surgery. 2021 Sep 1;93:106079.	No surgery
55	Uster A, Ruehlin M, Mey S, Gisi D, Knols R, Imoberdorf R, Pless M, Ballmer PE. Effects of nutrition and physical exercise intervention in palliative cancer patients: a randomized controlled trial. Clinical nutrition. 2018 Aug 1;37(4):1202-9.	No surgery
56	Adriaans DJ, Beijer S, Heesakkers FF, de Craen-Kat L, Horevoorts N, Dierick-van Daele A, Teijink JA, van Laarhoven HW, van de Poll-Franse L, Nieuwenhuijzen GA. Effect of a pre-operative web-based	Other malignancy

	dietary self-management intervention on patient satisfaction, body weight and quality of life of esophageal cancer patients: A prospective, observational study. Clinical Nutrition Open Science. 2022 Jun 1;43:42-55.	
57	Aslakson RA, Chandrashekaran SV, Rickerson E, Fahy BN, Johnston FM, Miller JA, Conca-Cheng A, Wang S, Morris AM, Lorenz K, Temel JS. A multicenter, randomized controlled trial of perioperative palliative care surrounding cancer surgery for patients and their family members (PERIOP-PC). Journal of palliative medicine. 2019 Sep 1;22(S1):S-44.	Other malignancy
58	Aslakson RA, Rickerson E, Fahy B, Waterman B, Siden R, Colborn K, Smith S, Verano M, Lira I, Hollahan C, Siddiqi A. Effect of perioperative palliative care on health-related quality of life among patients undergoing surgery for cancer: a randomized clinical trial. JAMA Network Open. 2023 May 1;6(5):e2314660-.	Other malignancy
59	Dimeo FC, Thomas F, Raabe-Menssen C, Pröpper F, Mathias M. Effect of aerobic exercise and relaxation training on fatigue and physical performance of cancer patients after surgery. A randomised controlled trial. Supportive care in cancer. 2004 Nov;12:774-9.	Other malignancy
60	Molenaar CJ, Minnella EM, Coca-Martinez M, Ten Cate DW, Regis M, Awasthi R, Martínez-Palli G, López-Baamonde M, Sebio-Garcia R, Feo CV, Van Rooijen SJ. Effect of multimodal prehabilitation on reducing postoperative complications and enhancing functional capacity following colorectal cancer surgery: the PREHAB randomized clinical trial. JAMA surgery. 2023 Jun 1;158(6):572-81.	Other malignancy
61	Nottelmann L, Groenvold M, Vejlgaard TB, Petersen MA, Jensen LH. Early, integrated palliative rehabilitation improves quality of life of patients with newly diagnosed advanced cancer: The Pal-Rehab randomized controlled trial. Palliative medicine. 2021 Jul;35(7):1344-55.	Other malignancy
62	West M, Bates A, Grimmett C, Allen C, Green R, Hawkins L, Moyses H, Leggett S, Levett DZ, Rickard S, Varkonyi-Sepp J. The Wessex Fit-4-Cancer Surgery Trial (WesFit): a protocol fo r a factorial-design, pragmatic randomised-controlled tria l investigating the effects of a multi-modal prehabilitatio n programme in patients undergoing elective major intra–cavity cancer surgery [version 1; peer review: awaiting.	Other malignancy
63	Woodfield JC, Clifford K, Wilson GA, Munro F, Baldi JC. Short-term high-intensity interval training improves fitness before surgery: A randomized clinical trial. Scandinavian journal of medicine & science in sports. 2022 May;32(5):856-65.	Other malignancy
64	Emond YE, Calsbeek H, Teerenstra S, Bloo GJ, Westert GP, Damen J, Wolff AP, Wollersheim HC. Improving the implementation of	Protocol

	perioperative safety guidelines using a multifaceted intervention approach: protocol of the IMPROVE study, a stepped wedge cluster randomized trial. Implementation Science. 2015 Dec;10:1-1.	
65	Fugazzaro S, Costi S, Mainini C, Kopliku B, Rapicetta C, Piro R, Bardelli R, Rebelo PF, Galeone C, Sgarbi G, Lococo F. PUREAIR protocol: randomized controlled trial of intensive pulmonary rehabilitation versus standard care in patients undergoing surgical resection for lung cancer. BMC cancer. 2017 Dec;17:1-0.	Protocol
66	Ji X, Ding H. The efficacy of enteral nutrition combined with accelerated rehabilitation in non-small cell lung cancer surgery: A randomized controlled trial protocol. Medicine. 2020 Nov 25;99(48):e23382.	Protocol
67	Lauscher J, Beyer K, Hellinger A, Croner RS, Ridwelski K, Krautz C, Lim C, Coplan PM, Kurepkat M, Ribaric G. Protocol: Impact of a digital surgical workflow including Digital Device Briefing Tool on morbidity and mortality in a patient population undergoing primary stapled colorectal anastomosis for benign or malignant colorectal disease: protocol for a multicentre prospective cohort study. BMJ Open. 2023;13(3).	Protocol
68	Missel M, Pedersen JH, Sommer MS, Hendriksen C, Tewes M, Adamsen L. The Importance of Pre-and Early Postoperative Rehabilitation in NSCLC Patient (Design and Rationale for the PROLUCA Study). InJOURNAL OF THORACIC ONCOLOGY 2015 Sep 1 (Vol. 10, No. 9, pp. S124-S124). 360 PARK AVE SOUTH, NEW YORK, NY 10010-1710 USA: ELSEVIER SCIENCE INC.	Protocol
69	Moyen A., Fleurent-Gregoire C., Gillis C., Carli F., Scheede-Bergdahl C., Morais J., et al. A Novel Multimodal Intervention for Surgical Prehabilitation on Functional Recovery and Muscle Characteristics in Patients With Lung Cancer - A Study Protocol. Curr Dev Nutr. 2023;7(Supplement 1):101130.	Protocol
70	Sheill G, Guinan E, O'Neill L, Normand C, Doyle SL, Moore S, Newell J, McDermott G, Ryan R, Reynolds JV, Hussey J. Preoperative exercise to improve fitness in patients undergoing complex surgery for cancer of the lung or oesophagus (PRE-HIIT): protocol for a randomized controlled trial. BMC cancer. 2020 Dec;20:1-1.	Protocol
71	Strijker D, van den Heuvel B, van Laarhoven KC, Meijerink JW, Drager LL. Multimodal prehabilitation to improve postoperative outcomes after high impact surgery–study protocol of the F4S PREHAB trial. European Journal of Surgical Oncology. 2023 Feb 1;49(2):e117-8.	Protocol
72	Lu HB, Wang YQ, Liu X, Ma RC, Yin YY, Song CY, Yang TT, Xie J. Effects of Preoperative High-Intensity Interval Training Combined	Quasi experimental design

	With Team Empowerment Education in Lung Cancer Patients With Surgery: A Quasi-experimental Trial. Cancer Nursing. 2022 Dec 1:10-97.	
73	Edvardsen E, Skjonsberg OH, Borchsenius F, Anderssen SA. Effect of training on maximal oxygen uptake and muscular strength after lung cancer surgery-a randomized controlled trial.	Rehabilitation only
74	Liu J, Wang Y, Du J, Wang G. Effects of respiratory rehabilitation nursing on improving postoperative respiratory function and quality of life of patients with lung cancer surgery. Int J Clin Exp Med. 2020 Jan 1;13(10):7920-7.	Rehabilitation only
75	Malik PR, Fahim C, Vernon J, Thomas P, Schieman C, Finley CJ, Agzarian J, Shargall Y, Farrokhyar F, Hanna WC. Incentive spirometry after lung resection: a randomized controlled trial. The Annals of Thoracic Surgery. 2018 Aug 1;106(2):340-5.	Rehabilitation only
76	Schwartz GS, Eden E, Reid M, Aguirre H, Mains S, Hawking K, Tartell L, Grossbard M, Bhora FY, Connery CP. Enhanced Post-Operative Inpatient Physical Therapy Decreases Post-Operative Length Of Stay For Patients Undergoing Major Pulmonary Surgery. InC102. QUALITY IMPROVEMENT IN PULMONARY MEDICINE 2012 May (pp. A5152-A5152). American Thoracic Society.	Rehabilitation only
77	Sommer MS, Vibe-Petersen J, Stærkind MB, Langer SW, Larsen KR, Trier K, Christensen M, Clementsen PF, Missel M, Christensen KB, Lillelund C. Early initiated postoperative rehabilitation enhances quality of life in patients with operable lung cancer: Secondary outcomes from a randomized trial. Lung Cancer. 2020 Aug 1;146:285-9.	Rehabilitation only
78	Yin H. Enhanced Recovery after Surgery (ERAS) in Postoperative Lung Cancer Patients: A Novel Perioperative Strategy for Preventing Venous Thromboembolism and Improving Quality of Life. The Tohoku Journal of Experimental Medicine. 2024;262(3):201-9.	Rehabilitation only
79	Yu Z, Xie G, Qin C, He H, Wei Q. Effect of postoperative exercise training on physical function and quality of life of lung cancer patients with chronic obstructive pulmonary disease: A randomized controlled trial. Medicine. 2024 Mar 8;103(10):e37285.	Rehabilitation only
80	Crandall K, Maguire R, Campbell A, Kearney N. Exercise intervention for patients surgically treated for Non-Small Cell Lung Cancer (NSCLC): a systematic review. Surgical oncology. 2014 Mar 1;23(1):17-30.	Review article
81	de Oliveira Vacchi C, Martha BA, Macagnan FE. Effect of inspiratory muscle training associated or not to physical rehabilitation in preoperative anatomic pulmonary resection: a systematic review	Review article

	and meta-analysis. Supportive Care in Cancer. 2022 Feb;30(2):1079-92.	
82	Debes C, Aissou M, Beaussier M. Prehabilitation. Preparing patients for surgery to improve functional recovery and reduce postoperative morbidity. InAnnales francaises d'anesthesie et de reanimation 2014 Jan 17 (Vol. 33, No. 1, pp. 33-40).	Review article
83	Ferreira V, Lawson C, Ekmekjian T, Carli F, Scheede-Bergdahl C, Chevalier S. Effects of preoperative nutrition and multimodal prehabilitation on functional capacity and postoperative complications in surgical lung cancer patients: a systematic review. Supportive Care in Cancer. 2021 Oct;29:5597-610.	Review article
84	Gravier FE, Smondack P, Prieur G, Medrinal C, Combret Y, Muir JF, Baste JM, Cuvelier A, Boujibar F, Bonnevie T. Effects of exercise training in people with non-small cell lung cancer before lung resection: a systematic review and meta-analysis. Thorax. 2022 May 1;77(5):486-96.	Review article
85	Jones LW. Physical activity and lung cancer survivorship. Physical activity and cancer. 2011:255-74.	Review article
86	Li TC, Yang MC, Tseng AH, Lee HH. Prehabilitation and rehabilitation for surgically treated lung cancer patients. Journal of cancer research and practice. 2017 Sep 1;4(3):89-94.	Review article
87	Mainini C, Rebelo PF, Bardelli R, Kopliku B, Tenconi S, Costi S, Tedeschi C, Fugazzaro S. Perioperative physical exercise interventions for patients undergoing lung cancer surgery: What is the evidence?. SAGE open Medicine. 2016 Oct 18;4:2050312116673855.	Review article
88	Mainini C, Rebelo PF, Bardelli R, Kopliku B, Tenconi S, Costi S, Tedeschi C, Fugazzaro S. Perioperative physical exercise interventions for patients undergoing lung cancer surgery: What is the evidence?. SAGE open Medicine. 2016 Oct 18;4:2050312116673855.	Review article
89	Matheny CR, Delis J, Kemezy D, Moore A, Woodrum C. Effectiveness of Cardiopulmonary Rehabilitation on Endurance and Dyspnea in Patients with Lung Cancer: Systematic Review. In2022 Combined Sections Meeting (CSM) 2022 Feb 3. APTA.	Review article
90	Michaels C. Importance of exercise in lung cancer treatment. InJOURNAL OF THORACIC ONCOLOGY 2015 Sep 1 (Vol. 10, No. 9, pp. S88-S88). 360 PARK AVE SOUTH, NEW YORK, NY 10010-1710 USA: ELSEVIER SCIENCE INC.	Review article
91	Ni HJ, Pudasaini B, Yuan XT, Li HF, Shi L, Yuan P. Exercise training for patients pre-and postsurgically treated for non–small cell lung	Review article

	cancer: a systematic review and meta-analysis. Integrative cancer therapies. 2017 Mar;16(1):63-73.	
92	Voorn MJ, Franssen RF, Hoogeboom TJ, van Kampen-van den Boogaart VE, Bootsma GP, Bongers BC, Janssen-Heijnen ML. Evidence base for exercise prehabilitation suggests favourable outcomes for patients undergoing surgery for non-small cell lung cancer despite being of low therapeutic quality: a systematic review and meta-analysis. European Journal of Surgical Oncology. 2023 May 1;49(5):879-94.	Review article
93	Zhu RY, Chen H, Gao YJ, Pan ZH, Wang JY. Effects of psychological nursing care on anxiety and depression in perioperative patients with lung cancer: A systematic review and meta-analysis. Medicine. 2022 Jul 22;101(29):e29914.	Review article
94	Avancini A, Cavallo A, Trestini I, Tregnago D, Belluomini L, Crisafulli E, Micheletto C, Milella M, Pilotto S, Lanza M, Infante MV. Exercise prehabilitation in lung cancer: getting stronger to recover faster. European Journal of Surgical Oncology. 2021 Aug 1;47(8):1847-55.	Review article
95	Vanessa Ferreira, Enrico Maria Minnella, Rashami Awasthi, Ann Gamsa, Lorenzo Ferri, David Mulder, Christian Sirois, Jonathan Spicer, Severin Schmid, Francesco Carli	Different comparator

MEDIASTINAL LYMPH NODE DISSECTION VERSUS SAMPLING IN PATIENTS WITH OPERABLE NON-SMALL CELL LUNG CANCER

Key Question in PICO format

In patients with operable non-small cell lung cancer (NSCLC), does systematic mediastinal lymph node dissection improve overall survival compared to mediastinal lymph nodal sampling?

Patient or population: Patients with operable non-small cell lung cancer
Subgroups: 1. T stage 2. Nodal involvement 3. Histology 4. PDL1 5. Smoking status
Intervention: Systematic mediastinal lymph node dissection

Comparison: Mediastinal lymph nodal sampling

Outcome: Critical outcomes - Overall survival, Surgery/surgical procedure related complications
Important outcome - Disease free survival, Length of hospital stay, Cost

Search Strategy

PubMed: (As on 31-May-2024)

Search domain	Search strategy	Number of hits
P	"Carcinoma, non-small cell lung" [MeSH Terms] OR "lung carcinomas, non-small cell" [tiab] OR "non-small cell lung cancer" [tiab] OR "non-small cell lung carcinoma" [tiab] OR "carcinoma, non-small cell lung" [tiab]OR "non-small cell lung cancer" OR " non-small cell lung carcinoma" [tiab] OR "carcinoma non-small cell lung"[tiab] OR "carcinomas, non-small cell lung" [tiab]	105,533
I	"Mediastinal lymph node sampling" [tiab] OR "Lymph Node Sampling" [tiab] OR "Lymph Node Sample" [tiab] OR "Node Dissections, Lymph" [tiab]	57,758
C	"Lymph node excision"[MeSH Terms] OR "Systematic mediastinal lymph node dissection" [tiab] OR "mediastinal lymph node dissection" [tiab] OR "Dissection, lymph node" [tiab] OR "Lymph Node Dissections" [tiab] OR "Node Dissection, Lymph"[tiab]	
O	"Overall survival" [tiab] OR "survival rate"[MeSH Terms] OR survival rate[tiab] OR "rate, survival" [tiab] OR "disease-free survival"[MeSH Terms] OR "disease free survival"[Tiab] OR "survival, disease free" OR "length of stay"[MeSH Terms] OR "hospital stay "[tiab] OR "stay, hospital" [tiab] OR "postoperative complications"[MeSH Terms] OR "complication postoperative"[tiab] OR "post-operative complications"[tiab] OR "costs and cost analysis"[MeSH Terms] OR "cost of treatment" [tiab]	1,521,383
Combined search domain (P AND I AND C AND O)	"Carcinoma, non-small cell lung" [MeSH Terms] OR "lung carcinomas, non-small cell" [tiab] OR "non-small cell lung cancer" [tiab] OR "non-small cell lung carcinoma" [tiab] OR "carcinoma, non-small cell lung" [tiab]OR "non-small cell lung cancer" OR " non-small cell lung carcinoma" [tiab] OR	643

	"carcinoma non-small cell lung"[tiab] OR "carcinomas, non-small cell lung" [tiab] **P AND** "Lymph node excision"[MeSH Terms] OR "Systematic mediastinal lymph node dissection" [tiab] OR "mediastinal lymph node dissection" [tiab] OR "Dissection, lymph node" [tiab] OR "Lymph Node Dissections" [tiab] OR "Node Dissection, Lymph"[tiab] OR "Mediastinal lymph node sampling" [tiab] OR "Lymph Node Sampling" [tiab] OR "Lymph Node Sample" [tiab] OR "Node Dissections, Lymph" [tiab] **I, C AND** "Overall survival" [tiab] OR "survival rate"[MeSH Terms] OR survival rate[tiab] OR "rate, survival" [tiab] OR "disease-free survival"[MeSH Terms] OR "disease free survival"[Tiab] OR "survival, disease free" OR "length of stay"[MeSH Terms] OR "hospital stay "[tiab] OR "stay, hospital" [tiab] OR "postoperative complications"[MeSH Terms] OR "complication postoperative"[tiab] OR "post-operative complications"[tiab] OR "costs and cost analysis"[MeSH Terms] OR "cost of treatment" [tiab] **O**	

EMBASE: (As on 31-May-2024)

Search domain	Search strategy	Number of hits
P	'non-small cell lung carcinoma'/exp OR 'non-small cell lung cancer'/exp OR 'non-small cell bronchogenic carcinoma'/exp OR 'non-small cell bronchogenic cancer'/exp	--
I	'Lymph node sampling/exp OR 'Mediastinal lymph node sampling'/exp	--
C	'Lymph node dissection'/exp OR 'mediastinal lymph node dissection'/exp OR 'Systematic mediastinal lymph node dissection'/exp	
O	'Overall survival'/exp OR 'post-operative complications'/exp OR 'disease free survival'/exp OR 'length of stay'/exp OR 'cost of treatment'/exp OR 'health expenditure'/exp	--
Combined search domain (P AND I AND C AND O)	'non-small cell lung carcinoma'/exp OR 'non-small cell lung cancer'/exp OR 'non-small cell bronchogenic carcinoma'/exp OR 'non-small cell bronchogenic cancer'/exp **P AND** 'lymph node sampling/exp OR 'Mediastinal lymph node sampling'/exp **I AND** 'lymph node dissection'/exp OR 'mediastinal lymph node dissection'/exp OR 'Systematic mediastinal lymph node dissection'/exp **C AND** 'overall survival'/exp OR 'post-operative complications'/exp OR 'disease free survival'/exp OR 'length of stay'/exp OR 'cost of treatment'/exp OR 'health expenditure'/exp **O**	242

SCOPUS: (As on 31-May-2024)

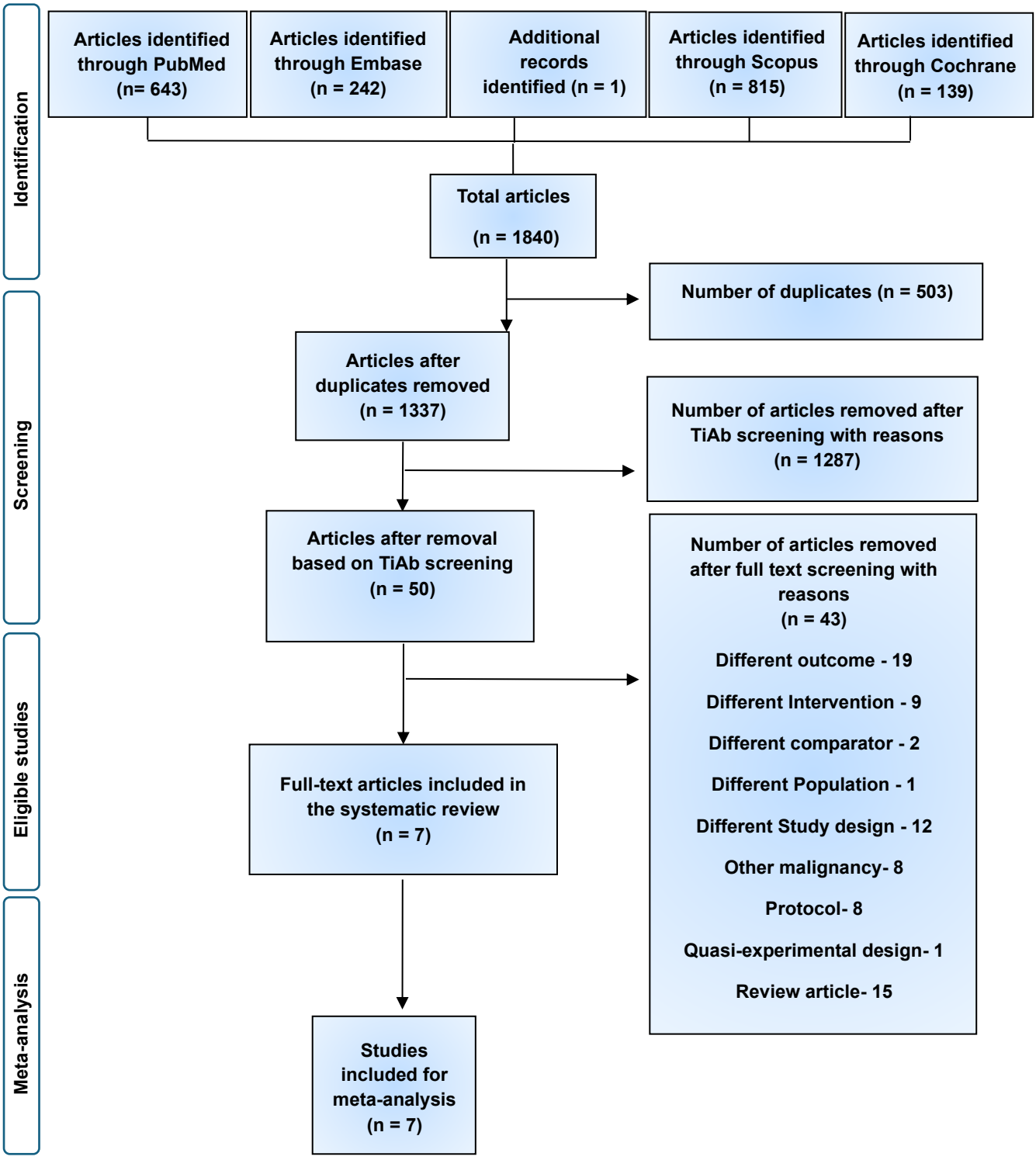
Search domain	Search strategy	Number of hits
P	TITLE-ABS-KEY (non-small cell lung cancer) OR TITLE-ABS-KEY (non-small cell lung carcinoma) OR TITLE-ABS-KEY (operable non-small cell lung carcinoma) OR TITLE-ABS-KEY (operable non-small cell lung cancer)	153,869
I	TITLE-ABS-KEY (mediastinal lymph node sampling) OR TITLE-ABS-KEY (lymph node sampling)	59,090
C	TITLE-ABS-KEY (mediastinal lymph node dissection) OR TITLE-ABS-KEY (systematic mediastinal lymph node dissection)	
O	(TITLE-ABS-KEY ("survival rate") OR TITLE-ABS-KEY ("surgical complications") OR TITLE-ABS-KEY ("disease-free survival") OR TITLE-ABS-KEY ("length of hospital stay") OR TITLE-ABS-KEY ("cost of treatment") OR TITLE-ABS-KEY (health expenditure))	743,941
Combined search domain (P AND I AND C AND O)	TITLE-ABS-KEY (non-small cell lung cancer) OR TITLE-ABS-KEY (non-small cell lung carcinoma) OR TITLE-ABS-KEY (operable non-small cell lung carcinoma) OR TITLE-ABS-KEY (operable non-small cell lung cancer) **P AND** TITLE-ABS-KEY(mediastinal lymph node sampling) OR TITLE-ABS-KEY(lymph node sampling) **I AND** TITLE-ABS-KEY(mediastinal lymph node dissection) OR TITLE-ABS-KEY(systematic mediastinal lymph node dissection) **C AND** (TITLE-ABS-KEY ("survival rate") OR TITLE-ABS-KEY("surgical complications") OR TITLE-ABS-KEY("disease-free survival") OR TITLE-ABS-KEY("length of hospital stay") OR TITLE-ABS-KEY("cost of treatment") OR TITLE-ABS-KEY(health expenditure)) **O**	815

Cochrane Central: (As on 31-May -2024)

Search domain	Search strategy	Number of hits
P	" non-small cell lung carcinoma" [tiab] OR "Carcinoma, non-small cell lung" [tiab] OR "Carcinoma, non-small cell lung" [MeSH Terms]	6922
I	"Node Dissection, Lymph"[tiab] OR "Mediastinal lymph node sampling" [tiab] OR "Lymph Node Sampling" [tiab] OR "Lymph Node Sample" [tiab] OR "Node Dissections, Lymph" [tiab]	2669
C	"Lymph node excision"[MeSH Terms] OR "Systematic mediastinal lymph node dissection" [tiab] OR "mediastinal lymph node dissection" OR "Dissection, lymph node" [tiab] OR "Lymph Node Dissections" [tiab]	
O	"Overall survival" [tiab] OR "survival rate"[MeSH Terms] OR survival rate[tiab] OR "rate, survival" [tiab] OR "disease-free survival"[MeSH Terms] OR "disease free survival"[Tiab] OR "survival, disease free" OR "length of stay"[MeSH Terms] OR "hospital stay "[tiab] OR "stay, hospital" [tiab] OR "postoperative complications"[MeSH Terms] OR "complication postoperative"[tiab] OR "post-operative complications"[tiab] OR	396077

	"costs and cost analysis"[MeSH Terms] OR "cost of treatment" [tiab]	
Combined search domain (P AND I AND C AND O)	" non-small cell lung carcinoma" [tiab] OR "Carcinoma, non-small cell lung" [tiab] OR "Carcinoma, non-small cell lung" [MeSH Terms] **P AND** "Node Dissection, Lymph"[tiab] OR "Mediastinal lymph node sampling" [tiab] OR "Lymph Node Sampling" [tiab] OR "Lymph Node Sample" [tiab] OR "Node Dissections, Lymph" [tiab] **I AND** "Lymph node excision"[MeSH Terms] OR "Systematic mediastinal lymph node dissection" [tiab] OR "mediastinal lymph node dissection" OR "Dissection, lymph node" [tiab] OR "Lymph Node Dissections" [tiab] **C AND** "Overall survival" [tiab] OR "survival rate"[MeSH Terms] OR survival rate[tiab] OR "rate, survival" [tiab] OR "disease-free survival"[MeSH Terms] OR "disease free survival"[Tiab] OR "survival, disease free" OR "length of stay"[MeSH Terms] OR "hospital stay "[tiab] OR "stay, hospital" [tiab] OR "postoperative complications"[MeSH Terms] OR "complication postoperative"[tiab] OR "post-operative complications"[tiab] OR "costs and cost analysis"[MeSH Terms] OR "cost of treatment" [tiab] **AND O.**	139

PRISMA flow diagram



Summary of Included Studies

S No.	Study ID	Population – Inclusion Criteria	Population – Exclusion Criteria	Intervention Characteristics	Comparator Characteristics	Outcome
1.	Izbicki et al. 1994	Patients of any age and sex with a curatively resectable non-small cell lung cancer	Tumour-associated exclusion criteria were evidence of distant metastasis; contralateral or supraclavicular nodal involvement; and confirmation of extensive N2 disease by computed tomography Patient-associated exclusion criteria were: previous or coexistent malignant disease; severe heart failure; renal insufficiency (creatinine level more than twice the normal upper limit); myocardial infarction less than 6 months previously; liver cirrhosis; and insu5cient pulmonary reserve, evidence of intrapulmonary metastases. Patients whose resection specimen exhibited residual tumour at the resection margin were also excluded,	Systematic mediastinal lymph node dissection	Mediastinal lymph nodal sampling	I. Length of hospital stay II. Surgery/ surgical procedure related complications

			as were those whose tumour was subsequently classified as small cell lung cancer.			
2.	Sugi et al. 1998	Patients with pathologic diagnosis of NSC lung cancer	Patients with a history of malignancy & Patients with hilar or mediastinal lymph nodes > 1 cm according to CT	Systematic mediastinal lymph node dissection	Mediastinal lymph nodal sampling	I. Overall survival II. Length of hospital stay III. Surgery/ surgical procedure related complications
3.	Izbicki et al. 1998	Patients of any age and either sex with a curatively resectable NSCLC	Patients with evidence of intrapulmonary metastases; whose resection specimen exhibited residual tumor at the resection margin and patients whose tumor was subsequently classified as small cell lung cancer. Patients with severe heart failure, renal insufficiency (creatinine > 2x upper normal limit), myocardial infarction less than 6 months ago, liver cirrhosis, and insufficient pulmonary reserve.	Systematic mediastinal lymph node dissection	Mediastinal lymph nodal sampling	I. Overall survival II. Disease free survival
4.	Wu et al. 2002	All patients who entered the trial must be 70 years old. Pathologic types must be NSCLC. cTNM must be Stage I–IIIA..	There must be not residual tumor at the resection margin or the operation is a complete resection (operation procedures include lobectomy and pneumonectomy).	Systematic mediastinal lymph node dissection	Mediastinal lymph nodal sampling	I. Overall survival

5.	Allen at a. 2006	Patients older than 18 years of age, an Eastern Cooperative Oncology Group (ECOG) performance score lower than 3, and a tissue diagnosis of a clinically resectable T1 or T2, N0 or nonhilar N1, M0 non–small cell lung cancer (squamous cell carcinoma, large cell carcinoma, or adenocarcinoma, including bronchoalveolar carcinoma) established before randomization	Exclusion criteria included patients who had T3 or T4 tumors, patients who were treated with pulmonary wedge excision, and patients who received prior chemotherapy or radiation therapy for their cancer.	Systematic mediastinal lymph node dissection	Mediastinal lymph nodal sampling	I. Length of hospital stay II. Surgery/ surgical procedure related complications
6.	Darling et al. 2011	Retrieving data. Wait a few seconds and try to cut or copy again.	Major violations including incorrect clinical stage, inadequate lymph node sampling, benign disease, insufficient documentation	Systematic mediastinal lymph node dissection	Mediastinal lymph nodal sampling	I. Overall survival II. Disease free survival
7.	Zhang et al. 2013	.All candidates were decided as clinical stage I-IIIa upon preoperative evaluation, which included fibrous bronchoscopy, computed tomography (CT) scan of the chest and brain, abdominal ultrasonography,	-	Complete mediastinal lymph node dissection	Minimal mediastinal lymph node dissection	I. Overall survival II. Surgery/ surgical procedure related complications

		positron emission tomography (PET) or single photon emission computed tomography (SPECT).				

Data Extraction

Name	Systematic Lymph Node Dissection for Clinically Diagnosed Peripheral Non-Small-Cell Lung Cancer Less Than 2 cm in Diameter
Author	Sugi et al
Study Type	Randomized controlled study
Countries and setting	Japan
Number of Participants	115
Duration of study follow up (in months)	>49
Inclusion Criteria	Patients with pathologic diagnosis of NSC lung cancer
Exclusion Criteria	Patients with a history of malignancy & Patients with hilar or mediastinal lymph nodes > 1 cm acc. to CT
Recruitment/Selection of Patients	Yamaguchi University School of Medicine
Intervention	Radical Systematic Lymphadenectomy
Outcome reported with time points	Clinically evaluated peripheral non-small-cell carcinomas smaller than 2 cm in diameter do not require radical systematic mediastinal and hilar lymph node dissection. The overall 5-year survival was 81% in the dissection group and 84% in the sampling group
Funding	
ROB 2 Assessment	Randomisation process - Some concerns Deviations from the intended interventions - Low Missing outcome data - Some concerns Measurement of the outcome - Low Selection of the reported result - Low Overall - Some concerns

Name	Effectiveness of Radical Systematic Mediastinal Lymphadenectomy in Patients With Resectable Non-Small Cell Lung Cancer
Author	Izbicki et al (1998)
Study Type	Randomized controlled study
Countries and setting	Germany

Number of Participants	169
Duration of study follow up (in months)	25-67
Inclusion Criteria	Patients of any age and sex with a curatively resectable NSCLC
Exclusion Criteria	Patients with evidence of intrapulmonary metastases; whose resection specimen exhibited residual tumor at the resection margin and patients whose tumor was subsequently classified as SCLC. Patients with severe heart failure, renal insufficiency, myocardial infarction less than 6 months ago, liver cirrhosis, and insufficient pulmonary reserve.
Recruitment/Selection of Patients	University of Munich, Central Hospital Gauting
Intervention	Radical Systematic Mediastinal Lymphadenectomy
Outcome reported with time points	After a median follow-up of 47 months, Lymphadenectomy (LA) did not improve survival in the overall group of patients. Although recurrences rates tended to be reduced among patients who underwent LA, these decreases were not statistically significant. So Radical SMLA does not influence disease-free or overall survival in patients with NSCLC and without overt lymph node involvement. However, a small subgroup of patients with limited mediastinal lymph node metastases might benefit from a systematic LA.
Funding	
ROB 2 Assessment	Randomisation process - Some concerns Deviations from the intended interventions - Low Missing outcome data - Some concerns Measurement of the outcome - Low Selection of the reported result - Low Overall - Some concerns

Name	**Radical systematic mediastinal lymphadenectomy in non-small cell lung cancer: a randomized controlled trial**
Author	Izbicki et al (1994)
Study Type	Randomized controlled study
Countries and setting	Germany
Number of Participants	182
Duration of study follow up (in months)	Median 26.8
Inclusion Criteria	Patients of any age and sex with a curatively resectable NSCLC

Exclusion Criteria	Evidence of distant metastasis; contralateral or supraclavicular nodal involvement; confirmation of extensive N2 disease by CT. Previous or coexistent malignant disease; severe heart failure; renal insufficiency (creatinine level more than twice the normal upper limit); Myocardial Infarction less than 6 months previously; liver cirrhosis; and insufficient pulmonary reserve, evidence of intrapulmonary metastases. Patients whose resection specimen exhibited residual tumour at the resection margin, whose tumour was subsequently classified as SCLC
Recruitment/Selection of Patients	University of Munich, Central Hospital Gauting
Intervention	Radical Systematic Mediastinal Lymphadenectomy
Outcome reported with time points	Comparison of short-term results revealed a significantly longer operating time in those undergoing systematic lymphadenectomy, but overall morbidity and mortality rates were comparable between groups. Interim analysis of results at a median follow-up of 26.8 months showed no significant influence of radical lymphadenectomy on local recurrence-free interval, metastasis-free interval or cancer-related survival.
Funding	
ROB 2 Assessment	Randomisation process - Some concerns Deviations from the intended interventions - Low Missing outcome data - Some concerns Measurement of the outcome - Low Selection of the reported result - Low Overall - Some concerns

Name	**A randomized trial of systematic nodal dissection in resectable non-small cell lung cancer**
Author	Wu et al
Study Type	Randomized controlled study
Countries and setting	China
Number of Participants	471
Duration of study follow up (in months)	60
Inclusion Criteria	Patients > 70 years old. Pathologic type NSCLC. cTNM Stage I–IIIA.
Exclusion Criteria	NA

Recruitment/Selection of Patients	Sun Yat-sen University of Medical Sciences, Guangzhou
Intervention	Radical Systematic Mediastinal Lymphadenectomy
Outcome reported with time points	For curative treatment, surgical resection remains the most effective therapy for non-small cell lung cancer. The 5-year survival rate for patients with resected NSCLC, including all stages and all types of resection, was 39.8%
Funding	
ROB 2 Assessment	Randomisation process - Some concerns Deviations from the intended interventions - Low Missing outcome data - Some concerns Measurement of the outcome - Low Selection of the reported result - Low Overall - Some concerns

Name	**Morbidity and Mortality of Major Pulmonary Resections in Patients With Early-Stage Lung Cancer: Initial Results of the Randomized, Prospective ACOSOG Z0030 Trial**
Author	Allen et. Al
Study Type	Prospective Randomized Trial
Countries and setting	USA
Number of Participants	1111
Inclusion Criteria	Patients older than 18 years of age, an Eastern Cooperative Oncology Group (ECOG) performance score lower than 3, and a tissue diagnosis of a clinically resectable T1 or T2, N0 or nonhilar N1, M0 non–smallcell lung cancer (squamous cell carcinoma, large cell carcinoma, or adenocarcinoma, including bronchoalveolar carcinoma) established before randomization

Exclusion Criteria	Exclusion criteria included patients who had T3 or T4 tumors, patients who were treated with pulmonary wedge excision, and patients who received prior chemotherapy or radiation therapy for their cancer
Recruitment/Selection of Patients	American College of Surgeons Oncology Study Group
Intervention	Radical Systematic Mediastinal Lymphadenectomy
Outcome reported with time points	Complete mediastinal lymphadenectomy adds little morbidity to a pulmonary resection for lung cancer.
ROB 2 Assessment	Randomisation process - Some concerns Deviations from the intended interventions - Low Missing outcome data - Some concerns Measurement of the outcome - Low Selection of the reported result - Low Overall - Some concerns

Name	**Randomized Trial of Mediastinal Lymph Node Sampling Versus Complete Lymphadenectomy During Pulmonary Resection in the Patient with N0 or N1 (Less Than Hilar) Non-Small Cell Carcinoma: Results of the ACOSOG Z0030 Trial**
Author	Darling et al
Study Type	Randomized control trial
Countries and setting	USA
Number of Participants	1,111
Duration of study follow up (in months)	Median follow-up of 6.5 years
Inclusion Criteria	Patients of any age and either sex with a curatively resectable NSCLC
Exclusion Criteria	Major violations including incorrect clinical stage, inadequate lymph node sampling, benign disease, insufficient documentation

Recruitment/Selection of Patients	Patients were randomized by 102 different surgeons from 63 institutions.
Intervention	Radical Systematic Mediastinal Lymphadenectomy
Outcome reported with time points	5 year disease free survival rate was 69% for MLNS and 68% for MLND. So If systematic, thorough pre-section sampling of the mediastinal and hilar lymph nodes is negative, MLND does not improve survival in patients with early stage NSCLC but these results are not generalizable to patients staged radiographically or those with higher stage tumors In a subgroup analysis of patients with stage II or IIIA NSCLC entered into Intergroup trial 0115 of adjuvant chemoradiotherapy vs. radiotherapy following resection, Keller15 reported improved long-term survival in patients with right upper lobe tumors who had MLND with a median survival of 57.5 months versus MLNS with a median survival of 29.2 months
ROB 2 Assessment	Randomisation process - Some concerns
	Deviations from the intended interventions - Low
	Missing outcome data - Some concerns
	Measurement of the outcome - Low
	Selection of the reported result - Low
	Overall - Some concerns

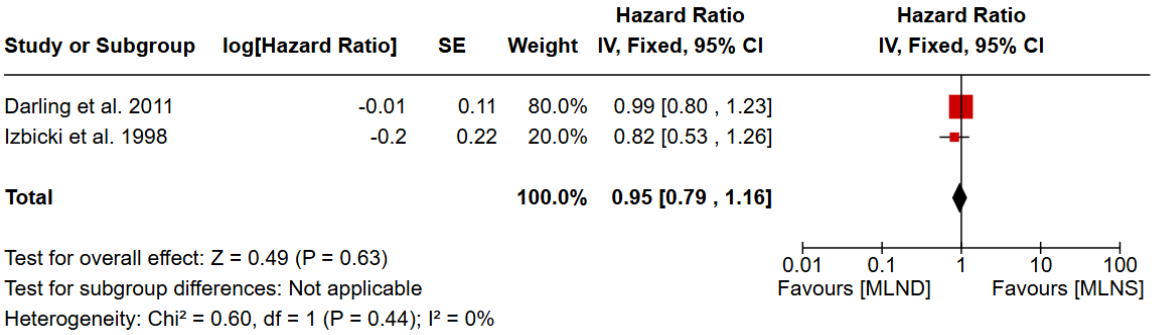
Name	**Comparison of complete and minimal mediastinal lymph node dissection for non-small cell lung cancer: Results of a prospective randomized trial**
Author	Zhang et al. 2013

Study Type	Prospective randomized trial
Countries and setting	Shanghai, China
Number of Participants	202
Duration of study follow up (in months)	The patients were under follow-up every four months during the first two years after surgery, and every six months after that, up to five years
Inclusion Criteria	Patients of any age and either sex with a curatively resectable NSCLC
Exclusion Criteria	Major violations including incorrect clinical stage, inadequate lymph node sampling, benign disease, insufficient documentation
Recruitment/Selection of Patients	Shanghai Chest Hospital from January 2006 to December 2007
Intervention	Radical Systematic Mediastinal Lymphadenectomy
Outcome reported with time points	The follow-up rate was 90.9%; the loss ratio of follow-up is 9.3% for the MLD group and 8.4% for the CLD. Overall five-year survival was 37.7% for the MLD group and 55.7% for the CLD group. Furthermore, CLD was associated with significantly superior five-year survival than MLD in subgroups of patients with a tumor size >3 cm, pleural invasion, pN1-N2, stage II-III, adenocarcinoma, or low cell differentiation.
ROB 2 Assessment	Randomisation process - Some concerns
	Deviations from the intended interventions - Low
	Missing outcome data - Some concerns
	Measurement of the outcome - Low
	Selection of the reported result - Low
	Overall - Some concerns

Forest Plots of Important Outcomes

Disease Free survival

Comparison of MLND Vs MLNS for perioperative complications of Disease-Free survival.



Evidence to Decision Framework

QUESTION	
Should Mediastinal lymph node dissection vs. sampling be used for patients with operable non-small cell lung cancer (NSCLC)?	
Population:	Patients with operable non-small cell lung cancer (NSCLC)
Intervention:	Mediastinal lymph node dissection
Comparison:	Mediastinal lymph node sampling
Main outcomes:	Overall survival Postoperative complications

ASSESSMENT

Problem **Is the problem a priority?**		
Judgement	**Research evidence**	**Additional considerations**
○ No ○ Probably no ○ Probably yes ● Yes	Two primary techniques for mediastinal lymph node assessment during surgery are mediastinal lymph node sampling (MLNS) and systematic mediastinal lymph node dissection (MLND). Despite MLND being considered the gold standard for staging, its superiority in terms of overall survival and disease-free survival compared to MLNS remains uncertain. Some studies suggest a potential therapeutic benefit of MLND, particularly in reducing locoregional recurrence, while others demonstrate no	No additional considerations

○ Varies ○ Don't know	significant advantage over MLNS. The decision between these two approaches can be influenced by several factors, including the tumor's T stage, extent of nodal involvement, histological subtype, PD-L1 expression, and patient smoking status. The clinical implications of selecting the optimal lymph node management strategy are profound. Inadequate staging may lead to under-treatment and poorer outcomes, while more aggressive approaches like MLND could increase postoperative complications, prolong hospital stays, and escalate healthcare costs. The trade-offs between surgical morbidity, cost, and potential survival benefit necessitate a careful evaluation of the evidence.	

Desirable Effects

How substantial are the desirable anticipated effects?

Judgement	Research evidence	Additional considerations
○ Trivial ○ Small ○ Moderate ● Large ○ Varies ○ Don't know	Given that the minimal clinically important difference (MCID) is 3%, the observed effect of MLND versus MLNS, with a hazard ratio of 0.74 (95% CI: 0.56 to 0.97), likely exceeds the threshold of clinical relevance. This suggests that MLND may provide a meaningful survival advantage over MLNS.	Conversion of HR to absolute effects discussed. It was decided that judgement would be made based on the values provided. Cancer staging as a sub group was discussed. The combined risk for all the stages up to 5 years - 50-55% in terms of absolute survival. 10-11% of absolute improvement in survival. For stage I,II,III 26% risk reduction would mean 12-13% difference in absolute survival rates. The rate is significantly higher than any other intervention. The HR

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)
	Risk with lymph node sampling	Risk with Mediastinal lymph node dissection			
Overall survival			**HR 0.74** (0.56 to 0.97)	1980 (5 RCTs)	⊕◯◯◯ Very low[a,b,c]

		value was discussed to be for mortality instead of overall survival.
Undesirable Effects How substantial are the undesirable anticipated effects?		
Judgement	**Research evidence**	**Additional considerations**
● Trivial ○ Small ○ Moderate ○ Large ○ Varies ○ Don't know	The evidence on undesirable effects of MLND compared to MLNS suggests no significant increase in most postoperative complications, with a trend toward reduced risk in several outcomes such as respiratory failure, atelectasis, and myocardial infarction.	Most of the individual complications have been reported in a very few RCTs. The complications may not be pertaining to LN dissection except for few like recurrent laryngeal nerve injury, chylothorax. Rest are general complications with lesser incidence.

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)
	Risk with lymph node sampling	Risk with Mediastinal lymph node dissection			
ARDS	10 per 1,000	**5 per 1,000** (1 to 19)	**OR 0.45** (0.11 to 1.83)	1205 (2 RCTs)	⊕⊕◯◯ Low[a,d]
Atelectasis	76 per 1,000	**52 per 1,000** (31 to 83)	**OR 0.66** (0.39 to 1.09)	1023 (1 RCT)	⊕⊕◯◯ Low[a,d]
Atrial fibrillation	18 per 1,000	**34 per 1,000** (3 to 285)	**OR 1.93** (0.17 to 21.90)	115 (1 RCT)	⊕⊕◯◯ Low[a,d]
Air leaks	30 per 1,000	**23 per 1,000** (12 to 42)	**OR 0.77** (0.41 to 1.44)	1522 (4 RCTs)	⊕⊕◯◯ Low[a,d]
Bronchopleural fistula	4 per 1,000	**6 per 1,000** (1 to 33)	**OR 1.43** (0.24 to 8.57)	1023 (1 RCT)	⊕⊕◯◯ Low[a,d]
Chylothorax	8 per 1,000	**17 per 1,000** (7 to 42)	**OR 2.16** (0.86 to 5.45)	1522 (4 RCTs)	⊕⊕◯◯ Low[a,d]
Haemorrhage	36 per 1,000	**27 per 1,000** (15 to 49)	**OR 0.74** (0.40 to 1.36)	1320 (3 RCTs)	⊕⊕◯◯ Low[a,d]
MI	16 per 1,000	**2 per 1,000** (0 to 15)	**OR 0.12** (0.01 to 0.94)	1023 (1 RCT)	⊕⊕⊕◯ Moderate[a]
Pneumonia	13 per 1,000	**12 per 1,000** (5 to 31)	**OR 0.98** (0.38 to 2.50)	1320 (3 RCTs)	⊕⊕◯◯ Low[a,d]
Recurrent nerve injury	16 per 1,000	**23 per 1,000** (11 to 45)	**OR 1.46** (0.71 to 2.98)	1589 (4 RCTs)	⊕⊕◯◯ Low[a,d]
Retained bronchial secretion	101 per 1,000	**136 per 1,000** (18 to 582)	**OR 1.39** (0.16 to 12.31)	297 (2 RCTs)	⊕⊕◯◯ Low[a,d]
Respiratory failure	68 per 1,000	**42 per 1,000** (24 to 71)	**OR 0.60** (0.34 to 1.04)	1023 (1 RCT)	⊕⊕◯◯ Low[a,d]
Seropneumothorax	98 per 1,000	**130 per 1,000** (55 to 276)	**OR 1.38** (0.54 to 3.52)	182 (1 RCT)	⊕⊕◯◯ Low[a,d]

Certainty of evidence What is the overall certainty of the evidence of effects?		
Judgement	**Research evidence**	**Additional considerations**
● Very low ○ Low ○ Moderate ○ High ○ No included studies	Overall certainty of evidence is very low due to risk of bias, inconsistency and imprecision	No additional considerations. For most surgical trials, the certainty of evidence would be very low due to limitations in the extent of blinding.
Values Is there important uncertainty about or variability in how much people value the main outcomes?		
Judgement	**Research evidence**	**Additional considerations**
○ Important uncertainty or variability ○ Possibly important uncertainty or variability ○ Probably no important	1. overall survival (36 out of 40), was highly valued by 92% patients who underwent lung surgery (Wong MSH, Pons A, De Sousa P, Proli C, Jordan S, Begum S, Buderi S, Lim E. Assessing patient perception and preferences for outcomes in lung cancer resection surgery: a cross-sectional study. J Thorac Dis. 2024 Jun 30;16(6):3844-3853) 2. Patients with lung cancer and caregivers demonstrated varying willingness to trade PFS for reduced severity of treatment-related side effects. Most participants (90%)	Very little data to support overall survival valued by patients. No direct evidence to support the same. A component of vulnerability has been taken into account in different studies, keeping different stakeholders in consideration. The is no variability in terms of patients valueing the overall survival as an outcome. There are two

uncertainty or variability ● No important uncertainty or variability	would accept treatment with more severe functional long-term effects for an 8.4-month PFS gain. (Janssen EM, et al. Analysis of Patient Preferences in Lung Cancer - Estimating Acceptable Tradeoffs Between Treatment Benefit and Side Effects. Patient Prefer Adherence. 2020 Jun 3;14:927-937)	outcomes being considered in the study, overall survival and adverse events. For stakeholders, the value is less likely to vary.
Balance of effects Does the balance between desirable and undesirable effects favor the intervention or the comparison?		
Judgement	**Research evidence**	**Additional considerations**
○ Favors the comparison ○ Probably favors the comparison ○ Does not favor either the intervention or the comparison ○ Probably favors the intervention ● Favors the intervention	The balance of effects appears to favor MLND over mediastinal lymph node MLNS. While the certainty of evidence is very low for overall survival, the observed hazard ratio (HR 0.74, 95% CI: 0.56 to 0.97) suggests a potential survival benefit with MLND, which exceeds the MCID of 3%. Additionally, undesirable effects do not appear to be substantially increased with MLND; in fact, certain complications (e.g., myocardial infarction, respiratory failure, atelectasis) may be reduced, though most evidence is of low certainty.	The panel decided in favour of the intervention, considering that the balance of effects appears to favour MLND over MLNS. Despite the very low certainty of evidence for overall survival, the observed hazard ratio suggests a clinically meaningful benefit, and the absence of a substantial increase in postoperative complications with MLND

○ Varies ○ Don't know		
Resources required		
Judgement	**Research evidence**	**Additional considerations**
○ Large costs ○ Moderate costs ● Negligible costs and savings ○ Moderate savings ○ Large savings ○ Varies ○ Don't know	No studies were identified that assessed the resources of MLND and MLNS in patients with lung cancer	In the absence of any studies supporting cost, the panel discussed that the difference in cost between two techniques would be negligible. Minimal increase in operative time, with no additional consumables used. Minor upskilling would be required for the human resource. Human resource, cost and upskilling were the three components considered for decision making
Certainty of evidence of required resources What is the certainty of the evidence of resource requirements (costs)?		
Judgement	**Research evidence**	**Additional considerations**

○ Very low ● Low ○ Moderate ○ High ○ No included studies	No studies were identified that assessed the resources of MLND and MLNS in patients with lung cancer	The panel's judgement was that there is low certainty of the evidence regarding resource requirements for MLND. This was due to limited and indirect cost data, variability in healthcare settings and surgical practices, and the absence of comprehensive economic evaluations specific to the context
Cost effectiveness Does the cost-effectiveness of the intervention favor the intervention or the comparison?		
Judgement	**Research evidence**	**Additional considerations**
○ Favors the comparison ○ Probably favors the comparison ○ Does not favor either the intervention or the comparison ○ Probably favors the intervention	No studies were identified that assessed the cost effectiveness of MLND and MLNS in patients with lung cancer	The panel's judgement was to favour the intervention despite the absence of direct evidence on cost-effectiveness of MLND versus MLNS in patients with lung cancer. This decision considered the potential clinical benefit and no substantial increase in postoperative complications, suggesting a likely acceptable cost-effectiveness profile, while acknowledging that contextual factors and resource availability may

● Favors the intervention ○ Varies ○ No included studies		influence economic value across settings.

Equity What would be the impact on health equity?		
Judgement	**Research evidence**	**Additional considerations**
○ Reduced ○ Probably reduced ● Probably no impact ○ Probably increased ○ Increased ○ Varies ○ Don't know	No studies were identified that assessed the equity of MLND and MLNS in patients with lung cancer	The panel's judgement was probably no impact on equity, as both MLNS and MLND are surgical staging techniques typically performed in tertiary care settings with similar requirements for infrastructure and specialist expertise. There is no clear evidence that recommending MLND over MLNS would disproportionately affect disadvantaged populations, and the intervention represents a modification to existing practice requiring minimal additional training, thereby not introducing significant new barriers to access.

Acceptability Is the intervention acceptable to key stakeholders?		
Judgement	**Research evidence**	**Additional considerations**
○ No ○ Probably no ○ Probably yes ● Yes ○ Varies ○ Don't know	No studies were identified that assessed the acceptability of MLND and MLNS in patients with lung cancer	While MLND is a more extensive and technically demanding procedure, the panel felt that it may be considered acceptable due to the potential survival advantage without significant increase in the postoperative complications, and superior staging.
Feasibility Is the intervention feasible to implement?		
Judgement	**Research evidence**	**Additional considerations**
○ No ○ Probably no ○ Probably yes ● Yes	No studies were identified that assessed the feasibility of MLND and MLNS in patients with lung cancer	Both MLNS and MLND are well-established procedures that are currently performed in thoracic surgical practice although MLNS is generally considered technically less demanding and quicker to perform.

○ Varies ○ Don't know		Their feasibility is further supported by the fact that they require similar surgical expertise and infrastructure, with no need for additional equipment or training for MLNS in centers capable of performing MLND.

Summary of judgements

	Judgement						
Problem	No	Probably no	Probably yes	**Yes**		Varies	Don't know
Desirable Effects	Trivial	Small	Moderate	**Large**		Varies	Don't know
Undesirable Effects	**Trivial**	Small	Moderate	Large		Varies	Don't know
Certainty of evidence	**Very low**	Low	Moderate	High			No included studies
Values	Important uncertainty or variability	Possibly important uncertainty or variability	Probably no important uncertainty or variability	**No important uncertainty or variability**			
Balance of effects	Favors the comparison	Probably favors the comparison	Does not favor either the intervention or the comparison	Probably favors the intervention	**Favors the intervention**	Varies	Don't know

	Judgement						
Resources required	Large costs	Moderate costs	**Negligible costs and savings**	Moderate savings	Large savings	Varies	Don't know
Certainty of evidence of required resources	Very low	**Low**	Moderate	High			No included studies
Cost effectiveness	Favors the comparison	Probably favors the comparison	Does not favor either the intervention or the comparison	Probably favors the intervention	**Favors the intervention**	Varies	No included studies
Equity	Reduced	Probably reduced	**Probably no impact**	Probably increased	Increased	Varies	Don't know
Acceptability	No	Probably no	Probably yes	**Yes**		Varies	Don't know
Feasibility	No	Probably no	Probably yes	**Yes**		Varies	Don't know

Type of recommendation

Strong recommendation against the intervention	Conditional recommendation against the intervention	Conditional recommendation for either the intervention or the comparison	Conditional recommendation for the intervention	**Strong recommendation for the intervention**
○	○	○	○	●

Conclusions

Recommendation
Mediastinal lymph node dissection is recommended as compared to mediastinal lymph node sampling, for treatment of patients with operable non-small cell lung cancer. Strength: Strong Certainty of evidence – Very low
Justification
The panel judged the desirable effects of mediastinal lymph node dissection to be large and the undesirable effects to be trivial. Cost-effectiveness was considered to favor dissection, and both acceptability and feasibility supported its use over sampling, contributing to the strength of the recommendation. Additionally, the panel concluded that favouring dissection over sampling would likely have no impact on health equity.
Research priorities

Given the absence of direct evidence on cost-effectiveness, equity, feasibility, and acceptability for mediastinal lymph node dissection (MLND) versus sampling (MLNS) in operable NSCLC, the following research priorities are recommended:

Health Economic Evaluations

Conduct formal cost–effectiveness and cost–utility analyses comparing MLND versus MLNS, incorporating Indian unit-cost data (operative time, hospital stay, complication management, and training/upskilling costs) and estimating QALY or life-year gains to inform resource-allocation decisions.

Equity-Focused Research

Investigate disparities in access to MLND, examining geographic (urban–rural), institutional (tertiary vs. district hospitals), and socioeconomic factors that influence whether patients receive systematic dissection versus sampling and identify strategies to ensure equitable staging.

Feasibility & Training Requirement Studies

Use implementation and hybrid effectiveness, implementation designs to assess the real-world practicability of MLND in diverse Indian surgical settings, focusing on:

a. Infrastructure and workflow: perioperative support services

b. Surgeon training needs: baseline skill assessment, upskilling programs, competency benchmarks

c. Long-term sustainability: integration into routine practice, continuing professional development pathways

Acceptability Studies

Undertake qualitative or mixed-method research with patients, caregivers, and thoracic surgeons to explore perceptions, preferred trade-offs (survival benefit vs. morbidity), and potential barriers or facilitators to adopting MLND over MLNS in routine practice.

List of Excluded Studies

Sr. No.	Citation of the study (Vancouver style only)	Reasons for exclusion
1.	Sun C, Liu Y, Zhang P, Wang X, Xu Y, Lin X, et al. Interim analysis of the efficiency and safety of neoadjuvant PD-1 inhibitor (sintilimab) combined with chemotherapy (nab-paclitaxel and carboplatin) in potentially resectable stage IIIA/IIIB non-small cell lung cancer: a single-arm, phase 2 trial. Journal of Cancer Research and Clinical Oncology. 2022 Feb 22;149(2):819–31.	Wrong comparator
2.	Dziedzic R. The role of sublobar resections in the treatment of early-stage non-small cell lung cancer-still awaiting evidence. J Thorac Dis. 2017 Nov;9(11):4146-4148.	Background article
3.	Toishi M, Yoshida K, Agatsuma H, Sakaizawa T, Eguchi T, Saito G, et al. Usefulness of vessel-sealing devices for ≤7 mm diameter vessels: a randomized controlled trial for human thoracoscopic lobectomy in primary lung cancer. Interact Cardiovasc Thorac Surg. 2014 Sep;19(3):448-55.	Wrong population
4.	Maniwa T, Kimura T, Ohue M, Okami J. Mediastinal lymph node dissection in older patients with non-small cell lung cancer. Surg Today. 2022 Mar;52(3):458-464.	Wrong study design
5.	Taylor M, Evison M, Clayton B, Grant SW, Martin GP, Shah R, et al. Adequacy of Mediastinal Lymph Node Sampling in Patients with Lung Cancer Undergoing Lung Resection. J Surg Res. 2022 Feb; 270:271-278.	Wrong study design
6.	Yoshida Y, Yotsukura M, Nakagawa K, Watanabe H, Motoi N, Watanabe SI. Surgical Results in Pathological N1 Nonsmall Cell Lung Cancer. Thorac Cardiovasc Surg. 2021 Jun;69(4):366-372.	Wrong study design
7.	Abughararah TZ, Jeong YH, Alabbood F, Chong Y, Yun JK, Lee GD, et al. Lobe-specific lymph node dissection in stage IA non-small-cell lung cancer: a retrospective cohort study. Eur J Cardiothorac Surg. 2021 Apr 29;59(4):783-790.	Wrong study design
8.	Katsumata S, Tane K, Suzuki J, Miyoshi T, Samejima J, Aokage K, et al. Mediastinal lymph node dissection for the elderly with clinical stage I non-small cell lung cancer. Gen Thorac Cardiovasc Surg. 2021 Dec;69(12):1560-1566.	Wrong study design
9.	De Giacomo T, Venuta F, Rendina EA. Role of lymphadenectomy in the treatment of clinical stage I non-small cell lung cancer. Thorac Surg Clin. 2007 May;17(2):217-21.	Wrong study design
10.	Isaka M, Kojima H, Imai T, Konno H, Mizuno T, Nagata T, et al. Lobe-specific nodal dissection with intraoperative frozen section analysis for clinical stage-I non-small cell lung cancer: a validation study by propensity score matching. Gen Thorac Cardiovasc Surg. 2022 Nov;70(11):977-984	Wrong study design
11.	Liu T, Liu H, Li Y. Systematic lymph node dissection is necessary for T1a non-small cell lung cancer. Asia Pac J Clin Oncol. 2015 Mar;11(1):49-53.	Wrong study design
12.	Chen J, Mao F, Song Z, Shen-Tu Y. [Retrospective study on lobe-specific lymph node dissection for patients with early-stage non-small cell lung cancer]. Zhongguo Fei Ai Za Zhi. 2012 Sep;15(9):531-8. Chinese.	Wrong study design

13.	Peng L, Deng HY, Yang Y. Lobe-specific Lymph Node Dissection for Clinical Stage IA Non-small-cell Lung Cancer: What do we know? Clin Lung Cancer. 2021 Sep;22(5):478-479.	Wrong study design
14.	Baisi A, Raveglia F, De Simone M, Cioffi U. Systemic lymphadenectomy is fundamental, especially in clinical N0 patients. Ann Thorac Surg. 2017 Oct;104(4):1436-7.	Wrong study design
15.	Zhao Y, Mao Y, He J, Gao S, Zhang Z, Ding N, et al. Lobe-specific Lymph Node Dissection in Clinical Stage IA Solid-dominant non-small-cell Lung Cancer: A Propensity Score Matching Study. Clin Lung Cancer. 2021 Mar;22(2): e201-e210.	Wrong outcome
16.	Ray MA, Fehnel C, Akinbobola O, Faris NR, Taylor M, Pacheco A, et al. Comparative Effectiveness of a Lymph Node Collection Kit Versus Heightened Awareness on Lung Cancer Surgery Quality and Outcomes. J Thorac Oncol. 2021 May;16(5):774-783.	Wrong outcome
17.	Long H, Tan Q, Luo Q, Wang Z, Jiang G, Situ D, et al. Thoracoscopic Surgery Versus Thoracotomy for Lung Cancer: Short-Term Outcomes of a Randomized Trial. Ann Thorac Surg. 2018 Feb;105(2):386-392.	Wrong outcome
18.	Zhou J, Liu C, Man S, Lyu M, Liao H, Chen N, et al. Comparison of the clinical benefits for non-small cell lung cancer patients between different volume of pleural lavage fluid following video-assisted thoracoscopic lobectomy and systematic mediastinal lymph node dissection: study protocol for a randomized controlled trial. Trials. 2020 Feb 27;21(1):232.	Wrong outcome
19.	Tada H. [Multimodality treatment for non-small cell lung cancer from the surgical standpoint]. Gan To Kagaku Ryoho. 1998 Jan;25(2):225-31.	Wrong outcome
20.	Zhai W, Duan F, Zheng Y, Yan Q, Dai S, Chen T, et al. Significance of accurate hilar and intrapulmonary lymph node examination and prognostication in stage IA-IIA non-small cell lung cancer, a retrospective cohort study. World J Surg Oncol. 2020 Sep 30;18(1):258.	Wrong outcome
21.	Annema JT, van Meerbeeck JP, Rintoul RC, Dooms C, Deschepper E, Dekkers OM, et al. Mediastinoscopy vs endosonography for mediastinal nodal staging of lung cancer: a randomized trial. JAMA. 2010 Nov 24;304(20):2245-52.	Wrong outcome
22.	Izbicki JR, Passlick B, Hosch SB, Kubuschock B, Schneider C, Busch C, et al. Mode of spread in the early phase of lymphatic metastasis in non-small-cell lung cancer: significance of nodal micrometastasis. J Thorac Cardiovasc Surg. 1996 Sep;112(3):623-30.	Wrong outcome
23.	Vansteenkiste JF, Cho BC, Vanakesa T, De Pas T, Zielinski M, Kim MS, et al. Efficacy of the MAGE-A3 cancer immunotherapeutic as adjuvant therapy in patients with resected MAGE-A3-positive non-small-cell lung cancer (MAGRIT): a randomised, double-blind, placebo-controlled, phase 3 trial. Lancet Oncol. 2016 Jun;17(6):822-835.	Wrong outcome

24.	Hamada A, Soh J, Hata A, Nakamatsu K, Shimokawa M, Yatabe Y, et al. Phase II Study of Neoadjuvant Concurrent Chemo-immuno-radiation Therapy Followed by Surgery and Adjuvant Immunotherapy for Resectable Stage IIIA-B (Discrete N2) non-small-cell Lung Cancer: SQUAT trial (WJOG 12119L). Clin Lung Cancer. 2021 Nov;22(6):596-600.	Wrong outcome
25.	Tournoy KG, De Ryck F, Vanwalleghem LR, Vermassen F, Praet M, Aerts JG, et al. Endoscopic ultrasound reduces surgical mediastinal staging in lung cancer: a randomized trial. Am J Respir Crit Care Med. 2008 Mar 1;177(5):531-5.	Wrong outcome
26.	O'Brien M, Paz-Ares L, Marreaud S, Dafni U, Oselin K, et al. Pembrolizumab versus placebo as adjuvant therapy for completely resected stage IB-IIIA non-small-cell lung cancer (PEARLS/KEYNOTE-091): an interim analysis of a randomised, triple-blind, phase 3 trial. Lancet Oncol. 2022 Oct;23(10):1274-1286.	Wrong outcome
27.	Huang J, Li C, Li H, Lv F, Jiang L, Lin H, et al. Robot-assisted thoracoscopic surgery versus thoracotomy for c-N2 stage NSCLC: short-term outcomes of a randomized trial. Transl Lung Cancer Res. 2019 Dec;8(6):951-958.	Wrong outcome
28.	Situ D, Long H, Tan Q, Luo Q, Wang Z, Jiang G, et al. OA13.02 Video-Assisted Thoracoscopic Surgery vs. Thoracotomy for Non-Small Cell Lung Cancer: Survival Outcome of a Randomized Trial. [cited 2024 Sep 11]; Available from: https://www.jto.org/article/S1556-0864(19)31161-X/fulltext	Wrong outcome
29.	D'Journo XB, Falcoz PE, Alifano M, Le Rochais JP, Danville T, Massard G, et al. Oropharyngeal and nasopharyngeal decontamination with chlorhexidine gluconate in lung cancer surgery: a randomized clinical trial. Intensive Care Med. 2018 May;44(5):578-587.	Wrong outcome
30.	Liu L, Liao H. A multi-center, prospective, randomized controlled clinical trial: Comparison between wedge resection and segmentectomy in the surgical treatment of ground glass opacity-dominant stage IA non-small cell lung cancer. J Thorac Oncol. 2018 Apr;13(4 Suppl)	Wrong outcome
31.	Eberhardt WE, Pöttgen C, Gauler TC, Friedel G, Veit S, Heinrich V, et al. Phase III Study of Surgery Versus Definitive Concurrent Chemoradiotherapy Boost in Patients with Resectable Stage IIIA(N2) and Selected IIIB Non-Small-Cell Lung Cancer After Induction Chemotherapy and Concurrent Chemoradiotherapy (ESPATUE). J Clin Oncol. 2015 Dec 10;33(35):4194-201.	Wrong outcome
32.	Karaiskos T, Ananiadou O, Diplaris K, Michael N, Sarigiannis G, Drossos G. Complete thoracoscopic lobectomy: A new era at the "G. Papanikolaou" hospital. Pneumon. 2013;26(2):157-161.	Wrong outcome
33.	Baumann M, Herrmann T, Koch R, Matthiessen W, Appold S, Wahlers B, et al. Final results of the randomized phase III CHARTWEL-trial (ARO 97-1) comparing hyperfractionated-accelerated versus conventionally fractionated radiotherapy in non-small cell lung cancer (NSCLC). Radiother Oncol. 2011 Jul;100(1):76-85.	Wrong outcome

34.	Patel YS, Hanna WC, Fahim C, Shargall Y, Waddell TK, Yasufuku K, et al. RAVAL trial: Protocol of an international, multi-centered, blinded, randomized controlled trial comparing robotic-assisted versus video-assisted lobectomy for early-stage lung cancer. PLoS One. 2022 Feb 2;17(2):e0261767.	Wrong intervention
35.	Huang J, Luo Q, Tan Q, Lin H, Qian L, Ding Z. Evaluation of the surgical fat-filling procedure in the treatment of refractory cough after systematic mediastinal lymphadenectomy in patients with right lung cancer. J Surg Res. 2014 Apr;187(2):490-5.	Wrong intervention
36.	Huynh C, Rayes R, Gaudreau P, Shieh B, Walsh L, Spicer J. Phase II randomized trial of neoadjuvant pembrolizumab +/- chemotherapy for operable stage IA3-IIA non-small cell lung cancer. J Thorac Oncol. 2021 Mar;16(3 Suppl)	Wrong intervention
37.	Vallieres E, Zielinski M, Stoelben E, Wu YL, Fu JH, Costas K, et al. Surgical approach and disease recurrence in NSCLC patients in the MAGRIT study. J Thorac Oncol. 2015 Jan;10(9 Suppl)	Wrong intervention
38.	Herbst RS, Majem M, Barlesi F, Carcereny E, Chu Q, Monnet I, et al. COAST: An Open-Label, Phase II, Multidrug Platform Study of Durvalumab Alone or in Combination With Oleclumab or Monalizumab in Patients With Unresectable, Stage III Non-Small-Cell Lung Cancer. J Clin Oncol. 2022 Oct 10;40(29):3383-3393.	Wrong intervention
39.	Westeel V, Foucher P, Scherpereel A, Domas J, Girard P, Trédaniel J, et al. Chest CT scan plus x-ray versus chest x-ray for the follow-up of completely resected non-small-cell lung cancer (IFCT-0302): a multicentre, open-label, randomised, phase 3 trial. Lancet Oncol. 2022 Sep;23(9):1180-1188.	Wrong intervention
40.	Mok TS, Cheng Y, Zhou X, Lee KH, Nakagawa K, Niho S, et al. Updated Overall Survival in a Randomized Study Comparing Dacomitinib with Gefitinib as First-Line Treatment in Patients with Advanced Non-Small-Cell Lung Cancer and EGFR-Activating Mutations. Drugs. 2021 Feb;81(2):257-266.	Wrong intervention
41.	Goldberg SB, Redman MW, Lilenbaum R, Politi K, Stinchcombe TE, Horn L, et al. Randomized Trial of Afatinib Plus Cetuximab Versus Afatinib Alone for First-Line Treatment of *EGFR*-Mutant Non-Small-Cell Lung Cancer: Final Results From SWOG S1403. J Clin Oncol. 2020 Dec 1;38(34):4076-4085.	Wrong intervention
42.	Zhou Q, Cheng Y, Yang JJ, Zhao MF, Zhang L, Zhang XC, et al. Pemetrexed versus gefitinib as a second-line treatment in advanced nonsquamous nonsmall-cell lung cancer patients harboring wild-type EGFR (CTONG0806): a multicenter randomized trial. Ann Oncol. 2014 Dec;25(12):2385-2391.	Wrong intervention
43.	Maniwa T, Okumura T, Isaka M, Nakagawa K, Ohde Y, Kondo H. Recurrence of mediastinal node cancer after lobe-specific systematic nodal dissection for non-small-cell lung cancer. Eur J Cardiothorac Surg. 2013 Jul;44(1): e59-64. doi: 10.1093/ejcts/ezt195. Epub 2013 May 3. PMID: 23644712.	Wrong comparator

RADICAL LOCAL TREATMENT OF THE PRIMARY & METASTATIC SITES IN PATIENTS WITH OLIGOMETASTATIC NON-SMALL CELL LUNG CANCE

Key Question in PICO format

In patients with oligometastatic non-small cell lung cancer (NSCLC), what is the comparative effectiveness of radical local treatment of the primary & metastatic sites compared to systemic therapy alone?
Patient or population: Patients with Oligometastatic Non-small cell Lung cancer
Subgroups: Single metastatic sites vs more than one metastatic sites
Site(s) of metastasis(es)
Setting: Tertiary Care Hospitals
Intervention: Radical local treatment in addition to systemic therapy (chemo /immune /targeted)
Comparison: Systemic therapy (chemo/immune/targeted) alone

Search Strategy

a) PubMed: (As on date 31/5/2024)

PubMed	
#1	"carcinoma, non-small-cell lung"[MeSH Terms] OR "non small cell lung cancer"[Title/Abstract] OR "non small cell"[Title/Abstract] OR "nonsmall cell"[Title/Abstract] OR nsclc[Title/Abstract]
#2	oligometasta*[Title/Abstract] OR "oligo-metastasis"[Title/Abstract] OR "oligo-metastases"[Title/Abstract] OR "oligo-metastatic"[Title/Abstract] OR oligoprogress*[Title/Abstract] OR "oligo-progression"[Title/Abstract] OR "oligo-progressive"[Title/Abstract] OR oligopersisten*[Title/Abstract] OR "oligo-persistent"[Title/Abstract] OR "oligopersistence"[Title/Abstract] OR oligorecurren*[Title/Abstract] OR "oligo-recurrent"[Title/Abstract] OR "oligo-recurrence"[Title/Abstract] OR "isolated metastasis"[Title/Abstract] OR "isolated metastases"[Title/Abstract] OR "limited metastasis"[Title/Abstract] OR "limited metastases"[Title/Abstract] OR "single organ metastasis"[Title/Abstract] OR "single organ metastases"[Title/Abstract] OR "solitary metastasis"[Title/Abstract] OR "solitary metastases"[Title/Abstract]
#3	(randomized controlled trial [pt] OR controlled clinical trial [pt] OR randomized [tiab] OR placebo [tiab] OR ("clinical trials as topic"[MeSH Terms]) OR randomly [tiab] OR trial [ti]) NOT (animals [mh] NOT humans [mh])
#4	#1 AND #2 AND #3

b) EMBASE: (As on date 31/05/2024)

Embase	
#1	'non small cell lung cancer'/exp OR 'non small cell lung cancer':ti,ab OR 'non small cell':ti,ab OR 'nonsmall cell':ti,ab OR nsclc:ti,ab
#2	'oligometastasis'/exp OR oligometasta*:ti,ab OR oligo-metastasis:ti,ab OR oligo-metastases:ti,ab OR oligo-metastatic:ti,ab OR oligoprogress*:ti,ab OR oligo-progression:ti,ab OR oligo-progressive:ti,ab OR oligopersisten*:ti,ab OR oligo-persistent:ti,ab OR oligopersistence:ti,ab OR oligorecurren*:ti,ab OR oligo-recurrent:ti,ab OR oligo-recurrence:ti,ab OR 'isolated metastasis':ti,ab OR 'isolated metastases':ti,ab OR 'limited metastasis':ti,ab OR 'limited metastases':ti,ab OR 'single organ metastasis':ti,ab OR 'single organ metastases':ti,ab OR 'solitary metastasis':ti,ab OR 'solitary metastases':ti,ab
#3	(('RANDOMIZED CONTROLLED TRIAL'/EXP OR 'SINGLE BLIND PROCEDURE'/EXP OR 'DOUBLE BLIND PROCEDURE'/EXP OR 'CROSSOVER PROCEDURE'/EXP) AND [EMBASE]/LIM OR ((RANDOM*:AB,TI OR PLACEBO*:AB,TI OR CROSSOVER*:AB,TI OR 'CROSS OVER':AB,TI OR ALLOCAT*:AB,TI OR TRIAL:TI OR ((DOUBL* NEXT/1 BLIND*):AB,TI)) AND [EMBASE]/LIM)) NOT (('ANIMAL'/DE OR 'NONHUMAN'/DE OR 'ANIMAL EXPERIMENT'/DE) AND [EMBASE]/LIM NOT ('HUMAN'/DE AND [EMBASE]/LIM))
#4	#1 AND #2 AND #3

c) SCOPUS: (As on date 31/05/2024)

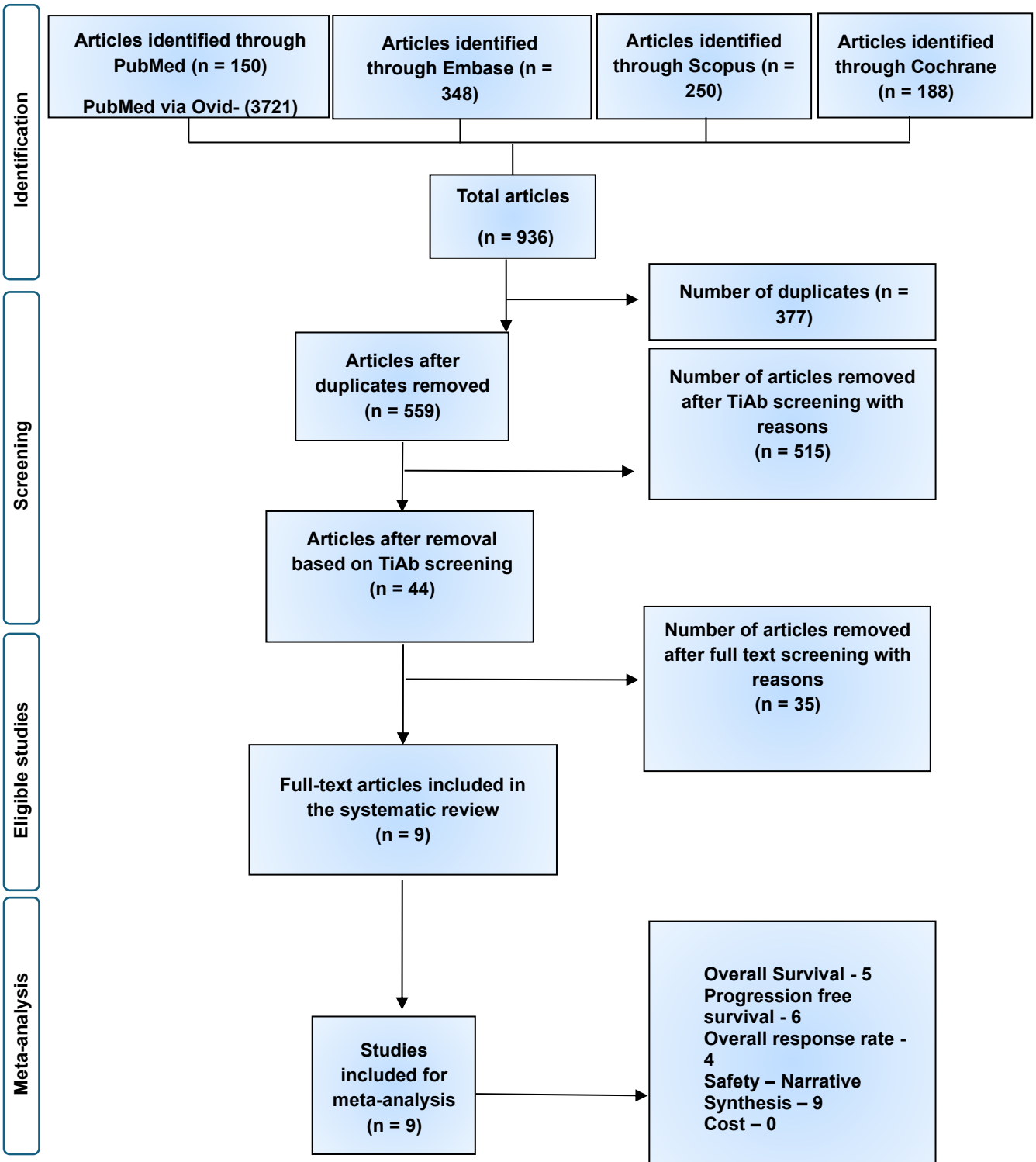
Scopus		
	#1	TITLE-ABS("non small cell lung cancer") OR TITLE-ABS("non small cell") OR TITLE-ABS("nonsmall cell") OR TITLE-ABS(nsclc)
	#2	TITLE-ABS(oligometasta*) OR TITLE-ABS(oligo-metastasis) OR TITLE-ABS(oligo-metastases) OR TITLE-ABS(oligo-metastatic) OR TITLE-ABS(oligoprogress*) OR TITLE-ABS(oligo-progression) OR TITLE-ABS(oligo-progressive) OR TITLE-ABS(oligopersisten*) OR TITLE-ABS(oligo-persistent) OR TITLE-ABS(oligopersistence) OR TITLE-ABS(oligorecurren*) OR TITLE-ABS(oligo-recurrent) OR TITLE-ABS(oligo-recurrence) OR TITLE-ABS("isolated metastasis") OR TITLE-ABS("isolated metastases") OR TITLE-ABS("limited metastasis") OR TITLE-ABS("limited metastases") OR TITLE-ABS("single organ metastasis") OR TITLE-ABS("single organ metastases") OR TITLE-ABS("solitary metastasis") OR TITLE-ABS("solitary metastases")
	#3	(TITLE-ABS(random*) OR TITLE-ABS(placebo) OR TITLE-ABS(blind*) OR TITLE-ABS(mask*) OR TITLE-ABS(trial*))

	#4	#1 AND #2 AND #3

d) Cochrane Central: (As on date 31/05/2024)

Cochrane Central	
#1	MeSH descriptor: [Carcinoma, Non-Small-Cell Lung] explode all trees
#2	non small cell lung cancer:ti,ab OR "non small cell":ti,ab OR "nonsmall cell":ti,ab OR nsclc:ti,ab
#3	oligometasta*:ti,ab OR oligo-metastasis:ti,ab OR oligo-metastases:ti,ab OR oligo-metastatic:ti,ab OR oligoprogress*:ti,ab OR oligo-progression:ti,ab OR oligo-progressive:ti,ab OR oligopersisten*:ti,ab OR oligo-persistent:ti,ab OR oligopersistence:ti,ab OR oligorecurren*:ti,ab OR oligo-recurrent:ti,ab OR oligo-recurrence:ti,ab OR "isolated metastasis":ti,ab OR "isolated metastases":ti,ab OR "limited metastasis":ti,ab OR "limited metastases":ti,ab OR "single organ metastasis":ti,ab OR "single organ metastases":ti,ab OR "solitary metastasis":ti,ab OR "solitary metastases":ti,ab
#4	(#1 OR #2) AND #3

PRISMA flow diagram



Summary of Included Studies

Sr. No.	Study ID	Study characteristics	Population characteristics			Intervention Characteristics	Comparator characteristics	Outcome characteristics
			Eligibility criteria	Demographics	Site(s) of Metastasis(es)			
1	Gomez et al. 2019	Place: Three institutes in United States of America and Canada Funding: MD Anderson Lung Cancer Priority Fund, MD Anderson Cancer Center Moon Shot Initiative, and Cancer Center Support (Core), National Cancer Institute, National Institutes of Health.	Inclusion Criteria: 1.An Eastern Cooperative Oncology Group performance status score of 2 or less, 2.Received standard first-line systemic therapy. Exclusion criteria: 1.Patients who had a complete response to chemotherapy with no lesions amenable to ablation.	Mean age: Intervention: 64 ± 10 Control: 63 ± 10 Sex distribution: Intervention: 12/13 Control: 10/14	CNS and outside CNS`	Patients who were randomly allocated to the local consolidative therapy group were treated with the intent to ablate all residual disease (primary tumor, lymph nodes, and metastatic sites as appropriate) with surgery, radiotherapy, or both. The type of local consolidative therapy was determined in consultation with multi-disciplinary teams. The choice of dose fractionation regimen was	The treating physician chose maintenance treatment from a predefined set of standard-of-care options.	1.Overall Survival

						made by the treating radiotherapist, with curative intent when possible. Stereotactic ablative body radiotherapy, intermediate hypofractionated radiotherapy, and concurrent chemoradiotherapy were allowed.		
2	Welsh et al. 2020	Place: United States of America Funding: Funding for and access to pembrolizumab was provided by Merck. Supported in part by NIH/NCI grant no. P30CA016672 to The University of Texas MD Anderson Cancer Center.	Inclusion Criteria: 1.Pathologically confirmed mNSCLC ,with one to four lung or liver lesions amenable to RT and at least one additional non-contiguous lesion amenable to radiographic evaluation for out-of-field responses. 2.Patients with brain metastases after undergoing	Sex distribution: Chemotherapy with SBRT: 13/6 Chemotherapy without SBRT: 16/5 Chemotherapy with RT: 13/8 Chemotherapy without RT: 9/10	Not Mentioned	Pembrolizumab + SBRT Or Pembrolizumab + RT	Pembrolizumab (salvage SBRT or RT if applicable)	1.Progression Free survival 2.Overall Response rate

			individualized treatment were included except for those presenting with neurological symptoms or requiring corticosteroids. Exclusion criteria: 1.Patients with brain metastases after presenting neurological symptoms or requiring corticosteroids. 2.A history of immunodeficiency or autoimmune disease.					
3	Peng et al. 2023	Place: Four institutes in China Funding: This work was supported by the National Science Foundation of China (No.	Inclusion Criteria: 1.Patients who had received first-line first-generation EGFR-TKIs for3 months and achieved stable	Mean age: Intervention 52.7 ±12 Control: 59.2 ±10.2 Sex distribution: Intervention: 11/19 Control: 12/19	Lung, mediastinum lymph node, liver, bone, adrenal gland, and brain	SBRT was performed 3 months after the EGFR-TKI administration in the study group with patients who had achieved SD or	Patients were treated with first-generation EGFR-TKIs including gefitinib, erlotinib, and Icotinib. The administration is as follow: Gefitinib or erlotinib or Icotinib, until disease	1.Overall Survival 2. Progression free Survival

		82172825, No. 82001785) and Chinese Society of Clinical Oncology Foundation (No. Y-BMS2019-070, Y-tongshu2021/qn-0082)	disease (SD) or partial response 2.Patients with measurable disease at baseline 3.No more than 5 metastatic Foci 4.Adequate normal organ and marrow function for EGFR-TKI treatment and radiotherapy Exclusion criteria: 1.Previous treatment with systemic therapy, such as targeted therapy, chemotherapy, or radiotherapy for the tumor site 2.Intolerance of radiotherapy or targeted therapy.			PR. A radiotherapy dose of 30–50 Gy in 5 fractions was recommended for the primary or metastatic lesions, or both, according to the investigators. It was recommended that SBRT be completed before the end of the fourth month of TKI treatment and that TKI be continued during SBRT.	progression or unable to tolerate	

4	Iyengar et al. 2018	Place: United States of America Funding: University of Texas Southwestern Medical Center	Inclusion Criteria: 1.Patients must have received 4 to 6 cycles of first-line platinum-based chemotherapy, achieving stable disease or partial response on imaging by RECIST (Response Evaluation Criteria In Solid Tumors) Exclusion criteria: 1.Previous treatment with systemic therapy, such as targeted therapy, chemotherapy, or radiotherapy for the tumor site 2.Intolerance of radiotherapy or targeted therapy	Mean age: Intervention 52.7 ±12 Control: 59.2 ±10.2 Sex distribution: Intervention: 9/5 Control: 11/4	brain, liver, lung, bone, and pancreas	SAbR to all sites of gross disease (including SAbR or hypo fractionated radiation to the primary) followed by maintenance chemotherapy (started within 1 week after all radiation, Maintenance chemotherapy included erlotinib, pemetrexed, docetaxel, gemcitabine, or bevacizumab)	Maintenance chemotherapy included erlotinib, pemetrexed, docetaxel, gemcitabine, or bevacizumab, initiated within 1week of randomization	1.Progression free survival

5	Shan et al. 2021	Place: China Funding: National Natural Science Foundation of China (81473071); Support Project for Young Teachers of Jining Medical University (JY2016KJ053Y); Shandong Medical and Health Science and Technology Development Plan Project (2017WS717)	Inclusion criteria: 1.Patients without radiotherapy, chemotherapy, or molecular-targeted therapy Exclusion criteria: 1.Patients with pathologically diagnosed small cell lung cancer. 2.Patients with stage I-IA by TNM stage who were able to undergo surgical resection 3. Patients who had been treated with chemotherapy or radiotherapy or surgery 4.Senile and weak patients who were not expected to tolerate interventional therapy and chemotherapy	Mean age: Intervention: 63.5 Control: 70 Sex distribution: Intervention: 9/5 Control: 11/4	NSCLC with hepatic solitary metastasis only	CT-guided microwave ablation for hepatic metastasis after 2 cycles of chemotherapy, then, 2 cycles of chemotherapy were performed and CT-guided microwave ablation was used to treat the pulmonary lesions, followed by another 2 cycles of chemotherapy.	The GP protocol was used in NSCLC patients with squamous cell carcinoma confirmed histologically: Gemcitabine, Cisplatin; or DP protocol: Docetaxel, Cisplatin. 1. The AP protocol was used in NSCLC patients with adenocarcinoma confirmed histologically: Pemetrexed, Cisplatin; or DP protocol: Docetaxel, Cisplatin.	1.Overall Response rate

6	Tsai et al. 2023	Place: United States of America Funding: National Cancer Institute	Inclusion criteria: 1.Metastatic disease detected on imaging and histologically confirmed breast cancer or NSCLC 2.Receipt of at least first-line systemic therapy, including maintenance therapies. 3.Extracranial oligo progression 4.Potential for all sites of oligo progression to be safely treated. 5.Patients with brain metastases could receive standard-of-care brain radiation before enrolment Exclusion criteria:	Mean age: Intervention: 71 Control: 70 Sex distribution: Intervention: 12/19 Control: 16/12	breast,lung, brain	The treating radiation oncologist determined the radiotherapy dose based on clinical parameter considerations, including tumor size and location. In most instances, regimens ranged from 27–30 Gy in three fractions to 30–50 Gy in five fractions. Other fractionation schemes were used infrequently, typically in patients whose lesions were in a location deemed unsafe to have the suggested radiation doses due to nearby organs at risk. No rigid tumor size cutoff for SBRT was set; however, the	Standard-of-care systemic therapy per physician's discretion.	1.Progression free survival

			1.leptomeningeal disease 2.Serious medical comorbidities precluding radiotherapy. 3.Re-irradiation to the same tumor location was not allowed.			lesion's diameter should typically be less than 4 cm.		
7	Lim et al. 2014	Place: South Korea Funding: This work was supported in part by Samsung Biomedical Research Institute Grant (SMX1132531) and by Elekta Korea research funds.	Inclusion criteria: 1.All patients had 1 to 4 parenchymal brain metastases by contrast-enhanced MRI, each with a maximum diameter of no more than 3cm with brain edema grade 0-1 2.None of the patients had prior surgical treatment or radiotherapy for brain metastases and	Mean age: Intervention: 58 Control: 57 Sex distribution: Intervention: 35/14 Control: 36/13	Cranial and extra cranial	The treatment of SRS involves a single high dose of stereotactically focused radiation. Gamma knife radiosurgery (GKS) is SRS using γ-rays from radioactive cobalt-60 installed in Gamma Knife (Elekta Instruments, Stockholm, Sweden).	3-week cycles of the following intravenous chemotherapy: cisplatin on day 1 plus gemcitabine on days 1 and 8 cisplatin plus pemetrexed or docetaxel on day 1 or cisplatin plus paclitaxel on day 1 or cisplatin on day 1 plus etoposide on days 1–3. Patients who were ineligible for cisplatin treatment received carboplatin.	1.Overall Survival 2. Overall Response rate

			leptomeningeal metastases Exclusion criteria: 1.Patients with uncontrolled extra-cranial disease 2.Severe comorbid illnesses 3.Active infections.					
8	Theelen et al. 2019	Place: 3 centres in Netherlands Funding: This study was an investigator-initiated trial, designed by the authors and financially supported by an unrestricted grant from Merck Sharp & Dohme that included medication supply.	Inclusion criteria: 1.At least 2 separate lesions were required, one of which was measurable according to the Response Evaluation Criteria in Solid Tumors and suitable for biopsy, and the other of which was amenable to irradiation Exclusion criteria: 1.Radiotherapy to any tumor site within 6	Mean age: Intervention: 62 Control:62 Sex distribution: Intervention: 9/12 Control: 17/9	Lung, metastasis Lymph node, intra thoracic, Lymph node, extrathoracic, Adrenal, Bone, Lung, primary tumor, Cutaneous, Liver, Pleural Retroperitoneal	SBRT High dose radiation (SBRT) followed by pembrolizumab treatment within 7 days after completion. Moreover, the minimal size of the tumor should be at least 0.5 cm with a maximum of 5 cm and radiotherapy treatment will be given 1-2 weeks prior to start of pembrolizumab. The designated tumor will receive	The dose amount required to prepare the pembrolizumab infusion solution will be four vials containing 50 mg.	1.Overall Survival 2. Progression free Survival 3. Overall Response rate

			months before randomization 2.Known, active central nervous system metastases and/or carcinomatous meningitis 3.Untreated driver alterations of epidermal growth factor receptor or anaplastic lymphoma kinase 4.Active autoimmune or interstitial lung disease			a treatment dose of 24 Gy, administered in fractions of 8 Gy on alternate days with a maximal overall treatment time of 10 days.		
9	Wang et al., 2022	Place: Five centres in China Funding: This study was supported in part by the National Science and Technology Foundation (No. 3035031263),	Included criteria: 1. All patients were required to have biopsy-proven EGFRm adenocarcinoma Exclusion criteria: 1.Presence of brain metastases as	Mean age: Intervention: 67 Control: 63 Sex distribution: Intervention: 25/43 Control: 26/39	Abdomen, contralateral lung	RT was directed to all metastases plus the primary tumor/involved regional nodes on imaging; it was performed in 5 fractions using well-recognized principles, such as 3-dimensional CT simulation, custom	All patients received a first-generation TKI (gefitinib, erlotinib, or icotinib) based on the discretion of the treating oncologist. TKI dose adjustment or interruption was allowed after grade 3-4 adverse events and was performed individually per the treating oncologist.	1.Overall Survival 2. Progression free Survival

		Sichuan Academy of Medical Sciences & Sichuan Provincial People's Hospital (No. 30305031017P), the Clinical Research and Transformation Fund of Sichuan Provincial People's Hospital (2021LY25), the Sichuan Science and Technology Office (No. 3050410336), and the Chengdu Science and Technology Innovation Research and Development Project	detected on contrast-enhanced MRI 2.prior irradiation to the thorax or metastatic sites 3.history of previous malignancies, prior receipt of any test drugs or investigational compounds within 4 weeks 4.Inadequate bone marrow or hepatorenal function, severe or uncontrolled cardiovascular comorbidities, any contraindications to receiving TKI therapy.			immobilization techniques, and daily image guidance. Because the total prescribed dose is highly dependent on tumor location and/or size, we allowed for a dose of 25-40 Gy (10-12), generally using the maximum dose that did not exceed 5-fraction dose tolerances to adjacent organs at risk.		

Data Extraction

Name	Local Consolidative Therapy Vs. Maintenance Therapy or Observation for Patients With Oligometastatic Non–Small-Cell Lung Cancer:Long-Term Results of a Multi-Institutional Phase II, Randomized Study
Author	Gomez et al., 2019
Study Type	Multicentre, randomised, controlled, phase 2 study
Number of Participants	49
Duration of study follow up (in months)	38.8 months (range, 28.3 to 61.4 months)
Inclusion Criteria	Diagnosis of pathologically confirmed NSCLC, stage IV disease according to the 7th edition of the American Joint Committee on Cancer staging system, three or fewer metastases, not including the primary tumour (as defined below), an Eastern Cooperative Oncology Group (ECOG) performance status score of 2 or less, were 18 years or older, and had received standard first-line systemic therapy, defined as four or more cycles of platinum doublet chemotherapy, erlotinib or another approved first-line EGFR tyrosine kinase inhibitor for 3 months or longer if the patient was known to harbour an EGFR mutation, or crizotinib for 3 months or longer if the patient was known to have an ALK rearrangement. Patients had no disease progression before randomization
Exclusion Criteria	Bevacizumab was not allowed within 2 weeks of the initiation of the radiotherapy course. Patients with malignant pleural eff usion or signifi cant third-space fluid that could not be controlled by drainage were excluded. Patients who had a history of uncontrolled angina, arrhythmias, or congestive heart failure also were excluded. Patients who had a complete response to chemotherapy with no lesions amenable to ablation (including the primary site) were also not eligible for randomization.
Recruitment/Selection of Patients	-
Intervention	Local consolodative therapy

Outcome reported with time points	The primary outcome, progression-free survival, was defined from the time of randomization to the time of disease progression or death, whichever occurred first. The secondary outcomes for the study were overall survival, defined as the time of randomization to the time of death from any cause, safety and tolerability, time to progression of previous metastatic lesions, defined from the time of randomisation to the progression of metastatic lesions or death, whichever occurred first, time to appearance of new metastatic lesions, defined as the time of randomization to the development of a previously unknown lesion or death, whichever occurred first, and quality of life
Funding	MD Anderson Lung Cancer Priority Fund, MD Anderson Cancer Center Moon Shot Initiative, and Cancer Center Support (Core), National Cancer Institute, National Institutes of Health.
ROB 2 Assessment	Randomisation process - Low
	Deviations from the intended interventions - Low
	Missing outcome data - Low
	Measurement of the outcome - Low
	Selection of the reported result - Low
	Overall - Low

Name	**Pembrolizumab with or without radiation therapy for metastatic non- small cell lung cancer: A randomized phase I/II trial**
Author	Welsh et al., 2020 (SBRT)
Study Type	Randomized phase I/II trial
Number of Participants	40
Duration of study follow up (in months)	20.4 months

Inclusion Criteria	Eligible patients were at least 18 years of age and had pathologically confirmed mNSCLC (PD-L1 testing was not mandated, but generally done when adequate tissue was available), with one to four lung or liver lesions amenable to RT and at least one additional non-contiguous lesion amenable to radiographic evaluation for out-of-field responses. Both newly diagnosed and previously treated cases were eligible. Prior RT and systemic therapy were allowed unless they precluded safe administration of immune radiotherapy on our study protocol. Patients with brain metastases after undergoing individualized treatment were included except for those presenting with neurological symptoms or requiring corticosteroids.
Exclusion Criteria	Patients with brain metastases after presenting with neurological symptoms or requiring corticosteroids. Notable exclusion criteria included a history of immunodeficiency or autoimmune disease.
Recruitment/Selection of Patients	-
Intervention	SBRT
Outcome reported with time points	The primary outcome, progression-free survival, was defined from the time of randomization to the time of disease progression or death, whichever occurred first. The secondary outcomes for the study were overall survival, defined as the time of randomization to the time of death from any cause, safety and tolerability, time to progression of previous metastatic lesions, defined from the time of randomisation to the progression of metastatic lesions or death, whichever occurred first, time to appearance of new metastatic lesions, defined as the time of randomization to the development of a previously unknown lesion or death, whichever occurred first, and quality of life
Funding	Funding for and access to pembrolizumab was provided by Merck. Supported in part by NIH/NCI grant no. P30CA016672 to The University of Texas MD Anderson Cancer Center.
ROB 2 Assessment	Randomisation process - Low
	Deviations from the intended interventions - Low
	Missing outcome data - Low

	Measurement of the outcome - Low
	Selection of the reported result - Low
	Overall - Low

Name	**EGFR-TKIs plus stereotactic body radiation therapy (SBRT) for stage IV Non-Small cell lung cancer (NSCLC): A prospective, multicentre study**
Author	Peng et al., 2023
Study Type	Investigator initiated, multicenter, openlabel, parallelgroup, phase 2, randomized study
Number of Participants	62
Duration of study follow up (in months)	29.6 Months
Inclusion Criteria	Patients were required to be in good performance status (Eastern Cooperative Oncology Group [ECOG] score 0–2), with biopsyproven metastatic NSCLC (Stage IV), and with an EGFR sensitive mutation (exon 19 deletion or exon 21 L858R). Further inclusion criteria included 1) Patients who had received first-line first generation EGFR-TKIs such as erlotinib, gefitinib, or icotinib for 3 months and achieved stable disease (SD) or partial response (PR); 2) Age above 18 years; 3) Patients with measurable disease at baseline; 4) No more than 5 metastatic foci; and 5) Adequate normal organ and marrow function for EGFR-TKI treatment and radiotherapy
Exclusion Criteria	The exclusion criteria included previously treatment with systemic therapy such as targeted therapy, chemotherapy or radiotherapy for the tumor site, intolerance of radiotherapy or targeted therapy, and pregnancy or lactation
Recruitment/Selection of Patients	Patients were enrolled at four hospitals (Tongji Hospital, Wuhan Union Hospital, Renmin Hospital of Wuhan University, and Hubei Cancer Hospital) in China
Intervention	SBRT with EGFR-TKI

Outcome reported with time points	The primary endpoint of this trial was progression-free survival, defined as the time from the induction randomization to either disease progression or death due to any cause, whichever came first. Prespecified secondary endpoints included: overall survival, defined as the time from randomization to death from any cause, and toxicity, assessed by the National Cancer Institute Common Terminology Criteria for Adverse Events Version 3.0 (CTCAE v3.0). Measurable lesions were evaluated according to RECIST 1.1
Funding	This work was supported by the National Science Foundation of China (No. 82172825, No. 82001785) and Chinese Society of Clinical Oncology Foundation (No. Y-BMS2019-070, Y-tongshu2021/qn-0082)
ROB 2 Assessment	Randomisation process - Low
	Deviations from the intended interventions - Low
	Missing outcome data - Low
	Measurement of the outcome - Low
	Selection of the reported result - Low
	Overall - Low

Name	**Consolidative Radiotherapy for Limited Metastatic Non–Small Cell Lung Cancer**
Author	Iyengar et al., 2018
Study Type	Phase 2 Randomized Clinical Trial
Number of Participants	29
Duration of study follow up (in months)	9.6 months
Inclusion Criteria	18 years or older, had a Karnofsky Performance Status score of 70 or better, and had biopsy-proven metastatic NSCLC. Patients must have received 4 to 6 cycles of first-line platinum-based chemotherapy, achieving stable disease or a partial response on imaging by RECIST (Response Evaluation Criteria In Solid Tumors)

Exclusion Criteria	Those receiving first-line targeted therapy for EGFR positive and/or ALK-positive NSCLC were excluded, Individuals were ineligible if previously irradiated primary disease progressed within 3 months of that treatment. Patients with untreated and/or uncontrolled brain metastases or disease involving the gastrointestinal tract and skin were ineligible
Recruitment/Selection of Patients	Patients were assessed within 21 to 42 days following completion of first-line chemotherapy with repeat diagnostics including computed tomography (CT) and/or positron emission tomography (PET)-CT
Intervention	SABR with Chemotherapy
Outcome reported with time points	The primary end point was PFS; secondary end points included toxic effects, local and distant tumor control, patterns of failure, and overall survival
Funding	Choy. Administrative, technical, or material support: Iyengar, Gerber, Hughes, Cheedella, Westover, Pulipparacharuvil, Choy, Timmerman
ROB 2 Assessment	Randomisation process - Some concerns
	Deviations from the intended interventions - Low
	Missing outcome data - Low
	Measurement of the outcome - Low
	Selection of the reported result - Low
	Overall - Some concerns

Name	**Chemotherapy combined with intermittent microwave ablation in the treatment of oligometastatic non-small cell lung cancer**
Author	Shan et al., 2021
Study Type	Randomised comparative study
Number of Participants	67

Duration of study follow up (in months)	6 months
Inclusion Criteria	1: Pathological diagnosis of lung cancer patients, also including patients with initial treatment; 2: Pulmonary solitary lesions with observable evaluation; with wild-type EGFR/ALK/ROS1; 3: Stage IV NSCLC with hepatic solitary metastasis only; 4: Patients without radiotherapy, chemotherapy, or molecular targeted therapy 3 weeks before treatment; 5: Normal function of heart and lung; 6: 18-70 years old regardless of gender; 7: The survival time was expected to be over 3 months; 8: Good physical condition, Karnofsky performance scale (KPS) score >70 points; 9: Patients with no serious diabetes or coagulopathy; 10: Routine examination showed no interventional treatment and chemotherapy contraindication
Exclusion Criteria	1: Patients with pathologically diagnosed small cell lung cancer; 2: Patients with stage I-IIIA by TNM stage who were able to undergo surgical resection; 3: Patients who had been treated with chemotherapy or radiotherapy or surgery; 4: Senile and weak patients who were not expected to tolerate interventional therapy and chemotherapy and were expected to survive for <6 months; 5: KPS score <60 points; 6: Patients with heart, liver, kidney and other serious dysfunctions, or combined with diabetes and coagulopathy; 7: Pregnant and lactating women and all unmarried young patients
Recruitment/Selection of Patients	-
Intervention	Microwave ablation plus chemotherapy
Outcome reported with time points	The effective rate was (CR+PR)/100*100%. For PD and dead patients, follow-up was terminated and PD patients received additional treatment. The PFS of the two groups was counted and the adverse reactions were observed in both groups at the same time.
Funding	National Natural Science Foundation of China (81473071); Support Project for Young Teachers of Jining Medical University (JY2016KJ053Y); Shandong Medical and Health Science and Technology Development Plan Project (2017WS717)
ROB 2 Assessment	Randomisation process - Some concerns
	Deviations from the intended interventions - Low
	Missing outcome data - Low
	Measurement of the outcome - Low
	Selection of the reported result - Low
	Overall - Some concerns

Name	Standard-of-care systemic therapy with or without stereotactic body radiotherapy in patients with oligoprogressive breast cancer or non-small-cell lung cancer (Consolidative Use of Radiotherapy to Block [CURB] oligoprogression): an open-label, randomised, controlled, phase 2 study
Author	Tsai et al., 2023
Study Type	Phase 2, open-label, randomised controlled trial
Number of Participants	59
Duration of study follow up (in months)	52 weeks
Inclusion Criteria	The eligibility criteria included: (1) patient's age of 18 years or older; (2) patient's willingness and ability to provide informed consent; (3) metastatic disease detected on imaging and histologically confirmed breast cancer or NSCLC; (4) receipt of at least first-line systemic therapy, including maintenance therapies; (5) extracranial oligoprogression, defined as having progression in up to five individual lesions according to either the Response Evaluation Criteria in Solid Tumours (RECIST) or the PET Response Criteria in Solid Tumours (PERCIST); and (6) potential for all sites of oligoprogression to be safely treated. Patients with brain metastases could receive standard-of-care brain radiation (either whole brain radiotherapy or stereotactic radiotherapy) before enrolment
Exclusion Criteria	The exclusion criteria included pregnancy, lepto-meningeal disease, and serious medical comorbidities precluding radiotherapy. Patients who had previously received any form of radiotherapy were eligible to enrol in the study; however, re-irradiation to the same tumour location was not allowed.
Recruitment/Selection of Patients	All patients were assessed by screening evaluations to determine eligibility within 28 days before randomisation. Permitted initial staging imaging methods were CT, PET-CT, or MRI (or any combination thereof) of the brain, neck, chest, abdomen, pelvis, or all other known sites of disease.
Intervention	SBRT (Sterotactic Body Radiotherapy)

Outcome reported with time points	The primary endpoint was progression-free survival, measured up to 12 months, for patients in the standard-of-care and SBRT groups, defined as the time from random assignment to systemic disease progression. Secondary outcomes were overall survival in the entire cohort and by disease group, defined as the time from random assignment to death or last follow-up; time to initiation of a new systemic therapy after the initial change of systemic therapy or no change at the time of enrolment, in the entire cohort and by disease site; toxicity of SBRT, measured by assessing adverse events according to the CTCAE criteria and with treatment-related adverse events defined by the treating physician; patient's quality of life, assessed by use of questionnaires; and progression-free survival by disease site—ie, for patients with breast cancer and for those with NSCLC in the standard-of-care and SBRT groups. As an exploratory objective, we also examined the mutational profiles of the tumours and paired blood samples collected at baseline and follow-up to assess possible changes in cell-free DNA.
Funding	National Cancer Institute
ROB 2 Assessment	Randomisation process - Low
	Deviations from the intended interventions - Low
	Missing outcome data - Low
	Measurement of the outcome - Low
	Selection of the reported result - Low
	Overall - Low

Name	**A randomized phase III trial of stereotactic radiosurgery (SRS) versus observation for patients with asymptomatic cerebral oligo-metastases in non-small-cell lung cancer**
Author	Lim et al., 2014
Study Type	Single center, randomized phase III trial
Number of Participants	105
Duration of study follow up (in months)	12 months

Inclusion Criteria	patients aged 18 years or older with histological confirmed NSCLC with synchronous brain metastases. All patients had 1 to 4 parenchymal brain metastases by contrast-enhanced MRI, each with a maximum diameter of no more than 3cm with brain edema grade 0-1. None of patients had prior surgical treatment or radiotherapy for brain metastases and leptomeningeal metastases
Exclusion Criteria	Patients with uncontrolled extra-cranial disease, severe comorbid illnesses and/or active infections were excluded.
Recruitment/Selection of Patients	patients aged 18 years or older with histological confirmed NSCLC with synchronous brain metastases
Intervention	stereotactically focused radiation.
Outcome reported with time points	The median OS time was 14.6 months [95% confidence interval (CI), 9.2–20.0] in the SRS group and 15.3 months (95% CI, 7.2–23.4) for the upfront chemotherapy group (P = 0.418). There was no significant difference in time to CNS disease progression [median, 9.4 months (SRS) versus 6.6 months (upfront chemotherapy),P = 0.248]. Symptomatic progression of brain metastases was observed more frequently in the upfront chemotherapy group (26.5%) than the SRS group (18.4%) but without statistical significance.
Funding	This work was supported in part by Samsung Biomedical Research Institute Grant (SMX1132531) and by Elekta Korea research funds.
ROB 2 Assessment	Randomisation process - Some concerns
	Deviations from the intended interventions - Low
	Missing outcome data - Low
	Measurement of the outcome - Low
	Selection of the reported result - Low
	Overall - Some concerns

Name	Effect of Pembrolizumab After Stereotactic Body Radiotherapy vs Pembrolizumab Alone on Tumor Response in Patients With Advanced Non–Small Cell Lung Cancer Results of the PEMBRO-RT
Author	Theelen et al., 2019
Study Type	Phase 2 Randomized Clinical Trial
Number of Participants	78
Duration of study follow up (in months)	12 weeks
Inclusion Criteria	Patients 18 years or older were eligible to participate if they had histological or cytological confirmed metastatic non–small cell lung cancer (NSCLC) that progressed after at least 1 regimen of chemotherapy but who were immunotherapy naive and had an Eastern Cooperative Oncology Group performance status of 1 or lower. At least 2 separate lesions were required, one of which was measurable according to the Response Evaluation Criteria in Solid Tumors and suitable for biopsy, and the other of which was amenable to irradiation
Exclusion Criteria	Patients were ineligible if they had (1) radiotherapy to any tumor site within 6 months before randomization; (2) known, active central nervous system metastases and/or carcinomatous meningitis; (3) untreated driver alterations of epidermal growth factor receptor or anaplastic lymphoma kinase; or (4) active autoimmune or interstitial lung disease
Recruitment/Selection of Patients	participate if they had histological or cytological confirmed metastatic non–small cell lung cancer (NSCLC)
Intervention	SBRT High dose radiation (SBRT) followed by pembrolizumab treatment within 7 days after completion.
Outcome reported with time points	Response rate, disease control rate, overall survival, progression free survival and toxicity as efficacy endpoints.
Funding	This study was an investigator-initiated trial, designed by the authors and financially supported by an unrestricted grant from Merck Sharp & Dohme that included medication supply.

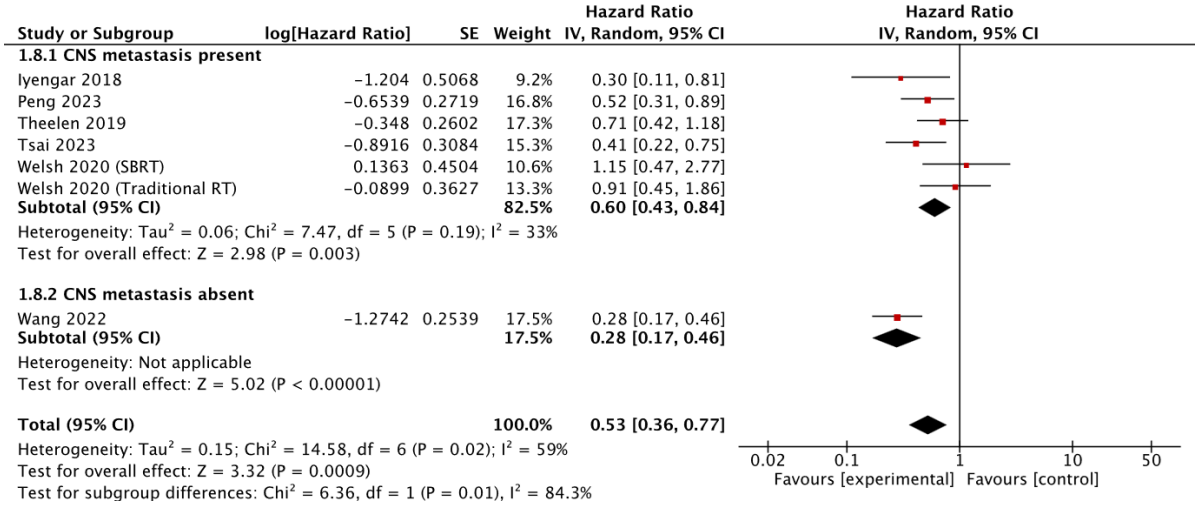
ROB 2 Assessment	Randomisation process - Some concerns
	Deviations from the intended interventions - Low
	Missing outcome data - Low
	Measurement of the outcome - Low
	Selection of the reported result - Low
	Overall - Some concerns

Name	**Randomized Trial of First-Line Tyrosine Kinase Inhibitor With or Without Radiotherapy for Synchronous Oligometastatic EGFR-Mutated Non-Small Cell Lung Cancer**
Author	Wang et al., 2022
Study Type	Open-label, parallel-group, phase III clinical trial
Number of Participants	133
Duration of study follow up (in months)	23.6 months
Inclusion Criteria	All patients were required to have biopsy-proven EGFRm adenocarcinoma (defined as any deletion in exon 19 or any mutation in exon 21, by means of either an amplification refractory mutation system or next generation sequencing) as well as synchronous (newly diagnosed, treatment-naïve) oligometastatic disease. Oligometastatic disease was defined as 5 or less discrete distant metastases with no more than 2 discrete areas of metastatic disease in any one organ (as confirmed by multidisciplinary review). The involved regional lymph nodes (regardless of nodal number) were not counted in the definition of metastatic disease and were grouped with the primary tumor. Involved nonregional lymph nodes were categorized as metastatic disease.

Exclusion Criteria	Further exclusion criteria were the presence of brain metastases as detected on contrast-enhanced magnetic resonance imaging (MRI), prior irradiation to the thorax or metastatic sites (or other contraindications to receiving RT, such as tumor within 5 mm of the spinal cord), history of previous malignancies, prior receipt of any test drugs or investigational compounds within 4 weeks, inadequate bone marrow or hepatorenal function, severe or uncontrolled cardiovascular comorbidities, any contraindications to receiving TKI therapy, mental illness or psychotropic substance abuse, and pregnant or breastfeeding women.
Recruitment/Selection of Patients	All patients were required to have biopsy-proven EGFRm adenocarcinoma (defined as any deletion in exon 19 or any mutation in exon 21, by means of either an amplification refractory mutation system or next generation sequencing) as well as synchronous (newly diagnosed, treatment-naïve) oligometastatic disease. Oligometastatic disease was defined as 5 or less discrete distant metastases with no more than 2 discrete areas of metastatic disease in any one organ (as confirmed by multidisciplinary review).
Intervention	TKI with RT
Outcome reported with time points	PFS, OS
Funding	This study was supported in part by the National Science and Technology Foundation (No. 3035031263), Sichuan Academy of Medical Sciences & Sichuan Provincial People's Hospital (No. 30305031017P), the Clinical Research and Transformation Fund of Sichuan Provincial People's Hospital (2021LY25), the Sichuan Science and Technology Office (No. 3050410336), and the Chengdu Science and Technology Innovation Research and Development Project
ROB 2 Assessment	Randomisation process - Low
	Deviations from the intended interventions - Low
	Missing outcome data - Low
	Measurement of the outcome - Low
	Selection of the reported result - Low
	Overall - Low

Forest Plots of Important Outcomes

Progression Free survival:



Evidence to Decision Framework

QUESTION

Should radical local treatment of the primary & metastatic sites vs. systemic therapy alone be used for patients with oligometastatic non-small cell lung cancer (NSCLC)?	
Population:	Patients with oligometastatic non-small cell lung cancer (NSCLC)
Intervention:	Radical local treatment of the primary & metastatic sites
Comparison:	Systemic therapy alone
Main outcomes:	Overall survival (Critical outcome) Adverse effects (Critical outcome) Quality of life (Critical outcome) Progression free survival (Important outcome) Response rate (Important outcome) Cost (Important outcome)
Setting:	India

ASSESSMENT

Problem Is the problem a priority?		
JUDGEMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
○ No ○ Probably no ○ Probably yes ● Yes ○ Varies ○ Don't know	The oligometastatic disease entity has a specific place on an apparent continuum that extends from localized, well-controlled disease to poly-metastatic, widespread disease. The tumor lacks fully developed metastatic pathogenicity. This reduces the tumour growth and distant seeding, and also makes it more recommended to disease control by radical local treatment. Using definitive local therapy in addition to systemic treatment has been shown to improve survival results in patients with oligometastatic non-small cell lung cancer. Radical treatment used to be mostly surgery, but it now includes radiation therapy as well. Radiotherapy is a non-invasive treatment that complements immunotherapy. For the treatment of individuals with oligometastatic non-small cell lung cancer, stereotactic radiosurgery is fast taking the place of other approaches.	
Desirable Effects How substantial are the desirable anticipated effects?		
JUDGEMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
○ Trivial ○ Small ○ Moderate ● Large ○ Varies ○ Don't know	The reduction in mortality, evidenced by hazard ratios ranging from 0.48 to 0.70, indicates that the intervention achieves a relative risk reduction (30–52%) well above the 5% MCID.	Studies that defined the condition as oligometastasis at the time of their conduct were included in the analysis. There is heterogeneity in population included and the definition has evolved over time. HR is indicative of mortality. The panel considered the desirable effects of radical local therapy to be large, particularly given the substantial relative reduction in mortality (HR 0.63;

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)
	Number survived with control	Number survived with Radical local therapy			
OS	640 per 1,000	**755 per 1,000** (654 to 833)	**HR 0.63** (0.41 to 0.95)	432 (5 RCTs)	⊕⊕◯◯ Low[a,b,c,d,e]
Subgroups: Type of intervention					
OS - Radiotherapy	640 per 1,000	**745 per 1,000** (623 to 833)	**HR 0.66** (0.41 to 1.06)	383 (4 RCTs)	⊕◯◯◯ Very low[a,b,c,e,f]
OS - radiotherapy or surgery or both	620 per 1,000	**803 per 1,000** (623 to 904)	**HR 0.46** (0.21 to 0.99)	49 (1 RCT)	⊕⊕◯◯ Low[c,e,g,h]
Subgroups: Site of metastasis					
OS - CNS Metastasis present	560 per 1,000	**666 per 1,000** (528 to 775)	**HR 0.70** (0.44 to 1.10)	299 (4 RCTs)	⊕◯◯◯ Very low[a,b,f]
OS - CNS Metastasis absent	850 per 1,000	**931 per 1,000** (895 to 956)	**HR 0.44** (0.28 to 0.68)	133 (1 RCT)	⊕⊕◯◯ Low[h]

95% CI: 0.41 to 0.95) observed across randomized controlled trials.

Undesirable Effects
How substantial are the undesirable anticipated effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS

○ Trivial ● Small ○ Moderate ○ Large ○ Varies ○ Don't know	Four out of nine studies reported adverse effects. Across most studies, there are a few of higher-grade (≥ Grade 3) toxicities in both the radical local therapy and systemic therapy arms. Overall, the undesirable effects associated with radical local therapy in oligometastatic disease appear limited to low frequencies of Grade 3 or higher toxicities. **Adverse events** **Study Grade events** / **Total** / **Radical local treatment** / **Systemic therapy alone** Iyengar et al., 2018 Grade 3 events: **6** / **4** / **2** Lim et al., 2014 >=Grade 3 events: **0** / **0** / **0** Theelen et al., 2019 >=Grade 3 events: **12*** / - / - Tsai et al., 2023 >=Grade 2 events: **9** / **9** / **0** Wang et al., 2022 Grade 5 events: **0** / **0** / **0** Welsh et al., 2020 Grade 3 events: **6*** / - / - Gomez et al., 2019 >=Grade 3: **0** / **0** / **0** Shan et al., 2021: No information about any grade events Peng et al., 2023 >=Grade 3 events: **0** / **0** / **0**	The panel decided to go with 'small' undesirable effects based on the limited and inconsistent reporting of adverse events across the included studies. Most studies did not provide statistical estimates or incidence rates, instead reporting the number of events without accounting for total sample size, and there was variability in the severity grading of adverse events considered (ranging from grade 2 and above).

Certainty of evidence
What is the overall certainty of the evidence of effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
● Very low ○ Low ○ Moderate ○ High ○ No included studies	The certainty of the evidence is very low due to high risk of bias, inconsistency and imprecision in the reported studies.	No additional considerations
Values Is there important uncertainty about or variability in how much people value the main outcomes?		
JUDGEMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
○ Important uncertainty or variability ○ Possibly important uncertainty or variability ○ Probably no important uncertainty or variability ● No important uncertainty or variability	1. overall survival (36 out of 40) 90%, and Health-related quality of life factors, (77.5%) were highly valued by patients who underwent lung surgery (Wong MSH, Pons A, De Sousa P, Proli C, Jordan S, Begum S, Buderi S, Lim E. Assessing patient perception and preferences for outcomes in lung cancer resection surgery: a cross-sectional study. J Thorac Dis. 2024 Jun 30;16(6):3844-3853) 2. For participants with early stage lung cancer, maintaining independence and QOL were more highly valued than survival or cancer recurrence. (Sullivan DR, Eden KB, Dieckmann NF, Golden SE, Vranas KC, Nugent SM, Slatore CG. Understanding patients' values and preferences regarding early-stage lung cancer treatment decision-making. *Lung Cancer*. 2019;131:47-57.) 3. Patients with lung cancer and caregivers demonstrated varying willingness to trade PFS for reduced severity of treatment-related side effects, with participants willing to trade up to 3.7 months of PFS for less severe functional long-term effects. While most participants (90%) would accept treatment with more severe functional long-term effects for an 8.4-month PFS gain. (Janssen EM, et al. Analysis of Patient Preferences in Lung Cancer - Estimating Acceptable Tradeoffs Between Treatment Benefit and Side Effects. Patient Prefer Adherence. 2020 Jun 3;14:927-937)	The panel decided on "no important variability" in values, considering the consistent prioritization of overall survival and quality of life (QoL) across studies. Evidence indicates that a high proportion of patients undergoing lung surgery (90%) valued overall survival, and a majority prioritized health-related QoL, functional independence, and acceptable trade-offs between progression-free survival (PFS) and treatment-related side effects, suggesting alignment in patient values across different clinical contexts.
Balance of effects		

Does the balance between desirable and undesirable effects favor the intervention or the comparison?		
JUDGEMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
○ Favors the comparison ○ Probably favors the comparison ○ Does not favor either the intervention or the comparison ● Probably favors the intervention ○ Favors the intervention ○ Varies ○ Don't know	The substantial improvements in overall survival (with reductions in mortality well above the clinically important threshold) come at the cost of relatively low and manageable increases in severe toxicity. The clinical benefits; especially the pronounced survival gains appear to outweigh the modest increase in undesirable events.	The panel decided the balance of effects as 'Probably favours the intervention" based on the substantial improvement in overall survival exceeding clinically important thresholds observed with radical local therapy, which appears to outweigh the relatively low and manageable increase in severe adverse events.
Resources required		
JUDGEMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
● Large costs ○ Moderate costs ○ Negligible costs and savings ○ Moderate savings ○ Large savings	The average cost for SABR per treatment is reported at approximately **$11,700**.Sensitivity analyses in the study indicated that SABR remains cost-effective even if treatment costs increase up to 7–8 times (up to roughly **$88,000–$93,750** per treatment in extreme scenarios). (Mehrens, D., Unterrainer, M., Corradini, S., Niyazi, M., Manapov, F., Westphalen, C. B., Froelich, M. F., Wildgruber, M., Seidensticker, M., Ricke, J., Rübenthaler, J.,	The panel judged the costs associated with radiotherapy as ‘large’. This decision was informed by the absence of studies from the India and the need for contextualization, taking into account factors such as high capital and maintenance costs of equipment, type of healthcare facility, treatment package costs, and the number of fractions administered.

○ Varies ○ Don't know	& Kunz, W. G. (2021). Cost-Effectiveness Analysis of Local Treatment in Oligometastatic Disease. *Frontiers in oncology*, *11*, 667993)	

Certainty of evidence of required resources What is the certainty of the evidence of resource requirements (costs)?		
JUDGEMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
○ Very low ○ Low ● Moderate ○ High ○ No included studies	The cost inputs for SABR, systemic therapy, and associated adverse events were derived from multiple reputable sources, including published literature, Medicare data, and established cost models. This triangulation of data sources increases confidence in the estimates.	The panel rated the certainty of evidence for required resources as 'moderate', given that the cost estimates were derived from multiple reputable sources, including peer-reviewed literature, Medicare reimbursement data, and validated cost-effectiveness models. Although these sources enhance confidence in the cost estimates through triangulation, their applicability to the Indian context remains limited, necessitating cautious interpretation.

Cost effectiveness Does the cost-effectiveness of the intervention favor the intervention or the comparison?		
JUDGEMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
○ Favors the comparison ○ Probably favors the comparison ○ Does not favor either the intervention or the	The cost-effectiveness evidence favors the addition of radical local treatment (SABR) to systemic therapy over systemic therapy alone in patients with oligometastatic NSCLC (Meherens et al). Incremental cost-effectiveness ratio (ICER) of $1,446 per QALY over a six-year horizon and $38,874 per QALY over a 16-year horizon, both well below the commonly accepted U.S. willingness-to-pay threshold of $100,000/QALY. These findings imply that the additional costs associated with radical local therapy are offset by the gain in quality-adjusted life years, making it a cost-effective option even if treatment costs were to increase substantially.	The panel acknowledged that while cost-effectiveness evidence from high-income settings (e.g., the United States) strongly supports the addition of radical local treatment (SABR) to systemic therapy—demonstrating low ICER values and robust model stability, its direct applicability to the Indian context is limited. However, considering the

comparison ● Probably favors the intervention ○ Favors the intervention ○ Varies ○ No included studies	• Both deterministic and probabilistic sensitivity analyses were conducted. These analyses demonstrated that even with significant increases in treatment costs (up to 7–8 times the base value), the model's conclusions regarding cost-effectiveness remained stable. • The robustness of the model across a wide range of cost assumptions supports a higher certainty in the resource requirement estimates. (Mehrens, D., Unterrainer, M., Corradini, S., Niyazi, M., Manapov, F., Westphalen, C. B., Froelich, M. F., Wildgruber, M., Seidensticker, M., Ricke, J., Rübenthaler, J., & Kunz, W. G. (2021). Cost-Effectiveness Analysis of Local Treatment in Oligometastatic Disease. *Frontiers in oncology*, *11*, 667993)	substantial survival benefit associated with the intervention, the panel concluded that cost-effectiveness *probably favours the intervention*, despite the higher equipment costs, limited infrastructure, and the need to account for purchasing power parity.
Equity What would be the impact on health equity?		
JUDGEMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
○ Reduced ● Probably reduced ○ Probably no impact ○ Probably increased ○ Increased ○ Varies ○ Don't know	No direct or indirect evidence was found in the literature	The panel decided it as probably reduced in view of the uneven distribution of specialized SABR services, which: • Are overwhelmingly concentrated in high-resource, urban centres possessing the requisite infrastructure and trained personnel • Impose substantial geographic and socioeconomic barriers for patients in under-resourced regions

		• Risk deepening existing disparities in cancer treatment availability and outcomes
Acceptability Is the intervention acceptable to key stakeholders?		
JUDGEMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
○ No ○ Probably no ● Probably yes ○ Yes ○ Varies ○ Don't know	No studies were identified that assessed the acceptability of radical treatment in patients with oligometastatic non-small cell lung cancer	The panel judged acceptability as probably yes given that patients favor interventions offering improved survival and manageable adverse events reinforce a favorable benefit-risk balance, enhancing patient willingness to undergo therapy
Feasibility Is the intervention feasible to implement?		
JUDGEMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
○ No ○ Probably no ○ Probably yes ○ Yes ● Varies ○ Don't know	No studies were identified that assessed the feasibility of radical treatment in patients with oligometastatic non-small cell lung cancer (NSCLC)	The panel judged feasibility as varies, given that the prerequisites for advanced radiotherapy technologies and specialized expertise, together with variable equipment availability, costs, and centre-specific implementation capacities that may limit broader uptake in resource-constrained environments. While direct evidence on the feasibility of radical local treatment in oligometastatic NSCLC is lacking, indirect indicators and experience from related settings suggest

		potential benefits contingent upon the affordability and technical capacity of individual centres.

SUMMARY OF JUDGEMENTS

	JUDGEMENT						
PROBLEM	No	Probably no	Probably yes	**Yes**		Varies	Don't know
DESIRABLE EFFECTS	Trivial	Small	Moderate	**Large**		Varies	Don't know
UNDESIRABLE EFFECTS	Trivial	**Small**	Moderate	Large		Varies	Don't know
CERTAINTY OF EVIDENCE	**Very low**	Low	Moderate	High			No included studies
VALUES	Important uncertainty or variability	Possibly important uncertainty or variability	Probably no important uncertainty or variability	**No important uncertainty or variability**			
BALANCE OF EFFECTS	Favors the comparison	Probably favors the comparison	Does not favor either the intervention or the comparison	**Probably favors the intervention**	Favors the intervention	Varies	Don't know
RESOURCES REQUIRED	**Large costs**	Moderate costs	Negligible costs and savings	Moderate savings	Large savings	Varies	Don't know
CERTAINTY OF EVIDENCE OF REQUIRED RESOURCES	Very low	Low	**Moderate**	High			No included studies
COST EFFECTIVENESS	Favors the comparison	Probably favors the comparison	Does not favor either the intervention or the comparison	**Probably favors the intervention**	Favors the intervention	Varies	No included studies

	JUDGEMENT						
EQUITY	Reduced	**Probably reduced**	Probably no impact	Probably increased	Increased	Varies	Don't know
ACCEPTABILITY	No	Probably no	**Probably yes**	Yes		Varies	Don't know
FEASIBILITY	No	Probably no	Probably yes	Yes		**Varies**	Don't know

TYPE OF RECOMMENDATION

Strong recommendation against the intervention	Conditional recommendation against the intervention	Conditional recommendation for either the intervention or the comparison	**Conditional recommendation for the intervention**	Strong recommendation for the intervention
○	○	○	●	○

CONCLUSIONS

Recommendation

Radical local treatment of primary and metastatic sites is **recommended** in comparison to treatment with systemic therapy alone for patients with oligometastatic non-small cell lung cancer.

Strength: Conditional
Certainty of evidence: Very low.

Justification

The panel judged that the desirable effects are large in magnitude, whereas the undesirable effects remain small and manageable. Cost-effectiveness was assessed as probably favouring the intervention, and patient acceptability further supports its use. Although the need for advanced technology and specialist expertise may constrain feasibility in some settings, the overall balance of benefits, harms, cost-effectiveness, and acceptability probably favours the intervention, leading to a conditional recommendation in its favour.

Research priorities

Given the absence of direct evidence on cost-effectiveness, equity, feasibility, and acceptability for radical local treatment in oligometastatic NSCLC, the following research priorities are recommended:

Health Economic Evaluations

Conduct formal cost-effectiveness analyses comparing radical local treatment plus systemic therapy versus systemic therapy alone, accounting for variations in health system resources and treatment settings.

Equity-Focused Research

Investigate disparities in access to radical local treatment, particularly examining geographic (urban–rural), socioeconomic, and health system–level factors that influence equitable delivery of care.

Feasibility Studies

Evaluate the implementation of SABR and other radical local treatments in diverse clinical settings, focusing on infrastructure requirements, workforce capacity, and institutional readiness.

Acceptability Studies

Assess patient and clinician perspectives on radical local treatment through qualitative or mixed-methods research to understand perceived benefits, burdens, and barriers to uptake.

List of Excluded Studies

Sr. No.	Citation of the study (Vancouver style only)	Reasons for exclusion
1	Bauml JM, Mick R, Ciunci C, Aggarwal C, Davis C, Evans T, et al. Pembrolizumab after completion of locally ablative therapy for oligometastatic non–small cell lung cancer: a phase 2 trial. JAMA Oncol. 2019 Sep 1;5(9):1283–90.	Single arm
2	Miyawaki T, Kenmotsu H, Harada H, Ohde Y, Chiba Y, Haratani K, Okimoto T, Sakamoto T, Wakuda K, Ito K, Uemura T, Sakata S, Kogure Y, Nishimura Y, Nakagawa K, Yamamoto N. Phase II study of multidisciplinary therapy combined with pembrolizumab for patients with synchronous oligometastatic non-small cell lung cancer TRAP OLIGO study (WJOG11118L). BMC Cancer. 2021 Oct 18;21(1):1121. doi: 10.1186/s12885-021-08851-z. PMID: 34663250; PMCID: PMC8524804.	Single arm
3	Blake-Cerda M, Lozano-Ruíz F, Maldonado-Magos F, de la Mata-Moya D, Díaz-García D, Lara-Mejía L, Zatarain-Barrón ZL, Cuevas-Góngora MF, Barron-Barron F, Corona-Cruz JF, Cabrera-Miranda L, Arroyo-Hernández M, Gerson R, Arrieta O. Consolidative stereotactic ablative radiotherapy (SABR) to intrapulmonary lesions is associated with prolonged progression-free survival and overall survival in oligometastatic NSCLC patients: A prospective phase 2 study. Lung Cancer. 2021 Feb;152:119-126. doi: 10.1016/j.lungcan.2020.12.029. Epub 2020 Dec 28. PMID: 33385737.	Single arm
4	De Ruysscher D, Wanders R, van Baardwijk A, Dingemans AM, Reymen B, Houben R, Bootsma G, Pitz C, van Eijsden L, Geraedts W, Baumert BG, Lambin P. Radical treatment of non-small-cell lung cancer patients with synchronous oligometastases: long-term results of a prospective phase II trial (Nct01282450). J Thorac Oncol. 2012 Oct;7(10):1547-55. doi: 10.1097/JTO.0b013e318262caf6. PMID: 22982655.	Single arm
5	Tjong MC, Louie AV, Iyengar P, Solomon BJ, Palma DA, Siva S. Local ablative therapies in oligometastatic NSCLC-upfront or outback?-a narrative review. Transl Lung Cancer Res. 2021 Jul;10(7):3446-3456. doi: 10.21037/tlcr-20-994. PMID: 34430379; PMCID: PMC8350079.	Single arm
6	Sundahl N, Lievens Y. Radiotherapy for oligometastatic non-small cell lung cancer: a narrative review. Transl Lung Cancer Res. 2021 Jul;10(7):3420-3431. doi: 10.21037/tlcr-20-1051. PMID: 34430377; PMCID: PMC8350107.	Single arm
7	Kroeze SGC, Schaule J, Fritz C, Kaul D, Blanck O, Kahl KH, Roeder F, Siva S, Verhoeff JJC, Adebahr S, Schymalla MM, Glatzer M, Szuecs M, Geier M, Skazikis G, Sackerer I, Lohaus F, Eckert F, Guckenberger M. Metastasis directed stereotactic radiotherapy in NSCLC patients progressing under targeted- or immunotherapy: efficacy and safety reporting from the 'TOaSTT' database. Radiat Oncol. 2021 Jan 6;16(1):4. doi: 10.1186/s13014-020-01730-0. PMID: 33407611; PMCID: PMC7788768.	Single arm
8	Li T, Jiahua Lv, Li L, Li F, Song Y, Li C, et al. A phase II prospective study of definitive thoracic concurrent chemoradiation followed by consolidation	Single arm

	chemotherapy for oligometastatic non-small cell lung cancer. Journal of Clinical Oncology. 2015 May 20;33(15_suppl):e19008–8.	
9	Bahig H, Aubin F, Stagg J, Gologan O, Ballivy O, Bissada E, Nguyen-Tan FP, Soulières D, Guertin L, Filion E, Christopoulos A, Lambert L, Tehfe M, Ayad T, Charpentier D, Jamal R, Wong P. Phase I/II trial of Durvalumab plus Tremelimumab and stereotactic body radiotherapy for metastatic head and neck carcinoma. BMC Cancer. 2019 Jan 14;19(1):68. doi: 10.1186/s12885-019-5266-4. PMID: 30642290; PMCID: PMC6332607.	Single arm
10	Iyengar P, Kavanagh BD, Wardak Z, Smith I, Ahn C, Gerber DE, Dowell J, Hughes R, Abdulrahman R, Camidge DR, Gaspar LE, Doebele RC, Bunn PA, Choy H, Timmerman R. Phase II trial of stereotactic body radiation therapy combined with erlotinib for patients with limited but progressive metastatic non-small-cell lung cancer. J Clin Oncol. 2014 Dec 1;32(34):3824-30. doi: 10.1200/JCO.2014.56.7412. Epub 2014 Oct 27. PMID: 25349291.	Single arm
11	Downey RJ, Ng KK, Kris MG, Bains MS, Miller VA, Heelan R, Bilsky M, Ginsberg R, Rusch VW. A phase II trial of chemotherapy and surgery for non-small cell lung cancer patients with a synchronous solitary metastasis. Lung Cancer. 2002 Nov;38(2):193-7. doi: 10.1016/s0169-5002(02)00183-6. PMID: 12399132.	Single arm
12	T. Berghmans. ES21.05 Clinical Trials to Advance the Field of OMD. Journal of Thoracic Oncology. 2019 Oct 1;14(10):S65–6.	Conference abstract
13	34th Annual Meeting & Pre-Conference Programs of the Society for Immunotherapy of Cancer (SITC 2019): part 1. *j. immunotherapy cancer* **7** (Suppl 1), 282 (2019). https://doi.org/10.1186/s40425-019-0763-1	Conference abstract
14	Newman NB, Anderson JL, Shinohara ET, Michael P, Attia A, Osmundson EC. Neoadjuvant Stereotactic Ablative and Hypofractionated Radiotherapy for Oligometastatic NSCLC. International Journal of Radiation Oncology*Biology*Physics. 2019 Aug 1;104(5):1196–6.	Conference abstract
15	Zhu X, Zheng Z, Li S. EP1.08-05 Local Non-Salvage Radiotherapy for Synchronous Oligometastatic NSCLC: A Multicenter, Randomized, Controlled, Phase 2 Study. Journal of Thoracic Oncology. 2019 Oct 1;14(10):S997–7.	Conference abstract
16	Peng P, Chen Y, Han G, Meng R, Zhang S, Liao Z, et al. MA01.09 Concomitant SBRT and EGFR-TKI Versus EGFR-TKI Alone for Oligometastatic NSCLC: A Multicenter, Randomized Phase II Study. Journal of Thoracic Oncology. 2019 Oct 1;14(10):S250–1.	Conference abstract
17	McDonald F, Guckenberger M, Popat S, C. Faivre-Finn, N. Andratschke, Riddell A, et al. EP08.03-005 HALT - Targeted Therapy with or without Dose-Intensified Radiotherapy in Oligo-Progressive Disease in Oncogene Addicted Lung Tumours. Journal of Thoracic Oncology. 2022 Sep 1;17(9):S492–2.	Conference abstract

18	Meeting abstracts from the 5th International Clinical Trials Methodology Conference (ICTMC 2019). *Trials* **20** (Suppl 1), 579 (2019). https://doi.org/10.1186/s13063-019-3688-6	Conference abstract
19	Tang C, Lee WC, Reuben A, Chang L, Tran H, Little L, Gumbs C, Wargo J, Futreal A, Liao Z, Xia X, Yi X, Swisher SG, Heymach JV, Gomez D, Zhang J. Immune and Circulating Tumor DNA Profiling After Radiation Treatment for Oligometastatic Non-Small Cell Lung Cancer: Translational Correlatives from a Mature Randomized Phase II Trial. Int J Radiat Oncol Biol Phys. 2020 Feb 1;106(2):349-357. doi: 10.1016/j.ijrobp.2019.10.038. Epub 2019 Oct 31. PMID: 31678224.	Conference abstract
20	Bestvina CM, Pointer KB, Karrison T, Al-Hallaq H, Hoffman PC, Jelinek MJ, Juloori A, Melotek JM, Murgu S, Partouche J, Vokes EE, Weichselbaum RR, Pitroda SP, Patel JD, Chmura SJ. A Phase 1 Trial of Concurrent or Sequential Ipilimumab, Nivolumab, and Stereotactic Body Radiotherapy in Patients With Stage IV NSCLC Study. J Thorac Oncol. 2022 Jan;17(1):130-140. doi: 10.1016/j.jtho.2021.08.019. Epub 2021 Sep 6. PMID: 34500113.	Both group radiotherapy
21	Han G, Bi J, Ma J, Yuan M, Li Y, Pi G, et al. 146P Stereotactic body radiotherapy plus anlotinib ± toripalimab in untreated oligometastatic brain metastases NSCLC patients. Immuno-Oncology Technology. 2022 Dec 1;16:100258–8.	Both group radiotherapy
22	Singh AK, Gomez-Suescun JA, Stephans KL, Bogart JA, Hermann GM, Tian L, Groman A, Videtic GM. One Versus Three Fractions of Stereotactic Body Radiation Therapy for Peripheral Stage I to II Non-Small Cell Lung Cancer: A Randomized, Multi-Institution, Phase 2 Trial. Int J Radiat Oncol Biol Phys. 2019 Nov 15;105(4):752-759. doi: 10.1016/j.ijrobp.2019.08.019. Epub 2019 Aug 22. PMID: 31445956; PMCID: PMC7043929.	Both group radiotherapy
23	Gregorc V, Novello S, Lazzari C, Barni S, Aieta M, Mencoboni M, Grossi F, De Pas T, de Marinis F, Bearz A, Floriani I, Torri V, Bulotta A, Cattaneo A, Grigorieva J, Tsypin M, Roder J, Doglioni C, Levra MG, Petrelli F, Foti S, Viganò M, Bachi A, Roder H. Predictive value of a proteomic signature in patients with non-small-cell lung cancer treated with second-line erlotinib or chemotherapy (PROSE): a biomarker-stratified, randomised phase 3 trial. Lancet Oncol. 2014 Jun;15(7):713-21. doi: 10.1016/S1470-2045(14)70162-7. Epub 2014 May 13. PMID: 24831979.	Both group chemotherapy
24	Chan OSH, Lam KC, Li JYC, Choi FPT, Wong CYH, Chang ATY, Mo FKF, Wang K, Yeung RMW, Mok TSK. ATOM: A phase II study to assess efficacy of preemptive local ablative therapy to residual oligometastases of NSCLC after EGFR TKI. Lung Cancer. 2020 Apr;142:41-46. doi: 10.1016/j.lungcan.2020.02.002. Epub 2020 Feb 11. PMID: 32088604.	Preference trial
25	Sutera P, Clump DA, Kalash R, D'Ambrosio D, Mihai A, Wang H, Petro DP, Burton SA, Heron DE. Initial Results of a Multicenter Phase 2 Trial of Stereotactic Ablative Radiation Therapy for Oligometastatic Cancer. Int J Radiat Oncol Biol Phys. 2019 Jan 1;103(1):116-122. doi: 10.1016/j.ijrobp.2018.08.027. Epub 2018 Aug 25. PMID: 30149056.	Preference trial
26	Tibdewal A, Agarwal JP, Srinivasan S, Mummudi N, Noronha V, Prabhash K, Patil V, Purandare N, Janu A, Kannan S. Standard maintenance therapy versus local consolidative radiation therapy and standard maintenance	Protocol

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