Evidence-based Guidelines for Lung Cancer Palliation

December 2025

Department of Health Research
Directorate General of Health Services

Ministry of Health and Family Welfare

Government of India

DISCLAIMER

The Evidence-based Guidelines for Lung Cancer Palliation published by the MoHFW/DHR-DGHS provide recommendations made after careful consideration of the available evidence. This evidence has been synthesized by collation of systematic reviews (SR) and meta-analysis (MA) of exisitng studies on well defined review questions on the subject matter. The guideline reflects the best avaialble data according to the study inclusion criteria set by the guideline development group. Considerable care has been taken to ensure that the information contained in the guidelines is accurate, evidence-based and up-to-date at the time of publication. However, there is a possbility that new studies may have been published too late during the development process or after publication and are not incorporated into the guideline.

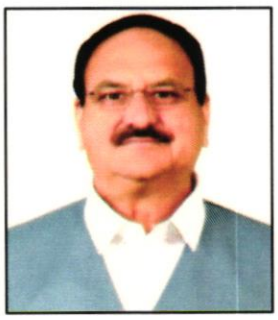
ICMR-DHR, DGHS and their scientists, members of the Steering Group, GDG and systematic review teams disclaim all liability for the accuracy or completeness of the guideline. The team further disclaims all the liability for any damage whatsoever (direct or indirect) arising out of the use or inability to use the information and procedures mentioned in this guideline. New studies in the future may lead to a revision in the exisiting recommendations. All MoHFW guidelines are subject to regular review and may be updated or withdrawn.

जगत प्रकाश नड्डा
JAGAT PRAKASH NADDA

सत्यमेव जयते

मंत्री
स्वास्थ्य एवं परिवार कल्याण
व रसायन एवं उर्वरक
भारत सरकार

Minister
Health & Family Welfare
and Chemicals & Fertilizers
Government of India



MESSAGE

In recent years, lung cancer has emerged as a major public health challenge, contributing significantly to morbidity and mortality across the country. It remains one of the leading causes of cancer-related deaths, imposing a substantial burden on individuals, families and the healthcare system. Late-stage diagnosis, complex treatment pathways and high symptom burden underscore the urgent need for standardized, evidence-based approaches to care.

I am happy that Ministry of Health & Family Welfare has developed evidence-based guidelines on Lung Cancer Treatment and Palliative Care to provide comprehensive guidance on disease-directed therapies and integrated supportive and palliative care across the course of illness. These guidelines emphasise a patient-centred approach, early integration of palliative care, multidisciplinary management and rational use of healthcare resources. The recommendations are based on rigorous appraisal of scientific evidence and expert consensus, ensuring clinical relevance and feasibility within our health system.

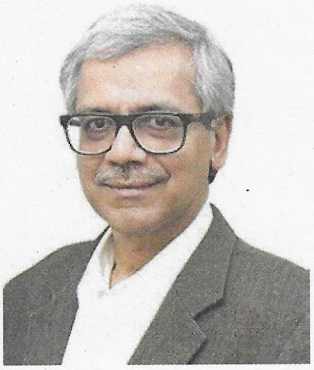
These guidelines will serve as a valuable resource for clinicians, programme managers and policymakers in strengthening service delivery and improving patient outcomes. It reinforces our commitment to expanding access to evidence-based treatment and comprehensive palliative care for people affected by lung cancer.

The Government of India remains steadfast in its commitment to addressing the growing burden of cancer in the country. I am confident that these guidelines will support healthcare professionals across the country in delivering compassionate, effective and evidence-based care to people affected by lung cancer.

(Jagat Prakash Nadda)

कार्यालयः कमरा नं. 12107, द्वितीय तल, 'सी' विंग, कर्त्तव्य भवन–1, नई दिल्ली–110001
Office: Room No. 12107, 2nd Floor, 'C' Wing, Kartavya Bhawan-1, New Delhi-110001
Tele.: (O): +91-11-24013301, 24013302, 24013303 • **E-mail:** min-hfm@gov.in

MESSAGE



In the face of India's rising burden of lung cancer, the development of robust, evidence-based lung cancer palliation guidelines has never been more critical. Lung cancer remains one of the leading causes of cancer-related mortality in our country, and its complex care pathways demand a clear, unified approach that integrates the latest scientific advances with real-world clinical practice.

These Evidence-based guidelines for the palliative care of lung Cancer have been crafted to support clinicians, researchers, and policymakers by offering transparent, practical recommendations for palliative care ensuring that every patient benefits from the most effective, scientifically validated interventions available today.

As we strive to improve outcomes and quality of life for those affected by lung cancer, it is imperative that we balance rapid innovation with patient safety and ethical rigor. We congratulate and thank all members of the Steering Group, Guideline Development Group, systematic review teams, and contributing experts for their dedication and meticulous work. Under the visionary leadership of the Ministry of Health & Family Welfare and with the unwavering support of the Department of Health Research and DGHS, we are confident that these guidelines will serve as a cornerstone for excellence in lung cancer care nationwide.

Dr Sunita Sharma
DGHS

Dr. Rajiv Bahl
Secretary DHR & DG, ICMR

CONTENTS

ACKNOWLEDGEMENTS

Lung cancer represents a significant and growing public health challenge in India, with rising incidence and mortality rates that underscore the urgent need for standardized, evidence-based management guidelines. In response to this pressing need, the Ministry of Health & Family Welfare envisioned one comprehensive guideline for the entire country based on the best available evidence.

The secretariat gratefully acknowledges the Steering Group for their leadership and strategic oversight throughout the guideline process. We extend our heartfelt appreciation to the members of the Guideline Development Group, whose expertise and dedication were instrumental in formulating the recommendations contained herein. We also acknowledge their commitment in attending multiple extended meetings to review and refine the evidence profiles and to participate fully in the Evidence-to-Decision process. We are indebted to our methodologist Prof. Joseph Mathew for his invaluable guidance and rigorous methodological support. Our sincere thanks also go to the systematic review teams, whose meticulous evidence syntheses provided the foundation for every recommendation.

We are profoundly grateful to Dr. Rajiv Bahl, Secretary, Department of Health Research and Director General, ICMR, whose steadfast guidance, visionary leadership, and relentless advocacy have been pivotal at every stage of this guideline's development. We also extend our sincere gratitude to Ms. Anu Nagar, Additional Secretary, Department of Health Research, for her exemplary administrative coordination and assistance throughout the process.

The constant support of the Centre for Evidence-Based Guidelines is deeply valued, and we greatly appreciate the logistical and administrative contributions of the Department of Health Research and the Delivery Division of ICMR staff.

ABBREVIATIONS

Abbreviation	Full Form
6MWD	6 - Minute Walking Distance
6MWD	6 - Minute Walking Distance
ALB	Albumin
ALK	Anaplastic Lymphoma Kinase
BMI	Body Mass Index
CBT	Cognitive Behavioural Theory
CNS	Central Nervous System
COPD	Chronic Obstructive Pulmonary Disease
CPET	Cardiopulmonary exercise testing
CPT	Chest Physical Therapy
CRT	Conventional resistance training
CTCAE	Common Terminology Criteria for Adverse Events
ECOG	Eastern Cooperative Oncology Group
EGFR	Epidermal Growth Factor Receptor
EORTC	European Organization for Research and Treatment of Cancer
ERAS	Enhanced Recovery After Surgery
FACT G	Functional Assessment of Cancer Therapy – General
FACT L	Functional Assessment of Cancer Therapy – Lung
FEV	Forced Expiratory Volume
FVC	Forced Vital Capacity
GDG	Guideline Development Group
GOLD	Global Initiative for Chronic Obstructive Lung Disease
GRADE	Grading of Recommendations, Assessment, Development and Evaluations
HADS A	Hospital Anxiety and Depression Scale - Anxiety
HADS D	Hospital Anxiety and Depression Scale - Depression
HIIT	High-Intensity Interval Training
IARC	International Agency for Research on Cancer
ICER	Incremental Cost-Effectiveness Ratio
IMT	Inspiratory Muscle Training
IPT	Intensive Physical Therapy

LMIC	Low- and Middle-Income Countries
MCID	Minimal Clinically Important Difference
MDASI	M. D. Anderson Symptom Inventory
MID	Minimal Important Difference
NPR	Non-Pulmonary Rehabilitation
NSCLC	Non-Small Cell Lung Cancer
OMD	Oligometastatic Disease
PEF	Peak Expiratory Flow
PET	Positron Emission Tomography
PFS	Progression Free Survival
PFT	Pulmonary Functional Tests
PHET	Preoperative Home-based Exercise Training
PHQ	Patient Health Questionnaire
PICO	Population, Intervention, Comparison, Outcome
PPC	Postoperative Pulmonary Complications
PRISMA	Preferred Reporting Items for Systematic Reviews and Meta-Analyses
PROSE	Patient-Reported Outcomes and Symptoms
PRP	Pulmonary rehabilitation programme
QALY	Quality-Adjusted Life Year
QLQ	Quality of Life Questionnaire
QOL	Quality of Life
RECIST	Response Evaluation Criteria in Solid Tumors
RMET	Respiratory Muscle Endurance Training
ROB	Risk of Bias
SMD	Standardized Mean Difference
TOI	Trial Outcome Index

EXECUTIVE SUMMARY

Background & Rationale:

Lung cancer remains a major global health burden, ranking among the leading causes of cancer-related mortality and profoundly affecting patient quality of life and healthcare systems. According to the latest Global Burden of Disease (GBD) estimates, lung malignancies contribute disproportionately to cancer deaths worldwide, in both high-income and resource-limited settings. Palliative care plays an indispensable role in alleviating physical symptoms, addressing psychosocial distress, and upholding patient dignity. Although interventions, such as advanced symptom management, early integration of psychosocial support, and multidisciplinary care pathways have enhanced comfort and well-being, many patients still endure significant physical and emotional burdens that require systematic, evidence-based attention. This guideline seeks to synthesize the current evidence base and provide methodologically sound recommendations for the palliative management of lung cancer.

Target Audience:

These guidelines are designed to inform a wide range of stakeholders, including policy makers, clinical practitioners specializing in palliative care, program managers, and health care administrators. The primary clinical audience comprises oncologists, pulmonologists, thoracic surgeons, radiation oncologists, palliative specialists, psychologists, and members of multidisciplinary oncology teams at secondary and tertiary care hospitals, dealing with palliative care. Academic researchers and implementation scientists engaged in translational studies and clinical trials will benefit from the consolidated review of current best practices as well as the identification of key research gaps and prioritized questions to guide future studies.

Guideline Development Methodology:

The guideline was developed using standard methodology as described by international agencies like the WHO and NICE. This involved the creation of a steering group, a guideline development group and systematic review teams. Briefly, the process involved: (i) Identifying priority review questions (PICOs), (ii) Evidence synthesis by systematic review & meta-analysis, (iii) Review of evidence profiles and grading the certainty of evidence (iv) Formulation of recommendations using the Evidence to Decision (EtD) framework (v) Drafting the guideline (vi) External review and (vii) Dissemination of guidelines. The GRADE approach (Grading of Recommendations Assessment, Development and Evaluation) was used to assess the certainty of evidence for each review question. The evidence generated was analyzed by the GDG to make judgments and formulate recommendations based on the EtD Framework in the GRADEpro GDT software. This included assessment of the effects (benefits to harms ratio) of the intervention, values and preferences of the patients, resource required, cost effectiveness, acceptability, feasibility of intervention and equity considerations. The GDG examined the evidence, made judgements for each disease condition, and finalized the wording of the recommendations. This was followed by external peer review, after which the draft guidelines were placed on the Department of Health Research (DHR) website for public consultation prior to final release.

Summary of Recommendations

Key Question	Recommendation	Rationale/Justification
For patients with lung cancer, does early integration of palliative care with standard oncological care compared to standard oncological care alone, improve patient outcomes?	Early integration of palliative care with standard oncological care is ***recommended*** as compared to standard oncological care alone for patients with lung cancer. Strength: Strong Certainty of evidence: Very low	The evidence showed moderate desirable effects, along with acceptability, feasibility, and cost-effectiveness probably favouring the early integration of palliative care. Despite very low certainty of evidence, the panel judged that the benefits clearly outweigh minimal harms. Given strong patient values and preferences for early supportive care, a strong recommendation was issued, while recognizing the need to address moderate resource requirements and potential equity concerns during implementation.
In patients with advanced lung cancer experiencing dyspnoea, how effective is multimodal treatment interventions compared to drug therapy alone in terms of improvement in dyspnoea?	Multi-modal treatment is ***recommended*** as compared to drug therapy alone for treatment of dyspnoea in patients with advanced lung cancer. Strength: Strong Certainty of evidence: Very low	The evidence showed moderate desirable effects with negligible additional costs, and cost-effectiveness probably favouring the use of multimodal interventions. The panel judged that the benefits outweigh minimal harms, supporting a strong recommendation.
For patients with newly diagnosed lung cancer, how efficacious is multi-modal approach to managing the symptom-cluster of insomnia, fatigue and depression, compare with psycho-social/ psychotherapeutic care alone?	Multimodal Approach of treatment is ***recommended*** in comparison to treatment with Psychotherapeutic Care alone for patients with lung cancer. Strength: Strong Certainty of Evidence: Very low	The evidence showed moderate desirable effects with trivial harms, alongside acceptability, feasibility, and cost-effectiveness probably favouring multimodal approach in managing the symptom cluster. The anticipated benefits outweigh potential downsides, supporting a strong recommendation.

GUIDELINE DEVELOPMENT PROCESS

Introduction:

A new process has been established within the Ministry of Health and Family Welfare (MoHFW) whereby comprehensive evidence-based guidelines are jointly developed by the Department of Health and Family Welfare (DoHFW), Directorate General of Health Services (DGHS), and the Department of Health Research (DHR) through a rigorous and robust scientific methodology. This initiative aims to bring clarity and consistency for key stakeholders, including patients, clinicians, and society at large. Evidence generation involved systematic reviews and meta-analyses of existing literature based on well-defined review questions structured using the PICO framework. The synthesized evidence was subsequently appraised for certainty using the Grading of Recommendations, Assessment, Development and Evaluation (GRADE) approach. This assessment informed the formulation of recommendations through structured Evidence-to-Decision (EtD) frameworks. Such rigorously developed evidence-based guidelines have the potential to bridge the research-to-policy gap by translating the best available evidence on healthcare interventions into routine clinical practice. (Figure 1).

Steps of Guideline development

Figure 1: Guideline Development Process - Adopted from NICE, WHO

Rationale/Scope:

Lung cancer often progresses rapidly to advanced stages, leaving patients with high symptom burden and a critical need for timely palliative support. There is a need to establish standardized guidance to enable consistent, effective, patient-centered and evidence-based palliative care across all levels of the health system. Realizing that therapeutic applications need to be based on rational and ethical premises, these guidelines aim to summarize the evidence available on the efficacy of lung cancer palliative care to guide informed decisions.

These guidelines aim to promote the responsible, safe, equitable, and effective delivery of lung cancer palliative care.

Contributors:

The following groups contributed to the development of guidelines (List Annexure 1):

Steering Group:

This group was jointly chaired by the Secretary, DHR & DG, ICMR and DGHS in overseeing the entire process of guideline development. The steering group identified priority disease conditions, helped in the formulation of GDG, reviewed the declaration of interest of members, reviewed the draft guidelines and managed the guideline publication and dissemination.

Guideline Development Group:

This group was constituted to formulate review questions relevant for the guidelines for conducting systematic reviews for addressing the question, decide on the critical outcomes and formulate recommendations based upon evidence generated by the systematic review teams. It is a multi-disciplinary group composed of methodologists, medical oncologists, surgical oncologists, radiation oncologists, palliative specialists, health economist, person with lived experience as well as patient group representatives. Potential members of the GDG were identified and approved by the Steering Group based on requisite technical skills and diverse perspectives needed for the formulation of the guidelines. These members were free from any conflict of interest in order to formulate unbiased recommendations. The subject experts and methodologists provided critical inputs on the formulation of review questions in the PICO format. After completion of the systematic reviews, the evidence profiles were reviewed by the DHR secretariat and guideline methodologists with the help of subject matter experts. Finally, the GDG examined and interpreted the whole body of evidence and made judgements in the meeting using GRADEpro EtD framework.

Systematic Review Teams:

These teams were commissioned to review and evaluate all available evidence in the form of randomized controlled trials (RCTs). The certainty of this evidence was assessed by the established GRADE criteria on the basis of risk of bias, imprecision, inconsistency, indirectness and publication bias.

External Reviewers:

Relevant subject experts were identified to review the final guideline document and comment upon the clarity of the recommendations, validity of the justification provided for each recommendation and the completeness of evidence.

DHR Secretariat:

The DHR Secretariat provided overall technical, methodological, and administrative coordination throughout the guideline development process. The Secretariat facilitated the establishment and functioning of the Guideline Development Group (GDG), and Systematic Review teams; coordinated meetings and communications among all stakeholder groups; and ensured adherence to the approved guideline development methodology and timelines. The Secretariat also monitored conduct of the systematic review process to ensure fidelity to approved protocols and internationally accepted reporting and methodological standards which included verification of PICO alignment, eligibility criteria, search strategy validation, duplicate screening and data-extraction processes, prespecified statistical and sensitivity analyses, risk-of-bias assessments, and

complete audit trails for protocols, amendments, correspondence, datasets, analysis scripts and final outputs. The Secretariat conducted a structured technical review of the evidence profiles received from the systematic review teams, verified the appropriate application of the GRADE and Evidence to Decision (EtD) frameworks in collaboration with guideline methodologists, and ensured systematic documentation of decisions at each stage of the guideline development process. The Secretariat also monitored timelines and key milestones, maintained and managed declarations of interest and conflicts (including procedures for their identification, management, and documentation), coordinated external and independent methodological peer review, and supported the finalisation of guideline recommendations.

Declaration of Interests:

Conflicts of interest (COIs) do not automatically preclude participation in guideline development, but they must be identified, transparently disclosed, and actively managed to minimise bias. A COI is any set of circumstances that creates a risk that professional judgement about a primary interest could be unduly influenced by a secondary interest; secondary interests may be financial or non-financial and include any interest that could be affected by a guideline recommendation. All potential GDG members completed a Declaration of Interests form adapted from WHO[1], and these declarations were reviewed by the Steering Group and managed appropriately. A summary of the Declaration of Interests (DoIs) and how they were managed is provided in Annexure.

Defining the Scope and Key Questions:

The Steering Group convened to define the full scope of the lung cancer guidelines, covering the entire continuum of care, from prevention and screening to diagnosis, treatment, and palliative care. Based on these priorities, the Guideline Development Group (GDG) formulated a total of 30 PICO-formatted review questions to guide the evidence synthesis process. These included 4 questions on prevention, 3 on screening, 8 on diagnosis, 12 on treatment, and 3 on palliation. Each question was developed with careful consideration of the Population, Intervention, Comparator, and Outcomes, ensuring alignment with the most pressing clinical and public health needs. The GDG emphasized relevance to patient priorities and feasibility within the Indian healthcare context, laying the foundation for evidence-based and context-specific recommendations.

Systematic Reviews:

Commissioning of Systematic Reviews: Once the review questions were identified, the ICMR-DHR secretariat floated an Expression of Interest inviting experts in the field from all over the country to conduct systematic reviews and meta-analysis. Out of a total of 152 applications received, 30 teams were selected. Criteria for evaluation included methodology expertise, subject expertise, quality of systematic reviews published, database access, strength of team and conflict of interests, if any. The systematic reviews in PICO format as finalized by the GDG. All the teams were provided with the methods provided oversight, including technical assessment and feedback on each systematic review protocol. The data extraction was checked to ensure uniformity and transparency in the entire process of guideline development.

Literature Search Strategy:

To maintain a uniform methodology, all the systematic review teams were instructed to design literature searches on the following databases: PubMed, Embase, Scopus, and Cochrane CENTRAL. Only randomized controlled trials were included in the systematic reviews of treatment and palliation related reviews. No grey literature was included. However, hand-searching of references of relevant review articles was done. Non-English articles were excluded only if translation was not possible. Subgroup analyses (if mentioned apriori in the protocol) was done wherever needed.

In addition, few criteria precluded the trial from being included in the final body of evidence in the evidence to decision framework. They were as follows:

- Flawed process of random sequence generation and/or concealment of allocation
- More than 30% deviated from allocated intervention post-randomization

Therefore, the systematic review teams were asked to do a meta-analysis excluding such trials and the evidence produced thereafter was presented to the GDG.

Data Extraction Methods:

Data extraction was conducted by the systematic review teams and reviewed by the ICMR-DHR secretariat and the methodologists. The teams were advised to use plot digitizer wherever feasible, if values were not available in text. Imputations and assumptions were best to be avoided. All methodological queries were resolved with the help of guideline methodologists and the teams were also advised to refer to the *Cochrane Handbook for Systematic Reviews of Interventions* to resolve any methodological queries[2]. While doing meta-analysis, the use of standardized mean difference (SMD) was to be minimized, as it is easier to compare mean difference (MD) with the minimal clinically important difference (MCID).

Risk of Bias Assessment:

Risk of bias for each study outcome was assessed using the Revised Cochrane Risk of Bias-2 tool. For assessment, the following terms of reference were agreed upon by the GDG and provided to all the systematic review teams:

- Use only the ROB-2 Tool for assessment of the risk of bias of RCTs and mention the reasons for the risk of bias judgments for all the domains of the ROB-2 Tool.
- The downgrading of evidence due to the risk of bias judgment should be decided by the following criteria:
  i. If ≥ 2/3rd (by weight in the pooled analysis) of RCTs are at low risk of bias (green), then label the overall risk of bias for that outcome as not serious in the GRADE Table.
  ii. If 1/3rd–2/3rd (by weight in the pooled analysis) of RCTs are at low risk of bias (green), then label the overall risk of bias for that outcome as serious in the GRADE Table.
  iii. If < 1/3rd (by weight in the pooled analysis) of RCTs are at low risk of bias (green), then label the overall risk of bias for that outcome as very serious in the GRADE Table.

The teams were asked to review the RCTs with extreme results in the pooled analysis cautiously, to search for any major methodological discrepancy.

The progress of the systematic review teams was monitored monthly and queries were resolved by the secretariat after discussion with the methodologists.

Determination of Minimal Clinically Important Difference (MCID):

The minimal clinically important difference (MCID) is defined as the smallest change in any outcome that is considered as clinically meaningful or important by the patient and the health care providers. It is the difference at which a large set of clinicians will be willing to change their practice for this benefit and the certainty of evidence is rated in relation to this threshold.

In this guideline, the GDG determined the MCID for each critical outcome based on their clinical expertise and the expected impact of the intervention. This included considerations such as the potential for meaningful improvement in patient outcomes, the relevance and magnitude of benefit, and whether the anticipated change would influence treatment decisions. The certainty of evidence for each outcome was assessed in relation to the established MCID thresholds, ensuring that recommendations were both evidence-based and clinically significant.

Grading of the Certainty of the Evidence:

The GRADE approach was used to assess the certainty of evidence using the GRADEpro GDT software (https://www.gradepro.org/). At baseline RCTs start with high certainty of evidence and this certainty can be downgraded based on pre-defined criteria like the risk of bias, inconsistency, imprecision, indirectness, and publication bias. Publication bias was evaluated using funnel plots if the number of studies for a particular meta-analysis was more than 10. If the studies were less than 10, Egger's test was used for evaluation. The systematic review teams completed their reviews and shared the evidence profiles with the guideline secretariat. The secretariat then reviewed the evidence profiles, with the help of guideline methodologist and any discrepancies in the review were resolved through discussion with the systematic review teams. The table below highlights the significance of the certainty of evidence as per GRADE[3]:

Certainty level	Significance
High	We are very confident that the true effect lies close to that of the estimate of the effect
Moderate	We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different
Low	Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect
Very Low	We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect

Drafting of Recommendations using Evidence to Decision Frameworks:

The DHR secretariat prepared the draft EtD frameworks. The EtD Framework available on the GRADEpro GDT software was used to draft recommendations. It consists of a set of criteria that determine the strength and direction of a recommendation to bring about transparency in the formulation of recommendations. These criteria include the certainty of evidence, the balance between benefits and harms, the acceptability and feasibility of the intervention, patient values and preferences, equity considerations, resource use and cost effectiveness. Prior to drafting recommendations, all the GDG members were apprised of this framework and every criterion was

explained in detail. The secretariat presented these frameworks along with a review of evidence profile and forest plots provided by the systematic review teams to the GDG.

Formulation of Recommendations:

The GDG members were asked to make judgments on each of the domain of the EtD framework based on the evidence presented to them. Judgments on the desirable and undesirable effects were made on the basis of the systematic reviews and meta-analysis. Review of literature/research evidence as well as the experience of the GDG members was used to inform the discussion. Patient values and preferences, resource use and cost effectiveness, acceptability and feasibility of the intervention along with equity considerations. Wherever research evidence unavailable, the option of the GDG was recorded in additional considerations. The entire body of evidence was put into the GRADE EtD framework for drafting the final recommendation for each review question.

Detailed deliberations and the rationale for each judgment were recorded explicitly in the "Additional Considerations" column of GRADEpro GDT using the PanelVoice feature to ensure transparency. Voting was convened only when differences of opinion arose, with each domain discussed thoroughly until consensus (≥75% agreement) was achieved. Following domain-level resolution, a final vote determined the strength and direction of each recommendation. Throughout this process, the GDG also identified evidence gaps and highlighted priority areas for future research.

Strength of Recommendations:

The strength of each recommendation reflects the GDG's confidence in the balance between an intervention's benefits and harms for the intended patient population, as well as considerations of resource use, equity, feasibility, and acceptability[4]. When the GDG was highly confident that desirable effects clearly outweighed undesirable effects and that the intervention was affordable, equitable, feasible, and acceptable, a strong recommendation was issued. Conversely, if uncertainty remained around the balance of benefits and harms, or if concerns arose regarding costs, implementation feasibility, equity, or stakeholder acceptability, a conditional recommendation was made. Conditional recommendations signal that clinicians should tailor decisions to individual patient circumstances, preferences, and local context.

Document Preparation and Peer Review:

After the completion of the ETD meetings, the ICMR-DHR secretariat prepared a draft of the guideline document to accurately reflect the deliberations and decisions taken by the GDG. This draft was reviewed by the guideline methodologists followed by the external review group. The external reviewers were requested to comment upon the clarity of the recommendations so that there is no ambiguity about the decision among the end-users, validity of the justification provided for each recommendation, accuracy and completeness of the evidence (randomized controlled trials only). The steering group carefully evaluated the input of the GDG members and the comments by the external reviewers. Revisions to the draft document were done as needed, to correct for any factual errors and the document was finalized, thereafter.

REFERENCES

1. WHO handbook for guideline development, second edition. Geneva: World Health Organization; GBD 2021 Nervous System Disorders Collaborators.
2. Higgins JPT, Thomas J, Chandler J, Cumpston M, Li T, Page MJ, Welch VA (editors). Cochrane Handbook for Systematic Reviews of Interventions.
3. Balshem H, Helfand M, Schünemann HJ, Oxman AD, Kunz R, Brozek J, Vist GE, Falck-Ytter Y, Meerpohl J, Norris S, Guyatt GH. GRADE guidelines: 3. Rating the quality of evidence. J Clin Epidemiol. 2011 Apr; 64(4):401-6. doi: 10.1016/j.jclinepi.2010.07.015. Epub 2011 Jan 5. PMID: 21208779.
4. Andrews J, Guyatt G, Oxman AD, Alderson P, Dahm P, Falck-Ytter Y, Nasser M, Meerpohl J, Post PN, Kunz R, Brozek J, Vist G, Rind D, Akl EA, Schünemann HJ. GRADE guidelines: 14. Going from evidence to recommendations: the significance and presentation of recommendations. J Clin Epidemiol. 2013 Jul; 66(7):719-25.

FOR PATIENTS WITH LUNG CANCER, DOES EARLY INTEGRATION OF PALLIATIVE CARE WITH STANDARD ONCOLOGICAL CARE COMPARED TO STANDARD ONCOLOGICAL CARE ALONE, IMPROVE PATIENT OUTCOMES?

Table of Contents

Background

Palliative care is one of the treatment modalities for cancer treatment. It is applicable throughout the cancer continuum from diagnosis to end of life. Most often, it is initiated once curative treatment isn't feasible or death is anticipated. The advantages of early palliative care (EPC) referral are timely assessment and treatment of physical and psychological symptoms, effective coping, improved communication and support for decision making and discussion of end-of-life preferences. Lung cancer is the most common cancer worldwide. It often presents in advanced and metastatic stages and is associated with significant symptoms like pain, dyspnoea, fatigue, and anorexia. Early palliative care in solid cancers has been shown to enhance the quality of life and symptom burden based on several randomised trials. The trials are heterogeneous, involving advanced incurable cancers across sites (head and neck, gastrointestinal and lung), with some showing benefit while others showing no impact of palliative care.

A meta-analysis on EPC among all cancers by Gautama et al. showed improved quality of life but no effect on mood or symptom control with palliative care. The trials have combined the outcomes for many or all cancers, and hence, it is difficult to estimate the effect of palliative care on individual cancers, particularly lung cancer. Temel et al. was the earliest randomised trial showing the benefit of palliative care in improving symptom control, mood and quality of life. This systematic review and meta-analysis aimed to comprehensively review all available evidence that has examined the effect of early integration of palliative care with standard oncological care compared to standard oncological care alone for lung cancer patients on symptom control, quality of life and survival. The secondary outcomes are to compare documented advance care plans, aggressive interventions in the last month of life and the cost of palliative care and oncological care with oncological care alone.

Recommendations

Early integration of palliative care with standard oncological care is ***recommended*** as compared to standard oncological care alone for patients with lung cancer

Strength: Strong
Certainty of evidence: Very low

Rationale/Justification

The evidence showed moderate desirable effects, along with acceptability, feasibility, and cost-effectiveness probably favouring the early integration of palliative care. Despite very low certainty of evidence, the panel judged that the benefits clearly outweigh minimal harms. Given strong patient values and preferences for early supportive care, a strong recommendation was issued, while recognizing the need to address moderate resource requirements and potential equity concerns during implementation.

Summary of Evidence

Key Question

For patients with lung cancer, does early integration of palliative care with standard oncological care compared to standard oncological care alone, improve patient outcomes?

Included Studies

A total of 3273 records from electronic databases were identified till date. Of the 3273 articles, 741 duplicate articles were removed. Further 2467 articles were removed after title and abstract screening because they were not relevant. Full text review was done for 13 articles. After application of inclusion and exclusion criteria, 7 articles were selected for systematic review.

Population and Study Characteristics

All the studies included patients diagnosed with lung cancer. The review includes adults of all ages and gender. Eligible studies are those that evaluate the effect of early integration of palliative care with standard oncological care compared to standard oncological care alone, in improving patient outcomes.

Subgroups:

a. Stage (Early-stage vs Advanced Stage)
b. Age
c. Comorbidities
d. Symptoms

Eligible studies reported on at least one of the following treatment outcomes:

1. Symptom burden control (7 studies)
2. Quality of life (7 studies)
3. Overall survival (3 studies)
4. Documented advance care-plan (2 studies)
5. Aggressive interventions in last month of patients' life [emergency visits/ ICU utilization/oncological intervention] (No studies)
6. Cost (one study)

Intervention

Standard oncological care with early integration of palliative care

Subgroup: 1. Within 8 weeks of diagnosis of lung cancer vs later

2. Various components of palliative care

Comparator

Standard oncological care without early integration of palliative care patients undergoing treatment for lung cancer.

Outcome

Different outcomes were evaluated and included the following critical and important outcomes:

1. Symptom burden control (*Critical outcome*)
2. Quality of life (*Critical outcome*)
3. Overall survival (*Critical outcome*)
4. Documented advance care-plan (*Important outcome*)
5. Aggressive interventions in last month of patients' life [emergency visits/ ICU utilization/oncological intervention] (*Important outcome*)
6. Cost (*Important outcome*)

Duration of Follow up

Critical Outcome reviewed and their MCID

Sr. No	Critical outcome reviewed	What does it measure	MCID decided by GDG
1	Overall Survival	OS (Proportion of people who have survived at a particular time point)	10% at any point of time
		OS (Proportion increase in median survival)	3 months for advanced stage 6 months for early stage
2	Symptom burden control	Difference in mean symptom score between intervention and standard of care	20%
3	Quality of Life	Quality of life (difference in the mean scores of QoL)	FACT L: 10% difference FACT G: 10% difference EORTC QLQ 30: 10% difference

PICO provided by GDG

Framework	Description
Population	Patients with lung cancer Subgroups: 1. Stage (Early-stage vs Advanced stage) 2. Age 3. Comorbidities 4. Symptoms
Intervention	Standard oncological care with early integration of palliative care *Subgroup*: 1. within 8 weeks of diagnosis of lung cancer vs later 2. Various components of palliative care
Comparator	Standard oncological care without early integration of palliative care
Outcome	• Symptom burden control (*Critical outcome*) • Quality of life (*Critical outcome*) • Overall survival (*Critical outcome*) • Documented advance care-plan (*Important outcome*) • Aggressive interventions in last month of patients' life [emergency visits/ ICU utilization/oncological intervention] (*Important outcome*) • Cost (*Important outcome*)

Risk of Bias Assessment

Symptom Burden Control

	D1	D2	D3	D4	D5	Overall
Temel et al 2010	-	+	-	-	+	-
Temel et al 2017	+	-	+	-	+	-
Krug et al 2021	+	+	+	-	+	-
Reinke et al 2022	+	+	+	-	X	X
Chen et al 2023	-	+	X	-	+	X
Dutta et al 2024	X	+	X	X	+	X
Allende et al 2024	-	+	X	X	+	X

Quality of life

	D1	D2	D3	D4	D5	Overall
Temel et al 2010	-	+	-	-	+	-
Temel et al 2017	+	-	+	-	+	-
Krug et al 2021	+	+	+	-	+	-
Reinke et al 2022	+	+	+	-	X	X
Chen et al 2023	-	+	X	-	+	X
Dutta et al 2024	X	+	X	X	+	X
Allende et al 2024	-	+	X	X	+	X

Overall Survival

	D1	D2	D3	D4	D5	Overall
Temel et al 2010	-	+	+	+	+	-
Chen et al 2023	-	+	-	+	+	-
Allende et al 2024	-	+	+	+	+	-

Documented Advance Care-Plan

	D1	D2	D3	D4	D5	Overall
Temel et al 2010	-	+	+	+	+	-
Reinke et al 2022	+	+	+	+	+	+

Cost

	D1	D2	D3	D4	D5	Overall
Temel et al 2010 and Greer et al 2012	-	+	+	+	+	-

D1	Randomisation process
D2	Deviations from the intended interventions
D3	Missing outcome data
D4	Measurement of the outcome
D5	Selection of the reported result

+	Low risk
-	Some concerns
X	High risk

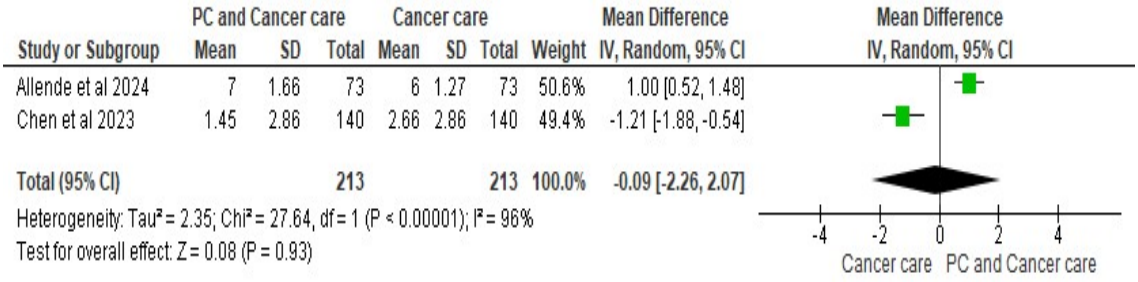
Desirable Effects

1. Symptom Burden

1.1 HADS Anxiety

Evidence shows no statistically significant or clinically meaningful difference between integrated palliative care and cancer care alone for HADS Anxiety. The analysis of studies comparing early integration of palliative care along with standard of care versus standard oncological care alone yielded a mean difference of 0.09 lower (95% CI: 2.26 lower to 2.07 higher). Substantial heterogeneity was observed across the studies. The evidence suggests that the addition of palliative care to cancer treatment does not produce a consistent benefit and that variability in study results limits the certainty of the evidence.

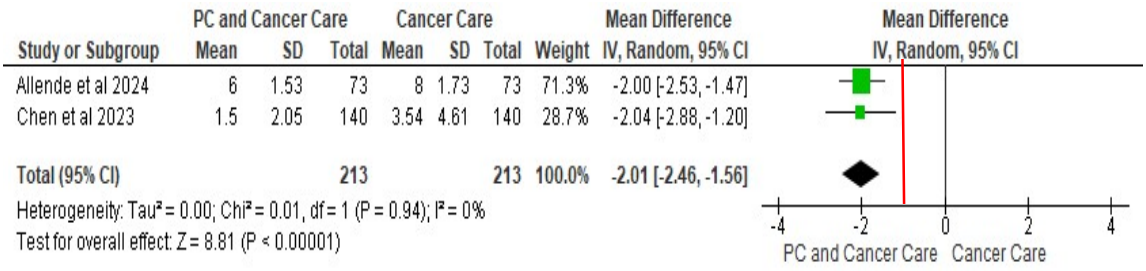
Figure 1.1 - Forest plot: Symptom Burden HADS Anxiety



1.2 HADS Depression

Evidence shows a significant and clinically meaningful benefit of integrating palliative care with cancer treatment in improving the assessed outcome. The analysis of two studies demonstrated a mean difference of 2.01 lower (95% CI: 2.46 lower to 1.56 lower), indicating a substantial reduction in the outcome score in favor of the intervention group. The score ranges from 0 to 14. Higher scores suggest high symptom burden. Higher scores were observed in patients receiving cancer care, suggesting better symptom control with the addition of palliative care.

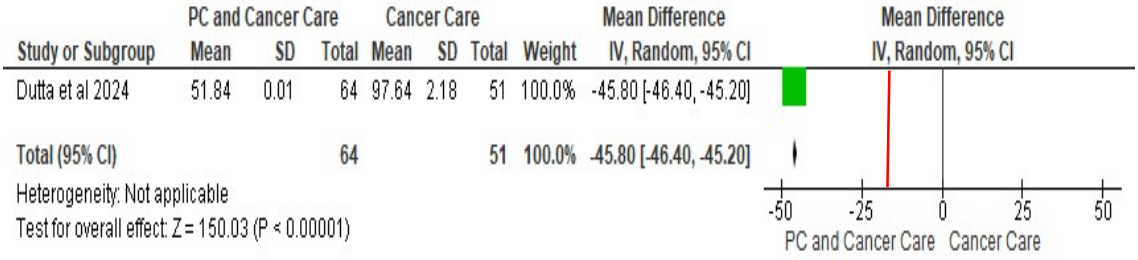
Figure 1.2 - Forest plot: Symptom Burden - HADS Depression



1.3 Edmonton Symptom Assessment Scale (ESAS)

Evidence shows a significant and clinically meaningful benefit of integrating palliative care with cancer treatment in improving the assessed outcome. The analysis of two studies demonstrated a mean difference of 2.01 lower (95% CI: 2.46 lower to 1.56 lower), indicating a substantial reduction in the outcome score in favor of the intervention group. The score ranges from 0 to 60. Higher scores were observed in patients receiving cancer care, suggesting better symptom control with the addition of palliative care.

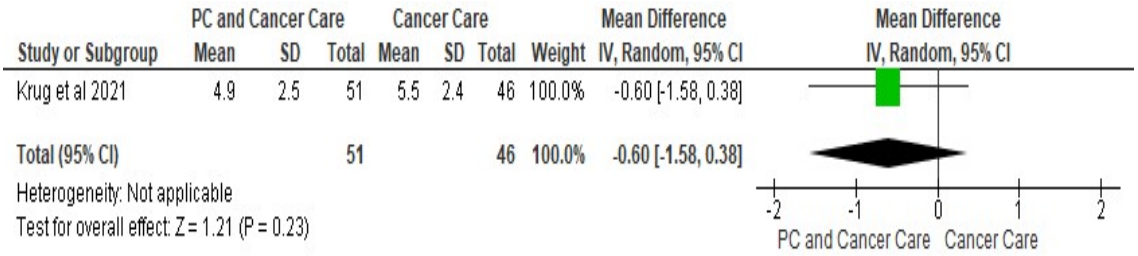
Figure 1.3 - Forest plot: Symptom Burden - ESAS



1.4 Distress Thermometer (DT)

Evidence shows no statistically significant or clinically meaningful difference between integrated palliative care and cancer care alone for Distress thermometer. The analysis of studies comparing early integration of palliative care along with standard of care versus standard oncological care alone yielded a mean difference of 0.60 lower (95% CI: 1.58 lower to 0.38 higher). The score ranges from 0 to 10. Higher scores suggest high symptom burden. Higher scores were observed in patients receiving cancer care, suggesting better symptom control with the addition of palliative care. This crosses the null line and is not significant.

Figure 1.4 - Forest plot: Symptom Burden - Distress Thermometer

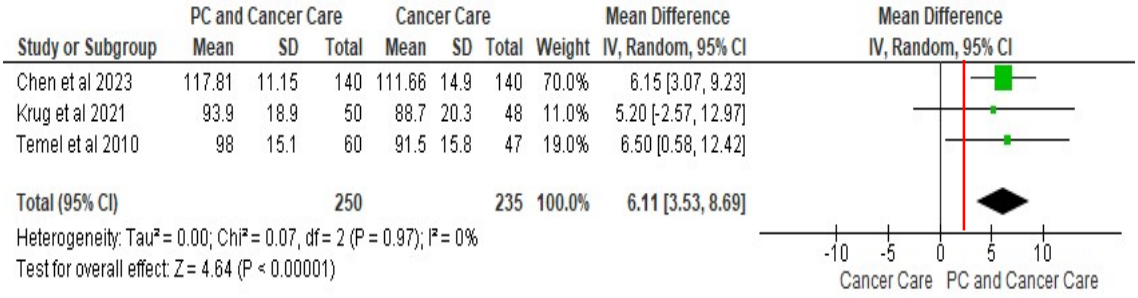


Quality of Life

1.5 FACT L

Evidence shows a significant and clinically meaningful benefit of integrating palliative care with cancer treatment in improving the assessed outcome. Pooled analysis of three randomized studies showed that integrated palliative and cancer care (intervention) was favoured over cancer care alone, with patients in the intervention group achieving higher outcome scores (mean difference 6.11 points; 95% CI: 3.53 to 8.69).

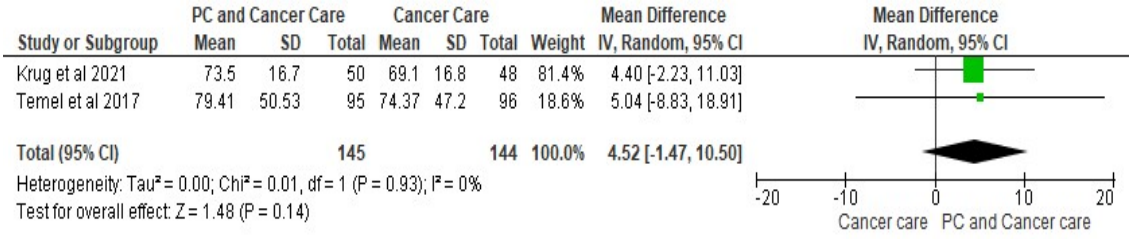
Figure 1.5 - Forest plot: Symptom Burden - FACT L



1.6 FACT G

Evidence shows no statistically significant or clinically meaningful difference between integrated palliative care and cancer care alone for FACT G. The analysis of studies comparing early integration of palliative care along with standard of care versus standard oncological care alone yielded a mean difference of 4.52 higher (95% CI: 1.47 lower to 10.50 higher).

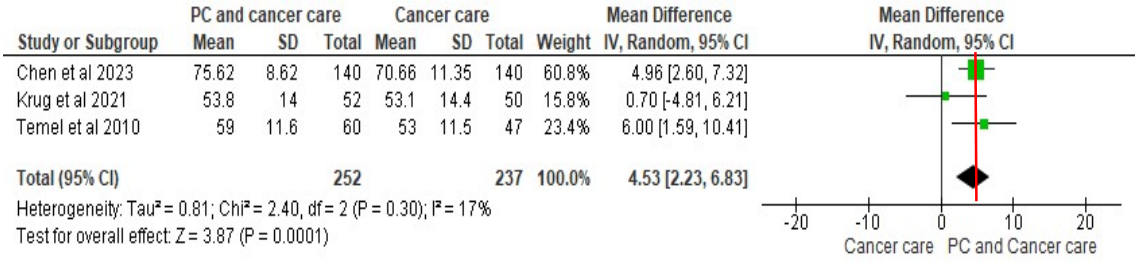
Figure 1.6 - Forest plot: Symptom Burden - FACT G



1.7 Trial Outcome Index (TOI)

Evidence shows a statistically significant benefit of integrating palliative care with cancer treatment in improving patient outcomes. The analysis of studies demonstrated a mean difference of 4.53 higher (95% CI: 2.23 higher to 6.83 higher; p = 0.0001) in favor of the integrated palliation approach, with low heterogeneity across studies. These findings suggest that adding palliative care to standard oncological treatment is consistently associated with improved outcomes.

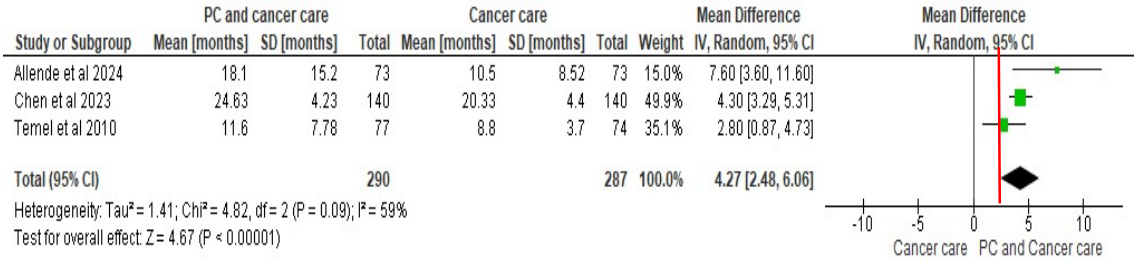
Figure 1.7 - Forest plot: Trial Outcome Index



1.8 Overall Survival

Pooled analysis of three randomized studies (total n = 577) found that adding palliative care to standard cancer treatment produced a statistically significant and clinically important improvement in the outcome: mean difference 4.27 months (95% CI 2.48 to 6.06 months; Z = 4.67, p < 0.00001), favoring the integrated palliative-and-cancer-care arm. All three studies point in the same direction, but there was moderate heterogeneity (Tau^2 = 1.41; Chi^2 = 4.82, df = 2, p = 0.09; I^2 = 59%), so the exact magnitude of benefit varies somewhat between trials.

Figure 1.8 - Forest plot: Overall Survival



*MCID Line in red (-)

Undesirable Effects

The evidence did not report any undesirable effects associated with the early integration of palliative care into cancer treatment, and potential harms remain unknown, indicating a need for further research to evaluate unintended consequences.

Table 1. Summary of Findings

Early Integration of Palliative Care along with Standard Oncological Care versus Standard Oncological Care alone

Patient or population: Patients with Lung Cancer

Intervention: Palliative care with standard oncological care

Comparison: Standard Oncological Care

Outcomes	Anticipated absolute effects* (95% CI)		Relative Effect (95% CI)	No. of Participants (Studies)	Certainty of the Evidence (GRADE)	Comments
	Risk with standard oncological care alone	Risk with Early integration of Palliative care with standard oncological care				
HADS A	Mean score 4.33	MD **0.09 lower** (2.26 lower to 2.07 higher)	-	426 (2 RCTs)	⊕◯◯◯ Very low[a,b,c]	The evidence is very uncertain about the effect of early integration of Palliative care with standard oncological care on HADS A.
HADS D	Mean score 5.77	MD **2.01 lower** (2.46 lower to 1.56 lower)	-	426 (2 RCTs)	⊕◯◯◯ Very low[a,d]	Early integration of Palliative care with standard oncological care may reduce HADS D slightly.
ESAS	Mean score 97.64	MD **45.8 lower** (46.4 lower to 45.2 lower)	-	115 (1 RCT)	⊕◯◯◯ Very low[a,d,e]	The evidence is very uncertain about the effect of early integration of Palliative care with standard oncological care on ESAS.
DT SCORE	Mean score 5.5	MD **0.6 lower** (1.58 lower to 0.38 higher)	-	97 (1 RCT)	⊕⊕◯◯ Low[c,e,f]	Early integration of Palliative care with standard oncological care likely reduces DT SCORE.
FACT L	Mean score 97.29	MD **6.11 higher** (3.53 higher to 8.69 higher)	-	485 (3 RCTs)	⊕⊕◯◯ Low[a,d]	Early integration of Palliative care with standard oncological care likely results in a large increase in FACT L.

FACT G	Mean score 71.73	MD **4.52 higher** (1.47 lower to 10.5 higher)	-	289 (2 RCTs)	⊕⊕◯◯ Low[a,c]	Early integration of Palliative care with standard oncological care may increase/have little to no effect on FACT G but the evidence is very uncertain.
Quality of life assessed with: TOI	Mean score 58.92	MD **4.53 higher** (2.23 higher to 6.83 higher)	-	489 (3 RCTs)	⊕◯◯◯ Very low[a,d]	Early integration of Palliative care with standard oncological care may increase/have little to no effect on quality of life but the evidence is very uncertain.[a,c]
Overall survival	The median overall survival was **13.2** months	MD **4.27 months higher** (2.48 higher to 6.06 higher)	-	577 (3 RCTs)	⊕◯◯◯ Very low[a,d]	The evidence suggests early integration of Palliative care with standard oncological care increases overall survival.

CI: Confidence Interval; **HR:** Hazard Ratio; **MD:** Mean Difference; **OR:** Odds Ratio

GRADE Working Group grades of evidence

High certainty: we are very confident that the true effect lies close to that of the estimate of the effect.

Moderate certainty: we are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.

Low certainty: our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect.

Very low certainty: we have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect.

Explanations

a. *The studies included are of high risk. As per the SOP, < 1/3rd (by weight in the pooled analysis) of RCTs are at low risk of bias (green), hence the overall risk of bias for this outcome has been downgraded by two level and is labeled as very serious in the GRADE table.*
b. *Heterogeneity is present with I2=96% and P<0.001.*
c. *Downgraded one level for imprecision as the 95% Confidence interval (CI) crosses the null effect line*
d. *Optimal Information size (OIS) is not met.*
e. *Single study was downgraded one level for inconsistency as it was inevaluable*
f. *One study had some concerns in the measurement of the outcome*

Table 2. Evidence Profile

Early Integration of Palliative Care along with Standard Oncological Care versus Standard Oncological Care alone

Patient or population: Patients with Lung Cancer

Intervention: Palliative care with standard oncological care

Comparison: Standard Oncological Care

Certainty Assessment							No. of Patients		Effect		Certainty	Importance
No. of Studies	Study Design	Risk of Bias	Inconsistency	Indirectness	Imprecision	Other Considerations	Early Integration of Palliative Care with Standard Oncological Care	Standard Oncological Care Alone	Relative (95% CI)	Absolute (95% CI)		
HADS A												
2	randomised trials	very serious[a]	Serious[b]	not serious	Serious[c]	none	213	213	-	MD **0.09 lower** (2.26 lower to 2.07 higher)	⨁◯◯◯ Very low[a,b,c]	CRITICAL

HADS D												
2	randomised trials	very serious[a]	not serious	not serious	Serious[d]	none	213	213	-	MD **2.01 lower** (2.46 lower to 1.56 lower)	⊕◯◯◯ Very low[a,d]	CRITICAL
ESAS												
1	randomised trials	very serious[a]	Serious[e]	not serious	Serious[d]	none	64	51	-	MD **45.8 lower** (46.4 lower to 45.2 lower)	⊕◯◯◯ Very low[a,d,e]	CRITICAL
DT SCORE												
1	randomised trials	serious[f]	Serious[e]	not serious	Serious[c]	none	51	46	-	MD **0.6 lower** (1.58 lower	⊕⊕◯◯ Low[c,e,f]	CRITICAL

										to 0.38 higher)		
FACT L												
3	randomised trials	serious[a]	not serious	not serious	Serious[d]	none	250	235	-	MD **6.11 higher** (3.53 higher to 8.69 higher)	⊕⊕◯◯ Low[a,d]	CRITICAL
FACT G												
2	randomised trials	Serious[a]	not serious	not serious	Serious[c]	none	145	144	-	MD **4.52 higher** (1.47 lower to 10.5 higher)	⊕⊕◯◯ Low[a,c]	CRITICAL
Quality of Life (Assessed with: TOI)												

3	randomised trials	very serious[a]	not serious	not serious	Serious[c]	none	252	237	-	MD **4.53 higher** (2.23 higher to 6.83 higher)	⊕◯◯◯ Very low[a,c]	CRITICAL
Overall Survival												
3	randomised trials	very serious[a]	not serious	not serious	Serious[d]	none	290	287	-	MD **4.27 months higher** (2.48 higher to 6.06 higher)	⊕◯◯◯ very low[a,d]	CRITICAL

CI: Confidence Interval; **MD:** Mean Difference

Explanations

a. *The studies included are of high risk. As per the SOP, < 1/3rd (by weight in the pooled analysis) of RCTs are at low risk of bias (green), hence the overall risk of bias for this outcome has been downgraded by two level and is labeled as very serious in the GRADE table.*
b. *Heterogeneity is present with I2=96% and P<0.001.*
c. *Downgraded one level for imprecision as the 95% Confidence interval (CI) crosses the null effect line*
d. *Optimal Information size (OIS) is not met.*
e. *Single study was downgraded one level for inconsistency as it was inevaluable*
f. *One study had some concerns in the measurement of the outcome*

Summary of Judgements

Problem	Yes
Desirable Effects	Moderate
Undesirable Effects	Don't Know
Certainty of evidence	Very Low
Values	No important uncertainty or variability
Balance of effects	Favors the intervention
Resources required	Moderate costs
Certainty of evidence of required resources	Low
Cost effectiveness	Probably favors the intervention
Equity	Probably reduced
Acceptability	Yes
Feasibility	Yes
Recommendation: Early integration of palliative care with standard oncological care is ***recommended*** as compared to standard oncological care alone for patients with lung cancer. **Strength**: Strong **Certainty of Evidence**: Very low	

Caveats in Existing Evidence:

The GDG opined that the existing evidence had the following limitations:

- Limited availability of high-quality randomized controlled trials directly comparing early integrated palliative care plus standard oncological care versus standard oncological care alone, particularly with respect to patient-reported outcomes.
- Insufficient evidence on the effect of early palliative care integration on key patient-centred outcomes, including symptom burden, quality of life, psychological distress, and functional status.
- Scarcity of evidence addressing caregiver-related outcomes, including caregiver burden, satisfaction, and psychosocial well-being, in the context of early palliative care integration.
- Paucity of health economic evaluations, including cost-effectiveness and budget impact analyses, comparing early integrated palliative care with standard oncological care alone.

IN PATIENTS WITH ADVANCED LUNG CANCER EXPERIENCING DYSPNOEA, HOW EFFECTIVE IS MULTIMODAL TREATMENT INTERVENTIONS COMPARED TO DRUG THERAPY ALONE IN TERMS OF IMPROVEMENT IN DYSPNOEA?

Table of Contents

Background

Dyspnoea, or the subjective experience of breathlessness, is a prevalent (45%) and distressing symptom among patients with advanced lung cancer, significantly impacting their quality of life (Damani et al., 2018). As the disease progresses, the physiological and psychological burden of dyspnoea intensifies, necessitating effective symptom management strategies (Hui et al., 2020). Traditional pharmacological interventions, while beneficial, may not provide adequate relief for all patients and can be accompanied by side effects (Hui et al., 2021). Consequently, there is a growing interest in multimodal interventions that combine pharmacological treatments with non-pharmacological approaches to enhance symptom relief (Zemel et al., 2021).

Multimodal interventions apart from pharmacological treatment may include a variety of strategies such as physical therapies, psychosocial support, breathing exercises, and assistive devices (Hui et al., 2021). These approaches aim to address the complex interplay of physiological, emotional, and social factors that contribute to dyspnoea in this population. For instance, incorporating physical rehabilitation can improve functional capacity and reduce respiratory distress (Jastrzębski et al., 2015, while psychological interventions can alleviate anxiety, which often exacerbates the sensation of breathlessness (Garcia et al., 2012).

Despite the theoretical benefits of multimodal strategies, the effectiveness of these interventions in managing dyspnoea in advanced lung cancer patients remains inadequately assessed. Systematic reviews and meta-analyses can provide valuable insights into the overall efficacy and safety of these interventions by synthesizing data from various studies (Hui et al., 2021). By analysing existing literature, this systematic review aims to evaluate the impact of multimodal interventions on the symptomatic management of dyspnoea in adult patients with advanced lung cancer. The findings could inform clinical practice, guiding healthcare providers in developing comprehensive care plans that address the multifaceted nature of dyspnoea and ultimately improve patient outcomes.

Recommendations

Multi-modal treatment is ***recommended*** as compared to drug therapy alone for treatment of dyspnoea in patients with advanced lung cancer.

Strength: Strong
Certainty of Evidence: Very low

Rationale/Justification

The evidence showed moderate desirable effects with negligible additional costs, and cost-effectiveness probably favouring the use of multimodal interventions. The panel judged that the benefits outweigh minimal harms, supporting a strong recommendation.

Summary of Evidence

Key Question

In patients with advanced lung cancer experiencing dyspnoea, how effective is multimodal treatment interventions compared to drug therapy alone in terms of improvement in dyspnoea?

Included Studies

A total of 1392 records from electronic databases were identified till date. Of the 1392 articles, 208 duplicate articles were removed. Further 1110 articles were removed after title and abstract screening because they were not relevant. Full text review was done for 72 articles. After application of inclusion and exclusion criteria, 13 articles were selected for systematic review and 12 studies were included in meta-analysis.

Population and Study Characteristics

All the studies included patients diagnosed with advanced lung cancer. The review includes adults of all ages and gender. Eligible studies are those that evaluate the effect of multimodal treatment interventions compared to drug therapy in improving dyspnoea.

Eligible studies reported on at least one of the following treatment outcomes:

a) Improvement in dyspnoea (13 studies)
b) Performance status (5 studies)
c) Quality of life (6 studies)
d) Cost (2 studies)

Intervention:

Multi-modal interventions (combination of drug and non-drug). Drug: (opioids in dose for breathlessness, non-opioid medications (bronchodilators, corticosteroids, other analgesics, anxiolytics, laxatives, crisis medications) Nondrug: position, psycho-social support, vaccination, education on self-management (physical/occupational therapy, energy conservation techniques, hand-held fan)

Comparator:

Drug therapy alone (opioids in dose for breathlessness, non-opioid medications (bronchodilators, corticosteroids, other analgesics, anxiolytics, laxatives)

Outcome

Different outcomes were evaluated and included the following critical and important outcomes:

e) Improvement in dyspnoea (*Critical outcome*)
f) Performance status (*Critical outcome*)
g) Quality of life (*Critical outcome*)
h) Cost (*Important outcome*)

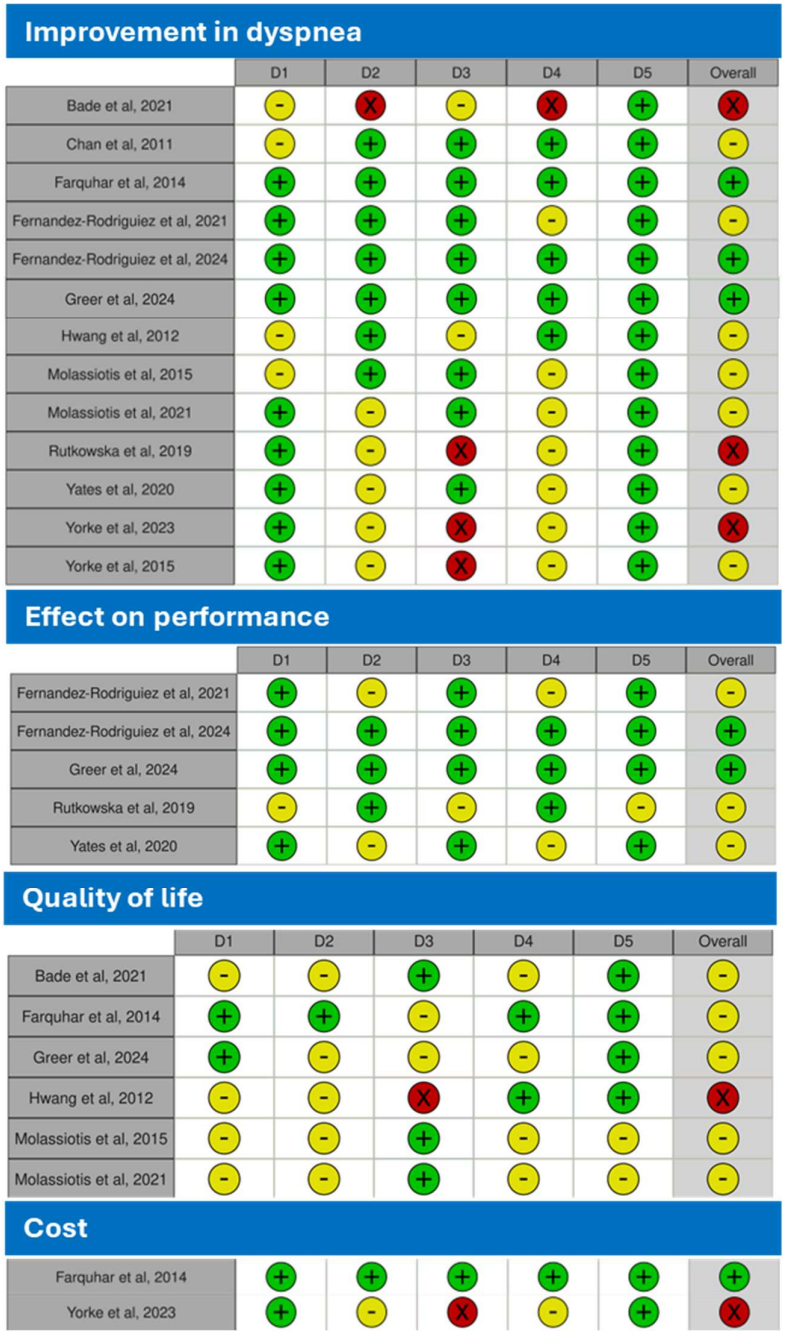
Critical Outcome reviewed and their MCID

Sr. No	Critical outcome reviewed	What does it measure	MCID decided by GDG
1	Improvement in dyspnoea	Difference in the mean scores	20%
2	Performance status	Difference in mean performance status between intervention and comparator	Difference of 1 point in KPS ECOG: difference of one point higher Reaching the best possible score
3	Quality of Life	Difference in the mean scores of QoL	10%

PICO

Framework	Description
Population	Adult patients with advanced lung cancer experiencing shortness of breath
Intervention	**Multi-modal interventions (combination of drug and non-drug)**. Drug: (opioids in dose for breathlessness, non-opioid medications (bronchodilators, corticosteroids, other analgesics, anxiolytics, laxatives, crisis medications) Nondrug: position, psycho-social support, vaccination, education on self-management (physical/occupational therapy, energy conservation techniques, hand-held fan)
Comparator	**Drug therapy alone** (opioids in dose for breathlessness, non-opioid medications (bronchodilators, corticosteroids, other analgesics, anxiolytics, laxatives)
Outcome	Improvement in dyspnoea (*critical outcome*) Performance status (*critical outcome*) Quality of life (*Critical outcome*) Cost (*Important outcome*)

Risk of Bias Assessment



D1	Randomisation process
D2	Deviations from the intended interventions
D3	Missing outcome data
D4	Measurement of the outcome
D5	Selection of the reported result

+	**Low risk**
-	**Some concerns**
X	**High risk**

Desirable Effects

Improvement in dyspnoea

Evidence shows no significant benefit of use of multi-modal treatment in reducing dyspnoea in advanced lung cancer patients in comparison to drug therapy alone. Multimodal intervention was associated with a non-significant reduction in symptom scores compared to usual care, with a pooled mean difference of 0.40 lower (95% CI: 0.95 lower to 0.14 higher; p = 0.15) based on data from 140 participants across three randomized controlled trials. While one study demonstrated a statistically significant benefit, the overall effect did not meet the threshold for statistical significance, and the presence of substantial heterogeneity (I^2 = 83%) warrants cautious interpretation. Multimodal interventions consistently reduced dyspnoea severity across validated scales, including the Numerical Rating Scale (pooled mean difference [MD] = 1.2 lower, 95% CI [1.8 lower, 0.6 lower]), modified Medical Research Council Dyspnoea Scale (MD = 0.33 lower, 95% CI [0.61 lower, 0.05 lower]), and Cancer Dyspnoea Scale discomfort subscale (MD = 0.59 lower, 95% CI [1.16 lower, 0.01 lower]). Nurse-led behavioural interventions (e.g., breathing techniques, posture adjustments, fan therapy) demonstrated statistically and clinically significant improvements, with sustained effects at 12 weeks.

Figure 1.1 (a): Forest plot: Improvement in Dyspnoea

Numerical rating scale (0-10)

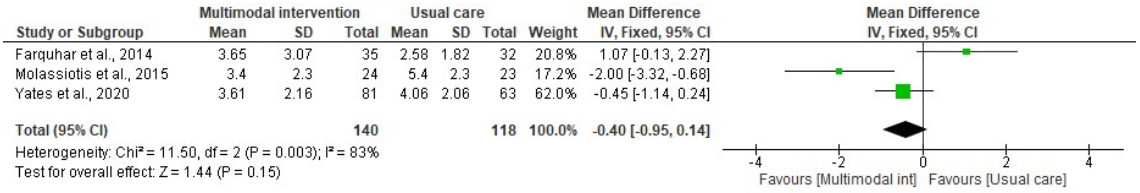


Figure 1.1 (b): Forest plot: Modified Medical Research Council (mMRC) Scale

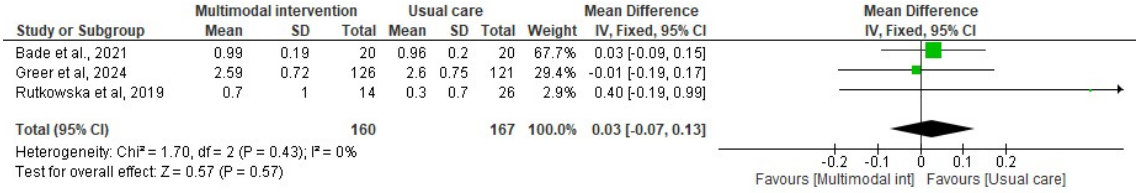
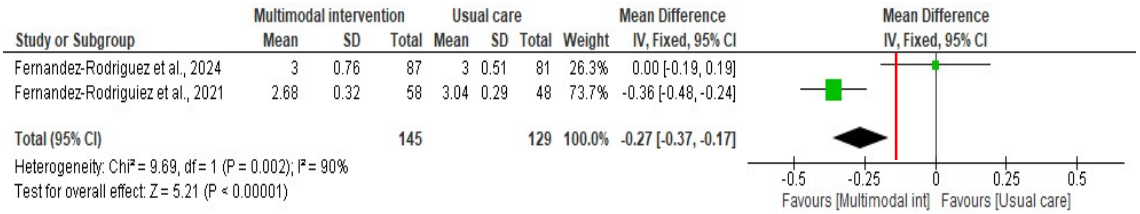


Figure 1.1 (c): Forest plot: Medical Research Council Dyspnoea Scale (MRC, 1-5)



*- Red line shows MCID given by GDG

Figure 1.1 (d): Forest plot: Cancer Dyspnoea Scale (CDS)

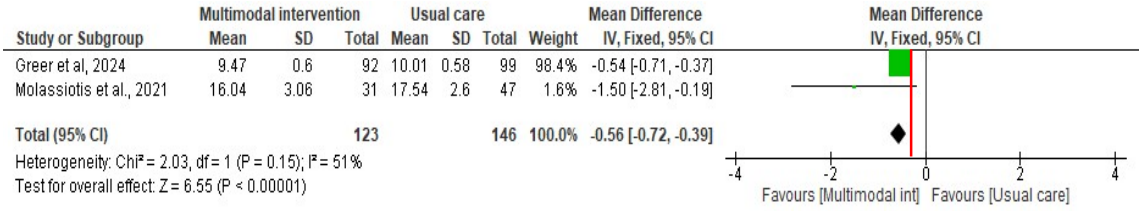
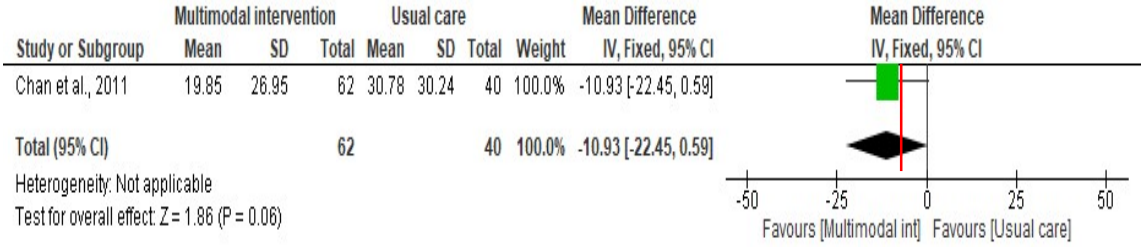


Figure 1.1 (e): Forest plot: 100mm visual analogue scale



*- Red line shows MCID given by GDG

Figure 1.1 (f): Forest plot: Dyspnea-12

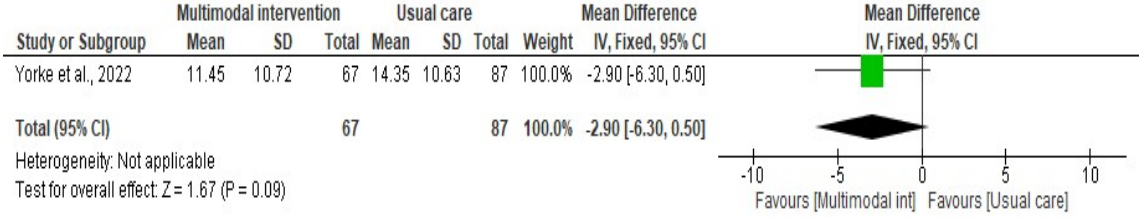
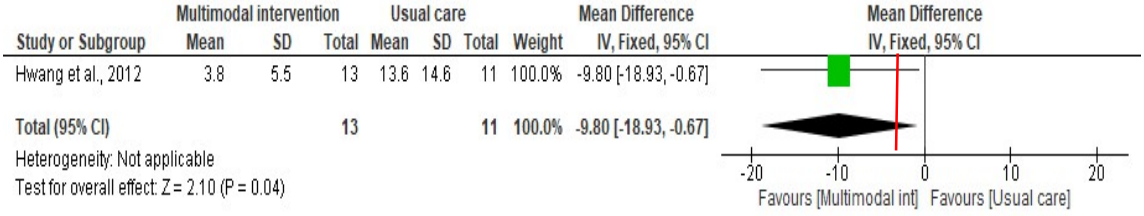


Figure 1.1 (g): Forest plot: European Organization for Research and Treatment of Cancer Quality of Life Questionnaire (EORTC QLQ-LC-13, Chinese language version) - Dyspnea subscale



*(-) Red line shows MCID given by GDG

Figure 1.1 (h): Forest plot: Borg scale

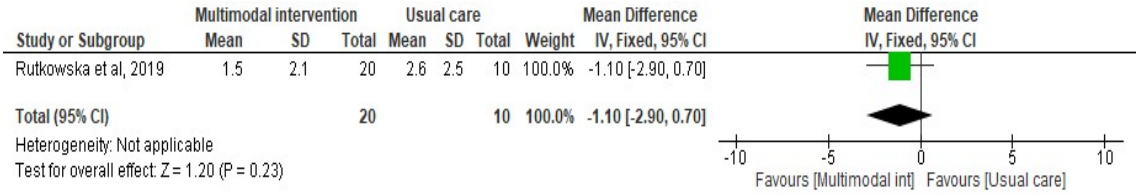


Figure 1.1 (i): Forest plot: Baseline dyspnoea index

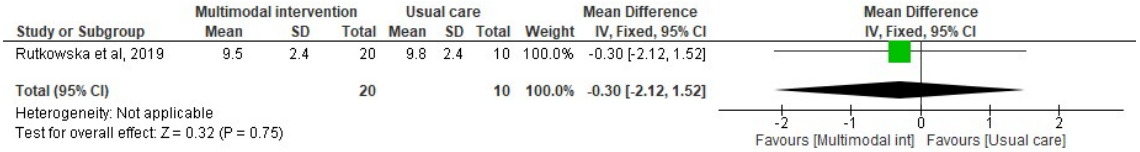
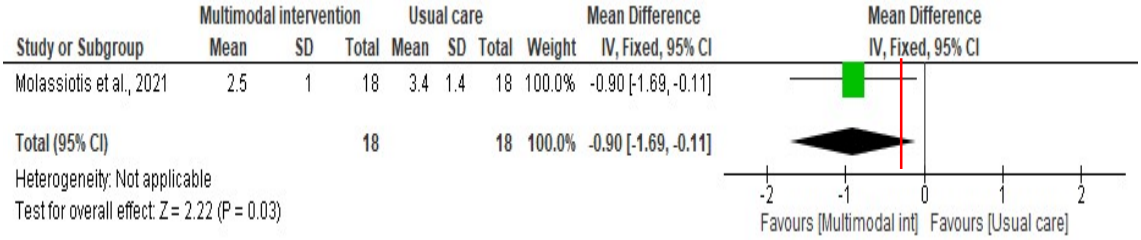


Figure 1.1 (j): Forest plot: Modified Borg scale



*(-) Red line shows MCID given by GDG

Effect on Performance Status

The evidence shows that the 6-minute walk test (6MWT) showed a mean difference of 41 higher (95% CI: 43.98 lower to 125.98 higher), which was not statistically significant (p = 0.34), indicating no clear benefit of multimodal intervention on walking endurance. In contrast, plot for percentage of time immobile in actinography shows a significant reduction in immobility time measured via actigraphy, favoring multimodal intervention with a mean difference of 1.62 higher (95% CI: 1.21 higher to 2.03 higher; p < 0.00001). For the Godin-Shephard questionnaire indicate a modest yet statistically significant improvement in leisure-time physical activity with a mean difference of 0.75 higher (95% CI: 0.62 higher to 0.89 higher; p < 0.00001), albeit with high heterogeneity (I^2 = 98%). However, plot 3.2(d) reflects a non-significant difference in physical activity (mean difference = 1.10 higher; 95% CI: 3.29 lower to 5.49 higher; p = 0.62). Furthermore, the evidence demonstrates a strong and statistically significant improvement in functional independence as measured by the Barthel Index (mean difference = 29.92 higher; 95% CI: 16.20 higher to 25.64 higher; p < 0.00001), showcasing the potential of multimodal interventions in enhancing activities of daily living.

Figure 1.2 (a): Forest Plot - 6MWT in minutes

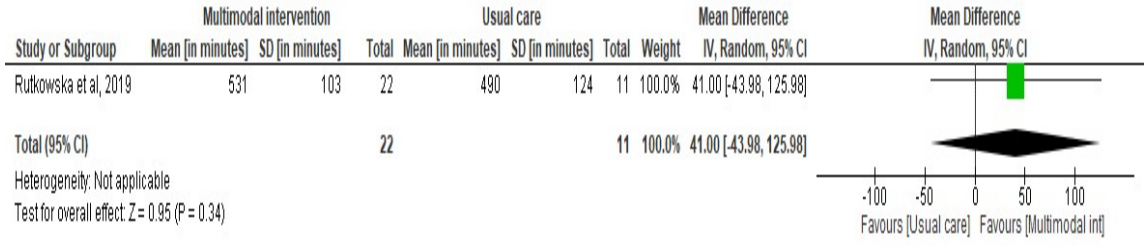
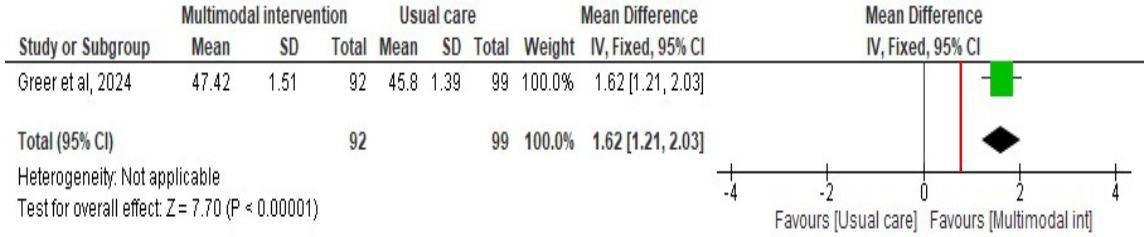
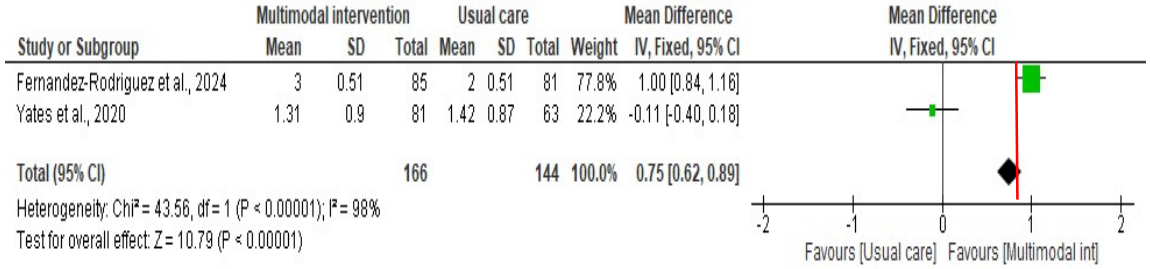


Figure 1.2 (b): Forest Plot - Percentage of time immobile in actigraphy



*(-) Red line shows MCID given by GDG

Figure 1.2 (c): Forest Plot - ECOG score



*(-) Red line shows MCID given by GDG

Figure 1.2 (d): Forest Plot - Godin-Shephard Leisure Time Physical Activity Questionnaire

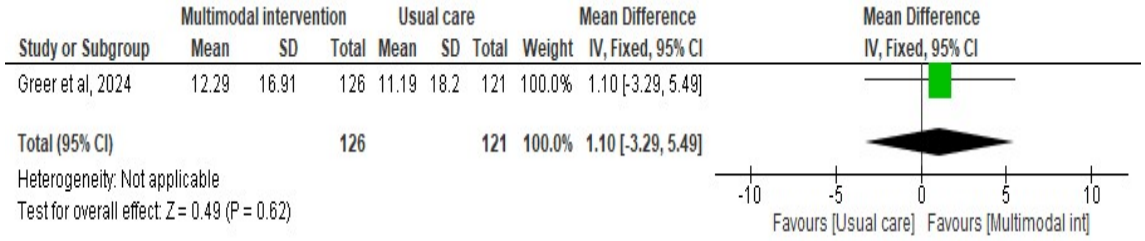
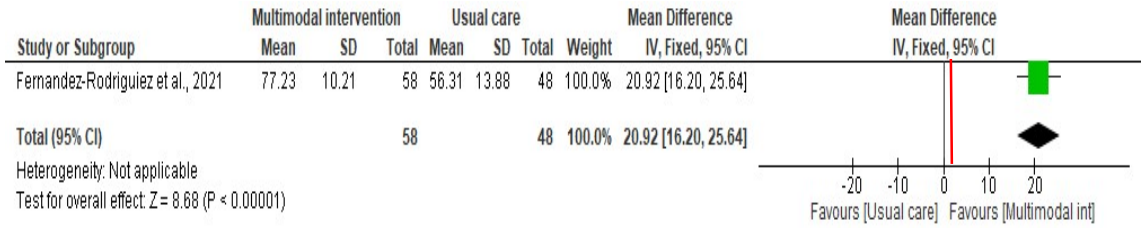


Figure 1.2 (e): Forest Plot - Barthel Index

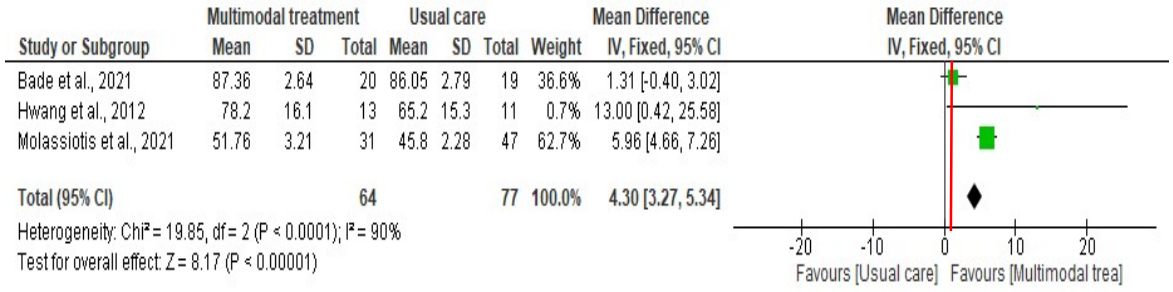


*(-) Red line shows MCID given by GDG

Quality of Life

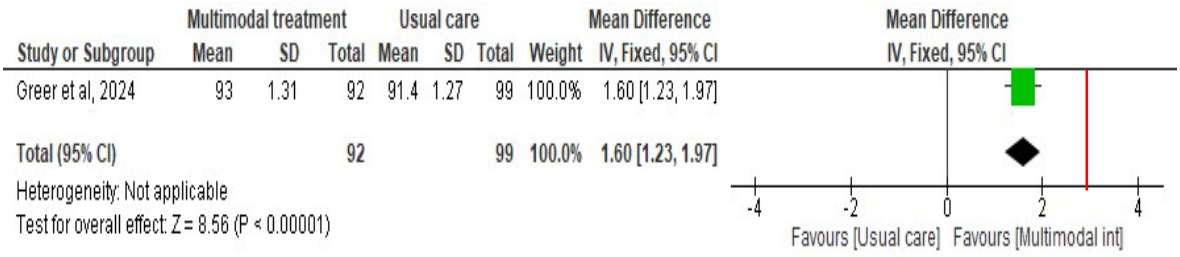
The evidence for EORTC-QLQ-C30 Global Health Status indicates a statistically significant improvement with multimodal intervention over usual care, with a mean difference of 4.30 higher [3.27 higher, 5.34 higher], although substantial heterogeneity is observed (I^2 = 90%). FACT-L scores also favor the multimodal intervention, showing a significant improvement in Quality-of-Life scores with a mean difference of 1.60 higher [1.23 higher, 1.97 higher], with no heterogeneity. In contrast, the Chronic Respiratory Questionnaire Mastery domain did not demonstrate a significant difference between groups, with a mean difference of 0.09 higher [0.58 lower, 0.76 higher], indicating no substantial improvement. The Chronic Respiratory Disease Questionnaire-short form fatigue scores, however, reflect a significant reduction in fatigue in the multimodal intervention group, with a mean difference of 2.00 higher [0.61 higher, 3.39 higher], suggesting a beneficial effect. These findings collectively suggest that multimodal interventions have a positive impact on general and disease-specific quality of life domains, although effectiveness may vary across different outcome measures.

Figure 1.3 (a): Forest Plot - EORTC-QLQ-C30 - Global Health Status



*(-) Red line shows MCID given by GDG

Figure 1.3 (b): Forest Plot - FACT L



*(-) Red line shows MCID given by GDG

Figure 1.3 (c): Forest Plot - Chronic Respiratory Questionnaire Mastery

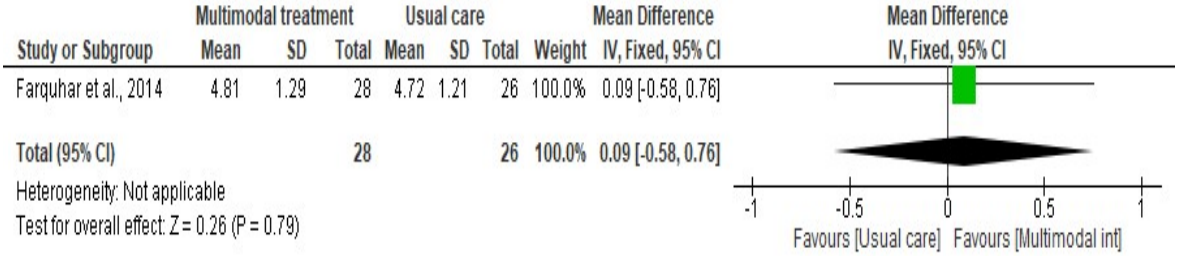
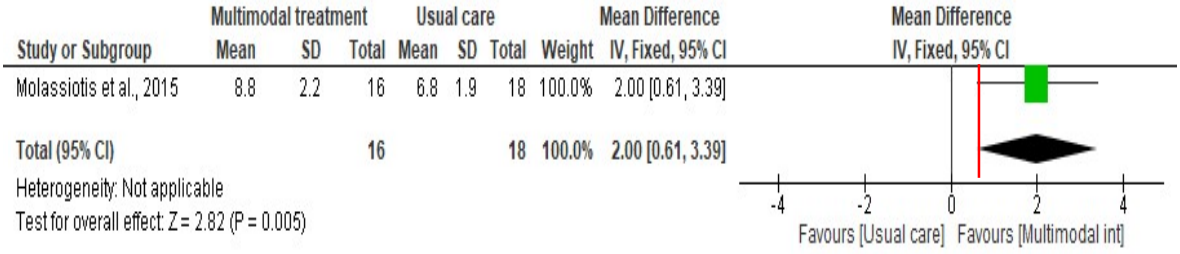


Figure 1.3 (d): Forest Plot - Chronic Respiratory Disease Questionnaire-Short Form Fatigue Scores



*(-) Red line shows MCID given by GDG

Undesirable Effects

The evidence did not report any undesirable effects associated with multimodal interventions in the treatment of dyspnoea in patients with advanced lung cancer, and potential harms remain unknown, indicating a need for further research to evaluate unintended consequences.

Table 1: Summary of Findings

Multimodal intervention compared to Usual care for management of dyspnoea

Patient or population: Advanced lung cancer patients with dyspnoea
Intervention: Multi-modal intervention (drug and non-drug)
Comparison: Standard of Care

Outcomes	Anticipated Absolute Effects* (95% CI)		Relative Effect (95% CI)	No. of Participants (studies)	Certainty of the Evidence (GRADE)
	Risk with Usual care	Risk with Multimodal Intervention			
Improvement in Dyspnoea					
Numerical rating scale (0-10)	Mean Score 4.01	MD 0.4 lower (0.95 lower to 0.14 higher)	-	258 (3 RCTs)	⊕◯◯◯ Very low[a,b,c]
Modified Medical Research Council (mMRC) Scale	Mean Score 1.28	MD 0.03 higher (0.07 lower to 0.13 higher)	-	327 (3 RCTs)	⊕◯◯◯ Very Low[a,c]
Medical Research Council Dyspnoea Scale (MRC, 1-5)	Mean Score 3.02	MD 0.27 lower (0.37 lower to 0.17 lower)	-	274 (2 RCTs)	⊕◯◯◯ Very Low[a,b,d]
Cancer Dyspnea scale (CDS)	Mean Score 13.77	MD 0.56 lower (0.72 lower to 0.39 lower)	-	269 (2 RCTs)	⊕⊕⊕◯ Moderate[d]
100mm visual analogue scale	Mean Score 30.78	MD 10.93 lower (22.45 lower to 0.59 higher)	-	102 (1 RCT)	⊕◯◯◯ Very Low[e,f,c]
Dyspnea-12	Mean score 14.35	MD 2.9 lower (6.3 lower to 0.5 higher)	-	154 (1 RCT)	⊕◯◯◯ Very Low[a,f,c]

European Organization for Research and Treatment of Cancer Quality of Life Questionnaire (EORTC QLQ-LC-13, Chinese language version) - Dyspnea subscale	Mean score 13.6	MD 9.8 lower (18.93 lower to 0.67 lower)	-	24 (1 RCT)	⊕◯◯◯ Very Low[e,f,c]
Borg scale	Mean score 2.6	MD 1.1 lower (2.9 lower to 0.7 higher)	-	30 (1 RCT)	⊕◯◯◯ Very Low[a,f,c]
Baseline Dyspnea Index	Mean score 9.8	MD 0.3 lower (2.12 lower to 1.52 higher)	-	30 (1 RCT)	⊕◯◯◯ Very Low[a,f,c]
Modified Borg scale	Mean score 3.4	MD 0.9 lower (1.69 lower to 0.11 lower)	-	36 (1 RCT)	⊕◯◯◯ Very Low[e,f,g]
Effect on Performance Status					
6MWT in minutes	Mean score 490	MD 41 higher (43.98 lower to 125.98 higher)	-	33 (1 RCT)	⊕◯◯◯ Very Low[a,f,c]
Actigraphy (percent time immobile)	Mean score 45.8	MD 1.62 higher (1.21 higher to 2.03 higher)	-	191 (1 RCT)	⊕⊕◯◯ Low[f,d]
ECOG	Mean score 1.71	MD 0.75 higher (0.62 higher to 0.89 higher)	-	310 (2 RCTs)	⊕⊕◯◯ Low[b,g]
Godin-Shephard Leisure Time Physical Activity Questionnaire	Mean score 11.19	MD 1.1 higher (3.29 lower to 5.49 higher)	-	247 (1 RCT)	⊕⊕◯◯ Low[f,c]
Barthel index	Mean score 56.31	MD 20.92 higher (16.2 higher to 25.64 higher)	-	106 (1 RCT)	⊕◯◯◯ Very low[e,f,d]
Quality of Life					
EORTC-QLQ-C30 - Global health status	Mean score 65.68	MD 4.3 higher (3.27 higher to 5.34 higher)	-	141 (3 RCTs)	⊕◯◯◯ Very Low[a,b,d]

FACT-L	Mean score 91.4	MD 1.6 higher (1.23 higher to 1.97 higher)	-	191 (1 RCT)	⊕⊕◯◯ Low[f,d]
Chronic Respiratory Questionnaire Mastery	Mean score 4.72	MD 0.09 higher (0.58 lower to 0.76 higher)	-	54 (1 RCT)	⊕◯◯◯ Very low[e,f,c]
Chronic Respiratory Disease Questionnaire-short form fatigue scores	Mean score 6.8	MD 2 higher (0.61 higher to 3.39 higher)	-	34 (1 RCT)	⊕◯◯◯ Very Low[e,f,,d]

*__The risk in the intervention group__ (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **risk difference** of the intervention (and its 95% CI).
CI: Confidence Interval, **MD:** Mean Difference

GRADE Working Group grades of evidence
High certainty: we are very confident that the true effect lies close to that of the estimate of the effect.
Moderate certainty: we are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
Low certainty: our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect.
Very low certainty: we have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect.

Explanations:

a. *Downgraded by two levels for risk of bias as less than 1/3rd studies (by weight) were at low risk of bias*
b. *High heterogeneity is present with significant I^2.*
c. Downgraded one level for imprecision as the 95% CI crossed the null effect line
d. *Small sample size, Optimal Information size (OIS) is not met.*
e. *Some concerns were identified in the study included for this outcome*
f. Single study was downgraded one level for inconsistency as it was inevaluable
g. *Confidence interval (CI) crosses the Minimal clinically important (MCID) line*

Table 2: Evidence Profile Table

Multimodal intervention compared to Usual care for management of dyspnoea

Patient or population: Advanced lung cancer patients with dyspnoea
Intervention: Multi-modal intervention (drug and non-drug)
Comparison: Standard of Care

Certainty Assessment							No. of Patients		Effect		Certainty	Importance
No. of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Multimodal intervention	Standard of Care	Relative (95% CI)	Absolute (95% CI)		
Improvement in Dyspnoea												
Numerical rating scale (0-10)												
3	randomised trials	very serious[a]	serious[b]	not serious	serious[c]	none	140	118	-	MD **0.4 lower** (0.95 lower to 0.14 higher)	⊕◯◯◯ Very low[a,b,c]	CRITICAL
Modified Medical Research Council (mMRC) Scale												
3	randomised trials	Very serious[a]	not serious	not serious	Serious[c]	none	160	167	-	MD **0.03 higher** (0.07 lower to 0.13 higher)	⊕◯◯◯ Very Low[a,c]	CRITICAL
Medical Research Council Dyspnea Scale (MRC, 1-5)												
2	randomised trials	Very serious[a]	Serious[b]	not serious	Serious[d]	none	145	129	-	MD **0.27 lower** (0.37 lower to 0.17 lower)	⊕◯◯◯ Very Low[a,b,d]	CRITICAL
Cancer Dyspnea scale (CDS)												

2	randomised trials	Not serious	not serious	not serious	Serious[d]	none	123	146	-	MD **0.56 lower** (0.72 lower to 0.39 lower)	⊕⊕⊕◯ Moderate[d]	CRITICAL
100mm visual analogue scale												
1	randomised trials	Serious[e]	Inevaluable[f]	not serious	Serious[c]	none	62	40	-	MD **10.93 lower** (22.45 lower to 0.59 higher)	⊕◯◯◯ Very Low[e,f,c]	CRITICAL
Dyspnea-12												
1	randomised trials	Very serious[a]	inevaluable[f]	not serious	Serious[c]	none	67	87	-	MD **2.9 lower** (6.3 lower to 0.5 higher)	⊕◯◯◯ Very Low[a,f,c]	CRITICAL
European Organization for Research and Treatment of Cancer Quality of Life Questionnaire (EORTC QLQ-LC-13, Chinese language version) - Dyspnea subscale												
1	randomised trials	Serious[e]	Inevaluable[f]	not serious	Serious[c]	none	13	11	-	MD **9.8 lower** (18.93 lower to 0.67 lower)	⊕◯◯◯ Very Low[e,f,c]	CRITICAL
Borg scale												
1	randomised trials	Very serious[a]	Inevaluable[f]	not serious	Serious[c]	none	20	10	-	MD **1.1 lower** (2.9 lower to 0.7 higher)	⊕◯◯◯ Very Low[a,f,c]	CRITICAL
Baseline Dyspnea Index												
1	randomised trials	Very serious[a]	Inevaluable[f]	not serious	Serious[c]	none	20	10	-	MD **0.3 lower** (2.12 lower to 1.52 higher)	⊕◯◯◯ Very Low[a,f,c]	CRITICAL
Modified Borg scale												

1	randomised trials	Serious[e]	Inevaluable[f]	not serious	Serious[g]	none	18	18	-	MD **0.9 lower** (1.69 lower to 0.11 lower)	⊕◯◯◯ Very Low[e,f,g]	CRITICAL
Effect on Performance Status												
6MWT in minutes												
1	randomised trials	Very serious[a]	Inevaluable[f]	not serious	Serious[c]	none	22	11	-	MD **41 higher** (43.98 lower to 125.98 higher)	⊕◯◯◯ Very Low[a,f,c]	CRITICAL
Actigraphy (percent time immobile)												
1	randomised trials	Not serious	Inevaluable[f]	not serious	serious[d]	none	92	99	-	MD **1.62 higher** (1.21 higher to 2.03 higher)	⊕⊕◯◯ Low[f,d]	CRITICAL
ECOG												
2	randomised trials	not serious	Serious[b]	not serious	Serious[g]	none	166	144	-	MD **0.75 higher** (0.62 higher to 0.89 higher)	⊕⊕◯◯ Low[b,g]	CRITICAL
Godin-Shephard Leisure Time Physical Activity Questionnaire												
1	randomised trials	not serious	Inevaluable[f]	not serious	Serious[c]	none	126	121	-	MD **1.1 higher** (3.29 lower to 5.49 higher)	⊕⊕◯◯ Low[f,c]	CRITICAL
Barthel index												
1	randomised trials	Serious[e]	Inevaluable[f]	not serious	serious[d]	none	58	48	-	MD **20.92 higher** (16.2 higher to 25.64 higher)	⊕◯◯◯ Very low[e,f,d]	CRITICAL

EORTC-QLQ-C30 - Global health status												
3	randomised trials	very serious[a]	Serious[b]	not serious	Serious[d]	none	64	77	-	MD **4.3 higher** (3.27 higher to 5.34 higher)	⊕◯◯◯ Very Low[a,b,d]	CRITICAL
FACT-L												
1	randomised trials	Not serious	Inevaluable[f]	not serious	Serious[d]	none	92	99	-	MD **1.6 higher** (1.23 higher to 1.97 higher)	⊕⊕◯◯ Low[f,d]	CRITICAL
Chronic Respiratory Questionnaire Mastery												
1	randomised trials	Serious[e]	Inevaluable[f]	not serious	serious[c]	none	28	26	-	MD **0.09 higher** (0.58 lower to 0.76 higher)	⊕◯◯◯ Very low[e,f,c]	CRITICAL
Chronic Respiratory Disease Questionnaire-short form fatigue scores												
1	randomised trials	Serious[e]	Inevaluable[f]	not serious	Serious[d]	none	16	18	-	MD **2 higher** (0.61 higher to 3.39 higher)	⊕◯◯◯ Very Low[e,f,,d]	CRITICAL

CI: Confidence Interval

Explanations:

a. *Downgraded by two levels for risk of bias as less than 1/3rd studies (by weight) were at low risk of bias*
b. *High heterogeneity is present with significant I^2.*
c. Downgraded one level for imprecision as the 95% CI crossed the null effect line
d. *Small sample size, Optimal Information size (OIS) is not met.*
e. *Some concerns were identified in the study included for this outcome*
f. Single study was downgraded one level for inconsistency as it was inevaluable
g. *Confidence interval (CI) crosses the Minimal clinically important (MCID) line*

Summary of Judgements

Problem	Yes
Desirable Effects	Moderate
Undesirable Effects	Don't Know
Certainty of evidence	Very Low
Values	No important uncertainty or variability
Balance of effects	Probably Favors the intervention
Resources required	Negligible costs and savings
Certainty of evidence of required resources	Very Low
Cost effectiveness	Probably Favors the intervention
Equity	Probably reduced
Acceptability	Yes
Feasibility	Probably Yes
Recommendations: Multi-modal treatment* is ***recommended*** as compared to drug therapy alone for treatment of dyspnoea in patients with advanced lung cancer. **Strength**: Strong **Certainty of evidence**: Very low	

*In this guideline, multimodal treatment for dyspnoea in patients with advanced lung cancer refers to the planned and concurrent delivery of standard pharmacological management alongside one or more structured non-pharmacological interventions, implemented as a coordinated package rather than as isolated or ad-hoc measures. Pharmacological therapy includes usual care with opioids, bronchodilators, corticosteroids, or oxygen therapy where clinically indicated. Non-pharmacological components include breathing retraining and pacing techniques, graded physical activity or pulmonary rehabilitation, posture optimisation, psychoeducational and behavioural support for symptom coping, and simple airflow interventions such as handheld fan use. These components are delivered by trained nurses or a multidisciplinary team, individually tailored to patient needs and disease stage, and may be provided in inpatient, outpatient, or home-based settings with scheduled follow-up. The emphasis of the multimodal approach is on coordinated implementation, patient education, and reinforcement over time, rather than reliance on pharmacological treatment alone.

Caveats in Existing Evidence:

The GDG opined that the existing evidence had the following limitations:

- Limited high-quality randomized controlled trials directly comparing multimodal dyspnoea management interventions (combining non-pharmacological, behavioural, and supportive strategies) with pharmacological therapy alone.
- Lack of studies employing a homogeneous and clearly defined comparator, with most available trials using "usual care" as the comparator rather than drug therapy alone, thereby limiting the ability to isolate the incremental benefit of multimodal interventions.
- Insufficient evidence on the added benefit of non-pharmacological components when used alongside standard drug therapy, including opioids, bronchodilators, and oxygen where indicated.
- Lack of health economic evaluations comparing multimodal interventions with drug therapy alone, including cost-effectiveness and impact on health-care utilisation.

FOR PATIENTS WITH NEWLY DIAGNOSED LUNG CANCER, HOW EFFICACIOUS IS MULTI-MODAL APPROACH TO MANAGING THE SYMPTOM-CLUSTER OF INSOMNIA, FATIGUE AND DEPRESSION, COMPARE WITH PSYCHO-SOCIAL/ PSYCHOTHERAPEUTIC CARE ALONE?

Table of Contents

Background

Multiple treatment approaches are available for patients with lung cancer including chemotherapy, radiotherapy, immunotherapy, and surgery. Additionally, most patients with lung cancer receive psychotherapeutic or psychosocial or supportive care, which can range from very structured approaches to simple educational strategies. Furthermore, patients could receive additional medications for specific symptom management including opioids, steroids, cough medications, antidepressants, etc. The symptom cluster of insomnia, fatigue, and depression are sometimes assessed and treated using these psychotherapeutic or psychosocial approaches or medications. Such multi-modal treatment approaches frequently also have a psychotherapy component that could help not only in symptom reduction but also improve quality of life of the patients. However, whether such multi-modal approaches including assessment and treatment are better than routine psychotherapeutic care alone for these symptom clusters has not been systematically studied. Therefore, this systematic review was aimed to comprehensively review all available evidence that has examined the effect of multimodal treatment approaches for newly diagnosed lung cancer patients on the symptom cluster of insomnia, fatigue, and depression, compared to psychotherapeutic care alone. Additionally, we intended to compare the quality of life, cost of treatment, and treatment adherence in those receiving multimodal treatment and psychotherapeutic care alone.

Recommendations

Multimodal Approach of treatment is ***recommended*** in comparison to treatment with Psychotherapeutic Care alone for patients with lung cancer.

Strength: Strong
Certainty of Evidence: Very low

Rationale/Justification

The evidence showed moderate desirable effects with trivial harms, alongside acceptability, feasibility, and cost-effectiveness probably favouring multimodal approach in managing the symptom cluster. The anticipated benefits outweigh potential downsides, supporting a strong recommendation.

Summary of Evidence

Key Question

For patients with newly diagnosed lung cancer, how efficacious is multi-modal approach to managing the symptom-cluster of insomnia, fatigue and depression, compared with psycho-social/ psychotherapeutic care alone?

Included Studies

A total of 5303 records from electronic databases were identified till date. Of the 5303 articles, 843 duplicate articles were removed. Further 4183 articles were removed after title and abstract screening because they were not relevant. Full text review was done for 274 articles. After application of inclusion and exclusion criteria, 15 articles were selected for systematic review and 10 studies were included in meta-analysis.

Population and Study Characteristics

All the studies included patients diagnosed with lung cancer undergoing psychotherapeutic care treatment for lung cancer using multimodal approach. The review includes adults of all ages and genders. Eligible studies are those that evaluate multi-modal interventions for psychotherapeutic care as a part of palliative care services for treatment of lung cancer. Studies also included a comparison group receiving psychotherapeutic care alone.

Eligible studies reported on at least one of the following **outcomes**:

- **Improvement in symptom** (10 studies)
- **Quality of life** (4 studies)
- Treatment adherence/compliance (10 studies)
- **Cost** (No studies)

Intervention

The intervention included multi-modal approach with clinical assessment and reversing the reversible (drugs, disease-conditions) and psychotherapeutic care (communication, counselling, expression therapies, sleep hygiene, problem solving, education) for treatment of patients with lung cancer.

Comparator

Psychotherapeutic care alone which includes communication, counselling, expression therapies, sleep hygiene, problem solving, education.

Outcome

Different outcomes were evaluated and included the following critical and important outcomes:

a) Improvement in symptom score (Critical outcome)
b) Quality of life (Critical outcome)
c) Cost (Important outcome)
d) Treatment adherence/compliance (important outcome)

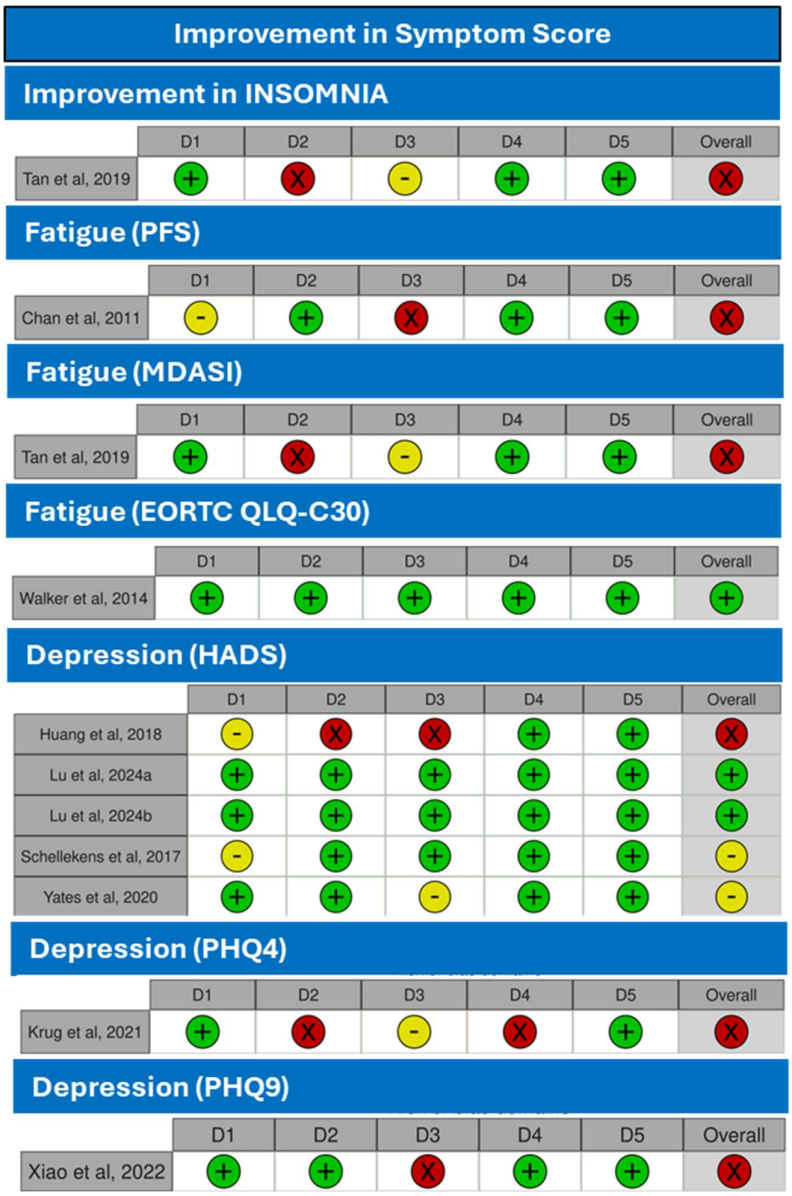
PICO

Framework	Description
Population	Patients with newly diagnosed lung cancer
Intervention	Multi-modal approach Clinical assessment and reversing the reversibles (drugs, disease-conditions) and psychotherapeutic care (communication, counselling, expression therapies, sleep hygiene, problem solving, education)
Comparator	Psychotherapeutic care alone (communication, counselling, expression therapies, sleep hygiene, problem solving, education)
Outcome	a. Improvement in symptom score (*critical outcome*) b. Quality of life (*Critical outcome*) c. Cost (*Important outcome*) d. Treatment adherence/compliance (Important outcome)

Critical Outcome reviewed and their MCID

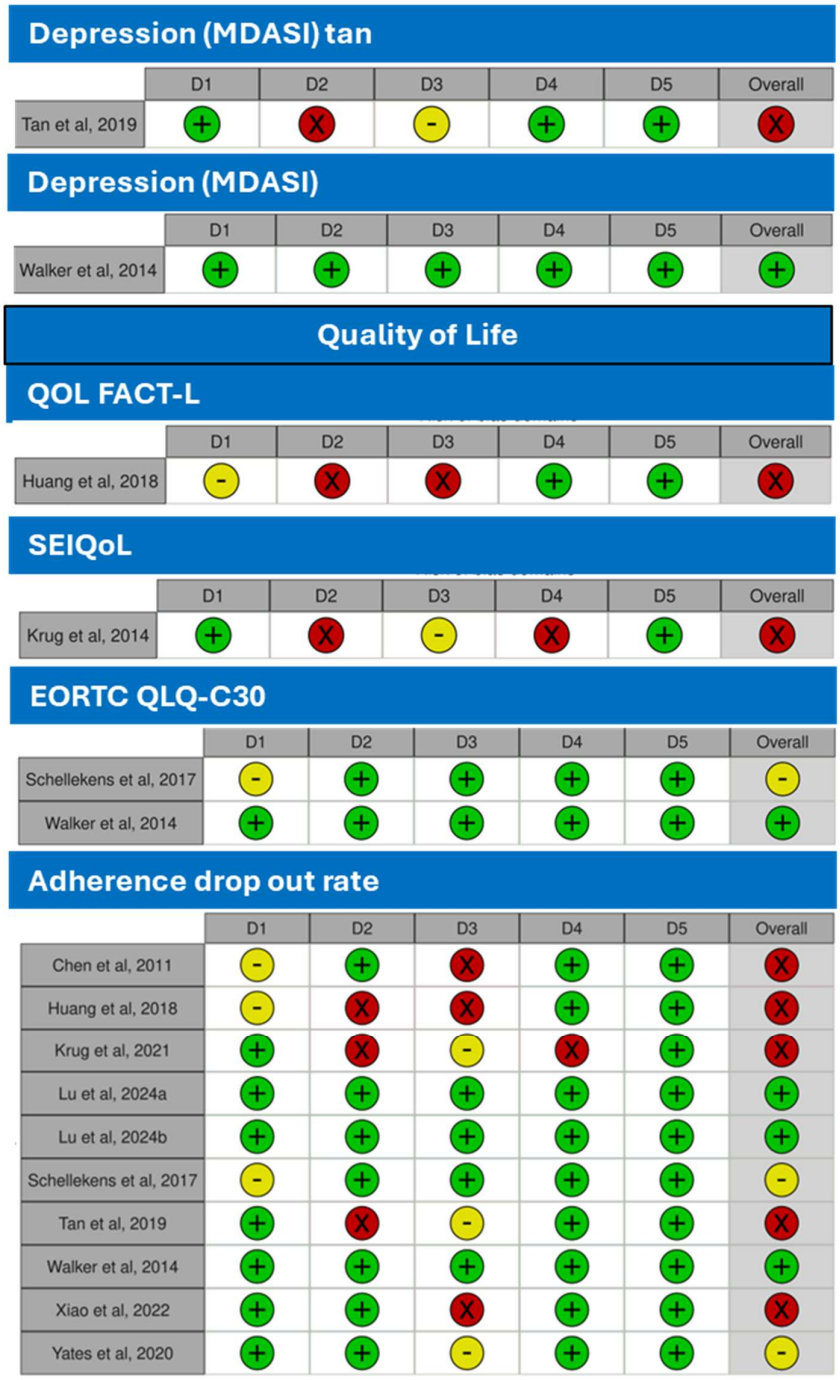
Sr. No	Critical Outcome Reviewed	What does it measure	MCID decided by GDG
1	Improvement in symptom score	Difference in the mean scores	20% difference
2	Quality of Life	Difference in the mean scores of QoL	10% improvement

Risk of Bias Assessment



D1	Randomisation Process
D2	Deviations from the Intended Interventions
D3	Missing outcome data
D4	Measurement of the outcome
D5	Selection of the reported result

+	Low risk
-	Some concerns
X	High risk



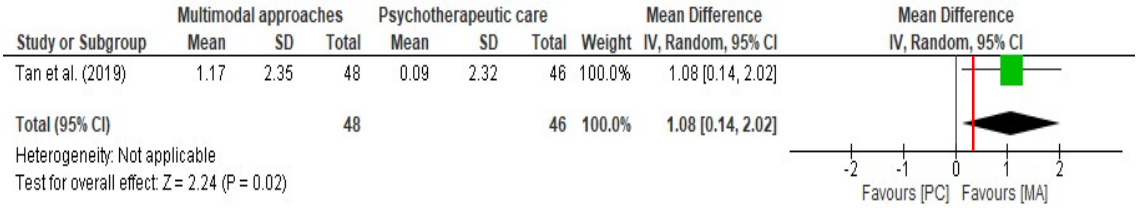
Desirable Effects

Total 12 studies were included for meta-analysis that examined the cluster of symptoms (insomnia, fatigue, and depression) comparing multimodal approaches with usual

psychotherapeutic or psychosocial care. Change in insomnia was found to be higher with multimodal approach (MD 1.08, 95% CI 0.14, 2.02). Fatigue was examined using three different scales; there was no difference between the approaches on PFS, whereas the other two studies showed multimodal approaches are better. Depression was better with multimodal approaches in 4 RCTs using HADS scores (MD 1.10, 95% CI 0.18, 2.02). Similar findings were seen with PHQ-9 scores, MDASI, and SCL-20, whereas the findings on PHQ-4 was not significantly different. All studies showed that QoL scores were better following multimodal approaches. However, dropout rates were not different between the different approaches.

Improvement in Symptom Score

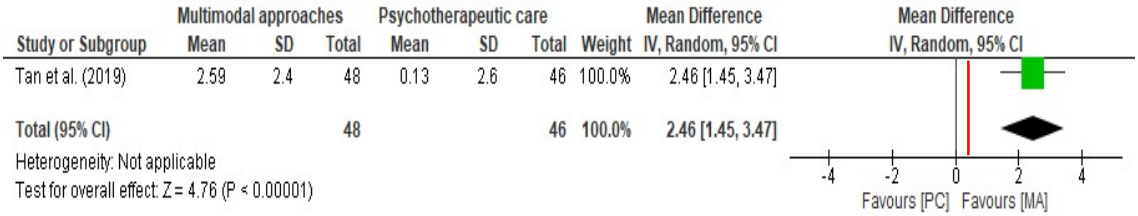
Figure 1.1 (a): Forest plot: Insomnia



*(-) Red line shows MCID given by GDG

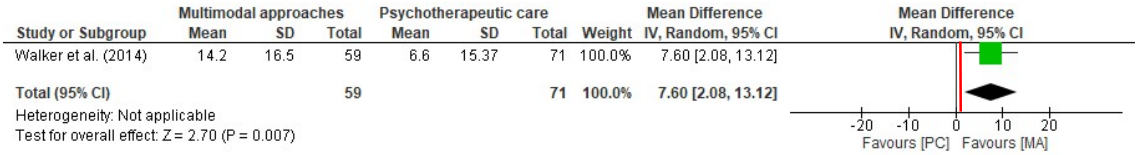
Figure 1.1 (b): Forest plot: Fatigue – PFS

Figure 1.1 (c): Forest plot: Fatigue - MDASI



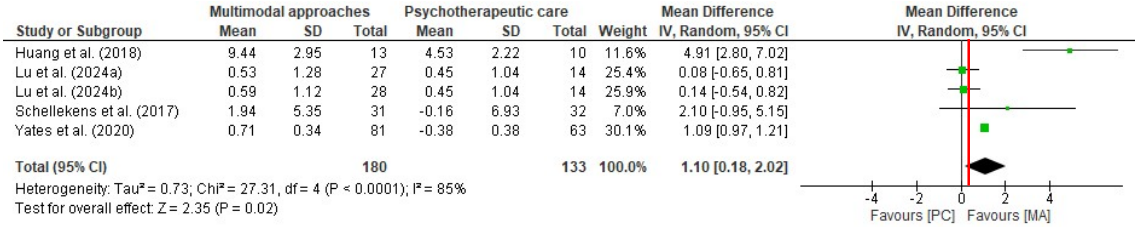
*(-) Red line shows MCID given by GDG

Figure 1.1 (d): Forest plot: Fatigue - EORTC QLQ-C30



*(-) Red line shows MCID given by GDG

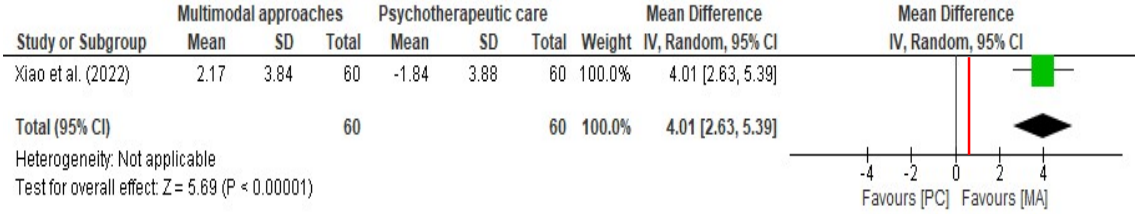
Figure 1.1 (e): Forest plot: Depression - HADS



*(-) Red line shows MCID given by GDG

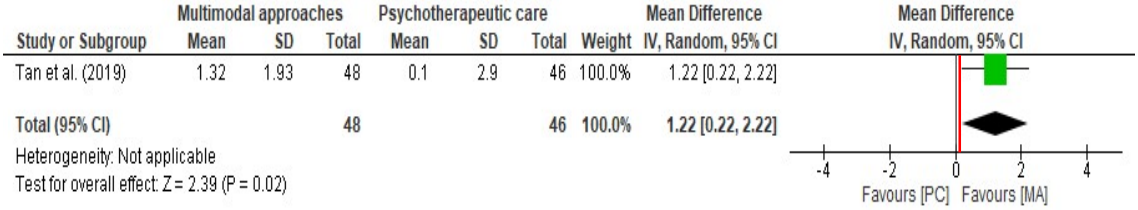
Figure 1.1 (f): Forest plot: Depression PHQ-4

Figure 1.1 (g): Forest plot: Depression PHQ-9



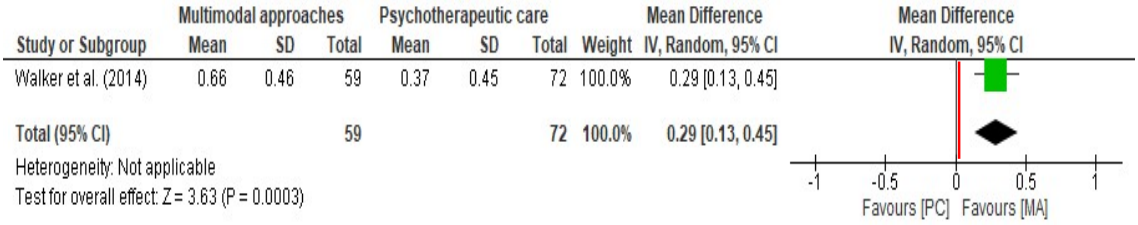
*(-) Red line shows MCID given by GDG

Figure 1.1 (h): Forest plot: Depression MDASI



*(-) Red line shows MCID given by GDG

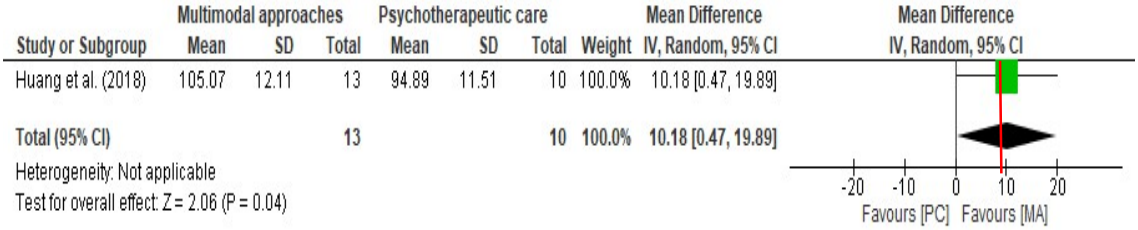
Figure 1.1 (i): Forest plot: Depression SCL-20



*(-) Red line shows MCID given by GDG

Quality of Life

Figure 1.2 (a): Forest Plot: QoL - FACT L



*(-) Red line shows MCID given by GDG

Figure 1.2 (b): Forest Plot: QoL – SEIQoL

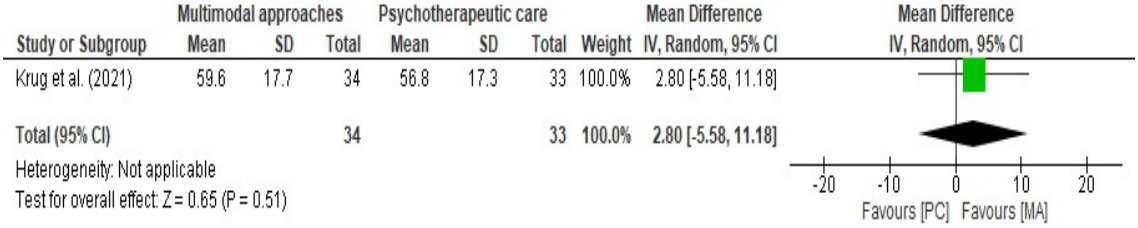
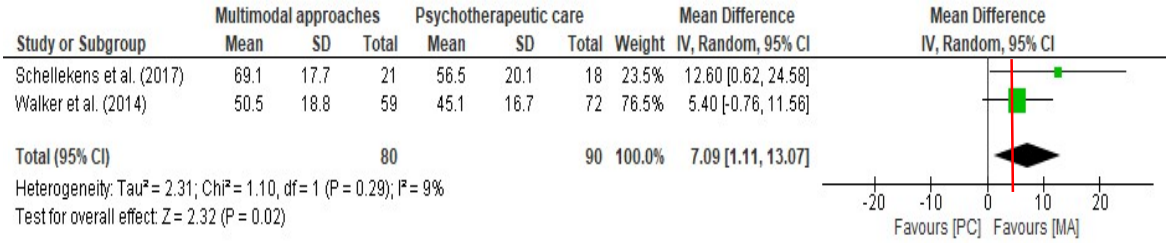


Figure 1.2 (c): Forest Plot: QoL EORTC QLQ-C30



*(-) Red line shows MCID given by GDG

Undesirable Effects

The evidence did not report any undesirable effects associated with the multimodal approach of treatment, and potential harms remain unknown.

Table 1: Summary of Findings

Multimodal approaches compared to psychotherapeutic care alone for newly diagnosed cases with lung cancer

Patient or population: Patients with Lung Cancer
Intervention: Multi-modal intervention (drug and non-drug)
Comparison: Psychotherapy alone

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	No. of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with Psychotherapeutic Care Alone	Risk with Multimodal intervention				
Improvement in Symptom Score						
Insomnia assessed with: MDASI	The mean insomnia was **0.09**	MD **1.08 higher** (0.14 higher to 2.02 higher)	-	94 (1 RCT)	⊕◯◯◯ Very Low[a,b,c]	Lower insomnia with multimodal approaches
Fatigue assessed with: PFS	The mean fatigue was **0.45**	MD **0.09 higher** (0.62 lower to 0.8 higher)	-	140 (1 RCT)	⊕◯◯◯ Very Low[a,b,d]	
Fatigue assessed with: MDASI	The mean fatigue was **0.13**	MD **2.46 higher** (1.45 higher to 3.47 higher)	-	94 (1 RCT)	⊕◯◯◯ Very Low[a,b,c]	Fatigue is less with multimodal approaches
Fatigue assessed with: QLQ-C30	The mean fatigue was **6.6**	MD **7.6 higher** (2.08 higher to 13.12 higher)	-	130 (1 RCT)	⊕⊕◯◯ Low[b,e]	Fatigue is less with multimodal approaches

Depression assessed with: HADS	The mean depression was **0.98**	**1.01 higher** (0.18 higher to 2.02 higher)	-	313 (5 RCTs)	⊕◯◯◯ Very low[f,g,c]	Lower depression with multimodal approaches
Depression assessed with: PHQ-4	The mean depression was **1.1**	MD **0.5 lower** (1.26 lower to 0.26 higher)	-	153 (1 RCT)	⊕◯◯◯ Very Low[a, b, d]	
Depression assessed with: PHQ-9	The mean depression was **-1.84**	MD **4.01 higher** (2.63 higher to 5.39 higher)	-	120 (1 RCT)	⊕◯◯◯ Very Low[a,b,e]	Lower depression with multimodal approaches
Depression assessed with: MDASI	The mean depression was **0.1**	MD **1.22 higher** (0.22 higher to 2.22 higher)	-	94 (1 RCT)	⊕◯◯◯ Very Low[a,b,e]	Lower depression with multimodal approaches
Depression assessed with: SCL-20	The mean depression was **0.37**	**0.29 higher** (0.13 higher to 0.45 higher)	-	131 (1 RCT)	⊕⊕◯◯ Low[b,e]	Lower depression with multimodal approaches
Quality of Life						
Quality of Life assessed with: FACT-L	The mean quality of Life was **94.89**	MD **10.18 higher** (0.47 higher to 19.89 higher)	-	23 (1 RCT)	⊕◯◯◯ Very Low[a,b,c]	Higher QoL with multimodal approaches
Quality of Life assessed with: SEIQoL	The mean quality of Life was **56.8**	MD **2.8 higher** (5.58 lower to 11.18 higher)	-	67 (1 RCT)	⊕◯◯◯ Very Low[a,b,d]	
Quality of life assessed with: QLQ-C30	The mean quality of Life was **50.8**	MD **7.09 higher** (1.11 higher to 13.07 higher)	-	170 (2 RCTs)	⊕⊕⊕◯ moderate[c]	Higher QoL in those receiving multimodal approaches

*__The risk in the intervention group__ (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **risk difference** of the intervention (and its 95% CI).
CI: Confidence Interval

GRADE Working Group grades of evidence
High certainty: we are very confident that the true effect lies close to that of the estimate of the effect.
Moderate certainty: we are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
Low certainty: our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect.
Very low certainty: we have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect.

Explanations

a. *Downgraded by two levels for risk of bias as less than 1/3rd studies (by weight) were at low risk of bias*
b. *Single study was downgraded one level for inconsistency as it was inevaluable*
c. *Downgraded one level for imprecision as the 95% CI crossed the MCID*
d. *Downgraded one level for imprecision as the 95% CI crossed the null effect line*
e. *Optimal Information Size (OIS) not met*
f. *Downgraded one level for risk of bias as less than 2/3rd studies (by weight) were at low risk of bias*
g. *Downgraded one level as the point estimates vary widely across the studies and significant heterogeneity with i2 of 85%*

Table 2: Evidence Profile Table

Multimodal approaches compared to psychotherapeutic care alone for newly diagnosed cases with lung cancer

Patient or population: Patients with Lung Cancer
Intervention: Multi-modal intervention (drug and non-drug)
Comparison: Psychotherapy alone

Certainty Assessment							No. of Patients		Effect		Certainty	Importance
No. of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Multimodal intervention	Standard of Care	Relative (95% CI)	Absolute (95% CI)		
Improvement in Symptom Score												
Insomnia (assessed with: MDASI)												
1	randomised trials	very serious[a,]	inevaluable[b]	not serious	serious[c]	none	48	46	-	MD **1.08 higher** (0.14 higher to 2.02 higher)	⊕◯◯◯ Very Low[a,b,c]	CRITICAL
Fatigue (assessed with: PFS)												
1	randomised trials	very serious[a]	inevaluable[b]	not serious	serious[d]	none	70	70	-	MD **0.09 higher** (0.62 lower to 0.8 higher)	⊕◯◯◯ Very Low[a,b,d]	CRITICAL
Fatigue (assessed with: MDASI)												

1	randomised trials	very serious[a,]	inevaluable[b]	not serious	serious[c]	none	48	46	-	MD **2.46 higher** (1.45 higher to 3.47 higher)	⊕◯◯◯ Very Low[a,b,c]	CRITICAL
Fatigue (assessed with: QLQ-C30)												
1	randomised trials	not serious	inevaluable[b]	not serious	serious[e]	none	59	71	-	MD **7.6 higher** (2.08 higher to 13.12 higher)	⊕⊕◯◯ Low[b,e]	CRITICAL
Depression (assessed with: HADS)												
5	randomised trials	serious[f]	serious[g]	not serious	serious[c]	none	180	133	-	**1.01 higher** (0.18 higher to 2.02 higher)	⊕◯◯◯ Very low[f,g,c]	CRITICAL
Depression (assessed with: PHQ-4)												
1	randomised trials	very serious[a]	inevaluable[b]	not serious	serious[d]	none	79	74	-	MD **0.5 lower** (1.26 lower to 0.26 higher)	⊕◯◯◯ Very Low[a, b, d]	CRITICAL
Depression (assessed with: PHQ-9)												
1	randomised trials	very serious[a]	inevaluable[b]	not serious	serious[e]	none	60	60	-	MD **4.01 higher** (2.63 higher to 5.39 higher)	⊕◯◯◯ Very Low[a,b,e]	CRITICAL

Depression (assessed with: MDASI)												
1	randomised trials	very serious[a]	inevaluable[b]	not serious	serious[e]	none	48	46	-	MD **1.22 higher** (0.22 higher to 2.22 higher)	⊕◯◯◯ Very Low[a,b,e]	CRITICAL
Depression (assessed with: SCL-20)												
1	randomised trials	not serious	inevaluable[b]	not serious	serious[e]	none	59	72	-	**0.29 higher** (0.13 higher to 0.45 higher)	⊕⊕◯◯ Low[b,e]	CRITICAL
Quality of Life												
Quality of Life (assessed with: FACT-L)												
1	randomised trials	very serious[a]	inevaluable[b]	not serious	serious[c]	none	13	10	-	MD **10.18 higher** (0.47 higher to 19.89 higher)	⊕◯◯◯ Very Low[a,b,c]	CRITICAL
Quality of Life (assessed with: SEIQoL)												
1	randomised trials	very serious[a]	inevaluable[b]	not serious	serious[d]	none	34	33	-	MD **2.8 higher** (5.58 lower to 11.18 higher)	⊕◯◯◯ Very Low[a,b,d]	CRITICAL

Quality of life (assessed with: QLQ-C30)												
2	randomised trials	not serious	not serious	not serious	serious[c]	none	80	90	-	MD **7.09 higher** (1.11 higher to 13.07 higher)	⊕⊕⊕◯ moderate[c]	CRITICAL

CI: Confidence Interval

Explanations:

a. *Downgraded by two levels for risk of bias as less than 1/3rd studies (by weight) were at low risk of bias*
b. *Single study was downgraded one level for inconsistency as it was inevaluable*
c. *Downgraded one level for imprecision as the 95% CI crossed the MCID*
d. *Downgraded one level for imprecision as the 95% CI crossed the null effect line*
e. *Optimal Information Size (OIS) not met*
f. *Downgraded one level for risk of bias as less than 2/3rd studies (by weight) were at low risk of bias*
g. *Downgraded one level as the point estimates vary widely across the studies and significant heterogeneity with i^2 of 85%*

Summary of Judgements

Problem	Yes
Desirable Effects	Moderate
Undesirable Effects	Trivial
Certainty of evidence	Very Low
Values	No important uncertainty or variability
Balance of effects	Probably Favors the intervention
Resources required	Moderate costs
Certainty of evidence of required resources	Low
Cost effectiveness	Probably Favors the intervention
Equity	Probably reduced
Acceptability	Yes
Feasibility	Yes
Recommendations: Multimodal Approach of treatment is recommended in comparison to treatment with Psychotherapeutic Care alone for patients with lung cancer. **Strength**: Strong **Certainty of Evidence:** Very low	

Caveats in Existing Evidence:

The GDG opined that the existing evidence had the following limitations

1. Limited availability of high-quality randomized controlled trials evaluating multi-modal interventions that simultaneously target insomnia, fatigue, and depression in patients with newly diagnosed lung cancer.
2. Insufficient comparative evidence directly contrasting multi-modal symptom management strategies with psychosocial or psychotherapeutic care alone, particularly in early phases following diagnosis.
3. Short duration of follow-up in existing studies, providing limited evidence on the sustainability of symptom control, relapse, or long-term mental health outcomes.
4. Limited data on the feasibility, acceptability, and resource requirements of delivering multi-modal interventions within routine oncology and palliative care pathways, especially in public-sector and resource-constrained settings.
5. Scarcity of health economic evaluations assessing the cost-effectiveness of multi-modal approaches compared with psychosocial or psychotherapeutic care alone.

REFERENCES

1. Kochovska S, Ferreira DH, Luckett T, Phillips JL, Currow DC. Earlier multidisciplinary palliative care intervention for people with lung cancer: a systematic review and meta-analysis. Transl Lung Cancer Res. 2020;9(4):1699-709.
2. Zimmermann C, Swami N, Krzyzanowska M, Hannon B, Leighl N, Oza A, et al. Early palliative care for patients with advanced cancer: a cluster-randomised controlled trial. Lancet. 2014;383(9930):1721-30.
3. Bakitas MA, Tosteson TD, Li Z, Lyons KD, Hull JG, Li Z, et al. Early Versus Delayed Initiation of Concurrent Palliative Oncology Care: Patient Outcomes in the ENABLE III Randomized Controlled Trial. J Clin Oncol. 2015;33(13):1438-45.
4. Patil VM, Singhai P, Noronha V, Bhattacharjee A, Deodhar J, Salins N, et al. Effect of Early Palliative Care on Quality of Life of Advanced Head and Neck Cancer Patients: A Phase III Trial. J Natl Cancer Inst. 2021;113(9):1228-37.
5. Gautama MSN, Damayanti A, Khusnia AF. Impact of Early Palliative Care to Improve Quality of Life of Advanced Cancer Patients: A Meta-Analysis of Randomised Controlled Trials. Indian J Palliat Care. 2023;29(1):28-35.
6. Temel JS, Greer JA, Muzikansky A, Gallagher ER, Admane S, Jackson VA, et al. Early Palliative Care for Patients with Metastatic Non–Small-Cell Lung Cancer. New England Journal of Medicine. 2010;363(8):733-42.
7. Temel JS, Greer JA, El-Jawahri A, Pirl WF, Park ER, Jackson VA, et al. Effects of Early Integrated Palliative Care in Patients with Lung and GI Cancer: A Randomized Clinical Trial. J Clin Oncol. 2017;35(8):834-41.
8. Krug K, Bossert J, Deis N, Krisam J, Villalobos M, Siegle A, et al. Effects of an Interprofessional Communication Approach on Support Needs, Quality of Life, and Mood of Patients with Advanced Lung Cancer: A Randomized Trial. Oncologist. 2021;26(8):e1445-e59.
9. Reinke LF, Sullivan DR, Slatore C, Dransfield MT, Ruedebusch S, Smith P, et al. A Randomized Trial of a Nurse-Led Palliative Care Intervention for Patients with Newly Diagnosed Lung Cancer. J Palliat Med. 2022;25(11):1668-76.
10. LF R. Nurse-Led, Telephone-Based Primary Palliative Care Intervention for Patients With Lung cancer: Domains of Quality Care. Journal of Hospice & Palliative Nursing. 2024;26(2):E91.
11. Chen M, Yu H, Yang L, Yang H, Cao H, Lei L, et al. Combined early palliative care for non-small-cell lung cancer patients: a randomized controlled trial in Chongqing, China. Front Oncol. 2023;13:1184961.
12. Datta A, Ostwal S, Das A. Role of Symptomatic Management in Understanding Effects of Early Integration of Palliative Care among Nonmetastatic Lung Cancer Patients on Psychological Well-Being. European Journal of Cancer Care. 2024;2024(1):6651067.
13. Allende S, Turcott JG, Verástegui E, Rodríguez-Mayoral O, Flores-Estrada D, Pérez Camargo DA, et al. Early Incorporation to Palliative Care (EPC) in Patients With Advanced Non-Small Cell Lung Cancer: The PACO Randomized Clinical Trial. Oncologist. 2024;29(10):e1373-e85.
14. McGrath S, Zhao X, Steele R, Thombs BD, Benedetti A. Estimating the sample mean and standard deviation from commonly reported quantiles in meta-analysis. Stat Methods Med Res. 2020;29(9):2520-37.
15. Bade BC, Gan G, Li F, Lu L, Tanoue L, Silvestri GA, Irwin ML. Randomized trial of physical activity on quality of life and lung cancer biomarkers in patients with advanced stage lung

cancer: a pilot study. BMC Cancer. 2021 Apr 1;21(1):352. doi:10.1186/s12885-021-08084-0. Erratum in: BMC Cancer. 2024 Nov 15;24(1):1409. doi:10.1186/s12885-024-13183-9. PMID: 33794808; PMCID: PMC8015735.

16. Barton R, English A, Nabb S, Rigby AS, Johnson MJ. A randomised trial of high vs low intensity training in breathing techniques for breathless patients with malignant lung disease: a feasibility study. Lung Cancer. 2010 Dec 1;70(3):313-9. doi:10.1016/j.lungcan.2010.03.005.
17. Chan CW, Richardson A, Richardson J. Managing symptoms in patients with advanced lung cancer during radiotherapy: results of a psychoeducational randomized controlled trial. J Pain Symptom Manage. 2011 Feb;41(2):347-57. doi:10.1016/j.jpainsymman.2010.04.024. PMID: 21131165.
18. Damani A, Ghoshal A, Salins N, Deodhar J, Muckaden M. Prevalence and Intensity of Dyspnea in Advanced Cancer and its Impact on Quality of Life. Indian J Palliat Care. 2018 Feb 15;24(1):44–50. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5801629/
19. Dhillon HM, Bell ML, van der Ploeg HP, Turner JD, Kabourakis M, Spencer L, et al. Impact of physical activity on fatigue and quality of life in people with advanced lung cancer: a randomized controlled trial. Ann Oncol. 2017 Aug 1;28(8):1889-1897. doi:10.1093/annonc/mdx205. PMID: 28459989.
20. Farquhar MC, Prevost AT, McCrone P, Brafman-Price B, Bentley A, Higginson IJ, et al. Is a specialist breathlessness service more effective and cost-effective for patients with advanced cancer and their carers than standard care? Findings of a mixed-method randomised controlled trial. BMC Med. 2014 Oct 31;12:194. doi:10.1186/s12916-014-0194-2. PMID: 25358424; PMCID: PMC4222435.
21. Fernandez-Rodriguez EJ, Sanchez-Gomez C, Fonseca-Sanchez E, Cruz-Hernandez JJ, Rihuete-Galve MI. Impact of a multimodal effort re-education programme on functionality, physical performance, and functional capacity in cancer patients with dyspnoea: a randomised experimental study. Support Care Cancer. 2024 Sep 6;32(10):639. doi:10.1007/s00520-024-08852-1. PMID: 39237780; PMCID: PMC11377624.
22. Fernández Rodríguez EJ, Rihuete Galve MI, Cruz Hernández JJ. Impact of a comprehensive functional rehabilitation programme on the quality of life of the oncological patient with dyspnoea. Med Clin (Barc). 2021 Jul 9;157(1):10-16. doi:10.1016/j.medcli.2020.05.058. Epub 2020 Aug 22. PMID: 32843213.
23. Garcia CC, Casas CA. Psychosocial distress among patients with lung cancer: an approach to assessment and intervention. Int J Radiat Oncol Biol Phys. 2012 Oct 25;84(3):S648. Available from: https://www.redjournal.org/article/S0360-3016(12)02674-0/fulltext
24. Greer JA, Post KE, Chabria R, Aribindi S, Brennan N, Eche-Ugwu IJ, et al. Randomized Controlled Trial of a Nurse-Led Brief Behavioral Intervention for Dyspnea in Patients With Advanced Lung Cancer. J Clin Oncol. 2024 Oct 20;42(30):3570-3580. doi:10.1200/JCO.24.00048. Epub 2024 Aug 1. PMID: 39088766; PMCID: PMC11483213.
25. Hui D, Maddocks M, Johnson MJ, Ekström M, Simon ST, Ogliari AC, et al. Management of breathlessness in patients with cancer: ESMO Clinical Practice Guidelines. ESMO Open. 2020 Jan 1;5(6):e001038. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7733213/
26. Hui D, Bohlke K, Bao T, Campbell TC, Coyne PJ, Currow DC, et al. Management of Dyspnea in Advanced Cancer: ASCO Guideline. J Clin Oncol. 2021 Feb 22;39(12):1389–411. Available from: https://ascopubs.org/doi/10.1200/JCO.20.03465
27. Hwang CL, Yu CJ, Shih JY, Yang PC, Wu YT. Effects of exercise training on exercise capacity in patients with non-small cell lung cancer receiving targeted therapy. Support Care Cancer.

2012 Dec;20(12):3169-77. doi:10.1007/s00520-012-1452-5. Epub 2012 Apr 14. PMID: 22526147.
28. Jastrzębski D, Maksymiak M, Kostorz S, Bezubka B, Osmanska I, Młynczak T, et al. Pulmonary rehabilitation in advanced lung cancer patients during chemotherapy. Adv Exp Med Biol. 2015 Jan 1;57–64. Available from: https://pubmed.ncbi.nlm.nih.gov/26017725/
29. Molassiotis A, Charalambous A, Taylor P, Stamataki Z, Summers Y. The effect of resistance inspiratory muscle training in the management of breathlessness in patients with thoracic malignancies: a feasibility randomised trial. Support Care Cancer. 2015 Jun;23(6):1637-45. doi:10.1007/s00520-014-2511-x. Epub 2014 Nov 23. PMID: 25417042.
30. Molassiotis A, Vu DV, Ching SSY. The Effectiveness of Qigong in Managing a Cluster of Symptoms (Breathlessness-Fatigue-Anxiety) in Patients with Lung Cancer: A Randomized Controlled Trial. Integr Cancer Ther. 2021 Jan-Dec;20:15347354211008253. doi:10.1177/15347354211008253. PMID: 33847150; PMCID: PMC8047940.
31. Rutkowska A, Jastrzebski D, Rutkowski S, Żebrowska A, Stanula A, Szczegielniak J, et al. Exercise Training in Patients With Non-Small Cell Lung Cancer During In-Hospital Chemotherapy Treatment: A RANDOMIZED CONTROLLED TRIAL. J Cardiopulm Rehabil Prev. 2019 Mar;39(2):127-133. doi:10.1097/HCR.0000000000000410. PMID: 30801436; PMCID: PMC6407827.
32. Yates P, Hardy J, Clavarino A, Fong KM, Mitchell G, Skerman H, et al. A Randomized Controlled Trial of a Non-pharmacological Intervention for Cancer-Related Dyspnea. Front Oncol. 2020 Dec 1;10:591610. doi:10.3389/fonc.2020.591610. PMID: 33335858; PMCID: PMC7737519.
33. Yorke J, Lloyd-Williams M, Smith J, Blackhall F, Harle A, Warden J, et al. Management of the respiratory distress symptom cluster in lung cancer: a randomised controlled feasibility trial. Support Care Cancer. 2015 Nov;23(11):3373-84. doi:10.1007/s00520-015-2810-x. Epub 2015 Jun 26. PMID: 26111954; PMCID: PMC4584102.
34. Yorke J, Johnson MJ, Punnett G, Smith J, Blackhall F, Lloyd Williams M, et al. Respiratory distress symptom intervention for non-pharmacological management of the lung cancer breathlessness-cough-fatigue symptom cluster: randomised controlled trial. BMJ Support Palliat Care. 2024 Jan 8;13(e3):e1181-e1190. doi:10.1136/spcare-2022-003924. PMID: 36283797; PMCID: PMC10850726.
35. Zemel RA. Pharmacologic and Non-Pharmacologic dyspnea management in advanced cancer patients. Am J Hosp Palliat Med. 2021 Sep 13;39(7):847–55. Available from: https://pubmed.ncbi.nlm.nih.gov/34510917/
36. Chan CW, Richardson A, Richardson J. Managing symptoms in patients with advanced lung cancer during radiotherapy: results of a psychoeducational randomized controlled trial. J Pain Symptom Manage 2011;41:347-57.
37. Huang FF, Yang Q, Zhang J, Han XY, Zhang JP, Ye M. A self-efficacy enhancing intervention for pulmonary rehabilitation based on motivational interviewing for postoperative lung cancers patients: modeling and randomized exploratory trial. Psychol Health Med 2018;23:804-22.
38. Huang X, Yan A, Liu Q, Wu L. Effects of magnanimous therapy on coping, adjustment, and living function in advanced lung cancer. Curr Oncol 2019;26:e48-e56. doi: 10.3747/co.26.4126
39. Krug K, Bossert J, Deis N, Krisam J, Villalobos M, Siegle A, et al. Effects of an interprofessional communication approach on support needs, quality of life, and mood of patients with advanced lung cancer: a randomized trial. Oncologist 2021;26:e1445-e1459. doi: 10.1002/onco.13790

40. Liu YY, Lu HB, Li YJ, Wang ZY, Liu YH, Qiao S, Xie J. Effects of mindful breathing training combined with diary-based rehabilitation guidance in lung cancer patients undergoing surgery: A randomized controlled trial. Complement Ther Clin Pract 2024;55:101849. doi: 10.1016/j.ctcp.2024.101849
41. Lu HB, Ma RC, Yin YY, Song CY, Yang TT, Xie J. Clinical Indicators of Effects of Yoga Breathing Exercises on Patients With Lung Cancer After Surgical Resection: A Randomized Controlled Trial. Cancer Nurs (in press). doi: 10.1097/NCC.0000000000001208
42. Milbury K, Li Y, Durrani S, Liao Z, Tsao AS, Carmack C, Cohen L, Bruera E. A mindfulness-based intervention as a supportive care strategy for patients with metastatic non-small cell lung cancer and their spouses: results of a three-arm pilot randomized controlled trial. Oncologist 2020;25:e1794-e1802. doi: 10.1634/theoncologist.2020-0125
43. Schellekens MPJ, van den Hurk DGM, Prins JB, Donders ART, Molema J, Dekhuijzen R, et al. Mindfulness-based stress reduction added to care as usual for lung cancer patients and/or their partners: A multicentre randomized controlled trial. Psychooncology 2017;26:2118-2126.
44. Tan X, Xiong H, Gui S, Wan Y, Yan W, Wang D, Tong L, Zeng G. Effects of cognitive education on the perceived control and symptom distress of lung cancer patients receiving chemotherapy: A randomised controlled trial. Eur J Cancer Care (Engl) 2019;28:e13120. doi: 10.1111/ecc.13120
45. Walker J, Hansen CH, Martin P, Symeonides S, Gourley C, Wall L, Weller D, Murray G, Sharpe M; SMaRT (Symptom Management Research Trials) Oncology-3 Team. Integrated collaborative care for major depression comorbid with a poor prognosis cancer (SMaRT Oncology-3): a multicentre randomised controlled trial in patients with lung cancer. Lancet Oncol 2014;15:1168-76.
46. Xiao J, Chow KM, Choi KC, Ng SNM, Huang C, Ding J, Chan WHC. Effects of family-oriented dignity therapy on dignity, depression and spiritual well-being of patients with lung cancer undergoing chemotherapy: A randomised controlled trial. Int J Nurs Stud 2022;129:104217. doi: 10.1016/j.ijnurstu.2022.104217
47. Yates P, Hardy J, Clavarino A, Fong KM, Mitchell G, Skerman H, Brunelli V, Zhao I. A randomized controlled trial of a non-pharmacological intervention for cancer-related dyspnea. Front Oncol 2020;10:591610. doi: 10.3389/fonc.2020.591610
48. Yuan T, Zhou Y, Wang T, Li Y, Wang Y. Impact research of pain nursing combined with hospice care on quality of life for patients with advanced lung cancer. Medicine (Baltimore) 2024;103:e37687. doi: 10.1097/MD.0000000000037687
49. Zeng D, Liao S. Effect of emotion regulation self-efficacy intervention on negative emotion and quality of life of lung cancer patients undergoing radiotherapy and chemotherapy. Acta Medica Mediterranea 2022;38:1021-26.
50. Zhao X, Cui L, Wang W, Su Q, Li X, Wu J. Influence of psychological intervention on pain and immune functions of patients receiving lung cancer surgery. Pak J Med Sci 2016;32:155-9.

CONTRIBUTORS

STEERING COMMITTEE MEMBERS

1. Dr Rajiv Bahl, Secretary DHR & DG ICMR, Chairperson
2. Dr Sunita Sharma, Directorate General of Health Services (DGHS), Co-Chairperson
3. Ms Anu Nagar, Additional Secretary, DHR
4. Shri Vijay Nehra, Joint Secretary, MoHFW
5. Maj Gen (Prof) Atul Kotwal, Ex-Executive Director, NHSRC
6. Dr Pragya Sharma, Executive Director, NHSRC
7. Dr A.Visala , Joint Drugs Controller, CDSCO
8. Dr Swasticharan, Addl.DDG, NCD, MoHFW
9. Dr Tanvir Kaur, Scientist G, ICMR
10. Dr Roopa Hariprasad, Scientist F, DHR
11. Dr Vikas Dhiman, Scientist D, DHR

GUIDELINE DEVELOPMENT GROUP (In Alphabetical Order)

1. Dr. Bhavani Shankara Bagepally, Scientist E, ICMR-NIE, Chennai, Health Economist
2. Dr. C S Pramesh, Professor and Director, Dept of Thoracic Surgery, TMH, Mumbai, Thoracic surgeon
3. Dr. Divya Khosla, Additional Professor, Dept of Radiation Oncology, PGIMER, Chandigarh, Radiation Oncologist
4. Mr D Manna, Treated at AIIMS Delhi in 2022, currently disease free, on follow up, Person with lived experience
5. Dr Jeremy L Pautu, Head of Department at Mizoram State Cancer Institute, India, Aizawl, Medical Oncologist, State nodal officer, north-east representative
6. Dr. Joseph Mathew, Professor, Department of Paediatrics, PGIMER, Chandigarh, Methodologist
7. Dr. Nandini Vallath, Prof & Head, Department of Pain and Palliative Medicine, St. John's National Academy of Health Sciences, BengaIuru, Palliative care specialist
8. Dr. Navneet Singh, Professor, Dept of Pulmonary Medicine, PGIMER, Chandigarh, Medical oncologist
9. Dr Neha Dumka, Advisor, NHSRC, New Delhi, NHSRC representative
10. Dr. Prabhat Malik, Additional Professor, Dept of Medical Oncology, AIIMS, New Delhi, Medical oncologist
11. Dr. Prasanth Penumadu, Consultant, SVICCAR Hospital, Tirupati, Thoracic surgeon
12. Dr. Priya Parmar, Director (Operations), Indian Cancer Society, Delhi, Representative, Patient Support group
13. Dr. Vikrant Kaushal, Head of Department, Radiation Oncology, Lady Hardinge Medical College, New Delhi, Radiation Oncologist

SYSTEMATIC REVIEW TEAMS

Effectiveness of early integration of palliative care with standard oncological care in lung cancer

1. Dr Shirley Lewis Salins, Dept. of Radiation Oncology, Kasturba Medical College, Manipal, Karnataka
2. Dr Naveen S Salins, Department of Palliative Medicine and Supportive Care, Kasturba Medical College, Manipal
3. Ms Vijay Shree Dhyani, Kasturba Medical College, Manipal, Manipal Academy of Higher Education, Manipal
4. Mr Mebin Mathew, Kasturba Medical College, Manipal, Manipal Academy of Higher Education, Manipal
5. Dr Anshul Singh, Dept. of Radiation Oncology, Kasturba Medical College, Manipal, Karnataka
6. Dr Umesh Velu, Dept. of Radiation Oncology, Kasturba Medical College, Manipal, Karnataka
7. Dr Jayshree NP, Dept. of Radiation Oncology, Kasturba Medical College, Manipal, Karnataka
8. Dr Sidharth Menon, Dept. of Radiation Oncology, Kasturba Medical College, Manipal, Karnataka

Impact of multimodal interventions on symptomatic management of dyspnea in adult patients with advanced lung cancer

1. Dr. Anuja Damani, Department of Palliative Medicine and Supportive Care, Kasturba Medical College, Manipal
2. Dr. Arun Ghoshal, Department of Palliative Medicine and Supportive Care, Kasturba Medical College, Manipal
3. Dr. Naveen S Salins, Department of Palliative Medicine and Supportive Care, Kasturba Medical College, Manipal
4. Mr. Mebin Mathew, Kasturba Medical College, Manipal, Manipal Academy of Higher Education, Manipal
5. Dr. Shreya Nair, Department of Palliative Medicine and Supportive Care, Kasturba Medical College, Manipal
6. Ms. Swathi Nayak Ammunje, Kasturba Medical College, Manipal, Manipal Academy of Higher Education, Manipal
7. Dr Aahan Agrawal, Kasturba Medical College, Manipal, Manipal Academy of Higher Education, Manipal
8. Dr. Krithika Rao, Department of Palliative Medicine and Supportive Care, Kasturba Medical College, Manipal
9. Dr. Vijay Shree Dhyani, Kasturba Medical College, Manipal, Manipal Academy of Higher Education, Manipal

Effectiveness of multimodal approaches versus psychotherapeutic care alone in newly diagnosed lung cancer patients

1. Dr. Naveen S Salins, Department of Palliative Medicine and Supportive Care, Kasturba Medical College, Manipal
2. Dr. Samir Kumar Praharaj, Dept. of Psychiatry, Kasturba Medical College, Manipal, Karnataka
3. Dr. Sonia Shenoy, Dept. of Psychiatry, Kasturba Medical College, Manipal, Karnataka
4. Dr Jithin Joseph, Dept. of Psychiatry, Kasturba Medical College, Manipal, Karnataka
5. Vijay Shree Dhyani, Kasturba Medical College, Manipal, Manipal Academy of Higher Education, Manipal
6. Mr Mebin Mathew, Kasturba Medical College, Manipal, Manipal Academy of Higher Education, Manipal
7. Nisha Abdul Khader, Kasturba Medical College, Manipal, Manipal Academy of Higher Education, Manipal

EXTERNAL REVIEWERS

1. Dr Shamali Poojary, Assistant Professor Department of Palliative Medicine, Tata Memorial Hospital, Mumbai
2. Dr. Jenifer Jeba S, Professor and Head (Palliative Medicine), Christian Medical College, Vellore
3. Dr Tejpal Gupta, Professor and Head, Radiation Oncology, Advanced Centre for Treatment, Research & Education in Cancer, Tata Memorial Centre- Mumbai

DHR-ICMR SECRETARIAT

1. Dr Roopa Hariprasad, Scientist F, DHR-ICMR
2. Dr Vikas Dhiman, Scientist D, DHR-ICMR
3. Dr. Ruchi Baghel, Scientist C, DHR
4. Ms Rozy Kumari, Young Professional, DHR

DECLARATION OF INTEREST

S. No.	Name of the GDG member	Declaration Interest	Management of Conflict(s) of Interest
01	Dr. Bhavani Shankara Bagepally, Scientist E, ICMR-NIE, Chennai	None declared	Not applicable
02	Dr. C S Pramesh, Professor and Director, Dept of Thoracic Surgery, TMH, Mumbai	None declared	Not applicable
03	Dr. Divya Khosla, Additional Professor, Dept of Radiation Oncology, PGIMER, Chandigarh,	None declared	Not applicable
04	Mr D Manna, Treated at AIIMS Delhi in 2022, currently disease free, on follow up	None declared	Not applicable
05	Dr Jeremy LPautu, Head of Department at Mizoram State Cancer Institute, Aizawl, India	None declared	Not applicable
06	Dr. Joseph Mathew, Professor, Dept. of Paediatrics, PGIMER, Chandigarh	None declared	Not applicable
07	Dr. Nandini Vallath, Prof & Head, Department of Pain and Palliative Medicine, St. John's National Academy of Health Sciences, BengaIuru	None declared	Not applicable
08	Dr. Navneet Singh, Professor, Dept of Pulmonary Medicine, PGIMER, Chandigarh	None declared	Not applicable
09	Dr Neha Dumka, Advisor, NHSRC, New Delhi	None declared	Not applicable
10	Dr. Prabhat Malik, Additional Professor, Dept of Medical Oncology, AIIMS, New Delhi	Principal Investigator for Industry sponsored academic clinical trials related to immunotherapy	For recommendations that directly involved immunotherapy, the PI stepped out of virtual call and abstained from voting
11	Dr. Prasanth Penumadu, Consultant, SVICCAR Hospital, Tirupati	None declared	Not applicable
12	Dr. Priya Parmar, Director (Operations), Indian Cancer Society, Delhi	None declared	Not applicable
13	Dr. Vikrant Kaushal, Head of Department, Radiation Oncology, Lady Hardinge Medical College, New Delhi	None declared	Not applicable