Ontario Health
Cancer Care Ontario

Guideline 26-3 Version 2

A Quality Initiative of the Program in Evidence-Based Care (PEBC), Ontario Health (Cancer Care Ontario)

Follow-up and Surveillance of Curatively Treated Patients with Lung Cancer

Y. Shargall, E.T. Vella, L. Del Giudice, S. Kulkarni, P.M. Ellis, C. Dennie, R. MacRae, Y.C. Ung, and the Lung Cancer Survivorship Guideline Development Group

Report Date: February 5, 2024

An assessment conducted in February 2026 deferred the review of Guideline 26-3 Version 2. This means that the document remains current until it is assessed again next year. The PEBC has a formal and standardized process to ensure the currency of each document (PEBC Assessment & Review Protocol)

Guideline 26-3 Version 2 is comprised of 5 sections. You can access the summary and full report here:

https://www.cancercareontario.ca/en/guidelines-advice/types-of-cancer/261

Section 1:	**Recommendations Summary**
Section 2:	**Guideline**
Section 3:	**Guideline Methods Overview**
Section 4:	**Evidence Review**
Section 5:	**Internal and External Review**

For information about this document, please contact Dr. Y. Shargall, the lead author, through the PEBC at:
Phone: 905-527-4322 ext. 42822 Fax: 905-526-6775 E-mail: ccopgi@mcmaster.ca

For information about the PEBC and the most current version of all reports, please visit the OH (CCO) website at https://www.cancercareontario.ca/en/guidelines-advice or contact the PEBC office at:
Phone: 905-527-4322 ext. 42822 Fax: 905-526-6775 E-mail: ccopgi@mcmaster.ca

PEBC Report Citation (Vancouver Style): Shargall Y, Vella ET, Del Giudice L, Kulkarni S, Ellis PM, Dennie C, et al. Follow-up and Surveillance of Curatively Treated Patients with Lung Cancer. Toronto (ON): Ontario Health (Cancer Care Ontario); 2024 February 5. Program in Evidence-Based Care Guideline No.: 26-3 Version 2.

Table of Contents

Follow-up and Surveillance of Curatively Treated Patients with Lung Cancer

Section 1: Recommendations

GUIDELINE OBJECTIVES

The primary objective of this guideline is to develop recommendations for the optimal management of patients with lung cancer after curative-intent treatment.

TARGET POPULATION

The target population includes adult patients with small cell lung cancer (SCLC) or non-small cell lung cancer (NSCLC) after curative-intent treatment.

INTENDED USERS

This guideline is targeted to thoracic surgeons, medical and radiation oncologists specializing in lung cancer, radiologists, primary care providers, respirologists, nurses, and psychosocial care providers.

RECOMMENDATIONS

These recommendations are a combination of endorsements of recommendations from other guidelines and new recommendations. Recommendations 1 to 5 were endorsed from the American Society of Clinical Oncology (ASCO) 2020 guideline [1] on imaging surveillance strategies. Recommendations 6, 8, 9, and 11 were endorsed from the previous PEBC 2014 version of this guideline. Recommendation 10 was endorsed from the OH (CCO) 2022 guideline on virtual care [4]. Recommendation 12 was endorsed from the vaccination schedule recommended by the Government of Canada [5]. Recommendations 7 and 13 were new recommendations.

RECOMMENDATIONS 1 to 5 (Endorsed from the ASCO 2020 [1] recommendations)

Note:

- These recommendations apply to patients with curatively treated stage I-III NSCLC and SCLC with no clinical suspicion of recurrent disease. This includes patients treated with surgery, stereotactic body radiotherapy, and chemoradiation.
- These recommendations pertain only to routine surveillance strategies. Imaging to evaluate symptoms and follow up on previous findings is not addressed by this guideline.
- These recommendations do not address the frequency of the clinical evaluation (history and physical examination) for either the suspicion of recurrence and/or to provide reassurance.

Recommendation 1.1

Patients should undergo surveillance imaging for recurrence every six months for two years.

Recommendation 1.2

Patients should undergo surveillance imaging for detection of new primary lung cancers annually after the first two years.

Recommendation 2.1
Clinicians should use a diagnostic or low-dose chest computed tomography (CT) that includes the adrenals, without contrast (preferred) or with contrast (when indicated) when conducting surveillance for recurrence during the first two years post treatment.

Qualifying statement for Recommendation 2.1
There is no evidence of added benefit for a CT of the abdomen and pelvis over a chest CT through the adrenals as a surveillance imaging modality for recurrence.

Recommendation 2.2
Clinicians should use a low-dose chest CT when conducting surveillance for new lung primaries after the first two years post treatment.

Recommendation 2.3
Clinicians should not use ^{18}F-labeled fluorodeoxyglucose positron emission tomography as a surveillance tool.

Recommendation 3
Surveillance imaging may be omitted in patients who are clinically unsuitable for or unwilling to accept further treatment. Age should not preclude surveillance imaging. Consideration of overall health status, chronic medical conditions, and patient preferences is recommended.

Recommendation 4
Clinicians should not use circulating biomarkers as a surveillance strategy for detection of recurrence in patients who have undergone curative-intent treatment of stage I-III NSCLC or SCLC.

Recommendation 5.1
For patients with stage I-III NSCLC, clinicians should not perform routine brain surveillance for recurrence with either magnetic resonance imaging (MRI) or CT in patients who have undergone curative-intent treatment.

Recommendation 5.2
In patients who have undergone curative-intent treatment of stage I-III SCLC and did not receive prophylactic cranial irradiation (PCI), clinicians should offer brain MRI every three months for the first year and every six months for the second year for surveillance. The same schedule may be offered for patients who did receive PCI.

Qualifying statement for Recommendation 5.2
Brain MRI should not be routinely offered to asymptomatic patients after two years of disease-free survival.

RECOMMENDATION 6
In the expert opinion of the authors, any new and persistent or worsening symptom warrants the consideration of a recurrence, especially:

Constitutional symptoms:
- Dysphagia
- Fatigue (new onset)
- Nausea or vomiting (unexplained)

- New finger clubbing
- Suspicious lymphadenopathy
- Sweats (unexplained)
- Thrombotic event
- Weight loss or loss of appetite

Pain:

- Bone pain
- Chest pain
- Caveat shoulder pain not related to trauma

Neurological symptoms:

- Headaches (if persistent)
- New neurological signs suggestive of brain metastases or cord compression such as leg weakness or speech changes
- Headache or focal neurological symptoms

Respiratory symptoms:

- Cough (despite use of antibiotics)
- Dyspnea
- Hemoptysis
- Hoarseness
- Signs of superior vena cava obstruction
- Stridor

RECOMMENDATION 7

There is insufficient evidence to recommend routine completion of patient-reported outcome tools at home for symptom monitoring or early detection of recurrence.

RECOMMENDATION 8

Health-related quality of life is very important for long-term survivors suffering from late side effects of their curative-intent therapy (including surgery, chemotherapy, and radiation therapy). Symptoms that are frequently experienced by lung cancer survivors include but are not limited to:

Constitutional issues:

- Anxiety
- Cough
- Decline in appetite
- Decrease in general health
- Depression
- Dysphagia
- Fatigue
- Fear of cancer recurrence
- Pain
- Physical ability restrictions
- Reduced sleep quality
- Shortness of breath

Long-term systemic therapy effects:

- Hearing loss
- Neuropathies
- Renal impairment
- Delayed immune-related adverse events
- Cumulative toxicities from ongoing therapy with tyrosine kinase inhibitors

Long-term radiation effects:

- Breathing complications
- Breathlessness/dyspnea

Long-term post-surgical effects:

- Empyema
- Oxygen dependence
- Post-thoracotomy pain syndrome
- Reduced exercise tolerance or activity limitations
- Shortness of breath

Patients should be encouraged to discuss these symptoms with their healthcare providers. Health care professionals need to aid lung cancer survivors in handling these symptoms to improve quality of life.

RECOMMENDATION 9
For lung cancer survivors who have completed curative-intent therapy, surveillance is required and may be provided by specialists, family physicians or nurse-led clinics.

RECOMMENDATION 10 (Endorsed from the OH (CCO) 2022 [2] recommendations)
Cancer survivorship considerations during virtual care

- Assess the need for in-person physical examination
- Cancer survivors under surveillance following curative intent treatment can be safely followed using virtual care, unless in-person physical examination is indicated and/or required.

Transition to virtual survivorship care

- Primary care providers and cancer survivors should be made aware of the potential for transition to virtual survivorship care.

RECOMMENDATION 11
Smoking cessation counselling is recommended for patients who have completed curative-intent therapy for NSCLC and SCLC. Although verbal cessation advice from a healthcare professional is of benefit, interventions that involve behavioural and pharmacotherapy support in addition to verbal advice is recommended.

RECOMMENDATION 12
Adult patients with lung cancer after curative-intent treatment living in Ontario should receive vaccinations as recommended by the Government of Canada [3]. The influenza and pneumococcal vaccine schedules for persons with chronic diseases, which includes cancer, or for immunocompromised persons should be followed. Further information can be found here: Canadian Immunization Guide - Canada.ca. The COVID-19 schedule for adults or

immunocompromised persons should followed. Further information can be found here: COVID-19 vaccine: Canadian Immunization Guide - Canada.ca.

RECOMMENDATION 13
Enrolling in an exercise or rehabilitation program is recommended.

IMPLEMENTATION CONSIDERATIONS

Patients in isolated areas or Indigenous populations may experience issues with accessing surveillance tests. Health care providers in the community-based setting might have more difficulty in following up a suspicion of recurrence than healthcare providers in the hospital-based setting. The cost of pharmacotherapy used in smoking cessation interventions may be a barrier for people on limited income. Currently, the pneumococcal polysaccharide vaccine is covered in Ontario, but the pneumococcal conjugate vaccine is not covered, which may influence patients' and healthcare providers' preferred vaccine. There may be issues with infrastructure in implementing exercise programs.

RELATED GUIDELINES

- Ontario Health (Cancer Care Ontario). Smoking Cessation Information for Healthcare Providers. Available from: https://www.cancercareontario.ca/en/guidelines-advice/cancer-continuum/prevention/smoking-cessation

FURTHER RESEARCH

Direct evidence from randomized controlled trials in adult patients with NSCLC or SCLC after curative-intent treatment are needed to provide a greater degree of certainty in the evidence to inform recommendations.

GUIDELINE LIMITATIONS

Systematic reviews were searched for some of the research questions and recent primary studies not included in systematic reviews may have been missed.

Follow-up and Surveillance of Curatively Treated Patients with Lung Cancer

Section 2: Guideline – Recommendations and Justifications

GUIDELINE OBJECTIVES

The primary objective of this guideline is to develop recommendations for the optimal management of patients with lung cancer after curative-intent treatment.

TARGET POPULATION

The target population includes adult patients with small cell lung cancer (SCLC) or non-small cell lung cancer (NSCLC) after curative-intent treatment.

INTENDED USERS

This guideline is targeted to thoracic surgeons, medical and radiation oncologists specializing in lung cancer, radiologists, primary care providers, respirologists, nurses, and psychosocial care providers.

RECOMMENDATIONS AND JUSTIFICATION

These recommendations are a combination of endorsements of recommendations from other guidelines and new recommendations. Recommendations 1 to 5 were endorsed from the American Society of Clinical Oncology (ASCO) 2020 guideline [1] on imaging surveillance strategies. Recommendations 6, 8, 9, and 11 were endorsed from the previous PEBC 2014 version of this guideline. Recommendation 10 was endorsed from the OH (CCO) 2022 guideline on virtual care [4]. Recommendation 12 was endorsed from the vaccination schedule recommended by the Government of Canada [5]. Recommendations 7 and 13 were new recommendations.

RECOMMENDATIONS 1 to 5 (Endorsed from the ASCO 2020 [1] recommendations)

Note:

- These recommendations apply to patients with curatively treated stage I-III NSCLC and SCLC with no clinical suspicion of recurrent disease. This includes patients treated with surgery, stereotactic body radiotherapy, and chemoradiation.
- These recommendations pertain only to routine surveillance strategies. Imaging to evaluate symptoms and follow up on previous findings is not addressed by this guideline.
- These recommendations do not address the frequency of the clinical evaluation (history and physical examination) for either the suspicion of recurrence and/or to provide reassurance.

Recommendation 1.1

Patients should undergo surveillance imaging for recurrence every six months for two years.

Recommendation 1.2

Patients should undergo surveillance imaging for detection of new primary lung cancers annually after the first two years.

Recommendation 2.1

Clinicians should use a diagnostic or low-dose chest computed tomography (CT) that includes the adrenals, without contrast (preferred) or with contrast (when indicated) when conducting surveillance for recurrence during the first two years post treatment.

Qualifying statement for Recommendation 2.1
There is no evidence of added benefit for a CT of the abdomen and pelvis over a chest CT through the adrenals as a surveillance imaging modality for recurrence.

Recommendation 2.2
Clinicians should use a low-dose chest CT when conducting surveillance for new lung primaries after the first two years post treatment.

Recommendation 2.3
Clinicians should not use ^{18}F-labeled fluorodeoxyglucose positron emission tomography as a surveillance tool.

Recommendation 3
Surveillance imaging may be omitted in patients who are clinically unsuitable for or unwilling to accept further treatment. Age should not preclude surveillance imaging. Consideration of overall health status, chronic medical conditions, and patient preferences is recommended.

Recommendation 4
Clinicians should not use circulating biomarkers as a surveillance strategy for detection of recurrence in patients who have undergone curative-intent treatment of stage I-III NSCLC or SCLC.

Recommendation 5.1
For patients with stage I-III NSCLC, clinicians should not perform routine brain surveillance for recurrence with either magnetic resonance imaging (MRI) or CT in patients who have undergone curative-intent treatment.

Recommendation 5.2
In patients who have undergone curative-intent treatment of stage I-III SCLC and did not receive prophylactic cranial irradiation (PCI), clinicians should offer brain MRI every three months for the first year and every six months for the second year for surveillance. The same schedule may be offered for patients who did receive PCI.

Qualifying statement for Recommendation 5.2
Brain MRI should not be routinely offered to asymptomatic patients after two years of disease-free survival.

Justification for Recommendations 1 to 5
This recommendation was endorsed from the ASCO 2020 guideline [1]. For recommendation 2.1, low-dose CT was added to reduce radiation exposure and without contrast was preferred over contrast because the use of intravenous contrast may pose a significant risk for patients with a contrast allergy or kidney dysfunction. For Recommendation 2.2, the word screening before chest CT was removed because these patients do not qualify for lung screening programs currently in Ontario. For recommendation 5.1, CT was added to clarify that routine brain surveillance should not be performed with CT as well as MRI.

RECOMMENDATION 6
In the expert opinion of the authors, any new and persistent or worsening symptom warrants the consideration of a recurrence, especially:

Constitutional symptoms:
- Dysphagia
- Fatigue (new onset)
- Nausea or vomiting (unexplained)
- New finger clubbing
- Suspicious lymphadenopathy
- Sweats (unexplained)
- Thrombotic event
- Weight loss or loss of appetite

Pain:
- Bone pain
- Chest pain
- Caveat shoulder pain not related to trauma

Neurological symptoms:
- Headaches (if persistent)
- New neurological signs suggestive of brain metastases or cord compression such as leg weakness or speech changes
- Headache or focal neurological symptoms

Respiratory symptoms:
- Cough (despite use of antibiotics)
- Dyspnea
- Hemoptysis
- Hoarseness
- Signs of superior vena cava obstruction
- Stridor

Justification for Recommendation 6
This recommendation was endorsed from the previous PEBC 2014 version of this guideline. Thrombosis was replaced with thrombotic event to represent a symptom that requires investigation rather than a condition.

RECOMMENDATION 7
There is insufficient evidence to recommend routine completion of patient-reported outcome (PRO) tools at home for symptom monitoring or early detection of recurrence.

Justification for Recommendation 7
Most low-quality studies did not find significant differences between using a PRO intervention versus usual care for any of the critical outcomes, including overall survival, progression-free survival, quality of life, distress, and patient or provider satisfaction. There was only a single trial that showed an overall survival benefit when patients were being monitored electronically at home weekly [4,5]. The current symptom monitoring system in Ontario was implemented for patients attending a clinic. There may be feasibility, cost, and equity issues in implementing a

more intensive system. For example, electronic tools would have to be available in multiple languages, which may be more costly and challenging to implement in rural compared with urban areas.

RECOMMENDATION 8
Health-related quality of life is very important for long-term survivors suffering from late side effects of their curative-intent therapy (including surgery, chemotherapy, and radiation therapy). Symptoms that are frequently experienced by lung cancer survivors include but are not limited to:

Constitutional issues:
- Anxiety
- Cough
- Decline in appetite
- Decrease in general health
- Depression
- Dysphagia
- Fatigue
- Fear of cancer recurrence
- Pain
- Physical ability restrictions
- Reduced sleep quality
- Shortness of breath

Long-term systemic therapy effects:
- Hearing loss
- Neuropathies
- Renal impairment
- Delayed immune related adverse events
- Cumulative toxicities from ongoing therapy with tyrosine kinase inhibitors

Long-term radiation effects:
- Breathing complications
- Breathlessness/dyspnea

Long-term post-surgical effects:
- Empyema
- Oxygen dependence
- Post-thoracotomy pain syndrome
- Reduced exercise tolerance or activity limitations
- Shortness of breath

Patients should be encouraged to discuss these symptoms with their healthcare providers. Health care professionals need to aid lung cancer survivors in handling these symptoms to improve quality of life.

Justification for Recommendation 8
This recommendation was endorsed from the previous PEBC 2014 version of this guideline and is based on expert opinion. Esophageal stricture was removed from the list because it is not a

symptom. Fear of cancer recurrence, delayed immune related adverse events, and cumulative toxicities from ongoing therapy with tyrosine kinase inhibitors were added to the list.

RECOMMENDATION 9
For lung cancer survivors who have completed curative-intent therapy, surveillance is required and may be provided by specialists, family physicians or nurse-led clinics.

Justification for Recommendation 9
This recommendation was endorsed from the previous PEBC 2014 version of this guideline. "Hospital-based nurses" was reworded to "nurse-led clinics" to be more inclusive.

RECOMMENDATION 10 (Endorsed from the OH (CCO) 2022 [2] recommendations)
Cancer survivorship considerations during virtual care

- Assess the need for in-person physical examination
- Cancer survivors under surveillance following curative intent treatment can be safely followed using virtual care, unless in-person physical examination is indicated and/or required.

Transition to virtual survivorship care

- Primary care providers and cancer survivors should be made aware of the potential for transition to virtual survivorship care.

Justification for Recommendation 10
This recommendation was endorsed from the OH (CCO) 2022 guideline on virtual care [2]. The words, "potential for", were added to the recommendation for clarity.

RECOMMENDATION 11
Smoking cessation counselling is recommended for patients who have completed curative-intent therapy for NSCLC and SCLC. Although verbal cessation advice from a healthcare professional is of benefit, interventions that involve behavioural and pharmacotherapy support in addition to verbal advice is recommended.

Justification for Recommendation 11
This recommendation was endorsed from the previous PEBC 2014 version of this guideline.

RECOMMENDATION 12
Adult patients with lung cancer after curative-intent treatment living in Ontario should receive vaccinations as recommended by the Government of Canada [3]. The influenza and pneumococcal vaccine schedules for persons with chronic diseases, which includes cancer, or for immunocompromised persons should be followed. Further information can be found here: Canadian Immunization Guide - Canada.ca. The COVID-19 schedule for adults or immunocompromised persons should followed. Further information can be found here: COVID-19 vaccine: Canadian Immunization Guide - Canada.ca.

Justification for Recommendation 12
For influenza, there was very low-quality evidence to suggest that hospitalizations would be reduced with vaccinations, but for all-cause mortality and influenza infections, the evidence was less certain. There was moderate-quality evidence to suggest the adverse effects would be mild.

For COVID-19 and pneumococcal vaccines, the included systematic reviews compared outcomes in patients with cancer versus patients without cancer. The effects of receiving COVID-19 or pneumococcal vaccinations versus not being vaccinated among patients with cancer were not reported in systematic reviews.
As a result of the limited evidence available in our target population, the Working Group decided to follow the immunization recommendations from the Government of Canada.

RECOMMENDATION 13
Enrolling in an exercise or rehabilitation program is recommended.

Justification for Recommendation 13
Low-quality evidence from four randomized controlled trials (RCTs) suggested that exercise training can improve general health-related quality of life in patients with lung cancer who had surgery. Furthermore, very-low quality evidence from three RCTs suggested that exercise training can improve dyspnea. The adverse events reported were minimal. Only one hip fracture was reported in four RCTs. The Working Group believed the potential benefits in quality of life and dyspnea would outweigh the adverse effects.

IMPLEMENTATION CONSIDERATIONS

Patients in isolated areas or Indigenous populations may experience issues with accessing surveillance tests. Health care providers in the community-based setting might have more difficulty in following up a suspicion of recurrence than healthcare providers in the hospital-based setting. The cost of pharmacotherapy used in smoking cessation interventions may be a barrier for people on limited income. Currently, the pneumococcal polysaccharide vaccine is covered in Ontario, but the pneumococcal conjugate vaccine is not covered, which may influence patients' and healthcare providers' preferred vaccine. There may be issues with infrastructure in implementing exercise programs.

RELATED GUIDELINES

- Ontario Health (Cancer Care Ontario). Smoking Cessation Information for Healthcare Providers. Available from: https://www.cancercareontario.ca/en/guidelines-advice/cancer-continuum/prevention/smoking-cessation

FURTHER RESEARCH

Direct evidence from RCTs in adult patients with NSCLC or SCLC after curative-intent treatment are needed to provide a greater degree of certainty in the evidence to inform recommendations.

GUIDELINE LIMITATIONS

Systematic reviews were searched for some of the research questions and recent primary studies not included in systematic reviews may have been missed.

Follow-up and Surveillance of Curatively Treated Patients with Lung Cancer

Section 3: Guideline Methods Overview

This section summarizes the methods used to create the guideline. For the systematic review, see Section 4.

THE PROGRAM IN EVIDENCE-BASED CARE

The Program in Evidence-Based Care (PEBC) is an initiative of the Ontario provincial cancer system, Ontario Health (Cancer Care Ontario). The PEBC mandate is to improve the lives of Ontarians affected by cancer through the development, dissemination, and evaluation of evidence-based products designed to facilitate clinical, planning, and policy decisions about cancer control.

The PEBC supports the work of Guideline Development Groups (GDGs) in the development of various PEBC products. The GDGs are composed of clinicians, other healthcare providers and decision makers, methodologists, and community representatives from across the province.

The PEBC is a provincial initiative of OH (CCO) supported by the Ontario Ministry of Health (OMH). All work produced by the PEBC is editorially independent from the OMH.

BACKGROUND FOR GUIDELINE

With advances in treatment options and effectiveness, lung cancer survivorship is increasing. However, this is a rapidly evolving field and as such, the regular review and update of lung cancer survivorship evidence-based guidance is paramount.

The original guideline objective was to develop recommendations for optimal clinical and imaging surveillance and disease control after curative-intent treatment for lung cancer. In addition, the guideline includes advice on assessment of late toxicity from cancer treatments, quality of life of lung cancer survivors, and the benefit of smoking cessation interventions.

The previous version of this guideline was published in 2014. In discussions with the Ontario Thoracic Cancers Advisory Committee, it was determined that this previous version of the guideline needed to be reviewed to incorporate more recent recommendations regarding imaging surveillance and any other new evidence on the additional topics covered in the previous version of this guideline.

GUIDELINE DEVELOPERS

This guideline was developed by the Lung Cancer Survivorship GDG (Appendix 1), which was convened at the request of the Disease Pathway Management Program. The project was led by a small Working Group of the Lung Cancer Survivorship GDG, which was responsible for reviewing the evidence base, drafting the guideline recommendations, and responding to comments received during the document review process. The Working Group had expertise in surgical oncology, radiation oncology, medical oncology, family medicine, diagnostic radiology, and health research methodology. Other members of the Lung Cancer Survivorship GDG served as the Expert Panel and were responsible for the review and approval of the draft document produced by the Working Group. Conflict of interest declarations for all GDG members are summarized in Appendix 1, and were managed in accordance with the *PEBC Conflict of Interest Policy*.

GUIDELINE DEVELOPMENT METHODS

The PEBC produces evidence-based and evidence-informed guidance documents using the methods of the Practice Guidelines Development Cycle [6,7]. This process includes a systematic review, interpretation of the evidence and drafting recommendations by the Working Group, internal review by content and methodology experts and external review by Ontario clinicians and other stakeholders.

The PEBC uses the AGREE II framework [8] as a methodological strategy for guideline development. AGREE II is a 23-item validated tool that is designed to assess the methodological rigour and transparency of guideline development and to improve the completeness and transparency of reporting in practice guidelines. PEBC guideline development methods are described in more detail in the *PEBC Handbook* and the *PEBC Methods Handbook*.

The currency of each document is ensured through periodic review and evaluation of the scientific literature and, where appropriate, the addition of newer literature to the original evidence base. This is described in the *PEBC Document Assessment and Review Protocol*.

RECOMMENDATIONS DEVELOPMENT METHODS

PEBC guideline recommendations are based on evidence of the magnitude of the desirable and undesirable effects of an intervention or accuracy of a test, and take into account the certainty of the evidence, the values of key stakeholders (e.g., patients, clinicians, policy makers, etc.), and the potential impact on equity, acceptability and feasibility of implementation according to Grading of Recommendations, Assessment, Development and Evaluations (GRADE)'s evidence-to-decision framework [9]. The results of the questions associated with this framework can be found in Appendix 2 and were discussed with the Working Group at five virtual meetings. If insufficient evidence was found, then the Working Group considered endorsing the recommendations from the previous version of this guideline (see Appendix 3). A list of any implementation considerations (e.g., costs, human resources, and unique requirements for special or disadvantaged populations, dissemination issues, etc.) was provided along with the recommendations for information purposes.

Search for Guidelines

The Working Group was aware of an ASCO 2020 guideline [1] on the benefits and harms of using different surveillance imaging strategies that they would consider for endorsement. The research questions of the ASCO 2020 guideline [1] included: 1. What should be the frequency of surveillance imaging? 2. What is the optimal imaging modality? 3. Are there any patient factors such as performance status or age limits that would preclude surveillance? 4. Is there a role for circulating biomarkers in surveillance? 5. What is the role of brain MRI for surveillance in curatively treated NSCLC and SCLC?

A search for other existing guidelines was undertaken to determine whether any other guideline could be endorsed. Evidence-based guidelines with systematic reviews that addressed at least one research question were included. Guidelines older than five years (published before 2017) were excluded.

The following sources were searched for guidelines on February 28, 2022, with the search terms lung cancer, cancer surveillance, cancer follow-up, cancer vaccine, cancer smoking, cancer symptoms, cancer virtual, cancer PROs, cancer type of clinician: National Institute for Health and Care Excellence Evidence Search, Canadian Medical Association Journal Infobase, Scottish Intercollegiate Guidelines Network, American Society of Clinical Oncology, ECRI database, and Cancer Council Australia – Cancer Guidelines Wiki. One other guideline met the inclusion criteria. This guideline by OH (CCO) 2022 [2] addressed the research question, what are the benefits and harms of virtual visits in providing follow-up care?

Assessment of Guidelines

The PEBC assesses the quality of guidelines using the AGREE II tool [8]. Guidelines that had the AGREE II rigour of development domain, which assesses the methodological quality of the guideline, above 50% were considered for endorsement. Both guidelines met this criterion (rigour of development domain score: ASCO 2020 = 100%, OH (CCO) 2022 = 86%) [1,2].

ENDORSEMENT PROCESS

The PEBC endorses guidelines using the process outlined in OH (CCO)'s Guideline Endorsement Protocol OH (CCO) Guideline Endorsement Protocol. The Working Group reviewed the recommendations from the ASCO 2020 [1] and OH (CCO) 2022 [2] guidelines (Appendix 4) to assess whether they agreed with the interpretation of the evidence with respect to the magnitude of the desirable and undesirable effects of treatment and took into account the certainty of the evidence, the values of key stakeholders (e.g., patients, clinicians, policy makers, etc.), and the potential impact on equity, acceptability and feasibility of implementation within Ontario according to GRADE's evidence-to-decision framework [9]. The evidence from each guideline for each comparison was summarized within this GRADE framework to help the Working Group members consider the evidence and make a judgement as to whether they agreed with the way the evidence was interpreted. The evidence from both guidelines and the judgements of the Working Group can be found in Appendices 2 and 4. The Working Group then reviewed each recommendation from both guidelines to determine whether it could be endorsed, endorsed with changes, or rejected. This determination was based on the agreement of the Working Group with the interpretation of the available evidence and considerations presented within the GRADE framework, and whether new evidence reported since the guideline was developed might change any of the recommendations.

Taking into consideration all these factors within the GRADE framework, the Working Group members decided to endorse the recommendations from ASCO 2020 [1] and OH (CCO) 2022 [2], with a few changes. For Recommendation 2.1 of the ASCO 2020 [1] guideline, low-dose CT was added to reduce radiation exposure and without contrast was preferred over contrast because the use of intravenous contrast may pose a significant risk for patients with a contrast allergy or kidney dysfunction. For Recommendation 2.2 of the ASCO 2020 [1] guideline, the word screening before chest CT was removed because these patients do not qualify for lung screening programs currently in Ontario. For Recommendation 5.1 of the ASCO 2020 [1] guideline, CT was added to clarify that routine brain surveillance should not be performed with CT as well as MRI. From the OH (CCO) 2022 [2] guideline, the words, "potential for", were added to Recommendation 10 for clarity.

The frequency of the surveillance strategy was based on consensus. The Working Group endorsed the ASCO 2020 [1] recommendations, which were less intense than the previous version of this guideline because it was more practical. The Working Group believed that lung imaging every six months would be easier to implement compared with every three months in the first two years. Also, McMurry et al. [10] demonstrated no difference in survival when comparing groups subjected to follow-up CT surveillance at three-month, six-month, and 12-month intervals after definitive surgical therapy for stage I-III NSCLC.

GUIDELINE REVIEW AND APPROVAL

Internal Review

For the guideline document to be approved, 75% of the content experts who comprise the GDG Expert Panel must cast a vote indicating whether or not they approve the document, or abstain from voting for a specified reason, and of those who vote, 75% must approve the document. In addition, the PEBC Report Approval Panel (RAP), a three-person panel with methodology expertise, must unanimously approve the document. The Expert Panel and RAP

members may specify that approval is conditional, and that changes to the document are required. If substantial changes are subsequently made to the recommendations during external review, then the revised draft must be resubmitted for approval by RAP and the GDG Expert Panel.

Patient Consultation Group

Three patient representatives participated as Consultation Group members of the Lung Cancer Survivorship Working Group. They reviewed drafts of the project plan and guideline and provided feedback on their comprehensibility, appropriateness, and feasibility to the Working Group's Health Research Methodologist. The Health Research Methodologist relayed the feedback to the Working Group for consideration.

External Review

Feedback on the approved draft guideline is obtained from content experts and the target users through two processes. Through the Targeted Peer Review, several individuals with content expertise are identified by the GDG and asked to review and provide feedback on the guideline document. Through Professional Consultation, relevant care providers and other potential users of the guideline are contacted and asked to provide feedback on the guideline recommendations through a brief online survey.

DISSEMINATION AND IMPLEMENTATION

The guideline will be published on the OH (CCO) website and may be submitted for publication to a peer-reviewed journal. The Professional Consultation of the External Review is intended to facilitate the dissemination of the guideline to Ontario practitioners. Section 1 of this guideline is a summary document to support the implementation of the guideline in practice. OH (CCO)-PEBC guidelines are routinely included in several international guideline databases including the CPAC Cancer Guidelines Database, the CMA/Joule CPG Infobase database, NICE Evidence Search (UK), and the Guidelines International Network (GIN) Library.

ACKNOWLEDGEMENTS

The Lung Cancer Survivorship GDG would like to thank the following individuals for their assistance in developing this report:

- Fulvia G. Baldassarre, Laurie Elit, Michelle Ghert, Ehsan Haider, Jonathan Isenberg, Sheila McNair, Jonathan Sussman, David Tiberi, Patrick James Villeneuve, and Xiaomei Yao for providing feedback on draft versions.
- Faith Maelzer for conducting a data audit.
- Sara Miller for copy editing.

Follow-up and Surveillance of Curatively Treated Patients with Lung Cancer

Section 4: Systematic Review

INTRODUCTION

More than 80% of patients with lung cancer are diagnosed with NSCLC and the remainder have mainly SCLC [11,12]. Patients with stage I-III NSCLC or limited stage SCLC may undergo curative-intent treatment through a combination of surgery, radiotherapy, and chemotherapy. Due to advances in treatment options and effectiveness, lung cancer survival has improved [13]. However, lung cancer survivors are at an increased risk of developing recurrence and second primary lung cancers [14]. Follow-up for patients after curative-intent treatment involves monitoring for recurrence through clinical and imaging surveillance strategies as well as additional efforts to improve their quality of life and survival.

The PEBC developed a follow-up and surveillance guideline for patients with curatively treated lung cancer in 2014. The guideline included recommendations for optimal clinical and imaging surveillance. In addition, the guideline included advice on the assessment of late toxicities from cancer treatments, the types of clinicians that should be involved in follow-up, and the benefit of smoking cessation interventions. In 2020, ASCO published recommendations on imaging surveillance in this patient population [1]. Therefore, an update of the PEBC guideline was undertaken to endorse these ASCO 2020 recommendations regarding imaging surveillance as well as to include new evidence through this systematic review on additional topics covered in the PEBC 2014 guideline.

The Working Group of the Lung Cancer Survivorship GDG developed this systematic review to update the evidence since the previous PEBC guideline and expand the scope to investigate the benefits of using PRO tools, and pneumococcal, influenza, and COVID-19 vaccines. This systematic review will inform the recommendations as part of a clinical practice guideline. Based on the objectives of this guideline, to develop recommendations for the optimal management of patients with lung cancer after curative-intent treatment, the Working Group derived the research questions outlined below. This systematic review has been registered on the PROSPERO website (International prospective register of systematic reviews) with the following registration number CRD42023338773 [15].

RESEARCH QUESTIONS

Table 4-1 includes the unique details of each research question. For all research questions the setting included primary or secondary care and the population included adult patients with SCLC or NSCLC after curative-intent treatment. Articles that were published in a language other than English were excluded.

Table 4-1 Details of each research question

Research Question	Intervention / Indicator	Comparator	Outcomes	Inclusion Criteria	Subgroups
1. What are the benefits and harms of different types of clinicians providing follow-up care?	Specialist-led or Nurse-led or Primary Care Provider-led follow-up	Specialist-led or Nurse-led or Primary Care Provider-led follow-up	Critical outcomes: Overall or recurrence-free survival, rate of late effects, or recurrence or metastasis, quality of life, patient satisfaction, health care provider satisfaction	Fully published studies or abstracts of RCTs with at least 30 patients per arm that analyzed data from patients with lung cancer who were being followed after curative-intent treatment	Age, sex, stage, smoking status, BMI, geographic location
2. What are the benefits and harms of using patient-reported outcome tools or measures in providing follow-up care?	Patient-reported outcome tools or measures	No patient-reported outcome tools or measures	Critical outcomes: Overall or recurrence-free survival, rate of late effects, or recurrence or metastasis, quality of life, patient satisfaction, health care provider satisfaction	Fully published studies or abstracts of RCTs with at least 30 patients per arm. If no/few RCTs are found that included patients with lung cancer who are being followed after curative-intent treatment, then RCTs that included other patients with lung cancer may be included.	Age, sex, smoking status, stage, setting, SES, comorbidities, type of cancer
3. What are the benefits and harms of pneumococcal, influenza, and COVID-19 vaccinations?	Pneumococcal, influenza, and COVID-19 vaccinations	No vaccinations	Critical outcomes: Overall or recurrence-free survival, rate of hospitalization, infection, or adverse effects Important outcomes: Immune response	Fully published studies or abstracts of RCTs with at least 30 patients per arm. If no/few RCTs are found that included patients with lung cancer who are being followed after curative-intent treatment, then RCTs that included other patients with lung cancer may be included. If no/few RCTs are found that included patients with lung cancer, then RCTs that included patients with any cancer may be included.	Age, sex, smoking status, stage, SES, comorbidities, type of cancer
4. What are the benefits and harms of smoking cessation interventions?	Smoking cessation strategies	Other smoking cessation strategies or usual care or no smoking cessation strategy	Critical outcomes: Overall or recurrence-free survival, rate of smoking cessation, cancer recurrence or metastasis, or adverse effects of treatment,	Fully published studies or abstracts of RCTs with at least 30 patients per arm. If no/few RCTs are found that included patients with lung cancer who are being followed after curative-intent treatment, then	Age, sex, smoking status, stage, setting, SES, comorbidities, type of cancer

Research Question	Intervention / Indicator	Comparator	Outcomes	Inclusion Criteria	Subgroups
			quality of life, patient satisfaction	RCTs that included other patients with lung cancer may be included.	
5. Which signs/symptoms/ risk factors/ comorbidities should be managed to improve their quality of life, risk of recurrence, survival, or risk of other primary cancers?	Signs/ symptoms/ risk factors/ comorbidities	Other signs/ symptoms/ risk factors/ comorbidities	Quality of life, risk of recurrence, survival, or risk of other primary cancers	This is a very broad question; therefore, only fully published systematic reviews will be included. Priority will be given to systematic reviews that included fully published studies with at least 30 patients that controlled for confounders.	Age, sex, smoking status, stage, setting, SES, comorbidities, type of cancer, prior treatment
6. What are the late toxicities after any treatment (surgical, radiotherapy, chemotherapy, immunotherapy) that should be managed to improve their quality of life?	Not applicable	Not applicable	Late toxicities from treatments (beyond acute and subacute)	This is a very broad question; therefore, only fully published systematic reviews will be included. Priority will be given to systematic reviews that included fully published studies with at least 30 patients	Not applicable
7. What are the benefits and harms of the treatment/ management strategies for signs/symptoms/risk factors/ comorbidities/ late toxicities?	Treatment/ management strategies for signs /symptoms/ risk factors/ comorbidities/late toxicities	No or alternate treatment/ management strategies	Critical outcomes: Overall or recurrence-free survival, rate of recurrence or metastasis, or adverse effects of treatment, quality of life, patient satisfaction	This is a very broad question; therefore, only fully published systematic reviews will be included. Priority will be given to systematic reviews that included RCTs with at least 30 patients per arm and/or fully published comparative studies that controlled for confounders with a sample size of at least 30 patients per arm.	Age, sex, smoking status, stage, setting, SES, comorbidities, type of cancer, prior treatment

Abbreviations: BMI, body mass index; RCTs, randomized controlled trials; SES, socioeconomic status

METHODS

Search for Systematic Reviews and Primary Literature

Systematic reviews were included if they met the following criteria: the review addressed the research question with similar inclusion or exclusion criteria, and the review had a low risk of bias as assessed with the ROBIS tool [16]. If more than one systematic review met the inclusion criteria, then one systematic review for each outcome per comparison was selected by EV based on its age, quality, and the best match with our study selection criteria stated above. For research questions one to four, for each outcome per comparison, if no systematic review was included, then a search for primary literature was conducted.

Literature Search Strategy

MEDLINE, EMBASE, the Cochrane Clinical Trials Registry, and the Cochrane Database of Systematic Reviews were searched since the time of the previous PEBC 2014 publication until June 1, 2022. PubMed was searched from June 1, 2022, until July 20, 2023. Conferences were searched for RCT abstracts in ASCO 2023, AATS 2023 (American Association for Thoracic Surgery), ASTRO 2022, IASLC 2022, ESMO 2022, and ESTRO 2023. Clinicaltrials.gov was searched on July 18, 2023, for ongoing trials and to identify data from any existing trials (see Appendix 5 for the full search strategies).

Study Selection Process, Data Extraction and Assessment of Risk of Bias

A review of the titles and abstracts was conducted by EV independently. For studies that warranted full-text review, EV reviewed each study in collaboration with the other authors, if uncertainty existed.

All included primary studies underwent data extraction by EV independently, with all extracted data and information audited subsequently by an independent auditor. Ratios, including hazard ratios (HRs), were expressed with a ratio of <1.0 indicating benefit for the intervention rather than the comparator.

Risk of bias (ROB) per outcome for each included RCT was assessed by EV in collaboration with the other authors, if uncertainty existed, using the Cochrane ROB for Interventions [17].

Synthesizing the Evidence

For time-to-event outcomes, when clinically and methodologically homogeneous results from two or more studies were available, a meta-analysis was conducted using Review Manager 5.4 software provided by the Cochrane Collaboration [18]. HRs, rather than the number of events at a specific time, were the preferred statistic for meta-analysis, and were used as reported. If the HR and/or its standard error were not reported, they were derived from other information reported in the study if available, using the methods described by Parmar et al. [19]. The generic inverse variance model with random effects was used. Adjusted effect measurements were used, if available. Sensitivity analyses by any variability in ROB may have been conducted. Subgroups listed in Table 4-1 were considered for separate analyses. Absolute values were reported for any ratios using baseline risks extracted from included studies.

The chi-squared (X^2) test was used to test the null hypothesis of homogeneity, and a probability level less than or equal to 5% ($p \leq 0.05$) was considered indicative of statistical heterogeneity. If heterogeneity was detected, then the I^2 index was used to quantify the percentage of the variability in the effect estimates that was due to heterogeneity.

Assessment of the Certainty of the Evidence

The certainty of the evidence per outcome for each comparison, taking into account ROB, inconsistency, indirectness, imprecision, and publication bias was assessed by EV in collaboration with the other authors using the GRADE method [20].

RESULTS

Search Results and ROB for Systematic Reviews and Primary Literature

There were 15,152 results from the combined MEDLINE, EMBASE, PubMed, and Cochrane search of which 27 systematic reviews and 21 studies, where one RCT had two publications, met the inclusion criteria. Furthermore, one systematic review and 11 studies were found from reference lists. Three abstracts of RCTs were included from the ASCO 2023 conference. A PRISMA flow chart with the reasons for exclusion can be found in Appendix 6. The assessment of the ROB of the systematic reviews can be found in Appendix 7. Since there were few systematic reviews that were found that addressed the research questions with similar inclusion and exclusion criteria, a decision was made to include systematic reviews with the lowest risk of bias for each comparison. The characteristics of the studies selected for inclusion can be found in Appendix 8. The assessment of the ROB of the included studies can be found in Appendix 9. The number of included systematic reviews or studies for each outcome per comparison or factor is reported in Table 4-2.

Table 4-2. Number of included systematic reviews and primary studies per outcome per comparison or factor.

Research Question	Comparisons / Factor	Outcomes	Number of systematic reviews (SRs) or primary studies
1	Nurse-led interventions vs. usual care	Overall survival	3 [21-23]
		Time to progression	1 [22]
		Quality of life	4 [23-26]
		Distress	4 [23,25-27]
		Patient satisfaction with nursing	6 [22,28-32]
		Hospital visits	3 [22,27,29]
2	Patient-reported outcome interventions vs. usual care or controls	Overall survival	5 [4,33-36]
		Progression-free survival	2 [5,33]
		Quality of life	10 [5,34-42]
		Distress	4 [34,36,38,43]
		Patient satisfaction	5 [36,37,41,43,44]
		Healthcare provider satisfaction	1 [41]
3	COVID-19 vaccine in cancer patients vs. COVID-19 vaccine in non-cancer patients	COVID-19 infection	1 SR [45] with 6 studies
		COVID-19 seroconversion	1 SR [46] with 5 studies
		COVID-19 vaccine grade 3-4 adverse events	1 SR [47] with 5 studies
	Influenza vaccine vs. no influenza vaccine	All-cause mortality	1 SR [48] with 2 studies
		Influenza infection	1 SR [48] with 1 study
		Hospitalization	1 SR [48] with 1 study
		Immune response	1 SR [48] with 1 study
		Influenza vaccine adverse events	1 SR [48] with 2 studies
	Pneumococcal vaccine in cancer patients vs. pneumococcal vaccine in non-cancer patients	Immune response	1 SR [49]
4		Smoking abstinence at 6 months	6 [50-55]

Research Question	Comparisons / Factor	Outcomes	Number of systematic reviews (SRs) or primary studies
	Smoking cessation intervention vs. usual care or placebo	Quality of life	2 [52,55]
		Medication adverse events	2 [52,53]
5	Symptoms associated with recurrence		1 SR [56]
	Symptoms associated with metastases		1 SR [57]
	Symptoms associated with quality of life		1 SR [58]
6	Late adverse events from interventions		7 SRs [59-65]
7	Exercise training vs. usual care or no exercise training	Adverse events	1 SR [66] with 4 studies
		General health-related quality of life	1 SR [66] with 4 studies
		Dyspnea	1 SR [66] with 3 studies
		Fatigue	1 SR [66] with 3 studies
		Anxiety and depression	1 SR [66] with 1 study

Outcomes and the Certainty of the Evidence for each Research Question

The outcomes reported from each primary study or systematic review can be found in Appendix 10.

1. What are the benefits and harms of different types of clinicians providing follow-up care?

Nurse-led interventions versus usual care

Twelve RCTs compared a nurse-led intervention with usual care, which could have included routine nursing (Table 4-3) [21-32]. The interventions included increasing the communication between patients, family physicians, and oncologists, symptom management, the addition of a nurse navigator, or nurse-led follow-up care. All studies included at least some patients with lung cancer who may have received curative-intent treatment, not just palliative care. All studies indicated that patients were being followed at some point after treatment, not just during treatment.

For all critical outcomes, either a significant effect was found in favour of the nurse-led intervention or no significant effect was found. There were no significant differences in overall survival, but for each of the other outcomes, including time to progression, change in quality of life from baseline, change in distress from baseline, patient satisfaction with nursing, and number of hospital visits, at least some studies reported favourable results for the nurse-led intervention. However, for PROs, there were issues with the blinding of the assessor in many of these studies as well as imprecision. Therefore, the certainty in these RCTs was very low.

Table 4-3. Summary of findings for nurse-led interventions vs. usual care

Certainty assessment							Summary of findings				Importance
							# of patients		Effect	Certainty	
# of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Nurse-led intervention	Usual care			
Overall survival (mean follow-up: range 1 to 2 years)											
3	RCT	serious [a]	not serious	serious [b]	serious [c]	none	334	335	All studies showed no significant effect. [d]	⨁◯◯◯ **VERY LOW**	**CRITICAL**
Time to progression (follow-up not reported)											
1	RCT	serious [e]	not serious	serious [f]	serious [g]	none	99	103	One study showed that nurses detected progression of symptoms sooner than doctors, but there was no difference in objective progression.	⨁◯◯◯ **VERY LOW**	**CRITICAL**
Quality of life											
4	RCT	serious [e]	serious [h]	serious [i]	serious [g]	none	253	254	Two studies showed significant differences favouring the nurse-led intervention and two studies showed no differences. [d]	⨁◯◯◯ **VERY LOW**	**CRITICAL**
Distress											
4	RCT	serious [e]	not serious	serious [i]	serious [g]	none	245	244	Most studies found no significant differences. [d]	⨁◯◯◯ **VERY LOW**	**CRITICAL**
Patient satisfaction with nursing											
6	RCT	serious [e]	not serious	serious [f]	serious [g]	none	313	303	Most studies showed greater satisfaction in the nurse-led intervention at some point in the study. [d]	⨁◯◯◯ **VERY LOW**	**CRITICAL**
Hospital visits											

3	RCT	serious [e]	serious [h]	serious [f]	serious [g]	none	192	194	One study found fewer visits, whereas another study found more visits, in the nurse-led intervention. The other study showed no differences at 3 months. [d]	⊕◯◯◯ **VERY LOW**	**IMPORTANT**

Abbreviations: RCT, randomized controlled trial

a. Some issues with baseline differences and deviations from intended interventions
b. McCorkle 2000 included patients with lung cancer or other cancers. Both studies included patients at early and advanced stages.
c. Number of deaths was less than 300.
d. A meta-analysis could not be performed because the populations and interventions were different.
e. Most studies had issues with blinding.
f. Some studies included patients who did not have curative-intent treatment.
g. Number of patients was less than 800.
h. The results were inconsistent. Only studies that reported a before and after change in quality of life were included.
i. Some studies included patients with non-lung cancers or patients who did not have curative-intent treatment.

2. What are the benefits and harms of using patient-reported outcome tools or measures in providing follow-up care?

PRO interventions versus usual care or controls

Ten fully published RCTs, where one trial had two publications, and three abstracts of RCTs compared using a PRO tool with usual care (Table 4-4) [4,5,36-44]. Usual care could have consisted of not using the tool or not reporting the information from the tool to the healthcare provider. All studies included patients with only lung cancer. Some studies included only patients with advanced stages of lung cancer. The certainty in this evidence was low, mainly due to issues with lack of blinding and imprecision. Several trials were stopped early due to issues with funding or were an interim analysis.

One fully published RCT found that patients who self-reported symptoms weekly with web-mediated follow-up had longer median overall survival at two years than patients who did not self-report symptoms weekly with web-mediated follow-up (HR, 0.59; 95% confidence interval [CI], 0.37 to 0.96, p=0.03) [4]. Progression-free survival at nine months was not significantly different between these groups (p=0.13) [5]. Another fully published study that compared using a self-report distress screening tool versus not using this tool found no differences in overall survival at six months (p=0.62) [36]. Three abstracts reported no differences in overall survival [33-35] and one abstract reported no difference in progression-free survival [33] between the PRO interventions and usual care.

Several studies reported on the change in quality of life from baseline, with most studies (8/10) showing no significant differences between groups [34-36,38-42]. Furthermore, four RCTs found no differences in change in distress from baseline between the arms [34,36,38,43]. Patient satisfaction was inconsistent and may have depended on the type of intervention being used. No differences in patient satisfaction were found in two studies that compared using self-administered tools versus not using the tools [36,37]. When studies compared reporting the information from the tool to healthcare providers versus not reporting, one study found greater satisfaction for patients receiving the intervention [44], whereas another study found no overall differences, but patient satisfaction was decreased for those receiving the intervention for some subscales [43]. One study did not compare patient satisfaction between groups, but only reported that the intervention was helpful [41]. This study also reported on healthcare provider satisfaction and found the intervention was acceptable among surgeons [41].

Table 4-4. Summary of findings for PRO interventions vs. usual care/control

Certainty assessment							Summary of findings				Importance
							# of patients		Effect	Certainty	
# of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	PRO intervention	Usual care/ control			
Overall survival (follow-up: 6 months to 2.6 years)											
5	RCT	serious [a]	not serious [b]	not serious	serious [c]	none	# of deaths 102/170 (60%)	# of deaths 120/174 (69%)	Median overall survival was significantly different favouring the intervention for one study, but all the other studies found no significant differences. [d]	⊕⊕◯◯ **LOW**	**CRITICAL**
Progression-free survival (median follow-up: 9 months)											
1	RCT	serious [e]	not serious	not serious	serious [f]	none	60	61	No significant difference was found.	⊕⊕◯◯ **LOW**	**CRITICAL**
Quality of life											
10	RCT	serious [g]	not serious	not serious	serious [h]	none	640	651	Eight studies found no differences. Two found differences; one favoured the intervention the other favoured the control. [i]	⊕⊕◯◯ **LOW**	**CRITICAL**
Distress											
4	RCT	serious [g]	not serious	not serious	serious [h]	none	432	444	All studies found no differences. [i]	⊕⊕◯◯ **LOW**	**CRITICAL**
Patient satisfaction											
5	RCT	serious [g]	not serious [b]	not serious	serious [h]	none	257	201	Two studies found no differences. Two found differences; one favoured the	⊕⊕◯◯ **LOW**	**CRITICAL**

									intervention the other favoured the control. One study found the intervention to be helpful. [i]		
Health care provider satisfaction											
1	RCT	not serious	not serious	not serious	very serious [h]	none	5	-	Study found high acceptability among surgeons.	⊕⊕◯◯ **LOW**	**CRITICAL**

Abbreviations: PRO, patient-reported outcome; RCT, randomized controlled trial

a. Cross-over may have occurred in one study and three studies were abstracts.
b. Inconsistency might be explained by differences in interventions.
c. Number of deaths was less than 300. One study stopped early and the other was an interim analysis. Three abstracts did not report number of deaths.
d. A meta-analysis could not be performed because the interventions were different.
e. Study not blinded and cross-over may have occurred.
f. Events not reported. Small sample size. Study stopped early.
g. Most studies had issues with lack of blinding.
h. Number of patients was less than 800.
i. A meta-analysis could not be performed because the measurement tools and follow-up times were different.

3. What are the benefits and harms of pneumococcal, influenza, and COVID-19 vaccinations (Table 4-5)?

There were no RCTs that compared COVID-19, influenza, or pneumococcal vaccinations with no vaccinations in patients with SCLC or NSCLC after curative-intent treatment.

Influenza vaccine vs. no influenza vaccine

There was a systematic review that compared influenza vaccination versus no vaccination in immunosuppressed adults with cancer [48]. The certainty of the evidence from the included studies was very low mainly due to issues with the risk of bias, imprecision, and indirectness. Influenza vaccination did not have a significant impact on all-cause mortality. One observational study that included patients with advanced colorectal cancer found an odds ratio of 0.88 (95% CI, 0.78 to 1.00) [67]. Likewise, a small RCT in patients who received an allogeneic bone marrow transplant found an odds ratio of 1.25 (95% CI, 0.43 to 3.62) [68]. Additionally, this RCT did not find a significant effect of influenza vaccination on reducing confirmed influenza (odds ratio, 0.69; 95% CI, 0.14 to 3.31). However, the vaccinated group had higher geometric mean titres for influenza A/H1N1 ($p=0.03$) and A/H3N2 ($p<0.001$) viruses, but not for influenza B virus ($p=0.07$) [68]. Another small RCT found that people with multiple myeloma who were vaccinated were less likely to be hospitalized (odds ratio, 0.09; 95% CI, 0.02 to 0.49) [69]. They also reported that 60% of the vaccinated group had mild adverse events at the injection site. Similarly, an observational study found 25% of vaccinated people experienced mild symptoms and 3% reported fever [70].

COVID-19 vaccine in cancer patients vs. COVID-19 vaccine in non-cancer patients

Six systematic reviews reported outcomes from COVID-19 vaccinations in people with cancer [45-47,71-73]. The included studies only compared COVID-19 vaccination in people with cancer versus COVID-19 vaccination in people without cancer. Only one systematic review reported on COVID-19 infection rates in people who had been vaccinated and found non-significantly higher infections in those with cancer compared with those without cancer (risk ratio [RR], 3.21; 95% CI, 0.35 to 29.04) [45]. All the systematic reviews reported on immune response. The results from Sakuraba et al. [46] were chosen because it had the lowest risk of bias and the largest sample size. They found that seroconversion was lower in people with solid tumours compared with people without cancer (RR, 1.05; 95% CI, 1.02 to 1.09). One systematic review reported no grade 3 to 4 adverse events from the COVID-19 vaccination [47].

Pneumococcal vaccine in cancer patients vs. pneumococcal vaccine in non-cancer patients

Two systematic reviews with a high risk of bias were found that included studies that compared pneumococcal vaccination in people with cancer versus pneumococcal vaccination in people without cancer [49,74]. The results of these systematic reviews were not reported by outcome. Only the La Torre et al. systematic review concluded that they found a worse immune response in patients with hematologic malignancies than in healthy controls or patients with other pathologies [49].

Table 4-5. Summary of findings for vaccines vs. controls

Certainty assessment						Summary of findings						Importance
						# of patients			Effect		Certainty	
# of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Vaccines	Control	Relative (95% CI)	Absolute (95% CI)		
COVID-19 (vaccine in cancer patients vs. vaccine in non-cancer patients)												
COVID-19 infection (from Becerril-Gaitan 2022 systematic review)												
6	observational (cancer)	not serious	not serious	serious [a]	serious [b]	none	20/2274 (0.88%)	0/733 (0%)	**RR 3.21** (0.35-29.04)		⊕⊕◯◯ **LOW**	**CRITICAL**
COVID-19 seroconversion (from Sakuraba 2022 systematic review)												
5	observational (solid tumours)	not serious	not serious	serious [c]	not serious	none	491/520 (94%)	189/189 (100%)	**RR 1.05** (1.02–1.09)		⊕⊕⊕◯ MODERATE	**IMPORTANT**
COVID-19 vaccine Grade 3-4 adverse events (from Cavanna 2021 systematic review)												
5	observational (cancer)	not serious	not serious	not serious	serious [b]	none	0	-			⊕⊕⊕◯ MODERATE	**CRITICAL**
Influenza (vaccine vs. no vaccine)												
All-cause mortality (from Bitterman 2018 systematic review)												
1	RCT (allogeneic bone marrow transplantation)	serious [d]	not serious	serious [e]	serious [d]	none	40	38 (211 per 1000) [d]	**OR 1.25** (0.43 to 3.62)	**250 per 1000** (103 to 491) [d]	⊕◯◯◯ **VERY LOW**	**CRITICAL**
1	observational (solid tumours)	serious [d]	not serious	serious [e]	serious [d]	none	626	951 (417 per 1000) [d]	**OR 0.88** (0.78-1.00)	**387 per 1000** (359 to 417) [d]	⊕◯◯◯ **VERY LOW**	**CRITICAL**
Influenza infection (from Bitterman 2018 systematic review)												
1	RCT (allogeneic bone marrow transplantation)	serious [d]	not serious	serious [e]	serious [b]	none	3/40 (7.5%)	4/38 (11%)	**OR 0.69** (0.14 to 3.31)		⊕◯◯◯ **VERY LOW**	**CRITICAL**
Hospitalization (from Bitterman 2018 systematic review)												
1	RCT (multiple myeloma)	serious [d]	not serious	serious [e]	serious [b]	none	2/25 (8%)	12/25 (48%)	**OR 0.09** (0.02 to 0.49)		⊕◯◯◯ **VERY LOW**	**CRITICAL**
Immune response (from Bitterman 2018 systematic review)												
1	RCT (allogeneic bone marrow transplantation)	serious [d]	not serious	serious [e]	serious [b]	none	40	38	Vaccinated group had significantly higher geometric mean titres for influenza A/H1N1 (p=0.03) and A/H3N2		⊕◯◯◯ **VERY LOW**	**IMPORTANT**

									(p<0.001) viruses, but not for influenza B virus (p=0.07).		
Influenza vaccine adverse events (from Bitterman 2018 systematic review)											
2	1 RCT 1 observational (cancer)	serious [d]	not serious	serious [e]	not serious	none	NR	NR	59% and 60% of vaccinated groups had local or mild adverse events. 3% reported fever in one study.	⊕⊕⊕◯ MODERATE	**CRITICAL**
Pneumococcal (vaccine in cancer patients vs. vaccine in non-cancer patients)											
Immune response (from La Torre 2016 systematic review)											
NR	observational (hematological cancers)	serious [f]	not serious	serious [e]	serious [g]	none	NR	NR	Found a worse response in hematologic patients than in healthy controls or patients with other pathologies	⊕◯◯◯ **VERY LOW**	**IMPORTANT**

Abbreviations: CI, confidence interval; NR, not reported; OR, odds ratio; RCT, randomized controlled trial; RR, risk ratio

a. Included patients with any type of cancer. Did not compare vaccinated versus not vaccinated among patients with cancer.
b. Number of events was less than 300.
c. Included patients with any type of solid tumour cancer. Did not compare vaccinated versus not vaccinated among patients with cancer.
d. From Bitterman 2018 assessment.
e. Not lung cancer
f. From La Torre 2016 assessment
g. Unsure of sample size

4. What are the benefits and harms of smoking cessation interventions?

Smoking cessation intervention vs. usual care or placebo

There was one systematic review that compared any psychosocial or pharmacological smoking cessation intervention or combinations of both versus no intervention, or a different psychosocial and/or pharmacological intervention, or a placebo, for pharmacological interventions, in patients with lung cancer [75]. No studies were found that met their inclusion criteria.

The primary studies compared a smoking cessation intervention with usual care or a placebo (Table 4-6) [50-55,76-78]. All studies included some patients with lung cancer as well as patients with other types of cancer. There were no studies that reported on survival. There was no statistically significant effect of a smoking cessation intervention on smoking abstinence at six months, but the point estimate favoured the intervention compared with the control (RR, 0.84; 95% CI, 0.68 to 1.03) (Figure 1). There was low certainty in this evidence due to risk of bias because some of the randomization methods were unclear or the outcomes assessors were not blinded. Also, there was an indirectness in the patient population since studies included patients with other types of cancer besides lung cancer. There were few studies that reported on quality of life or adverse events from medications. These studies reported no differences in these outcomes.

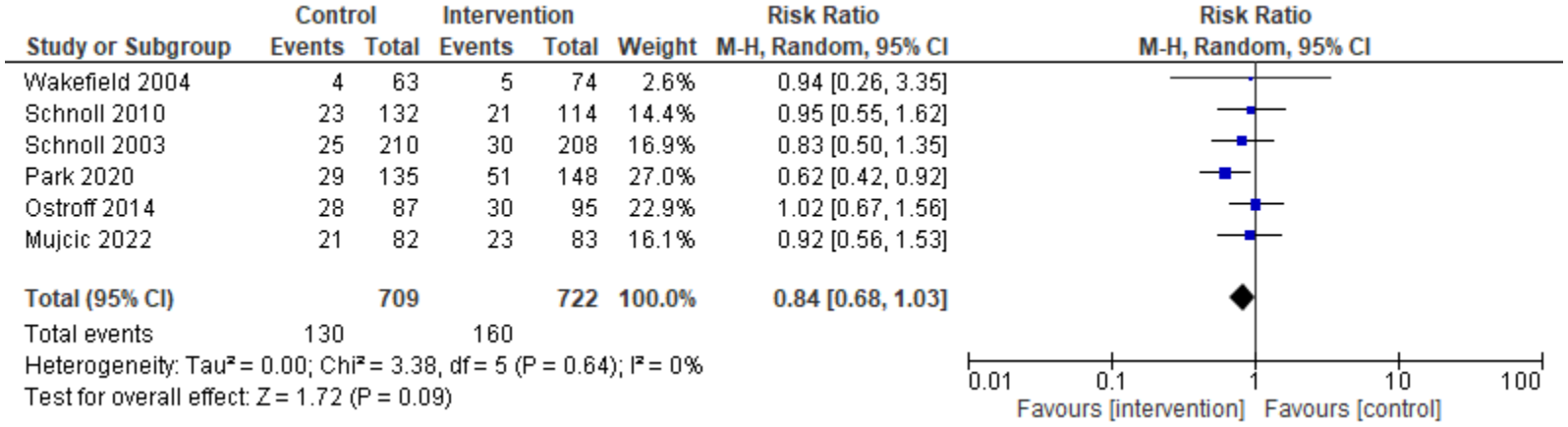
Table 4-6. Summary of findings for smoking cessation intervention vs. usual care/placebo

Certainty assessment							Summary of findings					
							# of patients		Effect			
# of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Smoking cessation intervention	Usual care/ placebo	Relative (95% CI)	Absolute (95% CI)	Certainty	Importance
Smoking abstinence (at 6 months)												
6	RCT	serious [a]	not serious	serious [b]	not serious	none	160/722 (22.2%)	130/709 (18.3%)	**RR 0.84** (0.68-1.03)	**29 more per 1000** (from 6 fewer to 59 more)	⊕⊕◯◯ **LOW**	**CRITICAL**
Quality of life												
2	RCT	serious [c]	not serious	serious [b]	serious [d]	none	197	214	No significant differences in quality of life were found for either of the studies. [e]		⊕◯◯◯ **VERY LOW**	**CRITICAL**
Medication adverse events												
2	RCT	serious [c]	not serious	serious [b]	serious [d]	none	262	267	No differences were reported for either of the studies. [e]		⊕◯◯◯ **VERY LOW**	**CRITICAL**

Abbreviations: CI, confidence interval; RCT, randomized controlled trial; RR, risk ratio

a. Outcomes assessors were not blinded and randomization process was unclear for some studies.
b. All studies included patients with lung cancer or other cancers.
c. Assessors not blinded.
d. Number of patients was less than 800.
e. A meta-analysis could not be performed because the measurement tools and follow-up times were different.

Figure 1: Smoking cessation intervention vs. usual care/placebo for smoking abstinence at six months



5. Which signs/symptoms/risk factors/comorbidities should be managed to improve their quality of life, risk of recurrence, survival, or risk of other primary cancers?

Symptoms associated with recurrence

One systematic review reported on signs or symptoms that were associated with recurrence in patients with lung cancer [56]. Walls et al. searched for predictors of local control in patients with stages I-III NSCLC after radical radiotherapy. However, predictive factors that would not be available before beginning radical radiotherapy were excluded. They found that weight loss was a statistically significant predictive factor in 4% of the studies investigating local control and in 8% of the studies investigating distant control. The risk of bias in these studies was considered to be high.

Symptoms associated with metastases

One systematic review reported on signs or symptoms that were associated with metastases in patients with lung cancer [57]. Wu et al. reported limb weakness (76.4%, n=161), paresthesia (61.5%), pain (49.7%), sphincter dysfunction (48.4%), and dysreflexia (18.0%) in patients with intramedullary spinal cord metastasis. The risk of bias was not reported in this systematic review.

Symptoms associated with quality of life

One systematic review found that fatigue, coughing, difficulty in walking, and dyspnea were significant predictors of quality of life in patients with SCLC [58]. The risk of bias was not reported in this systematic review.

6. What are the late toxicities after any treatment (surgical, radiotherapy, chemotherapy, immunotherapy) that should be managed to improve their quality of life?

The late adverse events from interventions for patients with lung cancer reported in seven included systematic reviews are listed in Table 4-7. Six studies reported on the long-term side effects after radiotherapy [59-62,64,65] including hypofractionated radiotherapy [59], prophylactic cranial irradiation [61], and stereotactic ablative radiation therapy [62,64,65]. Two studies reported on the late surgical effects [60,63].

Table 4-7. Late adverse events from interventions for patients with lung cancer

Studies	Populations	Outcomes	Overall bias
Guo 2017 [59]	Inoperable NSCLC treated after chemotherapy with hypofractionated radiotherapy	Esophagitis, pneumonitis, and hematological toxicity	Unclear
Iseli 2020 [60]	Stage III NSCLC	Nonsurgical late adverse events: anemia, anterior spinal cord syndrome, cough, dysphagia, dyspnea, esophageal perforation, esophageal stenosis, esophagitis, fatigue, hearing, lung fibrosis, lymphopenia, motor deficit, mucositis, neuropathy, pain, pancytopenia, pneumonitis, pulmonary hemorrhage, renal failure, radiotherapy injury, second malignancy, weight loss Late organ effects: blood/bone marrow, bone/osseous, cardiac, constitutional symptom, esophagus, gastrointestinal, neurological, renal, respiratory, skin Surgical late effects: chronic venous insufficiency, pneumonia	Unclear
Liu 2020 [61]	NSCLC treated with prophylactic cranial irradiation	Dyspnea, syncope, weakness, fatigue, soft tissue necrosis, headache, skin atrophy, significant decline in memory at 1 year	High
Morias 2018 [62]	Lung cancer after stereotactic ablative radiation therapy	Pulmonary (both acute and late): radiation pneumonitis, dyspnea, pleural effusion, cough, radiation-induced fibrosis Thoracic wall/ribs (both acute and late): rib fracture, chest wall pain, myositis Skin (both acute and late): dermatitis, erythema Other (both acute and late): esophagitis, heart disorders, atelectasis, fatigue, nausea (radiation sickness)	Unclear
Poghosyan 2013 [63]	NSCLC after surgery	Pain, fatigue, cough, dyspnea, anxiety, and depression	unclear
Prezzano 2019 [64]	Primary early-stage NSCLC definitively treated with stereotactic ablative radiation therapy	Esophageal perforation, fatal pulmonary hemorrhage	unclear
Voruganti 2020 [65]	Stage I NSCLC after stereotactic ablative radiation therapy	Pooled incidences of chest wall pain and rib fracture were estimated to be 8.94% and 5.27%, respectively	High

Abbreviations: NSCLC, non-small cell lung cancer

7. What are the benefits and harms of the treatment/management strategies for signs/symptoms/risk factors/comorbidities/late toxicities?

Exercise training versus usual care or no exercise training

Eight systematic reviews examined exercise training in patients with lung cancer following treatment [66,79-85]. The results of Cavalheri et al. were reported because it had a low risk of bias and included the most studies [66]. This systematic review examined the effect of exercise training started within 12 months of lung surgery in patients with NSCLC [66] (Table 4-8). One adverse event (hip fracture) related to exercise training was reported in one study and three other studies reported no adverse events. Exercise training improved the physical component of the general health-related quality of life (mean difference, 5.0 points; 95% CI, 2.3 to 7.7 points, four studies, 208 participants, low-certainty evidence) and lessened dyspnea (standardized mean difference, −0.43; 95% CI, −0.81 to −0.05, three studies, 110 participants, very low-certainty evidence). The effects on fatigue, the mental component of general health-related quality of life, and feelings of anxiety and depression were uncertain. Survival was not reported in the included studies.

Table 4-8. Summary of findings for exercise training vs. usual care or no exercise

Certainty assessment							Summary of findings					Importance
							# of patients		Effect			
# of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Exercise training	Usual care/no exercise	Relative (95% CI)	Absolute (95% CI)	Certainty	
General health-related quality of life (from Cavalheri 2019 systematic review)												
4	RCT	serious [a]	not serious	not serious	serious [b]	none	208	The mean general health-related quality of life (SF-36 - physical component score) ranged from 23.0 to 43.3		MD 5.02 higher (2.3 higher to 7.73 higher)	⊕⊕◯◯ **LOW**	**CRITICAL**
Adverse events (from Cavalheri 2019 systematic review)												
4	RCT	not serious	not serious	not serious	serious [c]	none	202		1 adverse event (a hip fracture) was reported in the intervention group of 1 RCT.		⊕⊕⊕◯ MODERATE	**CRITICAL**
Dyspnea (from Cavalheri 2019 systematic review)												
3	RCT	serious [a]	not serious	not serious	very serious [b]	none	110			SMD 0.43 lower (0.81 lower to 0.05 lower)	⊕◯◯◯ **VERY LOW**	**CRITICAL**
Fatigue (from Cavalheri 2019 systematic review)												
3	RCT	serious [d]	not serious	not serious	very serious [e]	none	68			SMD −0.05, 95% CI, −0.52 to 0.43	⊕◯◯◯ **VERY LOW**	**CRITICAL**
Anxiety and Depression (from Cavalheri 2019 systematic review)												
1	RCT	serious [d]	not serious	not serious	very serious [f]	none	Not reported			No significant differences between the intervention and control groups in feelings of anxiety and depression	⊕◯◯◯ **VERY LOW**	**CRITICAL**

Abbreviations: CI, confidence interval; MD, mean difference; RCT, randomized controlled trial; SF-36, Medical Outcomes Study Short Form 36 General Health Survey; SMD, standardized mean difference

a. Some studies rated as having a high risk of detection bias.
b. Some level of inconsistency across results of studies.
c. Outcome reported in only four of the eight included studies.
d. Studies had performance and reporting biases
e. Wide confidence interval and small sample size
f. Only one study

Ongoing or Unpublished Studies

See Appendix 11.

DISCUSSION

This systematic review examined the outcomes of using different types of clinicians, PRO tools, smoking cessation interventions, and pneumococcal, influenza, and COVID-19 vaccines in adult patients with NSCLC or SCLC after curative-intent treatment. Furthermore, this systematic review examined which signs or symptoms or risk factors or comorbidities or late toxicities should be managed to improve these patients' quality of life, risk of recurrence, survival, or risk of other primary cancers as well as which strategies were the most effective in managing these signs or symptoms or risk factors or comorbidities or late toxicities. There were no RCTs that included only our target population; therefore, conclusions were drawn from studies with broader populations.

When investigating which type of clinician should be following these patients, there were RCTs that compared a nurse-led intervention versus usual care. For all outcomes, either a significant effect was found in favour of the nurse-led intervention or no significant effect was found. The certainty in this evidence was very low; however, the Working Group did not believe there would be significant harm in using a nurse-led follow-up strategy versus follow-up with another clinician. There were no RCTs that examined follow-up with a family physician versus another type of clinician. Although the evidence was very low quality, the Working Group believed there would not be substantial harm in patients being followed by different clinicians.

RCTs compared using a PRO tool versus not using the tool or not reporting the information from the tool to the health care provider in the hospital or at home. The results were mixed, and this could be due to the differences in comparators and settings. Only one study found a difference in overall survival favouring using a tool when patients were asked to self-report symptoms weekly at home compared with routine follow-up with CT scans scheduled every three to six months [4,5]. In Ontario, symptom monitoring coincides with patients attending clinic. Therefore, the Working Group did not consider the evidence strong enough to support changing the current system to a more intense, at-home, system, especially because there were concerns about feasibility and accessibility.

There were issues with finding RCTs that compared using an influenza, COVID-19, or pneumococcal vaccine with not using a vaccine in our target population. Only studies that compared using the influenza vaccine versus not using the influenza vaccine could be found, but only among patients with solid tumours. Although the results for survival were not significant, one small study found that patients who were vaccinated were less likely to be hospitalized [69]. Furthermore, only mild adverse events were reported at the injection sites. The evidence for COVID-19 and pneumococcal vaccinations were less informative for recommendation development because the studies compared patients with cancer who were vaccinated with patients without cancer who were vaccinated. Since the evidence was limited in our target population, the Working Group decided to follow the immunization recommendations for patients who are moderately to severely immunocompromised from the Government of Canada [3].

Again, there was difficulty in finding RCTs that investigated smoking cessation interventions in our patient population. Studies that included patients with any cancer did not find a statistically significant increase in smoking abstinence at six months, but the point estimate favoured the intervention rather than the control or placebo groups. Evidence from studies that did not include patients with cancer and would not have met our inclusion criteria was reported in the PEBC systematic review used to inform the previous version of this guideline. A systematic review compared advice from physicians in promoting smoking cessation with no advice or usual care [86]. They found a statistically significant increase in smoking

cessation at the longest follow-up (RR, 1.66; 95% CI, 1.42 to 1.94, p<0.00001) when physicians provided smoking cessation advice with a moderate certainty in the evidence due to issues with risk of bias. Furthermore, their comparison of intensive versus minimal advice suggested that there was a small benefit in smoking cessation at the longest follow-up for more intensive advice (RR, 1.37; 95% CI, 1.20 to 1.56, p<0.00001) with a moderate certainty in the evidence due to concerns with risk of bias. Likewise, another systematic review found high-quality evidence for a benefit in smoking cessation at the longest follow-up for combined pharmacotherapy and behavioural treatment compared with usual care, brief advice, or less intensive behavioural support (RR, 1.83; 95% CI, 1.68 to 1.98, p<0.0001) [87]. Based on this evidence, and that it seemed to be consistent with the evidence found among patients with cancer, the Working Group endorsed the recommendation from the previous version of this guideline.

There were very few systematic reviews that investigated which specific symptoms or signs were associated with recurrence or risk of other primary cancers in our target population. The symptoms that were reported to have an association with local or distant control or metastases such as weight loss, limb weakness, and pain, were already included in the previous PEBC recommendation. Therefore, the Working Group endorsed the recommendation from the previous version of this guideline.

Likewise, few systematic reviews reported the manageable factors, besides smoking, that were associated with quality of life or survival in our patient population. The factors that were reported such as fatigue, coughing, and dyspnea as well as the long-term side effects from treatments such as renal impairment or hearing loss were already included in the previous PEBC recommendation that the Working Group decided to endorse.

Exercise training was the only management strategy conducted during the follow-up period after treatment in patients with lung cancer that was evaluated in systematic reviews. RCTs demonstrated that the physical component of quality of life and dyspnea seemed to improve in patients who received exercise training. The effects on fatigue, the mental component of quality of life, and feelings of anxiety and depression were less certain. There were few reported adverse effects. As such, the Working Group believed the benefits of exercise training might outweigh the harms and were recommended in this patient population.

There were several limitations in the evidence mainly due to the lack of studies in the target population. This required us to broaden our inclusion criteria to extend to patients outside of our target population. Therefore, the results may not always be directly applicable to our patients of interest. There were issues with lack of blinding in many of the RCTs. Furthermore, we only searched for systematic reviews for some of our research questions and may have missed some recent primary studies not captured in systematic reviews.

CONCLUSIONS

It was difficult to draw strong conclusions for this patient population. There was evidence to suggest that smoking cessation interventions could benefit these patients; however, the choice of the best intervention strategy could not be determined and evidence from broader populations would have to be used to inform recommendations. PRO tools may also benefit patients with lung cancer. Again, the choice of tools is difficult to recommend without taking into consideration feasibility and accessibility. There was no strong evidence to recommend any clinician over another in following these patients. However, there was evidence to suggest that exercise training may be beneficial and should be supported. More research in this patient population is needed to inform the optimal follow-up strategies for these patients.

Follow-up and Surveillance of Curatively Treated Patients with Lung Cancer

Section 5: Internal and External Review

INTERNAL REVIEW

The guideline was evaluated by the GDG Expert Panel and the PEBC Report Approval Panel (RAP) (Appendix 1). The results of these evaluations and the Working Group's responses are described below.

Expert Panel Review and Approval

Of the 23 members of the GDG Expert Panel, 19 (83%) members voted in September 2023. Of those who voted, 19 (100%) approved the document. The main comments from the Expert Panel and the Working Group's responses are summarized in Table 5-1.

Table 5-1. Summary of the Working Group's responses to comments from the Expert Panel.

Comments	Responses
1. Are we recommending annual CT indefinitely beyond five years, or is there a time limit?	The Working Group believed that people would likely be at a higher risk of recurrence beyond five years then people in a screening program. They believed that beyond five years, these people should still be followed with CT annually, similar to people in a screening program.

RAP Review and Approval

Three RAP members reviewed this document in October 2023. The RAP approved the document November 9, 2023. The main comments from the RAP and the Working Group's responses are summarized in Table 5-2.

Table 5-2. Summary of the Working Group's responses to comments from RAP.

Comments	Responses
1. The guideline recommendations with respect to frequency of lung imaging (every six months for two years) are based on endorsement of 2020 ASCO guidelines. However, the previous PEBC CCO recommendations were more intense, every three months for the first two years and every six months for the next year. The authors should provide some information on why the ASCO guidelines de-escalated and why the current guideline believes that these recommendations should be endorsed (as opposed to previous CCO guidelines). There are some data available in Appendix 4, but the reasons for these markedly different recommendations should be explicitly stated. This is important because clinicians will focus on Recommendations 1 and 2 and	The frequency of surveillance imaging was based on consensus. The Working Group endorsed the ASCO recommendations, which were less intense than the previous version of this guideline because it was more practical. The Working Group believed that lung imaging every six months would be easier to implement compared with every three months in the first two years. Also, McMurry et al. [10] demonstrated no difference in survival when comparing groups subjected to follow-up CT surveillance at three-month, six-month, and 12-month intervals after definitive surgical therapy for stage I-III NSCLC.

they are the backbone of post-treatment management.	

Patient Consultation Group

Three patient representatives participated as Consultation Group members for the Working Group. They reviewed the draft recommendations and provided feedback on its comprehensibility, appropriateness, and feasibility to the Working Group's Health Research Methodologist. The main comments from the Consultation Group are summarized in Table 5-3.

Table 5-3. Summary of the Working Group's responses to comments from the Consultation Group.

Comments	Responses
1. For Recommendation 8, should we add fear of cancer recurrence?	The Working Group added the fear of cancer recurrence to Recommendation 8.
2. For Recommendation 8, can we add how healthcare providers should manage the symptoms?	Research question 7 addressed this and few systematic reviews in our target patient population were found.
3. For Recommendation 11, should we include how to monitor smoking cessation?	The Working Group believed this was beyond the scope of this guideline.

EXTERNAL REVIEW

External Review by Ontario Clinicians and Other Experts

Targeted Peer Review

Five targeted peer reviewers from Ontario, who were considered to be clinical and/or methodological experts on the topic, were identified by the Working Group. Four agreed to be the reviewers (Appendix 1). Four responses were received. Results of the feedback survey are summarized in Table 5-4. The main comments from targeted peer reviewers and the Working Group's responses are summarized in Table 5-5.

Table 5-4. Responses to nine items on the targeted peer reviewer questionnaire.

	Reviewer Ratings (N=4)				
Question	Lowest Quality (1)	(2)	(3)	(4)	Highest Quality (5)
1. Rate the guideline development methods.	0	0	0	2	2
2. Rate the guideline presentation.	0	0	1	1	2
3. Rate the guideline recommendations.	0	0	0	2	2
4. Rate the completeness of reporting.	0	0	0	1	3
5. Does this document provide sufficient information to inform your decisions? If not, what areas are missing?	0	0	1	1	2
6. Rate the overall quality of the guideline report.	0	0	0	2	2
	Strongly Disagree (1)	(2)	Neutral (3)	(4)	Strongly Agree (5)
7. I would make use of this guideline in my professional decisions.	0	0	1	0	3

8. I would recommend this guideline for use in practice.	0	0	1	0	3
9. What are the barriers or enablers to the implementation of this guideline report?	The barriers mentioned included a lack of adequate funding, staff, infrastructure, or time, the lack of wide dissemination of the guideline, the lack of guidance on how to manage symptoms frequently experienced by lung cancer survivors that affect quality of life, the lack of a tool that succinctly summarizes surveillance recommendations for quick reference. Having key leaders in each cancer centre present this work may facilitate the wide dissemination of this guideline. Also, comprehensive training programs and ongoing support for staff may help them adapt to this guideline more effectively.				

Table 5-5. Summary of the Working Group's responses to comments from targeted peer reviewers.

Comments	Responses
1. Recommendation 2.1: While low-dose CT scans are recommended to minimize radiation exposure and reduce risks for specific patient populations, the use of contrast-enhanced CT scans may be preferred in these cases where there are no known contrast allergies and normal kidney function.	The Working Group believed that surveillance and follow-up is more closely related to screening, that uses CT without contrast, than diagnosis.

Professional Consultation

Feedback was obtained through a brief online survey of healthcare professionals and other stakeholders who are the intended users of the guideline. One hundred five individuals with an interest in lung cancer or survivorship care from the PEBC database and members from the Provincial Primary Care Network, the Ottawa Regional Cancer Foundation – survivorship program, Lung Cancer Canada, the Lung Health Foundation, and the Canadian Society of Thoracic Radiology were contacted by email to inform them of the survey. Twenty-two (21%) responses were received. Two stated that they were unavailable to review this guideline at the time. The results of the feedback survey from 20 people are summarized in Table 5-6. The main comments from the consultation and the Working Group's responses are summarized in Table 5-7.

Table 5-6. Responses to four items on the professional consultation survey.

	Reviewer Ratings (N=20)				
General Questions: Overall Guideline Assessment	Lowest Quality (1)	(2)	(3)	(4)	Highest Quality (5)
1. Rate the overall quality of the guideline report.	0	0	1 (5%)	9 (45%)	10 (50%)
	Strongly Disagree (1)	(2)	(3)	(4)	Strongly Agree (5)
2. I would make use of this guideline in my professional decisions.	0	1 (5%)	0	6 (30%)	13 (65%)

3. I would recommend this guideline for use in practice.	0	0	1 (5%)	6 (30%)	13 (65%)
4. What are the barriers or enablers to the implementation of this guideline report?	The most obvious and problematic barrier is the lack of formal low-dose screening CT programs across Ontario. Dissemination of the guidelines to the front-line primary care and specialist practitioners may be a barrier as well as patient compliance. Patients residing in isolated areas or Indigenous populations often encounter significant challenges in accessing surveillance tests. Healthcare providers operating within community-based settings may face heightened difficulties in effectively following up on suspicions of recurrence compared to their counterparts in hospital-based settings. The financial burden associated with pharmacotherapy used in smoking cessation interventions may pose a formidable barrier for individuals with limited incomes. Presently, in Ontario, while the pneumococcal polysaccharide vaccine is covered, the pneumococcal conjugate vaccine is not, potentially influencing the preferences of both patients and healthcare providers. Furthermore, the implementation of exercise programs may encounter hurdles related to insufficient infrastructure. These barriers collectively underscore the complexities and disparities that impact the successful execution of these healthcare interventions.				

Table 5-7. Summary of the Working Group's responses to comments from professional consultants.

Comments	Responses
1. When does follow-up start?	Follow-up and surveillance would start after curative-intent treatment as defined in the target population.
2. Recommendation 5.1: This recommendation specifically mentions excluding MRI brain surveillance for patients with NSCLC, but I think it should be stated explicitly that this also includes CT head. I am aware that there are some medical oncologists in the province who routinely perform CT head imaging in the follow up of patients with stage III NSCLC.	For Recommendation 5.1, CT was added to clarify that routine brain surveillance should not be performed with CT as well as MRI.
3. Recommendation 8: You do not include the long-term side effects of immunotherapy or targeted therapy.	For Recommendation 8, delayed immune-related adverse events, and cumulative toxicities from ongoing therapy with tyrosine kinase inhibitors were added to the list of long-term side effects.

CONCLUSION

The final guideline recommendations contained in Section 2 and summarized in Section 1 reflect the integration of feedback obtained through the external review processes with the

document as drafted by the GDG Working Group and approved by the GDG Expert Panel and the PEBC RAP.

References

1. Schneider BJ, Ismaila N, Aerts J, Chiles C, Daly ME, Detterbeck FC, et al. Lung cancer surveillance after definitive curative-intent therapy: ASCO guideline. J Clin Oncol. 2020;38(7):753-66.
2. Cheung MC FB, Meti N, Thawer A, Shankar A, Loblaw A, et al. Person-centred virtual cancer care clinical guidance https://www.cancercareontario.ca/en/guidelines-advice/types-of-cancer/69581. 2022.
3. Government of Canada. Vaccines and immunization. Available from: https://www.canada.ca/en/public-health/services/immunization-vaccines.html.
4. Denis F, Basch E, Septans AL, Bennouna J, Urban T, Dueck AC, et al. Two-year survival comparing web-based symptom monitoring vs routine surveillance following treatment for lung cancer. JAMA. 2019;321(3):306-7.
5. Denis F, Lethrosne C, Pourel N, Molinier O, Pointreau Y, Domont J, et al. Randomized Trial Comparing a Web-Mediated Follow-up With Routine Surveillance in Lung Cancer Patients. J Natl Cancer Inst. 2017;109(9).
6. Browman GP, Newman TE, Mohide EA, Graham ID, Levine MN, Pritchard KI, et al. Progress of clinical oncology guidelines development using the Practice Guidelines Development Cycle: the role of practitioner feedback. J Clin Oncol. 1998;16(3):1226-31.
7. Browman GP, Levine MN, Mohide EA, Hayward RS, Pritchard KI, Gafni A, et al. The practice guidelines development cycle: a conceptual tool for practice guidelines development and implementation. J Clin Oncol. 1995;13(2):502-12.
8. Brouwers MC, Kho ME, Browman GP, Burgers JS, Cluzeau F, Feder G, et al. AGREE II: advancing guideline development, reporting and evaluation in health care. CMAJ. 2010;182(18):E839-42.
9. Alonso-Coello P, Schunemann HJ, Moberg J, Brignardello-Petersen R, Akl EA, Davoli M, et al. GRADE Evidence to Decision (EtD) frameworks: a systematic and transparent approach to making well informed healthcare choices. 1: Introduction. BMJ. 2016;353:i2016.
10. McMurry TL, Stukenborg GJ, Kessler LG, Colditz GA, Wong ML, Francescatti AB, et al. More frequent surveillance following lung cancer resection is not associated with improved survival: A Nationally Representative Cohort Study. Ann Surg. 2018;268(4):632-9.
11. American Cancer Society. Cancer Facts & Figures 2019. Atlanta: American Cancer Society; 2019. Available from: https://www.cancer.org/content/dam/cancer-org/research/cancer-facts-and-statistics/annual-cancer-facts-and-figures/2019/cancer-facts-and-figures-2019.pdf.
12. Ganti AK, Klein AB, Cotarla I, Seal B, Chou E. Update of Incidence, Prevalence, Survival, and Initial Treatment in Patients With Non-Small Cell Lung Cancer in the US. JAMA Oncol. 2021;7(12):1824-32.
13. Statistics Canada. Ellison, LF. Health Reports. The cancer survival index: Measuring progress in cancer survival to help evaluate cancer control efforts in Canada. 2021. Available from: https://www150.statcan.gc.ca/n1/pub/82-003-x/2021009/article/00002-eng.htm#shr-pg0.
14. Lou F, Huang J, Sima CS, Dycoco J, Rusch V, Bach PB. Patterns of recurrence and second primary lung cancer in early-stage lung cancer survivors followed with routine computed tomography surveillance. J Thorac Cardiovasc Surg. 2013;145(1):75-81; discussion -2.
15. Yaron Shargall, Emily Vella, Lisa Del Giudice, Swati Kulkarni, Peter Ellis, Carole Dennie, Robert McRae, Yee Ung. Follow-up and Surveillance of Curatively Treated Patients with Lung Cancer. PROSPERO 2020 CRD42023338773 Available from: https://www.crd.york.ac.uk/PROSPERO/display_record.php?RecordID=338773.
16. Whiting P, Savovic J, Higgins JP, Caldwell DM, Reeves BC, Shea B, et al. ROBIS: A new tool to assess risk of bias in systematic reviews was developed. J Clin Epidemiol. 2016;69:225-34.

17. Sterne JAC, Savovic J, Page MJ, Elbers RG, Blencowe NS, Boutron I, et al. RoB 2: a revised tool for assessing risk of bias in randomised trials. BMJ. 2019;366:l4898.
18. Review Manager (RevMan) [Computer program]. Version 5.4. Copenhagen: The Nordic Cochrane Centre, The Cochrane Collaboration, 2020.
19. Parmar MK, Torri V, Stewart L. Extracting summary statistics to perform meta-analyses of the published literature for survival endpoints. [erratum appears in Stat Med. 2004;3(11):1817]. Stat Med. 1998;17(24):2815-34.
20. Guyatt GH, Oxman AD, Schunemann HJ. GRADE guidelines-an introduction to the 10th-13th articles in the series. J Clin Epidemiol. 2013;66(2):121-3.
21. McCorkle R, Strumpf NE, Nuamah IF, Adler DC, Cooley ME, Jepson C, et al. A specialized home care intervention improves survival among older post-surgical cancer patients. J Am Geriatr Soc. 2000;48(12):1707-13.
22. Moore S, Corner J, Haviland J, Wells M, Salmon E, Normand C, et al. Nurse led follow up and conventional medical follow up in management of patients with lung cancer: randomised trial. BMJ. 2002;325(7373):1145.
23. Edbrooke L, Aranda S, Granger CL, McDonald CF, Krishnasamy M, Mileshkin L, et al. Multidisciplinary home-based rehabilitation in inoperable lung cancer: A randomised controlled trial. Thorax. 2019.
24. Scherz N, Bachmann-Mettler I, Chmiel C, Senn O, Boss N, Bardheci K, et al. Case management to increase quality of life after cancer treatment: A randomized controlled trial. BMC Cancer. 2017;17(1) (no pagination).
25. Yun YH, Lim CI, Lee ES, Kim YT, Shin KH, Kim YW, et al. Efficacy of health coaching and a web-based program on physical activity, weight, and distress management among cancer survivors: A multi-centered randomised controlled trial. Psychooncology. 2020;29(7):1105-14.
26. Berezowska A, Passchier E, Bleiker E. Professional patient navigation in a hospital setting: a randomized controlled trial. Support Care Cancer. 2021;29(4):2111-23.
27. Aubin M, Vezina L, Verreault R, Simard S, Hudon E, Desbiens JF, et al. Continuity of Cancer Care and Collaboration Between Family Physicians and Oncologists: results of a Randomized Clinical Trial. Ann Fam Med. 2021;19(2):117-25.
28. Wang M, Sun Y, Zhang M, Yu R, Fu J. Effects of high-quality nursing care on quality of life, survival, and recurrence in patients with advanced nonsmall cell lung cancer. Medicine (Baltimore). 2022;101(37):e30569.
29. Perfors IAA, Helsper CW, Noteboom EA, Visserman EA, van Dorst EBL, van Dalen T, et al. Effects of structured involvement of the primary care team versus standard care after a cancer diagnosis on patient satisfaction and healthcare use: the GRIP randomised controlled trial. BMC Prim Care. 2022;23(1):145.
30. Yu J, Huang T, Xu J, Xiao J, Chen Q, Zhang L. Effect of Nursing Method of Psychological Intervention Combined with Health Education on Lung Cancer Patients Undergoing Chemotherapy. J Healthc Eng. 2022;2022 (no pagination).
31. Liu J, Wang Y, Du J, Wang G. Effects of respiratory rehabilitation nursing on improving postoperative respiratory function and quality of life of patients with lung cancer surgery. Int J Clin Exp Med. 2020;13(10):7920-7.
32. Su X, Li F, Zhao Q, Zhao T, Yang M, Xu M, et al. Quality of life levels and physical and mental states of dyspnoeic patients with advanced lung cancer effectively improved by comprehensive nursing intervention. Int J Clin Exp Med. 2019;12(9):11700-7.
33. Billingy NE, Hurk Cvd, Tromp VN, Aaronson NK, Belderbos J, Bogaard HJ, et al. Patient-reported symptom monitoring linked to an alert algorithm: Effects on progression-free and overall survival in the SYMPRO-Lung trial. J Clin Oncol. 2023;41(16_suppl):12099-.

34. Friis RB, Pappot H, Hjøllund NH, McCulloch T, Holt MI, Persson G, et al. Remote symptom-monitoring of patients with advanced lung cancer: A Danish national randomized controlled trial—The ProWide study. J Clin Oncol. 2023;41(16_suppl):1508-.
35. Noronha V, Goud S, Sharma R, More SB, Yadav A, Nakti D, et al. A randomized trial of patient navigation with symptom-monitoring in advanced lung cancer. J Clin Oncol. 2023;41(17_suppl):LBA1545-LBA.
36. Geerse OP, Hoekstra-Weebers JE, Stokroos MH, Burgerhof JG, Groen HJ, Kerstjens HA, et al. Structural distress screening and supportive care for patients with lung cancer on systemic therapy: A randomised controlled trial. Eur J Cancer. 2017;72:37-45.
37. Mills ME, Murray LJ, Johnston BT, Cardwell C, Donnelly M. Does a patient-held quality-of-life diary benefit patients with inoperable lung cancer? J Clin Oncol. 2009;27(1):70-7.
38. Schofield P, Ugalde A, Gough K, Reece J, Krishnasamy M, Carey M, et al. A tailored, supportive care intervention using systematic assessment designed for people with inoperable lung cancer: a randomised controlled trial. Psychooncology. 2013;22(11):2445-53.
39. Kuo JC, Graham DM, Salvarrey A, Kassam F, Le LW, Shepherd FA, et al. A randomized trial of the electronic lung cancer symptom scale for quality-of-life assessment in patients with advanced non-small-cell lung cancer. Curr Oncol. 2020;27(2):e156-e62.
40. Cooley ME, Mazzola E, Xiong N, Hong F, Lobach DF, Braun IM, et al. Clinical Decision Support for Symptom Management in Lung Cancer Patients: A group RCT. J Pain Symptom Manage. 2022;63(4):572-80.
41. Dai W, Feng W, Zhang Y, Wang XS, Liu Y, Pompili C, et al. Patient-reported Outcome-Based Symptom Management Versus Usual Care After Lung Cancer Surgery: A Multicenter Randomized Controlled Trial. J Clin Oncol. 2022;40(9):988-96.
42. Nimako K, Ayite B, Priest K, Severn J, Fries HM, Gunapala R, et al. A randomised assessment of the use of a quality of life questionnaire with or without intervention in patients attending a thoracic cancer clinic. Euro J Cancer Care. 2017;26(4).
43. Yount SE, Rothrock N, Bass M, Beaumont JL, Pach D, Lad T, et al. A randomized trial of weekly symptom telemonitoring in advanced lung cancer. J Pain Symptom Manage. 2014;47(6):973-89.
44. Cleeland CS, Wang XS, Shi Q, Mendoza TR, Wright SL, Berry MD, et al. Automated symptom alerts reduce postoperative symptom severity after cancer surgery: a randomized controlled clinical trial. J Clin Oncol. 2011;29(8):994-1000.
45. Becerril-Gaitan A, Vaca-Cartagena BF, Ferrigno AS, Mesa-Chavez F, Barrientos-Gutierrez T, Tagliamento M, et al. Immunogenicity and risk of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection after Coronavirus Disease 2019 (COVID-19) vaccination in patients with cancer: a systematic review and meta-analysis. Eur J Cancer. 2022;160:243-60.
46. Sakuraba A, Luna A, Micic D. Serologic response following SARS-COV2 vaccination in patients with cancer: a systematic review and meta-analysis. J Hematol Oncol. 2022;15(1) (no pagination).
47. Cavanna L, Citterio C, Toscani I. Covid-19 vaccines in cancer patients. Seropositivity and safety. systematic review and meta-analysis. Vaccines. 2021;9(9) (no pagination).
48. Bitterman R, Eliakim-Raz N, Vinograd I, Zalmanovici Trestioreanu A, Leibovici L, Paul M. Influenza vaccines in immunosuppressed adults with cancer. Cochrane Database Syst Rev. 2018;2018(2) (no pagination).
49. La Torre G, Mannocci A, Colamesta V, D'Egidio V, Sestili C, Spadea A. Influenza and pneumococcal vaccination in hematological malignancies: A systematic review of efficacy, effectiveness, and safety. Mediterr J Hematol Infect Dis. 2016;8(1) (no pagination).

50. Wakefield M, Olver I, Whitford H, Rosenfeld E. Motivational interviewing as a smoking cessation intervention for patients with cancer: randomized controlled trial. Nurs Res. 2004;53(6):396-405.
51. Schnoll RA, Zhang B, Rue M, Krook JE, Spears WT, Marcus AC, et al. Brief physician-initiated quit-smoking strategies for clinical oncology settings: a trial coordinated by the Eastern Cooperative Oncology Group. J Clin Oncol. 2003;21(2):355-65.
52. Schnoll RA, Martinez E, Tatum KL, Weber DM, Kuzla N, Glass M, et al. A bupropion smoking cessation clinical trial for cancer patients. Cancer Causes Control. 2010;21(6):811-20.
53. Park ER, Perez GK, Regan S, Muzikansky A, Levy DE, Temel JS, et al. Effect of Sustained Smoking Cessation Counseling and Provision of Medication vs Shorter-term Counseling and Medication Advice on Smoking Abstinence in Patients Recently Diagnosed with Cancer: A Randomized Clinical Trial. JAMA. 2020;324(14):1406-18.
54. Ostroff JS, Burkhalter JE, Cinciripini PM, Li Y, Shiyko MP, Lam CY, et al. Randomized trial of a presurgical scheduled reduced smoking intervention for patients newly diagnosed with cancer. Health Psychol. 2014;33(7):737-47.
55. Mujcic A, Blankers M, Boon B, Verdonck-de Leeuw IM, Smit F, van Laar M, et al. Effectiveness, Cost-effectiveness, and Cost-Utility of a Digital Smoking Cessation Intervention for Cancer Survivors: Health Economic Evaluation and Outcomes of a Pragmatic Randomized Controlled Trial. J Med Internet Res. 2022;24(3):e27588.
56. Walls GM, Hanna GG, Qi F, Zhao S, Xia J, Ansari MT, et al. Predicting outcomes from radical radiotherapy for non-small cell lung cancer: A systematic review of the existing literature. Front Oncol. 2018;8(OCT) (no pagination).
57. Wu L, Wang L, Yang J, Jia W, Xu Y. Clinical Features, Treatments, and Prognosis of Intramedullary Spinal Cord Metastases From Lung Cancer: A Case Series and Systematic Review. Neurospine. 2022;19(1):65-76.
58. Kossioris A, Karousi T. Determinants of health-related quality of life in patients with small cell lung cancer: A systematic PubMed review and meta-analysis. Russian Open Medical Journal. 2016;5(1) (no pagination).
59. Guo W, Gu X, Gao X, Ma M, Cui M, Xie M, et al. Concurrent versus sequential chemotherapy with hypofractionated radiotherapy in patients with inoperable locally advanced non-small cell lung cancer. Int J Clin Exp Med. 2017;10(7):10443-52.
60. Iseli T, Berghmans T, Glatzer M, Rittmeyer A, Massard G, Durieux V, et al. Adverse events reporting in stage iii nsclc trials investigating surgery and radiotherapy. ERJ Open Research. 2020;6(3):1-9.
61. Liu L, Zhao T, Zhong Q, Cui J, Xiu X, Li G. The role of prophylactic cranial irradiation in patients with non-small cell lung cancer: An updated systematic review and meta-analysis. Front Oncol. 2020;10 (no pagination).
62. Morias S, Marcu LG, Short M, Giles E, Bezak E. Do SABR-related toxicities for lung cancer depend on treatment delivery? Crit Rev Oncol Hematol. 2018;129:67-78.
63. Poghosyan H, Sheldon LK, Leveille SG, Cooley ME. Health-related quality of life after surgical treatment in patients with non-small cell lung cancer: A systematic review. Lung Cancer. 2013;81(1):11-26.
64. Prezzano KM, Ma SJ, Hermann GM, Rivers CI, Gomez-Suescun JA, Singh AK. Stereotactic body radiation therapy for non-small cell lung cancer: A review. World J Clin Oncol. 2019;10(1):14-27.
65. Voruganti IS, Donovan E, Walker-Dilks C, Swaminath A. Chest wall toxicity after stereotactic radiation in early lung cancer: A systematic review. Curr Oncol. 2020;27(4):179-89.
66. Cavalheri V, Burtin C, Formico VR, Nonoyama ML, Jenkins S, Spruit MA, et al. Exercise training undertaken by people within 12 months of lung resection for non-small cell lung cancer. Cochrane Database Syst Rev. 2019;2019(6) (no pagination).

67. Earle CC. Influenza vaccination in elderly patients with advanced colorectal cancer. J Clin Oncol. 2003;21(6):1161-6.
68. Ambati A, Boas LS, Ljungman P, Testa L, de Oliveira JF, Aoun M, et al. Evaluation of pretransplant influenza vaccination in hematopoietic SCT: A randomized prospective study. Bone Marrow Transplant. 2015;50(6):858-64.
69. Musto P, Carotenuto M. Vaccination against influenza in multiple myeloma. Br J Haematol. 1997;97(2):505-6.
70. Vinograd I, Eliakim-Raz N, Farbman L, Baslo R, Taha A, Sakhnini A, et al. Clinical effectiveness of seasonal influenza vaccine among adult cancer patients. Cancer. 2013;119(22):4028-35.
71. Corti C, Antonarelli G, Scotte F, Spano JP, Barriere J, Michot JM, et al. Seroconversion rate after vaccination against COVID-19 in patients with cancer-a systematic review. Ann Oncol. 2022;33(2):158-68.
72. Guven DC, Sahin TK, Kilickap S, Uckun FM. Antibody Responses to COVID-19 vaccination in cancer: A systematic review. Front Oncol. 2021;11 (no pagination).
73. Javadinia SA, Alizadeh K, Mojadadi MS, Nikbakht F, Dashti F, Joudi M, et al. COVID-19 Vaccination in Patients With Malignancy: A Systematic Review and Meta-Analysis of the Efficacy and Safety. Front Endocrinol (Lausanne). 2022;13:860238.
74. Vijenthira A, Gong I, Betschel SD, Cheung M, Hicks LK. Vaccine response following anti-CD20 therapy: A systematic review and meta-Analysis of 905 patients. Blood Advances. 2021;5(12):2624-43.
75. Zeng L, Yu X, Yu T, Xiao J, Huang Y. Interventions for smoking cessation in people diagnosed with lung cancer. Cochrane Database Syst Rev. 2019;2019(6) (no pagination).
76. Weaver KE, Urbanic JJ, Case D, Kaplan SG, Lesser GJ, Zbikowski S, et al. Preliminary efficacy of an enhanced quitline smoking cessation intervention for cancer patients. J Clin Oncol Conference. 2015;33(15 SUPPL. 1).
77. Simmons VN, Sutton SK, Meltzer LR, Martinez U, Palmer AM, Meade CD, et al. Preventing smoking relapse in patients with cancer: A randomized controlled trial. Cancer. 2020;126(23):5165-72.
78. Schnoll RA, Rothman RL, Wielt DB, Lerman C, Pedri H, Wang H, et al. A randomized pilot study of cognitive-behavioral therapy versus basic health education for smoking cessation among cancer patients. Ann Behav Med. 2005;30(1):1-11.
79. Cavalheri V, Tahirah F, Nonoyama M, Jenkins S, Hill K. Exercise training for people following lung resection for non-small cell lung cancer - a Cochrane systematic review. Cancer Treat Rev. 2014;40(4):585-94.
80. Ni HJ, Pudasaini B, Yuan XT, Li HF, Shi L, Yuan P. Exercise Training for Patients Pre- and Postsurgically Treated for Non-Small Cell Lung Cancer: A Systematic Review and Meta-analysis. Integr Cancer Ther. 2017;16(1):63-73.
81. Rowntree RA, Hosseinzadeh H. Lung cancer and self-management interventions: A Systematic Review of Randomised Controlled Trials. Int J Environ Res Public Health. 2022;19(1) (no pagination).
82. Sommer MS, Staerkind MEB, Christensen J, Vibe-Petersen J, Larsen KR, Holst Pedersen J, et al. Effect of postsurgical rehabilitation programmes in patients operated for lung cancer: A systematic review and meta-analysis. J Rehabil Med. 2018;50(3):236-45.
83. Li J, Guo NN, Jin HR, Yu H, Wang P, Xu GG. Effects of exercise training on patients with lung cancer who underwent lung resection: A meta-analysis. World J Surg Oncol. 2017;15(1) (no pagination).
84. Mainini C, Rebelo PF, Bardelli R, Kopliku B, Tenconi S, Costi S, et al. Perioperative physical exercise interventions for patients undergoing lung cancer surgery: What is the evidence? SAGE Open Medicine. 2016;4:2050312116673855.

85. Himbert C, Klossner N, Coletta AM, Barnes CA, Wiskemann J, LaStayo PC, et al. Exercise and lung cancer surgery: A systematic review of randomized-controlled trials. Crit Rev Oncol Hematol. 2020;156 (no pagination).
86. Stead LF, Buitrago D, Preciado N, Sanchez G, Hartmann-Boyce J, Lancaster T. Physician advice for smoking cessation. Cochrane Database Syst Rev. 2013;2013(5):CD000165.
87. Stead LF, Koilpillai P, Fanshawe TR, Lancaster T. Combined pharmacotherapy and behavioural interventions for smoking cessation. Cochrane Database Syst Rev. 2016;3(3):CD008286.

Appendix 1: Affiliations and Conflict of Interest Declarations

Name and Affiliation	Declarations of interest
Working Group	
Yaron Shargall Thoracic Surgeon St Joseph's Healthcare System	None declared
Lisa Del Giudice Family Physician Sunnybrook Health Sciences	• Received a stipend of $500 or more in a single year and is employed by the Toronto Regional Cancer Program, OH (CCO) • Received research support from the Canadian Institute Health Research as a co-investigator
Swati Kulkarni Medical Oncologist Lung Cancer Disease Site Group	None declared
Peter Ellis Medical Oncologist Lung Cancer Disease Site Group	Received $500 or more in a single year as an honorarium for advisory boards or speaking from Pfizer, AstraZeneca, BMS, Merck, Jazz, Eli Lilly, Jansen, Novartis, Sanofi, Takeda, Roche
Carole Dennie Diagnostic Radiologist Ottawa Hospital	Received $500 or more in a single year as a consultant for Astra Zeneca and as an honorarium for Boehringer Ingelheim
Robert MacRae Radiation Oncologist Lung Cancer Disease Site Group	Participated in an AstraZeneca advisory board meeting in 2019
Yee Ung Radiation Oncologist Lung Cancer Disease Site Group	None declared
Emily Vella Health Research Methodologist Program in Evidence-Based Care	None declared
Lung Cancer Disease Site Group Expert Panel	
Allison Ashworth Radiation Oncologist Lung Cancer Disease Site Group	None declared
Abdollah Behzadi Surgeon Lung Cancer Disease Site Group	None declared
Adrien Chan Medical Oncologist Lung Cancer Disease Site Group	None declared
Medhat El-Mallah Radiation Oncologist Lung Cancer Disease Site Group	Currently owns M. El-Mallah Medicine Professional Corporation
Michela Febbraro Medical Oncologist Lung Cancer Disease Site Group	None declared

Andrew Giles Surgeon Lung Cancer Disease Site Group	None declared
Natasha Leighl Medical Oncologist Lung Cancer Disease Site Group	None declared
Donna Maziak Surgeon Lung Cancer Disease Site Group	None declared
Rahul Nayak Surgeon Lung Cancer Disease Site Group	Received $500 or more in a single year to act in a consulting capacity for Merck and Co.
Andrew Pearce Radiation Oncologist Lung Cancer Disease Site Group	None declared
Lacey Pitre Medical Oncologist Lung Cancer Disease Site Group	• Received $500 or more in a single year to act in a consulting capacity for FUSE Health - Targeting BRCA-Mutated Solid Tumours: Ovarian Cancer November 2017, EMD Serono – Paid presenter February 2018, Novartis Canada – Ovarian cancer Advisory board September 2018, Novartis RIBBON program - September/October 2018, Merck Oncology – Speaker honoraria January 2021, Astra Zeneca – Speaker honoraria April 2021, Astra Zeneca – Rounds moderating January 2022, Astra Zeneca – Rounds moderating January 2023 • Was a local principal investigator only for BR.31
Kevin Ramchandar Radiation Oncologist Lung Cancer Disease Site Group	None declared
Andrew Robinson Medical Oncologist Lung Cancer Disease Site Group	• Received $500 or more in a single year to act in a consulting capacity for Merck, Astra Zeneca, and BMS • Received grants or other research support, either as principal or co-investigator, in any amount, from Roche, AstraZeneca, Merck, BMS, and Amgen sponsorship • Was a National Investigator for a study with a Merck Product (BRC7 trial)
Simon Sun Surgeon Lung Cancer Disease Site Group	None declared
Anand Swaminath Radiation Oncologist Lung Cancer Disease Site Group	None declared
Julius Toth Surgeon Lung Cancer Disease Site Group	None declared

Paul Wheatley-Price Medical Oncologist Lung Cancer Disease Site Group	• Received $500 or more in a single year on advisory boards or received speaking honoraria from the following companies in the last 5 years: Roche, AstraZeneca, BMS, Merck, Amgen, Lilly, Novartis, Sanofi, Pfizer, Guardant, Janssen, Jazz Pharmaceuticals, EMD Serono, Bayer, and AbbVie • Received any grants or other research support, either as principal or co-investigator, in any amount, from Roche, Pfizer and BMS regarding a COVID-19-related lung cancer study. These grants were in an OHRI (Ottawa Hospital Research Institute) cost centre.
Kazuhiro Yasufuku Surgeon Lung Cancer Disease Site Group	None declared
Edward Yu Radiation Oncologist Lung Cancer Disease Site Group	None declared
Patient Consultation Group	
Lester Krames	None declared
Randy Conrod	Received a $500 stipend from the University Health Network
Abeer Salim	None declared
Report Approval Panel	
Laurie Elit Gynecologic Oncology Professor Emeritus McMaster University	None declared
Michelle Ghert Professor Orthopaedic Surgery McMaster University	None declared
Jonathan Sussman Professor and Chair Department of Oncology McMaster University	None declared
Targeted Peer Reviewers	
Ehsan Haider Diagnostic Radiologist St. Joseph's Healthcare Hamilton, Ontario	None declared
Jonathan Isenberg Family Medicine Toronto, Ontario	None declared
David Tiberi Radiation Oncologist The Ottawa Hospital General Campus Ottawa, Ontario	None declared

Patrick James Villeneuve Thoracic Surgeon The Ottawa Hospital General Campus Ottawa, Ontario	• Received $500 or more in a single year for a panelist honorarium and for a multicentre review for the management of early-stage lung cancer • Received $500 or more in a single year for a travel grant and training support from Intuitive Surgical

Appendix 2: Responses to GRADE's evidence-to-decision framework

Population: Adult patients with small cell lung cancer or non-small cell lung cancer after curative-intent treatment

Comparison	Desirable effects	Undesirable effects	Certainty of evidence	Values	Balance of effects	Equity	Acceptability	Feasibility	Generalizable
Surveillance strategy vs. another surveillance strategy or usual care	-Trivial between different intensities and frequencies -Unknown between different tests, but expect CT to be better than X-ray based on screening studies -Incidence of brain metastases is higher in patients with SCLC (especially for those who did not receive PCI) than in patients with NSCLC. In metastatic setting, treatment of asymptomatic brain metastases improves outcomes in	-Trivial between different intensities and frequencies -Small effects of radiation exposure for CT. Current diagnostic CT can be at reduced radiation doses for lung. Harm may be greater with intravenous contrast CT for select groups. ^{18}F-FDG PET/CT results in more radiation exposure than CT.	Ranged from moderate to low	Most patients would value overall survival	The benefits of CT surveillance would outweigh the harms. The benefits of brain MRI surveillance might outweigh the harms for patients with SCLC, especially for those who did not receive PCI.	Patients in isolated areas or Indigenous populations may experience issues with accessing these tests.	Some patients may be unwillingly to accept further treatment.	^{18}F-FDG PET/CT is associated with increased cost compared with CT without added benefit as an initial surveillance tool.	These tests can be used with all patients in the target population, taking into account patients' acceptability for further treatment, co-morbidities and their overall health status.

Comparison	Desirable effects	Undesirable effects	Certainty of evidence	Values	Balance of effects	Equity	Acceptability	Feasibility	Generalizable
	patients who did not receive PCI.								
Virtual follow-up visits vs. in-person follow-up visits (usual care)	Small	Trivial	Moderate	No important uncertainty or variability	Benefits ≥ Harms	Probably increased	Yes	Yes	It remains unknown if these findings in the area of endometrial cancer can be generalized to follow up of asymptomatic patients in other cancer disease sites.
Nurse-led interventions vs. usual care	Trivial	Trivial	Very low	No important uncertainty or variability	The balance of effects does not favour either the intervention or the comparison	Probably reduced because health care providers in the community-based setting might have more difficulty in following up a suspicion of recurrence than health care providers in the hospital-based setting	Don't know	Yes	Yes
Patient reported outcome	Trivial	Trivial	Low	No important uncertainty	The balance of effects does not	There may be issues with equity	Probably no. There may be patient	There may be feasibility and cost issues in	Yes

Comparison	Desirable effects	Undesirable effects	Certainty of evidence	Values	Balance of effects	Equity	Acceptability	Feasibility	Generalizable
interventions vs. usual care or controls				or variability	favour either the intervention or the comparison	since patients would require access to electronic tools, which may be more challenging in rural compared with urban areas. Also, any new tools would have to be available in multiple languages.	who would not complete the surveys.	implementing a more intensive system.	
COVID-19 vaccine in cancer patients vs. COVID-19 vaccine in non-cancer patients	Don't know	Trivial	Low	Possibly important uncertainty or variability	Don't know. Need to base decisions on outcomes from non-cancer populations	Probably no impact	Possibly important uncertainty or variability	Yes	Yes
Influenza vaccine vs. no influenza vaccine	Small	Trivial	Very low	Possibly important uncertainty or variability	Benefits ≥ Harms	Probably no impact	Possibly important uncertainty or variability	Yes	Yes
Pneumococcal vaccine in cancer patients vs. pneumococcal vaccine in non-cancer patients	Don't know	Trivial	Very low	Possibly important uncertainty or variability	Don't know. Need to base decisions on outcomes from non-cancer populations	Probably no impact	Possibly important uncertainty or variability	Yes	Yes

Comparison	Desirable effects	Undesirable effects	Certainty of evidence	Values	Balance of effects	Equity	Acceptability	Feasibility	Generalizable
Smoking cessation intervention vs. usual care or placebo	Small	Trivial	Very low	No important uncertainty or variability	Benefits > Harms	Probably no impact	Yes	Varies because cost of pharmacotherapy may be a barrier for people on limited income	Yes
Exercise training vs. usual care or no exercise training	Small	Trivial	Very low	No important uncertainty or variability	Benefits ≥ Harms	Probably Yes. Access to exercise facilities may be an issue.	Yes	Probably Yes. There may be issues with infrastructure in implementing exercise programs.	Yes

Abbreviations: CT, computed tomography; ^{18}F-FDG, 18-F-labeled fluorodeoxyglucose; MRI, magnetic resonance imaging; NSCLC, non-small cell lung cancer; PCI, prophylactic cranial irradiation; PET, positron emission tomography; SCLC, small-cell lung cancer

Appendix 3: Recommendations from the previous Program in Evidence-Based Care 2014 version of the guideline 'Follow-up and surveillance of curatively treated lung cancer patients'

RECOMMENDATION 1
Following curative-intent treatment for NSCLC, survivors should receive scheduled follow-up visits that include a medical history, physical examination, and chest imaging. Clinical evaluations should be conducted every three months in years 1 and 2, every six months in year 3 and annually thereafter.

RECOMMENDATION 2
Following curative-intent treatment for SCLC, survivors should receive scheduled follow-up visits that include a medical history, physical examination, and chest imaging. Clinical evaluations should be conducted every three months in years 1 and 2, every six months in year 3 and annually thereafter.

RECOMMENDATION 3
For both NSCLC and SCLC survivors, no recommendation can be made in relation to positron emission tomography/CT.

RECOMMENDATION 4
In the expert opinion of the authors, any new and persistent or worsening symptom warrants the consideration of a recurrence, especially:
Constitutional symptoms:

- Dysphagia
- Fatigue (new onset)
- Nausea or vomiting (unexplained)
- New finger clubbing
- Suspicious lymphadenopathy
- Sweats (unexplained)
- Thrombosis
- Weight loss or loss of appetite

Pain:

- Bone pain
- Chest pain
- Caveat shoulder pain not related to trauma

Neurological symptoms:

- Headaches (if persistent)
- New neurological signs suggestive of brain metastasis or cord compression such as leg weakness or speech changes
- Headache or focal neurological symptoms

Respiratory symptoms:

- Cough (despite use of antibiotics)
- Dyspnea
- Hemoptysis
- Hoarseness

- Signs of superior vena cava obstruction
- Stridor

RECOMMENDATION 5
Health-related quality of life (QoL) is very important for long-term survivors suffering from late side effects of their curative-intent therapy (including surgery, chemotherapy, and radiation therapy). The following is a summary of issues reported by survivors. Health care professionals need to aid lung cancer survivors in handling these symptoms to improve QoL.

Constitutional issues:
- Anxiety
- Cough
- Decline in appetite
- Decrease in general health
- Depression
- Dysphagia
- Esophageal stricture
- Fatigue
- Pain
- Physical ability restrictions
- Reduced sleep quality
- Shortness of breath

Long-term chemotherapy effects:
- Hearing loss
- Neuropathies
- Renal impairment

Long-term radiation effects:
- Breathing complications
- Breathlessness/Dyspnea

Long-term surgery effects:
- Empyema
- Oxygen dependence
- Post-thoracotomy pain syndrome
- Reduced exercise tolerance or activity limitations
- Shortness of breath

RECOMMENDATION 6
For lung cancer survivors who have completed curative-intent therapy, surveillance is required and may be provided by specialists, family physicians, or hospital-based nurses.

RECOMMENDATION 7
Smoking cessation counselling is recommended for patients who have completed curative-intent therapy for NSCLC and SCLC. Although verbal cessation advice from a health care professional is of benefit, interventions that involve behavioural and pharmacotherapy support in addition to verbal advice is recommended.

Appendix 4: Evidence from ASCO 2020 and CCO (OH) 2022 guidelines

ASCO 2020 guideline

Criteria	Evidence/Considerations
Desirable effects	Pg 757: McMurry et al. demonstrated no difference in survival when comparing groups subjected to follow-up CT surveillance at three-month, six-month, and 12-month intervals after definitive surgical therapy for stage I-III NSCLC. A meta-analysis by Calman et al. included nine studies (seven retrospective, one prospective cohort, and one RCT) and evaluated patient survival with intensive follow-up (typically medical examination plus routine imaging) versus non-intensive follow-up (medical examination alone with further testing as clinically indicated). This report described a nonsignificant trend for improved survival with intensive follow-up that included routine surveillance imaging (HR, 0.83; 95% CI, 0.66 to 1.05). Pg 758: Westeel 2022: survival was not significantly different between follow-up groups (every six months for first two years and yearly until five years) (8.5 years [95% CI, 7.4 to 9.6] in the minimal follow-up group vs. 10.3 years [8.1–not reached] in the CT-based follow-up group; adjusted HR, 0.95; 95% CI, 0.83 to 1.10; log-rank p=0.49). Pg 758: After curative-intent resection, CT imaging is more sensitive than conventional chest X-ray for detecting tumour recurrence. Pg 759: ^{18}F-FDG PET/CT may have similar sensitivity and specificity compared with CT alone in detecting recurrence. Pg 760: While several studies have demonstrated an association with elevated CEA in the postoperative period and reduced survival, other studies have failed to confirm these findings. Pg 760: Two small studies have demonstrated detection of cfDNA to be a robust predictor of recurrence in patients who have received curative therapy. However, the detection of recurrence two to five months before standard imaging modalities may not enhance overall survival, as this short time period is unlikely to allow a curable recurrence to progress to an incurable one. Pg 760: There have been no RCTs to date evaluating the use of brain MRI for surveillance in NSCLC. There have been no RCTs assessing the role of brain MRI surveillance compared with observation alone in SCLC. The incidence of brain metastases is higher in SCLC than in NSCLC. A Japanese RCT found no survival benefit with PCI potentially because they used MRI (every three months for year 1 and every six months during year 2) that detected lesions earlier when radiotherapy may be effective.
Undesirable effects	Pg 757: None of the studies identified a harm introduced by more intensive imaging. Pg 758: Current imaging technology, in particular iterative reconstruction techniques, allows for diagnostic CT to be obtained at reduced radiation doses. Pg 759: The use of intravenous contrast [CT] may pose a significant risk for patients with a contrast allergy or kidney dysfunction. Pg 759: ^{18}F-FDG PET/CT is associated with increased radiation exposure
Certainty of evidence	Evidence quality ranged from intermediate to low.
Values	The patients' values of the outcomes were not reported.
Balance of effects	Pg 758: The panel determined that biannual imaging for the first two years rather than three years was indicated based on the limited body of evidence combined with patient factors, resource availability, and expert opinion. In totality, the panel believes the potential benefit of surveillance imaging is modestly stronger than potential harm in this high-risk patient population.
Equity	No information was provided about equity when comparing surveillance strategies vs. other surveillance strategies or usual care.
Acceptability	Pg 759: Some patients may be unwilling to accept further treatment.
Feasibility	Pg 759: ^{18}F-FDG PET/CT is associated with increased cost

Criteria	Evidence/Considerations
Generalizable	Pg 758: Specific patient subpopulations that may benefit from more- or less-frequent imaging are not clearly defined but may emerge from future studies. Pg 759: Since studies are lacking about any potential harm attributable to screening elderly and frail lung cancer survivors, this cohort may be offered the same schedule of CT surveillance (as for young and fit survivors) if the provider believes that the risk of death from cancer recurrence is greater than competing comorbidities. Discussion of potential risks and benefits with patients is recommended. Pg 762: Clearly, the ability to safely receive further anticancer therapy is an important factor to consider to avoid the identification of a recurrence or new primary NSCLC that the patient will more likely die with rather than from. The management of patients with significant chronic conditions is a challenge, but the use of the geriatric assessment in clinical practice may avoid unnecessary radiographic imaging and testing that ultimately reduces the patient's quality of life. The Expert Panel notes that physicians must make surveillance decisions based on physiologic age rather than chronological age so the optimal program can be developed. A few comorbid conditions often may be identified in a fit older patient who otherwise has no functional deficits. These patients are candidates for surveillance programs offered to younger patients. Conversely, a frail older adult patient with multiple chronic conditions and limited independence is at higher risk of serious adverse events from anticancer therapies versus younger patients with same malignancy. Patients with cancer with comorbid conditions often have trouble with treatment adherence that may reduce efficacy, ultimately affecting cancer survival. These comorbidities may also affect patients' survival independently from their cancer disease itself.

Abbreviations: ASCO, American Society of Clinical Oncology; CEA, carcinoembryonic antigen; cfDNA, cell-free deoxyribonucleic acid; CI, confidence interval; CT, computed tomography; 18F-FDG, 18-F-labeled fluorodeoxyglucose; HR, hazard ratio; MRI, magnetic resonance imaging; NSCLC, non-small cell lung cancer; PCI, prophylactic cranial irradiation; PET, positron emission tomography; Pg, page; RCT, randomized controlled trial; SCLC, small-cell lung cancer

OH (CCO) 2022 guideline

Criteria	Evidence/Considerations
Desirable effects	Pg. 3503: The ENDCAT trial, evaluated as high quality, was conducted in patients with stage I endometrial cancer. It found high patient satisfaction and noninferior psychological morbidity for telephone versus in-person follow-up. All recurrences were symptomatic and detected between scheduled virtual or in-person visits, suggesting that virtual follow-up in early-stage endometrial cancer does not place patients at increased risk. Most other studies measured outcomes of patient satisfaction, feasibility, and cost, and one studied pain management, but they did not include long-term outcomes.
Undesirable effects	No specific harms were reported with virtual care.
Certainty of evidence	Pg. 3490: The overall certainty of evidence per outcome and per study was evaluated as moderate to very low for RCTs and very low for non-RCTs.
Values	Pg. 3489: Preferred (critical) outcomes were recurrence, survival, or other long-term objective outcomes. Patient experience outcomes, including acceptance of virtual care, symptoms, and quality of life, were considered important outcomes.
Balance of effects	Pg. 3504: Virtual care does not appear to be inferior to in-person care when considering patient satisfaction.
Equity	Pg. 3502: Transportation costs were reduced and care for some was more accessible [with virtual care].
Acceptability	Pg. 3503: Overall, the results were consistent in showing patient acceptance of virtual care.
Feasibility	Pg. 3503: Overall, the results were consistent in showing feasibility of virtual care.

Criteria	Evidence/Considerations
Generalizable	Pg. 3503: It remains unknown if these findings in the area of endometrial cancer can be generalized to follow up of asymptomatic patients in other cancer disease sites.

Abbreviations: CCO, Cancer Care Ontario; ENDCAT, Endometrial Cancer Telephone trial; OH, Ontario Health; Pg, Page; RCT, randomized controlled trial

Appendix 5: Literature Search Strategy

Database(s): **Embase** 1996 to 2022 May 27**, OVID Medline Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily and Ovid MEDLINE(R) 1946 to Present, EBM Reviews - Cochrane Central Register of Controlled Trials** April 2022**, EBM Reviews - Cochrane Database of Systematic Reviews** 2005 to May 25, 2022

Search Strategy:

exp neoplasms/ or exp cancer/
(cancer$ or neoplas$ or carcinom$ or malignan$ or tumo?r$ or adenocarcinoma$ or oncolog$ or metasta$ or leukemi$ or leukaemi$ or lymphoma$ or myeloma$ or sarcoma$ or melanoma$).mp.
exp lung neoplasms/ or exp lung cancer/
((lung or thorax or thoracic or pulmonary) adj3 (cancer$ or neoplasm$ or carcinom$ or malignan$ or tumo?r$ or adenocarcinoma$ or metasta$)).mp.
exp non small cell lung cancer/ or exp small cell carcinoma/ or exp carcinoma, non-small-cell lung/ or exp small cell lung carcinoma/ or exp Carcinoma, Small Cell/
(NSCLC or SCLC or small cell).mp.
1 or 2 or 3 or 4 or 5 or 6
3 or 4 or 5 or 6
5 or 6
exp primary health care/ or exp general practitioner/ or exp family physician/ or exp general practice/ or exp specialist/ or exp nurse/
(((family or general) adj (practitioner$ or physician$ or doctor$ or practice$)) or ((primary or tertiary or community or hospital or institution$) adj2 care) or specialist$ or oncologist$ or radiologist$ or surgeon$ or nurse$ or clinician$ or rn or apn or gp or cancer centre or cancer center or clinic).ti.
patient-reported outcome/ or outcome assessment/ or patient reported outcome measures/ or diagnostic self evaluation/ or symptom assessment/ or population surveillance/ or patient health questionnaire/ or self report/
(patient-reported or self-reported).mp.
Influenza, Human/ or exp influenzavirus a/ or exp Influenzavirus B/ or Influenzavirus C/ or exp influenza/
(influenza$ or grippe or flu or orthomyxovir$ or myxovirus$).mp.
exp coronavirus disease 2019/ or exp COVID-19/
(covid* or coronavirus* or corona* virus* or coronovirus* or corono* virus* or coronavirinae* or corona* virinae* or Cov or "2019-nCoV*" or 2019nCoV* or "19-nCoV*" or 19nCoV* or nCoV2019* or "nCoV-2019*" or nCoV19* or "nCoV-19*" or "HCoV19*" or HCoV19* or "HCoV-2019*" or HCoV2019* or "2019 novel*" or Ncov* or "n-cov" or "SARS-CoV-2*" or "SARSCoV-2*" or "SARSCoV2*" or "SARS-CoV2*" or SARSCov19* or "SARS-Cov19*" or "SARSCov-19*" or "SARS-Cov-19*" or SARSCov2019* or "SARSCov2019*" or "SARSCov-2019*" or "SARS-Cov-2019*" or SARS2* or

"SARS-2*" or SARScoronavirus2* or "SARS-coronavirus-2*" or "SARScoronavirus 2*" or "SARS coronavirus2*" or SARScoronovirus2* or "SARS-coronovirus-2*" or "SARScoronovirus 2*" or "SARS coronovirus2*" or "severe acute respiratory syndrome*").mp.
exp pneumococcal infection/ or exp Streptococcus pneumoniae/ or exp Pneumococcal Infections/ or exp Streptococcus pneumoniae/
(Pneumococc$ or (Streptococcus and pneumoniae)).mp.
14 or 15 or 16 or 17 or 18 or 19
exp vaccine/ or exp immunization/ or exp Vaccines/
(vaccin$ or immuniz$ or Pfizer or Moderna or Johnson or Janssen or AstraZeneca or CAIV or LAIV or pcv or pps).mp.
21 or 22
20 and 23
Influenza Vaccines/ or exp influenza vaccine/ or exp SARS-CoV-2 vaccine/ or exp COVID-19 Vaccines/ or exp pneumococcus vaccine/ or exp Pneumococcal Vaccines/
(flumist or trivalent or fluzone or fluarix or fluinsure or fluviral or invivac or influvac or flublok or fluvirin or vaxigrip or mutagrip or flushield or fluogen or Novavax or Medicago or SYNFLORIX or Prevnar or VAXNEUVANCE or PNEUMOVAX).mp.
25 or 26
24 or 27
exp "smoking and smoking related phenomena"/ or exp smoking/ or exp smoking cessation/ or exp smoking reduction/ or exp "tobacco use cessation"/ or exp smoking cessation agents/ or exp bupropion/ or exp nicotine/ or exp nicotine chewing gum/ or exp varenicline/
(smok$ or tobacco$ or nicotine$).mp.
disease management/ or multivariate analysis/ or cancer prognosis/ or complication/ or quality of life/ or risk/ or rehabilitation/ or rehabilitation care/ or comorbidity/ or aftercare/ or follow up/ or risk reduction/ or scoring system/ or cancer survivor/ or long term care/ or prognosis/ or Follow-Up Studies/ or Cancer Survivors/ or recurrence/ or neoplasm recurrence, local/ or "signs and symptoms"/ or exp recurrent cancer/ or exp recurrent disease/ or clinical feature/ or symptom/ or dysphagia/ or pain/ or chest pain/ or shoulder pain/ or cough/ or coughing/ or weight change/ or weight gain/ or weight reduction/ or body weight changes/ or dyspnea/ or hemoptysis/ or hoarseness/ or respiratory sounds/ or wheezing/
(continuity or (follow adj up) or follow-up or (shared adj care) or (after adj care) or aftercare or surveillance$ or survivo$ or recurren$ or metasta$ or (second$ adj primar$) or (radiation adj induced adj malignanc$) or dysphagia or pain or cough$ or (weight adj (loss or gain or change$)) or (appetite adj loss) or (neurological adj symptom$) or neuropath$ or (finger adj clubbing) or lymphadenopathy or dyspn$ or headach$ or hemoptysis or haemoptysis or

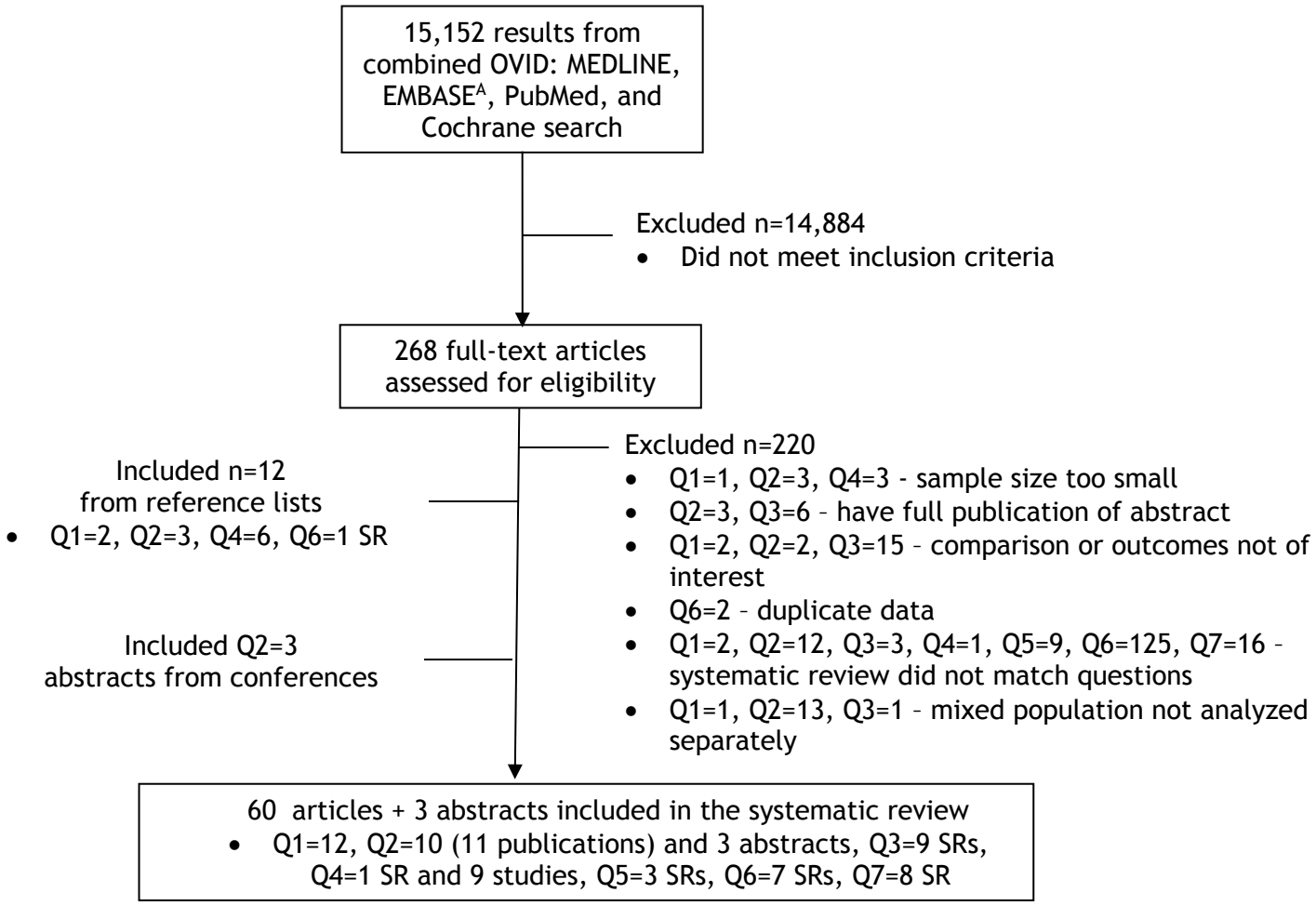
hoarse$ or (superior adj vena adj cava adj obstruction) or thrombosis or cardi$ or stridor or wheez$ or (short$ adj2 breath) or (breath$ adj complication$) or (lung adj toxicit$) or (hearing adj loss) or (chronic adj obstructive adj pulmonary adj disease) or COPD or fatigue or (esophageal adj stricture) or (renal adj impair$) or (renal adj function) or (quality adj of adj life) or signs or symptoms or comorbid$ or (risk adj factor$) or qol).mp.
exp Drug Therapy/ae or exp Radiotherapy/ae or exp Combined Modality Therapy/ae or exp Immunotherapy/ae
((late or chronic or delayed or post or long or ongoing or endur$ or persist$ or prolong$ or extend$ or linger$ or lasting$ or continuous$ or continual$ or continuing$) adj2 (effect$ or toxic$ or event$ or complication$ or consequence$ or outcome$ or impact$ or reaction$ or problem$ or issue$ or sequela$)).mp.
((((systematic adj (review: or overview:)) or (meta-analy: or metaanaly:) or (pooled analy: or statistical pooling or mathematical pooling or statistical summar: or mathematical summar: or quantitative synthes?s or quantitative overview:)).mp. or (exp review literature as topic/ or review.pt. or exp review/)) and systematic.tw.) or (cochrane or embase or psychlit or psyclit or psychinfo or psycinfo or cinhal or cinahl or science citation index or scisearch or bids or sigle or cancerlit or pubmed or pub-med or medline or med-line or (reference list: or bibliograph: or hand-search: or handsearch: or relevant journal: or manual search:)).ab. or ((selection criteria or data extract: or quality assess: or jadad score or jadad scale or methodologic: quality or (stud: adj1 select:)).ab. and review.pt.) or (guideline or practice guideline).pt. or practice guideline/ or exp consensus development conference/ or consensus/ or *consensus development/ or *consensus/ or *standard/ or (guideline: or recommend: or consensus or standards).ti. or (guideline: or recommend: or consensus or standards).kw.
exp phase 3 clinical trial/ or exp "phase 3 clinical trial (topic)"/ or exp clinical trial, phase iii/ or exp clinical trials, phase iii as topic/ or exp phase 4 clinical trial/ or exp "phase 4 clinical trial (topic)"/ or exp clinical trial, phase iv/ or exp clinical trials, phase iv as topic/ or exp randomized controlled trial/ or exp "randomized controlled trial (topic)"/ or exp randomized controlled trials as topic/ or exp controlled clinical trial/ or "controlled clinical trial (topic)"/ or controlled clinical trials as topic/ or exp randomization/ or exp random allocation/ or exp double-blind method/ or exp single-blind method/ or exp double blind procedure/ or exp single blind procedure/ or exp triple blind procedure/ or exp placebos/ or exp placebo/ or ((exp phase 2 clinical trial/ or exp "phase 2 clinical trial (topic)"/ or exp clinical trial, phase ii/ or exp clinical trials, phase ii as topic/ or exp clinical trial/ or exp prospective study/) and random$.tw.) or (((phase II or phase 2 or clinic$) adj3 trial$) and random$).tw. or ((singl$ or double$ or treble$ or tripl$) adj3 (blind$ or mask$ or dummy)).tw. or placebo?.tw. or (allocat: adj2 random:).tw. or (rct or phase III or phase IV or phase 3 or phase 4 or randomi$: or randomly).tw. or (random$ adj3 trial$).mp. or "clinicaltrials.gov".mp.
35 or 36
10 or 11 or 12 or 13 or 29 or 30
8 and 37 and 38
7 and 37 and 28
31 or 32 or 33 or 34

9 and 35 and 41
39 or 40 or 42
limit 43 to yr="2014 -Current"
exp animal/ not (exp human/ or humans/)
44 not 45
(comment or letter or editorial or note or erratum or short survey or news or newspaper article or patient education handout or case report or historical article).pt.
46 not 47
(editorial or note or letter erratum or short survey).pt. or letter/ or case study/
48 not 49

PubMed was searched on July 20, 2023, with the following search strategy:
((lung or thorax or thoracic or pulmonary) AND (cancer* or neoplasm* or carcinoma* or malignan* or tumor* or tumour* or adenocarcinoma* or metasta*)) Filters: Humans, English, Randomized Controlled Trial, Systematic Review, Meta-analysis, custom publication date – June 1, 2022, to July 20, 2023

Appendix 6: PRISMA Flow Diagram

Figure 1: Flow diagram of results from literature search strategies



[A] Online search strategy available in Appendix 5
Abbreviations: EMBASE, Excerpta Medica; MEDLINE, Medical Literature Analysis and Retrieval System Online; Q, Question; SR, systematic review

Appendix 7: Risk of Bias of Systematic Reviews assessed with the ROBIS tool

Study	Population	Comparison(s)/ Factor(s)/ Outcome(s)	1. Concerns regarding specification of study eligibility criteria	2. Concerns regarding methods used to identify and/or select studies	3. Concerns regarding methods used to collect data and appraise studies	4. Concerns regarding the synthesis and findings	Risk of bias in the review
Question 3. What are the benefits and harms of pneumococcal, influenza, and COVID-19 vaccinations?							
Becerril-Gaitan 2022	Cancer	COVID-19 vaccination in people with cancer vs. COVID-19 vaccination in people without cancer	Low	Low	Low	High (risk of bias not incorporated into findings)	High
Bitterman 2018	Cancer	Inactivated or recombinant influenza vaccines vs. placebo, no vaccination, or a different vaccine	Low	Low	Low	Low	Low
Cavanna 2021	Cancer	COVID-19 vaccination in people with cancer vs. COVID-19 vaccination in healthy controls	Low	Low	High (no risk of bias assessment)	High (no risk of bias assessment)	High
Corti 2022	Cancer	COVID-19 vaccination	High (ambiguous eligibility criteria)	Low	Low	High (risk of bias not incorporated into findings)	High
Guven 2021	Cancer	COVID-19 vaccination in people with cancer vs. COVID-19 vaccination in healthy controls	High (ambiguous eligibility criteria)	Low	Low	High (risk of bias not incorporated into findings)	High
Javadinia 2022	Cancer	COVID-19 vaccination	Low	Low	Low	High (risk of bias not incorporated into findings)	High
La Torre 2016	Hematological malignancies	Influenza/ pneumococcal vaccine vs. not reported	High (ambiguous eligibility criteria)	Low	Low	High (risk of bias not incorporated into findings)	High
Sakuraba 2022	Cancer	COVID-19 vaccination in people with cancer vs. COVID-19 vaccination in people without cancer	Low	Low	Low	Low	Low
Vijenthira 2021	Hematologic malignancy or autoimmune disease who have received anti-CD20 therapy	Influenza/ pneumococcal vaccine in patients receiving anti-CD20 therapy vs. influenza/ pneumococcal vaccine in healthy or disease controls not receiving anti-CD20 therapy	Low	Low	Low	High (risk of bias not incorporated into findings)	High
Question 4. What are the benefits and harms of smoking cessation interventions?							
Zeng 2019	Lung cancer	Any psychosocial and/or pharmacological smoking cessation intervention vs. no intervention, a different psychosocial and/or pharmacological intervention, or placebo for pharmacological interventions	Low	Low	Low	Low	Low
Question 5. Which signs/symptoms/risk factors/comorbidities should be managed to improve their quality of life, risk of recurrence, survival, or risk of other primary cancers?							

Study	Population	Comparison(s)/ Factor(s)/ Outcome(s)	1. Concerns regarding specification of study eligibility criteria	2. Concerns regarding methods used to identify and/or select studies	3. Concerns regarding methods used to collect data and appraise studies	4. Concerns regarding the synthesis and findings	Risk of bias in the review
Kossioris 2016	SCLC	Clinical and sociodemographic determining factors of health-related quality of life	Low	Low	High (no risk of bias assessment)	High (no risk of bias assessment, data analysis unclear)	High
Walls 2018	NSCLC following radical radiotherapy	Predictors of local control in NSCLC with radical radiotherapy	Low	Low	High (insufficient study characteristics)	Low	High
Wu 2022	Lung cancer	Clinical features of intramedullary spinal cord metastasis	Low	Low	High (risk of bias not reported)	High (risk of bias not incorporated into findings)	High
Question 6. What are the late toxicities after any treatment (surgical, radiotherapy, chemotherapy, immunotherapy) that should be managed to improve their quality of life?							
Guo 2017	Inoperable NSCLC treated with chemotherapy with hypofractionated radiotherapy	Adverse effects after treatment	Low	High (ambiguous search strategy)	High (no risk of bias assessment)	High (no risk of bias assessment)	High
Iseli 2020	Stage III NSCLC	Adverse events after radiotherapy and/or surgery	Low	Low	High (no risk of bias assessment)	High (no risk of bias assessment)	High
Liu 2020	NSCLC treated with prophylactic cranial irradiation	Adverse events after treatment	Low	Low	Low	Low	Low
Morias 2018	Lung cancer	Toxicities after stereotactic ablative radiation therapy	High (ambiguous eligibility criteria)	High (not reported)	High (no risk of bias assessment)	High (no risk of bias assessment)	High
Poghosyan 2013	NSCLC after surgery	Symptoms after surgery	High (ambiguous eligibility criteria)	High (ambiguous search strategy)	High (no risk of bias assessment)	High (no risk of bias assessment)	High
Prezzano 2019	Primary early-stage NSCLC definitively treated with stereotactic ablative radiation therapy	Adverse events after treatment	Low	High (ambiguous search strategy)	High (no risk of bias assessment)	High (no risk of bias assessment)	High
Voruganti 2020	Stage I NSCLC after stereotactic ablative radiation therapy	Incidence of chest wall pain and rib fracture	Low	Low	Low	Low	Low
Question 7. What are the benefits and harms of the treatment/ management strategies for signs/symptoms/risk factors/ comorbidities/ late toxicities?							
Cavalheri 2019	NSCLC after surgery	Exercise training vs. usual care or no exercise	Low	Low	Low	Low	Low
Cavalheri 2014	NSCLC after surgery	Exercise vs. usual care or no exercise	Low	Low	Low	Low	Low
Himbert 2020	Lung cancer after surgery (subgroup)	Exercise vs. usual care or other exercise intervention	Low	Low	Low	Low	Low
Li 2017	Lung cancer after surgery	Exercise training vs. usual care or standard postoperative care	Low	Low	Low	Low	Low

Study	Population	Comparison(s)/ Factor(s)/ Outcome(s)	1. Concerns regarding specification of study eligibility criteria	2. Concerns regarding methods used to identify and/or select studies	3. Concerns regarding methods used to collect data and appraise studies	4. Concerns regarding the synthesis and findings	Risk of bias in the review
Mainini 2016	Underwent surgery for NSCLC with curative intent	Exercise training vs. control	Low	Low	Low	Low	Low
Ni 2017	NSCLC postoperative (subgroup)	Exercise training vs. control	Low	High (full search strategy not reported)	Low	Low	High
Rowntree 2022	Lung cancer	Self-management interventions vs. standard care	Low	High (full search strategy not reported)	Low	Low	High
Sommer 2018	NSCLC	Post exercise program vs. usual care	Low	Low	Low	Low	Low

Abbreviations: NSCLC, non-small cell lung cancer; SCLC, small cell lung cancer

Appendix 8: Characteristics of the Included Studies

Study Location Protocol ID Study period	Population Target sample size	Intervention (# randomized) Deviations?	Control (# randomized) Deviations?	Outcome(s) of interest	Concealment/ Blinding Confounder(s)/ Adjusted factor(s)
Question 1. What are the benefits and harms of different types of clinicians providing follow-up care?					
Aubin 2021 Quebec, Canada NCT01389739 2010-2014	Nonsurgical lung cancer Inclusion: have an FP, expected survival ≥3 months Target sample size = 206	Nurse-facilitated increased communication between FP, oncologist, and patient plus usual care (104)	Usual care (102)	Secondary: Distress, hospital visits	Concealed No blinding Patient perception of pattern of care differed between groups
Berezowska 2021 Netherlands METC16.1493 2016-2017	Newly diagnosed ovarian, vulvar, endometrial, melanoma stage III/IV, lung, or renal cancer Inclusion: Dutch-speaking, ≥18 years old Target sample size = 62	Nurse navigator plus usual care (42) (18 with lung cancer)	Usual care (47) (21 with lung cancer)	Primary: Quality of life Secondary: Distress	Concealment & blinding not reported No differences in patient characteristics
Edbrooke 2019 Australia ACTRN12614001268639 2014-2016	Inoperable lung cancer Inclusion: Non-surgical treatment planned for the primary lung tumour, started treatment ≤4 weeks prior to recruitment, ≥18 years old, proficient in English, ECOG-PS of ≤2, Clinical Frailty Scale score of <7, life expectancy of >6 months, for newly diagnosed recurrent disease, for recurrent cancer must have completed previous treatment >6 months prior to recruitment Exclusion: Concurrent, actively treated other malignancy (or 1-year history of other malignancy)	Home-based rehabilitation program to improve physical function via physiotherapists and patient symptom management via nurses plus usual care (45) (21 curative)	Usual care (47) (21 curative) May have exercised	Secondary: Health-related quality of life, distress, anxiety, depression Exploratory: Survival	Concealed Patients and personnel not blinded Outcome assessors blinded People who declined to participate were older (p=0.04) and had higher scores on the Colinet Co-morbidity Scale than people in the trial (p=0.006) P-values for differences between patient characteristics not reported

Study Location Protocol ID Study period	Population Target sample size	Intervention (# randomized) Deviations?	Control (# randomized) Deviations?	Outcome(s) of interest	Concealment/ Blinding Confounder(s)/ Adjusted factor(s)
	other than in situ melanoma or non-melanoma skin cancer, physical activity self-report has met guidelines for past month, unstable psychiatric or cognitive disorder, participation in exercise program prohibited by comorbidities or pelvic or lower limb bony metastases Target sample size = 92				
Liu 2020 China ID not reported 2016-2018	After radical surgery for lung cancer Inclusion: between 55 and 75 years old Exclusion: contraindications to surgery, severe liver and kidney dysfunction, coagulation disorders, other malignant tumors, severe immune system diseases, cognitive impairment and communication impairment, did not cooperate with the experiment Target sample size not reported	Respiratory rehabilitation training and nursing after surgery (53)	Routine nursing (53)	Nursing satisfaction	Concealment and blinding not reported No differences in gender, age, BMI, and pathological types of patients in both groups ($p>0.05$)
McCorkle 2000 USA ID not reported 1993-1995	Post-surgical cancer aged ≥60 years Inclusion: diagnosed with solid tumor in 2 months immediately preceding primary surgical removal of cancers, life expectancy ≥6 months after surgery	Nurse-led home-based care follow-up (190) (36 lung cancer)	Usual care in ambulatory setting (185) (37 lung cancer)	Primary: Overall survival	Concealed Blinding not reported Adjusted for stage and total length of hospitalization during surgery

Study Location Protocol ID Study period	Population Target sample size	Intervention (# randomized) Deviations?	Control (# randomized) Deviations?	Outcome(s) of interest	Concealment/ Blinding Confounder(s)/ Adjusted factor(s)
	Target sample size not reported				
Moore 2002 England ID not reported Year not reported	Lung cancer completed initial treatment Inclusion: expected to survive for ≥3 months Target sample size = 200 Final assessment at 12 months Target sample size = 200	Nurse-led follow up (100)	Usual care (103)	Primary: patients' satisfaction at 3 months Secondary: overall survival, time to progression	Concealed Blinding not reported P-values for differences between patient characteristics not reported
Perfors 2022 Netherlands NTR5909 2015-2017	Curatively treated for breast, lung, colorectal, gynecologic cancer or melanoma Inclusion: aged ≥18 years Exclusion: unable to fill in questionnaires, had a major psychiatric disease or personality disorder, already started cancer treatment, patient's general practitioner worked outside the study area or did not agree to participate Target sample size = 150	Time Out consultation with the general practitioner after diagnosis, and follow-up during and after treatment by a home care oncology nurse in cooperation with the general practitioner plus usual care (77) (3 with lung cancer)	Usual care (77) (6 with lung cancer)	Primary: patient satisfaction with care and healthcare utilization during the year after inclusion	Concealed Not blinded Higher presence of comorbidity in the intervention group (68% versus 49%) Characteristics of the analyzed patients and the patients who dropped out did not differ p > 0.05
Scherz 2017 Switzerland ISRCTN41474586 2010-2012	Received curatively intent cancer treatment Inclusion: at least 18, expected survival ≥1 year, temporary and increased distress scale (≥3), need of and intention to undertake rehabilitation according to patient's perspective Exclusion: treatment completed >1 month ago, metastasis and/or advanced stage disease, cancer	Nurse case manager (51) (1 with lung cancer)	Usual care (53) (0 with lung cancer)	Primary: Quality of life at 12 months	Concealed Blinding not reported Adjusted for differences in quality of life and distress at baseline

Study Location Protocol ID Study period	Population Target sample size	Intervention (# randomized) Deviations?	Control (# randomized) Deviations?	Outcome(s) of interest	Concealment/ Blinding Confounder(s)/ Adjusted factor(s)
	relapse during study, palliative treatment, insufficient knowledge of German, or severe psychiatric disease Target sample size = 132				
Su 2019 China ID not reported Year not reported	Advanced lung cancer Inclusion: stage III or IV, complete clinicopathologic data, willing to cooperative with the work, did not receive medical treatment before admission, received surgery and postoperative chemotherapy, KPS ≥ 70 points, verbal Exclusion: Pregnant or lactating, family psychiatric history, autoimmune system defects, liver dysfunction and/or severe organ disease Target sample size not reported	Comprehensive nursing intervention (120)	Routine nursing (120)	Nursing satisfaction levels	Concealment & blinding not reported No differences in patient characteristics
Wang 2022 China ID not reported 2014-2016	Postoperative advanced non-small cell lung cancer Inclusion: scheduled for adjuvant chemotherapy, >18 years, BMI >18 kg/m^2, follow study protocol Exclusion: cancer history, concurrent surgery, congestive heart disease, depression, pregnant, history of childhood trauma	High-quality nursing (normal nursing plus additional care including postoperative complications care, postoperative mental communication, and medication reminder) (192)	Normal nursing (202)	Satisfaction with provider	Concealment & blinding not reported No differences in patient characteristics
Yu 2022 China ID not reported 2017-2020	Received chemotherapy for lung cancer Inclusion: High treatment compliance, stable vital	Nurse-led psychological intervention combined with health education (35)	Routine nursing (35)	Nursing satisfaction	Concealment & blinding not reported

Study Location Protocol ID Study period	Population Target sample size	Intervention (# randomized) Deviations?	Control (# randomized) Deviations?	Outcome(s) of interest	Concealment/ Blinding Confounder(s)/ Adjusted factor(s)
	signs, no disturbance of consciousness, communication barriers, and psychiatric history, KPS ≥60 points Exclusion: Incomplete clinical data, need surgical treatment, had severe organic diseases in the heart, liver, kidney, etc. Target sample size not reported				No differences in patient characteristics
Yun 2020 South Korea NCT02650661 2015-2016	Cancer survivors within 2 months of completing primary cancer treatment Inclusion: ≥20 years old, not met ≥1 of these behavioural goals: (i) conducting moderate physical activity for ≥150 minutes/week or strenuous exercise for >75 minutes per week or, in the case of lung cancer patients, low or moderate intensity exercise for > 12.5 MET per week, (ii) maintaining normal weight, and (iii) attaining a score >72 in the Post Traumatic Growth Inventory Exclusion: Progressive malignant disease or a recurrent, metastasized, or additional primary cancer, had a condition that might compromise adherence to an unsupervised exercise program, had a condition	Nurse-led health coaching plus web-based program (135) (36 with lung cancer) or Web-based program only (125) (33 with lung cancer)	Usual care (134) (34 with lung cancer)	Secondary: Anxiety, depression, quality of life	Concealed Patients not blinded Outcome assessors blinded Patients stratified by cancer type (breast, stomach, colon, or lung), sex, and the enrollment hospital No differences in patient characteristics

Study Location Protocol ID Study period	Population Target sample size	Intervention (# randomized) Deviations?	Control (# randomized) Deviations?	Outcome(s) of interest	Concealment/ Blinding Confounder(s)/ Adjusted factor(s)
	that could interfere with a diet high in vegetables and fruit, had a serious psychological disorder, had an infection, had a visual or motor dysfunction, or pregnancy Target sample size 477				
Question 2. What are the benefits and harms of using patient reported outcome tools or measures in providing follow-up care?					
Billingy 2023 Abstract Netherlands NL7897 Year not reported Home	Non-small cell lung cancer Inclusion: Age 18 years or older, stage I-IV, starting treatment, ECOG-PS classification should be 0, 1 or 2 Exclusion: Participating in a treatment study when a structured symptom reporting is already part of such a study, life expectancy is shorter than 15 weeks, treatment and follow up does not remain in an affiliated hospital Target sample size not reported	Online PRO symptom monitoring via the active and reactive approach (reported PRO symptoms weekly up to 1 year follow-up. If symptoms exceeded a pre-determined threshold, an alert was sent to a physician/nurse (active intervention group) or to the patient themselves (reactive intervention group) (249)	Usual care (266)	Secondary: 1-year progression-free survival, overall survival	Concealment unclear Not blinded Active intervention group had significantly more stage IV patients compared to the control group and the reactive intervention group (63% vs. 44% vs. 44%, p=0.001) Age, sex, cancer staging, ECOG-PS and some baseline EORTC domain scores were included as covariates in the analyses.
Cleeland 2011 Stopped early due to lack of funding USA ID not reported Year not reported Home	Lung cancer or lung metastasis Inclusion: Receiving thoracotomy, ≥18 years old, understand English and study requirements, willing and able to respond to a repeated interactive voice response-administered	Usual care plus email alert to clinicians about severe symptoms (50)	Usual care (after hospital discharge patients rated postoperative symptoms twice weekly for 4 weeks via automated telephone calls) (50)	Secondary: Patient satisfaction with symptom treatment	Concealed Not blinded No differences in patient characteristics

Study Location Protocol ID Study period	Population Target sample size	Intervention (# randomized) Deviations?	Control (# randomized) Deviations?	Outcome(s) of interest	Concealment/ Blinding Confounder(s)/ Adjusted factor(s)
	symptom rating scale, surgical clinician had to be willing to receive e-mail alerts, to consult with these patients by phone about alerted symptoms, and to inform study staff about actions taken in response to the alert Target sample size = 118				
Cooley 2022 USA NCT00852462 Year not reported Hospital	Advanced lung cancer Inclusion: English speaking, ≥21 years old, stage III or IV non-small cell lung cancer, any stage small cell lung cancer, or recurrent lung cancer, receiving treatment with chemotherapy or combined treatment Exclusion: Needed emergent care or had fewer than monthly visits Target sample size not reported	Symptom Assessment and Management Intervention (patient-report of symptoms and delivery of recommendations to manage pain, fatigue, dyspnea, depression, and anxiety) (88)	Attention control (symptom reporting prior to the visit) (91)	Secondary: Quality of life	Concealment unclear Not blinded Randomized medical oncologists, stratified by clinical site and clinician volume. Patients were assigned to the same group as their medical oncologist. Attention control group was slightly older (p=0.06), had higher percentage of females (p=0.06), and were less educated (p=0.07).
Dai 2022 China ChiCTR1900020846 2019-2020 Hospital and home	Lung cancer Inclusion: Aged 18 to 75 years, stage I-IIIA, planning to receive surgery, able and willing to respond to a repeated electronic Questionnaire Exclusion: History of neoadjuvant therapy, have	E-questionnaire in hospital and home with alerts sent to clinician (83)	Usual care (e-questionnaire in hospital, no alerts) (83)	Secondary: Quality of life, surgeon acceptability, patient satisfaction	Concealed Patients and personnel not blinded Outcome assessors blinded No differences in patient characteristics

Study Location Protocol ID Study period	Population Target sample size	Intervention (# randomized) Deviations?	Control (# randomized) Deviations?	Outcome(s) of interest	Concealment/ Blinding Confounder(s)/ Adjusted factor(s)
	other malignant tumours, unable to understand study requirements				
Denis 2017, 2019 Stopped early due to pre-planned interim analysis France NCT02361099 2014-2016 Home	Advanced lung cancer Inclusion: Nonprogressive small cell or non–small cell lung cancer staged as at least cTxN1/pTxpN1 to TxNxMþ cancer before their last treatment, performance status between 0 and 2, initial symptom score of less than 7, each patient or one of his close relatives had internet access and prior email experience Target sample size = 224, stopped early	Web-mediated follow-up algorithm (based on weekly self-scored patient symptoms) plus usual care (67)	Usual care (routine follow-up with CT scans scheduled every three to six months according to the disease stage) (66) Cross-over may have occurred	Primary: Overall survival Secondary: Progression-free survival, change from baseline in health-related quality of life score at 6 months	Concealed Not blinded Stratified according to sex, performance status, stage of disease, and type of ongoing treatment Mean baseline FACT-L score was higher in intervention than control (99.6, SD=16.3 & 91.4, SD=16.2, p=0.01)
Friis 2023 Abstract Denmark NCT03608410 Year not reported Home	Stage III-IV lung cancer treated with palliative intent Inclusion: ECOG-PS status ≤2, internet access and non-progressive disease after completed induction treatment, maintenance treatment allowed Exclusion: Dementia, mental alteration or psychiatric disease that can compromise informed consent or adherence to the protocol and monitoring, pregnant or breastfeeding, participating in another interventional study during the surveillance period that	Remote symptom-monitoring plus standard of care (weekly electronic questionnaire from home covering 13 common symptoms related to lung cancer. When severity-threshold was exceeded, a notification was sent to a clinical nurse. The nurse was instructed to contact the patient and offer best supportive care. If disease progression was suspected, a CT scan was performed) (239)	Standard of care (254)	Primary: Overall survival Secondary: Health-related quality of life, anxiety, depression	Concealed Not blinded

Study Location Protocol ID Study period	Population Target sample size	Intervention (# randomized) Deviations?	Control (# randomized) Deviations?	Outcome(s) of interest	Concealment/ Blinding Confounder(s)/ Adjusted factor(s)
	might interfere with the intervention Target sample size = 492				
Geerse 2017 Interim analysis due to pre-planned analysis from high drop-out rates Netherlands NTR3540 2010-2013 Home	Lung cancer Inclusion: Newly diagnosed or recurrent, starting systemic therapy, ECOG-PS between 0 and 2 Exclusion: psychiatric co-morbidity, receiving palliative care Target sample size = 250	Self-administered distress screening tool (Distress Thermometer and Problem List) (110)	Usual care (113)	Primary: Quality of life Secondary: Patient satisfaction Post-hoc: Distress, overall survival	Concealed Not blinded Stratified by performance score and disease stage More patients smoked and more received chemo-radiation in the experimental group
Kuo 2020 Stopped early due to slow accrual Ontario, Canada ID not reported 2004-2011 Hospital	Advanced non-small cell lung cancer Inclusion: Incurable, commencing first-line systemic therapy, stage IIIb or IV, no prior chemotherapy, performance status 0–3, written fluency in English, French, Portuguese, Spanish, Italian, or Chinese Exclusion: Unable to independently complete or understand the assessment process, receiving concurrent radical radiotherapy, did not commence chemotherapy, participating in another clinical trial involving first-line therapy Target sample size not reported	Oncologists receive patients' quality of life data in real time (44)	Oncologists did not receive patients' quality of life data in real time (55)	Secondary: Health-related quality of life	Concealment unclear Blinding unclear Stratified by treating oncologist, planned treatment, and performance status 0 or 1 compared with 2 or greater Patients in the control arm were older, more likely to have stage IV disease, and more likely to have a worse performance status

Study Location Protocol ID Study period	Population Target sample size	Intervention (# randomized) Deviations?	Control (# randomized) Deviations?	Outcome(s) of interest	Concealment/ Blinding Confounder(s)/ Adjusted factor(s)
Mills 2009 Ireland ID not reported 2005-2007 Home	Advanced lung cancer Inclusion: Inoperable, ability to give written informed consent, performance status of 0 to 2, ability to complete questionnaires Target sample size = 84	Quality of life diary (encouraged to share results with health care provider) (57)	Usual care (58)	Primary: Quality of life - Trial Outcome Index subscale Secondary: Quality of life – other measures, patient satisfaction	Concealed Blinding unclear No differences in patient characteristics
Nimako 2017 United Kingdom NCT01213745 Year not reported Hospital	Lung cancer Inclusion: Able to understand written and spoken English, recently completed treatment, no plan to commence treatment within 6 weeks Exclusion: Taking part in any other studies that required completion of a quality of life questionnaire, had received any anti-cancer treatment within previous 3 weeks, ongoing toxicities from their treatment, which had not been stabilized Target sample size = 138	Quality of life questionnaire plus feedback (EORTC-Core Quality of Life Questionnaire and Lung Cancer Module at baseline and received feedback during a clinic) (45)	Attention group (completed quality of life questionnaire at baseline without feedback) (47) Control group (did not complete the questionnaire) (46) These groups may have discussed quality of life issues in clinic.	Secondary: Changes in quality of life from baseline to 6 weeks	Concealed Not blinded Stratified by different cancer therapies No differences in patient characteristics
Noronha 2023 Abstract India 2022 CTRI/2020/023511 Hospital visits	Advanced lung cancer planned for palliative intent therapy Inclusion: ≥18 years old Target sample size = 150	Patient navigator with symptom monitoring (administered weekly, navigator alerted clinician for any symptom marked severe) (75)	Standard care (75)	Primary: Change in quality of life from baseline to 12 weeks Secondary: overall survival	Concealed Not blinded Stratified according to sex, ECOG-PS, age and histopathology
Schofield 2013 Stopped early due to insufficient funds Australia ID not reported 2005-2007 Hospital/clinic/virtual	Lung or pleural cancer Inclusion: Inoperable, scheduled to receive palliative external beam radiotherapy, palliative chemotherapy or radical radiotherapy and	Self-completed needs assessment, active listening, self-care education and communication of unmet psychosocial and symptom needs to the	Usual care (53) May have received support from a multidisciplinary team	Distress, health-related quality of life	Concealed Blinding unclear Stratified by scheduled treatment

Study Location Protocol ID Study period	Population Target sample size	Intervention (# randomized) Deviations?	Control (# randomized) Deviations?	Outcome(s) of interest	Concealment/ Blinding Confounder(s)/ Adjusted factor(s)
	chemotherapy, understand English Exclusion: Psychiatric disorder or serious cognitive impairment, performance status score ≥3, ≤2 months since a previous treatment Target sample size = 200	multidisciplinary team for management and referral (55)			No differences in patient characteristics
Yount 2014 Stopped early due to funding USA ID not reported Year not reported Home	Advanced lung cancer Inclusion: Stages III or IV non-small cell lung cancer or small cell lung cancer, at least 18 years old, English speaking, receiving active treatment with traditional chemotherapy no later than day 1 of cycle 2 or receiving oral therapy, access to a telephone, life expectancy ≥6 months Target sample size = 360	Technology-based symptom monitoring and reporting to the clinical team (123)	Monitoring alone (130) Physicians exposed to intervention may have affected the management of patients in this group. Patients may have experienced an enhancement of symptom awareness in this group.	Primary: Overall symptom burden/distress Secondary: Patient satisfaction	Concealment unclear Not blinded Stratified by institution No differences in patient characteristics
Question 4. What are the benefits and harms of smoking cessation interventions?					
Mujcic 2022 Netherlands NTR6011 2016-2019	Cancer Inclusion: ≥18 years old, diagnosed with any form of cancer in past 10 years, had Internet connection at home, had ability & intention to participate in the 12-month study, smoked ≥5 cigarettes per day in past 7 days, intention to quit smoking Exclusion: Insufficient mastery of the Dutch language, pregnant, self-reported suicidal ideation, acute psychosis, severe	Digital interactive smoking cessation intervention (MyCourse-Quit Smoking) plus usual care (83) (14 with lung cancer)	Noninteractive web-based information brochure plus usual care (82) (9 with lung cancer)	Primary: Self-reported 7-day smoking abstinence at 6-months Secondary: Quality-adjusted life years gained	Concealed Participants not blinded Randomized to minimize age, sex, and education level differences No difference in the proportion of missing data between groups at any of the time points (p=0.77)

Study Location Protocol ID Study period	Population Target sample size	Intervention (# randomized) Deviations?	Control (# randomized) Deviations?	Outcome(s) of interest	Concealment/ Blinding Confounder(s)/ Adjusted factor(s)
	alcohol dependence, dementia, or severe depression Target sample size = 204				P-values for differences between patient characteristics not reported
Ostroff 2014 USA ID not reported Year not reported	Cancer Inclusion: English-speaking, adults, localized solid mass likely to be cancer, awaiting surgical treatment no less than 7 days from study entry, smoked ≥8 cigarettes per day within the past week, sufficient visual acuity and manual dexterity to use a handheld computer Exclusion: Psychopathology or cognitive impairment severe enough to prevent informed consent or completion of study Target sample size not reported	Best practice plus a behavioural tapering regimen (scheduled reduced smoking) administered by a handheld computer before hospitalization for surgery (96) (25 with lung cancer)	Best practice, presurgical, hospital-based, tobacco cessation intervention (cessation counseling and nicotine replacement therapy) (89) (30 with lung cancer)	Primary: 6 months posthospitalization biochemically verified smoking abstinence Secondary: Hospital admission and 3 months biochemically verified smoking abstinence	Concealed Blinding not reported Stratified by baseline daily cigarette consumption No differences in patient characteristics No group differences in misreporting of smoking status
Park 2020 USA NCT01871506 2013-2017	Cancer Inclusion: Adults, smoked ≥1 cigarette within 30 days, spoke English or Spanish, had telephone access, recently diagnosed breast, gastrointestinal, genitourinary, gynecological, head and neck, lung, lymphoma, or melanoma cancers Exclusion: Medical and cognitive impairment likely to interfere with study participation, uncontrolled	Intensive treatment (sustained telephone counseling and medication) (153) (46 with lung cancer)	Standard treatment (shorter-term telephone counseling and medication advice) (150) (47 with lung cancer)	Primary: Biochemically confirmed 7-day point prevalence tobacco abstinence at 6-month follow-up Secondary: Biochemically confirmed past 7-day abstinence at 3 months, adverse events	Concealed Not blinded Stratified by study site and cancer center clinic Hispanic or race other than White were significantly less likely to be randomized Participants who did not complete 3- or 6-

Study Location Protocol ID Study period	Population Target sample size	Intervention (# randomized) Deviations?	Control (# randomized) Deviations?	Outcome(s) of interest	Concealment/ Blinding Confounder(s)/ Adjusted factor(s)
	psychosis or suicide attempt in past year, insufficient comprehension/literacy, not receiving cancer care at a study site Target sample size = 296				month follow-up were significantly more likely to be younger and have later stages of cancer P-values for differences between patient characteristics not reported
Schnoll 2010 USA ID not reported 2002-2008	Cancer (32.2% with lung or head and neck cancer) Inclusion: ≥18 years of age, speak English, possess a telephone, smoke ≥2 cigarettes/day on average Exclusion: No current smoking, had stage IV lung cancer or brain metastases, current drug, or alcohol dependence, current Axis I psychiatric conditions, pregnant/lactating, seizure disorder, cardiac, renal, pulmonary, endocrine, or neurological disorders, using MAO inhibiter or a pharmacotherapy for nicotine dependence, recent discontinuation of benzodiazepines Target sample size not reported	Bupropion plus usual care (transdermal nicotine and behavioural counseling) (114)	Placebo plus usual care (transdermal nicotine and behavioural counseling) (132)	Primary: 7-day point prevalence abstinence, biochemically confirmed, at end of treatment (week 12), and at 6 months post quit day (week 27) Secondary: Quality of life, side effects	Concealment unclear Double-blind Stratified by pre-treatment depression symptoms No differences in patient characteristics between treatment arms Women and those with less than a college education were more likely to be in the depression symptoms group
Schnoll 2005 USA ID not reported Year not reported	Lung or head and neck cancer Inclusion: Smoking in last 30-day period, speak English,	Cognitive-behavioural therapy plus nicotine replacement therapy (52)	Basic health education plus nicotine replacement therapy (57)	30-day point-prevalence abstinence at 1-month or 3-months	Concealment and blinding unclear

Study Location Protocol ID Study period	Population Target sample size	Intervention (# randomized) Deviations?	Control (# randomized) Deviations?	Outcome(s) of interest	Concealment/ Blinding Confounder(s)/ Adjusted factor(s)
	able to attend a 2-hour counseling session at the hospital, reachable by phone Target sample size not reported	(24 with lung cancer)	(40 with lung cancer)		Decliners, compared to enrollees, were significantly more likely to have head and neck cancer (vs. lung cancer), exhibit fewer physical symptoms, report a lower readiness to quit smoking, indicate no intention to quit smoking, and smoke fewer cigarettes No difference in rate of compliance or smoking rates or side effects with patch use across study conditions ($p>0.05$) Adjusted for mean time since diagnosis and initiation of treatment
Schnoll 2003 USA ID not reported 1990-1991	Cancer Inclusion: ≥19 years old, stage I-II cancer (of any type) or stage III-IV breast, prostate, or testicular cancer or lymphoma, ECOG-PS score of 0 or 1, informed consent, have been scheduled to return to treatment site, smoking ≥1 cigarettes in past 30 days or	National Institutes of Health physician-based smoking intervention (215) (12 with lung cancer)	Usual care (217) (17 with lung cancer) Patients in usual care arm might have been provided with physician quit advice and/or may have sought assistance with quitting	Primary: 7-day point prevalence abstinence at 6 and 12 months after study entry	Not blinded More males in usual care arm than intervention (39% vs. 29%, respectively), lower proportion of patients in usual care arm reported experiencing heart trouble or a heart attack in the past

Study Location Protocol ID Study period	Population Target sample size	Intervention (# randomized) Deviations?	Control (# randomized) Deviations?	Outcome(s) of interest	Concealment/ Blinding Confounder(s)/ Adjusted factor(s)
	have self-identified as a smoker Target sample size not reported				year than did patients in intervention (3.7% vs. 11.6%, respectively) No significant difference between study arms in attrition caused by death or refusal to complete the assessment
Simmons 2020 USA NCT01630161 Year not reported	Cancer Inclusion: Aged ≥18 years; fluent in English, smoking history of ≥10 cigarettes per day over past year, had quit since diagnosis and had been continuously abstinent for at least 24 hours but for ≤90 days at time of recruitment Exclusion: Metastatic disease Target sample size not reported	Smoking relapse prevention intervention (targeted educational DVD plus a validated self-help intervention for preventing smoking relapse (203) (40 with lung cancer)	Usual care (209) (33 with lung cancer)	Primary: Smoking abstinence at 2 months, 6 months, and 12 months	Personnel blinded Stratified by sex, length of smoking abstinence, and cancer site
Wakefield 2004 Australia ID not reported 1999-2001	Cancer (12% with lung cancer) Inclusion: Smoke tobacco more than weekly, speak English, be cognitively able to consent, have a prognosis exceeding 6 months, live close enough to maximize biochemical confirmation at follow-up assessment Target sample size not reported	Motivational interviewing intervention (smoking cessation counselor, smoking cessation booklets, nicotine replacement therapy, family advice to quit, in-person or telephone follow-up conversation) (74)	Usual care (brief advice to quit, widely available quit-smoking information brochures, information about a well-promoted telephone quit-line service if they wanted further assistance for quitting) (63)	Primary: Biochemically confirmed 3-month continued abstinence or at least 7-day abstinence at 6 months	Concealment and blinding unclear No difference in percentage of patients who completed follow-up interview between groups No differences in baseline

Study Location Protocol ID Study period	Population Target sample size	Intervention (# randomized) Deviations?	Control (# randomized) Deviations?	Outcome(s) of interest	Concealment/ Blinding Confounder(s)/ Adjusted factor(s)
					characteristics between patients who did and those who didn't complete 6-month follow-up Patients in intervention group more likely to have ever tried to quit and to have made more quit attempts in preceding year. Also, more control patients lived in remote areas
Weaver 2015 Abstract USA NCT01434342 2012-2104	Cancer Inclusion: ≥18 years old, stages 0, I, II, & III lung (53%), breast, prostate, colorectal, bladder, head & neck, and cervical cancers, smoking any amount in last 7 days, scheduled to receive or currently receiving surgery, radiation or chemotherapy OR have received one or more of the following in the last 6 months surgery, last radiation treatment or last chemotherapy treatment, KPS of 70-100, can understand & willingness to sign consent, willing to consider quitting smoking Exclusion: Unstable cardiac disease, current use or planned use of varenicline,	Quitline smoking cessation intervention (98)	Usual care (48) Crossover use of counseling and nicotine replacement therapy by usual care participants was common	Secondary: Self-reported smoking status at 12 and 24 weeks	Concealed No blinding Study completion at 12 and 24 weeks was 73% and 57%, with no difference by group assignment Whether there were differences in patient characteristics not reported in abstract

Study Location Protocol ID Study period	Population Target sample size	Intervention (# randomized) Deviations?	Control (# randomized) Deviations?	Outcome(s) of interest	Concealment/ Blinding Confounder(s)/ Adjusted factor(s)
	buproprion or any other nicotinic receptor agonist, current probable alcohol abuse, use of illegal drugs or use of prescription medications for non-medical reasons in the past month, current use of chewing, dipping and pipe tobacco, or cigars, no regular access to phone, history of allergic reactions attributed to nicotine replacement therapy, active peptic ulcer disease, ongoing, psychiatric illness/social situations that would limit compliance with study requirements, pregnant women do not receive the nicotine replacement therapy Target sample size = not reported				

Abbreviations: BMI, body mass index; CT, computed tomography; ECOG-PS, Eastern Cooperative Oncology Group Performance Status; EORTC, European Organisation for Research and Treatment of Cancer; FACT-L, Functional Assessment of Cancer Therapy-Lung; FP, family physician; ID, identifier; KPS, Karnofsky performance status; MAO, monoamine oxidase; MET, metabolic equivalent of task; PRO, patient-reported outcome; SD, standard deviation

Appendix 9: Risk of Bias of Included Studies assessed with Version 2 of the Cochrane risk-of-bias tool for randomized trials

Study	Population	Comparison(s)	Outcomes	Randomization Process	Deviation from intended interventions	Missing data	Measurement of outcomes	Selection of reported result	Overall bias
Question 1. What are the benefits and harms of different types of clinicians providing follow-up care?									
Aubin 2021	Nonsurgical lung cancer	Nurse-facilitated increased communication between FP, oncologist, and patient plus usual care vs. usual care	Distress, hospital visits	Some (difference between groups)	Low	Low	High (nurse does assessments)	Low	High
Berezowska 2021	Newly diagnosed ovarian, vulvar, endometrial, melanoma stage III/IV, lung, or renal cancer	Nurse navigator plus usual care vs. usual care	Quality of life Distress	Some (no information)	Low	Low	High (no information)	Low	High
Edbrooke 2019	Inoperable lung cancer	Home-based rehabilitation program to improve physical function via physiotherapists and patient-reported outcomes via nurses plus usual care vs. usual care	Health-related quality of life, distress, anxiety, depression, survival	Low	Some (OS) High (others) (patients not blinded, usual care group may have exercised)	Low	Low	Low	Some (OS) High (Others)
Liu 2020	After radical surgery for lung cancer	Respiratory rehabilitation training and nursing after surgery vs. routine nursing	Nursing satisfaction	Low	Low	Low	High (no information)	Low	High
McCorkle 2000	Post-surgical cancer aged ≥60 years	Nurse-led home-based care follow-up vs. usual care in ambulatory setting	OS	Some (differences due to stage)	Low	Low	Low	Low	Some
Moore 2002	Lung cancer completed initial treatment	Nurse-led follow-up vs. usual care	Patients' satisfaction, OS, time to progression	Low	Low	Low (OS and at 3 months) High (others) (more not	Low (OS) High (others) (no information)	Low (OS) Some (others) (not all time points	Low (OS) High (Others)

Study	Population	Comparison(s)	Outcomes	Randomization Process	Deviation from intended interventions	Missing data	Measurement of outcomes	Selection of reported result	Overall bias
						compliant in intervention)		reported, objective progression not defined)	
Perfors 2022	Curatively treated for breast, lung, colorectal, gynecologic cancer or melanoma	Follow-up by home care oncology nurse in cooperation with general practitioner plus usual care vs. usual care	Patient satisfaction with care, healthcare utilization	Some (baseline differences)	Low	High (higher drop out in intervention groups)	High (not blinded)	Low	High
Scherz 2017	Received curatively intent cancer treatment	Nurse case manager vs. usual care	Quality of life at 12 months	Some (baseline differences)	Low	Low	High (nurse does assessments)	Low	High
Su 2019	Advanced lung cancer	Comprehensive nursing intervention vs. routine nursing	Nursing satisfaction levels	Some (no information)	Some (no information)	High (no information)	High (no information)	Low	High
Wang 2022	Postoperative advanced non-small cell lung cancer	High-quality nursing vs. normal nursing	Nursing satisfaction	Some (no information)	Some (no information)	High (no information)	High (no information)	High (baseline & 5-year not reported)	High
Yu 2022	Received chemotherapy for lung cancer	Nurse-led psychological intervention combined with health education vs. routine nursing	Nursing satisfaction	Some (no information)	Some (no information)	Low	High (no information)	Low	High
Yun 2020	Cancer survivors within 2 months of completing primary cancer treatment	Nurse-led health coaching plus web-based program vs. web-based program only vs. usual care	Anxiety, depression, quality of life	Low	Low	High (higher drop out in intervention groups)	Low	Low	High
Question 2. What are the benefits and harms of using patient reported outcome tools or measures in providing follow-up care?									
Billingy 2023 Abstract	Non-small cell lung cancer	Online PRO symptom monitoring via the active and reactive approach vs. usual care	1-year progression-free survival, OS	Some (baseline differences)	Some (no information)	High (no information)	Low (OS) High (others) (not blinded)	Low	High

Study	Population	Comparison(s)	Outcomes	Randomization Process	Deviation from intended interventions	Missing data	Measurement of outcomes	Selection of reported result	Overall bias
Cleeland 2011	Lung cancer or lung metastasis	Usual care plus email alert to clinicians about severe symptoms vs. usual care	Patient satisfaction with symptom treatment	Low	Low	Low	High (not blinded)	Low	High
Cooley 2022	Advanced lung cancer	Symptom Assessment and Management Intervention vs. attention control	Quality of life	Some (baseline differences)	Low	Low	High (not blinded)	Low	High
Dai 2022	Lung cancer	PRO-based symptom management vs. usual care	Quality of life, surgeon acceptability, patient satisfaction	Low	Low	Low	Low	Low	Low
Denis 2017, 2019	Advanced lung cancer	Web-mediated follow-up algorithm plus usual care vs. usual care	OS, progression-free survival, change from baseline in health-related quality of life score at 6 month	Some (baseline differences)	High (cross-over)	Low	Low (OS) High (others)	Low	High
Friis 2023 Abstract	Stage III-IV lung cancer treated with palliative intent	Remote symptom-monitoring plus standard of care vs. standard of care	OS, health-related quality of life, anxiety, depression	Low (no information)	Some (no information)	High (no information)	Low (OS) High (others) (not blinded)	Low	High
Geerse 2017	Lung cancer	Self-administered distress screening tool vs. usual care	Quality of life, patient satisfaction, distress, OS	Some (baseline differences)	Low	Low	Low (OS) High (others) (not blinded)	Low	Some (OS) High (Others)
Kuo 2020	Advanced non-small cell lung cancer	Oncologists receive patients' quality of life data in real time vs. oncologists did not receive patients' quality of life data in real time	Health-related quality of life	High (baseline differences)	Low	Low	High (no information)	Low	High
Mills 2009	Advanced lung cancer	Quality of life diary vs. usual care	Quality of life - Trial Outcome Index subscale, quality of life -	Low	Low	Low	High (no information)	Low	High

Study	Population	Comparison(s)	Outcomes	Randomization Process	Deviation from intended interventions	Missing data	Measurement of outcomes	Selection of reported result	Overall bias
			other measures, patient satisfaction						
Nimako 2017	Lung cancer	Quality of life questionnaire plus feedback vs. quality-of-life questionnaire at baseline without feedback vs. no questionnaire	Changes in quality of life from baseline to 6 weeks	Low	Some (potential deviation)	Low	High (not blinded)	Low	High
Noronha 2023 Abstract	Advanced lung cancer planned for palliative intent therapy	Patient navigator with symptom monitoring vs. standard care	Change in quality of life from baseline to 12 weeks, OS	Low (no information)	Some (no information)	High (no information)	Low (OS) High (others) (not blinded)	Low	High
Schofield 2013	Lung or pleural cancer	Self-completed needs assessment plus management and referral vs. usual care	Distress, health-related quality of life	Low	Some (potential deviation)	Low	High (no information)	Low	High
Yount 2014	Advanced lung cancer	Technology-based symptom monitoring and reporting to the clinical team vs. monitoring alone	Overall symptom burden/distress, patient satisfaction	Some (unclear)	Some (potential deviation)	Low	High (not blinded)	Low	High
Question 4. What are the benefits and harms of smoking cessation interventions?									
Mujcic 2022	Cancer	Digital interactive smoking cessation intervention plus usual care vs. noninteractive web-based information brochure plus usual care	Self-reported 7-day smoking abstinence at 6-months, quality-adjusted life years gained	Low	Low	Low	High (not blinded)	Low	High
Ostroff 2014	Cancer	Best practice plus a behavioural tapering regimen vs. best practice alone	6 months posthospitalization biochemically verified smoking abstinence, hospital admission and 3 months biochemically	Low	Low	Low	Low	Low	Low

Study	Population	Comparison(s)	Outcomes	Randomization Process	Deviation from intended interventions	Missing data	Measurement of outcomes	Selection of reported result	Overall bias
			verified smoking abstinence						
Park 2020	Cancer	Intensive treatment vs. standard treatment	Biochemically confirmed 7-day point prevalence tobacco abstinence at 6-month follow-up, biochemically confirmed past 7-day abstinence at 3 months, adverse events	Low	Low	Low	Low (biochemically verified adherence) High (others) (not blinded)	Low	Low (biochemically verified adherence) High (others)
Schnoll 2010	Cancer	Bupropion plus usual care vs. placebo plus usual care	7-day point prevalence abstinence, biochemically confirmed, at end of treatment (week 12), and at 6 months post quit day (week 27), quality of life, side effects	Some (unclear)	Low	Low	Low (biochemically verified adherence) High (others) (no information)	Low	Some (biochemically verified adherence) High (others)
Schnoll 2005	Lung or head and neck cancer	Cognitive-behavioural therapy plus nicotine replacement therapy vs. basic health education plus nicotine replacement therapy	30-day point-prevalence abstinence at 1-month or 3-months	Some (unclear)	Low	Low	High (no information)	Low	High
Schnoll 2003	Cancer	National Institutes of Health physician-based smoking intervention vs. usual care	7-day point prevalence abstinence at 6 and 12 months after study entry	Some (unclear)	High (crossover in usual care group)	Low	High (not blinded)	Low	High
Simmons 2020	Cancer	Smoking relapse prevention intervention vs. usual care	Smoking abstinence at 2 months, 6 months, and 12 months	Some (unclear)	Low	High (more withdrawn in intervention?)	High (no information if assessors blinded)	Low	High

Study	Population	Comparison(s)	Outcomes	Randomization Process	Deviation from intended interventions	Missing data	Measurement of outcomes	Selection of reported result	Overall bias
Wakefield 2004	Cancer	Motivational interviewing intervention vs. usual care	Biochemically confirmed 3-month continued abstinence or at least 7-day abstinence at 6 months	Some (unclear)	Low	Low	Low	Low	Some
Weaver 2015 Abstract	Cancer	Quitline smoking cessation intervention vs. usual care	Self-reported smoking status at 12 and 24 weeks	Low	High (crossover in usual care group)	Low	High (self-report)	Low	High

Abbreviations: FP, family physician; OS, overall survival; PRO, patient-reported outcome; vs., versus

Appendix 10: Outcomes Reported from each Primary Study or Systematic Review per Comparison

Comparisons	Outcomes	Studies	Populations Sample sizes (intervention vs. comparator)	Measurement tools (assessment times) or Follow-up or Type of vaccine	Results (intervention vs. comparator)	Overall bias
Nurse-led intervention vs. usual care	Overall survival	Edbrooke 2019	Inoperable lung cancer (45 vs. 47)	Average follow-up 1.1 vs. 1.0 years	48 deaths (21 vs. 27) p=0.15 HR 0.658 (95% CI, 0.372 to 1.164)	Some
		McCorkle 2000	Post-surgical cancer aged ≥60 years (190 vs. 185)	Mean follow-up 24 months (range 1-44 months)	93 deaths (41 vs. 52) p=0.129 HR 0.728 (95% CI, 0.484 to 1.097)	Some
		Moore 2002	Lung cancer completed initial treatment (99 vs. 103)	Follow-up not reported	141 deaths (72 vs. 69) p=0.99 HR 1.002 (95% CI, 0.720 to 1.394)	Low
	Time to progression	Moore 2002	Lung cancer completed initial treatment (99 vs. 103)	No definition for objective progression provided	Nurses (6.0 [95% CI, 4.7 to 7.3] months) recorded progression of symptoms sooner than doctors (10.2 [95% CI, 5.9 to 14.6] months) (p=0.01). No differences were seen in objective progression, (8.3 [95% CI, 5.5 to 12.2] months vs. 10.2 [95% CI, 5.9 to 14.5] months [p=0.47]).	High

Comparisons	Outcomes	Studies	Populations Sample sizes (intervention vs. comparator)	Measurement tools (assessment times) or Follow-up or Type of vaccine	Results (intervention vs. comparator)	Overall bias
	Quality of life	Berezowska 2021	Newly diagnosed cancer (33 vs. 38 with all times)	EORTC QLQ-C30 summary score (1, 3, 5 months)	No significant differences (p>0.05)	High
		Edbrooke 2019	Inoperable lung cancer (38 vs. 34)	Assessment of Quality of Life (9 weeks, 6 months)	No significant differences (p>0.05)	High
				FACT-L (9 weeks, 6 months)	Significant 6-month change from baseline favouring nurse-led intervention 13.0 (95% CI, 3.9 to 22.1) (p=0.005)	
		Scherz 2017	Received curative-intent cancer treatment (47 vs. 48)	FACT-G questionnaire (3, 6, 12 months)	Significant 12-month change from baseline favouring nurse-led intervention (mean (SE) 16.2 (2.0) vs. 9.2 (1.5) points (p=0.006), mean difference in change between groups of 7.0 (2.5) points	High
		Yun 2020	Cancer survivors within 2 months of completing primary cancer treatment (nurse-led 61	Social support spiritual scales of the McGill Quality of Life scale (3, 6, 12 months)	No significant difference at 12 months (p>0.05)	High

Comparisons	Outcomes	Studies	Populations Sample sizes (intervention vs. comparator)	Measurement tools (assessment times) or Follow-up or Type of vaccine	Results (intervention vs. comparator)	Overall bias
			vs. web-only 72 vs. usual care 85 at 12 months)			
	Distress	Aubin 2021	Nonsurgical lung cancer (39 vs. 38 at 18 months)	HADS (every 3 months until 18 months)	No significant difference (p=0.39)	High
		Berezowska 2021	Newly diagnosed cancer (33 vs. 38 with all times)	Distress thermometer (1, 3, 5 months)	No significant difference (p>0.05)	High
		Edbrooke 2019	Inoperable lung cancer (38 vs. 34)	HADS (9 weeks, 6 months)	No significant differences (p>0.05)	High
		Yun 2020	Cancer survivors within 2 months of completing primary cancer treatment (nurse-led 61 vs. web-only 72 vs. usual care 85) at 12 months	HADS (3, 6, 12 months)	Significant 12-month change in anxiety score from baseline favouring nurse-led intervention vs. usual care (difference = 1.89 points, p=0.045) No other significant differences were found	High
	Patient satisfaction with nursing	Liu 2020	After radical surgery for lung cancer (53 vs. 53)	Self-made nursing satisfaction questionnaire (1 month)	Nursing satisfaction higher in nurse-led intervention (96%)	High

Comparisons	Outcomes	Studies	Populations Sample sizes (intervention vs. comparator)	Measurement tools (assessment times) or Follow-up or Type of vaccine	Results (intervention vs. comparator)	Overall bias
					than usual care (75%) p=0.002	
		Moore 2002	Lung cancer completed initial treatment (75 vs. 71)	Newcastle satisfaction with nursing scales (3, 6, 12 months)	Overall support rated higher in nurse-led group than usual care at 3 & 6 months (p<0.05), no difference at 12 months	High
		Perfors 2022	Curatively treated for breast, lung, colorectal, gynecologic cancer or melanoma (30 vs. 24)	Adjusted EORTC-INPATSAT 32 (up to 12 months after inclusion)	No difference concerning experience or knowledge, availability, attention and willingness	High
		Su 2019	Advanced lung cancer (120 vs. 120)	Not reported	Nursing satisfaction higher in nurse-led intervention (93%) than usual care (80%) (p<0.05)	High
		Wang 2022	Postoperative advanced NSCLC (not reported)	Consumer Assessment of Healthcare Providers and Systems General Survey satisfaction of provider item (over a 5-year period)	High-quality nursing increased satisfaction compared with normal nursing group (p<0.05)	High

Comparisons	Outcomes	Studies	Populations Sample sizes (intervention vs. comparator)	Measurement tools (assessment times) or Follow-up or Type of vaccine	Results (intervention vs. comparator)	Overall bias
		Yu 2022	Received chemotherapy for lung cancer (35 vs. 35)	Self-made nursing satisfaction questionnaire (not reported)	Nursing satisfaction higher in nurse-led intervention (94%) than usual care (66%) (p<0.05)	High
	Hospital visits	Aubin 2021	Nonsurgical lung cancer (39 vs. 38 at 18 months)	Hospitalizations and visits to the emergency department as found in patients' medical files (every 3 months until 18 months)	At 3 months, fewer visits for nurse-led intervention (hospitalizations: 17% vs. 29% (p=0.05), emergency department: 24% vs. 36%, (p=0.05) No other differences were found at other time points	High
		Moore 2002	Lung cancer completed initial treatment (76 vs. 79)	Admissions to hospital or hospice (3, 6, 12 months)	No significant difference at 3 months (p>0.99) Other times not reported	High
		Perfors 2022	Curatively treated for breast, lung, colorectal, gynecologic cancer or melanoma (77 vs. 77)	Electronic Medical Records registrations in hospital (up to 12 months after inclusion)	Intervention group had significantly higher emergency department visits (RR: 1.9 [95% CI, 1.01 to 3.45]; p=0.04) compared with control group	High

Comparisons	Outcomes	Studies	Populations Sample sizes (intervention vs. comparator)	Measurement tools (assessment times) or Follow-up or Type of vaccine	Results (intervention vs. comparator)	Overall bias
PRO tools vs. usual care/control/no monitoring	Overall survival	Billingy 2023 Abstract	NSCLC (249 vs. 266)	Median follow-up duration was 12 months	No significant differences of interventions compared with usual care (active: HR 0.80, 95% CI, 0.55 to 1.15, reactive: HR 0.69, 95% CI, 0.42 to 1.15)	High
		Denis 2019	Advanced lung cancer (60 vs. 61)	Two years of follow-up	69 deaths (29 vs. 40) p=0.03 HR 0.59 (95% CI, 0.37 to 0.96), median OS (22.5 vs. 14.9 months) without censoring for crossover HR 0.50 (95% CI, 0.31 to 0.81), p=0.005, median OS (22.5 vs. 13.5 months) with censoring for crossover	High
		Friis 2023 Abstract	Stage III-IV lung cancer treated with palliative intent (239 vs. 254)	Median follow-up of 2.6 years	No significant improvement, HR 0.93 (95% CI, 0.75 to 1.16, p=0.54)	High
		Geerse 2017	Lung cancer (110 vs. 113)	Follow-up was until death or at least 25 weeks	153 deaths (73 vs. 80) p=0.62, median OS (10.3 95% CI, 6.5 to 14.1 vs. 10.1 95% CI, 7.6 to 12.6 months)	Some

Comparisons	Outcomes	Studies	Populations Sample sizes (intervention vs. comparator)	Measurement tools (assessment times) or Follow-up or Type of vaccine	Results (intervention vs. comparator)	Overall bias
		Noronha 2023 Abstract	Advanced lung cancer planned for palliative intent therapy (75 vs. 75)	Median follow-up of 6.4 months	6-month was 66% (SE, 0.057) vs. 68.1% (SE, 0.056) (p=0.343)	High
	Progression-free survival	Billingy 2023 Abstract	NSCLC (249 vs. 266)	Median follow-up duration was 12 months	No significant difference between active intervention group compared with usual care (HR 0.78 95% CI, 0.58 to 1.04)	High
		Denis 2017	Advanced lung cancer (60 vs. 61)	Median follow-up 9 months	No significant difference (p=0.13)	High
	Quality of life	Cooley 2022	Advanced lung cancer (151 at 2 months, 131 at 4 months, 125 at 6 months)	Trial Outcome Index subscales (2, 4, 6 months)	No significant differences (p≥0.05)	High
		Dai 2022	Lung cancer (65 vs. 69)	SIQOL (4 weeks after discharge)	No significant difference (adjusted mean difference, -0.10, 95% CI, -0.85 to 0.65, p=0.790)	Low
		Denis 2017	Advanced lung cancer (31 vs. 29)	FACT (6 months)	Significantly more stable or improved scores for intervention (80.6% vs. 58.6%, p=0.04)	High
		Friis 2023 Abstract	Stage III-IV lung cancer treated	EORTC-QoL-30 (every 2 months)	No clinically meaningful effects	High

Comparisons	Outcomes	Studies	Populations Sample sizes (intervention vs. comparator)	Measurement tools (assessment times) or Follow-up or Type of vaccine	Results (intervention vs. comparator)	Overall bias
			with palliative intent (239 vs. 254)		were found. For physical functioning, mean overall change from baseline was 3.1 points (95% CI, 0.1 to 6.2, p=0.043), for pain, -3.9 points (95% CI; -8.4 to 0.7, p=0.096)	
		Geerse 2017	Lung cancer (61 vs. 50)	EORTC-QLQ-C30, European Quality of Life 5-Dimensions questionnaire (EQ-5D) (25 weeks)	No significant differences (p>0.05)	High
		Kuo 2020	Advanced NSCLC (44 vs. 51)	eLCSS-QL (up to 12 months follow-up)	No significant difference (p=0.19)	High
		Mills 2009	Advanced lung cancer (28 vs. 25)	FACT (4 months)	No significant difference in Trial Outcome Index subscale (p=0.10) Significant decreases in quality of life over time for intervention compared with control in FACT-L (p=0.04) and FACT-G (p=0.04)	High
		Nimako 2017	Lung cancer (42 vs. 45)	EORTC QLQ-C30 (6 weeks)	No significant difference (p>0.05)	High
		Noronha 2023 Abstract	Advanced lung cancer planned	FACT-L (baseline & every 12 weeks)	Trial Outcome index improved by at least 5	High

Comparisons	Outcomes	Studies	Populations Sample sizes (intervention vs. comparator)	Measurement tools (assessment times) or Follow-up or Type of vaccine	Results (intervention vs. comparator)	Overall bias
			for palliative intent therapy (75 vs. 75)		points from baseline in 34 (58.6%) patients in intervention arm, vs. 32 (56.1%) in control arm (p=0.788). Mean Trial Outcome Index increased by 7.76 points in intervention arm vs. 10.85 points in control arm (p=0.257), effect size = -1.41. Mean quality of life score increased by 7.21 points in intervention group vs. 13.68 points in control group (p=0.160), effect size = 1.17	
		Schofield 2013	Lung or pleural cancer (55 vs. 53)	EORTC QLQ-C30 (8, 12 weeks)	No differences (p-value not reported)	High
	Distress	Friis 2023 Abstract	Stage III-IV lung cancer treated with palliative intent (239 vs. 254)	HADS (every 2 months)	No clinically meaningful effects were found. For HADS-anxiety, mean overall change from baseline was, -0.5 points (95% CI, -1.0 to 0.0 (p=0.070)	High
		Geerse 2017	Lung cancer (61 vs. 50)	HADS (25 weeks)	No significant differences (p>0.05)	High

Comparisons	Outcomes	Studies	Populations Sample sizes (intervention vs. comparator)	Measurement tools (assessment times) or Follow-up or Type of vaccine	Results (intervention vs. comparator)	Overall bias
		Schofield 2013	Lung or pleural cancer (55 vs. 53)	HADS (8, 12 weeks)	No differences (p-value not reported)	High
		Yount 2014	Advanced lung cancer (77 vs. 87)	Symptom Distress Scale (12 weeks)	No significant difference (p=0.505)	High
	Patient satisfaction	Cleeland 2011	Lung cancer or lung metastasis (38 vs. 41)	Not reported (4 to 6 weeks after discharge)	Intervention group found symptom recording system more comfortable (9.4 vs. 8.4, p<0.03) and easier to use (9.7 vs. 8.8, p<0.01) than control group	High
		Dai 2022	Lung cancer (56)	Trial-specific survey (4 weeks after discharge)	In the intervention group, 96.4% of patients thought that the PRO-based symptom management approach was helpful.	Low
		Geerse 2017	Lung cancer (61 vs. 50)	PSQ-III (25 weeks)	No significant difference (p>0.05)	High
		Mills 2009	Advanced lung cancer (25 vs. 23)	Trial-specific questionnaire (4 months)	No significant differences (p>0.05)	High
		Yount 2014	Advanced lung cancer (77 vs. 87)	FACIT-TS-PS (12 weeks)	No significant difference on total FACIT-TS-PS score Intervention group had lower satisfaction on Comprehensive	High

Comparisons	Outcomes	Studies	Populations Sample sizes (intervention vs. comparator)	Measurement tools (assessment times) or Follow-up or Type of vaccine	Results (intervention vs. comparator)	Overall bias
					Care (p=0.012) and Decision Making (p=0.027) subscales	
	Health care provider satisfaction	Dai 2022	Lung cancer (5)	Trial-specific survey (4 weeks after discharge)	Acceptability of the PRO-based symptom management approach among the surgeons was high, with a minimum median score of 8 on 0-to-10-point scale	Low
COVID-19 vaccination in patients with cancer vs. in patients without cancer	COVID-19 infection	Becerril-Gaitan 2022	Cancer (complete: 2274 vs. 733, partial: 577 vs. 400)	mRNA vaccines	Increased COVID-19 infection for cancer patients compared with controls after complete (RR 2.04, 95% CI, 0.38 to 11.10) and partial (RR 3.21, 95% CI, 0.35 to 29.04) COVID-19 immunization	Moderate using ROBINS-I
	Seroconversion	Sakuraba 2022	Cancer (520 vs. 189)	mRNA vaccines	Solid tumour cancers had lower seroconversion compared with controls OR 0.24, 95% CI, 0.062–0.90 (p=0.035)	Low using Joanna Briggs Institute Critical Appraisal Checklist
	Adverse events	Cavanna 2021	Cancer (not reported)	mRNA vaccines	Mostly mild and moderate adverse	Low

Comparisons	Outcomes	Studies	Populations Sample sizes (intervention vs. comparator)	Measurement tools (assessment times) or Follow-up or Type of vaccine	Results (intervention vs. comparator)	Overall bias
			See Table 3		effects were reported. No grade 3-4 adverse events were reported.	
Influenza (vaccine vs. no vaccine)	All-cause mortality	Bitterman 2018	Cancer (observational: 626 vs. 951, RCT: 40 vs. 38)	Inactivated or recombinant influenza vaccines	No significant differences Observational: Adjusted OR for death 0.88 (95% CI, 0.78 to 1.00) RCT: OR for death 1.25 (95% CI, 0.43 to 3.62)	High*
	Influenza infection	Bitterman 2018	Cancer (40 vs. 38)	Inactivated or recombinant influenza vaccines	Lower infection, but not significant, with vaccination OR 0.69 (95% CI, 0.14 to 3.31)	High*
	Hospitalization	Bitterman 2018	Cancer (25 vs. 25)	Inactivated or recombinant influenza vaccines	Significantly lower rate of hospitalizations in vaccinated participants OR 0.09 (95% CI, 0.02 to 0.49)	High*
	Immune response	Bitterman 2018	Cancer (40 vs. 38)	Inactivated or recombinant influenza vaccines	Vaccinated group had significantly higher geometric mean titres for influenza A/H1N1 ($p=0.03$) and A/H3N2 ($p<0.001$) viruses, but not for influenza B virus ($p=0.07$).	High*

Comparisons	Outcomes	Studies	Populations Sample sizes (intervention vs. comparator)	Measurement tools (assessment times) or Follow-up or Type of vaccine	Results (intervention vs. comparator)	Overall bias
	Adverse events	Bitterman 2018	Cancer (not reported)	Inactivated or recombinant influenza vaccines	25% and 60% of vaccinated groups had local or mild adverse events. 3% reported fever in one study.	High*
Pneumococcal vaccination in patients with cancer vs. in patients without cancer	Immune response	La Torre 2016	Hematological malignancies (not reported)	14-valent, 23-valent polysaccharide, 7-valent conjugate and 13-valent conjugate	Found a worse response in hematologic patients than in healthy controls or patients with other pathologies	High using Newcastle-Ottawa Scale or the Jadad scale
Smoking cessation intervention vs. usual care/placebo	Smoking abstinence	Mujcic 2022	Cancer (83 vs. 82)	Self-reported smoking abstinence (6 months)	No significant difference at 6 months, 28% vs. 26% (p=0.6, OR=0.47, 95% CI, 0.03 to 7.86)	High
		Ostroff 2014	Cancer (95 vs. 87)	Biochemically verified smoking abstinence (hospital admission, 3 months, 6 months posthospitalization)	No significant difference at 6 months, 32% for both groups (p=1.0, OR=1.028, 95% CI, 0.525 to 2.012) No significant difference at 3 months, 36% vs. 34% (p=0.878, OR=0.944, 95% CI, 0.490 to 1.816) No significant difference at admission, 45% for both groups (p=1.0 by	Low

Comparisons	Outcomes	Studies	Populations Sample sizes (intervention vs. comparator)	Measurement tools (assessment times) or Follow-up or Type of vaccine	Results (intervention vs. comparator)	Overall bias
					Fisher's test, OR=0.987, 95% CI, 0.530 to 1.839)	
		Park 2020	Cancer (148 vs. 135)	Biochemically verified smoking abstinence (3 and 6 months)	Significantly different at 6 months, 34.5% vs. 21.5% (p<0.2, OR=1.92, 95% CI, 1.13 to 3.27) Significantly different at 3 months, 31.1% vs. 20.7% (p=0.048, OR=1.72, 95% CI, 1.00 to 2.96)	Low
		Schnoll 2010	Cancer (114 vs. 132)	Biochemically verified smoking abstinence (12 and 27 weeks)	No significant difference at 27 weeks, 18.4% vs. 17.4% (p=0.64, OR=1.36, 95% CI, 0.38 to 4.81) No significant difference at 12 weeks, 27.2% vs. 24.2% (data not reported)	Some
		Schnoll 2005	Lung or head and neck cancer (49 vs. 55 at 1 month, 44 vs. 51 at 3 months)	Self-reported smoking abstinence (1 and 3 months)	No significant difference at 3 months, 43.2% vs. 39.2% (p=0.835, OR=0.821, 95% CI, 0.327 to 2.066)	High

Comparisons	Outcomes	Studies	Populations Sample sizes (intervention vs. comparator)	Measurement tools (assessment times) or Follow-up or Type of vaccine	Results (intervention vs. comparator)	Overall bias
					No significant difference at 1 month, 44.9% vs. 47.3% (p=0.846, OR=1.065, 95% CI, 0.450 to 2.518)	
		Schnoll 2003	Cancer (208 vs. 210 at 6 months, 203 vs. 206 at 12 months)	Self-reported smoking abstinence (6 and 12 months)	No significant difference at 12 months, 13.3% vs. 13.6% (p=0.52) No significant difference at 6 months, 14.4% vs. 11.9% (p=0.27)	High
		Simmons 2020	Cancer (size not reported per group)	Self-reported smoking abstinence (2, 6 and 12 months)	No significant difference at 12 months, 67.5% vs. 62.7% (p=0.384, OR=1.24, 95% CI, 0.77 to 2.00) No significant difference at 6 months, 68.8% vs. 64.8% (p=0.300, OR=1.27, 95% CI, 0.81 to 2.00) No significant difference at 2 months, 75.0% vs. 71.5% (p=0.202, OR=1.37, 95% CI, 0.85 to 2.23)	High

Comparisons	Outcomes	Studies	Populations Sample sizes (intervention vs. comparator)	Measurement tools (assessment times) or Follow-up or Type of vaccine	Results (intervention vs. comparator)	Overall bias
		Wakefield 2004	Cancer (74 vs. 63)	Biochemically verified smoking abstinence (6 months)	No significant difference at 6 months for 7-day abstinence, 7% vs. 6% (p=1.00) No significant difference at 6 months for 3-month abstinence, 5% vs. 6% (p=1.00)	Some
		Weaver 2015 abstract	Cancer (size not reported by group)	Self-reported smoking abstinence (12 and 24 weeks)	No significant differences at 12 or 24 weeks, 15% vs. 13% (p=0.65)	High
	Quality of life	Mujcic 2022	Cancer (83 vs. 82)	EQ-5D-5L (12 months?)	No significant difference 0.75 (SD 0.18) vs. 0.78 (SD 0.15) (B=−0.03, SE 0.03; p=0.26)	High
		Schnoll 2010	Cancer (114 vs. 132)	SF-12 (week 5?)	No significant effects of bupropion on changes in withdrawal (p=0.39), negative (p=0.41) and positive (p=0.77) affect, and physical (p=0.31) and mental (p=0.42) quality of life	High
	Medication adverse events	Park 2020	Cancer (148 vs. 135)	Self-reported (at each weekly/biweekly	Most common: nausea (13 vs. 6), rash (4 vs. 1), hiccups (4 vs. 1), mouth irritation (4 vs.	High

Comparisons	Outcomes	Studies	Populations Sample sizes (intervention vs. comparator)	Measurement tools (assessment times) or Follow-up or Type of vaccine	Results (intervention vs. comparator)	Overall bias
				session over 2 months)	0), difficulty sleeping (3 vs. 2), vivid dreams (3 vs. 2)	
		Schnoll 2010	Cancer (114 vs. 132)	32-item side-effects checklist from bupropion and transdermal nicotine (week 5)	No significant differences in total (p=0.80) or individual (e.g., headache, nausea, seizures) side effects	High
Exercise training vs. usual care or no exercise	Adverse events	Cavalheri 2019	NSCLC after surgery 202 (4 RCTs)	Follow-up not reported	Three of these four studies reported no adverse events, whereas one reported a hip fracture during balance training	Moderate
	General health-related quality of life	Cavalheri 2019	NSCLC after surgery 208 (4 RCTs)	SF-36 - physical and mental component scores	Mean difference 5.02 higher (2.3 higher to 7.73 higher) for exercise group for physical component score Mean difference 2.32 lower (11.26 lower to 6.62 higher) for exercise group for mental component score	Low
	Dyspnea	Cavalheri 2019	NSCLC after surgery 110 (3 RCTs)	EORTC QLQC30 Dyspnea and VAS Dyspnea	Standardized mean difference 0.43 lower (0.81 lower to 0.05	Very low

Comparisons	Outcomes	Studies	Populations Sample sizes (intervention vs. comparator)	Measurement tools (assessment times) or Follow-up or Type of vaccine	Results (intervention vs. comparator)	Overall bias
					lower) for exercise group	
	Fatigue	Cavalheri 2019	NSCLC after surgery 68 (3 RCTs)	FACIT fatigue or fatigue component score of the EORTC QLQ-C30	Standardized mean difference 0.05 lower (0.52 lower to 0.43 higher) for exercise group	Not reported
	Anxiety and depression	Cavalheri 2019	NSCLC after surgery Not reported (1 RCT)	HADS	No significant difference between the intervention and control groups in feelings of anxiety (mean ± SD intervention group: 3 ± 2 points to 5 ± 4 points and control group: 2 ± 2 points to 4 ± 5 points; p=0.17) and depression (mean ± SD intervention group: 2 ± 2 points to 4 ± 5 points and control group: 3 ± 3 points to 4 ± 3 points; p=0.40)	Not reported

Abbreviations: CI, confidence interval; eLCSS-QL, Electronic Lung Cancer System Scale for Quality of Life; EORTC, European Organization for Research and Treatment of Cancer; EORTC-INPATSAT 32, European Organization for Research and Treatment of Cancer in-patient satisfaction with cancer care questionnaire; EQ-5D-5L, EuroQol-5 Dimension-5 Levels; FACIT, Functional Assessment of Chronic Illness Therapy; FACIT-TS-PS, Functional Assessment of Chronic Illness Therapy-Treatment Satisfaction-Patient Satisfaction; FACT, Functional Assessment of Cancer Therapy; FACT-G, Functional Assessment of Cancer Therapy-General; FACT-L, Functional Assessment of Cancer Therapy-Lung; HADS, Hospital anxiety and depression scale; HR, hazard ratio; mRNA,

messenger ribonucleic acid; NSCLC, non-small cell lung cancer; OR, odds ratio; OS, overall survival; PRO, patient-reported outcome; PSQ-III, Patient Satisfaction Questionnaire-III; QLQ-C30, EORTC Core Quality of Life questionnaire; RCT, randomized controlled trial; ROBINS-I, Risk of Bias in Non-randomized Studies - of Interventions; RR, risk ratio; SD, standard deviation; SE, standard error; SF-36, Medical Outcomes Study Short Form 36 General Health Survey; SIQOL, single-item quality of life; VAS, visual analogue scale; vs, versus

* Using Cochrane's tool for assessing risk of bias or an Adapted Newcastle-Ottawa Scale

Appendix 11: Ongoing or Unpublished Trials
Searched clinicaltrials.gov on July 18, 2023, with the following keyword: lung cancer

Study Title ID
Web-based Symptom Monitoring and Survival in Advanced Stage Lung Cancer (LUCA-S) NCT05621902
Implementation of Smoking Cessation Support During Lung Cancer Workup NCT05192031
The Effect of Interventional Pulmonary Rehabilitation Exercise with Advanced Lung Cancer NCT05279521
Impact of Telemonitoring for the Management of Side Effects in Patients With Melanoma, Lung or Renal Cancer, Treated With Immunotherapy Combination of Nivolumab and Ipilimumab (MONITOR) NCT04605146
Improving Supportive Care For Patients With Thoracic Malignancies NCT03216109
Effectiveness of an Enhanced Tobacco Intervention Protocol Compared to Standard Treatment in Helping Head and Neck and Lung Cancer Patients Starting Treatment to Reduce Cigarette Use NCT04694846
Immunization With IMM-101 vs Observation for Prevention of Respiratory and Severe COVID-19 Related Infections in Cancer Patients at Increased Risk of Exposure (COV-IMMUNO) NCT04442048
SARS-CoV-2 Vaccine (COH04S1) Versus EUA SARS-COV-2 Vaccine for the Treatment of COVID-19 in Patients With Blood Cancer NCT04977024
A Vaccine Booster (GEO-CM04S1) for the Prevention of COVID-19 in Patients With Chronic Lymphocytic Leukemia NCT05672355
Bringing Optimised COVID-19 Vaccine Schedules To ImmunoCompromised Populations (BOOST-IC): an Adaptive Randomised Controlled Clinical Trial NCT05556720