Clinical practice guidelines for the prevention and diagnosis of lung cancer

Please note there are further questions under development for this guideline and they will be released for public consultation and published in a staged approach. To be notified about updates, please email guidelines (at) cancer.org.au.

See also: Clinical practice guidelines for the treatment of lung cancer.

5 Diagnosis and staging

- When is IHC required for subtyping of NSCLC and what is the optimal IHC panel?
- What specimen types are suitable for mutation testing in NSCLC patients?
- In people undergoing lung cancer evaluation, does concurrent diagnosis and staging provide greater benefit for patient outcomes compared to sequential testing for diagnosis followed by staging?
- For patients undergoing workup for known or suspected lung cancer, what is the optimal timing of PET/CT? Before or after tissue biopsy confirmation?

6 Follow up

- Does routine follow-up improve patient outcomes in people who have curative intent treatments for lung cancer?
- What are the optimal follow-up tests for people with lung cancer who have had curative intent treatment?
- What is the optimal model (provider) of care for the follow up of people with lung cancer who have had curative intent treatment?

6.1 Questions under development

- What is the most effective way to manage small solid, sub-solid and non-solid nodules?
- For suspected lung cancer in the periphery of the lung (peripheral pulmonary lesions), what is the most effective diagnostic modality?

6.2 Appendices

- Guideline development process
- List of clinical questions
- Working party members and contributors
- Conflict of interest register

6.3 Further information for health professionals

Investigating symptoms of lung cancer: a guide for all health professionals

6.4 Information for consumers

Understanding Lung Cancer

Back to top

1 Foreword

1.1 Clinical practice guidelines for the diagnosis of lung cancer (screening draft guidelines)

1.1.1 Foreword

This work consolidates the internationally unique, wiki-based revision of the 2004 first Australian evidence-based “Clinical guidelines for the prevention, diagnosis and management of lung cancer” paperback format with endorsement by the National Health and Medical Research Council.

The work, initially commissioned by Cancer Australia (CA), was undertaken by the CCA to develop a sustainable web-based wiki platform with revised guidelines for the treatment of lung cancer with the first phase being restricted to the treatment of non-small cell and small cell lung cancer (chapters 5 and 6 respectively of the 2004 version) and supporting the patient and palliative care (chapters 4, 7 and 8), now publicly available and widely used at Clinical practice guidelines for the treatment of lung cancer.

The success of the treatment recommendations in guiding clinical practice in Australia has now enabled CCA to move to the second phase, addressing topics of prevention, screening, diagnosis and assessment. To kick off this next phase, we present 3 draft guidelines pertaining to the screening of lung cancer, timely given the increasing interest in low dose CT (LDCT) screening around the world based on the pivotal NLST trial.

Specifically, the multidisciplinary working group, including consumers and New Zealand participation, has carefully examined the evidence for 3 focused questions:

- In people at risk of lung cancer, does population based screening with chest radiography reduce mortality?
- In people at risk of lung cancer, does population based CT screening reduce mortality?
- Which population group would potentially most benefit from CT screening for lung cancer?

As with other wiki guidelines, despite an extensive and rigorous review progress, these online resources will not be final, and as intended represent a living and evolving document, suitable for interactive comment and debate, in addition to the guideline writing tradition of modification to learn from emerging evidence. We have targeted this guidance for practice in Australia, and expect that the evidence base and therefore their clinical implications may be similarly applied in New Zealand.

Consequently, we invite readers and stakeholders, who become aware of new evidence to create a personal account on the wiki and contribute comment online, so that their views are duly considered by the public and to enable the working party to consider any subsequent changes or refinement to the recommendations.

Further work on this second phase of the Australian diagnostic and evaluation lung cancer wiki guidelines will continue, with the areas of prevention, diagnosis and assessment to be considered next.

We sincerely hope the wiki will be an accessible up-to-date resource for multi-disciplinary teams, individual clinicians, students and consumers, and look forward to your feedback and discourse.

I thank the CCA for intense backroom work that underpins these guidelines, this output is only achieved by an enormous amount of support from the project team at CCA; Jutta von Dincklage, Laura Wuellner, Emma Dickins, Christine Vuletich and Clara Ha, working closely with members of the working party who have given up weekends and evenings to contribute their expertise to help address the heavy burden of lung cancer in Australia.

Professor Kwun Fong

Chair, Cancer Council Australia Lung Cancer Prevention and Diagnosis Guidelines Working Party

2 Summary of recommendations

2.1 Summary of recommendations

This page provides a summary of the recommendations in the published guidelines.

This guideline includes evidence-based recommendations (EBR), consensus-based recommendations (CBR) and practice points (PP) as defined in the table below. Recommendations and practice points were developed by working party members and sub-committee members.

Each EBR was assigned a grade by the expert working group, taking into account the volume, consistency, generalisability, applicability and clinical impact of the body of evidence according to NHMRC Level and Grades for Recommendations for Guidelines Developers.[1]

2.1.1 NHMRC approved recommendation types and definitions

Type of recommendation	Definition
Evidence-based recommendation	A recommendation formulated after a systematic review of the evidence, indicating supporting references
Consensus-based recommendation	A recommendation formulated in the absence of quality evidence, after a systematic review of the evidence was conducted and failed to identify admissible evidence on the clinical question
Practice point	A recommendation on a subject that is outside the scope of the search strategy for the systematic review, based on expert opinion and formulated by a consensus process

Source: National Health and Medical Research Council. Procedures and requirements for meeting the NHMRC standard for clinical practice guidelines. Melbourne: National Health and Medical Research Council, 2011

You may also like to refer to the Guideline Development Handbook for details on the levels of evidence and recommendation grades.

2.2 Recommendations

2.2.1 Screening and early detection

2.2.2 In people at risk of lung cancer, does population based screening with chest radiography reduce mortality?

Evidence-based recommendation	Grade
Chest radiography is not recommended for lung cancer screening in asymptomatic individuals.	**A**

Back to top

2.2.3 In people at risk of lung cancer, does population based CT screening reduce mortality?

Evidence-based recommendation	Grade
There is insufficient evidence to recommend population-based CT Screening.* * Despite the existing evidence from North America that computed tomography (CT) screening can reduce lung cancer specific and all-cause mortality in some people at high risk for lung cancer, current uncertainties including the generalisability of this international trial result to the Australian setting, the lack of local cost effectiveness evidence, and concerns as how best to implement a safe and effective screening program in Australia, mean that the available evidence is insufficient to recommend population based CT screening in Australia at the current time.	**B**

Back to top

2.2.4 Which population group would potentially most benefit from CT screening for lung cancer?

Evidence-based recommendation	Grade
CT scans for the early detection of lung cancer in asymptomatic individuals should only be considered in those at high risk of lung cancer and who meet the following minimum criteria: aged 55-74 with heavy smoking histories (at least 30 pack years, current or former smokers who have quit within the prior 15 years).* *See the section on population-based CT screening for more information.Available evidence is insufficient to recommend populated based CT screening.	**C**

Practice point
Current evidence does not support population-based screening with CT scanning. For the asymptomatic individual at high risk for lung cancer who is considering a CT scan to detect early lung cancer, it is recommended that they discuss any potential benefits against the potential harms of a low dose CT scan with their GP.

Back to top

2.2.5 Diagnosis and staging

2.2.6 When is IHC required for subtyping of NSCLC and what is the optimal IHC panel?

Evidence-based recommendation	Grade
A small panel of IHC markers should be used to subtype morphologically undifferentiated NSCLC in small biopsy and cytology samples, with 2 markers usually sufficient (1 adenocarcinoma marker and 1 squamous marker).	**C**

Practice point

IHC to assist in subtyping NSCLC is only required when there is no morphological evidence of glandular or squamous differentiation.The optimal panel of IHC markers is not clear from the literature with many studies using a different range of markers (eg TTF-1, Napsin A, CK5, CK5/6, p40, p63, CK7, surfactant protein A, as well as histochemical markers for mucin such as PAS.) The WHO Classification of Tumours of the Lung (Travis WD et al 2015) recommends using only one squamous marker (ie p40, p63 or CK5/6) and one adenocarcinoma marker (TTF-1 or a histochemical stain for mucin) so as to preserve tissue for molecular testing in the setting of a small biopsy showing a non-small cell carcinoma lacking definite squamous or glandular morphology.

Practice point

It is advisable to limit the number of IHC markers used to 2 so as to preserve tissue for molecular testing if required (1 adenocarcinoma marker such as TTF1, and 1 squamous marker such as p40).

Practice point

In some instances, IHC may also be needed to help determine if the tumour is of lung origin or a metastasis. Clinicopathological correlation and multidisciplinary team meeting discussion can often assist in excluding the possibility of a metastasis to the lung in the setting of a solitary lung lesion, and can help avoid unnecessary use of IHC markers and thereby preserve tissue for molecular testing. IHC markers are not useful in distinguishing primary from metastatic disease in the case of a squamous cell carcinoma in the lung.

Back to top

2.2.7 What specimen types are suitable for mutation testing in NSCLC patients?

Evidence-based recommendation	Grade
Any tumour sample can be used for mutation testing (sample from primary or metastatic site; histology or cytology sample).	**C**

Practice point

It is advisable to use the optimal specimen available from each patient for mutation testing (if more than one specimen is available). This would be the specimen with the highest content and proportion of tumour cells and could be a histology specimen such as a core biopsy or a cytology specimen. This should be determined on a case by case basis by a pathologist.

Back to top

2.2.8 In people undergoing lung cancer evaluation, does concurrent diagnosis and staging provide greater benefit for patient outcomes compared to sequential testing for diagnosis followed by staging?

Consensus-based recommendation

In suspected lung cancer, where possible, clinicians should select a first diagnostic procedure which can provide diagnosis and staging concurrently. However, other considerations include the safety of each test for an individual patient, and the need to obtain an adequate sample for required pathological testing. CT PET scanning should be obtained prior to endobronchial/endoscopic ultrasound in potentially curative cases.

Back to top

2.2.9 For patients undergoing workup for known or suspected lung cancer, what is the optimal timing of PET/CT? Before or after tissue biopsy confirmation?

Practice point

In the absence of evidence to guide optimal timing of PET/CT in the workup of known or suspected lung cancer (NSCLC) it is advisable to:

1. Offer PET/CT to all patients who are considered for curative therapy.
2. Consider the use of PET/CT prior to biopsy in order to guide biopsy as well as to stage disease.
3. Consider the use of PET/CT at any stage in order to evaluate the extent of metastatic disease.
4. Consider the use of "flat-top" table position for PET/CT as this is the radiotherapy planning position; this may avoid the need for a second scan to plan for radiotherapy.

Back to top

2.2.10 For patients undergoing workup for known or suspected lung cancer, what is the optimal timing of PET/CT? Before or after tissue biopsy confirmation?

Practice point
In the absence of evidence to guide optimal timing of PET/CT in the workup of known or suspected lung cancer (NSCLC) it is advisable to: 1. Offer PET/CT to all patients who are considered for curative therapy. 2. Consider the use of PET/CT prior to biopsy in order to guide biopsy as well as to stage disease. 3. Consider the use of PET/CT at any stage in order to evaluate the extent of metastatic disease. 4. Consider the use of "flat-top" table position for PET/CT as this is the radiotherapy planning position; this may avoid the need for a second scan to plan for radiotherapy.

Back to top

2.2.11 Follow-up

2.2.12 Does routine follow-up improve patient outcomes in people who have curative intent treatments for lung cancer?

Evidence-based recommendation	Grade
It is recommended that patients undergoing curative treatment for lung cancer have regular follow up.	**D**

Evidence-based recommendation	Grade
It is recommended that patients undergo follow up after treatment for non-small cell carcinoma.	**D**

Practice point
It is advisable to utilise the many clinical guidelines available for follow up. There are no local Australian guidelines and the clinician may use the NICE guidelines.

Back to top

2.2.13 What are the optimal follow-up tests for people with lung cancer who have had curative intent treatment?

Evidence-based recommendation	Grade
Low dose CT should be considered as part of the protocol for follow up of lung cancer patients.	**C**

Evidence-based recommendation	Grade
Consideration should be given to including PET-CT in the follow up for detection of recurrences after 6 months.	**D**

Practice point
It is advisable to consider utilising PET-CT for follow up. There is no evidence to suggest a clear survival benefit even though the probability of detecting early recurrence is higher with PET-CT.

Practice point
PET-CT is not reimbursed for follow up of lung cancer patients.

Practice point
It is suggested that the use of PET-CT for follow up be initiated following discussion at a lung cancer multidisciplinary meeting (MDT).

Back to top

2.2.14 What is the optimal model (provider) of care for the follow up of people with lung cancer who have had curative intent treatment?

Evidence-based recommendation	Grade
A multidisciplinary approach to follow up is ideal, involving the treating specialists, family physician and clinical nurse specialists.	**C**

Evidence-based recommendation	Grade
It is recommended that a nurse specialist ideally be involved, as an member of the team, in the follow up team for patients receiving curative intent treatment for lung cancer.	**B**

Back to top

Back to top

2.3 References

1. ↑ National Health and Medical Research Council. *NHMRC levels of evidence and grades for recommendations for guideline developers.* Canberra: National Health and Medical Research Council; 2009 Available from: https://www.nhmrc.gov.au/_files_nhmrc/file/guidelines/developers/nhmrc_levels_grades_evidence_120423.pdf.

2.1 Chest radiography screening

Contents

2.1.1 Systematic Review Evidence

In the previous Australian lung cancer guidelines, it was noted that no forms of population screening for lung cancer, including regular chest radiography, with or without sputum cytology even in high-risk groups, have been shown to improve outcomes and screening is not recommended.

Since then a number of articles have been published (as linked) with two notable papers, the results of the PLCO (prostate, lung, colon and ovarian) cancer screening study of chest radiography in male and female subjects aged 55–74 years[1] and a high quality Cochrane Systematic Review by Manser et al.[2]

PLCO started in 1992, recruiting 154,901 participants, with 50% women and 45% never smokers; randomly assigned to screening or usual care.[1] The research question was whether annual single-view (posterior-anterior) chest radiograph reduced lung cancer mortality compared to usual care. Initially all participants randomised to screening were invited to receive a baseline and three annual chest x-ray screens; the protocol later changed to screen never-smokers only three times. Screening adherence was 86.6% at baseline and 79% to 84% at years 1 through 3; the rate of screening use in the usual care group was 11%.

Cumulative lung cancer incidence rates through 13 years of follow-up were 20.1 per 10 000 person-years in the intervention group and 19.2 per 10 000 person-years in the usual care group (rate ratio [RR]; 1.05, 95% CI, 0.98-1.12). At 13 years of follow-up, 1,213 lung cancer deaths were observed in the intervention group, compared with 1,230 lung cancer deaths in the usual-care group (mortality relative risk, 0.99; 95% CI, 0.87–1.22). Sub-analyses suggested no differential effect by sex or smoking status.

Some Investigators have suggested that a possible small benefit from chest radiography may be possible as the reporting time of PLCO may have been too late.[3] Also, a benefit, smaller than the 20% reduction in lung cancer mortality resulting from the 90% study power is not excluded. For instance, in higher risk PLCO participants matching the National Lung Screening Trial (NLST) criteria[1], an absolute reduction in the number of deaths was observed 316 versus 334 (rate ratio 0.94; with 95% CI 0.81 - 1.10).

The 2013 Cochrane Review is an updated version of the original review published in The Cochrane Library in 1999 and updated in 2004 and 2010.[2] The Authors reported that the meta-analysis of studies comparing different frequencies of chest x-ray screening, frequent screening with chest x-rays was associated with an 11% relative increase in mortality from lung cancer compared with less frequent screening (RR 1.11, 95% CI 1.00 to 1.23); noting though that several included had potential methodological weaknesses. Manser et al also observed a non-statistically significant trend to reduced lung cancer mortality with chest x-ray and sputum cytology was compared with chest x-ray alone (RR 0.88, 95% CI 0.74 to 1.03).[2]

Overall, the bulk and consistency of evidence, as well as the lack of significant benefit observed in the PLCO trial supports the conclusion that lung cancer screening with chest radiology does not reduce lung cancer mortality.

Back to top

2.1.2 Evidence summary and recommendations

Evidence summary	Level	References
There is no evidence to support reduced lung cancer mortality through screening for lung cancer with chest x-rays.	I	[2]

Evidence-based recommendation	Grade
Chest radiography is not recommended for lung cancer screening in asymptomatic individuals.	**A**

2.1.3 Research underway

The National Health and Medical Research Council (NHMRC) has recently funded an international multicentre trial (Australia-Canada) of risk stratification to improve the performance of lung cancer CT screening (the International Lung Screen Trial (ILST)), which will in the near future provide additional data likely to be highly relevant to screening in the Australian context.

Back to top

2.1.4 References

1. ↑ 1.0 1.1 1.2 Oken MM, Hocking WG, Kvale PA, Andriole GL, Buys SS, Church TR, et al. *Screening by chest radiograph and lung cancer mortality: the Prostate, Lung, Colorectal, and Ovarian (PLCO) randomized trial.* JAMA 2011 Nov 2;306(17):1865-73 Available from: http://www.ncbi.nlm.nih.gov/pubmed/22031728.
2. ↑ 2.0 2.1 2.2 2.3 Manser R, Lethaby A, Irving LB, Stone C, Byrnes G, Abramson MJ, et al. *Screening for lung cancer.* Cochrane Database Syst Rev 2013 Jun 21;6:CD001991 Available from: http://www.ncbi.nlm.nih.gov/pubmed/23794187.
3. ↑ Sagawa M, Nakayama T, Sobue T, JECS Study Group. *A different interpretation of the efficacy of lung cancer screening in the PLCO trial.* Eur J Epidemiol 2015 Jul 22 Available from: http://www.ncbi.nlm.nih.gov/pubmed/26197850.

Back to top

2.1.5 Appendices

View recommendation components	View pending evidence	View body of evidence	View literature search	View PICO

Back to top

2.1.1 Introduction

2.1.1.1 Introduction

Lung cancer is the leading cause of cancer death in Australia. Globally, 1.59 million deaths were due to lung cancer in 2012, by far the greatest single cause of cancer death.[1] The independent Council of Australian Governments (COAG) Reform Council highlighted lung cancer as one of six emerging areas of concern.[2] Despite overall incidence falling between 2007 and 2013, lung cancer rate among women has increased substantially, reinforcing the need for ongoing emphasis on prevention, early identification and treatment of this disease.

The advent of low dose computed tomography (LDCT) has provided an opportunity to detect lung cancers in its early stage, and the potential to reduce the overall mortality of lung cancer affected patients. This has generated much clinical and public interest in lung cancer screening. However, there is ongoing debate about the benefits and feasibility of screening and the topic remains controversial.

Only one high quality randomised control trial, NLST, demonstrated a reduction in lung cancer mortality from screening.[3]The American College of Radiology has taken the lead in setting standards in the US. Australian Government guidelines[4] call for robust governance for all screening programs, however the practicalities of this for lung cancer screening in Australia have yet to be established.

Aside from NLST, all other RCTs have been conducted in Europe and have either shown no mortality benefit or are yet to report mortality data. Only the NELSON trial is large enough to independently provide an answer on mortality. The European trials used different eligibility criteria to NLST and probably recruited slightly lower risk participants than NLST although all RCTs have included only current and former smokers.

Many expert bodies in North America, such as the U.S. Preventive Services Task Force (USPSTF)[5] and Centers for Medicare and Medicaid Services (CMS)[6], and some professional organisations in Europe, such as the ESR /ERS[7] now recommend screening. Lung cancer screening is now available in the U.S. where over 2000 U.S.

radiology providers have registered with The American College of Radiology (ACR) Lung Cancer Screening Registry™ to meet quality reporting requirements and receive Medicare CT lung cancer screening payments.[8] However, opinion in the US is not uniform; the U.S. Department of Veterans Affairs elected to conduct its own pilot program and the American Academy of Family Physicians[9] concluded that the evidence was insufficient to make a recommendation. Other experts are more conservative and do not recommend screening at the present time in their country or healthcare setting.[10] In addition, some guidelines adhere firmly to NLST inclusion criteria[11][12][13][14], others based on modelling and expert opinion, have broader inclusion criteria.[5][6][7][15] The International Association for the Study of Lung Cancer (IASLC) recognizes the difficulty generalising US results to non-US health settings and recommends each country/ health care setting comes to its own independent decision[16]. There are no high level implementation studies in the Australian context supporting population-based CT screening. Furthermore there are no recent Australian cost-effectiveness data; one Australian modelled study (pre-NLST) was circumspect in its conclusions.[17] For these reasons, the Australian Department of Health Standing Committee on Screening viewpoint is that screening cannot be adopted in Australia at the present time.[18]

It is clear that worldwide expert opinion differs on a) whether or not screening should be recommended and b) which criteria should be used to determine screening eligibility. This guideline does not attempt to make general lung cancer screening recommendations; rather it attempts to make recommendations that are specific to the *Australian situation at the current time*. Specifically to Australia, the potential cost and cost-effectiveness of screening in this country are unknown, the generalisability of NLST results outside of the US healthcare system are uncertain and the mechanisms to ensure high quality screening practice are lacking.

Although the situation pertaining to Australia is uncertain at present, this guideline will be regularly updated as new evidence becomes available. It is likely that the situation will become clearer as time moves on, and when the NELSON results are published. In this respect we offer evidence based guidance on whether population-based screening should be offered in Australia at the current time (In people at risk of lung cancer, does population based CT screening reduce mortality?) and if it were offered, who it would potentially benefit (In people at risk of lung cancer, does population based CT screening reduce mortality?) in the context of the current international and Australia-specific uncertainties. We also highlight research gaps that need addressing in the section "Issues requiring more clinical research study to address gaps in the Australian context".

2.1.1.2 Systematic review questions

Two clinical questions in regards to CT Screening were addressed via systematic review:

- In people at risk of lung cancer, does population based CT screening reduce mortality?
- Which population group would potentially most benefit from CT screening for lung cancer?

2.1.1.3 References

1. ↑ World Health Organisation. *Cancer fact sheet.* [homepage on the internet] World Health Organisation; [cited 2015 Feb 4; updated 2015 Feb]. Available from: http://www.who.int/mediacentre/factsheets/fs297/en/#.
2. ↑ COAG Reform Council. *Healthcare in Australia 2012-13: Five years of performance.* Sydney: COAG Reform Council; 2014 Available from: http://apo.org.au/files/Resource/coag_healthcare-in-australia-2012-13_2014.pdf.
3. ↑ Aberle DR, Adams AM, Berg CD, Black WC, Clapp JD, Fagerstrom RM, et al. *Reduced lung-cancer mortality with low-dose computed tomographic screening.* N Engl J Med 2011 Aug 4;365(5):395-409 Available from: http://www.ncbi.nlm.nih.gov/pubmed/21714641.
4. ↑ Australian Population Health Development Principle Committee Screening Subcommittee. *Population Based Screening Framework.* Canberra: Commonwealth of Australia; 2008 Available from: http://www.cancerscreening.gov.au/internet/screening/publishing.nsf/Content/lung-cancer-screening.
5. ↑ [5.0] [5.1] Moyer VA, U.S. Preventive Services Task Force. *Screening for lung cancer: U.S. Preventive Services Task Force recommendation statement.* Ann Intern Med 2014 Mar 4;160(5):330-8 Available from: http://www.ncbi.nlm.nih.gov/pubmed/24378917.
6. ↑ [6.0] [6.1] Centers for Medicare & Medicaid Services (CMS). *Decision Memo for Screening for Lung Cancer with Low Dose Computed Tomography (LDCT) (CAG-00439N).* [homepage on the internet]; 2015 Dec 1 Available from: https://www.cms.gov/medicare-coverage-database/details/nca-decision-memo.aspx?NCAId=274.
7. ↑ [7.0] [7.1] Kauczor HU, Bonomo L, Gaga M, Nackaerts K, Peled N, Prokop M, et al. *ESR/ERS white paper on lung cancer screening.* Eur Respir J 2015 Jul;46(1):28-39 Available from: http://www.ncbi.nlm.nih.gov/pubmed/25929956.
8. ↑ American College of Radiology (ACR). *LCSR Registrants as of November 28, 2016.* ACR; Available from: https://www.acr.org/~/media/ACR/Documents/PDF/QualitySafety/NRDR/Lung%20Cancer%20Screening%20Practice%20Registry/List%20of%20LCSR%20Participants.pdf.
9. ↑ American Academy of Family Physicians (AAFP). *AAFP Summary of Recommendations For Clinical Preventive Services.* AAFP; 2016 Dec Available from: http://www.aafp.org/dam/AAFP/documents/patient_care/clinical_recommendations/cps-recommendations.pdf.
10. ↑ Field JK, Baldwin D, Brain K, Devaraj A, Eisen T, Duffy SW, et al. *CT screening for lung cancer in the UK: position statement by UKLS investigators following the NLST report.* Thorax 2011 Aug;66(8):736-7 Available from: http://www.ncbi.nlm.nih.gov/pubmed/21724746.
11. ↑ Bach PB, Mirkin JN, Oliver TK, Azzoli CG, Berry DA, Brawley OW, et al. *Benefits and harms of CT screening for lung cancer: a systematic review.* JAMA 2012 Jun 13;307(22):2418-29 Available from: http://www.ncbi.nlm.nih.gov/pubmed/22610500.
12. ↑ Frauenfelder T, Puhan MA, Lazor R, von Garnier C, Bremerich J, Niemann T, et al. *Early detection of lung cancer: a statement from an expert panel of the Swiss university hospitals on lung cancer screening.* Respiration 2014;87(3):254-64 Available from: http://www.ncbi.nlm.nih.gov/pubmed/24458197.

13. ↑ Couraud S, Cortot AB, Greillier L, Gounant V, Mennecier B, Girard N, et al. *From randomized trials to the clinic: is it time to implement individual lung-cancer screening in clinical practice? A multidisciplinary statement from French experts on behalf of the French intergroup (IFCT) and the groupe d'Oncologie de langue francaise (GOLF).* Ann Oncol 2013 Mar;24(3):586-97 Available from: http://www.ncbi.nlm.nih.gov/pubmed/23136229.
14. ↑ Roberts H, Walker-Dilks C, Sivjee K, Ung Y, Yasufuku K, Hey A, et al. *Screening high-risk populations for lung cancer.* Toronto (ON): Cancer Care Ontario; 2013 Available from: https://www.cancercare.on.ca/common/pages/UserFile.aspx?fileId=287881.
15. ↑ NCCN. *National Comprehensive Cancer Network Guidelines. Version 2.* Fort Washington, PA, USA: National Comprehensive Cancer Network (NCCN); 2016.
16. ↑ Field JK, Aberle DR, Altorki N, Baldwin DR, Dresler C, Duffy SW, et al. *The International Association Study Lung Cancer (IASLC) Strategic Screening Advisory Committee (SSAC) response to the USPSTF recommendations.* J Thorac Oncol 2014 Feb;9(2):141-3 Available from: http://www.ncbi.nlm.nih.gov/pubmed/24419409.
17. ↑ Manser R, Dalton A, Carter R, Byrnes G, Elwood M, Campbell DA. *Cost-effectiveness analysis of screening for lung cancer with low dose spiral CT (computed tomography) in the Australian setting.* Lung Cancer 2005 May;48(2):171-85 Available from: http://www.ncbi.nlm.nih.gov/pubmed/15829317.
18. ↑ Department of Health Standing Committee on Screening.. *Position Statement: Lung Cancer Screening using Low-Dose Computed Tomography.* Canberra: Commonwealth of Australia; 2015 Available from: http://www.cancerscreening.gov.au/internet/screening/publishing.nsf/Content/lung-cancer-screening.

2.1.2 Population-based CT screening

Contents

2.1.2.1 Systematic Review Evidence

There is evidence that low dose computed tomography (LDCT) screening reduces lung cancer specific mortality and all-cause mortality in people at high risk of lung cancer. Evidence of lung cancer specific mortality reduction came from the National Lung Screening Trial (NLST) in the US which showed a 20% reduction, p=0.004[1] and also from a meta-analysis with a odds ratio of 0.84, 95% CI 0.74-0.96[2] using pooled data from four randomised trials, including NLST, Danish Lung Cancer Screening Trial (DLCST)[3][4], Detection and Screening of Early Lung Cancer by Novel Imaging Technology and Molecular Essays (DANTE trial)[5][6] and the Multicentric Italian Lung

Detection study (MILD study)[7]. Evidence of all-cause mortality reduction came from the largest and high quality NLST study alone, which has a study population of 53,434, with their results showing a reduction of 6.7%, p=0.02.[1] The other smaller randomised trials (DLCST, DANTE and MILD) each had study populations of fewer than 5000 and did not have sufficient statistical power to demonstrate a statistically significant all-cause mortality reduction.

There however remain uncertainties and ongoing questions about the generalisability of these international trial results, and the cost effectiveness of LDCT screening in the Australian context.[8][2][9] (see also CT Screening) How best to implement lung cancer screening outside a research environment is also uncertain.

The currently available evidence is therefore insufficient to recommend population based LDCT screening in Australia, and we await future local studies to clarify the efficacy, cost effectiveness and feasibility of implementing such screening program in an Australian setting (see also 'Which population group would most benefit from CT screening for lung cancer?'). We also await further results from the existing screening trials with longer follow up time and pooled analysis of European screening trials to provide a sample size with adequate power to confirm the mortality reduction from LDCT.

Back to top

2.1.2.2 Evidence summary and recommendations

Evidence summary	Level	References
Computed tomography (CT) screening reduces lung cancer specific mortality in high risk patients.	I, II	[1], [2]
Computed tomography (CT) screening slightly reduces all-cause mortality in people at high risk for lung cancer.	II	[1]
There is no high level implementation studies in the Australian context supporting population-based CT screening.	N/A	

Evidence-based recommendation	Grade
There is insufficient evidence to recommend population-based CT Screening.* * Despite the existing evidence from North America that computed tomography (CT) screening can reduce lung cancer specific and all-cause mortality in some people at high risk for lung cancer, current uncertainties including the generalisability of this international trial result to the Australian setting, the lack of local cost effectiveness evidence, and concerns as how best to implement a safe and effective screening program in Australia, mean that the available evidence is insufficient to recommend population based CT screening in Australia at the current time.	**B**

Back to top

2.1.2.3 Issues requiring more clinical research study

Critical research questions that should be addressed by Australian CT screening projects include:

1. Is population based CT screening cost-effective in Australia?
2. How best to implement safe and effective population based CT screening in Australia?

2.1.2.4 Key implementation issues

1. How will eligible ever-smokers be approached and recruited into a screening program in a way that maximises uptake from eligible individuals, yet minimises distress and/or screening demand from lower-risk screening-ineligible individuals?
2. How can access to screening with appropriate low-dose CT technology be provided to those living in rural and remote Australia?
3. How can quality and consistency in eligibility assessment, screening adherence, CT dosimetry and nodule management be implemented?
4. How should incidental findings be reported? How will such incidental findings be communicated to participants and general practitioners?

Back to top

2.1.2.5 References

1. ↑ [1.0] [1.1] [1.2] [1.3] Aberle DR, Adams AM, Berg CD, Black WC, Clapp JD, Fagerstrom RM, et al. *Reduced lung-cancer mortality with low-dose computed tomographic screening.* N Engl J Med 2011 Aug 4;365(5):395-409 Available from: http://www.ncbi.nlm.nih.gov/pubmed/21714641.
2. ↑ [2.0] [2.1] [2.2] Fu C, Liu Z, Zhu F, Li S, Jiang L. *A meta-analysis: Is low-dose computed tomography a superior method for risky lung cancers screening population?* Clin Respir J 2014 Oct 13 Available from: http://www.ncbi.nlm.nih.gov/pubmed/25307063.
3. ↑ Saghir Z, Dirksen A, Ashraf H, Bach KS, Brodersen J, Clementsen PF, et al. *CT screening for lung cancer brings forward early disease. The randomised Danish Lung Cancer Screening Trial: status after five annual screening rounds with low-dose CT.* Thorax 2012 Apr;67(4):296-301 Available from: http://www.ncbi.nlm.nih.gov/pubmed/22286927.
4. ↑ Wille MM, Dirksen A, Ashraf H, Saghir Z, Bach KS, Brodersen J, et al. *Results of the Randomized Danish Lung Cancer Screening Trial with Focus on High-risk Profiling.* Am J Respir Crit Care Med 2015 Oct 20 Available from: http://www.ncbi.nlm.nih.gov/pubmed/26485620.
5. ↑ Infante M, Cavuto S, Lutman FR, Brambilla G, Chiesa G, Ceresoli G, et al. *A randomized study of lung cancer screening with spiral computed tomography: three-year results from the DANTE trial.* Am J Respir Crit Care Med 2009 Sep 1;180(5):445-53 Available from: http://www.ncbi.nlm.nih.gov/pubmed/19520905.
6. ↑ Infante M, Cavuto S, Lutman FR, Passera E, Chiarenza M, Chiesa G, et al. *Long-term Follow-up Results of the DANTE Trial, a Randomized Study of Lung Cancer Screening with Spiral Computed Tomography.* Am J Respir Crit Care Med 2015 Mar 11 Available from: http://www.ncbi.nlm.nih.gov/pubmed/25760561.

7. ↑ Pastorino U, Rossi M, Rosato V, Marchianò A, Sverzellati N, Morosi C, et al. *Annual or biennial CT screening versus observation in heavy smokers: 5-year results of the MILD trial.* Eur J Cancer Prev 2012 May;21(3):308-15 Available from: http://www.ncbi.nlm.nih.gov/pubmed/22465911.
8. ↑ Bach PB, Mirkin JN, Oliver TK, Azzoli CG, Berry DA, Brawley OW, et al. *Benefits and harms of CT screening for lung cancer: a systematic review.* JAMA 2012 Jun 13;307(22):2418-29 Available from: http://www.ncbi.nlm.nih.gov/pubmed/22610500.
9. ↑ Humphrey LL, Deffebach M, Pappas M, Baumann C, Artis K, Mitchell JP, et al. *Screening for lung cancer with low-dose computed tomography: a systematic review to update the US Preventive services task force recommendation.* Ann Intern Med 2013 Sep 17;159(6):411-20 Available from: http://www.ncbi.nlm.nih.gov/pubmed/23897166.

Back to top

2.1.2.6 Appendices

View recommendation components	View pending evidence	View body of evidence	View literature search	View PICO

Back to top

2.1.3 Population benefiting from CT screening

Contents

Note: *This question was open for public comment from 19 August 2016 to 3 October 2016. This content is not part of the public consultation from 3-30 July 2017 and is therefore not open for comment.*

2.1.3.1 Systematic Review Evidence

Although these guidelines do not currently recommend CT screening for lung cancer in Australia, it is possible this recommendation may change in future as more Australian-specific data is generated. The aim of this question is therefore to consider, should screening become recommended, which population stands to gain most from screening?

It is worth considering the definition of screening at this point. According to The Australian Population Based Screening Framework, population-based screening is where "a test is offered systematically to all individuals in the defined target group within a framework of agreed policy, protocols, quality management, monitoring and evaluation. A population-based screening program is an organised integrated process where all activities along the screening pathway are planned, coordinated, monitored and evaluated through a quality improvement framework. All of these activities must be resourced adequately to ensure benefits are maximised".[1] In addition it is required that a screening program "offers more benefit than harm to the target population".[1] On the other hand, opportunistic case-finding occurs when a test is offered to an individual without symptoms of the disease when they present to a health care practitioner for reasons unrelated to that disease.

CT screening carries potential benefit and potential harm. Although some individuals may find great comfort in knowing they have a negative screening CT scan, and others may be motivated to quit smoking on the basis of a positive CT scan, arguably the only individuals who will benefit from screening are those who harbour early-stage, curable lung cancer. All other participants are at risk of the harms of screening without any benefit. Harms include detriments to health-related quality of life, exposure to medical radiation, decreased motivation to quit smoking with negative scan results, exposure to invasive diagnostic procedures for benign lesions and even risk of death. This variable risk benefit ratio was illustrated in post hoc analysis of the NLST participants.[2] When stratified into quintiles of lung cancer risk, the ratio of false positive screening results (risk) to CT-prevented lung-cancer death (benefit) improved from 1648:1 in the lowest risk quintile to 65:1 in the highest risk quintile. Thus individuals at low risk of lung cancer are unlikely to gain any benefit from screening (i.e. early detection of occult lung cancer) but will be exposed to the harms of screening.

Eligibility criteria for NLST were age 55-74 years, current or former smokers who had smoked ≥30 pack years (20 cigarettes per day for 1 year = 1 pack year). Former smokers had to have quit less than 15 years before study entry.[3] The European screening RCTs determined eligibility based on slightly different age and smoking criteria. They mostly found prevalence lung cancer rates similar or slightly lower than NLST (Table 1). DLCST[4], MILD[5] and DANTE[6] reported no mortality benefit but lacked statistical power. In addition, all three trials accepted fewer smoking pack year history than NLST (≥30 years). Furthermore, MILD and DLCST recruited younger participants (from age 49 and 50 respectively). The estimated 10 year lung cancer risk for former smokers meeting minimum inclusion criteria were 1% for DLSCT, and less than 1% for NELSON compared to 2% in NLST.[7] Thus a population risk at least equivalent to NLST is probably mandatory to obtain the population benefit. The lower risk profile from younger participants with lighter smoking histories is reflected in lower baseline lung cancer prevalence rates (Table 1).

Lung cancer risk factors other than older age and smoking history are well recognised in the literature and might be useful additions when determining risk. Post hoc analysis of several screening trials has shed light on risk: Analysis of NLST data found weak evidence of slightly improved mortality benefit in women[8] and increased mortality reduction in African Americans[9]. Regarding age, participants ≥65years of age had higher cancer prevalence but also a higher rate of false-positive screening results.[10] DLCST found risk of death from lung cancer was associated with older age, COPD diagnosis and heavier smoking history.[11] Multivariable risk estimation in NLST showed improved cost-effectiveness and increased mortality reduction in higher risk individuals[2][12] and was more efficient than NLST criteria improving sensitivity and decreasing false-positive rates.[13][14] The UKLS[15] which used multivariable risk assessment showed slightly higher rates of prevalent lung cancer compared to other trials suggesting a higher risk group had been successfully targeted (Table 1).

Despite this suggestive evidence, there are no primary data to support mortality reduction in individuals who fall outside NLST criteria.

Back to top

2.1.3.2 Evidence summary and recommendations

Evidence summary	Level	References
Men and women aged 55-74 with heavy smoking histories (at least 30 pack years, current or former smokers who had quit within the prior 15 years) had reduced lung cancer mortality in a large, high quality randomised lung cancer CT screening trial.	II	[3], [7], [16]

Evidence-based recommendation	Grade
CT scans for the early detection of lung cancer in asymptomatic individuals should only be considered in those at high risk of lung cancer and who meet the following minimum criteria: aged 55-74 with heavy smoking histories (at least 30 pack years, current or former smokers who have quit within the prior 15 years).* *See the section on population-based CT screening for more information.Available evidence is insufficient to recommend populated based CT screening.	**C**

Practice point
Current evidence does not support population-based screening with CT scanning.

Practice point

For the asymptomatic individual at high risk for lung cancer who is considering a CT scan to detect early lung cancer, it is recommended that they discuss any potential benefits against the potential harms of a low dose CT scan with their GP.

2.1.3.2.1 Benefits and harms of screening

2.1.3.2.1.1 Screening benefits

2.1.3.2.1.1.1 Smoking cessation

Participation in lung cancer screening may prompt smokers to try and quit. Alternatively a negative scan result may give false reassurance and reduce motivation to quit. The evidence is not compelling either way. No primary data were found in the search however two systematic reviews of screening have noted limited data showing no difference or mixed results either way.[7][16]

Back to top

2.1.3.2.1.2 Screening harms

2.1.3.2.1.2.1 Medical radiation

No studies were identified. Systematic reviews reported dose ranges from RCTs and cohort trials of between 0.61 to 1.50mSv and cumulative dose across 4 annual screens of 6 to 7mSv.[16] Bach estimated NLST cumulative dose was ~8mSv per participant over 3 years, including both screening and diagnostic examinations.[7] The immediate potential benefit of diagnosing early lung cancer in some participants has to be weighed against the postponed potential risk of radiation-induced cancer many years later.

2.1.3.2.1.2.2 Over-diagnosis

The rate of over-diagnosis is uncertain.[16][7] NLST estimated the rate as 18.5% (95% CI, 5.4%–30.6%).[17]

2.1.3.2.1.2.3 False-positive rate

Varying definitions of what constitutes a positive scan result and difference in reporting make comparisons between RCTs difficult. FPR tends to be higher in baseline rounds. Cumulative positive scan rates were highest in NLST with an average of 24% across all three rounds and a cumulative rate of 39%. Of the positive scans, 96.4% were false positive. Most positive scans were followed with further imaging tests.[3]

2.1.3.2.1.2.4 Risks of major complications and death

In NLST, the risk of death following diagnostic events (including imaging) for benign nodules was 4.1 per 10,000 screened.[7] The risks of major complications following diagnostic events (including imaging) for benign nodules was 4.5 per 10,000 screened.[7] In comparison, the number needed to screen to prevent one lung cancer death in NLST was 320 (~31 deaths avoided per 10,000 screened).[3]

2.1.3.2.1.2.5 Anxiety, quality of life

When screening large numbers of individuals, participant reported health related quality of life (HRQoL) is an important consideration; even small decrements in HRQoL may have important implications when applied across large populations. Three RCTs reported HRQoL using generic and specific measures. Generic questionnaires allows comparison across a range of health problems, treatments and screening programs, whereas screening-specific questionnaires may be more sensitive to the impact of screening which might not be captured by generic tools.

NLST found participants with True Positive scans had worse generic HRQoL outcomes at 1 and 6 months after the first screening scan, but those with False Positive Scans or Significant Incidental Findings were similar to participants with Negative Scans at both time points.[18] NELSON assessed generic HRQoL. There were some statistically, but not clinically significant changes in HRQoL up to 6 months after baseline CT. Participants with higher levels of anxiety reported more discomfort in connection with having to wait for the results of the CT scan.[19] After 2 years follow-up, there was no significant difference between the screen and control groups. Participants with an indeterminate baseline result reported a temporary increase in lung cancer-specific distress compared to participants with a negative baseline scan, but this was no longer apparent at 2 years follow-up and an indeterminate result at the second screening round had no impact on HRQoL.[20][21] DLCST used a validated screening-specific instrument. There were statistically significant adverse HRQoL effects across all screening rounds for screen and control groups which were differentially worse in the control group. These negative effects tended to persist. Although statistically significant, a minimal clinically important difference was not defined a priori.[22][23] Evidence suggests individuals undergoing screening are at risk of negative HRQoL effects. Those most at risk are individuals diagnosed with lung cancer and individuals with pre-existing higher levels of anxiety. Positive scans may cause temporary adverse effects on HRQoL.

Back to top

2.1.3.3 References

1. ↑ 1.0 1.1 Australian Population Health Development Principle Committee Screening Subcommittee. *Population Based Screening Framework.* Canberra: Commonwealth of Australia; 2008 Available from: http://www.cancerscreening.gov.au/internet/screening/publishing.nsf/Content/lung-cancer-screening.
2. ↑ 2.0 2.1 Kovalchik SA, Tammemagi M, Berg CD, Caporaso NE, Riley TL, Korch M, et al. *Targeting of low-dose CT screening according to the risk of lung-cancer death.* N Engl J Med 2013 Jul 18;369(3):245-54 Available from: http://www.ncbi.nlm.nih.gov/pubmed/23863051.

3. ↑ 3.0 3.1 3.2 3.3 Aberle DR, Adams AM, Berg CD, Black WC, Clapp JD, Fagerstrom RM, et al. *Reduced lung-cancer mortality with low-dose computed tomographic screening.* N Engl J Med 2011 Aug 4;365(5):395-409 Available from: http://www.ncbi.nlm.nih.gov/pubmed/21714641.
4. ↑ Saghir Z, Dirksen A, Ashraf H, Bach KS, Brodersen J, Clementsen PF, et al. *CT screening for lung cancer brings forward early disease. The randomised Danish Lung Cancer Screening Trial: status after five annual screening rounds with low-dose CT.* Thorax 2012 Apr;67(4):296-301 Available from: http://www.ncbi.nlm.nih.gov/pubmed/22286927.
5. ↑ Pastorino U, Rossi M, Rosato V, Marchianò A, Sverzellati N, Morosi C, et al. *Annual or biennial CT screening versus observation in heavy smokers: 5-year results of the MILD trial.* Eur J Cancer Prev 2012 May;21(3):308-15 Available from: http://www.ncbi.nlm.nih.gov/pubmed/22465911.
6. ↑ Infante M, Cavuto S, Lutman FR, Passera E, Chiarenza M, Chiesa G, et al. *Long-term Follow-up Results of the DANTE Trial, a Randomized Study of Lung Cancer Screening with Spiral Computed Tomography.* Am J Respir Crit Care Med 2015 Mar 11 Available from: http://www.ncbi.nlm.nih.gov/pubmed/25760561.
7. ↑ 7.0 7.1 7.2 7.3 7.4 7.5 7.6 Bach PB, Mirkin JN, Oliver TK, Azzoli CG, Berry DA, Brawley OW, et al. *Benefits and harms of CT screening for lung cancer: a systematic review.* JAMA 2012 Jun 13;307(22):2418-29 Available from: http://www.ncbi.nlm.nih.gov/pubmed/22610500.
8. ↑ Pinsky PF, Church TR, Izmirlian G, Kramer BS. *The National Lung Screening Trial: results stratified by demographics, smoking history, and lung cancer histology.* Cancer 2013 Nov 15;119(22):3976-83 Available from: http://www.ncbi.nlm.nih.gov/pubmed/24037918.
9. ↑ Tanner NT, Gebregziabher M, Hughes Halbert C, Payne E, Egede LE, Silvestri GA. *Racial Differences in Outcomes within the National Lung Screening Trial: Implications for Widespread Implementation.* Am J Respir Crit Care Med 2015 Apr 30 Available from: http://www.ncbi.nlm.nih.gov/pubmed/25928649.
10. ↑ Pinsky PF, Gierada DS, Hocking W, Patz Jr EF, Kramer BS. *National Lung Screening Trial Findings by Age: Medicare-Eligible Versus Under-65 Population.* Ann Intern Med 2014 Sep 9 Available from: http://www.ncbi.nlm.nih.gov/pubmed/25199624.
11. ↑ Wille MM, Dirksen A, Ashraf H, Saghir Z, Bach KS, Brodersen J, et al. *Results of the Randomized Danish Lung Cancer Screening Trial with Focus on High-risk Profiling.* Am J Respir Crit Care Med 2015 Oct 20 Available from: http://www.ncbi.nlm.nih.gov/pubmed/26485620.
12. ↑ Black WC, Gareen IF, Soneji SS, Sicks JD, Keeler EB, Aberle DR, et al. *Cost-effectiveness of CT screening in the National Lung Screening Trial.* N Engl J Med 2014 Nov 6;371(19):1793-802 Available from: http://www.ncbi.nlm.nih.gov/pubmed/25372087.
13. ↑ Tammemägi MC, Church TR, Hocking WG, Silvestri GA, Kvale PA, Riley TL, et al. *Evaluation of the lung cancer risks at which to screen ever- and never-smokers: screening rules applied to the PLCO and NLST cohorts.* PLoS Med 2014 Dec;11(12):e1001764 Available from: http://www.ncbi.nlm.nih.gov/pubmed/25460915.
14. ↑ Tammemägi MC, Katki HA, Hocking WG, Church TR, Caporaso N, Kvale PA, et al. *Selection criteria for lung-cancer screening.* N Engl J Med 2013 Feb 21;368(8):728-36 Available from: http://www.ncbi.nlm.nih.gov/pubmed/23425165.
15. ↑ Field JK, Duffy SW, Baldwin DR, Whynes DK, Devaraj A, Brain KE, et al. *UK Lung Cancer RCT Pilot Screening Trial: baseline findings from the screening arm provide evidence for the potential implementation of lung cancer screening.* Thorax 2015 Dec 8 Available from: http://www.ncbi.nlm.nih.gov/pubmed/26645413.

16. ↑ 16.0 16.1 16.2 16.3 Humphrey LL, Deffebach M, Pappas M, Baumann C, Artis K, Mitchell JP, et al. *Screening for lung cancer with low-dose computed tomography: a systematic review to update the US Preventive services task force recommendation.* Ann Intern Med 2013 Sep 17;159(6):411-20 Available from: http://www.ncbi.nlm.nih.gov/pubmed/23897166.
17. ↑ Patz EF Jr, Pinsky P, Gatsonis C, Sicks JD, Kramer BS, Tammemägi MC, et al. *Overdiagnosis in low-dose computed tomography screening for lung cancer.* JAMA Intern Med 2014 Feb 1;174(2):269-74 Available from: http://www.ncbi.nlm.nih.gov/pubmed/24322569.
18. ↑ Gareen IF, Duan F, Greco EM, Snyder BS, Boiselle PM, Park ER, et al. *Impact of lung cancer screening results on participant health-related quality of life and state anxiety in the National Lung Screening Trial.* Cancer 2014 Nov 1;120(21):3401-9 Available from: http://www.ncbi.nlm.nih.gov/pubmed/25065710.
19. ↑ van den Bergh KA, Essink-Bot ML, Bunge EM, Scholten ET, Prokop M, van Iersel CA, et al. *Impact of computed tomography screening for lung cancer on participants in a randomized controlled trial (NELSON trial).* Cancer 2008 Jul 15;113(2):396-404 Available from: http://www.ncbi.nlm.nih.gov/pubmed/18484588.
20. ↑ van den Bergh KA, Essink-Bot ML, Borsboom GJ, Scholten ET, van Klaveren RJ, de Koning HJ. *Long-term effects of lung cancer computed tomography screening on health-related quality of life: the NELSON trial.* Eur Respir J 2011 Jul;38(1):154-61 Available from: http://www.ncbi.nlm.nih.gov/pubmed/21148229.
21. ↑ van den Bergh KA, Essink-Bot ML, Borsboom GJ, Th Scholten E, Prokop M, de Koning HJ, et al. *Short-term health-related quality of life consequences in a lung cancer CT screening trial (NELSON).* Br J Cancer 2010 Jan 5;102(1):27-34 Available from: http://www.ncbi.nlm.nih.gov/pubmed/19935789.
22. ↑ Aggestrup LM, Hestbech MS, Siersma V, Pedersen JH, Brodersen J. *Psychosocial consequences of allocation to lung cancer screening: a randomised controlled trial.* BMJ Open 2012;2(2):e000663 Available from: http://www.ncbi.nlm.nih.gov/pubmed/22382119.
23. ↑ Rasmussen JF, Siersma V, Pedersen JH, Brodersen J. *Psychosocial consequences in the Danish randomised controlled lung cancer screening trial (DLCST).* Lung Cancer 2014 Nov 20 Available from: http://www.ncbi.nlm.nih.gov/pubmed/25433982.

Back to top

2.1.3.4 Appendices

View recommendation components	View pending evidence	View body of evidence	View literature search	View PICO

Back to top

2.2 Optimal IHC panel for subtyping NSCLC

Contents

2.2.1 Systematic Review Evidence

For patients with advanced stage disease, accurate subclassification of different subtypes of NSCLC is needed to help determine optimal treatment.[1][2] In small biopsy and cytology specimens of non-small cell lung carcinoma (NSCLC), however, it is not always possible to distinguish squamous cell carcinoma from adenocarcinoma or other subtypes of NSCLC using morphological features alone. In these cases, immunohistochemical stains can be used to help distinguish those tumours likely to be adenocarcinomas from those more likely to represent squamous cell carcinomas.[3] Review of the literature shows that various IHC markers can be used to assist in distinction of squamous cell carcinoma from adenocarcinoma subtypes of NSCLC, although the number of IHC markers used and which specific combinations of IHC markers is quite variable, and most of the studies were at risk of bias. In addition, many of the studies that assessed reliability of IHC subtyping did not provide information regarding how morphologically undifferentiated the tumours were or if subtyping could be inferred from morphology alone.

Back to top

2.2.2 Evidence summary and recommendations

Evidence summary	Level	References
IHC is useful in subtyping NSCLC using a small panel of IHC markers.	III-2	[4], [5], [6], [7], [8], [9], [10], [11]

Evidence-based recommendation	Grade
A small panel of IHC markers should be used to subtype morphologically undifferentiated NSCLC in small biopsy and cytology samples, with 2 markers usually sufficient (1 adenocarcinoma marker and 1 squamous marker).	**C**

Practice point

IHC to assist in subtyping NSCLC is only required when there is no morphological evidence of glandular or squamous differentiation.The optimal panel of IHC markers is not clear from the literature with many studies using a different range of markers (eg TTF-1, Napsin A, CK5, CK5/6, p40, p63, CK7, surfactant protein A, as well as histochemical markers for mucin such as PAS.) The WHO Classification of Tumours of the Lung (Travis WD et al 2015) recommends using only one squamous marker (ie p40, p63 or CK5/6) and one adenocarcinoma marker (TTF-1 or a histochemical stain for mucin) so as to preserve tissue for molecular testing in the setting of a small biopsy showing a non-small cell carcinoma lacking definite squamous or glandular morphology.

Practice point

It is advisable to limit the number of IHC markers used to 2 so as to preserve tissue for molecular testing if required (1 adenocarcinoma marker such as TTF1, and 1 squamous marker such as p40).

Practice point

In some instances, IHC may also be needed to help determine if the tumour is of lung origin or a metastasis. Clinicopathological correlation and multidisciplinary team meeting discussion can often assist in excluding the possibility of a metastasis to the lung in the setting of a solitary lung lesion, and can help avoid unnecessary use of IHC markers and thereby preserve tissue for molecular testing. IHC markers are not useful in distinguishing primary from metastatic disease in the case of a squamous cell carcinoma in the lung.

Back to top

2.2.3 References

1. ↑ Cooper WA, O'toole S, Boyer M, Horvath L, Mahar A. *What's new in non-small cell lung cancer for pathologists: the importance of accurate subtyping, EGFR mutations and ALK rearrangements.* Pathology 2011 Feb;43(2):103-15 Available from: http://www.ncbi.nlm.nih.gov/pubmed/21233671.
2. ↑ Cancer Council Australia Lung Cancer Guidelines Working Party. *Clinical practice guidelines for the treatment of lung cancer.* [homepage on the internet] Sydney: Cancer Council Australia; Available from: http://wiki.cancer.org.au/australia/Guidelines:Lung_cancer.
3. ↑ Travis WD, Brambilla E, Nicholson AG, Yatabe Y, Austin JH, Beasley MB, et al. *The 2015 World Health Organization Classification of Lung Tumors: Impact of Genetic, Clinical and Radiologic Advances Since the 2004 Classification.* J Thorac Oncol 2015 Sep;10(9):1243-60 Available from: http://www.ncbi.nlm.nih.gov/pubmed/26291008.

4. ↑ Ikeda S, Naruse K, Nagata C, Kuramochi M, Onuki T, Inagaki M, et al. *Immunostaining for thyroid transcription factor 1, Napsin A, p40, and cytokeratin 5 aids in differential diagnosis of non-small cell lung carcinoma.* Oncol Lett 2015;9(5):2099-2104 Available from: http://www.ncbi.nlm.nih.gov/pubmed/26137020.
5. ↑ Pelosi G, Rossi G, Bianchi F, Maisonneuve P, Galetta D, Sonzogni A, et al. *Immunhistochemistry by means of widely agreed-upon markers (cytokeratins 5/6 and 7, p63, thyroid transcription factor-1, and vimentin) on small biopsies of non-small cell lung cancer effectively parallels the corresponding profiling and eventual diagnoses on surgical specimens.* J Thorac Oncol 2011 Jun;6(6):1039-49 Available from: http://www.ncbi.nlm.nih.gov/pubmed/21512408.
6. ↑ Jorda M, Gomez-Fernandez C, Garcia M, Mousavi F, Walker G, Mejias A, et al. *P63 differentiates subtypes of nonsmall cell carcinomas of lung in cytologic samples: implications in treatment selection.* Cancer 2009 Feb 25;117(1):46-50 Available from: http://www.ncbi.nlm.nih.gov/pubmed/19347829.
7. ↑ Ocque R, Tochigi N, Ohori NP, Dacic S. *Usefulness of immunohistochemical and histochemical studies in the classification of lung adenocarcinoma and squamous cell carcinoma in cytologic specimens.* Am J Clin Pathol 2011 Jul;136(1):81-7 Available from: http://www.ncbi.nlm.nih.gov/pubmed/21685035.
8. ↑ Righi L, Graziano P, Fornari A, Rossi G, Barbareschi M, Cavazza A, et al. *Immunohistochemical subtyping of nonsmall cell lung cancer not otherwise specified in fine-needle aspiration cytology: a retrospective study of 103 cases with surgical correlation.* Cancer 2011 Aug 1;117(15):3416-23 Available from: http://www.ncbi.nlm.nih.gov/pubmed/21246522.
9. ↑ Koh J, Go H, Kim MY, Jeon YK, Chung JH, Chung DH. *A comprehensive immunohistochemistry algorithm for the histological subtyping of small biopsies obtained from non-small cell lung cancers.* Histopathology 2014 Dec;65(6):868-78 Available from: http://www.ncbi.nlm.nih.gov/pubmed/25130792.
10. ↑ da Cunha Santos G, Lai SW, Saieg MA, Geddie WR, Pintilie M, Tsao MS, et al. *Cyto-histologic agreement in pathologic subtyping of non small cell lung carcinoma: review of 602 fine needle aspirates with follow-up surgical specimens over a nine year period and analysis of factors underlying failure to subtype.* Lung Cancer 2012 Sep;77(3):501-6 Available from: http://www.ncbi.nlm.nih.gov/pubmed/22656670.
11. ↑ Montezuma D, Azevedo R, Lopes P, Vieira R, Cunha AL, Henrique R. *A panel of four immunohistochemical markers (CK7, CK20, TTF-1, and p63) allows accurate diagnosis of primary and metastatic lung carcinoma on biopsy specimens.* Virchows Arch 2013 Dec;463(6):749-54 Available from: http://www.ncbi.nlm.nih.gov/pubmed/24126803.

Back to top

2.2.4 Appendices

View recommendation components	View pending evidence	View body of evidence	View all comments	View literature search
View PICO				

Back to top

2.3 Specimen types mutation testing NSCLC

Contents

2.3.1 Systematic Review Evidence

Advanced stage lung adenocarcinomas, NSCLC with any glandular differentiation or NSCLC, not otherwise specified, all require mutation testing to assess for targetable mutations in the *epidermal growth factor receptor (EGFR)* gene or translocations involving the anaplastic lymphoma kinase (ALK) gene.[1][2][3] This information is required to help determine the most appropriate 1st line treatment due to the availability of tyrosine kinase inhibitors that specifically target these alterations.[1][2][3] Pathologists and treating physicians need to know which specimens are suitable for mutation testing to ensure the mutation status of each patient's tumour is accurately determined.

Most studies compared the concordance of mutation status in tissue samples obtained from primary tumours versus metastases; or the mutation status in histology tissue samples versus cytology samples. While there was generally high concordance across the different groups in keeping with the underlying biology of these genetic alterations as driver alterations, slightly lower rates of mutations were sometimes found in samples obtained

from metastatic tumours compared to primary tumours, possibly relating to technical factors such as smaller tumour samples from these sites. Little information was provided on the sample size, quantity or proportion of tumour cells which could all effect the results. Lower concordance was also generally found when lower sensitivity techniques were used to assess mutation status. To avoid false negatives, primary tumours or samples with the greatest tumour volume should be used for mutation testing where available. In the setting of *EGFR* mutant tumours that have developed resistance to an EGFR-TKI, repeat testing may be undertaken to assess for acquisition of targetable resistance mutations (such as *EGFR* T790M mutation) and tissue or "liquid biopsy" specimens (circulating tumour DNA in plasma) could potentially be used, however, this was not specifically addressed in the literature review.

Back to top

2.3.2 Evidence summary and recommendations

Evidence summary	Level	References
There is generally high concordance in the mutation status of tumours obtained by using samples from histology or cytology samples, or from primary tumours versus metastases	III-1, III-2	[4], [5], [6]

Evidence-based recommendation	Grade
Any tumour sample can be used for mutation testing (sample from primary or metastatic site; histology or cytology sample).	**C**

Practice point

It is advisable to use the optimal specimen available from each patient for mutation testing (if more than one specimen is available). This would be the specimen with the highest content and proportion of tumour cells and could be a histology specimen such as a core biopsy or a cytology specimen. This should be determined on a case by case basis by a pathologist.

2.3.3 References

1. ↑ [1.0] [1.1] Lindeman NI, Cagle PT, Beasley MB, Chitale DA, Dacic S, Giaccone G, et al. *Molecular testing guideline for selection of lung cancer patients for EGFR and ALK tyrosine kinase inhibitors: guideline from the College of American Pathologists, International Association for the Study of Lung Cancer, and Association for Molecular Pathology.* J Thorac Oncol 2013 Jul;8(7):823-59 Available from: http://www.ncbi.nlm.nih.gov/pubmed/23552377.

2. ↑ [2.0] [2.1] Cooper WA, O'toole S, Boyer M, Horvath L, Mahar A. *What's new in non-small cell lung cancer for pathologists: the importance of accurate subtyping, EGFR mutations and ALK rearrangements.* Pathology 2011 Feb;43(2):103-15 Available from: http://www.ncbi.nlm.nih.gov/pubmed/21233671.
3. ↑ [3.0] [3.1] Cancer Council Australia Lung Cancer Guidelines Working Party. *Clinical practice guidelines for the treatment of lung cancer.* [homepage on the internet] Sydney: Cancer Council Australia; Available from: http://wiki.cancer.org.au/australia/Guidelines:Lung_cancer.
4. ↑ Bruno P, Mariotta S, Ricci A, Duranti E, Scozzi D, Noto A, et al. *Reliability of direct sequencing of EGFR: comparison between cytological and histological samples from the same patient.* Anticancer Res 2011 Dec;31(12):4207-10 Available from: http://www.ncbi.nlm.nih.gov/pubmed/22199282.
5. ↑ Park S, Holmes-Tisch AJ, Cho EY, Shim YM, Kim J, Kim HS, et al. *Discordance of molecular biomarkers associated with epidermal growth factor receptor pathway between primary tumors and lymph node metastasis in non-small cell lung cancer.* J Thorac Oncol 2009 Jul;4(7):809-15 Available from: http://www.ncbi.nlm.nih.gov/pubmed/19487967.
6. ↑ Wang F, Fang P, Hou DY, Leng ZJ, Cao LJ. *Comparison of epidermal growth factor receptor mutations between primary tumors and lymph nodes in non-small cell lung cancer: a review and meta-analysis of published data.* Asian Pac J Cancer Prev 2014;15(11):4493-7 Available from: http://www.ncbi.nlm.nih.gov/pubmed/24969875.

Back to top

2.3.4 Appendices

View recommendation components | View pending evidence | View body of evidence | View all comments | View literature search

View PICO

Back to top

2.4 Concurrent vs sequential diagnosis and staging

Contents

2.4.1 Introduction

In suspected lung cancer, tissue diagnosis may be obtained from the primary mass, or from lymph node or distal metastases. Accurate staging is critical to inform optimum treatment decisions. Timely work up of lung cancer is encouraged to enable patients to receive treatment prior to further disease progression. Staging modalities such as endobronchial and endoscopic ultrasound, have made both diagnosis and staging feasible during the first diagnostic procedure in selected cases.[1].

2.4.2 Systematic Review Evidence

Systematic literature searches did not identify any studies directly comparing concurrent versus sequential diagnosis and staging for improving patient outcomes. The search strategies and inclusion and exclusion criteria are described in detail in the Appendices.

2.4.3 Overview of additional evidence (Non-systematic review)

Timely work up of lung cancer is strongly encouraged or mandated in order to avoid disease progression prior to treatment.[2] In addition, patients report the period during the diagnostic process and waiting for tests in secondary care as the most stressful part off the pathway.[3]

Non-invasive staging of suspected lung cancer is undertaken with staging CT chest and/or CT PET scanning. However, imaging may be insufficiently accurate to obviate the need for tissue sampling, particularly in the mediastinum ; CT size significant or FDG-avid nodes require confirmatory sampling to exclude “false positives”. Endobronchial and/or endoscopic ultrasound guided transbronchial or fine needle aspiration (EBUS-TBNA / EUS-FNA) have allowed nodal sampling to be accurately achieved during a day case procedure with minimal morbidity. Therefore, in selected cases with accessible mediastinal and/or hilar lymph nodes on either CT or CT PET, it is now feasible to achieve staging and diagnosis with EBUS-TBNA/EUS-FNA as the first diagnostic test. If the staging CT shows potentially curable disease, CT PET is recommended. CT PET is more sensitive and specific for mediastinal and hilar nodal metastases, and thus it is best to have CT PET available prior to EBUS-TBNA or EUS-FNA to guide appropriate nodal sampling.

In patients with positive cervical and/or axillary (N3) nodes, pleural disease (M1a) or distal metastases (M1b), percutaneous sampling of such nodes, effusions or deposits to achieve diagnosis and staging may also be considered as the first diagnostic test. This approach may shorten work up times and expedite treatment, and is consistent with guidance issued elsewhere. [4] Despite this however, direct evidence linking the strategy of concurrent rather than sequential to improved outcomes is lacking.

The size and adequacy of samples obtained via each approach needs to also be factored into the diagnostic algorithm, as does in turn the likely treatment strategy for each individual patient. EBUS-TBNA is usually undertaken with 21G and 22G needles obtaining cytology samples, although 19G needles are in development. There is little specific evidence addressing the adequacy of samples obtained by needles of different gauges. Percutaneous biopsies of metastatic lesions and lung primaries may include both FNA and core biopsies, the latter obtaining samples for histopathological analysis as would endobronchial biopsies of primary lesions. Core biopsies may be associated with a higher complication rate in some patients. Thoracic multidisciplinary meeting discussion may be considered prior to tissue sampling, in order to help select the most appropriate initial modality. Specific guidance with examples has also been published elsewhere in 2011.[5]

Back to top

2.4.4 Evidence summary and recommendations

Consensus-based recommendation

In suspected lung cancer, where possible, clinicians should select a first diagnostic procedure which can provide diagnosis and staging concurrently. However, other considerations include the safety of each test for an individual patient, and the need to obtain an adequate sample for required pathological testing. CT PET scanning should be obtained prior to endobronchial/endoscopic ultrasound in potentially curative cases.

2.4.5 Issues requiring more clinical research study

Due to the widespread adoption of minimally invasive staging, it is unlikely that this question will be addressed in prospective, randomised trials. However, the development of standardised lung cancer datasets should be encouraged to promote prospective data capture and subsequent audit at a local, regional and national level. This can drive changes in practice.[6][7] Comparison of diagnostic and staging data with outcomes would then be informative.

Back to top

2.4.6 References

1. ↑ Fielding D, Windsor M. *Endobronchial ultrasound convex-probe transbronchial needle aspiration as the first diagnostic test in patients with pulmonary masses and associated hilar or mediastinal nodes.* Intern Med J 2009 Jul;39(7):435-40 Available from: http://www.ncbi.nlm.nih.gov/pubmed/19371395.
2. ↑ Cancer Council Victoria. *Optimal care pathway for people with lung cancer.*; Available from: http://www.cancer.org.au/content/ocp/health/optimal-care-pathway-for-people-with-lung-cancer-june-2016.pdf.
3. ↑ W Stevens. *Recommendations to Expedite the Diagnosis of Lung Cancer. Final Report of the HRC_DHBNZ Funded Project: "Identification of barriers to the early diagnosis of people with lung cancer and description of best practice solutions".* New Zealand: Northern Cancer Network; Available from: http://www.northerncancernetwork.org.nz/LinkClick.aspx?fileticket=Xgn%2bFhw6HAQ%3d&tabid=101&language=en-US.

4. ↑ Rivera MP, Mehta AC, Wahidi MM. *Establishing the diagnosis of lung cancer: Diagnosis and management of lung cancer, 3rd ed: American College of Chest Physicians evidence-based clinical practice guidelines.* Chest 2013 May;143(5 Suppl):e142S-65S Available from: http://www.ncbi.nlm.nih.gov/pubmed/23649436.
5. ↑ National Collaborating Centre for Cancer for NICE. *The Diagnosis and Treatment of Lung Cancer (Update).* 2011 Apr Available from: http://www.nice.org.uk/nicemedia/live/13465/54199/54199.pdf.
6. ↑ Sethi T, Lim E, Peake M, Field J, White J, Nicolson M, et al. *Improving care for patients with lung cancer in the UK.* Thorax 2013 Dec;68(12):1181-5 Available from: http://www.ncbi.nlm.nih.gov/pubmed/24204006.
7. ↑ Evison M, Crosbie P, Martin J, Shah R, Doran H, Borrill Z, et al. *EBUS-guided mediastinal lung cancer staging: monitoring of quality standards improves performance.* Thorax 2016 Aug;71(8):762-3 Available from: http://www.ncbi.nlm.nih.gov/pubmed/27146201.

Back to top

2.4.7 Appendices

View recommendation components | View pending evidence | View body of evidence | View all comments | View literature search

View PICO

Back to top

2.5 Optimal timing of PET/CT

Contents

2.5.1 Introduction

The use of PET/CT scanning in the diagnostic and staging workup for lung cancer varies according to local availability and practice. International guidelines vary in their detailed recommendations but generally include PET/CT in diagnostic and staging algorithms for lung cancer. [1][2][3][4] International guidelines for evaluation of pulmonary nodules also include PET/CT in the diagnostic workup.[5][6] However, this guideline will focus on the role and optimal timing of PET/CT in the evaluation of patients with more than a pulmonary nodule, where lung cancer has been either confirmed on tissue biopsy or where lung cancer is suspected and where the clinical effort underway aims to confirm this suspicion and to correctly ascertain the disease stage. This guideline restricts its recommendations to the use of PET/CT in the diagnosis and work up of non-small cell lung cancer (NSCLC). The term PET/CT refers to FDG-PET/CT throughout.

2.5.2 Non-systematic Review Evidence

Ideally, guideline recommendations on this question would draw upon high-level evidence that specifically investigated the best timing for PET/CT in the work up of NSCLC. However, extensive literature searches have not identified such evidence so a combination of published recommendations and clinical expertise inform this content.

Even though this section of the guidelines will focus particularly on PET/CT for workup of lung cancer, there exists some overlap with the use of PET/CT for the assessment of pulmonary nodules. Two publications give relatively clear recommendations for the use of PET/CT in the evaluation of pulmonary nodules where lung cancer is suspected.[5][6] Both papers concentrate on evaluation of pulmonary nodules per se, but pertinent recommendations for lesions suspicious for malignancy are summarized in Table 1. Levels of evidence are given where available.

2.5.2.1 Table 1. Summarised recommendations for PET/CT in the evaluation of pulmonary nodules suspicious for lung cancer

Gould 2013	Callister 2015
PET/CT is recommended for solid, indeterminate nodules >8mm with low-moderate pre-test probability of malignancy (estimated by clinical judgement or by using a validated model. (Grade 2C) *	The pre-test probability of malignancy influences interpretation of PET/CT, with high-risk individuals at risk of false-negative results, and low-risk individuals at risk of false-positive results. (Grade D)
PET/CT is not recommended to characterize nodules with a high pre-test probability of malignancy. (Grade 2C) (Although it is reasonable to use PET/CT for pre-treatment staging in such cases).**	Combined clinical and PET/CT information results in best diagnostic accuracy.
PET/CT has high sensitivity (95%) and specificity (82%) for malignancy in pulmonary nodules compared with other imaging modalities. [7]	PET/CT is most efficacious in nodules with low-moderate pre-test probability of malignancy.
Negative PET/CT scan does not reliably exclude malignancy.	PET/CT is the preferred investigation for evaluation of pulmonary nodules as no other imaging modality is superior and PET/CT is widely available.
No data exist to compare integrated PET/CT with PET /CT combined with dedicated CT imaging.	PET/CT should be offered to patients with a >10% risk of malignancy (according to the Brock model***).[8][9][10] (Grade B)
	PET/CT should be used for staging if resection is considered.

*Where factors contributing to a pre-test likelihood of malignancy include age, smoking history, extra-thoracic cancer diagnosis > 5 years prior, size of lesion, spiculation and upper lobe location.

**In practice this would be a common point at which PET/CT would be used, whatever the intent of the clinician.

***The Brock model comprises four smoking variables (smoking intensity, smoking duration, quit time in former smokers, and current smoking status [current versus former]) and seven non-smoking variables (age, race/ethnicity, socioeconomic circumstance estimated by education level, body mass index, personal history of cancer, chronic obstructive pulmonary disease, family history of lung cancer).

Back to top

2.5.2.2 PET/CT for staging of known or suspected NSCLC

The other significant use of PET/CT is for non-invasive staging of NSCLC. Again, little data exist to inform us on optimal timing. However, recommendations from published guidelines are summarized in Table 2. Levels of evidence are given where available.

2.5.2.2.1 Table 2. Summarised recommendations for PET/CT from published lung cancer guidelines (with key references included)

NICE 2011	Silvestri 2013	SIGN 2014	NCCN 2016
Offer PET/CT as a first test for patients with low to intermediate probability of mediastinal malignancy potentially suitable for curative treatment. Every cancer network should have rapid access to PET/CT. PET/CT is appropriate to confirm the presence of isolated distant metastases /synchronous tumours in patients considered for curative treatment. Consider research into the use of MRI and PET /CT in routine brain imaging prior to treatment with curative intent.	In patients with clinical (and CT) early stage disease considered for curative intent treatment, PET/CT is recommended to evaluate for metastases (except the brain). (Grade 1B) PET/CT has multiple purposes in lung cancer workup including diagnostic accuracy, guiding biopsy and staging. In patients with lower risk of metastatic disease (such as clinical stage IA peripheral tumours) PET/CT may not be indicated (possible false positive rates for metastases).[11]	After FDG PET/CT scanning of solitary lung lesions pathological confirmation of results is still required. (Grade C) [12] All patients considered for radical treatment should have a staging FDG PET/CT scan before treatment. (Grade B) [13][2][14][15][16] For adrenal metastases, negative PET/CT reliably excludes metastases (Grade B); after positive PET/CT tissue confirmation usually required unless metastatic disease is extensive. (Grade B) [17]	PET/CT imaging is frequently best performed before biopsy. (Grade 2A) PET/CT is recommended for pre-treatment evaluation for all stages of disease. (Grade 2A) PET/CT can play a role in evaluation and more accurate staging of NSCLC. [2][14] PET/CT is even more sensitive and is therefore recommended by NCCN.[18][19][16][20] The presence of post-obstructive pneumonitis means

NICE 2011	Silvestri 2013	SIGN 2014	NCCN 2016
			that the size of mediastinal lymph nodes has no correlation with tumour involvement. [21] The use of PET/CT for staging of early stage disease avoids inappropriate surgical resection. [22] PET/CT positive nodes generally require pathological confirmation. [2][23]

Back to top

2.5.3 Evidence summary and recommendations

Of four major international guidelines, only one comments on the timing of PET/CT in the work up of lung cancer [4], observing that PET/CT is often best performed before biopsy. In patients potentially suitable for curative therapy, UK guidelines [1] recommend PET/CT as (i) the first test with low likelihood of mediastinal involvement and as (ii) an early test (along with EBUS TBNA) for patients with possible mediastinal involvement. In patients potentially suitable for curative therapy, the Chest guidelines[2] include PET/CT as an early test for patients without extra thoracic involvement on CT and acknowledge the multiple roles of PET/CT including guiding biopsy and staging. The Scottish national guidelines[3] recommend PET/CT for patients potentially suitable for curative therapy and discuss the utility of a negative PET/CT in the exclusion of adrenal metastases. The NCCN guidelines [4] give detailed recommendations for the use of PET/CT across all stages of NSCLC; these guidelines note that PET/CT may be best performed prior to biopsy. The recommendations are based on a range of studies (details in Table 2) evaluating the sensitivity and specificity of PET/CT compared with other imaging modalities and with tissue sampling.

Investigators have explored the use of PET/CT early in the diagnostic algorithm, performed directly after suspicious CXR without the use of interventing diagnostic CT and indicate the potential for greater efficiency without major increases in cost.[24]

Practice point

In the absence of evidence to guide optimal timing of PET/CT in the workup of known or suspected lung cancer (NSCLC) it is advisable to:

1. Offer PET/CT to all patients who are considered for curative therapy.
2. Consider the use of PET/CT prior to biopsy in order to guide biopsy as well as to stage disease.
3. Consider the use of PET/CT at any stage in order to evaluate the extent of metastatic disease.
4. Consider the use of "flat-top" table position for PET/CT as this is the radiotherapy planning position; this may avoid the need for a second scan to plan for radiotherapy.

Back to top

2.5.4 Issues requiring more clinical research study

1. Does the use of PET/CT prior to biopsy improve the efficiency and accuracy of diagnosis and staging?
2. What factors weigh against the use of PET/CT in the workup of known or suspected NSCLC?
3. What are the potential benefits of early PET/CT, following CXR without intervening diagnostic CT? What is the cost-benefit analysis of this approach?

Back to top

2.5.5 Approach to Content Development

The development of the content addressing this question was based on a non-systematic approach to the literature. There is a relative lack of papers that specifically address the question of optimal timing of PET/CT in the diagnosis and workup of lung cancer. This guideline has therefore explored available international recommendations as well as, appropriate papers that address aspects of the question and has combined these findings with practical clinical expertise.

Back to top

2.5.6 References

1. ↑ [1.0] [1.1] National Comprehensive Cancer Network. *NCCN Clinical Practice Guidelines in Oncology. Non-Small Cell Lung Cancer.* NCCN 2011;Version 3 Available from: http://www.nccn.org/professionals/physician_gls/pdf/nscl.pdf.
2. ↑ [2.0] [2.1] [2.2] [2.3] [2.4] Silvestri GA, Gonzalez AV, Jantz MA, Margolis ML, Gould MK, Tanoue LT, et al. *Methods for staging non-small cell lung cancer: Diagnosis and management of lung cancer, 3rd ed: American College of Chest Physicians evidence-based clinical practice guidelines.* Chest 2013 May;143(5 Suppl): e211S-50S Available from: http://www.ncbi.nlm.nih.gov/pubmed/23649440.

3. ↑ 3.0 3.1 Scottish Intercollegiate Guidelines Network (SIGN). *Sign 137: Management of lung cancer. A national clinical guideline.* Edinburgh: Scottish Intercollegiate Guidelines Network; 2014 Available from: http://www.sign.ac.uk/guidelines/fulltext/137/index.html.
4. ↑ 4.0 4.1 4.2 National Comprehensive Cancer Network (NCCN). *Non small cell lung cancer. Version 4.2016.* Fort Washington (PA): National Comprehensive Cancer Network; 2016 Available from: https://www.nccn.org/store/login/login.aspx?ReturnURL=https://www.nccn.org/professionals/physician_gls/pdf/nscl.pdf.
5. ↑ 5.0 5.1 Gould MK, Donington J, Lynch WR, Mazzone PJ, Midthun DE, Naidich DP, et al. *Evaluation of individuals with pulmonary nodules: when is it lung cancer? Diagnosis and management of lung cancer, 3rd ed: American College of Chest Physicians evidence-based clinical practice guidelines.* Chest 2013 May; 143(5 Suppl):e93S-120S Available from: http://www.ncbi.nlm.nih.gov/pubmed/23649456.
6. ↑ 6.0 6.1 Callister ME, Baldwin DR, Akram AR, Barnard S, Cane P, Draffan J, et al. *British Thoracic Society guidelines for the investigation and management of pulmonary nodules.* Thorax 2015 Aug;70 Suppl 2:ii1-ii54 Available from: http://www.ncbi.nlm.nih.gov/pubmed/26082159.
7. ↑ Cronin P, Dwamena BA, Kelly AM, Carlos RC. *Solitary pulmonary nodules: meta-analytic comparison of cross-sectional imaging modalities for diagnosis of malignancy.* Radiology 2008 Mar;246(3):772-82 Available from: http://www.ncbi.nlm.nih.gov/pubmed/18235105.
8. ↑ McWilliams A, Tammemagi MC, Mayo JR, Roberts H, Liu G, Soghrati K, et al. *Probability of cancer in pulmonary nodules detected on first screening CT.* N Engl J Med 2013 Sep 5;369(10):910-9 Available from: http://www.ncbi.nlm.nih.gov/pubmed/24004118.
9. ↑ Tammemägi MC, Church TR, Hocking WG, Silvestri GA, Kvale PA, Riley TL, et al. *Evaluation of the lung cancer risks at which to screen ever- and never-smokers: screening rules applied to the PLCO and NLST cohorts.* PLoS Med 2014 Dec;11(12):e1001764 Available from: http://www.ncbi.nlm.nih.gov/pubmed/25460915.
10. ↑ Al-Ameri A, Malhotra P, Thygesen H, Plant PK, Vaidyanathan S, Karthik S, et al. *Risk of malignancy in pulmonary nodules: A validation study of four prediction models.* Lung Cancer 2015 Jul;89(1):27-30 Available from: http://www.ncbi.nlm.nih.gov/pubmed/25864782.
11. ↑ Kozower BD, Meyers BF, Reed CE, Jones DR, Decker PA, Putnam JB Jr. *Does positron emission tomography prevent nontherapeutic pulmonary resections for clinical stage IA lung cancer?* Ann Thorac Surg 2008 Apr;85(4):1166-9; discussion 1169-70 Available from: http://www.ncbi.nlm.nih.gov/pubmed/18355490.
12. ↑ Gould MK, Maclean CC, Kuschner WG, Rydzak CE, Owens DK. *Accuracy of positron emission tomography for diagnosis of pulmonary nodules and mass lesions: a meta-analysis.* JAMA 2001 Feb 21;285 (7):914-24 Available from: http://www.ncbi.nlm.nih.gov/pubmed/11180735.
13. ↑ Silvestri GA, Gould MK, Margolis ML, Tanoue LT, McCrory D, Toloza E, et al. *Noninvasive staging of non-small cell lung cancer: ACCP evidenced-based clinical practice guidelines (2nd edition).* Chest 2007 Sep; 132(3 Suppl):178S-201S Available from: http://www.ncbi.nlm.nih.gov/pubmed/17873168.
14. ↑ 14.0 14.1 Pieterman RM, van Putten JW, Meuzelaar JJ, Mooyaart EL, Vaalburg W, Koëter GH, et al. *Preoperative staging of non-small-cell lung cancer with positron-emission tomography.* N Engl J Med 2000 Jul 27;343(4):254-61 Available from: http://www.ncbi.nlm.nih.gov/pubmed/10911007.
15. ↑ MacManus MP, Hicks RJ, Matthews JP, Hogg A, McKenzie AF, Wirth A, et al. *High rate of detection of unsuspected distant metastases by pet in apparent stage III non-small-cell lung cancer: implications for radical radiation therapy.* Int J Radiat Oncol Biol Phys 2001 Jun 1;50(2):287-93 Available from: http://www.ncbi.nlm.nih.gov/pubmed/11380213.

16. ↑ 16.0 16.1 Fischer B, Lassen U, Mortensen J, Larsen S, Loft A, Bertelsen A, et al. *Preoperative staging of lung cancer with combined PET-CT.* N Engl J Med 2009 Jul 2;361(1):32-9 Available from: http://www.ncbi.nlm.nih.gov/pubmed/19571281.
17. ↑ Boland GW, Dwamena BA, Jagtiani Sangwaiya M, Goehler AG, Blake MA, Hahn PF, et al. *Characterization of adrenal masses by using FDG PET: a systematic review and meta-analysis of diagnostic test performance.* Radiology 2011 Apr;259(1):117-26 Available from: http://www.ncbi.nlm.nih.gov/pubmed/21330566.
18. ↑ R Chin Jr, R Ward , J W Keyes , R H Choplin , J C Reed , S Wallenhaupt , A S Hudspeth , and E F Haponik. *Mediastinal staging of non-small-cell lung cancer with positron emission tomography.* AJRCCM 1995 Dec 1; Volume 152; No.6 Available from: http://www.atsjournals.org/doi/abs/10.1164/ajrccm.152.6.8520780.
19. ↑ Kernstine KH, Stanford W, Mullan BF, Rossi NP, Thompson BH, Bushnell DL, et al. *PET, CT, and MRI with Combidex for mediastinal staging in non-small cell lung carcinoma.* Ann Thorac Surg 1999 Sep;68(3):1022-8 Available from: http://www.ncbi.nlm.nih.gov/pubmed/10510001.
20. ↑ De Wever W, Stroobants S, Coolen J, Verschakelen JA. *Integrated PET/CT in the staging of nonsmall cell lung cancer: technical aspects and clinical integration.* Eur Respir J 2009 Jan;33(1):201-12 Available from: http://www.ncbi.nlm.nih.gov/pubmed/19118231.
21. ↑ Kerr KM, Lamb D, Wathen CG, Walker WS, Douglas NJ. *Pathological assessment of mediastinal lymph nodes in lung cancer: implications for non-invasive mediastinal staging.* Thorax 1992 May;47(5):337-41 Available from: http://www.ncbi.nlm.nih.gov/pubmed/1609375.
22. ↑ Maziak DE, Darling GE, Inculet RI, Gulenchyn KY, Driedger AA, Ung YC, et al. *Positron emission tomography in staging early lung cancer: a randomized trial.* Ann Intern Med 2009 Aug 18;151(4):221-8, W-48 Available from: http://www.ncbi.nlm.nih.gov/pubmed/19581636.
23. ↑ Darling GE, Maziak DE, Inculet RI, Gulenchyn KY, Driedger AA, Ung YC, et al. *Positron emission tomography-computed tomography compared with invasive mediastinal staging in non-small cell lung cancer: results of mediastinal staging in the early lung positron emission tomography trial.* J Thorac Oncol 2011 Aug;6(8):1367-72 Available from: http://www.ncbi.nlm.nih.gov/pubmed/21587082.
24. ↑ Macpherson R, Benamore R, Panakis N, Sayeed R, Breen D, Bradley K, et al. *A proposed new imaging pathway for patients with suspected lung cancer.* Clin Radiol 2012 Jun;67(6):564-73 Available from: http://www.ncbi.nlm.nih.gov/pubmed/22300820.

Back to top

2.5.7 Appendices

View recommendation components | View pending evidence | View body of evidence | View all comments | View literature search

View PICO

2.6 Routine follow-up & patient outcomes

Contents

2.6.1 Systematic Review Evidence

Routine clinical follow up following curative intent treatment is variably applied. There is variation in both the time intervals of follow up and the required investigations, with most guidelines recommending 3 monthly follow up for the first 2 years and 6 monthly to annually for the next 3 years. Clinical follow up is standard with chest imaging, including chest x-rays, CT scanning and occasionally PET scans.

The potential benefits include the early detection of recurrence or second primary cancer with the option for aggressive treatment resulting in a survival benefit. The surveillance programme can have significant cost implications.

The evidence for this is limited and is largely consensus and guideline driven and distinction needs to be made between small and non-small cell carcinoma. Westeel 2000, in a prospective, randomised controlled trial found that follow up was feasible and may improve survival. Three year survival was 31% if recurrence was found on follow up vs 4% if found on unscheduled visits. [1] Only 15 out of 136 recurrences could be treated with curative intent. A cost analysis showed a cost per life year gained of US$13415 which was felt to be feasible.[1] In a meta-analysis, Calman 2011 found no clear cut benefit to intensive follow up with a trend to improved survival favouring intensive follow up.[2]

Looking at small cell carcinoma, Sugiyama compared intensive (CXR, CT, MR/CT brain, bone scans bimonthly for 6 months and then quarterly for 18 months) with non-intensive follow up in patients with small cell cancer. Survival following recurrence was 9 months in the intensive group and 4 months in the non-intensive group ($p = 0.001$). Overall survival was also better, 20 vs 13 months ($p = 0.04$). Salvage treatment was possible in more of the patients undergoing intensive follow up and with better survival - 8 vs 1 month ($p = 0.001$).[3] Whilst the evidence on non-small cell carcinoma is not clear, there appears to be come survival benefit in small cell carcinoma.

In most studies, recurrences occurred more often within 2 years, justifying the intensive follow up in the first 2 years. Subsequent follow up investigations are mainly aimed at identifying new primaries. Subotic 2009, prospectively reported 88 patients treated surgically for NSCLC. This included 35(39.8%) patients with stage IIIA disease. They compared an intensive follow up consisting of monthly phone calls to the patient with standard follow up clinically. There was no increase in the detection of asymptomatic recurrence.[4]

Returning to the cost involved, a further cost analysis by Egermann 2002 found a cost per life year gained of 90000 Swiss Francs.[5] Goucerol 2013 demonstrated a survival benefit with asymptomatic recurrences of 15.5 months vs 7.2 months (p = 0.001 CI 1.33-3.28) and a cost per life year gained of USD32700.[6]

There are no local Australian guidelines for follow up and it is left to the discretion of the clinician to determine which guideline to follow.

Back to top

2.6.2 Evidence summary and recommendations

Evidence summary	Level	References
Routine follow up is feasible following curative intent treatment of lung cancer.	IV	[1]

Evidence-based recommendation	Grade
It is recommended that patients undergoing curative treatment for lung cancer have regular follow up.	**D**

Evidence summary	Level	References
Intensive follow up may improve survival following curative intent treatment for non-small cell carcinoma.	III-2, IV	[1], [2]

Evidence-based recommendation	Grade
It is recommended that patients undergo follow up after treatment for non-small cell carcinoma.	**D**

Practice point

It is advisable to utilise the many clinical guidelines available for follow up. There are no local Australian guidelines and the clinician may use the NICE guidelines.

2.6.3 Issues requiring more clinical research study

1. What is the most appropriate time interval for surveillance in patients following curative intent treatment for lung cancer?
2. What are the ideal follow up investigations following curative intent treatment for lung cancer?
3. Is routine follow up cost-effective in an Australian setting?
4. Should we be following up non-small and small-cell carcinoma with different protocols?
5. Are there specific patient characteristics that predict improved survival during follow up for lung cancer?

Back to top

2.6.4 References

1. ↑ [1.0] [1.1] [1.2] [1.3] Westeel V, Choma D, Clément F, Woronoff-Lemsi MC, Pugin JF, Dubiez A, et al. *Relevance of an intensive postoperative follow-up after surgery for non-small cell lung cancer.* Ann Thorac Surg 2000 Oct;70(4):1185-90 Available from: http://www.ncbi.nlm.nih.gov/pubmed/11081867.
2. ↑ [2.0] [2.1] Calman L, Beaver K, Hind D, Lorigan P, Roberts C, Lloyd-Jones M. *Survival benefits from follow-up of patients with lung cancer: a systematic review and meta-analysis.* J Thorac Oncol 2011 Dec;6(12):1993-2004 Available from: http://www.ncbi.nlm.nih.gov/pubmed/21892108.
3. ↑ Sugiyama T, Hirose T, Hosaka T, Kusumoto S, Nakashima M, Yamaoka T, et al. *Effectiveness of intensive follow-up after response in patients with small cell lung cancer.* Lung Cancer 2008 Feb;59(2):255-61 Available from: http://www.ncbi.nlm.nih.gov/pubmed/17900754.
4. ↑ Subotic D, Mandaric D, Radosavljevic G, Stojsic J, Gajic M, Ercegovac M. *Relapse in resected lung cancer revisited: does intensified follow up really matter? A prospective study.* World J Surg Oncol 2009 Nov 12;7:87 Available from: http://www.ncbi.nlm.nih.gov/pubmed/19909550.
5. ↑ Egermann U, Jaeggi K, Habicht JM, Perruchoud AP, Dalquen P, Solèr M. *Regular follow-up after curative resection of nonsmall cell lung cancer: a real benefit for patients?* Eur Respir J 2002 Mar;19(3):464-8 Available from: http://www.ncbi.nlm.nih.gov/pubmed/11936523.
6. ↑ Gourcerol D, Scherpereel A, Debeugny S, Porte H, Cortot AB, Lafitte JJ. *Relevance of an extensive follow-up after surgery for nonsmall cell lung cancer.* Eur Respir J 2013 Nov;42(5):1357-64 Available from: http://www.ncbi.nlm.nih.gov/pubmed/23520312.

Back to top

2.6.5 Appendices

View recommendation components | View pending evidence | View body of evidence | View all comments | View literature search

View PICO

Back to top

2.7 Optimal follow-up tests

Contents

2.7.1 Systematic Review Evidence

There is little evidence to support the absolute benefit of follow up in patients following curative intent treatment for lung cancer. The appropriate follow up investigations are also not fully defined. The NCCN, ACCP and ESMO guidelines recommend 6 monthly CT scans for the first 2 years with subsequent annual low-dose CT scans.[1][2][3] There is no recommendation on the role of PET-CT scans at present. The questions guiding the use of the investigations relate to the ability of the test to pick up progressive disease that would result in salvage /curative treatment and also cost-effectiveness.

History and clinical examination are recommended in all guidelines for follow up. There is limited evidence to support the role of chest radiography but it is still included in most guidelines.

Evaluating low-dose CT (LDCT), Chiu et al found that LDCT detected 85.7% of recurrences compared to standard dose scans. They suggest that they may be comparable to standard dose CT for follow up ($p<0.001$).[4] In this study, there was correlation between SDCT and LDCT for detection of pulmonary, pleural and mediastinal recurrences. Low dose CT does have limitations in detecting distant and mediastinal metastases.

PET-CT has been demonstrated to have a high sensitivity and specificity with a low false positive rate.[5][6][7] Antoniou evaluated the prognostic value of PET-CT when done after 6months following completion of treatment and found PET positivity to be associated with a lower survival in younger patients. The median survival with a positive PET was 32.9months compared to 81.6months with a negative scan ($p = 0.0001$). [8]

PET CT, done at 3months, was shown to be more cost effective than CT, especially in asymptomatic patients.[9] The caveat to this was that the imaging depends on what society can afford.There is no evidence for cost-efficacy in the Australian setting and PET-CT is not reimbursed for follow up of lung cancer patients.

Pan et al found that the addition of PET-CT following curative chemoradiation allowed for higher probability of early detection of progression and these patients had a better performance status than those detected on CT ($p=0.02$).[10]

There is no clear evidence demonstrating a survival benefit with the routine use of PET-CT for follow up after management of lung cancer. In consideration of the above, requests for PET-CT should be ideally discussed in the setting of a multi-disciplinary meeting.

Back to top

2.7.2 Evidence summary and recommendations

Evidence summary	Level	References
Low dose CT can be performed for follow up following curative treatment of lung cancer.	III-2	[4]

Evidence-based recommendation	Grade
Low dose CT should be considered as part of the protocol for follow up of lung cancer patients.	**C**

Evidence summary	Level	References
PET-CT is an effective tool in detecting recurrence of lung cancer.	IV	[5], [6], [7]

Evidence-based recommendation	Grade
Consideration should be given to including PET-CT in the follow up for detection of recurrences after 6 months.	**D**

Practice point
It is advisable to consider utilising PET-CT for follow up. There is no evidence to suggest a clear survival benefit even though the probability of detecting early recurrence is higher with PET-CT.

Practice point
PET-CT is not reimbursed for follow up of lung cancer patients.

Practice point
It is suggested that the use of PET-CT for follow up be initiated following discussion at a lung cancer multidisciplinary meeting (MDT).

2.7.3 Issues requiring further clinical research study

1. Is PET-CT routinely required in the follow up of asymptomatic patients following curative treatment for lung cancer?
2. What is the optimal timing and frequency for follow up surveillance with PET-CT?
3. Is it cost-effective in an Australian setting for PET-CT to be included in the follow up investigations?
4. Does PET-CT follow up improve survival compared to standard clinical follow up?

Back to top

2.7.4 References

1. ↑ National Comprehensive Cancer Network (NCCN). *Non small cell lung cancer. Version 4.2016.* Fort Washington (PA): National Comprehensive Cancer Network; 2016 Available from: https://www.nccn.org/store/login/login.aspx?ReturnURL=https://www.nccn.org/professionals/physician_gls/pdf/nscl.pdf.

2. ↑ Colt HG, Murgu SD, Korst RJ, Slatore CG, Unger M, Quadrelli S. *Follow-up and surveillance of the patient with lung cancer after curative-intent therapy: Diagnosis and management of lung cancer, 3rd ed: American College of Chest Physicians evidence-based clinical practice guidelines.* Chest 2013 May;143(5 Suppl):e437S-54S Available from: http://www.ncbi.nlm.nih.gov/pubmed/23649451.
3. ↑ Vansteenkiste J, De Ruysscher D, Eberhardt WE, Lim E, Senan S, Felip E, et al. *Early and locally advanced non-small-cell lung cancer (NSCLC): ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up.* Ann Oncol 2013 Oct;24 Suppl 6:vi89-98 Available from: http://www.ncbi.nlm.nih.gov/pubmed/23860613.
4. ↑ [4.0] [4.1] Chiu CH, Chern MS, Wu MH, Hsu WH, Wu YC, Huang MH, et al. *Usefulness of low-dose spiral CT of the chest in regular follow-up of postoperative non-small cell lung cancer patients: Preliminary report.* J Thorac Cardiovasc Surg 2003 Jun;125(6):1300-5 Available from: http://www.ncbi.nlm.nih.gov/pubmed/12830048.
5. ↑ [5.0] [5.1] Muzaffer Metin, Makbule Ergin, Okan Solak, Adnan Sayar, Murat Sezer, Atilla Pekcolaklar, Atilla Gürses. *Effectiveness of PET Scan in Postoperative Long Term Follow up of Patients with Nonsmall Cell Lung Cancer.* JCAM ;3(1):30-2 Available from: http://www.jcam.com.tr/files/KATD-489.pdf.
6. ↑ [6.0] [6.1] Hiroaki Toba, Shoji Sakiyama, Hideki Otsuka, Yukikiyo Kawakami, Hiromitsu Takizawa, Koichiro Kenzaki, Kazuya Kondo,vand Akira Tangokua. *18F-fluorodeoxyglucose positron emission tomography /computed tomography is useful in postoperative follow-up of asymptomatic non-small-cell lung cancer patients.* Interact Cardiovasc Thorac Surg. ;15(5): 859–864. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3480619/.
7. ↑ [7.0] [7.1] Dane B, Grechushkin V, Plank A, Moore W, Bilfinger T. *PET/CT vs. non-contrast CT alone for surveillance 1-year post lobectomy for stage I non-small-cell lung cancer.* Am J Nucl Med Mol Imaging 2013 Sep 19;3(5):408-16 Available from: http://www.ncbi.nlm.nih.gov/pubmed/24116349.
8. ↑ Antoniou AJ, Marcus C, Tahari AK, Wahl RL, Subramaniam RM. *Follow-up or Surveillance (18)F-FDG PET /CT and Survival Outcome in Lung Cancer Patients.* J Nucl Med 2014 Jul;55(7):1062-8 Available from: http://www.ncbi.nlm.nih.gov/pubmed/24777290.
9. ↑ van Loon J, Grutters JP, Wanders R, Boersma L, Dingemans AM, Bootsma G, et al. *18FDG-PET-CT in the follow-up of non-small cell lung cancer patients after radical radiotherapy with or without chemotherapy: an economic evaluation.* Eur J Cancer 2010 Jan;46(1):110-9 Available from: http://www.ncbi.nlm.nih.gov/pubmed/19944595.
10. ↑ Pan Y, Brink C, Schytte T, Petersen H, Wu YL, Hansen O. *Planned FDG PET-CT Scan in Follow-Up Detects Disease Progression in Patients With Locally Advanced NSCLC Receiving Curative Chemoradiotherapy Earlier Than Standard CT.* Medicine (Baltimore) 2015 Oct;94(43):e1863 Available from: http://www.ncbi.nlm.nih.gov/pubmed/26512597.

Back to top

2.7.5 Appendices

View recommendation components	View pending evidence	View body of evidence	View all comments	View literature search
View PICO				

Back to top

2.8 Optimal model (provider) of follow up care

Contents

2.8.1 Systematic Review Evidence

There is limited evidence on the optimal follow up model, either specialist (surgeon or physician), clinical nurse specialist or family physician driven.

In a randomised controlled trial, Moore et al, evaluated nurse led follow up looking at patient quality of life (QOL) and patient satisfaction.They found that patients had more satisfaction at 3 months with nurse led follow up, fewer medical consultations and a shorter time to symptomatic progression possibly related to the education they received regarding the symptoms - 6 vs 10.2 months ($p = 0.004$). There was no survival difference with nurse led follow up ($p = 0.99$). [1] This led to the NICE and Scottish guidelines being amended to include the role of the clinical nurse specialist in the follow up of lung cancer patients in a complementary fashion.[2][3]

Gilbert 2000 found no survival differences between surgeon and general practitioner follow up although the costs were higher with surgical follow up. In addition, more recurrences were found by the GP, mainly with history and clinical examination. [4]

Evaluating the role of telephonic nurse led follow up on symptoms and QOL in a quasi-experimental study of non-surgical patients, it was found that patients in this group had better social functioning and QOL and less side-effects with chemotherapy - believed to be related to the education regarding symptoms and more support. [5]

Comparing specialist with nurse and GP follow up, Cox 2006 found patients were happier with specialist follow up over nursing ($p = 0.018$) but favoured nurses over GP ($p = 0.012$). In an outpatient setting, 20% of patients were suitable for nurse led follow up.[6]

The American College of Chest Physicians (ACCP) have a level 1C recommendation for follow up with the original physician.[7] In a systematic review, Schmidt-Hansen 2012 suggested that all patients be offered an initial 6 week review with a specialist to discuss the ongoing review and follow up plan with early involvement of a clinical nurse specialist.[8] Nakamura 2010 found that physician led follow up was associated with a better survival over surgical follow up ($p = 0.0009$). This was confounded by the fact that the methods of follow up were different in the 2 groups with surgeons not using CT scans. In addition, looking at the more recent cases (post 1994), there was no survival difference.[9]

There is insufficient evidence to support a specific follow up model. Current follow up with a multidisciplinary approach is advocated with specialist (either surgeon or physician) follow up, complemented by clinical nurse specialists and involvement of the GP.[3]

Back to top

2.8.2 Evidence summary and recommendations

Evidence summary	Level	References
Specialist follow up should be offered to all patients following curative intent treatment for lung cancer.	III-2	[8]

Evidence-based recommendation	Grade
A multidisciplinary approach to follow up is ideal, involving the treating specialists, family physician and clinical nurse specialists.	**C**

Evidence summary	Level	References
The evidence suggests that patient satisfaction is improved with nurse involvement	II	[1]

Evidence summary	Level	References
in the follow up team.		

Evidence-based recommendation	Grade
It is recommended that a nurse specialist ideally be involved, as an member of the team, in the follow up team for patients receiving curative intent treatment for lung cancer.	**B**

2.8.3 Issues requiring more clinical research study

1. How do we streamline the follow up to reduce duplication of tests and follow up appointments?
2. How do we incorporate modern technology and social media in the follow up of patients following curative treatment for NSCLC?
3. Can we incorporate apps to facilitate follow up for lung cancer?

Back to top

2.8.4 References

1. ↑ [1.0] [1.1] 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 Nov 16;325(7373):1145 Available from: http://www.ncbi.nlm.nih.gov/pubmed/12433764.
2. ↑ National Institute for Health and Care Excellence (NICE). *Lung cancer:diagnosis and management (update).* Manchester, UK; 2011 Available from: https://www.nice.org.uk/guidance/cg121/resources/lung-cancer-diagnosis-and-management-35109444863941.
3. ↑ [3.0] [3.1] Scottish Intercollegiate Guidelines Network (SIGN). *Sign 137: Management of lung cancer. A national clinical guideline.* Edinburgh: Scottish Intercollegiate Guidelines Network; 2014 Available from: http://www.sign.ac.uk/guidelines/fulltext/137/index.html.
4. ↑ Gilbert S, Reid KR, Lam MY, Petsikas D. *Who should follow up lung cancer patients after operation?* Ann Thorac Surg 2000 Jun;69(6):1696-700 Available from: http://www.ncbi.nlm.nih.gov/pubmed/10892909.
5. ↑ Hintistan S, Nural N, Cilingir D, Gursoy A. *Therapeutic Effects of Nurse Telephone Follow-up for Lung Cancer Patients in Turkey.* Cancer Nurs 2016 Dec 12 Available from: http://www.ncbi.nlm.nih.gov/pubmed/27977427.
6. ↑ Cox K, Wilson E, Heath L, Collier J, Jones L, Johnston I. *Preferences for follow-up after treatment for lung cancer: assessing the nurse-led option.* Cancer Nurs 2006 May;29(3):176-87 Available from: http://www.ncbi.nlm.nih.gov/pubmed/16783116.
7. ↑ Colt HG, Murgu SD, Korst RJ, Slatore CG, Unger M, Quadrelli S. *Follow-up and surveillance of the patient with lung cancer after curative-intent therapy: Diagnosis and management of lung cancer, 3rd ed: American College of Chest Physicians evidence-based clinical practice guidelines.* Chest 2013 May;143(5 Suppl):e437S-54S Available from: http://www.ncbi.nlm.nih.gov/pubmed/23649451.

8. ↑ 8.0 8.1 Schmidt-Hansen M, Baldwin DR, Hasler E. *What is the most effective follow-up model for lung cancer patients? A systematic review.* J Thorac Oncol 2012 May;7(5):821-4 Available from: http://www.ncbi.nlm.nih.gov/pubmed/22481234.
9. ↑ Nakamura R, Kurishima K, Kobayashi N, Ishikawa S, Goto Y, Sakai M, et al. *Postoperative follow-up for patients with non-small cell lung cancer.* Onkologie 2010;33(1-2):14-8 Available from: http://www.ncbi.nlm.nih.gov/pubmed/20164657.

Back to top

2.8.5 Appendices

View recommendation components	View pending evidence	View body of evidence	View all comments	View literature search
View PICO				

Back to top

2.9 Guideline development process

2.9.1 Project background

In 2010, Cancer Council Australia embarked on the revision of the treatment and follow-up section of the *2004 Clinical Practice Guidelines for the Prevention, Diagnosis and Management of Lung Cancer* as wiki-based, electronic guidelines with funding received from Cancer Australia. The revision covering Management and Follow-up was finalised in 2012 developed by the multi-disciplinary Lung Cancer Treatment Guidelines Working Party.

In 2012, the Management Committee of the Lung Cancer Guidelines Revision project was contacted to propose suitable lead authors and working party members for the prevention and diagnosis guidelines (see: Lung Cancer Treatment Guidelines Working Party).

In November 2012, Cancer Council Australia convened the first working party meeting to determine the included clinical questions to be part of the prevention and diagnosis section of the revised lung cancer guidelines.

2.9.1.1 Funding

The revised *Clinical practice guidelines for the prevention and diagnosis of lung cancer* are developed by Cancer Council Australia. No external funding has been received. Cancer Council Australia contributed in kind resources consisting of project staff, facilities, systems and travel budget to fund the prevention and diagnosis section revision of the 2004 lung cancer guidelines.

Back to top

2.9.2 Project governance, guidelines scope and guidelines development group

The small Management Committee appointed in 2009 is responsible to oversee the guidelines revision project. The Management Committee is responsible for the overall management and strategic leadership of the guidelines review process.

The Management Committee proposed lead authors for each included clinical question. The nominated individuals were invited to join (see multidisciplinary working party). In addition, the Management Committee identified and nominated a consumer representative to join the multidisciplinary working party.

In consultation with the question lead author, sub-committees consisting of members with relevant expertise and experience were established for each question (see multidisciplinary working party).

Declarations of interest were collected from all nominated members and evaluated (see COI register). All members were advised to update their declarations of interest over the course of the project and received reminders to review their declarations prior to every formal working party meeting.

Back to top

2.9.3 Guidelines development approach

The Management Committee agreed to use Cancer Council Australia's Cancer Guidelines Wiki Platform and approach to develop the guidelines. The Wiki Platform is web-based and supports all processes of guidelines development, such as the literature search, critical appraisal, data extraction, evidence assessment and summary processes, as well as content and recommendation development, online consultation, review and web publication. It is in line with the NHMRC guidelines requirements, designated standards of quality, process and grading system for recommendations.[1][2] An infrastructure is set in place to process literature updates and continuously update content as new evidence emerges and is reviewed.

The Development of Clinical Practice Guidelines using Cancer Council Australia's Cancer Guidelines Wiki Handbook[3] illustrates the steps in the development of Cancer Council Australia's web-based clinical practice guidelines. It provides information to assist working party members and staff members to develop concise clinical questions in PICO format, construct sound search strategies, systematically search the literature, critically appraise, summarise the evidence and formulate guidelines recommendations.

Rather than waiting until systematic reviews and content for all included clinical questions have been finalised, the working party agreed to publish finalised question content and the associated recommendations in stages. The group decided that it is important to publish content and results as soon as it is finalised by the working party to ensure that the medical community receives up-to-date information without any publication delay. Prior to publication, feedback would be sought from guidelines stakeholders about the clinical questions content (See also Public Consultation).

The first set of completed draft contents regarding screening and early detection is now being released for public consultation:

- In people at risk of lung cancer, does population based screening with chest radiography reduce mortality?
- In people at risk of lung cancer, does population based CT screening reduce mortality?
- Which population group would most benefit from CT screening for lung cancer?

Subsequent clinical questions and associated recommendations will be published in 2017 and 2018.

The detailed steps in preparing the question content, conducting the literature searches, appraising the literature and formulating and grading recommendations, are outlined below.

Back to top

2.9.4 Steps in preparing clinical practice guidelines

For every clinical question the following steps were completed:

1. Develop a structured clinical question in PICO format

2. Search for existing relevant guidelines and systematic reviews answering the clinical question

3. Perform systematic review process

    Developing the systematic review protocol and systematic literature search strategy for each PICO question

    Conducting the systematic literature search according to protocol

    Screening of literature results against pre-defined inclusion and exclusion criteria

    Critical appraisal and data extraction of each included article

    Body evidence table of all included literature

4. Summarise the relevant data

5. Assess the body of evidence and formulate recommendations

6. Write the content narrative

Back to top

2.9.4.1 Step 1. Develop a structured clinical question

All included questions were reviewed on the basis of their purpose, scope and clinical importance to the target audience and were structured according to the PICO (populations, interventions, comparisons, outcomes) framework. The lead authors provided the systematic review team with feedback to refine the PICO questions and inclusion and exclusion criteria for the systematic review.

Back to top

2.9.4.2 Step 2. Search for existing relevant guidelines and systematic reviews

For each PICO question, the National Guideline Clearinghouse, the Guidelines Resource Centre and the scoping search for the PICO question were scanned for relevant clinical practice guidelines to inform the question.

Back to top

2.9.4.3 Step 3. Perform systematic review process

2.9.4.3.1 Developing a systematic search strategy

For each PICO question, systematic literature search strategies were developed by the technical team. Searches were limited or widened as necessary according to the PICO structure using keywords or MESH and subject terms. Systematic search strategies were derived from these terms for each included electronic databases. The included standard databases searched were Pubmed, Embase, Trip database, Cochrane Database of Systematic Reviews and Database of Abstracts of Reviews of Effects and Health Technology Assessment for all questions. The psychosocial questions also included CINAHL and PsycINFO databases to retrieve relevant literature.

Back to top

2.9.4.3.2 Conducting the systematic literature search according to protocol

Clinical practice guidelines should be based on systematic identification and synthesis of the best available scientific evidence.[1] For each clinical question that required a systematic literature review, literature searches were conducted systematically from 1990 onwards. The following electronic databases were part of the systematic literature search strategy:

- **PubMed –** bibliographic references and abstracts to articles in a range of languages on topics such as clinical medical information and biomedicine, and including the allied health fields, biological and physical sciences.
- **EMBASE –** major pharmacological and biomedical database indexing drug information from 4550 journals published in 70 countries.
- **Trip Database –** A medical database with focus on Evidence based medicine and clinical practice guidelines with content available from Cochrane and Bandolier.
- **Database of Abstracts of Reviews of Effects and Health Technology Assessment –** Contains details of systematic reviews that evaluate the effects of healthcare interventions and the delivery and organisation of health services.
- **The Cochrane Database of Systematic Reviews**.
- **Cinahl –** Bibliographic references and abstracts to journal articles, book chapters, pamphlets, audiovisual materials, software, dissertations, critical paths, and research instruments on topics including nursing and allied health, biomedicine, consumer health, health sciences librarianship, behavioral sciences, management, and education
- **Psychinfo –** Bibliographic references and abstracts to journal articles, book chapters, dissertations and technical reports on psychology; social, clinical, cognitive and neuropsychology; psychiatry, sociology, anthropology and education, with source material from a wide range of languages.

Additional relevant papers from reference lists and, where appropriate, clinical trial registries, were also identified for retrieval as part of the snowballing process.

The full detailed systematic literature search strategy for every clinical question is fully documented in the appendix of the clinical question.

Back to top

2.9.4.3.3 Screening of literature results against pre-defined inclusion and exclusion criteria

Part of the systematic review process is to screen all retrieved literature results against the pre-defined inclusion and exclusion criteria in two stages.

a) First screen – During the first screening round, the titles and abstracts of all retrieved literature were screened by the Project Officer. All irrelevant, incorrect and duplicates were removed.

b) Second screen – A second screen was undertaken based on the full article. The Project Officer and the allocated Lead Author assessed each article for inclusion against the pre-defined inclusion and exclusion criteria for each question. In the case of a disagreement between the reviewers, a third independent reviewer assessed the article against the inclusion and exclusion criteria. Articles that met the inclusion criteria were forwarded for quality assessment and data extraction to the lead author.

Back to top

2.9.4.3.4 Critical appraisal and data extraction of each included article

The risk of bias of each of the included studies was assessed using a study design specific assessment tool and where necessary pre-specified criteria. For all quality assessment tools, see Guideline Development Handbook.

For all included articles, the relevant data was extracted and summarised in study characteristics and evidence tables. Each risk of bias assessment and data extraction was checked by the Project Officer. These tables are available in the appendix of each question.

Back to top

2.9.4.4 Step 4. Summarise the relevant data

The study results, level of the evidence, risk of bias due to study design and the relevance of the evidence for each included study were summarised in a body of evidence table.

The NHMRC levels of evidence are outlined below:

2.9.4.4.1 Table 1. Designations of levels of evidence according to type of research question (NHMRC, 2009)

Level	Intervention	Diagnosis	Prognosis	Aetiology	Screening
I	A systematic review of level II studies	A systematic review of level II studies	A systematic review of level II studies	A systematic review of level II studies	A systematic review of level II studies
II	A randomised controlled trial	A study of test accuracy with: an independent, blinded comparison with a valid reference standard, among consecutive patients with a defined	A prospective cohort study	A prospective cohort study	A randomised controlled trial

		clinical presentation			
III-1	A pseudo-randomised controlled trial (i.e. alternate allocation or some other method)	A study of test accuracy with: an independent, blinded comparison with a valid reference standard, among non-consecutive patients with a defined clinical presentation	All or none	All or none	A pseudo-randomised controlled trial (i.e. alternate allocation or some other method)
III-2	A comparative study with concurrent controls: Non-randomised, experimental trial Cohort study Case-control study Interrupted time series with a control group	A comparison with reference standard that does not meet the criteria required for Level II and III-1 evidence	Analysis of prognostic factors amongst untreated control patients in a randomised controlled trial	A retrospective cohort study	A comparative study with concurrent controls: Non-randomised, experimental trial Cohort study Case-control study
III-3	A comparative study without concurrent controls: Historical control study Two or more single arm study	Diagnostic case-control study	A retrospective cohort study	A case-control study	A comparative study without concurrent controls: Historical control study

	Interrupted time series without a parallel control group				Two or more single arm study
IV	Case series with either post-test or pre-test/post-test outcomes	Study of diagnostic yield (no reference standard)	Case series, or cohort study of patients at different stages of disease	A cross-sectional study	Case series

Source: National Health and Medical Research Council. NHMRC additional levels of evidence and grades for recommendations for developers of guidelines. Canberra: NHMRC; 2009. (https://www.nhmrc.gov.au/_files_nhmrc/file/guidelines/developers/nhmrc_levels_grades_evidence_120423.pdf)

Back to top

2.9.4.5 Step 5. Assess the body of evidence and formulate recommendations

The body of evidence table for each clinical question was forwarded to the lead author for assessment. The lead author in collaboration with the Project Officer assessed the body of evidence and completed the evidence assessment matrix in regard to the volume of the evidence, its consistency, clinical impact, generalisability and applicability and developed evidence statements for each recommendation.

The process is described in NHMRC additional levels of evidence and grades for recommendations for developers of guidelines (2009).[4]

Following grading of the body of evidence and development of evidence statements, authors were asked to formulate evidence-based recommendations based on the results of the systematic review summarised in the body of evidence table. The method of grading recommendations is shown in Table 2.

2.9.4.5.1 Table 2. Grading of recommendations

Component of Recommendation	**Recommendation Grade**			
	A **Excellent**	**B** **Good**	**C** **Satisfactory**	**D** **Poor**
	one or more level I studies with a low risk of	one or two level II studies with a low risk of bias	one or two level III studies with a low risk	level IV studies, or level I to III studies

Volume of evidence [1]**	bias or several level II studies with a low risk of bias	or a systematic review/several level III studies with a low risk of bias	of bias, or level I or II studies with a moderate risk of bias	/systematic reviews with a high risk of bias
Consistency [2]**	all studies consistent	most studies consistent and inconsistency may be explained	some inconsistency reflecting genuine uncertainty around clinical question	evidence is inconsistent
Clinical impact	very large	substantial	moderate	slight or restricted
Generalisability	population/s studied in body of evidence are the same as the target population for the guideline	population/s studied in the body of evidence are similar to the target population for the guideline	population/s studied in body of evidence differ to target population for guideline but it is clinically sensible to apply this evidence to target population[3]	population/s studied in body of evidence different to target population and hard to judge whether it is sensible to generalise to target population
Applicability	directly applicable to Australian healthcare context	applicable to Australian healthcare context with few caveats	probably applicable to Australian healthcare context with some caveats	not applicable to Australian healthcare context

[1] Level of evidence determined from level of evidence criteria

[2] If there is only one study, rank this component as 'not applicable'

[3] For example results in adults that are clinically sensible to apply children OR psychosocial outcomes for one cancer that may be applicable to patients with another cancer.

[**]For a recommendation to be graded A or B, the volume and consistency of evidence must also be graded either A or B!

Source: National Health and Medical Research Council. NHMRC additional levels of evidence and grades for recommendations for developers of guidelines. Canberra: NHMRC; 2009. (https://www.nhmrc.gov.au /_files_nhmrc/file/guidelines/developers/nhmrc_levels_grades_evidence_120423.pdf)

The overall recommendations grade are shown in Table 3.

2.9.4.5.2 Table 3. Overall recommendation grades

Grade of recommendation	Description
A	Body of evidence can be trusted to guide practice
B	Body of evidence can be trusted to guide practice in most situations
C	Body of evidence provides some support for recommendation(s) but care should be taken in its application
D	Body of evidence is weak and recommendation must be applied with caution

Source: National Health and Medical Research Council. NHMRC levels of evidence and grades for recommendations for developers of guidelines. Canberra: NHMRC; 2009. (https://www.nhmrc.gov.au/_files_nhmrc/file/guidelines/developers/nhmrc_levels_grades_evidence_120423.pdf)

The NHMRC approved recommendation types and definitions are shown in Table 4.

2.9.4.5.3 Table 4. NHMRC approved recommendation types and definitions

Type of recommendation	Definition
Evidence-based recommendation	A recommendation formulated after a systematic review of the evidence, indicating supporting references
Consensus-based recommendation	A recommendation formulated in the absence of quality evidence, after a systematic review of the evidence was conducted and failed to identify admissible evidence on the clinical question
Practice point	A recommendation on a subject that is outside the scope of the search strategy for the systematic review, based on expert opinion and formulated by a consensus process

Source: National Health and Medical Research Council. Procedures and requirements for meeting the NHMRC standard for clinical practice guidelines. Melbourne: National Health and Medical Research Council, 2011

In addition to developing evidence-based recommendations as a result of the systematic review for a clinical question, expert authors could also draft consensus-based recommendations in the absence of evidence after having performed a systematic review or practice points, when a matter was outside the scope of the search strategy for the systematic review.

Back to top

2.9.4.6 Step 6. Write the content narrative

For each question, the assigned lead authors were asked to draft their guidelines chapter using the following format:

- Background to the clinical question, including its clinical importance and historical evidence, where relevant
- Review of the evidence, including the number, quality and findings of studies identified by the systematic review
- Evidence summary in tabular form including evidence statements, levels of evidence of included studies, and reference citations
- Evidence-based recommendation(s) and corresponding grade(s), consensus-based recommendations and practice points
- Discussion, including unresolved issues, relevant studies currently underway, and future research priorities
- References.

The content draft was then reviewed by the working party and feedback incorporated where required.

Back to top

2.9.5 Review of the draft chapters

Draft content was circulated to the working party. Members were asked to submit further suggestions on consensus-based recommendations and practice points.

A teleconference with all working party members was scheduled to review and finalise the draft content for public consultation. Prior to this teleconference, the latest iteration drafts were circulated. All panelists were asked to review the content, individual recommendations and practice points in detail, identify and note any controversies and points to be discussed at the meeting. During the meeting, each recommendation and practice point was tabled as an agenda point. Each was reviewed and approved by consensus, which was reached by voting. The Chairperson nominated a particular recommendation/practice point to be reviewed and the panelists had the opportunity to discuss any issues and suggest revisions to recommendations and practice points. Each recommendation and practice point was approved once the eligible panelists reached consensus.

Back to top

2.9.6 Public consultation

This guideline is being developed in a staged process.

- The first set of draft clinical questions (screening and early detection questions) was made available on the wiki for public consultation from 19 August to 19 September 2016.
- The second set of draft clinical questions was made available on the wiki for public consultation from 3-30 July 2017.

During each public consultation period, submissions are invited from the general public and professional societies and groups and other relevant stakeholders. Relevant professional societies and groups, consumer groups and other relevant stakeholders are contacted.

All feedback on the draft received during the consultation periods is compiled and sent to the relevant lead author (and subcommittee, when required) to review the draft content, assessing and considering the submitted comments. Any additional submitted papers are assessed by the methodologist team against the review protocol.

Wider Working Party review of the public consultation comments and suggested amendments is facilitated by email or teleconference. Subsequent changes to the draft are agreed by consensus, based on consideration of the evidence and, in the absence of evidence, expert opinion. The same consensus process that was followed during the face-to-face Working Party meeting prior to public consultation is followed.

All changes resulting from the public consultation submission reviews will be documented and made accessible by request once the guidelines are published.

Back to top

2.9.7 Dissemination and implementation

A multi-strategy approach will be followed for the dissemination and implementation of the guidelines, as this has shown to positively influence guidelines uptake.[5][6]

Once all clinical questions that are part of the guidelines revision are completed, the guidelines will be distributed directly to relevant professional and other interested groups and through meetings, national and international conferences, and other professional development and continuing medical education (CME) events. Local expert leaders will be identified and approached to facilitate dissemination and act as champions for the guidelines.

A significant effort will be made to have the guidelines introduced to senior undergraduate medical students and to encourage the relevant learned colleges to support the guidelines and to foster their integration into hospital and community practice through resident and registrar education activities.

The guidelines will be made available as online guidelines via the Cancer Council Australia Cancer Guidelines Wiki. The online guidelines version increases availability as well as accessibility, and usage will be tracked and analysed with a web analytics solution. The Cancer Guidelines Wiki is a responsive website that is optimised for mobile and desktop access.

Interlinking and listing the guidelines on national and international guideline portal is also an important part of the digital dissemination strategy. Important Australian health websites, such as EviQ and healthdirect Australia will be approached to link to the online guidelines. The guidelines will also be listed on national and international guideline portals such as Australia’s Clinical Practice Guidelines Portal, Guidelines International Network guidelines library and National Guidelines Clearinghouse.

The Cancer Guidelines Wiki is based on semantic web technology, so the guidelines are available in a machine-readable format, which offers the possibility to easily integrate the guidelines content with systems and web applications used in the Australian healthcare context. Use of the guidelines as part of core curriculum in specialty exams will be encouraged.

It is recognised that a planned approach is necessary to overcome specific barriers to implementation in particular settings and to identify appropriate incentives to encourage uptake of guidelines recommendations. Implementation of the guidelines will require a combination of effective strategies and may include further CME initiatives and interactive learning, the development and promotion of computer-assisted decision aids and electronic decision-support systems, and the creation of audit and other clinical tools.

Back to top

2.9.8 Future updates

The handbook *Development of Clinical Practice Guidelines Using Cancer Council Australia's Cancer Guidelines Wiki. Handbook for section authors and the guideline working party.* outlines Cancer Council Australia's guidelines updating processes. The incoming literature updates will continue to be monitored for each systematic review question. The Working Party will notify the Project Officer if any clinical question requires revision because new high level evidence has been published. External stakeholders are encouraged to use the comment feature and notify us of any new evidence for a specific topic.

2.9.9 References

1. ↑ [1.0] [1.1] National Health and Medical Research Council. *Procedures and requirements for meeting the NHMRC standard for clinical practice guidelines.* Melbourne; 2011.
2. ↑ National Health and Medical Research Council. *NHMRC levels of evidence and grades for recommendations for guideline developers.* Canberra: National Health and Medical Research Council; 2009 Available from: https://www.nhmrc.gov.au/_files_nhmrc/file/guidelines/developers/nhmrc_levels_grades_evidence_120423.pdf.
3. ↑ Clinical Guidelines Network Cancer Council Australia. *Development of Clinical Practice Guidelines using Cancer Council Australia's Cancer Guidelines Wiki. Handbook for section authors and the guideline working party.* CCA Sydney; 2014 Available from: http://wiki.cancer.org.au/australiawiki/images/9/9b/CCA_Clinical_Practice_Guideline_Development_Handbook.pdf.
4. ↑ National Health and Medical Research Council. *NHMRC levels of evidence and grades for recommendations for guideline developers.* Canberra: National Health and Medical Research Council; 2009 Available from: https://www.nhmrc.gov.au/_files_nhmrc/file/guidelines/developers/nhmrc_levels_grades_evidence_120423.pdf.
5. ↑ National Institute of Clinical Studies. *Do guidelines make a difference to health outcomes?*; 2006 Available from: https://www.nhmrc.gov.au/_files_nhmrc/file/nics/material_resources/Do%20guidelines%20make%20a%20difference%20to%20health%20care%20outcomes.pdf.
6. ↑ Francke AL, Smit MC, de Veer AJE, Mistiaen P. *Factors influencing the implementation of clinical guidelines for health care professionals: A systematic meta-review.* BMC Med Inform Decis Mak 2008;8, (38).

Back to top

2.10 List of clinical questions

2.10.1 Published

- In people at risk of lung cancer, does population based screening with chest radiography reduce mortality
- In people at risk of lung cancer, does population based CT screening reduce mortality?
- Which population group would potentially most benefit from CT screening for lung cancer?
- What specimen types are suitable for mutation testing in NSCLC patients?
- When is IHC required for subtyping of non-small cell lung cancer and what is the optimal IHC panel?
- In people undergoing lung cancer evaluation, does concurrent diagnosis and staging provide greater benefit for patient outcomes compared to sequential testing for diagnosis followed by staging?
- Does routine follow-up improve patient outcomes in people who have curative intent treatments for lung cancer?
- What is the optimal test and timing for the follow-up of people with lung cancer who have had curative intent treatment?
- What is the optimal model (provider) of care for the follow up of people with lung cancer who have had curative intent treatment?
- For patients undergoing workup for known or suspected lung cancer, what is the optimal timing of PET/CT? Before or after tissue biopsy confirmation?

2.10.2 Underway or pending

- What is the most effective way to manage small solid, sub-solid and non-solid nodules?
- In people with suspected early stage lung cancer considered for curative treatment (surgery, radiation therapy, ablation), does pathological diagnosis improve outcomes?
- For suspected lung cancer in the periphery of the lung (peripheral pulmonary lesions), what is the most effective diagnostic modality?
- In patients considered for curative treatment of lung cancer, is MRI more effective that CT scan for the diagnosis of brain metastases?
- What are the most effective smoking cessation strategies for smokers who have been diagnosed with lung cancer?
- In smokers or former smokers at risk of lung cancer, is chemoprevention effective?
- In people with lung cancer referred for active treatment, does smoking cessation result in improved outcomes?
- Which histological subtype should undergo testing?
- What are the validated patient and tumour prognostic markers in NSCLC and SCLC?

2.10.3 Suggestions

If you would like to submit any proposed questions to be considered for inclusion in the guidelines, please submit a comment below for consideration by the Working Party.

Back to top

2.11 Working party members and contributors

2.11.1 Working Party membership and contributors

2.11.2 Working Party members

Working Party Member	Affiliation	State or country
Prof Kwun Fong (Chairperson)	Thoracic and Sleep Physician, Dept of Thoracic Medicine, The Prince Charles Hospital	QLD
A/Prof Eddie Lau	Consultant radiologist and nuclear medicine specialist, Austin Health, Melbourne	VIC
Prof David Ball	Deputy Director, Division of Radiation Oncology and Cancer Imaging Chair, Lung Service, Peter MacCallum Cancer Centre	VIC
Dr Steven Leong	Thoracic and Sleep Physician, Dept of Thoracic Medicine, The Prince Charles Hospital	QLD
A/Prof Rayleen Bowman	Staff Specialist (Thoracic), The Prince Charles Hospital	QLD
Dr Christopher Lewis	Respiratory Physician, Auckland City Hospital	NZ
A/Prof Wendy Cooper	Staff Specialist, Department of Tissue Pathology and Diagnostic Oncology, Royal Prince Alfred Hospital	NSW
Dr Henry Marshall	Thoracic Physician, Dept of Thoracic Medicine, The Prince Charles Hospital	QLD
A/Prof	Head, Health Services Research, MCRI and Clinical Epidemiologist, Cancer Strategy	

Working Party Member	Affiliation	State or country
Michael Coory	and Development, Murdoch Children's Research Institute and Department of Health Victoria	VIC
Dr Lucy Morgan	Senior Staff Specialist, Department of Respiratory Medicine, Concord Hospital	NSW
Dr Emily Stone	Senior Staff Specialist, Department of Thoracic Medicine, St Vincent’s Hospital	NSW
Dr Morgan Windsor	Cardiothoracic Surgeon, Holy Spirit Northside Private Hospital	QLD
Dr Rishendran Naidoo	Cardiothoracic Surgeon, The Prince Charles Hospital	QLD
Ms Ingrid Pleuckhahn	Nurse, Peter MacCallum Cancer Centre	VIC
Dr Fraser Brims	Consultant Respiratory Physician, Sir Charles Gairdner Hospital	WA
Ms Amanda Watson	Consumer representative	QLD

2.11.3 Cancer Council Australia team members

Individual	Role
Christine Vuletich	Manager, Clinical guidelines Network, Cancer Council Australia, 2012-July 2014
Jutta von Dincklage	Head, Clinical Guidelines Network, Cancer Council Australia, July 2012-present Product Manager, Wiki Development, Cancer Council Australia, January 2010-June 2012
Laura Wuellner	Project Manager, Clinical Guidelines Network, Cancer Council Australia, Sept 2014-Nov 2016 Acting Head, Clinical Guidelines Network, November 2017-December 2017
Katrina Anderson	Project Manager, Clinical Guidelines Network, Cancer Council Australia, November 2016-December 2017
Emma Dickins	Project Officer, Systematic Literature Review, Clinical Guidelines Network, Cancer Council Australia, 2014-June 2016
Clara Ha	Project Officer, Systematic Literature Review, Clinical Guidelines Network, Cancer Council Australia August 2016-December 2017

2.11.3.1 Lead authors of published questions or questions currently open for public consultation

Working party member	Published clinical questions
Prof Kwun Fong	In people at risk of lung cancer, does population based screening with chest radiography reduce mortality? (published)
A/Prof Eddie Lau	In people at risk of lung cancer, does population based CT screening reduce mortality? (published)
Dr Henry Marshall	Which population group would most benefit from CT screening for lung cancer? (published)
A/Prof Wendy Cooper	■ When is IHC required for subtyping of NSCLC and what is the optimal IHC panel? (public consultation) ■ What specimen types are suitable for mutation testing in NSCLC patients? (public consultation)
Dr Chris Lewis	In people undergoing lung cancer evaluation, does concurrent diagnosis and staging provide greater benefit for patient outcomes compared to sequential testing for diagnosis followed by staging? (public consultation)
Dr Emily Stone	For patients undergoing workup for known or suspected lung cancer, what is the optimal timing of PET/CT? Before or after tissue biopsy confirmation? (public consultation)
Dr Rishendran Naidoo	■ Does routine follow-up improve patient outcomes in people who have curative intent treatments for lung cancer? (public consultation) ■ What are the optimal follow-up tests for people with lung cancer who have had curative intent treatment? (public consultation) ■ What is the optimal model (provider) of care for the follow up of people with lung cancer who have had curative intent treatment? (public consultation)

Back to top

2.12 Conflict of interest register

Conflict of interest register