

CADTH RAPID RESPONSE REPORT: REFERENCE LIST

# Lung Cancer Screening: Clinical Utility and Guidelines

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#### **Research Questions**

- 1. What is the clinical utility of screening for lung cancer in the general adult population?
- 2. What is the clinical utility of screening for lung cancer in adults at high risk of lung cancer?
- 3. What are the evidence-based guidelines regarding screening for lung cancer?

# **Key Findings**

Five health technology assessments, 10 systematic reviews (six with meta-analyses), and 14 randomized controlled trials were identified regarding the clinical utility of screening for lung cancer in adults at high risk of lung cancer. Ten evidence-based guidelines were identified regarding screening for lung cancer. No literature was identified regarding the clinical utility of screening for lung cancer in the general adult population.

#### Methods

#### Literature Search Methods

A limited literature search was conducted by an information specialist on key resources including MEDLINE, the Cochrane Library, the University of York Centre for Reviews and Dissemination (CRD) databases, the websites of Canadian and major international health technology agencies, as well as a focused internet search. The search strategy was comprised of both controlled vocabulary, such as the National Library of Medicine's MeSH (Medical Subject Headings), and keywords. The main search concepts were lung neoplasms and mass screening. Search filters were applied to limit retrieval to health technology assessments, systematic reviews, meta-analyses, or network meta-analyses, randomized controlled trials or controlled clinical trials and guidelines. Where possible, retrieval was limited to the human population. The search was also limited to English language documents published between January 1, 2015 and September 22, 2020. Internet links were provided, where available.

#### Selection Criteria

One reviewer screened literature search results (titles and abstracts) and performed limited handsearching, and selected publications according to the inclusion criteria presented in Table 1. Full texts of study publications were not reviewed. Open access full-text versions of evidence-based guidelines were reviewed when abstracts were not available.

# **Table 1: Selection Criteria**

Population	Q1,3: General adult population Q2,3: Adults at high risk of lung cancer (e.g., diagnosis of emphysema, smoking history, exposure to asbestos, radon gas)
Intervention	Q1-3: Any lung cancer screening method (e.g., low-dose computed tomography, thorax radiography, sputum cytology, positron-emission tomography, biomarkers)
Comparator	Q1,2: A different lung cancer screening method; no screening Q3: Not applicable



Outcomes	Q1,2: Clinical utility (e.g., all-cause mortality, morbidity, time to diagnosis and treatment, quality of life), and safety (e.g., harms of screening test, consequences of false positives and false negatives, overdiagnosis)  Q3: Recommendations regarding lung cancer screening.
Study Designs	Health technology assessments, systematic reviews, randomized controlled trials, evidence-based guidelines

# Results

Five health technology assessments, <sup>1-5</sup> 10 systematic reviews<sup>6-15</sup> (six with meta-analyses<sup>6,9-11,13,15</sup>), and 14 randomized controlled trials <sup>16-29</sup> were identified regarding the clinical utility of screening for lung cancer in adults at high risk of lung cancer. Ten evidence-based guidelines <sup>30-39</sup> were identified regarding screening for lung cancer. No literature was identified regarding the clinical utility of screening for lung cancer in the general adult population.

Additional references of potential interest that did not meet the inclusion criteria are provided in the appendix.

# Health Technology Assessments

Low-Dose Computed Tomography (LDCT)

- Sahakyan Y, Krahn M. Lung cancer screening with low dose computed tomography. Guidance for business case development. Toronto (ON): Canadian Partnership Against Cancer; 2020.
  - See: Health Technology Assessment (p. 26-33)
- Glinz D, Shaw D, Tomonaga Y. Low-dose CT screening for lung cancer. Basel (CH):
   Basel Institute for Clinical Epidemiology and Biostatistics; 2020:
   <a href="https://cancerscreeningcommittee.ch/wp-content/uploads/2020/05/scoping-report-low-dose-ct-screening-for-lung-cancer-20200430.pdf">https://cancerscreeningcommittee.ch/wp-content/uploads/2020/05/scoping-report-low-dose-ct-screening-for-lung-cancer-20200430.pdf</a>. Accessed 2020 Sep 25.
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   2016; <a href="https://www2.gov.bc.ca/gov/content/health/about-bc-s-health-care-system/partners/health-authorities/bc-health-technology-assessment/health-technology-assessments/low-dose-ct-screening-lung-cancer. Accessed 2020 Sep 25</a>



### Systematic Reviews and Meta-analyses

Low-Dose Computed Tomography (LDCT)

 Sadate A, Occean BV, Beregi JP, et al. Systematic review and meta-analysis on the impact of lung cancer screening by low-dose computed tomography. Eur J Cancer. 2020 Jul;134:107-114.

PubMed: PM32502939

- Screening for lung cancer with low-dose computed tomography: an evidence review for the U.S. Preventive Services Task Force. Rockville (MD): Agency for Healthcare Research and Quality; 2020.
- 8. Coureau G, Delva F. [Lung cancer screening among the smoker population]. Bull Cancer. 2019;106(7):693-702.
- Huang KL, Wang SY, Lu WC, Chang YH, Su J, Lu YT. Effects of low-dose computed tomography on lung cancer screening: a systematic review, meta-analysis, and trial sequential analysis. *BMC Pulm Med*. 2019 Jul 11;19(1):126.
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- Tang X, Qu G, Wang L, Wu W, Sun Y. Low-dose CT screening can reduce cancer mortality: a meta-analysis. Rev Assoc Med Bras. 2019 Dec;65(12):1508-1514. PubMed: PM31994634
- Yang H, Varley-Campbell J, Coelho H, et al. Do we know enough about the effect of low-dose computed tomography screening for lung cancer on survival to act? A systematic review, meta-analysis and network meta-analysis of randomised controlled trials. *Diagn Progn Res.* 2019;3:23.
   PubMed: PM31890897
- Coureau G, Salmi LR, Etard C, Sancho-Garnier H, Sauvaget C, Mathoulin-Pelissier S. Low-dose computed tomography screening for lung cancer in populations highly exposed to tobacco: a systematic methodological appraisal of published randomised controlled trials. *Eur J Cancer*. 2016 07;61:146-156.
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- 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. 2016 May;10(3):333-341.
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# Multiple Screening Methods

 Usman Ali M, Miller J, Peirson L, et al. Screening for lung cancer: a systematic review and meta-analysis. *Prev Med.* 2016;89:301-314.
 PubMed: PM27130532



#### Randomized Controlled Trials

Low-Dose Computed Tomography (LDCT)

 Becker N, Motsch E, Trotter A, et al. Lung cancer mortality reduction by LDCT screening-results from the randomized German LUSI trial. *Int J Cancer*. 2020;146(6):1503-1513.

PubMed: PM31162856

 de Koning HJ, van der Aalst CM, de Jong PA, et al. Reduced lung-cancer mortality with volume CT screening in a randomized trial. N Engl J Med. 2020;382(6):503-513.
 PubMed: PM31995683

 de-Torres JP, Wisnivesky JP, Bastarrika G, Wilson DO, Celli BR, Zulueta JJ. Exploring the impact of lung cancer screening on lung cancer mortality of smokers with obstructive lung disease: analysis of the NLST-ACRIN cohort. *Arch Bronconeumol*. 2020;S0300-2896(20)30104-6.

PubMed: PM32409195

 Gonzalez Maldonado S, Motsch E, Trotter A, et al. Overdiagnosis in lung cancer screening - estimates from the German Lung Cancer Screening Intervention Trial. Int J Cancer. 2020.

PubMed: PM32930386

20. Paci E, Puliti D, Carozzi FM, et al. Prognostic selection and long-term survival analysis to assess overdiagnosis risk in lung cancer screening randomized trials. *J Med Screen*. 2020;969141320923030.

PubMed: PM32437229

 Pinsky PF, Bellinger CR, Miller DP, Jr. False-positive screens and lung cancer risk in the National Lung Screening Trial: implications for shared decision-making. *J Med Screen*. 2018;25(2):110-112.

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22. Paci E, Puliti D, Lopes Pegna A, et al. Mortality, survival and incidence rates in the ITALUNG randomised lung cancer screening trial. *Thorax*. 2017;72(9):825-831. PubMed: PM28377492

23. Brain K, Lifford KJ, Carter B, et al. Long-term psychosocial outcomes of low-dose CT screening: results of the UK lung cancer screening randomised controlled trial. *Thorax*. 2016;71(11):996-1005.

PubMed: PM27471048

 Wille MM, Dirksen A, Ashraf H, et al. Results of the randomized Danish Lung Cancer Screening Trial with focus on high-risk profiling. Am J Respir Crit Care Med. 2016;193(5):542-551.

PubMed: PM26485620

25. Rasmussen JF, Siersma V, Pedersen JH, Brodersen J. Psychosocial consequences in the Danish randomised controlled lung cancer screening trial (DLCST). *Lung Cancer*. 2015;87(1):65-72.

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#### Multiple Screening Methods

 Gierada DS, Pinsky PF. Survival after detection of stage I lung cancer by screening in the National Lung Screening Trial. *Chest.* 2020;S0012-3692(20)34234-3.
 PubMed: PM32822676

 National Lung Screening Trial Research T. Lung cancer incidence and mortality with extended follow-up in the National Lung Screening Trial. *J Thorac Oncol*. 2019;14(10):1732-1742.

PubMed: PM31260833

 Doroudi M, Pinsky PF, Marcus PM. Lung Cancer mortality in the lung screening study feasibility trial. JNCI Cancer Spectr. 2018;2(3):pky042.
 PubMed: PM31360863

#### Biomarkers

 Sullivan FM, Mair FS, Anderson W, et al. Earlier diagnosis of lung cancer in a randomised trial of an autoantibody blood test followed by imaging. *Eur Respir J.* 2020. PubMed: PM32732334

#### **Guidelines and Recommendations**

#### **Biomarkers**

30. Prabhash K, Advani SH, Batra U, et al. Biomarkers in non-small cell lung cancers: Indian consensus guidelines for molecular testing. *Adv Ther*. 2019;36(4):766-785. PubMed: PM30864106

#### Low-Dose Computed Tomography (LDCT)

31. Armstrong C. Lung cancer screening recommendations from the ACCP. *Am Fam Physician*. 2018;98(11):688-689.

PubMed: PM30485036

 Mazzone PJ, Silvestri GA, Patel S, et al. Screening for lung cancer: CHEST guideline and expert panel report. Chest. 2018;153(4):954-985.
 PubMed: PM29374513

33. Canadian Association of Radiologists: guide on CT screening for lung cancer. Ottawa (ON): Canadian Association of Radiologists; 2016: <a href="https://car.ca/wp-content/uploads/CT-Screening-for-Lung-Cancer-2017.pdf">https://car.ca/wp-content/uploads/CT-Screening-for-Lung-Cancer-2017.pdf</a>. Accessed 2020 Sep 25. See: Screening recommendations of the Canadian Association of Radiologists (p. 12)

#### Multiple Screening Methods

NCCN clinical practice guidelines in oncology (NCCN guidelines): lung cancer screening. Version 1.2020. Plymouth Meeting (PA): National Comprehensive Cancer Network (NCCN); 2019: <a href="www.nccn.org">www.nccn.org</a>. Accessed 2020 Sep 25.
 See: LDCT as Part of a Lung Screening Program (p. MS-3)



35. Lung cancer: diagnosis and management. (NICE guideline NG122). London (GB): National Institute for Health and Care Excellence; 2019: https://www.nice.org.uk/guidance/ng122/resources/lung-cancer-diagnosis-and-management-pdf-66141655525573. 2020 Sep 25. See: Section 1.3 Diagnosis and staging (p. 7-8)

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37. Canadian Task Force on Preventive Health Care. Recommendations on screening for lung cancer. *CMAJ*. 2016;188(6):425-432.

<u>PubMed: PM26952527</u> See: Key Points (p. 425)

Providing guidance on lung cancer screening to patients and physicians: an update.
 Chicago (IL): American Lung Association; 2015:
 <a href="https://www.lung.org/getmedia/0f9f6821-8817-4444-a647-e6ca0c82104c/lung-cancer-screening-report.pdf">https://www.lung.org/getmedia/0f9f6821-8817-4444-a647-e6ca0c82104c/lung-cancer-screening-report.pdf</a>. Accessed 2020 Sep 25.

 See: VIX. Conclusions (p. 29)

 Zhou QH, Fan YG, Bu H, et al. China national lung cancer screening guideline with low-dose computed tomography (2015 version). *Thorac Cancer*. 2015;6(6):812-818. <u>PubMed: PM26557925</u>



# **Appendix** — Further Information

# Previous CADTH Reports

- Artificial intelligence for classification of lung nodules: a review of clinical utility, diagnostic accuracy, cost-effectiveness, and guidelines. (CADTH Rapid response report: summary with critical appraisal). Ottawa (ON): CADTH; 2020: <a href="https://www.cadth.ca/sites/default/files/pdf/htis/2020/RC1228%20Al%20for%20Lung%20Nodules%20Final.pdf">https://www.cadth.ca/sites/default/files/pdf/htis/2020/RC1228%20Al%20for%20Lung%20Nodules%20Final.pdf</a>. Accessed 2020 Sep 25.
- Low-dose computed tomography for lung cancer screening: a review of the clinical effectiveness, diagnostic accuracy, cost-effectiveness, and guidelines. (CADTH Rapid response report: summary with critical appraisal). Ottawa (ON): CADTH; 2015: <a href="https://www.cadth.ca/sites/default/files/pdf/htis/oct-2015/RC0706-LDCT-LungCancer%20Final.pdf">https://www.cadth.ca/sites/default/files/pdf/htis/oct-2015/RC0706-LDCT-LungCancer%20Final.pdf</a>. Accessed 2020 Sep 25.

# Systematic Reviews & Meta-analyses

#### No Comparator

- Hoffman RM, Atallah RP, Struble RD, Badgett RG. Lung cancer screening with low-dose CT: a meta-analysis. *J Gen Intern Med*. 2020.
   PubMed: PM32583338
- Wang BJ, Tang YD, Yu BY, Gui D, Xu H. Expression of autophagy-related factor p62 for lung cancer diagnosis and prognosis: a systematic review and meta-analysis. *Math Biosci Eng.* 2019;16(6):6805-6821.
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#### Meta-analyses without a Systematic Review

- Brodersen J, Voss T, Martiny F, Siersma V, Barratt A, Heleno B. Overdiagnosis of lung cancer with low-dose computed tomography screening: meta-analysis of the randomised clinical trials. Breathe. 2020;16(1):200013.
   PubMed: PM32194774
- Yang Q, Chen L, Yang L, Huang Y. Diagnostic and prognostic values of circular RNAs for lung cancer: a meta-analysis. *Postgrad Med J.* 2020.
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PubMed: PM28404921

 Pei D, Li Y, Liu X, et al. Diagnostic and prognostic utilities of humoral fibulin-3 in malignant pleural mesothelioma: evidence from a meta-analysis. *Oncotarget*. 2017;8(8):13030-13038.
 PubMed: PM28103581



#### Unclear Comparator

49. Shao C, Yang F, Qin Z, Jing X, Shu Y, Shen H. The value of miR-155 as a biomarker for the diagnosis and prognosis of lung cancer: a systematic review with meta-analysis. *BMC Cancer*. 2019;19(1):1103.

PubMed: PM31727002

 Wu GX, Raz DJ, Brown L, Sun V. Psychological burden associated with lung cancer screening: a systematic review. *Clin Lung Cancer*. 2016;17(5):315-324.
 PubMed: PM27130469

#### Unclear Methodology

 Hua Q, Zhu Y, Liu H. Detection of volatile organic compounds in exhaled breath to screen lung cancer: a systematic review. *Future Oncol.* 2018;14(16):1647-1662. PubMed: PM29939068

#### Randomized Controlled Trials

#### Alternative Outcomes

52. Puliti D, Mascalchi M, Carozzi FM, et al. Decreased cardiovascular mortality in the ITALUNG lung cancer screening trial: analysis of underlying factors. *Lung Cancer*. 2019;138:72-78.

PubMed: PM31654837

#### Alternative Comparators

53. Pastorino U, Sverzellati N, Sestini S, et al. Ten-year results of the Multicentric Italian Lung Detection trial demonstrate the safety and efficacy of biennial lung cancer screening. *Eur J Cancer*. 2019;118:142-148.

PubMed: PM31336289

#### Alternative Outcomes

 Pinsky PF, Gierada DS, Black W, et al. Performance of Lung-RADS in the National Lung Screening Trial: a retrospective assessment. *Ann Intern Med.* 2015;162(7):485-491.

PubMed: PM25664444

# Guidelines and Recommendations

#### Unclear Methodology

55. Garrido P, Conde E, de Castro J, et al. Updated guidelines for predictive biomarker testing in advanced non-small-cell lung cancer: a National Consensus of the Spanish Society of Pathology and the Spanish Society of Medical Oncology. Clin Transl Oncol. 2020;22(7):989-1003.

PubMed: PM31598903

 Koegelenberg CFN, Dorfman S, Schewitz I, et al. Recommendations for lung cancer screening in Southern Africa. *J Thorac Dis.* 2019 Sep;11(9):3696-3703.
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   (Medtech innovation briefing MIB209). London (GB): National Institute for Health and
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   See: Population, setting and intended user (p. 3)
- Lung cancer screening in Canada: environmental scan. Toronto (ON): Canadian Partnership Against Cancer; 2018: <a href="https://s22457.pcdn.co/wp-content/uploads/2019/04/Lung-Cancer-Screening-Environmental-Scan\_EN\_2018\_final.pdf">https://s22457.pcdn.co/wp-content/uploads/2019/04/Lung-Cancer-Screening-Environmental-Scan\_EN\_2018\_final.pdf</a>. Accessed 2020 Sep 25.

See: Lung Cancer Screening Programs and Guidelines (p. 6)

- 60. Companion implementation resource: lung cancer screening. Toronto (ON): Canadian Partnership Against Cancer; 2018: <a href="https://s22457.pcdn.co/wp-content/uploads/2019/01/Lung-Companion-Implementation-Resource-2018-EN.pdf">https://s22457.pcdn.co/wp-content/uploads/2019/01/Lung-Companion-Implementation-Resource-2018-EN.pdf</a>. Accessed 2020 Sep 25. See: Lung Cancer Screening Guidelines (p. 2)
- 61. Frequently asked questions (FAQs) for healthcare providers: lung cancer screening in Ontario for people at high risk. Toronto (ON): Cancer Care Ontario; 2017: <a href="https://www.lungcancercanada.ca/LungCancerCanada/media/Documents/Screening/CC-Lung-Cancer-Screening-Program-FAQs-2017.pdf">https://www.lungcancercanada.ca/LungCancerCanada/media/Documents/Screening/CC-Lung-Cancer-Screening-Program-FAQs-2017.pdf</a>. Accessed 2020 Sep 25.