CADTH

Lung Cancer Screening: Clinical Utility and Guidelines

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,[1-5] 10 systematic reviews[6-15] (six with meta-analyses[6,9-11,13,15]), and 14 randomized controlled trials[16-29] were identified regarding the clinical utility of screening for lung cancer in adults at high risk of lung cancer. Ten evidence-based guidelines[30-39] 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)

1. 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)

2. Glinz D, Shaw D, Tomonaga Y. Low-dose CT screening for lung cancer. Basel (CH) : Basel Institute for Clinical Epidemiology and Biostatistics; 2020: https://cancerscreeningcommittee.ch/wp-content/uploads/2020/05/scoping-report-low-dose-ct-screening-for-lung-cancer-20200430.pdf. Accessed 2020 Sep 25.

3. Snowsill T, Yang H, Griffin E, et al. Low-dose computed tomography for lung cancer screening in high-risk populations: a systematic review and economic evaluation. *Health Technol Assess.* 2018 11;22(69):1-276.
PubMed: PM30518460

4. Sarimin R, Abdul Rahim KNK, Ghani BA. Low dose computed tomography for lung cancer screening. Putrajaya (MY): Malaysian Health Technology Assessment Section (MaHTAS), Medical Development Division, Ministry of Health Malaysia; 2018: https://www.moh.gov.my/moh/resources/Penerbitan/MAHTAS/HTA/HTA-LDCT%20for%20lung%20ca%20screening.pdf. Accessed 2020 Sep 25

5. Government of British Columbia. Low dose CT screening for lung cancer (LDCT). 2016; 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

Systematic Reviews and Meta-analyses

Low-Dose Computed Tomography (LDCT)

6. 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

7. 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.

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9. 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.
PubMed: PM31296196

10. 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

11. 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

12. 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.
PubMed: PM27211572

13. 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? C*lin Respir J.* 2016 May;10(3):333-341.
PubMed: PM25307063

14. Sánchez González MC, Cantero Muñoz P, Atienza Merino G. [Low-dose computed tomography screening for lung cancer]. 2016; https://avalia-t.sergas.es/Paxinas/web.aspx?tipo=paxtxt&idLista=4&idContido=655&migtab=38%3b39%3b655&idTax=12028. Accessed 2020 Sep 25.

Multiple Screening Methods

15. 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)

16. 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

17. 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

18. 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

19. 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

21. 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.
PubMed: PM28929865

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

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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.
PubMed: PM25433982

Multiple Screening Methods

26. 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

27. 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

28. 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

29. 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

32. 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: https://car.ca/wp-content/uploads/CT-Screening-for-Lung-Cancer-2017.pdf. Accessed 2020 Sep 25.
    See: Screening recommendations of the Canadian Association of Radiologists (p. 12)

Multiple Screening Methods

34. NCCN clinical practice guidelines in oncology (NCCN guidelines): lung cancer screening. Version 1.2020. Plymouth Meeting (PA): National Comprehensive Cancer Network (NCCN); 2019: www.nccn.org. 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)

36. Expert Panel on Thoracic Imaging, Donnelly EF, Kazerooni EA, et al. ACR appropriateness criteria® lung cancer screening. *J Am Coll Radiol*. 2018;15(11S):S341-S346.
PubMed: PM30392603

37. Canadian Task Force on Preventive Health Care. Recommendations on screening for lung cancer. *CMAJ*. 2016;188(6):425-432.
PubMed: PM26952527
See: Key Points (p. 425)

38. Providing guidance on lung cancer screening to patients and physicians: an update. Chicago (IL): American Lung Association; 2015: https://www.lung.org/getmedia/0f9f6821-8817-4444-a647-e6ca0c82104c/lung-cancer-screening-report.pdf.pdf. Accessed 2020 Sep 25.
See: VIX. Conclusions (p. 29)

39. 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.
PubMed: PM26557925

Appendix — Further Information

Previous CADTH Reports

40. 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: https://www.cadth.ca/sites/default/files/pdf/htis/2020/RC1228%20AI%20for%20Lung%20Nodules%20Final.pdf. Accessed 2020 Sep 25.

41. 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: https://www.cadth.ca/sites/default/files/pdf/htis/oct-2015/RC0706-LDCT-LungCancer%20Final.pdf. Accessed 2020 Sep 25.

Systematic Reviews & Meta-analyses

No Comparator

42. 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

43. 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. PubMed: PM31698589

Meta-analyses without a Systematic Review

44. 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

45. 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. PubMed: PM32518074

46. Wang X, Liu H, Shen Y, Li W, Chen Y, Wang H. Low-dose computed tomography (LDCT) versus other cancer screenings in early diagnosis of lung cancer: a meta-analysis. *Medicine.* 2018;97(27):e11233. PubMed: PM29979385

47. Ma Y, Chen Y, Lin J, et al. Circulating miR-31 as an effective biomarker for detection and prognosis of human cancer: a meta-analysis. *Oncotarget.* 2017;8(17):28660-28671. PubMed: PM28404921

48. 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

50. 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

51. 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

54. 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

56. 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.
PubMed: PM31656641

Additional References

57. Evaluation of the benefits and harms of lung cancer screening with low-dose computed tomography: a collaborative modeling study for the U.S. Preventive Services Task Force. Rockville (MD): Agency for Health Research and Quality (AHRQ); 2020.

58. EarlyCDT-lung for cancer risk classification of indeterminate pulmonary nodules. *(Medtech innovation briefing MIB209).* London (GB): National Institute for Health and Care Excellence; 2020: https://www.nice.org.uk/advice/mib209/resources/earlycdtlung-for-cancer-risk-classification-of-indeterminate-pulmonary-nodules-pdf-2285965399480261. Accessed 2020 Sep 25.
See: Population, setting and intended user (p. 3)

59. Lung cancer screening in Canada: environmental scan. Toronto (ON): Canadian Partnership Against Cancer; 2018: https://s22457.pcdn.co/wp-content/uploads/2019/04/Lung-Cancer-Screening-Environmental-Scan_EN_2018_final.pdf. 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: https://s22457.pcdn.co/wp-content/uploads/2019/01/Lung-Companion-Implementation-Resource-2018-EN.pdf. 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: https://www.lungcancercanada.ca/LungCancerCanada/media/Documents/Screening/CCO-Lung-Cancer-Screening-Program-FAQs-2017.pdf. Accessed 2020 Sep 25.