Lung cancer screening primer

Key information for primary care providers

Anna N. Wilkinson MSc MD CCFP FCFP Stephen Lam MD FRCPC

Abstract

Objective To review new evidence reported since the 2016 publication of the Canadian Task Force on Preventive Health Care recommendations and to summarize key facets of lung cancer screening to better equip primary care providers (PCPs) in anticipation of wider implementation of the recommendations.

Quality of evidence A new, large randomized controlled trial has been published since 2016, as have updates from 4 other trials. PubMed was searched for studies published between January 1, 2004, and December 31, 2020, using search words including *lung cancer screening eligibility, lung cancer screening criteria,* and *lung cancer screening guidelines*. All information from peer-reviewed articles, reference lists, books, and websites was considered.

Main message Lung cancers diagnosed at stage 4 have a 5-year survival rate of only 5% and have a disproportionate impact on those with lower socioeconomic status, rural populations, and Indigenous populations. By *downstaging,* or diagnosing lung cancers at an earlier and more treatable stage, lung cancer screening reduces mortality with a number needed to screen of 250 to prevent 1 death. Practical aspects of lung cancer screening are reviewed, including criteria to screen, appropriate low-dose computed tomography screening, and management of findings. Harms of screening, such as overdiagnosis and incidental findings, are discussed to allow PCPs to appropriately counsel their patients in the face of ongoing implementation of new lung cancer screening programs.

Conclusion Lung cancer screening, with its embedded emphasis on smoking cessation, is an excellent addition to PCPs' preventive health care tools. The implementation of formal and pilot lung cancer screening programs across Canada means that PCPs will be increasingly required to counsel their patients around the uptake of lung cancer screening.

Lung cancer kills more people annually than colon, breast, and pancreatic cancers combined, accounting for 1 in 4 cancer deaths.[1] The 5-year survival rate for lung cancer is 19%, primarily because approximately half of all lung cancers are diagnosed at stage 4, when survival is abysmal. Seventy-two percent of lung cancers are attributable to smoking, creating an opportunity for targeted screening for lung cancer. The primary benefit of lung cancer screening is *downstaging*—diagnosing lung cancers at an earlier stage when there are potential curative therapies with improved survival rates. Lung cancers diagnosed at stage 1 have a 3-year net survival rate of 71%, compared with 5% at stage 4.[1]

In 2016, the Canadian Task Force on Preventive Health Care (CTFPHC) recommended lung cancer screening (**Box 1**).[2] Across Canada, there is currently a patchwork of lung cancer screening implementation, including an organized program in Ontario as of April 1, 2021, a program in British Columbia starting in 2022, and pilot programs in Quebec and Alberta. Business case proposals are being submitted by several other provinces. In the absence of organized programs, opportunistic screening is ongoing, a practice that

Editor's key points

- Lung cancer screening is unique because it targets a specific high-risk group. More accurate identification of this high-risk cohort is critical to avoid harms of screening for those who have a lower incidence of lung cancer. Primary care providers should be aware that Canadian screening programs are using risk stratification models like the PLCOm2012 to determine eligibility for screening. Individual health jurisdictions may adjust their screening thresholds based on health care resources.
- Low-dose computed tomography (LDCT) is the only imaging modality recommended for lung cancer screening. There is no contrast required for LDCT and the radiation dose is 4 times less than a standard computed tomography scan. The optimal frequency and length of screening are not yet known. The greatest predictors of malignancy are size, rate of growth, and increase in density of semisolid or nonsolid nodules. An increase of 1.5 mm or greater in the diameter of an existing solid nodule is considered substantial and should be investigated.
- In an organized screening program, standardized reports would be provided to the primary care provider and the screenee, indicating appropriate follow-up. For individuals with a low risk of lung cancer, this would include routine annual or biennial screening, while those individuals with nodules that should be monitored would be recalled for repeat LDCT in 1 to 6 months.

Box 1. 2016 CTFPHC lung cancer screening recommendation

The following is a weak recommendation with low-quality evidence.

- In those 55 to 74 years of age who currently smoke or who quit within the past 15 years, and have ≥ 30 pack-years' smoking history, screen with low-dose CT for up to 3 consecutive years, in centres with adequate expertise

CT—computed tomography, CTFPHC—Canadian Task Force on Preventive Health Care.
Data from the CTFPHC.[2]

potentially has increased harms, such as regular-dose computed tomography (CT) that has 4 to 5 times higher radiation, unnecessary repeat imaging studies, or biopsies, and there is no organized manner for abnormalities to be worked up.[3]

The number needed to screen (NNS) to prevent 1 lung cancer death is 250,[4] which compares favorably to the optimal NNS for mammography of 645.[5] A simulation of lung cancer screening over the next 20 years projected 7000 to 17 000 fewer stage 4 diagnoses and 5000 to 11 000 fewer deaths should screening be implemented.[1]

Primary care provider (PCP) understanding of eligibility for screening and associated harms is suboptimal.[6] This update on lung cancer screening will review new evidence reported since the 2016 publication of the CTFPHC recommendations and will summarize key facets of lung cancer screening to better equip PCPs in anticipation of wider implementation.

Quality of evidence

Since the meta-analysis that informed the 2016 CTFPHC recommendations,[7] a new large randomized controlled trial, NELSON *(Nederlands–Leuvens Longkanker Screenings Onderzoek)*,[8] has been published, as have updates on several other trials (**Table 1**).[8-12] We searched PubMed for studies published between January 1, 2004, and December 31, 2020, using search words including *lung cancer screening eligibility, lung cancer screening criteria,* and *lung cancer screening guidelines*. All information from peer-reviewed articles, reference lists, books, and websites was considered.

Main message

New evidence. A significant relative reduction in lung cancer mortality was shown in NELSON (24%) and the National Lung Screening Trial (NLST) (20%).[8-10] Other smaller randomized controlled trials were not sufficiently powered to show a mortality difference due to screening; however, specific issues in low-dose CT (LDCT) screening were addressed.[13] The MILD (Multicentric Italian Lung Detection) study highlighted that prolonged annual or biennial screening beyond 5 years is needed to show a lung cancer mortality reduction benefit.[11] The German LUSI (Lung Cancer Screening Intervention) trial[12] suggested women may benefit more from LDCT screening than men (**Table 1**).[8-12] Recent meta-analyses have reported statistically and clinically significant relative reductions in lung cancer death of 17%[14,15] and 19%,[4] but no difference in all-cause mortality.

Cost effectiveness of LDCT. Low-dose CT is cost-effective, with an incremental cost of $20 724 per quality-adjusted life-year gained.[16] Cost effectiveness is driven not only by lung cancer outcomes, but also by a reduction in tobacco-related diseases. The cost savings of lung cancer screening are amplified when the rising costs of immunotherapy and targeted therapy in stage 3 and 4 lung cancer treatment are considered. The average cost to screen an individual once is $500,[16] while the cost of a single dose of pembrolizumab is $8800,[17] which is given every 21 days for up to 2 years in metastatic lung cancer.

Who should be screened? Lung cancer screening is unique because it targets a specific high-risk group. More accurate identification of this high-risk cohort is critical to avoid harms of screening in those who have a lower incidence of lung cancer. The subgroup analysis of the NLST divided participants into risk quintiles and found an NNS of 61 in the highest-risk subgroup, compared with an NNS of 5276 in the lowest-risk subgroup. This translated into a decrease in false-positive results from 1648 in the low-risk quintile to only 65 in the high-risk quintile.[18]

The PLCOm2012 is a risk calculator that is available online (**https://brocku.ca/lung-cancer-screening-and-risk-prediction/risk-calculators/**) and has been validated as a superior method to determine eligibility for screening.[19] This tool incorporates several predictors to generate a percentage risk of developing lung cancer in the next 6 years (**Box 2**).[19] The prospective observational PanCan (Pan-Canadian Early Detection of Lung Cancer) study was not included in the CTFPHC guidelines or meta-analyses and assessed the efficacy of an earlier version of this risk-based model to select individuals for lung cancer screening with a 6-year lung cancer risk of 2% or greater. The PanCan study had an improved detection of lung cancer with statistically significant downstaging, with 77% of screen-detected lung cancers diagnosed at stage 1 or 2.[20] When a PLCOm2012 score cutoff of 1.7% was compared with the criteria of age and pack-years alone, 18.5% more lung cancers were found when screening the same number of people.[21] Primary care providers should be aware that Canadian screening programs are using risk stratification models like the PLCOm2012 to determine eligibility for screening. Individual health jurisdictions may adjust their screening thresholds based on health care resources. British Columbia screens individuals with a greater than 1.5% risk of developing lung cancer within a 6-year period, while Ontario uses a cutoff of 2% or greater.[19,22]

Table 1. Lung cancer screening trials published since 2016

TRIAL NAME, COUNTRY	MEDIAN FOLLOW-UP, Y	SAMPLE SIZE, N	CRITERIA	INTERVENTION	LUNG CANCER MORTALITY	ALL-CAUSE MORTALITY
LDCT vs CXR						
• NLST,[9,10] USA	12.3	53 454	• Age 55-74 y • ≥ 30 pack-years smoking • ≤ 15 y since quitting	3 annual scans	• RR = 0.80 (95% CI 0.73-0.93)	• RR = 0.97 (95% CI 0.94-1.01)
LDCT vs no screening						
• NELSON,[8] the Netherlands and Belgium	> 10	13 195 men, 2594 women	• Age 50-74 y • ≥ 15 cigarettes/d for ≥ 25 y or ≥ 10 cigarettes/d for ≥ 30 y • ≤ 10 y since quitting	4 scans (at 0, 1, 3, and 5.5 y)	• RR = 0.76 for men • RR = 0.67 for women	NA
• MILD,[11] Italy	> 10	4099	• Age 49-75 y • ≥ 20 pack-years smoking • ≤ 10 y since quitting	10 annual scans or 5 biennial scans	• HR = 0.61 (95% CI 0.39-0.95)	• HR = 0.80 (95% CI 0.62-1.03)
• LUSI,[12] Germany	8.8	4052	• Age 50-69 y • ≥ 15 cigarettes/d for ≥ 25 y or ≥ 10 cigarettes/d for ≥ 30 y • ≤ 10 y since quitting	5 annual scans	• HR = 0.74 (95% CI 0.46-1.19) • HR = 0.94 (95% CI 0.54-1.61) for men • HR = 0.31 (95% CI 0.10-0.96) for women	• HR = 0.99 (95% CI 0.79-1.25)

CXR—chest x-ray, HR—hazard ratio, LDCT—low-dose computed tomography, LUSI—Lung Cancer Screening Intervention, MILD—Multicentric Italian Lung Detection, NA—not applicable, NELSON—*Nederlands–Leuvens Longkanker Screenings Onderzoek*, NLST—National Lung Screening Trial, RR—rate ratio, USA—United States of America.

Box 2. PLCOm2012 predictors

The following are predictors used by the PLCOm2012 to generate a percentage risk of developing lung cancer in the next 6 years:

- Age
- Education
- Family history of lung cancer
- Body mass index
- Chronic obstructive pulmonary disease
- Smoking duration
- Smoking intensity
- Smoking quit time
- Personal history of cancer
- Race or ethnic origin

Data from Tammemägi et al.[19]

What should screening consist of? Low-dose CT, in the form of multidetector helical CT with a slice thickness of 1.25 mm or less, is the only imaging modality recommended for lung cancer screening. There is no contrast required for LDCT and the radiation dose is 1.5 mSv or less, more than 4 times less than that of a traditional CT scan (8 mSv).[23]

The optimal frequency and length of screening are not yet known. Although the CTFPHC recommends 3 annual screens, prolonged annual or biennial screening beyond 5 years shows a lung cancer mortality reduction benefit[11] (**Table 1**).[8-12] The US Preventive Services Task Force recommends annual screening until the upper age limit of 80, unless the screenee is no longer eligible owing to comorbidities.[24] A personalized approach to screening intervals is under investigation, with the aim of optimally balancing the costs and harms of screening with the risk of a missed cancer diagnosis.[25]

How should findings be managed? Nodules can be solid, semisolid, or nonsolid (eg, ground-glass nodules), and size can be expressed as diameter or volume. Calcified or "popcorn" and perifissural nodules are generally benign and do not require further follow-up.[25] The greatest predictors of malignancy are size, rate of growth, and increase in density of semisolid or nonsolid nodules. An increase of 1.5 mm or greater in the diameter of an existing solid nodule is considered substantial and should be investigated. The appearance of new nodules after a baseline or subsequent LDCT is more suggestive of malignancy, triggering investigation at a smaller diameter.[26] New nonsolid nodules have less malignant potential, and large nodules (>20 mm) that appear suddenly are more likely infectious or inflammatory.[27]

In an organized screening program, standardized reports would be provided to the PCP and the screenee,

indicating appropriate follow-up. For individuals with a low risk of lung cancer, this would include routine annual or biennial screening, while those individuals with nodules that should be monitored would be recalled for repeat LDCT in 1 to 6 months. Findings that arouse suspicion of cancer should trigger referral for diagnostic workup.[25] In the absence of standardized reporting, **Table 2** provides a guide to management.[13,19,25] These recommendations are based on the Canadian Partnership Against Cancer Pan-Canadian Lung Cancer Screening Network evidence-based framework for management of screen-detected lung nodules.[25]

What are the harms of screening? The application of targeted screening selection criteria and standardized lung nodule workup protocols are paramount in mitigating harms of screening. False-positive findings are not uncommon and precipitate a workup that may include further radiation exposure, unnecessary procedures, and psychological distress. A systematic review of psychological distress associated with lung cancer screening showed that individuals with indeterminate scan results had an initial increase in psychological burden, but after 6 months, health-related quality of life and anxiety had returned to baseline.[28] The NELSON trial had a 1.2% false-positive rate (264 of 22 600 participants), with 23% of these individuals undergoing invasive procedures.[8] The NLST had a higher false-positive rate of 23%, which was related to the definition of positive screen findings.[9] Protocols for lung nodule management have subsequently been refined.[25,29] This is why organized screening instead of opportunistic or ad hoc screening is important.

Incidental findings in the thyroid, heart, lung, kidneys, adrenal glands, and liver are common in lung cancer screening. The identification of coronary calcification is also common and can trigger important lifestyle and risk management discussions for these patients.[30] Although up to 20% of incidental findings will require investigation, their clinical significance is less than 1%.[31,32] At about $12 per screen, the workup of incidental findings contributes substantially to the cost of screening programs.[33] In the absence of specific recommendations in the radiology report, **Table 3** provides a guide to management.[34-36]

Overdiagnosis refers to the diagnosis of cancers that would not have become clinically significant during the life of the individual. A comparison of the incidence of lung cancer in the screening and control groups over time generally allows for an estimation of this value. The 12.3-year follow-up of the NLST yielded an overdiagnosis estimate of 3%,[9] the NELSON trial with 10 years of follow-up had an estimate of 8.9%,[8] and the US Preventive Services Task Force has modeled a rate of 10% to 12%.[24] A longer follow-up duration is required to determine the true rate of overdiagnosis.

Table 2. Management of screen-detected lung nodules

SCREENING	CONTINUE ROUTINE SCREENING	EARLY RECALL (REPEAT LDCT AT 1 TO 6 MO)	DIAGNOSTIC WORKUP
Baseline screening			
• Solid nodule	No nodule *or* PanCan risk score* < 5% *or* nodule < 5 mm	PanCan risk score* ≥ 5% to < 30% *or* nodule ≥ 5 to < 15 mm	PanCan risk score* ≥ 30% *or* nodule ≥ 15 mm
• Part-solid nodule†	PanCan risk score* < 5% *or* nodule < 6 mm	PanCan risk score* ≥ 5% to < 30% *or* nodule ≥ 6 to < 8 mm	PanCan risk score* ≥ 30% *or* nodule ≥ 8 mm
• Nonsolid nodule	PanCan risk score* < 5% *or* nodule < 6 mm	PanCan risk score* ≥ 5% to < 30% *or* nodule 6 to < 15 mm	PanCan risk score* ≥ 30% *or* nodule ≥ 15 mm persistent at 3 mo *or* nodule develops solid component
Annual or biennial repeat screening			
• New solid nodule	< 4 mm	4 to < 8 mm	≥ 8 mm
• Pre-existing solid nodule	NA	< 8 mm and increase in mean diameter by ≥ 1.5 mm *or* volume doubling time 400 to 600 d	≥ 8 mm and increase in mean diameter by ≥ 1.5 mm *or* volume doubling time < 400 d
• Part-solid nodule†	< 6 mm	≥ 6 to < 8 mm	≥ 8 mm
• Nonsolid nodule	< 15 mm	≥ 15 mm	Development of solid component ≥ 6 mm *or* becomes solid

LDCT—low-dose computed tomography, NA—not applicable.
*Pan-Canadian lung nodule malignancy risk score.[25] This is different than the PLCOm2012 screening selection criteria.[19]
†Refers to the size of the solid component.
Reproduced with permission of the ©European Respiratory Society.[13]

Table 3. Management of common incidental findings

FINDING	RECOMMENDATION
Severe coronary artery calcification	• Optimize cardiac risk factors • If symptomatic: coronary artery disease workup or cardiology consultation
Moderate or severe aortic valve calcification	• Echocardiogram to rule out aortic stenosis • Cardiology consultation if indicated
Moderate or severe pulmonary emphysema	• Pulmonary function test. If result is abnormal: optimize COPD management • Respirology consultation if indicated
Pulmonary fibrosis	• > 5% in any lung zones: pulmonary function test. Respirology consultation if result is abnormal
Bronchiectasis	• Respirology consultation if symptomatic
Renal abnormality	• Abdominal ultrasound or CT if not cystic
Adrenal nodule	• Abdominal CT with adrenal protocol if enlarging or ≥ 40 mm; biochemical test if clinical signs or symptoms of pheochromocytoma or Cushing syndrome
Breast mass	• Mammography or ultrasound
Thyroid nodule	• ≥ 15 mm on long axis: dedicated thyroid ultrasound

COPD—chronic obstructive pulmonary disease, CT—computed tomography.
Data from the International Early Lung Cancer Action Program,[34] Munden et al,[35] and Berland et al.[36]

Smoking cessation. A pillar of any lung cancer screening program must be an integrated smoking cessation program. Individuals presenting for screening may be uniquely receptive to smoking cessation given their increased awareness of the health impacts of smoking. The Alberta Lung Cancer Screening Study demonstrated the efficacy of embedded smoking cessation with a quit rate of 13%, more than double that of the general population (5%).[37] Increased smoking cessation has been modeled to be cost-effective and, independent of screening, would prevent the development of lung cancers and improve mortality.[38]

Equity. A higher smoking incidence is strongly associated with lower socioeconomic status (SES), rurality, and Indigenous populations. The smoking rate in the highest income quintile is only 12% compared with 22% in the lowest income quintile. Smoking rates in First Nations people living off reserves are twice as high as in non-Indigenous populations, and 69% of Inuit living in Nunavut are daily smokers.[39-41] As a result, these populations are disproportionately diagnosed with lung cancer. The lung cancers diagnosed in these individuals are typically later stage (stage 3 or 4), resulting in poorer survival rates compared with lung cancers diagnosed in urban populations, non-Indigenous individuals, and those of higher SES.[1] Inequitable access to health care means that even when cancers are diagnosed at the same stage, those with lower incomes will have lower survival rates than individuals with higher incomes. Lung cancer screening presents a unique opportunity to address the disparities in health outcomes for those with low SES, Indigenous populations, and rural populations. For example, attaching lung screening to an in-community general health check (eg, detection of chronic obstructive pulmonary disease using spirometry and CT evidence of emphysema, detection of coronary artery disease from the screening LDCT, smoking cessation counseling), using telehealth, providing free transportation to screening centres, or using mobile screening may help to overcome the access barriers. Improved access to smoking cessation programs and coordinated diagnosis and management of lung cancers have considerable potential to have survival benefits greater than those reported in clinical trials.

Conclusion

This update has provided a review of the key evidence and the harms and benefits of screening, as well as the practicalities of results management, to better equip family doctors to support their patients. Lung cancer screening, with its embedded emphasis on smoking cessation, is an excellent addition to PCPs' armamentarium of preventive health care tools. The innate ability of lung cancer screening to target people who have smoked or who are still smoking who are often found in underserved or underserviced populations with the poorest lung cancer outcomes provides a key means for PCPs to standardize access to care for their patient populations. The implementation of formal and pilot lung cancer screening programs across Canada means that PCPs will be increasingly required to counsel their patients on the uptake of lung cancer screening.

Dr Anna N. Wilkinson is Assistant Professor in the Department of Family Medicine at the University of Ottawa in Ontario, a family physician with the Ottawa Academic Family Health Team, a general practitioner oncologist at The Ottawa Hospital Cancer Centre, Program Director of PGY-3 FP-Oncology, Chair of the Cancer Care Member Interest Group at the College of Family Physicians of Canada, and Regional Cancer Primary Care Lead for Champlain Region. **Dr Stephen Lam** is Professor of Medicine at the University of British Columbia in Vancouver, a respirologist at BC Cancer, and Distinguished Scientist Leon Judah Blackmore Chair in Lung Cancer Research and Medical Director of the BC Lung Screening Program at the BC Cancer Research Centre.

Contributors
Both authors contributed to the literature review and interpretation, and to preparing the manuscript for submission.

Competing interests
None declared

Correspondence
Dr Anna N. Wilkinson; e-mail **anwilkinson@toh.ca**

References

1. Canadian Cancer Statistics Advisory Committee. *Canadian cancer statistics. A 2020 special report on lung cancer*. Toronto, ON: Canadian Cancer Society; 2020. Available from: **cancer.ca/Canadian-Cancer-Statistics-2020-EN**. Accessed 2020 Dec 17.
2. Canadian Task Force on Preventive Health Care. Recommendations on screening for lung cancer. *CMAJ* 2016;188(6):425-32. Epub 2016 Mar 7.
3. *Lung cancer screening in Canada: environmental scan*. Toronto, ON: Canadian Partnership Against Cancer; 2018. Available from: **https://s22457.pcdn.co/wp-content/uploads/2019/04/Lung-Cancer-Screening-Environmental-Scan_EN_2018_final.pdf**. Accessed 2021 Sep 27.
4. Ebell MH, Bentivegna M, Hulme C. Cancer-specific mortality, all-cause mortality, and overdiagnosis in lung cancer screening trials: a meta-analysis. *Ann Fam Med* 2020;18(6):545-52. Erratum in: *Ann Fam Med* 2021;19(4):292.
5. Klarenbach S, Sims-Jones N, Lewin G, Singh H, Thériault G, Tonelli M, et al. Recommendations on screening for breast cancer in women aged 40-74 years who are not at increased risk for breast cancer. *CMAJ* 2018;190(49):E1441-51.
6. Duong DK, Shariff-Marco S, Cheng I, Naemi H, Moy LM, Haile R, et al. Patient and primary care provider attitudes and adherence towards lung cancer screening at an academic medical center. *Prev Med Rep* 2017;6:17-22.
7. Ali MU, Miller J, Peirson L, Fitzpatrick-Lewis D, Kenny M, Sherifali D, et al. Screening for lung cancer: a systematic review and meta-analysis. *Prev Med* 2016;89:301-14. Epub 2016 Apr 26.
8. De Koning HJ, van der Aalst CM, de Jong PA, Scholten ET, Nackaerts K, Heuvelmans MA, et al. Reduced lung-cancer mortality with volume CT screening in a randomized trial. *N Engl J Med* 2020;382(6):503-13. Epub 2020 Jan 29.
9. National Lung Screening Trial Research Team. Lung cancer incidence and mortality with extended follow-up in the National Lung Screening Trial. *J Thorac Oncol* 2019;14(10):1732-42. Epub 2019 Jun 28.
10. National Lung Screening Trial Research Team; Aberle DR, Adams AM, Berg CD, Black WC, Clapp JD, et al. Reduced lung-cancer mortality with low-dose computed tomographic screening. *N Engl J Med* 2011;365(5):395-409. Epub 2011 Jun 29.
11. Pastorino U, Silva M, Sestini S, Sabia F, Boeri M, Cantarutti A, et al. Prolonged lung cancer screening reduced 10-year mortality in the MILD trial: new confirmation of lung cancer screening efficacy. *Ann Oncol* 2019;30(7):1162-9. Erratum in: *Ann Oncol* 2019;30(10):1672.
12. Becker N, Motsch E, Trotter A, Heussel CP, Dienemann H, Schnabel PA, et al. Lung cancer mortality reduction by LDCT screening—results from the randomized German LUSI trial. *Int J Cancer* 2020;146(6):1503-13. Epub 2019 Jun 20.
13. Lam S, Tammemagi M. Contemporary issues in the implementation of lung cancer screening. *Eur Respir Rev* 2021;30(161):200288.
14. Sadate A, Occean BV, Beregi JP, Hamard A, Addala T, de Forges H, et al. Systematic review and meta-analysis on the impact of lung cancer screening by low-dose computed tomography. *Eur J Cancer* 2020;134:107-14. Epub 2020 Jun 2.
15. 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;19(1):126.
16. Cressman S, Peacock SJ, Tammemägi MC, Evans WK, Leighl NB, Goffin JR, et al. The cost-effectiveness of high-risk lung cancer screening and drivers of program efficiency. *J Thorac Oncol* 2017;12(8):1210-22. Epub 2017 May 10.
17. Pan-Canadian Oncology Drug Review. *pCODR Expert Review Committee (pERC) final recommendation*. Canadian Agency for Drugs and Technologies in Health; 2019. Available from: **https://www.cadth.ca/sites/default/files/pcodr/Reviews2019/10153PembroNSQ-NSCLC_FnRec_approvedbyChair_Post_NOREDACT_31May2019_final.pdf**. Accessed 2021 Feb 3.
18. 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;369(3):245-54.
19. 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;368(8):728-36. Erratum in: *N Engl J Med* 2013;369(4):394.
20. Tammemagi MC, Schmidt H, Martel S, McWilliams A, Goffin JR, Johnston MR, et al. Participant selection for lung cancer screening by risk modelling (the Pan-Canadian Early Detection of Lung Cancer [PanCan] study): a single-arm, prospective study. *Lancet Oncol* 2017;18(11):1523-31. Epub 2017 Oct 18.
21. Lam S, Myers R, Ruparel M, Atkar-Khattra S, Stone E, Manser R, et al. PL02.02. Lung cancer screenee selection by USPSTF versus PLCOm2012 criteria—interim ILST findings [abstract]. *J Thorac Oncol* 2019;14(10 Suppl):S4-5.
22. Darling GE, Tammemägi MC, Schmidt H, Buchanan DN, Leung Y, McGarry C, et. Organized lung cancer screening pilot: informing a province-wide program in Ontario, Canada. *Ann Thorac Surg* 2021;111(6):1805-11. Epub 2020 Oct 8.
23. Rampinelli C, Origgi D, Bellomi M. Low-dose CT: technique, reading methods and image interpretation. *Cancer Imaging* 2012;12(3):548-56.
24. Moyer VA; US Preventive Services Task Force. Screening for lung cancer: US Preventive Services Task Force recommendation statement. *Ann Intern Med* 2014;160(5):330-8.
25. Lam S, Bryant H, Donahoe L, Domingo A, Earle C, Finley C, et al. Management of screen-detected lung nodules: a Canadian Partnership Against Cancer guidance document. *Can J Respir Crit Care Sleep Med* 2020;4(4):236-65.
26. Walter JE, Heuvelmans MA, de Jong PA, Vliegenthart R, van Ooijen PMA, Peters RB, et al. Occurrence and lung cancer probability of new solid nodules at incidence screening with low-dose CT: analysis of data from the randomised, controlled NELSON trial. *Lancet Oncol* 2016;17(7):907-16. Epub 2016 Jun 6.
27. Pinsky PF, Gierada DS, Nath PH, Munden R. Lung cancer risk associated with new solid nodules in the national lung screening trial. *AJR Am J Roentgenol* 2017;209(5):1009-14. Epub 2017 Sep 12.
28. Wu GX, Raz DJ, Brown L, Sun V. Psychological burden associated with lung cancer screening: a systematic review. *Clin Lung Cancer* 2016;17(5):315-24. Epub 2016 Mar 30.
29. Tammemagi MC, Lam S. Screening for lung cancer using low dose computed tomography. *BMJ* 2014;348:g2253.
30. Mitchell JD, Fergestrom N, Gage BF, Paisley R, Moon P, Novak E, et al. Impact of statins on cardiovascular outcomes following coronary artery calcium scoring. *J Am Coll Cardiol* 2018;72(25):3233-42.
31. Van de Wiel JCM, Wang Y, Xu DM, van der Zaag-Loonen HJ, van der Jagt EJ, van Klaveren RJ, et al. Neglectable benefit of searching for incidental findings in the Dutch-Belgian lung cancer screening trial (NELSON) using low-dose multidetector CT. *Eur Radiol* 2007;17(6):1474-82. Epub 2007 Jan 6.
32. Kucharczyk MJ, Menezes RJ, McGregor A, Paul NS, Roberts HC. Assessing the impact of incidental findings in a lung cancer screening study by using low-dose computed tomography. *Can Assoc Radiol J* 2011;62(2):141-5. Epub 2010 Apr 10.
33. Priola AM, Priola SM, Giaj-Levra M, Basso E, Veltri A, Fava C, et al. Clinical implications and added costs of incidental findings in an early detection study of lung cancer by using low-dose spiral computed tomography. *Clin Lung Cancer* 2013;14(2):139-48. Epub 2012 Aug 4.
34. *Baseline screening protocol, results and workup recommendations*. Tempe, AZ: International Early Lung Cancer Action Program; 2021. Available from: **https://www.ielcap.org/sites/default/files/I-ELCAP-protocol-summary.pdf**. Accessed 2021 Jan 30.
35. Munden RF, Carter BW, Chiles C, MacMahon H, Black WC, Ko JP, et al. Managing incidental findings on thoracic CT: mediastinal and cardiovascular findings. A white paper of the ACR Incidental Findings Committee. *J Am Coll Cardiol* 2018;15(8):1087-96. Epub 2018 Jun 22.
36. Berland LL, Silverman SG, Gore RM, Mayo-Smith WW, Megibow AJ, Yee J, et al. Managing incidental findings on abdominal CT: white paper of the ACR Incidental Findings Committee. *J Am Coll Cardiol* 2010;7(10):754-73.
37. Tremblay A, Taghizadeh N, Huang J, Kasowski D, MacEachern P, Burrowes P, et al. A randomized controlled study of integrated smoking cessation in a lung cancer screening program. *J Thorac Oncol* 2019;14(9):1528-37. Epub 2019 May 8.
38. Evans WK, Gauvreau CL, Flanagan WM, Memon S, Yong JHE, Goffin JR, et al. Clinical impact and cost-effectiveness of integrating smoking cessation into lung cancer screening: a microsimulation model. *CMAJ Open* 2020;8(3):E585-92.
39. Gionet L, Roshanafshar S. *Select health indicators of First Nations people living off reserve, Métis and Inuit*. Ottawa, ON: Statistics Canada; 2013.
40. Bougie E, Kohen D. *Smoking prevalence among Inuit in Canada*. Ottawa, ON: Statistics Canada; 2017.
41. Mazereeuw MV, Withrow DR, Nishri ED, Tjepkema M, Marrett LD. Cancer incidence among First Nations adults in Canada: follow-up of the 1991 Census Mortality Cohort (1992–2009). *Can J Public Health* 2018;109(5-6):700-9. Epub 2018 Jun 28.

This article is eligible for Mainpro+ certified Self-Learning credits. To earn credits, go to **www.cfp.ca** and click on the Mainpro+ link.
This article has been peer reviewed.
Can Fam Physician 2021;67:817-22. DOI: 10.46747/cfp.6711817
Cet article se trouve aussi en français à la **page 823**.