Lung Cancer Screening- Guideline Presentation

Speaker deck

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OVERVIEW

We will review the following:

1. Background on Lung Cancer Screening
2. Methods of the CTFPHC
3. Recommendations and Key Findings
4. Implementation of Recommendations
5. Conclusions
6. Questions and Answers

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CTFPHC WORKING GROUP MEMEBERS

The Lung Cancer Screening Working Group included members from the Canadian Task Force on Preventive Health Care (CTFPHC), the Public Health Agency of Canada (PHAC) and the Evidence Review Synthesis Centre (ERSC) at McMaster University.

Task Force Members:

- Gabriela Lewin (Chair)
- James Dickinson
- Neil Bell
- Maria Bacchus
- Harminder Singh
- Marcello Tonelli

Public Health Agency of Canada:

- Kate Morissette*
- Lesley Dunfield*
- Alejandra Jaramillo Garcia*

Evidence Review and Synthesis Centre:

- Donna Fitzpatrick-Lewis*
- Ali Usman*

*non-voting member

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SCREENING FOR LUNG CANCER: BACKGROUND

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BACKGROUND

Lung cancer is the most common cause of cancer-related deaths and the most commonly diagnosed cancer among Canadians – an estimated 26,600 Canadians will be diagnosed and 20,900 will die from lung cancer in 2015. In Canada, the incidence of lung cancer is currently higher in men than women (although this gap is beginning to narrow) and more than 85% of cases are related to smoking tobacco.

Mortality is extremely high in late stage lung cancer but much lower in earlier stages (5-year relative survival rates for stage 4 and 1A lung cancer were 1% and 49% respectively in 2007). Screening for lung cancer aims to detect disease at an early stage, when it may respond better to treatment and be less likely to cause serious illness or death.

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SMOKING HISTORY

Approximately 44% of Canadians (12.6 million) are current or former smokers. Those with a history of heavy smoking are at the greatest risk for lung cancer. Smoking history is often measured in pack-years, which is the product of the average number of packs smoked daily and the number of years of smoking. For example, individuals who smoked 1 pack a day (20 cigarettes) for 30 years, or 2 packs a day for 15 years, would both have a 30 pack-year history.

Screening has been proposed as an adjunct to other methods for reducing the burden of lung cancer, including global tobacco control initiatives and interventions designed to encourage smoking cessation.

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SCREENING TESTS FOR LUNG CANCER

The CTFPHC examined three different screening tests for lung cancer: low dose computed tomography (LDCT), and chest x-ray (CXR) both with and without sputum cytology. Tobacco control and smoking cessation initiatives are critical for prevention and for reducing the morbidity and mortality due to lung cancer.

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SCREENING FOR LUNG CANCER: METHODS

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METHODS OF THE CTFPHC

The CTFPHC is an independent panel of clinicians and methodologists with expertise in prevention, primary care, literature synthesis, and critical appraisal. The mandate of the CTFPHC is to apply the latest evidence in preventive health care research to primary care practice and policy across Canada.

The Lung Cancer Working Group is composed of 7 CTFPHC members who work with PHAC science officers to establish the guidelines research questions and analytical framework.

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METHODS OF THE CTFPHC

The Evidence Review and Synthesis Centre (ERSC), in consultation with field experts, then undertakes a systematic review of literature based on this analytical framework, and prepares a systematic review of the evidence with GRADE tables. The ERSC participates in working group and CTFPHC meeting

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CTFPHC REVIEW PROCESS

The CTFPHC review process is composed of an (i) internal review process and an (ii) external review process. The internal review process involves the guideline working group, the full CTFPHC, PHAC science officers and ERSC staff.

The external review process involves review of the guidelines by key stakeholders from generalist and disease specific organizations, federal, provincial and territorial stakeholders. The Canadian Medical Association Journal (CMAJ), where most of the CTFPHC guidelines are published, undertakes its own independent peer review journal process.

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RESEARCH QUESTIONS

The systematic review for screening for lung cancer included 2 key research questions (with 2 sub-questions) and 7 supplemental or contextual questions.

For more detailed information please access the systematic review
www.canadiantaskforce.ca

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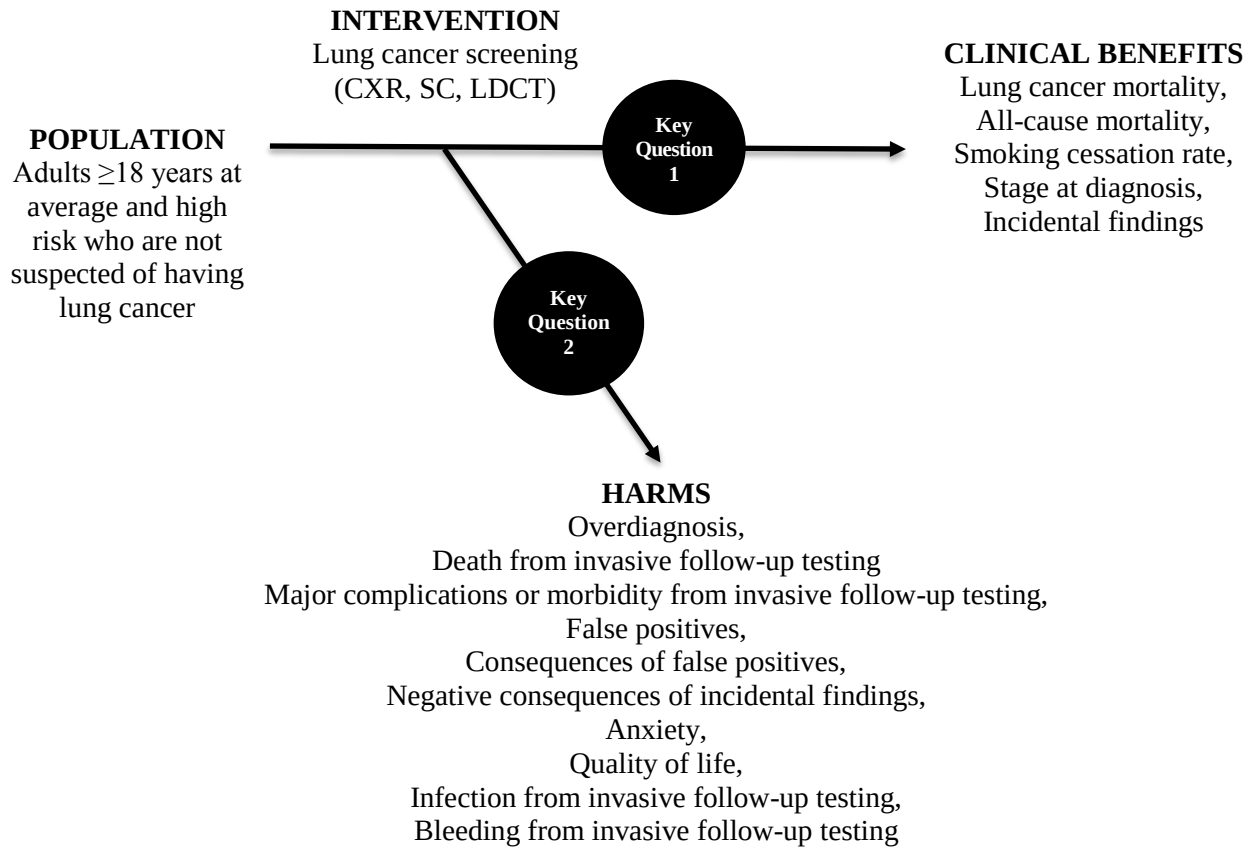
ANALYTICAL FRAMEWORK: SCREENING



The analytical framework outlines the scope of the evidence review and guideline recommendations. The purpose of the analytical framework is to show practicing physicians what the guideline includes and does not include and to visually display the relationship between the key concepts.

This guideline applies to Adults ≥18 years at average and high risk who are not suspected of having lung cancer. As outlined in the analytical framework, this guideline looks at the impact of screening on clinical benefits (e.g., lung cancer mortality, all-cause mortality, smoking cessation, stage at diagnosis) as well as associated adverse effects (e.g., overdiagnosis, major complications from invasive follow-up testing, false positives, or death).

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ELIGIBLE STUDY TYPES

The primary population of interest for the lung cancer screening guideline was adults over the age of 18 at average and high risk, who are not suspected of having lung cancer.

The studies included were in English and in French.

The study types for benefits of screening were restricted to randomized control trials (RCTs), either with comparison groups of no screening, or comparison groups between tests. The study types for harms of screening included any quantitative study design, with or without comparison groups.

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HOW IS EVIDENCE GRADED?

The CTFPHC utilizes the GRADE system for providing clinical practice guideline recommendations based on a systematic review of the available evidence. The **GRADE** acronym stands for: **G**rading of **R**ecommendations, **A**ssessment, **D**evelopment and **E**valuation.

The GRADE system is composed of two main components:

1. **The quality of the evidence**: The quality of the evidence measures the degree of confidence that the available evidence correctly reflects the theoretical true effect of the intervention or service. It is graded as high, moderate, low or very low based on how likely further research is to change our confidence in the estimate of effect.
2. **The strength of recommendation:** The strength of the recommendation (strong/weak) is based on the quality of supporting evidence, the degree of

uncertainty about the balance between desirable and undesirable effects, the degree of uncertainty or variability in values and preferences, and the degree of uncertainty about whether an intervention represents a wide use of resources.

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HOW IS THE STRENGTH OF RECOMMENDATIONS DETERMINED?

GRADE: How is the strength of the recommendations graded?

The strength of the recommendations (strong or weak) is based on four factors:

1. The quality of the supporting evidence
2. The certainty about the balance between desirable and undesirable effects
3. The certainty or variability in the values and preferences of individuals
4. The certainty about whether the intervention represents a wise use of resources

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INTERPRETATIONS OF RECOMMENDATIONS

Implications	Strong,Recommendation	Weak,Recommendations
For patients	Most individuals would want the recommended course of action; Only a small proportion would not.	The majority of individuals in this, situation would want the suggested course of action but many would not.
For clinicians	Most individuals should receive the intervention.	Recognize that different choices will be appropriate for individual patients; Clinicians must help patients make management decisions consistent with values and preferences.
For policy makers	The recommendation can be adapted as, policy in most situations.	Policy making will require substantial debate and involvement of various stakeholders.

This is a standard GRADE table which outlines how weak or strong recommendations should be interpreted and implemented by different groups or stakeholders. It is important to consider the strength of the recommendations when interpreting the Task Force guidelines for implementation in clinical practice, for policy, or for patients in decision making.

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SCREENING FOR LUNG CANCER: RECOMMENDATIONS & KEY FINDINGS

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LUNG CANCER 2016 GUIDELINES

This guideline provides recommendations for practitioners on preventative health screening in a primary care setting. This guideline applies to adults aged 18 years and older who are not suspected of having lung cancer. These recommendations do not apply to individuals who have a history of lung cancer, or suspected lung cancer.

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LOW DOSE COMPUTED TOMOGRAPHY (LDCT)

Recommendation: For adults aged 55 to 74 years with at least a 30 pack-year smoking history, who currently smoke or quit less than 15 years ago, we recommend annual screening with LDCT up to three consecutive times (Weak recommendation; low quality evidence).

It's important to note that screening should ONLY be carried out in health care setting with expertise in early diagnosis and treatment of lung cancer

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LOW DOSE COMPUTED TOMOGRAPHY (LDCT)

Basis of the recommendation: The CTFPHC recommendation to screen the high-risk population places a relatively high value on a small benefit for reduced lung cancer mortality and the known poor prognosis of untreated lung cancer; but a relatively lower value on the risk of side effects, overdiagnosis, and the lack of data comparing LDCT to no screening

A weak recommendation means that most eligible people would want to be screened for lung cancer, but many may appropriately choose not to be screened.

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LOW DOSE COMPUTED TOMOGRAPHY (LDCT)

Recommendation: For all other adults, regardless of age, smoking history, or other risk factors, **we recommend not screening for lung cancer with LDCT**. (Strong recommendation; very low quality evidence)

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LOW DOSE COMPUTED TOMOGRAPHY (LDCT) CONTINUED…

Basis of the recommendation: People who are not at high risk for lung cancer would be expected to have lower absolute benefit of screening than high risk patients, but would still be susceptible to some of the harms association with screening (e.g., false positives, consequences from invasive follow-u p tests, and overdiagnosis)

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CHEST X-RAY (CXR)

Recommendation: We recommend that chest x-ray not be used to screen for lung cancer, with or without sputum cytology (*Strong recommendation; low quality evidence)*

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CHEST X-RAY (CXR)

Basis of the recommendation: Screening with CXR detected more early-stage and fewer late-stage lung cancers, compared to groups receiving usual care. However, such screening did not reduce lung cancer specific mortality or all-cause mortality.

This recommendation against screening is strong, based on low quality evidence, since available evidence suggests no benefit of screening with CXR on lung cancer specific or

all-cause mortality; but there are established harms (e.g., overdiagnosis, false positives, and complications from follow-up testing)

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PERFORMANCE CHARACTERISTICS OF LDCT

The test characteristics of various low-dose CT technologies (e.g., multislice or helical) (but not chest radiography) were examined in the review performed for the task force. The sensitivity of low-dose CT is high (80%–100%), but the specificity varies widely (28%–100%), likely contributing to the high frequency of false-positive results. Studies reporting on test performance found that a multislice CT, along with computer assisted reading and diagnosis and two independent radiologist readers, showed the highest sensitivity (94.6%) and specificity (98.3%).

The cut points for a positive low-dose CT result varied across studies (ranging from > 3 to > 10 mm). At present, there is no agreement on which cut point will optimize the balance between a reduction in mortality and minimizing harm.

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SCREENING INTERVALS

The CTFPHC is taking a more conservative approach in recommending three annual scans, rather than continuous annual or biennial scans

It is possible that ongoing screening might yield additional benefits, but this is speculative, since there is no supporting RCT data. It is unclear whether it could lead to more false positives and invasive follow up testing, potentially disrupting the balance between the benefits and harms.

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HARMS AND BENEFITS FOR SCREENING

The systematic review performed for CTFPHC included 33 studies on lung cancer screening, including 13 RCTs on the benefits of screening. Seven low quality studies examined screening with CXR (with or without sputum cytology) compared to no screening or less intensive screening (e.g., screening with CXR at longer intervals, or being advised to have a CXR), and found small benefits in terms of early disease detection.

Two studies were found that compared LDCT to CXR. One of the studies included mortality outcomes (National Lung Screening Trial, NLST). The NLST was a high quality RCT that demonstrated a 15% reduction in lung cancer mortality and 6% reduction in all-cause mortality associated with screening with LDCT compared to CXR after 6.5 years follow up. Screening with LDCT reduced the absolute risk of lung cancer mortality by 0.31%, and of all-cause mortality by 0.46%. LDCT also detected significantly more cases of early-stage lung cancer (8 more per 1000 people screened) and significantly fewer cases of late-stage lung cancer (4 fewer per 1000 people screened) with LDCT compared to CXR.

Evidence from 4 studies indicated no significant differences in smoking cessation rates between the screened (LDCT or CXR) groups and the control groups(13). The risk of bias for these studies was unclear due to the self-reported nature of this outcome.

The harms of screening and invasive follow up tests were informed by 31 studies, many with observational designs(13). The main harms included false positives, death or major complications from invasive follow up testing, and overdiagnosis.

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HARMS AND BENEFITS FOR SCREENING

322 people would need to be screened with LDCT to prevent one death from lung cancer over 6.5 years.

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OVERALL FINDINGS SUMMARY – BENEFITS (CRITICAL AND SELECTED IMPORTANT OUTCOMES)

Outcome	CXR vs Usual Care	CXR plus SC vs CXR	Annual LDCT vs Usual Care	LDCT vs CXR
Lung Cancer Mortality	RR 0.99 95% CI 0.92, 1.07 I^2 = 0%	RR 1.01 95% CI 0.74, 1.42 I^2 = na	RR 1.35 95% CI 0.79, 2.29 I^2 = na	RR 0.80 95% CI 0.70, 0.92, I^2 = na Absolute value per million 3,250 fewer, range from 1,271 fewer to 4,972 fewer ARR 0.33% NNS 308 (95% CI 201, 787)
All-Cause Mortality	RR 0.98 95% CI 0.96, 1.00 I^2 = 0%	–	RR 1.42 95% CI 0.91, 2.22 I^2 = 67%	RR 0.94 95% CI 0.88,1.00, I^2 = na Absolute value per million 4,571 fewer, range from 180 fewer to 8,709 fewer ARR 0.46% NNS 219 (95% CI115, 5,556)
Stage at Diagnosis (Early Stage)	RR 1.14 95% CI 1.03, 1.25 I^2 = na	–	RR 1.59 95% CI 1.11, 2.28 I^2 = 0%	RR 1.46 95% CI 1.33, 1.61 I^2 = na
Stage at Diagnosis (Late Stage)	RR 0.93 95% CI 0.87, 0.98 I^2 = na	–	RR 0.59 95% CI 0.43, 0.83 I^2 = 0%	RR 0.71 95% CI 0.65, 0.77 I^2 = na

AAR = Absolute Risk Reduction; NNS = Number Needed to Screen

This table shows the various benefit outcomes compared for different screening tests, including CXR vs usual care; CXR plus SC (sputum cytology) vs. CXR; Annual LDCT vs. usual care; and LDCT vs CXR.

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OVERALL FINDINGS SUMMARY – HARMS (CRITICAL OUTCOMES)

Outcome	CXR	CXR plus SC	LDCT
Overdiagnosis	—	TVDT >400 days: 2.27% to 6.98% of all cases of lung cancer diagnosed in the screened population were overdiagnosed TVDT >300 days: 4.55% to 16.28% of all cases of lung cancer diagnosed in the screened population were overdiagnosed	10.99% to 25.83% of all cases of lung cancer diagnosed in the screened population were overdiagnosed
Death from Invasive Follow-up Testing	28.60 deaths (95% CI 16.02, 41.17) per 1,000 patients undergoing invasive follow-up testing	47.67 deaths (95% CI 23.86, 71.49) per 1,000 patients undergoing invasive follow-up testing	11.18 deaths (95% CI 5.07, 17.28) per 1,000 patients undergoing invasive follow-up testing
Major Complications from Invasive Follow-up Testing	63.32 major complications (95% CI 42.92, 92.49) per 1,000 patients undergoing invasive follow-up testing	—	43.29 major complications (95% CI 32.00, 54.58) per 1,000 patients undergoing invasive follow-up testing

TVDT = Tumor volume doubling time
This table shows the various harmful outcomes compared for different screening tests, including CXR, CXR plus SC, and LDCT.

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COMPARISON: CTFPHC GUIDELINE VS. OTHER RECOMMENDATIONS

The CTFPHC guideline is generally in line with other Canadian and international guidelines on screening for lung cancer; however, the CTFPHC is taking a more conservative approach in recommending three annual scans, rather than continuous annual or biennial scans.

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SCREENING FOR LUNG CANCER: IMPLEMENTATION OF RECOMMENDATIONS

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VALUES AND PREFERENCES

The CTFPHC looked at patient preference on lung cancer screening through seven studies included in the systematic review as well as de novo data collection via focuse groups and surveys with members of the public.
The systematic review concluded that most participants in the high risk group (i.e., current or former smokers) had high willingness to participate in screening for lung cancer, motivated by their smoking history, beliefs that early detection improves health outcomes, and family history o flung cancer. Potential barriers to participation included inconvenience of screening, and negative experiences with health care workers or settings.
In the judgment of the CTFPHC, the consistent evidence indicating that high risk patients are willing to be screened for lung cancer supports the recommendation for screening in this group.
The CTFPHC conducted a series of focus groups and a survey with members of the public; and in general, participants agreed that these recommendations were appropriate, beneficial, and feasible; though some had concerns about access to LDCT scans, and limiting eligibility to those between 55 to 74 years.

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KNOWLEDGE TRANSLATION TOOLS

The CTFPHC creates KT tools to support the implementation of guidelines into clinical practice. A clinician recommendation table and patient FAQ has been developed for the lung cancer screening guideline.

After the public release, these tools will be freely available for download in both French and English on the website: www.canadiantaskforce.ca

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SCREENING FOR LUNG CANCER: CONCLUSIONS

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CONCLUSIONS: KEY POINTS

Adults between 55-74 years who are at high risk for lung cancer (i.e., current or former smokers who quit within the past 15 years, and who have at least a 30 pack-year smoking history) may benefit from screening for lung cancer with LDCT annually for

three consecutive years. Because of the potential for screening-related harms, LDCT and subsequent management should be carried out in health care setting with expertise in early diagnosis and treatment of lung cancer

In order to prevent one death from lung cancer, 322 people would need to be screened with LDCT over 6.5 years.

The weak recommendation implies that practitioners should have a discussion with their patients about the benefits and harms of screening for lung cancer with LDCT including false positives, side effects of invasive follow-up testing, and overdiagnosis. There is no clear benefit of LDCT screening for lung cancer in adults younger than 55 years, older than 74 years, or who have a lower risk based on smoking history (i.e., smokers with less than a 30 pack-year smoking history, or former smokers who quit more than 15 years prior).

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CONCLUSIONS: KEY POINTS

There is no benefit of screening for lung cancer with chest x–rays (with or without sputum cytology), but there are known harms including false positives, side effects of invasive follow up testing, and overdiagnosis.

Since smoking is associated with 85% of incident lung cancer in Canada, tobacco control and smoking cessation are critical for reducing the morbidity and mortality due to lung cancer.

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CONCLUSIONS: KEY POINTS

For more information on the details of this guideline or to access the KT tools please refer to the evidence review in the resources section of the website www.canadiantaskforce.ca**.**

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QUESTIONS AND ANSWERS

Thank you.