

Controlled settings for lung cancer screening: why do they matter? Considerations for referring clinicians

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The updated guideline on lung cancer screening released in March 2016 by the Canadian Task Force on Preventive Health Care recommends screening for people at high risk for lung cancer. Annual screening with low-dose computed tomography (LDCT) is recommended for up to 3 consecutive years for adults 55–74 years of age with a minimum 30 pack-year smoking history who are current smokers or who have quit within the preceding 15 years¹. The Task Force recommendations also underscore the importance of delivering lung cancer screening in controlled health care settings so as to both minimize potential risks and replicate the 20% reduction in lung cancer mortality achieved in the U.S. National Lung Screening Trial (NLST)², a major trial that informed the guideline.

Lung cancer screening is not a test but a process that requires the integration of many elements^{3–8}:

- Identification of individuals with sufficient lung cancer risk to benefit from screening
- Strategies for effective screening uptake and retention, especially for underserved populations
- Provision of smoking cessation services to current smokers, including those who express an interest in screening but who do not meet screening criteria
- Use of defined LDCT imaging and interpretation protocols
- Adoption of a standardized algorithm to manage abnormal findings
- Availability of expertise to diagnose and treat early lung cancer
- Mechanisms for data collection, outcome evaluation, and quality assurance

Clinicians looking to replicate the benefits of lung cancer screening play an important role by ensuring that their patients are screened within controlled settings. The purpose of the present commentary is to outline the importance of such settings, which has been an area of focus for the Pan-Canadian Lung Cancer Screening Network (PLCSN), a group that aims to leverage expertise and evidence-based recommendations to support policy and best practices in lung cancer screening.

The PLCSN's Lung Cancer Screening Framework for Canada addresses key considerations for the delivery of lung cancer screening and highlights key components of controlled settings⁴. The framework consists of 34 consensus

statements developed by pan-Canadian working groups comprising PLCSN members and other expert clinicians, pathologists, radiologists, smoking cessation experts, and thoracic surgeons. The framework not only provides guidance for organizations considering the implementation of organized lung cancer screening, but, to maximize benefits and minimize potential harms, it also includes key considerations relevant to clinicians contemplating referral of their patients for lung cancer screening.

Unlike population-based screening for breast, cervical, and colorectal cancers, whose guidelines base eligibility primarily on age, lung cancer screening is currently restricted to a high-risk population based on age and smoking history^{1,8}. Controlled settings for screening can help to ensure that screening is limited to those for whom there is evidence of benefit, thus limiting “eligibility creep” or unintentional screening of low-risk groups. Such selectivity is particularly important because the absolute benefit of lung cancer screening for those who do not meet, at minimum, NLST eligibility criteria is unknown (but presumably lower), and the risk of associated harms with screening is likely similar¹. Providing screening in controlled settings can help both to ensure appropriate participation and to facilitate systematic monitoring and evaluation of eligibility assessment to ensure that patients benefit from screening.

A recent retrospective analysis showed that fewer than one third of patients with newly diagnosed lung cancer would meet current screening criteria based on age and pack-years⁹. The impact of screening at the population level might be much smaller than estimated. Screening based on risk prediction models that incorporate additional variables—for example, family history of lung cancer, personal history of cancer, diagnosis of chronic obstructive pulmonary disease, socioeconomic status, ethnicity, and body mass index—in determining who is at high risk for lung cancer and eligible for screening have demonstrated greater predictive accuracy than does screening using age and smoking history alone^{5,6}. The use of risk prediction models such as the PLCO_{m2012}⁷ might also avoid patient misunderstanding by basing eligibility on a more comprehensive and incremental assessment of risk rather than on age and smoking history cut-offs. The use of risk prediction models also offers an opportunity for clinicians to counsel patients about their lung cancer risk and eligibility for screening, particularly those with

lower-than-threshold smoking histories (28 pack-years, for instance) but with other lung cancer risk factors that might sufficiently elevate their risk to merit screening. To date, risk prediction models have not been evaluated prospectively outside a clinical trial setting. Capacity for prospective measurement and evaluation in controlled settings means that the evidence for using risk prediction models can be evaluated in real-world settings.

Although lung cancer screening with LDCT lowers lung cancer mortality, the potential harms associated with any kind of cancer screening are also well documented and can include false-positive results and adverse effects of invasive follow-up¹. The harms associated with downstream investigations of suspicious lung nodules can be more severe than the harms associated with the diagnostic follow-up from other screening tests such as mammography. Screening participants would be exposed to radiation from annual repeat LDCT scans and potentially to additional radiation as a result of diagnostic work-up such as further computed tomography or positron-emission tomography imaging¹⁰, which increases risk for lung and other cancers¹¹. In controlled settings, standardized technical parameters and dosage levels for LDCT and standardized algorithms to manage abnormal findings can reduce the need for repeat scans and can minimize cumulative radiation exposure.

One of the challenges with lung cancer screening is the high rate of indeterminate or suspicious pulmonary nodules requiring diagnostic follow-up. The NLST demonstrated that decreases in mortality from LDCT screening occurred alongside relatively high rates of false-positive findings requiring follow-up examinations and, in a smaller subset of cases, invasive follow-up⁶. Significant computed tomography reader variability was found in the NLST, with false-negative rates ranging from 3.5% to 8.1% and false-positive rates ranging from 3.8% to 69.0%¹². False-negative readings can increase the chance of missing a cure, and false-positive readings can increase radiologist workload and downstream investigations.

Although most screen-detected nodules require only a repeat LDCT scan, additional work-up might include biopsy or surgical resection, which can cause undue harm if the result were ultimately to be a false positive¹. Complications from, for example, a lung biopsy can include pulmonary bleeding and pneumothorax¹³. Surgical mortality from lung resections can vary depending on the level of specialization of the medical facility in which the procedure is performed¹⁴. Delivering lung cancer screening in a controlled setting facilitates prospective cross-jurisdictional evaluation of the consistency and quality of computed tomography imaging interpretation and of nodule follow-up algorithms, including nodule malignancy probability calculators^{1,6,15,16}. By providing screening in a controlled setting closely resembling that of the NLST, the opportunity to achieve comparable reductions in lung cancer mortality is greater.

It is well known that physician advice to quit significantly increases smoking cessation rates¹⁷. Conversations about referral to lung cancer screening in controlled settings are a window of opportunity for clinicians to engage eligible screening participants who are current smokers or who have recently quit, helping them to become aware of

the effects of tobacco, to change their smoking behavior, or to sustain a recent quit attempt¹⁸. Lung cancer screening activities should complement evidence-based and ethno-culturally appropriate smoking cessation interventions¹⁹. Evidence suggests that smoking cessation interventions embedded in lung cancer screening increase quit and abstinence rates regardless of the lung cancer screening result¹³. Controlled settings can align comprehensive smoking cessation interventions with screening activities, thereby providing smoking cessation interventions that are complementary and reinforcing to those provided by referring clinicians. Data collected on an ongoing basis from controlled settings could provide further information on how to optimize smoking cessation, particularly within the context of screening¹⁹. Smoking cessation interventions combined with lung cancer screening are also more cost-effective than screening delivered alone^{20,21}. For patients diagnosed with lung cancer through screening, smoking cessation interventions improve therapeutic benefit and prognosis. The effect of smoking cessation can equal, or even exceed, the positive therapeutic effects of chemotherapeutic agents²².

Although the Task Force recommendations support lung cancer screening for specific high-risk individuals in Canada, further questions remain, including optimal screening interval, duration of screening, and follow-up for abnormal results. As an example, the Task Force recommends 3 consecutive annual screens for the high-risk population, but other Canadian guidelines might recommend annual ongoing screening similar to that outlined in the guideline recommendations from the U.S. Preventive Services Task Force²³. Data coming from the delivery of lung cancer screening in real-world controlled settings is especially important for guiding future practice, because those settings actively follow screening participants and have organized mechanisms for measuring and evaluating screening outcomes.

In preparation for the future implementation of screening in controlled settings, the PLCSN is working on the development of a set of lung cancer screening quality indicators for reporting at the national level. Some differences in lung cancer screening implementation across Canada are expected. However, the anticipated heterogeneity from those differences in implementation could provide insights for further maximizing the benefits of lung cancer screening with LDCT, especially if performed in controlled settings with consistent mechanisms for monitoring, reporting, and evaluating various outcomes.

To replicate the results achieved in the NLST, the Task Force guidelines for lung cancer screening underscore the importance of delivering lung cancer screening in controlled settings in which expertise in the early diagnosis and treatment of lung cancer is available. For clinicians who are considering referring patients for screening, the PLCSN framework further addresses some of the key considerations for the delivery of lung cancer screening within those controlled settings.

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We have read and understood *Current Oncology's* policy on disclosing conflicts of interest, and we declare that we have none.

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