Review Article

Lung cancer screening—contemporary issues: a narrative review

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Contributions: (I) Conception and design: Both authors; (II) Administrative support: S Lam; (III) Provision of study materials or patients: None; (IV) Collection and assembly of data: Both authors; (V) Data analysis and interpretation: Both authors; (VI) Manuscript writing: Both authors; (VII) Final approval of manuscript: Both authors.

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Background and Objective: Randomized clinical trials and meta-analyses have firmly established low-dose computed tomography (LDCT) screening is an effective intervention to reduce lung cancer mortality. The purpose of this review is to address the contemporary issues relevant to health professionals and policymakers regarding lung cancer screening and the optimal approach to integrating smoking cessation with screening.

Methods: A narrative review was conducted based on evidence in the literature from PubMed, Cochrane Library, and Web of Science using the keywords related to lung cancer screening.

Key Content and Findings: There is a risk threshold below which there is no mortality reduction benefits from LDCT screening. An accurate lung cancer risk prediction tool such as the PLCOm2012 is more cost-effective and has significantly higher sensitivity and positive predictive value for identifying individuals who will be diagnosed with lung cancer compares to age and pack-years criteria. Screening of light and never smokers in the general population who do not currently qualify for LDCT screening will require development of an accurate risk assessment tool that includes other important risk factors such as cumulative ambient air pollution exposures. The use of geospatial mapping tools that take into account screening, diagnostic work-up and treatment resource capacities, disparity in access by social-economically deprived and underserved populations to guide screening program improvement need to be evaluated. An accurate, personalized screening LDCT management protocol is key to minimize potential harms from radiation exposure due to unnecessary imaging studies, and adverse events from biopsy or surgery for benign disease. Artificial intelligence (AI)/deep learning tools incorporating time-dependent changes in smoking behavior, age and CT findings are promising approaches to tailor individual screening intervals or diagnostic work-up referral. Improvement in the smoking cessation rate in a screening population who are older and nicotine dependent requires wider use of pharmacotherapy in addition to counselling. Primary care providers play an important role in providing smoking cessation pharmacotherapy and management of additional findings.

Conclusions: Tremendous progress has been made in lung cancer screening. Additional studies to optimize screening eligibility criteria, overcome barriers to screening uptake, and personalized screening protocol can further improve the benefits/harms trade-offs.

Keywords: Lung cancer; screening; chest computed tomography (chest CT); smoking cessation

Received: 06 May 2023; Accepted: 30 October 2023; Published online: 30 October 2023.

doi: 10.21037/ccts-23-3

View this article at: https://dx.doi.org/10.21037/ccts-23-3

Introduction

Background

Lung cancer is the second most diagnosed cancer and the leading cause of cancer deaths globally with 1.8 million annual deaths (1). This high mortality rate is largely due to late diagnosis. Reduction in lung cancer mortality by screening with low-dose computed tomography (LDCT) versus no screening or chest X-ray in high-risk individuals who have ever smoked has been firmly established by meta-analyses and randomized controlled trials that included the pivotal National Lung Screening Trial (NLST) and the Dutch-Belgian NELSON trial (2-6). Lung cancer CT screening programs have been implemented at the country or regional level in various settings including the United States, Canada, South Korea, Poland, China, Croatia, Czech Republic, Taiwan and the United Arab Emirates. A further six countries—the United Kingdom, Australia, Italy, Slovakia, Romania and Kazakhstan, have formal commitment to implement LDCT screening with a number of other countries in the planning process (7). Successful implementation of an effective, high quality lung cancer screening program that can improve lung cancer outcomes requires attention to several key areas. The purpose of this review is to address the contemporary issues relevant to health professionals and policymakers regarding lung cancer screening and the optimal approach to integrating smoking cessation with screening.

Rationale and knowledge gaps

Unlike other cancer screening programs such as mammography screening for breast cancer that are based on age criteria, only those with sufficient risk for lung cancer that outweigh the potential harms of screening are screened. For a screening program to have substantial public health impact, major issues such as the proportion of high-risk individuals potentially covered by the screening eligibility criteria, workforce and technical capacity, equitable access to screening services, screening uptake, efficiency and safety of the screening management protocol and optimal smoking cessation intervention for participants who are still smoking need to be addressed.

Objective

The purpose of this narrative review is to discuss the contemporary issues in lung cancer screening relevant to health professionals, and policy development in the implementation of an effective lung screening program at the population level and the optimal approach to integrating smoking cessation into screening programs. We present this article in accordance with the Narrative Review reporting checklist (available at https://ccts.amegroups.com/article/view/10.21037/ccts-23-3/rc).

Methods

An English language literature search of PubMed, Cochrane Library and Web of Science was conducted using the keywords related to lung cancer screening [lung cancer, lung cancer screening, early detection, tobacco smoking, smoking cessation, disparities in lung cancer, biomarkers, cost-effectiveness]. The date of the last search was 6th April 2023 (*Table 1*).

Contemporary issues

Screening eligibility

Unlike other cancer screenings such as cervix, breast and colorectal cancer screening, lung screening only benefits those with sufficient risk of lung cancer and not everyone within a certain age group. For example, in the NLST, individuals who had a 6-year lung cancer risk <0.64%, had no significant reduction in lung cancer deaths in the LDCT group compared to the chest X-ray group (8) (*Figure 1*).

There are two major approaches to select high-risk ever smokers for LDCT screening. The first is categorical age (age 50/55 to 74/77/80 years), smoking (15/18.8/20/30 pack-years) and time since quitting (10/15 years for former smokers) that has been used by NELSON and NLST, and recommended by the US Medicare and Medicaid Services, the US Preventive Services Task Force (USPSTF 2013 and 2021) and the 2016 Canadian Task Force on Preventive Health Care as screening criteria (5,6,9-12). A second approach is to use risk prediction models that are based on incidence lung cancer risk or risk of lung cancer death (13). In contrast to using limited categorical risk criteria, accurate lung cancer risk prediction models use additional predictors and quantify risk by modeling continuous predictors. Over 20 lung cancer risk prediction models have been proposed (14). Several models have been identified as being accurate and possibly suitable for guiding selection of individuals for lung cancer screening and they include the Bach, LCDRAT, LLP and PLCOm2012 models (13,15-17).

Table 1 The search strategy summary

Items	Specification
Date of search	04/06/2023
Databases and other sources searched	PubMed, Cochrane Library, Web of Science
Search terms used	Lung cancer; lung cancer screening; early detection, tobacco smoking, smoking cessation; disparities in lung cancer; biomarkers; cost-effectiveness
Timeframe	2000 to 2023
Inclusion and exclusion criteria	Inclusion: English language literature, clinical trials, screening guidelines or statements by professional societies or regulatory agencies
	Exclusion: opinion articles, non-scientific or regulatory documents
Selection process	By authors following review and discussion

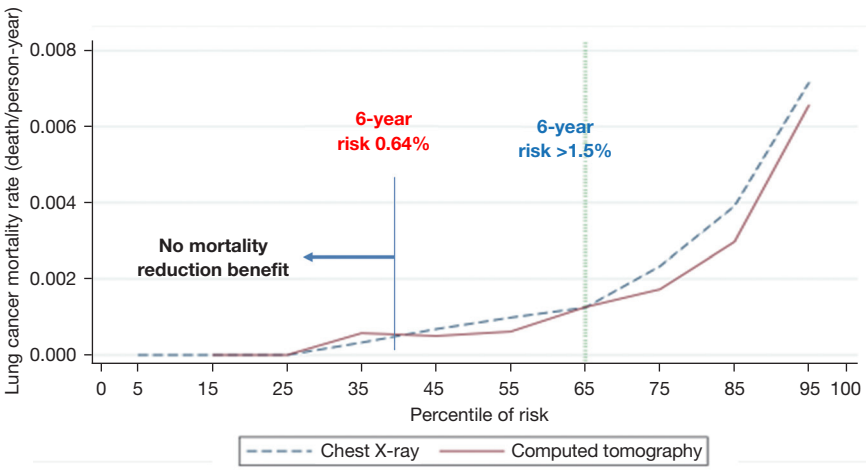

Figure 1 LDCT screening only benefits individuals with sufficient lung cancer risk that outweighs potential harms. A lung cancer mortality reduction benefit could not be demonstrated when the 6-year lung cancer risk is below 0.64%. LDCT screening had a consistently lower mortality compared to chest X-ray when the 6-year lung cancer risk is above 1.5%. Adapted from Reference (8). Courtesy of Professor Martin Tammemagi. LDCT, low-dose computed tomography.

To date, the PLCOm2012 is the lung cancer risk prediction model that has been most validated by different research teams in multiple countries around the world, including the United States, Germany, Australia, the UK, Canada and Brazil (14-16,18-26). It is being used in Canada and the UK. The PLCOm2012 model has the following predictors: age, race/ethnicity, education (estimator of socioeconomic circumstance), body mass index, history of chronic obstructive pulmonary disease (COPD), personal history of cancer, family history of lung cancer, smoking status (current *vs.* former), smoking intensity (cigarettes per day), smoking duration and smoking quit-years in former smokers. In retrospective and cost-effectiveness analyses, Canada yields more life years gained, has smaller number needed to screen to avert one lung cancer death and is more cost-effective compared to USPSTF 2013 categorical criteria (8,13,22,27-32). A recent cost-effectiveness analysis compared risk-based strategies with the USPSTF 2013 and 2021 recommendations showed that PLCOm2012 was cost-effective down to a risk threshold of 1.2%/6 years with an incremental cost-effectiveness being more cost-effective than the USPSTF 2013 or 2021 recommendations, which were both under the analysis' efficiency frontier and strongly dominated by other strategies that result in more quality-adjusted life years (QALYs) for similar costs, while having a similar level of screening coverage (person ever

screened 21.7% with PLCOm2012 1.2%/6 years versus 22.6% with USPSTF) (33). Head-to-head comparison between USPSTF 2013 and PLCOm2012 showed the PLCOm2012 prediction tool was 15.8% more sensitive in identifying individuals with lung cancer screening the same number of participants (34). The positive predictive value was also significantly higher (4.0% *vs.* 3.4%, P=0.01). Of those deemed ineligible for lung screening based on PLCOm2012 or USPSTF criteria, lung cancer developed in 0.5% *vs.* 0.85%, respectively (P<0.001). Females typically accumulate fewer pack-years than male smokers (35). As a result, age and pack-years criteria underestimates lung cancer risk in females. Compared to non-indigenous people, indigenous people have a higher risk of lung cancer despite smoking less tobacco (36). PLCOm2012 race model removes race/ethnicity disparity and reduce sex disparity more than USPSTF 2021 screening criteria (34,35,37). The USPSTF 2021 criteria also exclude those who have stopped smoking for more than 15 years. A recent meta-analysis showed the reducible relative risk after smoking cessation only marginally declines after 15 years from 26.7% [95% confidence interval (CI): 20.2–34.3%] to 19.7% (95% CI: 13.3–26.4%) at 20 years (38). The duration of smoking cessation is not an exclusion criterion in PLCOm2012. In people who have stopped smoking, LDCT screening is one of the best options to reduce the risk of dying from lung cancer (39). An additional advantage of using the PLCOm2012 to determine screening eligibility is that screening can be prioritized according to individual risk scores, with the highest scoring individuals being offered screening first. This aspect is particularly beneficial when LDCT resources are limited, such as during the COVID-19 pandemic (40).

Since risk prediction models developed in a predominant North American-European population need to be validated in an Asian population to inform policy makers to design lung cancer screening programs, methodologies for recalibrating or adapting risk models were developed by synthesizing data sources without large prospective cohorts with long term follow-up. The PLCOm2012 was recalibrated for a Taiwanese population with high predictive performance and calibration (41). Prospective validation of the model is needed.

Lung cancer deaths related to tobacco smoking are projected to decrease in the next 25 years but the number and proportion of lung cancers in people who have never smoked will continue to increase (42). In some East Asian countries and regions, the incidence of lung adenocarcinoma has been increasing over time, despite a steady decline in male smoking since the 1990's and a constant low smoking rate among females (43). The TALENT trial in Taiwan recruited people who have never smoked and had risk factors such as a family history of lung cancer, secondhand tobacco smoke exposure, chronic lung diseases such as tuberculosis or chronic obstructive pulmonary disease, high cooking index and cooking in poorly ventilated spaces (44). Among 12,011 participants, the first screening round revealed a 2.1% detection rate of stage I or higher lung cancers (44), a rate that is higher than in NLST (5) and NELSON (6). A prior 8-year population-based screening study was conducted in Hitachi City, Japan among individuals 50 to 74 years of age. In 17,935 participants who underwent LDCT and 15,548 controls who underwent one or more chest radiographs, 54% and 66% in the LDCT and chest-ray group respectively, had never smoked (45). Using regional cancer registry data, LDCT screening increased the lung cancer detection rate [hazard ratio (HR): 1.79] and decreased the lung cancer mortality rate (HR: 0.41) among the never smokers during year 4 to 8 of the screening compared to the first 4 years (45). However, a study in Taiwan showed a 6-fold increase in the incidence of stages 0–I lung cancer from 2004 to 2018 with no significant change in the incidence of stages II–IV lung cancer (46). The Shanghai Cancer Surveillance Study in China from 2002 to 2017 also showed a sharp rise in early-stage adenocarcinoma, particularly among young women with no significant decline in late-stage disease and mortality (47). These studies raised concern about overdiagnosis especially in younger females without identifiable lung cancer risk factor(s) (46,47). However, these studies did not discuss LDCT screening as a general health examination that includes younger individuals with no known lung cancer risk factor is different than screening based on risk factors such as family history of lung cancer, genetics, outdoor and indoor exposures (48). In addition, overdiagnosis related to the relatively high proportion of adenocarcinomas *in-situ* (stage 0) can be reduced by improvement in our understanding of the molecular biology of non-solid (ground-glass) nodules (GGNs) and refinement of the lung nodule management protocol (48).

Several lung cancer risk assessment tools for people who have never smoked have been published. Without the addition of blood biomarkers such as carcinoembryonic antigen (CEA), alpha-fetal protein, single nucleotide polymorphisms (SNPs) or spirometry data, the accuracy

of these prediction models was modest (8,48-54). None of these models included ambient particulate matter pollution, the second most important cause of lung cancer deaths contributing to 15.1% of lung cancer deaths globally (55). Although the age-standardized death and incidence rates of lung cancer for both sexes combined decreased globally over the past decade, rates trended upwards for some populations, particularly females in certain countries lower on the socio-demographic index (SDI) (55). The age-standardized death rates of lung cancer attributable to ambient particulate matter pollution rose significantly in these populations over the past decade, while the age-standardized death rates attributable to household air pollution from solid fuels remained stagnant. Time-weighted mean exposure to particulate matter PM2.5 at the individual level since 1996 can be obtained from satellite observations, chemical transport models and ground measurements at high resolution (56). Research incorporating past air pollution exposure in lung cancer risk assessment to identify high-risk never smokers who may benefit from LDCT screening is urgently needed.

Equity in screening services

In the United States, screening uptake has been slow and varied widely across the country (57). Lung cancer screening rates were found not to be aligned with lung cancer burden across the US (57). Screening uptake was higher among individuals with insurance than among the uninsured (15.2% *vs.* 4.0%, P<0.001) (58). Uptake declined with age, higher education level, lack of primary care, lower provider knowledge of lung screening guideline and socioeconomic deprivation (59-61). Social deprivation is an independent predictor of lung cancer incidence and mortality (62). Using a social deprivation index constructed from community level education, income, unemployment, welfare assistance, and individual level covariates, the odds of lung cancer and death from lung cancer in the most deprived neighborhood were 1.27 and 1.32, respectively (62). Increasing travel time and level of urbanization have been associated with lower screening rates in established screening programs such as breast mammography and colorectal cancer screening (63-65). To facilitate planning for screening program growth and investment in the areas of greatest need, the American Cancer Society National Lung Cancer Round Table developed a geospatial mapping tool on the geographic distribution of tobacco use, incidence, and mortality of lung cancer, access to lung screening facilities, geographic disparities by race/ethnicity, income, health insurance, and rural/urban location in relation to travel distance (66,67). A similar geospatial mapping approach was used in the implementation of the British Columbia Lung Screening Program in Canada to map the location of the 36 screening sites. Utilizing lung cancer cases in health units across British Columbia as a proxy for the screen-eligible population, the impact of urbanization, individual components of the Statistics Canada's Canadian Index of Multiple Deprivation, composed of sociodemographic and economic indicators, were considered in addition to vehicle travel time (68). Ninety-two percent of the lung cancer patients could access one of the 36 sites within one hour of driving. Longer drive times were found to be associated with situational vulnerability, economic dependency, residential instability, sex, and ethnocultural composition. The potential advantage of using lung cancer prevalence as a proxy for the screen-eligible population is that smoking history from electronic health records can be inaccurate and the smoking criteria for screening eligibility can change over time. The use of geospatial tools that take into account screening, diagnostic work-up and treatment resource capacity, disparity in access by Indigenous people, immigrants, social-economically deprived and underserved populations, to guide screening program improvement need to be evaluated. The potential application of machine learning tool using routine laboratory data such as complete blood count, in addition to clinical information to determine if a LDCT is warranted or the use of a point of care blood test as a pre-screening tool to optimize screening eligibility assessment (69,70) in underserved populations deserves further investigation.

Lung nodule management

An accurate, personalized screening LDCT management protocol is key to maximizing the benefits of screening in detecting lung cancer early while minimizing potential harms by reducing radiation exposure from unnecessary imaging studies, adverse events from biopsy or surgery for benign disease.

Most current lung cancer screening programs are based on a fixed, annual, screening interval until the upper age limit or until the participant would no longer benefit from screening, with shorter follow-up intervals to determine growth rate of suspicious nodules. Examples of these are the Lung Imaging Reporting and Data System (Lung-RADS) (71,72) and the EU-NELSON volumetric protocol (73).

The International Lung Screening Trial (ILST) protocol is the only clinical protocol that has a biennial screening provision based on an individual's lung cancer risk after the baseline (first) screening LDCT which comprise of approximately two-thirds of the screening population (74). The ILST protocol was based on the PanCan lung nodule malignancy risk calculator (75), that was reviewed by the Canadian Agency For Drugs And Technologies In Health comparing the diagnostic test accuracy of the PanCan versus Lung-RADS version 1.0 (76). In nine published studies, six indicate that the PanCan risk calculator performs better at determining which lung nodules identified by LDCT are cancerous compared to Lung-RADS with significantly better specificity and positive predictive value. PanCan had similar diagnostic test accuracy in three other studies—one case-control study, one study that only included subsolid nodules and the third study with a small sample size (76). A prospective study in Vancouver as part of the ILST showed a significantly higher sensitivity and positive predictive value of the PanCan protocol compared to Lung-RADS or the NELSON management protocols (77). A screening protocol with a biennial screening provision for lower risk individuals is currently used in the BC Lung Screening Program in British Columbia, Canada (78). This management protocol has significant implication in reducing health care resource utilization, cost and cumulative radiation exposure.

Other studies such as the randomized Multicentric Italian Lung Detection (MILD) trial compared annual *vs.* biennial LDCT screening interval and reported similar reduction in mortality with biennial screening which saved 44% of follow-up LDCT in subjects with negative baseline LDCT without increase in the occurrence of advanced lung cancer (79). A multicenter, multi-national trial, the 4-IN-THE-LUNG-RUN (4ITLR), is an on-going study in the EU to address the question if a 2 year instead of 1 year follow-up scan can be safely implemented in a screening program in participants with a negative baseline screen and lower lung cancer risk (80). Since findings in a prior scan (e.g., nodules versus no nodules, change in nodule size or attenuation), changes in smoking behavior and increasing age can modify lung cancer risk, several studies attempted to integrate this information to determine the timing of the next screening LDCT based on individual risk (33,81-85). Deep learning tools have also been developed to reduce the proportion of participants with indeterminate or intermediate risk lung nodules, personalize surveillance screening intervals and reduce radiologist workload (84,86-91). The risk thresholds to determine individually tailored screening schedules that optimize the benefits/harms trade-offs have not been prospectively evaluated in these studies. Whether one protocol is superior to another will require prospective randomized studies. Retrospective validation, while informative, is susceptible to bias due to the way individuals are followed based on recommendations from the standard of care rather than an artificial intelligence (AI) algorithm. For example, if AI recommends an earlier imaging study or biopsy for a more aggressive tumor, this benefit cannot be observed in retrospective data because the patient did not have a visit at this earlier time point, and it is unknown whether the patient already had lung cancer at that time.

The management of GGN is an area that requires further research; it has the greatest variation in management because of few high-quality studies on the natural history of these lesions (92). Lung-RADS version 1.1 increased the allowable nodule size for GGNs in category 2 from 20 to 30 mm. Chinese and Japanese guidelines, as well as the British Thoracic Society guideline, recommend early recall LDCT in 3–6 months for GGNs of at least 6 mm but less than 15 mm. Japanese and Chinese guidelines recommend diagnostic work-up for persistent nonsolid nodules of 15 mm or larger (93). The recommendation was based on the finding that a nodule larger than 15 mm is a significant determinant for invasive adenocarcinoma (94). A study using the NLST database suggested that if Lung-RADS categories for GGNs were based on malignancy probability similar to solid nodules, the GGN size threshold for early recall CT should be revised lower (6–19 mm) and not higher (95). In both Lung-RADS version 1.0 and version 1.1, no recommendation is made for biopsy until the nodule becomes part-solid or solid. Revising the size of GGNs from 20 to 30 mm showed no benefit but potentially missing some invasive adenocarcinoma (71).

Diagnostic work-up

Diagnostic work-up of a suspected lesion is an important part of the screening pathway as significant morbidity or even mortality can result from the diagnostic or surgical procedure. Balance must be made between over- and under-investigation of lesions, avoiding delays to diagnosis and treatment on one hand while minimizing harms of unnecessary procedures (5,6,96-98). Screen-detected early lung cancers create diagnostic challenges due to their small size and often peripheral location. In a screening trial,

participants with a suspected early lung cancer on their CT scan who underwent surgical resection, the benign disease resection rate was as high as 34% (99). Pre-operative fine needle aspiration of the lung nodule can significantly reduce the nonmalignant surgical resection rate from 25.9% to 7.9% (100).

Positron emission tomography (PET) is recommended in several international guidelines for assessment of screen detected lung nodules (72,101,102). However, PET/CT has limited role for diagnosis of solid nodules in areas with endemic granulomatous diseases or for the diagnosis of non-solid nodules (103,104). Absent, or minimal increase in FDG uptake should not prevent biopsy or surgical resection of a sufficiently fast-growing nodule (93,103,105,106). The cost-effectiveness of routine PET/CT imaging for investigation of intermediate risk lung nodules versus volumetric growth measurement with repeat LDCT requires further investigation. The on-going Watch the Spot Trial may provide additional evidence to inform recommendations about management of patients with small lung nodules <15 mm (107).

PET/CT remains the mainstay of staging for lung cancer because the detection of unsuspected distant metastases or suspicious nodal disease on PET may profoundly influence selection of treatment. Patients with peripheral stage cIA1 tumors or ground glass opacities may not require a PET/CT for staging as nodal metastasis is known to be low in these lesions (108,109).

Tissue confirmation of malignancy in a small lung lesion can be challenging and requires an experienced operator. Options include bronchoscopic biopsy, CT-guided transthoracic biopsy or surgical resection. The choice of technique varies depending on nodule type and location, need for nodal sampling, patient comorbidities, operability and preference, as well as available local expertise and equipment. The overall diagnostic yield of navigational bronchoscopy with radial ultrasound-guided transbronchial lung biopsy showed an average diagnostic yield of 66% for lesions ≤20 mm and 81% for lesions between 20 to 30 mm compared to 92% and 96% respectively with CT-guided transthoracic biopsy (110). Bronchoscopic biopsies had significantly lower rates of pneumothorax and bleeding (93,110,111). 'Real-world' experience with CT-guided biopsies of small screen-detected lesions can be lower (78%) (112).

Since the major downsides of screening are complications related to radiation exposure, biopsies or surgery for benign disease, best practices need to be evaluated using quality indicators such as percent of LDCT screens which recommended additional imaging studies, positive predictive values of a diagnostic work-up biopsy and resection rate of benign lesions (113).

Additional findings on screening LDCT

Additional findings (incidental findings) are commonly encountered in a screening LDCT. These findings are unrelated to the goal of the study which is for lung cancer screening, Examples of these are moderate or greater coronary artery calcification (CAC), moderate or severe emphysema, interstitial lung disease including pulmonary fibrosis, a mass in the neck, chest or upper abdomen, aortic aneurysms, bronchiectasis or osteoporosis (114-116). Only findings that have clinical implication should be reported as investigations may add considerable cost to screening program and cause harm to the patient (117). When reported, information should be provided to the health care provider regarding the recommended next step.

Smoking cessation

By design, lung cancer screening programs attract participants with smoking rates above the community average. In the 50 to 80 years age group, about 50% of screening participants are still smoking (5,6,18,19,34,118-121) compared to 10% to 15% in the general population. In the Italian COSMOS study, a significantly higher incidence of lung cancer was observed in those who continued to smoke following the first screening LDCT (122). In the NLST, 7 years of abstinence from tobacco smoking alone was associated with 20% reduction in lung cancer mortality (123). Combining smoking abstinence with LDCT screening resulted in 38% reduction in death from Lung cancer (123). A 39% reduction in all-cause mortality was observed in former compared to current smokers undergoing repeated LDCT screening in the MILD trial (124). One-third of the current smokers in NLST were found to be highly dependent on tobacco (125). High tobacco dependency was associated with higher lung cancer rates, all-cause mortality and lung cancer-specific mortality (125). A recent lung cancer risk modeling study that integrates past screening findings and changes in smoking behavior of individuals suggested people who continued to smoke heavily would require annual screening above the age of 61 even with two consecutive negative screens while those who stopped smoking could have biennial screening (126). Since smoking cessation prevents the development of lung

cancer, reduces lung cancer specific and all-cause mortality and is cost-effective (127-129), it is imperative that smoking cessation programs are integrated in lung cancer screening programs (130).

The optimal interventions to facilitate smoking cessation in the screening setting is the subject of ongoing clinical trials (131,132). The average quit rate with counseling is between 11% to 14% (133). The cessation rates are higher with more than one screening round and longer duration in the screening program (134,135). Abnormal findings on a CT scan may increase initial quit attempts especially if the finding is new and suspicious for lung cancer but the behavior for less significant abnormality may not be sustained (133,136,137). A randomized telephone-based smoking cessation counseling intervention incorporating lung cancer screening results did not result in increased 12-month cessation rates versus written information alone in unselected smokers undergoing lung cancer screening (138). In another randomized trial, more intensive telephone counseling comparing eight 20 minutes phone sessions + 8 weeks nicotine patch was compared with minimal three 20 minutes phone sessions + 2 weeks of optional nicotine patch. A higher quit rate was observed with the intensive intervention only in the first 3 months which was probably related to the addition of nicotine replacement therapy (139).

A significant proportion of the current smokers in screening studies such as the NLST were found to be highly dependent on tobacco with 34% reported time to first cigarette of less than 5 minutes (125). The likelihood of cessation decreased with incremental increases in severity of dependence. Studies have shown combining counseling with pharmacotherapy can double the quit rate and that those with high nicotine dependence benefitted most from dual pharmacologic therapy (140-142). In the NLST, only a minority of smoking participants were offered smoking cessation pharmacotherapy (142). In a Veterans Health Administration study, only 1.1% received the recommended combination of pharmacotherapy and counseling; of those receiving pharmacotherapy, only one in four received one of the most effective medications: varenicline (12.1%) or combination nicotine replacement therapy (14.3%) (143). Cost and the need for a prescription may be the issue. Cytisine, an inexpensive partial agonist binding nicotine acetylcholine receptor nicotinic receptor similar to varenicline may be an option—achieving a 32% 12-month quit rate compared to 7% with counselling alone (144). Treatment of tobacco dependency and evaluation of the success of smoking cessation programs should consider the level of nicotine dependency which can be readily assessed by asking a simple question on time to first cigarette upon waking (125). Engagement of primary care providers to provide pharmacotherapy needs to be improved. Lobbying governments to provide free nicotine replacement therapy and other smoking cessation drugs should be a priority.

Individuals who are still smoking but are ineligible for lung cancer screening should be offered smoking cessation. Only a minority of this group was found to participate in smoking cessation programs but almost all were interested in quitting and in receiving help with quit attempts (145).

Conclusions

LDCT screening for lung cancer significantly reduces mortality from lung cancer. To maximize the benefits of LDCT screening, research is needed to identify high risk individuals who are not currently eligible but would benefit from LDCT screening. The role of blood or breath biomarkers should be evaluated for potential application to identify high risk individuals for LDCT screening (146). AI and deep learning methods integrating clinical, demographic and imaging information are promising approaches to personalize the screening interval and duration should be evaluated in randomized controlled studies. Future studies are needed to determine the most effective approaches to deliver smoking cessation services to large numbers of older individuals who have been smoking for several decades and are still smoking. LDCT screening goes beyond detecting and treating lung cancer early; it provides the framework for improving lung cancer care in the general population through prevention, risk assessment, early detection, rapid diagnosis and timely treatment.

Acknowledgments

Funding: None.

Footnote

Provenance and Peer Review: This article was commissioned by the Guest Editors (Donna E. Maziak and Patrick J. Villeneuve) for the series "Comprehensive Lung Cancer Care: A Continuum" published in *Current Challenges in Thoracic Surgery*. The article has undergone external peer review.

Reporting Checklist: The authors have completed the

Narrative Review reporting checklist. Available at https://ccts.amegroups.com/article/view/10.21037/ccts-23-3/rc

Peer Review File: Available at https://ccts.amegroups.com/article/view/10.21037/ccts-23-3/prf

Conflicts of Interest: Both authors have completed the ICMJE uniform disclosure form (available at https://ccts.amegroups.com/article/view/10.21037/ccts-23-3/coif). The series "Comprehensive Lung Cancer Care: A Continuum" was commissioned by the editorial office without any funding or sponsorship. SL received research grants from the Terry Fox Research Institute and the National Institute of Health (USA). He receives consultant fee as an expert advisor for the Canadian Partnership Against Cancer. He is a member of the Medical Advisory Board of Nucelix Inc. (unpaid). He has partial travel support from the International Association for the Study of Lung Cancer to participate in the World Conference on Lung Cancer. The authors have no other conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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doi: 10.21037/ccts-23-3
Cite this article as: Baeza SM, Lam S. Lung cancer screening—contemporary issues: a narrative review. Curr Chall Thorac Surg 2023;5:47.

