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BRN Rev. 2024;10(1):1-15

BRN Reviews

REVIEW ARTICLE

Quality requirements to establish a successful lung cancer screening program

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ABSTRACT

Lung cancer is the leading cause of cancer-related deaths globally. There is a strong body of evidence from the last two decades to support the effectiveness of lung cancer screening (LCS) with low radiation dose computed tomography (LDCT) in reducing lung cancer mortality and all-cause mortality. National programmes are approved and either ongoing or in planning in Poland, Croatia, the UK, Canada, Australia and the US. Other countries are proceeding with pilot programmes, some of which are framed as research studies. The European Commission's Group of Chief Scientific Advisors recommended that lung cancer screening (LCS) be added to the other established cancer screening programs in Europe and the European Council recommended that LCS be implemented in a stepwise approach depending on national priorities. However, it is essential that clinical and cost-effectiveness shown in studies and pilot programmes are replicated in national programmes. This is achieved through the use of evidence-based strategies across each element of screening from participant selection to treatment. This review addresses key quality requirements identified in the literature which must form part of a successful LCS program. We describe the challenges and, where possible, suggest solutions for the implementation of screening. We will highlight the areas for further research including risk-prediction models for screening eligibility, optimising recruitment methods, personalisation of screening intervals, biomarkers, smoking cessation integration, and artificial intelligence.

Keywords: Computed tomography. Lung cancer. Screening.

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Received: 19-12-2024
Accepted: 06-03-2024
DOI: 10.23866/BRNRev:2024-M0102
www.brnreviews.com

INTRODUCTION

Lung cancer is the leading cause of cancer-related deaths worldwide. Several randomized controlled trials have shown that screening for lung cancer with low radiation dose CT (LDCT) reduces disease-specific mortality by detecting lung cancer at earlier stages when prognosis is better and it is more amenable to treatment with curative intent[1,2]. National programmes are approved and either ongoing or in planning in Poland, Croatia, the UK, Canada, Australia and the U, whilst other countries are proceeding with pilot programmes, some of which are framed as research studies[3]. This growing body of evidence led the European Council in November 2022, to adopt a recommendation to implement screening for lung cancer in a stepwise approach[4,5]. It is estimated that 130-320 people need to be screened with LDCT to avoid one lung cancer death, depending on the selected screening interval[6,7]. Furthermore, in contrast to both breast and bowel cancer screening, meta-analyses have shown a 3-5% all-cause mortality reduction[1,2,8].

Careful consideration must now be given to how to optimise design and delivery to ensure the program is clinically and cost-effective. However, many challenges remain across key aspects such as defining screening eligibility, maximising participation and adherence, screening intervals and smoking cessation integration. This review will describe crucial quality requirements which should form part of a successful lung cancer screening program and discuss current challenges to full implementation.

SCREENING ELIGIBILITY

Establishing robust and targeted eligibility criteria reduces the number needed to screen to detect lung cancer. Whilst this improves the efficiency of the programme and likely reduces the level of harm in those who do not develop lung cancer, it limits the population that can benefit and will inevitably miss some cancers. Selection criteria should therefore provide an acceptable balance between these considerations. Several approaches exist to identify high-risk individuals. Earlier studies such as the National Lung Screening Trial (NLST) and Dutch-Belgian randomised lung cancer screening trial (NELSON) used age and cumulative smoking exposure alone in their selection criteria[7,9]. The US preventive services task force (USPSTF) subsequently recommended annual screening in 2013 for those aged 55-80 with a 30 pack-year smoking history and currently smoke or have quit in the past 15 years[10]. In 2020, the eligibility was extended to individuals aged 50-80 years and a smoking history of 20 pack-years to increase the proportion of individuals who may develop lung cancer with lower smoking histories and reduce racial disparities[11]. The latter substantially increases the size of the eligible population and hence the total cost of the programme. However, age and smoking history alone may oversimplify lung cancer risk prediction by not considering important risk factors, such as family history of lung cancer, smoking intensity, personal history of lung disease and exposure to asbestos[12].

Several multi-variable lung cancer risk-prediction models have been developed to improve pre-test probability and efficiency of screening. Although they have not been adopted

widely, the Prostate, Lung, Colorectal and Ovarian ($PLCO_{m2012}$) model[13] and modified Liverpool Lung Project (LLP_{v2}) model[14] have been particularly well evaluated and are recommended in the NHS Targeted Lung Health Check (TLHC) Standard Protocol[15]. However, the models remain heavily dependent on age and smoking history (for Western populations). Detailed smoking history is often lacking in routine electronic health records, even those with comprehensive population coverage such as the UK primary care dataset[16]. Most countries do not have a comprehensive record of the smoking history of individuals and so the whole population within the eligible age range has to be approached. Where records do exist, it may be possible to at least contact people who have ever smoked, thus avoiding contacting many people who are not at high enough risk. In the English programme, all ever-smokers are identified and invited for screening and then eligibility is determined in a second step. It is crucial to identify methods to improve smoking data completeness to maximise efficiency. There is an emerging role for digital health "apps" and social media (e.g. the NHS Health app) where users can input their smoking habits. However, retrospective analyses found the $PLCO_{m2012}$ and LLP_{v2} models had only moderate discrimination and were not well calibrated once externally validated in the English primary care population[17].

Compared to seven other models, the CanPredict (lung) model has recently been shown to have the best performance for discrimination, calibration, and net benefit. It demonstrates higher sensitivity than both LLP_{v2} and $PLCO_{m2012}$ in the UK primary care population[18]. The study proposed that the model could be used as a single-step alternative to the process of determining eligibility, thereby also improving cost-effectiveness. Further research is required to determine if the CanPredict (lung) model will continue to outperform the LLP_{v2} and $PLCO_{m2012}$ when compared in the context within which they were designed to be used i.e., CanPredict (lung) applied directly on the primary care record, compared with LLP_{v2} and $PLCO_{m2012}$ where data are collected directly from participants[19].

Models developed for ever-smokers in the Western population were found to have moderate discrimination in the Korean population, prompting the development of a risk model tailored to the population that showed better discrimination and calibration[20]. It is important that different risk prediction models are validated for target population demographics where risk factors may differ before they are implemented into guidelines and practice[21].

Multi-variable models may also select a population with a greater proportion of individuals with significant comorbidity. Concern about this has led some groups not to recommend risk prediction models. Individuals must have a reasonable chance of benefiting from early detection of lung cancer to maximise the effectiveness of screening. Their fitness must also be reassessed at each screening round to ensure ongoing benefit. Better attention to treatment of comorbid disease and the impact on all-cause mortality is a subject of ongoing research[22,23].

There is further emerging evidence for integration and validation of biomarkers into risk prediction models to improve accuracy,

particularly in populations with lower smoking histories[20,24,25]. Machine learning tools applied to chest x-ray prediction of lung cancer are also in development which would further reduce reliance on accurate and detailed smoking histories[26].

Further models have been developed to better predict risk after the prevalence round. These have not yet been deployed but may significantly improve efficiency and allow stratification by screen interval[27,28].

RECRUITMENT, PARTICIPATION AND ADHERENCE

Maximising recruitment, participation, and adherence of those at highest risk of lung cancer is crucial to ensuring optimal clinical and cost effectiveness. Participation rates in the US, where LDCT screening has been funded since 2015, were estimated to be only 14-19% in 2018, although only 4-7% in the uninsured group, demonstrating challenges in real-world uptake[29,30].

The main approaches to recruitment have largely involved local strategies such as invitation letters, advertising, and community outreach. The pilot UK Lung Cancer Screening (UKLS) trial used a true population-level approach in recruitment (all people aged 50 to 75) and found that only 3.5% were eligible and willing to participate, albeit with a risk threshold of > 5% over five years[31]. Current smokers and socioeconomically deprived groups were less likely to participate, despite them being at highest risk[32,33] a finding that is replicated in many studies and pilots and in other screening programmes[33]. Female sex and older age were also associated with lower participation rates[32,34]. Ensuring equitable uptake is therefore key to maximising benefit and overall effectiveness.

Table 1. Practical and psychological barriers to lung cancer screening[37]

Practical barriers	Psychological barriers
Travel (physical distance, access) Employment Costs of screening (including access to medical insurance) Comorbidity Other commitments	Fatalism Fear Stigma Guilt Low perceived efficacy of treatment Misunderstanding

Numerous psychological and practical barriers to participation and adherence to screening have been identified (Table 1), often more common in the more deprived socioeconomic groups. In the Lung Screen Uptake Trial (LSUT), "targeted, stepped and low burden" materials for recruitment were used to minimise psychological barriers[35] as well as a number of measures known to improve participation in other screening programmes[33]. The participation rate was 52.6%, (compared to 24.9% in NELSON) with uptake particularly improved among those living in areas of highest deprivation. Methods included a primary care approach, pre-invitation letters, reminder letters for non-responders, pre-scheduled appointments and framing to "lung health check". The latter may reduce fear compared to the word "cancer" and encourage participation. Given the improved participation rate, these methods could form a minimum standard. Facilitation of transport or provision of mobile CT scanners in hard-to-reach communities may address distance and access issues to screening[33].

Individuals with a documented history of smoking or diagnosis of chronic obstructive pulmonary disorder (COPD) recorded in primary care records were invited to the Liverpool Lung Health Check[36]. This pilot had an uptake rate of 40% in the first round providing further evidence of the importance of the electronic health record in identifying eligibility.

Further research is needed to evaluate how participation and adherence to subsequent screening rounds can be improved. It is also necessary to test whether these methods translate into different populations across Europe.

MANAGEMENT OF SCREEN-DETECTED FINDINGS

Clinical management of pulmonary nodules and lung cancer are well established across international guidelines[38,39] and will not be addressed in this review.

Over two thirds of individuals screened with LDCT for lung cancer have findings not relevant to the primary aim of screening – so-called "incidental findings"[40]. However, the vast majority of these are coronary artery calcification and/or emphysema, probably better termed "expected" findings given the population selection criteria. A retrospective review of participants in the Cleveland Clinic LCS program observed that incidental findings were present in 94% of participants screened but only 15% warranted further evaluation[41]. Actions relating to these findings risk physical harm from unnecessary investigations and psychological harm such as anxiety[42]. These will in turn place a significant burden on the health care system. Clear guidance and protocols can standardise the approach to incidental findings and reduce the proportion of screening participants that require onward referral, thereby minimising harms and financial impact[43,44]. A European Consensus Statement on management of incidental findings has recently been published that was based on an extensive systematic review of the literature on the commonest findings[45]. Table 2 shows the suggested management of common incidental findings.

WORKFORCE AND TECHNICAL CAPACITY

The US 10-pillar model reflects the elements required to support a successful LCS program. A well-staffed and well-trained workforce as well as sufficient technical capacity are essential to maximising clinical and cost effectiveness. The NHS TLHC Standard Protocol has outlined the specific requirements that services across England are expected to meet to ensure equitable provision and monitoring of LCS[15]. Although workforce and technical capacity vary by country, concerns remain about the ability to deliver a full screening program with many healthcare systems still recovering from the effects of the Covid-19 pandemic.

Before the start of a programme, careful evaluation of current workforce and technical capacity to deliver LCS is crucial. In Europe, there is widespread variation in availability of CT scanners with 9.64 per million population in Hungary compared to 46.39 per million population in Iceland in 2020[46]. Uneven distribution is also seen within countries such as the UK. This has been mitigated through the

Table 2. Management of incidental findings on LDCT screening based on recommendations from the European Consensus Statement

Finding	Reporting recommendation	Suggested action if baseline or new
If clinical information is available (as in some European sites), this should be considered in producing the report and recommendation. However, this table assumes no clinical information is available.		
Pulmonary		
Emphysema	Classify as: – Mild (< 25%) – Moderate (25-50%) – Severe > 50%	Refer those with moderate to severe radiological emphysema for clinical assessment Smoking cessation referral for all current smokers
Interstitial lung abnormalities (ILA)	Report all ILA	Surveillance as part of a screening programme *or* ILA involving more than 5% of either the whole lungs or a lung zone could be referred for specialist review
Bronchiectasis	Report bronchiectasis when moderate or severe (defined as internal bronchial luminal diameter > 2x adjacent artery)	Refer for clinical assessment if moderate or severe
Respiratory bronchiolitis interstitial lung disease (RB-ILD)	Report presence of RB-ILD	Smoking cessation referral
Consolidation	Classify as: – likely inflammatory – possibly malignant	Refer to lung cancer service if cancer is possible. Repeat CT at 6 weeks or 3 months if likely inflammatory
Pleural effusion/ thickening	Report size and laterally	Refer for clinical assessment and work-up if suspicious appearances including a new effusion, malignant appearing pleural thickening or mass
Pleural plaques	Reporting pleural plaques may be appropriate where compensation is offered for their presence* Reporting of pleural plaques may be appropriate is their presence is to be used in lung cancer risk assessment*	Ensure that no clinical activity is generated for benign appearances
Tuberculosis (TB)	Report if active TB likely and differential diagnoses	Referral into local TB service
Bronchial wall thickening	Do not report	No action required
Extrapulmonary		
Coronary calcification (CAC)	Report CAC Classify (using simple visual scoring) as: – None – Mild – Moderate – Severe	Clinician assessment of cardiovascular risk if moderate or severe CAC present Primary preventive measures (if not already taking)
Aortic valve disease	Report aortic valve calcification (AVC) if moderate or severe Classify using simple visual scoring	Refer those with moderate or severe AVC for evaluation with echocardiography
Thoracic aortic calcification/ dilatation	Do not report thoracic aortic calcification Thoracic aorta diameter – < 45 do not report – ≥ 45 report	Referral for further assessment for those with thoracic aorta > 45 mm diameter according to local guidelines/ pathways
Mediastinal mass	Report size, position and density/ texture	Cystic lesions do not require further assessment* Options for management include surveillance as part of the screening programme *or* work-up with PET/CT/MRI, depending on clinical assessment
Mediastinal lymph nodes	Report mediastinal and hilar lymphadenopathy ≥ 15 mm short axis	≥ 15 mm short axis and no explainable cause refer for clinical assessment Surveillance options include short interval CT scan at 3- 6 months
Thyroid abnormalities	Report nodules ≥ 15 mm* or those with suspicious features such as local lymphadenopathy or punctate calcification	Referral for further investigation for nodules ≥ 20 mm or those with suspicious features
Cardiac decompensation/ pericardial effusion	Pericardial fluid – Trivial/ small- do not report – Moderate/ large- report	Referral for echocardiography/ clinical assessment for those with moderate/ large pericardial effusions
Oesophageal lesions	Report significant dilatation, diffuse wall thickening, or focal lesions	Referral for further assessment according to local guidelines/ pathways
Abdominal aortic aneurysm (AAA)	Report all AAA	Referral for further assessment/ surveillance according to local guidelines/ pathways
Breast nodules	Report size, site, calcification and density	Refer any breast lesion that is not previously known, or lesions that are not clearly cystic, and/or not coarsely calcified, for triple assessment according to local guidelines/pathways
Liver lesions	Report size and attenuation	Benign features: sharp margin and homogenous low attenuation (≤ 20 Hounsfield Unit (HU)), (focal) fatty sparing or deposition do not require further investigation* Lesions < 1 cm – No further investigation (unless the patient is high risk- cirrhosis or other hepatic risk factors)* Lesions ≥ 1 cm and no benign features: – Referral for further investigation with CE CT/ ultrasound/ MRI
Renal lesions	Report size, site, attenuation, calcification	Homogenous hypodense or hyperdense cysts < 3 cm do not require further investigation*, larger lesions should be evaluated in the next screening round. Soft tissue or mixed density renal mass > 1 cm - refer for further assessment with CE CT or MRI
Bone abnormalities	Check HU at level of L1 and report if: – 100-130 HU- osteopenia – < 100 HU- osteoporosis An alternative approach is: – Report > 50% loss of vertebral height in at least one vertebra	Referral for risk assessment (+/- DEXA) and bone protection for HU ≤ 130 or > 50% loss of vertebral height
Adrenal lesions	Report size and attenuation	Lesions < 10 mm or < 10 HU in density do not require further investigation* Lesions 10-40 mm or with attenuation > 10 HU can be followed up at the next annual screening round *or* referred for further evaluation with CE CT or MRI Adrenal lesions stable on CT over 12 months may not require further investigation

* Where there is no action required it may not be required to report the finding at all. This is at the discretion of individual programs.
DEXA: dual-energy X-ray absorptiometry; MRI: magnetic resonance imaging; PET: positron emission tomography. Reproduced with permission of the ERS 2024: European Respiratory Journal 62 (4) 2300533; DOI: 10.1183/13993003.00533-2023. Published 19 October 2023..

development a hybrid approach to screening with decentralised units (e.g. mobile CT scanners in trucks) in hard-to-reach communities to improve equity in coverage[33]. In the UK, the Royal College of Radiologists Clinical Radiology Workforce Census 2022 report found radiology capacity insufficient to meet demand, with an estimated shortage of 29% of radiologists, projected to rise over the next 10 years[47]. Inequities also exist in access to radiotherapy equipment, radiation oncologists and medical physicists[48]. US models have predicted that the radiology workforce there can absorb lung cancer screening in most areas of the country, except in areas of most deprivation and low income, ironically those areas with the highest burden of disease[49]. LCS will inevitably give rise to more surgical demand. Blom et al.[50], estimated 37% more lung cancer surgeries in the US in 2015-2040 compared to no screening. Thus, successful implementation will require investment in workforce and equipment, with approaches in place to optimise and/or redistribute available resources. Artificial intelligence (AI) applied to detection and analysis of pulmonary nodules, quantification of findings such as coronary artery calcification, ILA and emphysema, has great potential to improve accuracy and efficiency[51]. Additional research and evaluation are needed urgently to ensure AI performs as expected in terms of accuracy and without generating unmanageable numbers of false positive findings.

CLINICAL GOVERNANCE

Robust and clearly defined clinical governance structures will provide mechanisms to support high-quality, effective and safe screening practices. A national standardised screening protocol should be provided with minimum requirements outlined to optimise accuracy and consistency across different localised programs[52]. This should be accompanied by a quality assurance standard that includes aspects of the structural requirements and monitoring of performance standards. In the UK, this has been addressed by the NHSE TLHC with requirements clearly documented in its Standard Protocol[15] and Quality Assurance Standard[53]. The American College of Radiology (ACR) and the Royal College of Radiologists and the British Society of Thoracic Imaging (BSTI) in the UK have defined thoracic radiology standards[54-56].

Clear leadership and accountability need to be established from the start of the program[57]. Hierarchical structures with defined roles and responsibilities have been favoured in several programs and pilots including the NHSE TLHC. National organizations have been set up to oversee screening programs and ensure equitable coverage and standards. Multidisciplinary collaborative groups allow stakeholders to advise on all aspects of the screening program, guide program development and ensure governance is consistent and effective[58]. Further essential roles and responsibilities involved in clinical governance of a central or local lung cancer screening program have recently been defined by a European Taskforce (Table 3).

Communities targeted by lung cancer screening programs, especially those considered "hard to reach", must be involved early in the program to advocate on behalf of that community and inform program planning and development[59]. Establishing clear governance is therefore key to the implementation of a successful screening program.

Table 3. Key roles and responsibilities in the governance of a lung cancer screening program as outlined by a European Respiratory Society Taskforce[60]

Title of role	Function
National Screening Advisory Body	Evaluates clinical and cost effectiveness. Makes national recommendations.
National Cancer Board/Team	Translates recommendations for screening, national cancer plans into national LCS program.
National LCS Steering Committee or Collaborative Group	Develops protocol. Advises on all aspects of the program including outcome and QA data.
Local LCS Steering Committee	Direct oversight of the local program ensuring adherence to protocol. .
Director/Lead of local program	Takes overall responsibility for local delivery of LCS including adherence to the agreed protocol and QA standards.
Responsible Radiologist	Responsible for adherence of radiology team to defined standards.
Responsible Clinician	Responsible for adherence of the clinical team managing indeterminate, incidental and positive findings from LDCT.
Responsible Assessor	Responsible for ensuring the correct selection and recruitment processes.

LCS: lung cancer screening; LDCT: low-dose CT; QA:quality assurance. Reproduced with permission of the ERS 2024: European Respiratory Journal 61 (6) 2300128; DOI: 10.1183/13993003.00128-2023. Published 15 June 2023.

SMOKING CESSATION INTERVENTIONS

Up to 55% of participants in trials and pilots identify as current smokers compared to 15-20% in the general population aged 55-80 years[7,9,31,61]. Lung cancer screening therefore offers an important opportunity to provide smoking cessation services in a high-risk group. The NLST trial demonstrated that seven years of smoking abstinence was associated with a reduction in lung cancer mortality comparable to LDCT screening[62]. Integration of evidence-based smoking cessation interventions maximises mortality reduction from lung cancer and other tobacco-related diseases such as chronic obstructive pulmonary disorder and ischaemic heart disease compared to screening alone[62]. Even short-term smoking cessation of three weeks prior to lung cancer surgery can reduce postoperative morbidity and mortality[64]. A cohort study demonstrated that postdiagnosis smoking cessation in patients with early-stage lung cancer was associated with reduced lung cancer progression, increased survival time and decreased lung cancer and all-cause mortality during a seven-year follow-up period, compared to those that continued to smoke[65]. Smoking cessation is therefore a key component of lung cancer screening.

Most trials have offered brief advice and referral to smoking cessation services. The NELSON trial observed that participants in the screening arm had higher smoking cessation rates than the background general population rate (14.5% versus 6-7%)[66]. The UKLS trial also demonstrated higher smoking cessation rates in the screened population, especially in participants receiving an abnormal result[67]. There are multiple opportunities throughout the screening process to support participants with smoking cessation, i.e. as "teachable moments"[68]. Offering these at multiple points can lead to an accrued benefit of improving reach, thereby maximising clinical and cost-effectiveness.

Smoking remains a highly stigmatised behavioural risk factor. Alongside screening-associated psychological barriers e.g. fear and fatalism, a real challenge exists to address uptake of smoking cessation advice. Motivation for smoking cessation will vary within the screened population, therefore services presented on an 'opt-out' basis and co-located within the screening program can improve effectiveness. The Yorkshire Enhanced Stop Smoking (YESS) recently co-developed a personalised cessation booklet that incorporated individual LDCT images[69]. This included artistic impressions to improve interpretation and language targeting personal threat and efficacy perceptions. The study, so far published in abstract, showed 12-month confirmed smoking cessation rates of 30% in both the control and intervention arms. These high quit rates are attributed to the opt-out support from a trained smoking cessation practitioner, with the option of pharmacotherapy located on the screening mobile unit[70,71]. The study highlights the importance of a comprehensive and easily accessed smoking cessation intervention. In another study, immediate provision of an intensive telephone-based smoking cessation intervention with follow-up, at the time of participation in lung cancer screening, showed a self-reported quit rate of 21% at three months[72]. The optimal and most cost-effective approach is still being debated but very brief verbal advice is unlikely to be able to achieve equivalent potential benefits in all-cause mortality. Provision of pharmacotherapy has been associated with improved engagement and adherence[73]. Multiple counselling sessions with or without provision of pharmacotherapy may be most effective[74]. A recent simulation study observed that all smoking cessation interventions delivered within the screening process improved lung cancer mortality compared to screening alone with small differences in cost between approaches[75]. The choice of specific smoking cessation interventions should therefore be based on practical issues such as availability, staff training and patient preference. Barriers to successful provision include time pressures, inadequate staff training and reimbursement issues[76].

REQUIREMENTS FOR CT EQUIPMENT, SOFTWARE, IMAGE ACQUISITION AND REPORTING

Advances in technology have led to reductions in effective radiation doses, improving the risk-benefit ratio of lung cancer screening[77]. The NHS THLC Standard Protocol outlines specific requirements for technology, hardware, and software for lung cancer screening in the UK (Table 4) and has been adopted in the ERS Technical Standard for a comprehensive high-quality lung cancer screening program.

SCREENING INTERVALS

Determining the optimal LDCT screening interval will require balancing the benefits of screening, namely lung cancer mortality reduction, with total cost and potential harms. Increasing screen intervals risks an increase in interval cancers whereas reducing the interval increases radiation exposure and increases the total cost[78] NLST used three annual screening rounds and was the main source of evidence for the USPSTF and Centers for Medicare & Medicaid Services (CMS) recommendation for annual screening. USPSTF

Table 4. Standards for imaging acquisition and reporting as set out by the NHS THLC Standard Protocol and ERS Technical Standard[15,60]

CT equipment	16-channel multi-detector CT calibrated according to manufacturer's specifications, capable of delivering low radiation dose protocols
Volumetric software	Preferred method for assessment of pulmonary nodules Remain constant to compare volumes accurately Where upgrades/updates are required by the supplier: – Dates must be recorded – Evidence must be provided that the upgrade provides the same measurements or that the user is prompted to re-measure nodules from previous scans if measurement capability changes – Integrated (directly or indirectly) into picture archiving and communications systems, capable of automated retrieval of, and comparison with previous imaging Computer aided detection (CAD) is to be used as a concurrent or second reader with a false positive rate of < 2 per case
Image acquisition: – Patient position	Participant to lie supine, arms above their head and thorax in the midline of the scanner Maximal inspiration should be rehearsed prior to the scan Imaging to be performed during suspended maximal inspiration No intravenous contrast administered
– Localiser	Programs should use their standard scanogram to localise the start and end positions of the scan Frontal localiser should be performed in the posteroanterior (PA) projection and at the lowest possible setting to minimise breast dose
– Volumetric CT scan	Lung parenchyma (lung apices to bases) must be scanned in its entirety in a single cranio-caudal acquisition Field of view selected as the smallest diameter as measured from widest point of outer rib to outer rib large enough to accommodate the entire lung parenchyma Thin detector collimation (≤ 1.25 mm) to be used
– Exposure factors	Calculated radiation dose < 2 mSv Vary kVp and mAs settings according to participant height and weight Ultra LDCT to be used where available where considered to be of equivalent diagnostic sensitivity to LDCT
– Image reconstruction	Standardisation of image reconstruction for subsequent follow-up examination where possible, with emphasis on ensuring slice thickness, reconstruction increment, and reconstruction algorithm are constant Slice thickness ≤ 1.25 mm Iterative reconstruction should be kept constant at follow up if used
Reading and reporting	Image interpretation should be performed on systems which permit scrolling through the data set with variable thickness and orientation using multi-planar reformations and maximum intensity projection. Volumetric segmentation of nodules should be visually checked by radiologists All scan data acquired should be archived and retained at a local or central site Radiologists should report a minimum of 500 thoracic CTs annually as part of their routine clinical practice, a significant proportion of which should be lung cancer CTs Readers must be familiar with the use and limitations of nodule volumetry software and apply guidelines for nodule management Structured reporting proforma should be used to allow consistency and audit
– Quality assurance	Minimum level of training and expertise of readers should be ensured with continuing professional development Initial CT reads (e.g. first 50) of radiologists inexperienced in the lung cancer screening setting should be reviewed by more experienced readers Periodic review of CT readers reports by expert panels Evaluation of all readers' recall rates, false positive rates and false negative rates, with identification of outliers Evaluation of readers against validated cases

LDCT: low radiation dose computed tomography.

modelling demonstrated that compared to biennial models, annual screening led to improved lung cancer mortality but was associated with a higher cost[79].

The NELSON trial was not able to show that a two-year interval led to a higher proportion of more advanced-stage interval lung cancers compared to a one-year interval, but may have

been underpowered for this. NELSON did demonstrate that the final 2.5-year interval was too long[80]. Significantly more stage 3B/4 lung cancers were detected at the final 2.5-year interval compared to the one-year interval (17.3% versus 6.8%, p = 0.02).

The Multicentric Italian Lung Detection (MILD) study demonstrated that biennial screening following a negative baseline LDCT almost halved the number of follow-up LDCTs required whilst maintaining comparable mortality benefits to annual screening[81].

Personalised risk stratification leveraging CT findings and established risk factors for lung cancer may help determine the most appropriate LDCT interval and further improve screening efficiency and cost-effectiveness. For example, individuals stratified to lower risk of lung cancer could have an extended LDCT interval, thereby reducing total scans, exposure to radiation, radiologist workload and programme costs. The inclusion of CT findings such as emphysema and consolidation to the Lung Cancer Risk Assessment Tool (LCRAT) extended screen intervals in low-risk participants following a negative LDCT[82]. However, this was also associated with increased incidence of delayed lung cancer diagnoses. The NHSE TLHC employs a much simpler method of stratification with all participants with actionable lung nodules having screens at three months and one year whilst those without nodules have a biennial screen. This was based on findings from both NLST and NELSON that cancer detection rates were more than double if nodules were present[83,84].

There is ongoing research and debate on how to optimise the LDCT interval to improve cost-effectiveness, limit total cost and reduce the harm of screening. The 4-In-The-Lung-Run (4ITLR) trial plans to randomise 24,000 participants across several European countries, to evaluate the safety of risk-stratified screening intervals following a negative baseline CT, compared to annual screens. Further research is also needed to define the role of artificial intelligence and biomarkers in refining optimal screening intervals.

COMMUNICATION OF RESULTS

Timely and consistent communication of results to participants is essential to reduce psychological distress associated with LCS[85]. Results must also be communicated promptly and effectively among healthcare staff to enable timely management and follow-up of findings. A recent ERS Technical Standard recommends outcomes are communicated within four weeks of the LDCT[60].

Communication of results may involve a variety of healthcare staff including primary care physicians, lung cancer specialists, or patient navigators who have been used to provide "end-to-end" support for participants throughout the screening pathway[86].

Studies have explored patient preferences regarding methods for communication of results. Serious findings should be communicated face-to-face at clinic visits[15]. A qualitative study in the US highlighted many patients were dissatisfied with the communication of normal or low-risk findings by letter in the LCS setting[87]. Reasons included the lack of opportunity to ask questions, leaving them feeling confused and concerned. Conversations can be time-consuming and not feasible

in the context of national screening programs. The Study to Understand Mortality and Morbidity in COPD (SUMMIT) study in the UK however demonstrated high rates of satisfaction with receiving results by letter in preference to verbal communication via telephone appointment[88]. Further work is required to understand the geographical variation in rates of satisfaction. Provision of an advice line and support resources may mitigate some dissatisfaction where results are not received face-to-face. Communication of normal or low-risk findings should accompany education about smoking cessation and continued risk of lung cancer to encourage participants to adhere to the screening process.

Health literacy is a key consideration and has been found to be an independent predictor of participation in population-based screening programs for breast, cervical and colorectal cancer[89]. Lower health literacy levels are associated with patients from lower income backgrounds who we know are at higher risk of lung cancer[90]. Communication of results must therefore address varying levels of health literacy to enable shared decision making among a diverse population.

DATA MANAGEMENT

An effective data management system (DMS) is central in successful implementation of lung cancer screening. Despite this being well managed in trials, approaches to data management within programs such as the NHS THLC have been variable. Simple spreadsheets for data collection have been used by many sites which limits the ability to review real-time data and monitor program performance. The NHS THLC[53] and US roundtable group[55] have suggested minimum required dataset items which would allow monitoring of key performance indicators. Further integration with imaging platforms and risk stratification tools is ideal. Establishing a single national DMS with standardised protocols for data management would optimise consistency and accuracy. Interoperability with national health data systems is a key consideration whilst maintaining adherence to information governance and General Data Protection Regulation (GDPR) guidelines.

CONCLUSION

Evidence from randomised control trials and pilot programs have confirmed the efficacy of LDCT screening in detecting lung cancer at an early stage. This growing body of evidence has supported pilot implementation across many health systems that are now engaged in the process of wider implementation. If the results of the trials are to be replicated and improved upon, it is crucial that programs proactively adopt evidence-based strategies with clear protocols and quality assurance standards to maximise public health benefit. Reliable population-level data is crucial to identify those at highest risk of lung cancer who are most likely to benefit from screening. Further research is required in areas that can improve clinical and cost-effectiveness of lung cancer screening such as improved eligibility criteria and recruitment methods, which will need to be validated for the target population. Personalised screening intervals will likely play an important role in balancing risks and benefits of screening, thereby improving effectiveness. Finally, as recommended by the

European Commission, countries need to use the evidence base from research, and that accumulating from the programmes already underway, to model the impact on capacity and resources to determine a feasible timeline to achieve a substantial reduction in their mortality from lung cancer.

DISCLOSURES

AB has nothing to disclose.

DRB has received honoraria for speaking from Astra Zeneca, Roche and Bristol-Myers-Squib. He has current research grants from Cancer Research UK, the National Institute for Health Research, Horizon Europe, the Small Business Research Institute, Innovate UK and Yorkshire Cancer. He is advisor to the UK National Screening Committee.

REFERENCES

1. Field JK, Vulkan D, Davies MPA et al. Lung cancer mortality reduction by LDCT screening: UKLS randomised trial results and international meta-analysis. Lancet Reg Health Eur. 2021;10:100179.
2. Sadate A, Occean BV, Beregi JP et al. Systematic review and meta-analysis on the impact of lung cancer screening by low-dose computed tomography. Eur J Cancer. 2020;134:107-14.
3. Global Lung Cancer Coalition's lung cancer screening resource centre. (https://www.lungcancercoalition.org/screening-resource/).
4. Scientific Advice For Policy By European Academies (SAPEA). Improving Cancer Screening in the European Union. 12/11/22 (https://sapea.info/wp-content/uploads/cancer-screening-report.pdf).
5. Council of the European Union. Council Recommendation on strengthening prevention through early detection: A new EU approach on cancer screening replacing Council Recommendation 2003/878/EC. 29/11/2022 (https://data.consilium.europa.eu/doc/document/ST-14770-2022-INIT/en/pdf).
6. Wait S, Alvarez-Rosete A, Osama T et al. Implementing Lung Cancer Screening in Europe: Taking a Systems Approach. JTO Clin Res Rep. 2022;3:100329.
7. National Lung Screening Trial Research Team, Aberle DR, Adams AM et al. Reduced lung-cancer mortality with low-dose computed tomographic screening. N Engl J Med. 2011;365:395-409.
8. Bonney A, Malouf R, Marchal C et al. Impact of low-dose computed tomography (LDCT) screening on lung cancer-related mortality. Cochrane Database Syst Rev. 2022;8:CD013829.
9. de Koning HJ, van der Aalst CM, de Jong PA et al. Reduced Lung-Cancer Mortality with Volume CT Screening in a Randomized Trial. N Engl J Med. 2020;382:503-13.
10. Humphrey LL, Deffebach M, Pappas M et al. Screening for lung cancer with lowdose computed tomography: a systematic review to update the US Preventive services task force recommendation. Ann Intern Med. 2013;159:411-20.
11. Force USPST, Krist AH, Davidson KW et al. Screening for Lung Cancer: US Preventive Services Task Force Recommendation Statement. JAMA. 2021;325:962-70.
12. Tammemagi MC, Church TR, Hocking WG et al. Evaluation of the Lung Cancer Risks at Which to Screen Ever- and Never-Smokers: Screening Rules Applied to the PLCO and NLST Cohorts. PLoS Med. 2014;11:e1001764.
13. Tammemagi MC, Katki HA, Hocking WG et al. Selection criteria for lung-cancer screening. New Engl J Med. 2013;368:728-36.
14. Cassidy A, Myles JP, van Tongeren M et al. The LLP risk model: an individual risk prediction model for lung cancer. Br J Cancer. 2008;98:270-6.
15. National Health Service England, - National, Cancer, Programme. Targeted Screening for Lung Cancer with Low Radiation Dose Computed Tomography. Standard Protocol prepared for the Targeted Lung Health Checks Programme. (https://www.england.nhs.uk/publication/targeted-screening-for-lung-cancer/).
16. O'Dowd EL, Ten Haaf K, Kaur J et al. Selection of eligible participants for screening for lung cancer using primary care data. Thorax. 2022;77:882-90.
17. Robbins HA, Alcala K, Swerdlow AJ et al. Comparative performance of lung cancer risk models to define lung screening eligibility in the United Kingdom. Br J Cancer. 2021;124:2026-34.
18. Liao W, Coupland CAC, Burchardt J et al. Predicting the future risk of lung cancer: development, and internal and external validation of the CanPredict (lung) model in 19.67 million people and evaluation of model performance against seven other risk prediction models. Lancet Respir Med. 2023;11:685-97.
19. Crosbie PAJ, Callister MEJ. Optimising eligibility criteria for lung cancer screening. Lancet Respir Med. 2023;11:665-6.
20. Park B, Kim Y, Lee J, Lee N, Jang SH. Risk-based prediction model for selecting eligible population for lung cancer screening among ever smokers in Korea. Transl Lung Cancer Res. 2021;10:4390-4402.
21. Park S, Nam BH, Yang HR et al. Individualized risk prediction model for lung cancer in Korean men. PLoS One. 2013;8:e54823.
22. Vonder M, van der Aalst CM, Vliegenthart R et al. Coronary Artery Calcium Imaging in the ROBINSCA Trial: Rationale, Design, and Technical Background. Acad Radiol. 2018;25:118-28.
23. van der Aalst CM, Denissen S, Vonder M et al. Screening for cardiovascular disease risk using traditional risk factor assessment or coronary artery calcium scoring: the ROBINSCA trial. Eur Heart J Cardiovasc Imaging. 2020;21:1216-24.
24. Wu FZ, Huang YL, Wu CC et al. Assessment of Selection Criteria for Low-Dose Lung Screening CT Among Asian Ethnic Groups in Taiwan: From Mass Screening to Specific Risk-Based Screening for Non-Smoker Lung Cancer. Clin Lung Cancer. 2016;17:e45-e56.
25. Li N, Tan F, Chen W et al. One-off low-dose CT for lung cancer screening in China: a multicentre, population-based, prospective cohort study. Lancet Respir Med. 2022;10:378-91.
26. Patel BN, Langlotz CP. Beyond the AJR: "Deep Learning Using Chest Radiographs to Identify High-Risk Smokers for Lung Cancer Screening Computed Tomography: Development and Validation of a Prediction Model". AJR Am J Roentgenol. 2021;217:521.
27. Mikhael PG, Wohlwend J, Yala A et al. Sybil: A Validated Deep Learning Model to Predict Future Lung Cancer Risk From a Single Low-Dose Chest Computed Tomography. J Clin Oncol. 2023;41:2191-2200.
28. Robbins HA, Cheung LC, Chaturvedi AK, Baldwin DR, Berg CD, Katki HA. Management of Lung Cancer Screening Results Based on Individual Prediction of Current and Future Lung Cancer Risks. J Thorac Oncol. 2022;17:252-63.
29. Jemal A, Fedewa SA. Lung Cancer Screening With Low-Dose Computed Tomography in the United States-2010 to 2015. JAMA Oncol. 2017;3:1278-81.
30. Zahnd WE, Eberth JM. Lung Cancer Screening Utilization: A Behavioral Risk Factor Surveillance System Analysis. Am J Prev Med. 2019;57:250-5.

31. Field JK, Duffy SW, Baldwin DR et al. UK Lung Cancer RCT Pilot Screening Trial: baseline findings from the screening arm provide evidence for the potential implementation of lung cancer screening. Thorax. 2016;71:161-70.
32. Ali N, Lifford KJ, Carter B et al. Barriers to uptake among high-risk individuals declining participation in lung cancer screening: a mixed methods analysis of the UK Lung Cancer Screening (UKLS) trial. BMJ Open. 2015; 5:e008254.
33. Baldwin DR, Brain K, Quaife S. Participation in lung cancer screening. Transl Lung Cancer Res. 2021;10:1091-8.
34. Ruparel M, Quaife S, Baldwin D, Waller J, Janes S. Defining the information needs of lung cancer screening participants: a qualitative study. BMJ Open Respir Res. 2019;6:e000448.
35. Quaife SL, Ruparel M, Dickson JL et al. Lung Screen Uptake Trial (LSUT): Randomized Controlled Clinical Trial Testing Targeted Invitation Materials. Am J Respir Crit Care Med. 2020;201:965-75.
36. Ghimire B, Maroni R, Vulkan D et al. Evaluation of a health service adopting proactive approach to reduce high risk of lung cancer: The Liverpool Healthy Lung Programme. Lung Cancer. 2019;134:66-71.
37. Quaife SL, Waller J, Dickson JL et al. Psychological Targets for Lung Cancer Screening Uptake: A Prospective Longitudinal Cohort Study. J Thorac Oncol. 2021;16:2016-28.
38. Callister ME, Baldwin DR, Akram AR et al. British Thoracic Society guidelines for the investigation and management of pulmonary nodules. Thorax. 2015;70 Suppl 2:ii1-ii54.
39. American College Radiology. Lung RADS v 1.1. (https://www.acr.org/-/media/ACR/Files/RADS/Lung-RADS/LungRADSAssessmentCategories v1-1.pdf?la=en).
40. Tisi S, Creamer AW, Dickson J et al. Prevalence and clinical characteristics of non-malignant CT detected incidental findings in the SUMMIT lung cancer screening cohort. BMJ Open Respir Res. 2023;10.
41. Morgan L, Choi H, Reid M, Khawaja A, Mazzone PJ. Frequency of Incidental Findings and Subsequent Evaluation in Low-Dose Computed Tomographic Scans for Lung Cancer Screening. Ann Am Thorac Soc. 2017;14:1450-6.
42. Quaife SL, Vrinten C, Ruparel M et al. Smokers' interest in a lung cancer screening programme: a national survey in England. BMC Cancer. 2018;18: 497.
43. Bartlett EC, Belsey J, Derbyshire J et al. Implications of incidental findings from lung screening for primary care: data from a UK pilot. NPJ Prim Care Respir Med. 2021;31:36.
44. Horst C, Patel S, Nair A. Reporting and management of incidental lung findings on computed tomography: beyond lung nodules. Br J Radiol. 2023;96:20220207.
45. O'Dowd EL, Tietzova I, Bartlett E et al. ERS/ESTS/ESTRO/ESR/ESTI/EFOMP statement on management of incidental findings from low dose CT screening for lung cancer. Eur Respir J. 2023.
46. OECD. Computed tomography (CT) scanners. Total / In hospitals / In ambulatory care providers, Per 1 000 000 inhabitants, 2022 or latest available. (https://data.oecd.org/healtheqt/computed-tomography-ct-scanners.htm).
47. Royal C, of, Radiologists, Clinical Radiology Census Reports. Workforce Census 2022. (https://www.rcr.ac.uk/news-policy/policy-reports-initiatives/clinical-radiology-census-reports/).
48. Rodin D, Grover S, Xu MJ et al. Radiotherapeutic Management of Non-Small Cell Lung Cancer in the Minimal Resource Setting. J Thorac Oncol. 2016;11:21-9.
49. Smieliauskas F, MacMahon H, Salgia R, Shih YC. Geographic variation in radiologist capacity and widespread implementation of lung cancer CT screening. J Med Screen. 2014;21:207-15.
50. Blom EF, Ten Haaf K, Arenberg DA, de Koning HJ. Treatment capacity required for full-scale implementation of lung cancer screening in the United States. Cancer. 2019;125:2039-48.
51. Chamberlin J, Kocher MR, Waltz J et al. Automated detection of lung nodules and coronary artery calcium using artificial intelligence on low-dose CT scans for lung cancer screening: accuracy and prognostic value. BMC Med. 2021;19:55.
52. The Health Policy Partnership. Lung cancer screening Building resilience and sustainability of healthcare systems. (www.healthpolicypartnership.com/app/uploads/Lung-cancer-screening-Building-resilience-and-sustainability-of-healthcare-systems.pdf).
53. National Health Service. England. Targeted Screening for Lung Cancer with Low Radiation Dose Computed Tomography. Quality Assurance Standards prepared for the Targeted Lung Health Checks Programme. (https://www.england.nhs.uk/wp-content/uploads/2019/02/B1647-quality-assurance-standards-targeted-lung-health-checks-programme-v2.pdf).
54. Kazerooni EA, Armstrong MR, Amorosa JK et al. ACR CT Accreditation Program and the Lung Cancer Screening Program Designation. J Am Coll Radiol. 2016;13:R30-4.
55. Mazzone PJ, White CS, Kazerooni EA, Smith RA, Thomson CC. Proposed Quality Metrics for Lung Cancer Screening Programs: A National Lung Cancer Roundtable Project. Chest. 2021;160:368-78.
56. British Society of Thoracic Imaging and The Royal College of Radiologists (RCR). Considerations to ensure optimum roll-out of targeted lung cancer screening over the next five years. (https://www.rcr.ac.uk/sites/default/files/final_pdf_considerations_to_ensure_optimum_roll-out_of_targeted_lung_cancer_screening.pdf).
57. World Health Organisation. A short guide to cancer screening: increase effectiveness, maximize benefits and minimize harm. (https://www.who.int/europe/publications/i/item/9789289057561).
58. Association ATSaAL. Implementation Guide for Lung Cancer Screening. (https://www.lungcancerscreeningguide.org/wp-content/uploads/2018/10/implementation-guide-for-lung.pdf).
59. Cancer Council Australia. Plan and deliver a cancer screening project. How do I work with communities? (https://screeningresources.cancervic.org.ausections/how-to-deliver-screening-projects/how-do-i-work-with-communities).
60. Baldwin D, O'Dowd E, Tietzova I et al. Developing a Pan-European Technical Standard for a Comprehensive High-quality Lung Cancer CT Screening Program. An ERS Technical Standard. Eur Respir J. 2023.
61. Lam S, Tammemagi M. Contemporary issues in the implementation of lung cancer screening. Eur Respir J. 2021;30:30.
62. Tanner NT, Kanodra NM, Gebregziabher M et al. The Association between Smoking Abstinence and Mortality in the National Lung Screening Trial. Am J Respir Crit Care Med. 2016;193:534-41.
63. Zhu D, Zhao G, Wang X. Association of Smoking and Smoking Cessation With Overall and Cause-Specific Mortality. Am J Prev Med. 2021;60: 504-12.
64. Heiden BT, Eaton DB, Jr., Chang SH et al. Assessment of Duration of Smoking Cessation Prior to Surgical Treatment of Non-small Cell Lung Cancer. Ann Surg. 2023;277:e933-40.
65. Sheikh M, Mukeriya A, Shangina O, Brennan P, Zaridze D. Postdiagnosis Smoking Cessation and Reduced Risk for Lung Cancer Progression and Mortality: A Prospective Cohort Study. Ann Intern Med. 2021;174:1232-39.
66. van der Aalst CM, van den Bergh KA, Willemsen MC, de Koning HJ, van Klaveren RJ. Lung cancer screening and smoking abstinence: 2 year follow-up data from the Dutch-Belgian randomised controlled lung cancer screening trial. Thorax. 2010;65:600-5.
67. Brain K, Carter B, Lifford KJ et al. Impact of low-dose CT screening on smoking cessation among high-risk participants in the UK Lung Cancer Screening Trial. Thorax. 2017;72:912-8.
68. Slatore CG, Baumann C, Pappas M, Humphrey LL. Smoking behaviors among patients receiving computed tomography for lung cancer screening. Systematic review in support of the U.S. preventive services task force. Ann Am Thorac Soc. 2014;11:619-27.
69. Murray RL, Brain K, Britton J et al. Yorkshire Enhanced Stop Smoking (YESS) study: a protocol for a randomised controlled trial to evaluate the effect of adding a personalised smoking cessation intervention to a lung cancer screening programme. BMJ Open. 2020;10:e037086.
70. Quinn-Scoggins HD, Murray RL, Quaife SL et al. Co-development of an evidence-based personalised smoking cessation intervention for use in a lung cancer screening context. BMC Pulm Med. 2022;22:478.

71. Murray RL, Brain K, Britton J et al. The Yorkshire Enhanced Smoking Cessation Study. World Conference on Lung Cancer. Barcelona 2021.
72. Williams PJ, Philip KEJ, Gill NK et al. Immediate, Remote Smoking Cessation Intervention in Participants Undergoing a Targeted Lung Health Check: Quit Smoking Lung Health Intervention Trial, a Randomized Controlled Trial. Chest. 2023;163:455-63
73. Kocak ND, Akturk UA. What Factors Influence Non-Adherence to the Smoking Cessation Program? Turk Thorac J. 2019;20:168-74
74. Iaccarino JM, Duran C, Slatore CG, Wiener RS, Kathuria H. Combining smoking cessation interventions with LDCT lung cancer screening: A systematic review. Prev Med. 2019;121:24-32.
75. Cadham CJ, Cao P, Jayasekera J et al. Cost-Effectiveness of Smoking Cessation Interventions in the Lung Cancer Screening Setting: A Simulation Study. J Natl Cancer Inst. 2021;113:1065-73.
76. Park ER, Gareen IF, Japuntich S et al. Primary Care Provider-Delivered Smoking Cessation Interventions and Smoking Cessation Among Participants in the National Lung Screening Trial. JAMA Intern Med. 2015;175:1509-16.
77. Murugan VA, Kalra MK, Rehani M, Digumarthy SR. Lung Cancer Screening: Computed Tomography Radiation and Protocols. J Thorac Imaging. 2015;30:283-9.
78. Ten Haaf K, van der Aalst CM, de Koning HJ, Kaaks R, Tammemagi MC. Personalising lung cancer screening: An overview of risk-stratification opportunities and challenges. Int J Cancer. 2021;149:250-63.
79. de Koning HJ, Meza R, Plevritis SK et al. Benefits and harms of computed tomography lung cancer screening strategies: a comparative modeling study for the U.S. Preventive Services Task Force. Ann Intern Med. 2014;160:311-20.
80. Yousaf-Khan U, van der Aalst C, de Jong PA et al. Final screening round of the NELSON lung cancer screening trial: the effect of a 2.5-year screening interval. Thorax. 2017;72:48-56.
81. Pastorino U, Silva M, Sestini S et al. Prolonged lung cancer screening reduced 10-year mortality in the MILD trial: new confirmation of lung cancer screening efficacy. Ann Oncol. 2019;30:1162-9.
82. Robbins HA, Berg CD, Cheung LC, Chaturvedi AK, Katki HA. Identification of Candidates for Longer Lung Cancer Screening Intervals Following a Negative Low-Dose Computed Tomography Result. J Natl Cancer Inst. 2019;111:996-9.
83. Yousaf-Khan U, van der Aalst C, de Jong PA et al. Risk stratification based on screening history: the NELSON lung cancer screening study. Thorax. 2017;72:819-24.
84. Patz EF, Jr., Greco E, Gatsonis C, Pinsky P, Kramer BS, Aberle DR. Lung cancer incidence and mortality in National Lung Screening Trial participants who underwent low-dose CT prevalence screening: a retrospective cohort analysis of a randomised, multicentre, diagnostic screening trial. Lancet Oncol. 2016;17:590-9.
85. Quaife SL, Marlow LAV, McEwen A, Janes SM, Wardle J. Attitudes towards lung cancer screening in socioeconomically deprived and heavy smoking communities: informing screening communication. Health Expect. 2017;20:563-73.
86. Darling GE, Tammemagi MC, Schmidt H et al. Organized Lung Cancer Screening Pilot: Informing a Province-Wide Program in Ontario, Canada. Ann Thor Surg. 2021;111:1805-11.
87. Wiener RS, Clark JA, Koppelman E et al. Patient vs Clinician Perspectives on Communication About Results of Lung Cancer Screening: A Qualitative Study. Chest. 2020;158:1240-9.
88. Dickson JL, Bhamani A, Quaife SL et al. The reporting of pulmonary nodule results by letter in a lung cancer screening setting. Lung Cancer. 2022;168:46-9.
89. Baccolini V, Isonne C, Salerno C et al. The association between adherence to cancer screening programs and health literacy: A systematic review and meta-analysis. Prev Med. 2022;155:106927.
90. Haas K, Brillante C, Sharp L et al. Lung cancer screening: assessment of health literacy and readability of online educational resources. BMC Public Health. 2018;18:1356.