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Early View

Task force report

Developing a Pan-European Technical Standard for a Comprehensive High-quality Lung Cancer CT Screening Program. An ERS Technical Standard

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Developing a Pan-European Technical Standard for a Comprehensive High-quality Lung Cancer CT Screening Program. An ERS Technical Standard

Abstract

Screening for lung cancer with low radiation dose computed tomography (LDCT) has a strong evidence base. The European Council adopted a recommendation in November 2022 that lung cancer screening be implemented using a stepwise approach. The imperative now is to ensure that implementation follows an evidence-based process that delivers clinical and cost effectiveness. This ERS Taskforce was formed to provide a technical standard for a high-quality lung cancer screening program.

Method

A collaborative group was convened to include members of multiple European societies (see below). Topics were identified during a scoping review and a systematic review of the literature was conducted. Full text was provided to members of the group for each topic. The final document was approved by all members and the ERS Scientific Advisory Committee.

Results

Ten topics were identified representing key components of a screening program. The action on findings from the LDCT were not included as they are addressed by separate international guidelines (nodule management and clinical management of lung cancer) and by a linked taskforce (incidental findings). Other than smoking cessation, other interventions that are not part of the core screening process were not included (e.g. pulmonary function measurement). Fifty-three statements were produced and areas for further research identified.

Conclusion

This European collaborative group has produced a technical standard that is a timely contribution to implementation of LCS. It will serve as a standard that can be used, as recommended by the European Council, to ensure a high quality and effective program.

Author Disclosure Statement

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The final document has received endorsements from the European Society of Radiology (ESR), European Society of Thoracic Imaging (ESTI) and the European Society of Thoracic Surgeons (ESTS).

1.0 Introduction and Scope

A recent independent report commissioned by 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[1]. The subsequent European Council adopted recommendation was that LCS "…can be implemented in a stepwise approach to ensure the gradual and appropriate planning, piloting, and roll-out of the screening programmes within national priorities."[2] Furthermore the recommendation stressed the need to follow evidence-based guidelines and standards. Prior to this, two European expert consensus statements recommended preparation for LCS implementation in Europe[3,4] and more recently the European Respiratory Society (ERS) recommended implementation in an updated statement on LCS[5]. However, to replicate and improve on the results of the trials that have provided the evidence on which these recommendations were made, there needs to be careful adherence to optimal practice, and this requires that screening programs are well-organised with clear guidance, protocols and quality assurance. Although individual national consensus statements exist, none amount to a protocol that can be followed from a pan-European perspective. Rather, there is a risk that a heterogeneous lung cancer screening landscape will develop among, and even within, European countries. There is therefore a pressing need to develop a harmonized Technical Standard bringing together existing protocols and the latest evidence.

A number of screening initiatives have protocols supporting them. In the US the International Early Lung Cancer Action Program (I-ELCAP) have produced protocol documents covering nodule workup and surveillance, management of incidental findings and quality assurance which their screening sites should adhere to[6]. A joint policy statement was published in 2015 by the American Thoracic Society (ATS) and American College of Chest Physicians[7] and more recently, Chest lung cancer guidelines[8] and an extensive ATS/American Lung Association ALA) implementation guide including a detailed website[9,10] have added to the complexity of the available resources, in the US. In the United Kingdom (UK), the National Health Service England (NHSE) has made significant progress with a phased implementation of a targeted lung cancer screening program called the "the Targeted Lung Health Check (TLHC)". To ensure a standardized approach, a protocol and quality assurance standard were developed[11,12]. A pan-European Technical Standard offers the potential to improve the consistency of approach to lung cancer screening, but the challenge is to make it sufficiently adaptable to be useful across the spectrum of healthcare systems in Europe.

The clinical management of findings from screening is not part of the scope of this standard. Guidelines exist for the management of pulmonary nodules and for the investigation and treatment of lung cancer so this Technical Standard will not include detail of either of these although both are essential parts of a screening program[4,13-16]. The management of incidental findings by CT is also a substantial topic and is being addressed in a separate ERS Taskforce (ERS MILCa Statement, TF 2019-14), which should be read with this Standard. Health economics was not included in the scope although adhering to high quality standards should maximize cost effectiveness. It is important that each country use existing or new models to determine both cost effectiveness and total financial impact to determine feasibility and speed of implementation, as indicated in the European Council recommendation.

The primary aim of the Taskforce (TF) was to formulate and agree a pan-European Technical Standard for a comprehensive high-quality lung cancer CT screening program. Additional work that the TF will undertake includes setting up a pan-European network of experts along with a network of early career members; establishing which components of a screening program are missing in different countries and which components require a clinical guideline; identifying topics for research; and disseminating the work.

2.0 Methods

The assembly of the Taskforce was coordinated by the ERS following approval by the ERS Guidelines Working Group and ERS Council in January 2021. The work was conducted by members with expertise in pulmonology, radiology, thoracic surgery and radiation oncology and thus covered most of the core specialisms involved in lung cancer screening (LCS). The Taskforce received support from ERS methodologists throughout the project. The Taskforce was further enhanced by involvement of a patient representative (A B-K). Six meetings were held (five virtual and one in person at the ERS Congress 2022). All members of the Taskforce signed conflict of interest disclosures at the beginning of the project and updated them at project finalisation or when any new relevant conflict of interest appeared. Conflicts of interest were managed according to ERS policy.

The first exercise was to identify and agree the essential components required for a high quality LCS program and list these as topics. Following this, a literature search was performed. The evidence reviewed was restricted to that drawn from CT screening trials and programs for all topics unless stated in the relevant section. MEDLINE and Cochrane Library records from 2010 to 2021 were searched. The search terms are shown in the Appendix A. Selected references considered to be of particular relevance were included up to June 2021 (although additional references identified by TF members were included up to July 2022, see below). In addition, TF members were asked to source government and other institutional documents that might be of relevance. All retrieved references were uploaded to Covidence (www.covidence.org). This systematic review software allows for review of abstracts by more than one evaluator. EOD and TGB reviewed all abstracts and excluded those of no relevance to the topic. Include articles were classified according to which component of a LCS program to which they pertained (they could have multiple classifications). Some articles potentially covered all components and were given a general classification for review by all leads for each topic. Discordant abstracts were arbitrated by a third reviewer (DRB). Full text review of the remaining articles was conducted by two or more TF members and relevant reference lists were examined for additional citations and these were included up to July 2022. Only studies written in English, or for which an English translation was available, were included. The article screening results are presented in the flow diagram in Appendix B. A total of 1341 abstracts were reviewed and 660 full text articles reviewed. Lead TF members for each section drafted a summary of the evidence and statements. This work was then reviewed by all TF members and both the evidence summary, statements and research recommendations were finalised.

3.0 Results

3.1 Topics relating to components of a LCS program

Appendix C shows the list of topics identified by TF members. The questions relating to each topic are also shown. The clinical management of the findings from the LDCT, was not included in the scope due to existing clinical guidelines (lung cancer management and pulmonary nodules); incidental findings are addressed in the linked TF.

3.1.1 Summary of Technical Standards

Capacity and infrastructure standards

1. Prior to commencement, and at regular intervals during the expansion and full implementation of a LCS program, there should be a full assessment of the essential components where the capacity and/or infrastructure could jeopardise the safety and effectiveness of the program. These are shown in Table 1.

Governance and roles standards

2. LCS programs should have a clearly defined and documented governance structure.
3. There should be a national oversight committee or a collaborative group to ensure a uniform approach and appropriate equity in coverage and standards; this should involve capacity considerations.
4. There should be regionally and locally based steering committees to oversee and monitor the screening programs which should report to the national committee.
5. There should be defined roles to which individuals are appointed to take overall responsibility for standards of the assessment and recruitment process, radiology reporting and clinical work-up.
6. There should be documented mechanisms to ensure equity of access to the program.

Invitation Methods Standards

7. Identification of the potentially eligible population should be via electronic records containing data on smoking habit where these exist.
8. National programs should consider creating a population record of individual smoking habits as part of health surveys.
9. Where there is no such national record, invitation methods should be deployed in a variety of settings that may include high-risk geographic locations, smoking cessation clinics, community centres, occupational health clinics and via other screening programs.
10. Materials providing accurate information about LCS should be distributed to high-risk individuals via mail and social media and should include written material and educational videos.
11. Information and invitations should be tailored to account for potential inequity in access and uptake in minority groups
12. The first approach to potential participants should be via primary care, where possible.
13. Invitation methods should include: provision of information in a format sensitively designed for the demographic and designed to reduce fear; pre-invitation letters, texts, reminders, and pre-scheduled appointments; and repeat appointments for non-attenders.
14. There should be easy geographical and physical access to screening and appointments with easy rescheduling for participants.
15. Feedback from non-attenders should be sought and used to improve invitation methods.
16. Patient advocacy groups should be part of the engagement with potential participants.

Risk assessment for entry into screening programs standards

17. Multivariable models that have been externally validated in the local population or one very similar are preferred over age and smoking history alone.
18. Multivariable models or single criteria (e.g. presence of pulmonary nodules) may be used to stratify participants into annual or biennial screening intervals.
19. Participants should be reassessed for eligibility by risk threshold; this can be done *in silico* if using multivariable model(s).
20. Participants should be reassessed for fitness at each screening round to ensure they can still benefit from screening.

Smoking cessation standards

21. CT screening programs should include an integrated smoking cessation intervention for participants who are smokers.
22. The smoking cessation service should be comprehensive and include smoking cessation practitioners, availability of pharmacotherapy and regular follow up.
23. Smoking cessation services should be co-located with the screening services, and offered at the same time on an opt-out basis.

Non-attendance and exiting the program standards

24. Methods effective in increasing baseline participation should be employed to reduce non-attendance (see invitation methods).
25. In addition, appointments for ongoing screening should be made as soon as possible after the previous screen and reminders provided nearer the time of the scan..
26. Information for participants should emphasise the importance of ongoing screening for the individual.
27. Programs should have Navigators (nurse, patient, or both) to support the participants in ongoing screening as well as helping with administration such as reminders, identifying travel needs and facilitating rescheduling.
28. Participants should exit the program once they no longer meet the eligibility criteria; they should be given clear information why they should no longer be screened and information about what to do if they have symptoms that could be due to lung cancer.

Imaging acquisition and reporting standards

CT and software

29. The minimum specification is a 16 multi-detector CT calibrated according to the manufacturer's specifications, capable of delivering low radiation dose protocols (see below). There should be regular checks on the equipment according to local protocol.
30. For volumetric software:

    a. It is the preferred method for assessment of solid pulmonary nodules
    b. The same software should be used to compare volumes.
    c. Where there are software updates these should be recorded and the supplier provide evidence that:
        i. the upgrade provides the same measurements or;
        ii. ensure that the user is prompted to re-measure nodules from preceding scans.
    d. It must be directly or indirectly integrated into PACS systems, capable of automated image retrieval of historical imaging.

31. Computer aided detection (CAD) should be used as a concurrent or second reader. A false positive rate of <2 per case is desirable for CAD systems.

CT Image Acquisition Protocol

32. Participants should be comfortably positioned supine, arms above their head and thorax in the midline of the scanner. Maximal inspiration should be rehearsed prior to the scan and imaging should be performed during suspended maximal inspiration. No intravenous contrast material should be administered.
33. Programs should use their standard scanogram to localise the start and end positions of the scan. The frontal localiser should be performed in the PA projection and at the lowest possible setting to minimize breast dose.
34. The lung parenchyma (lung apices to bases) must be scanned in its entirety in a single cranio-caudal acquisition. The 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 (≤1.25mm) will be used.

35. The CTDIvol must be kept as low as possible with the effective radiation dose well below 2 mSv. The kVp and mAs settings are adjusted according to the height and weight of participants. Ultra LDCT should be used where considered to be of equivalent diagnostic sensitivity to LDCT.
36. Image reconstruction should be standardised and used for any follow-up examinations, with particular emphasis on ensuring that slice thickness, reconstruction increment, reconstruction algorithm and field of view are identical. Slice thickness should be ≤ 1.25mm. If iterative reconstruction is used, this should be kept constant at follow up.

Reporting

37. 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 checked visually.
38. All scan data should be archived and retained; a national repository should be considered to facilitate education and research.
39. Readers must report a substantial number of thoracic CTs annually as part of their normal clinical practice (>500), including a significant proportion of lung cancer CTs.
40. Readers must be familiar with the use and limitations of nodule volumetry software and apply agree guidelines for nodule management.
41. A structured reporting proforma must be used to promote consistency and assist audit.

Thoracic CT Reader Quality Assurance (QA)

42. Each program should have documented quality assurance mechanisms in place for CT reading. QA for CT reading may include:

    e. Ensuring a minimum level of training and expertise of readers including continuous professional development in LCS.
    f. Ensuring initial CT reads of radiologists without experience of LCS are reviewed by more experienced readers (e.g. first 50 cases).
    g. Periodic review of CT readers reports by expert panels, including referral recommendations.
    h. Evaluation of all readers' recall rates, false positive rates and false negative rates, with identification of outliers. This includes incidental findings.
    i. Evaluation of readers against validated cases.

43. National or regional consortia of expert radiologists may be the best way to address capacity, education and QA.

Interval and surveillance standards

44. Annual LDCT is the preferred interval if capacity and total economic and health service impact allow.
45. Biennial intervals may be applied for lower risk groups using LDCT findings or multivariable risk prediction models to select participants.
46. Participants should be aware of the reason they have been stratified.
47. Screening intervals should not exceed 2 years.
48. Surveillances scans with a shorter interval that 1 year should follow pulmonary nodule guidelines.

Communication of results technical standard

49. Communication of results for each finding needs to be systematically designed for local populations, with local patient representative input.
50. The outcome should be communicated within a timeframe not exceeding 4 weeks from the LDCT.
51. Communication of negative and indeterminate findings can be via mail with an offer of support via telephone or videocall. Communications should include a reminder of the symptoms of lung cancer and the importance of smoking cessation.
52. Communication of positive findings should be face to face, usually within an urgent clinic.
53. Feedback from participants should be collected via a formal process and the results used to improve the participant experience.

Data Management Technical Standards

54. An end-to-end, validated data management system is the optimum system for an organised lung cancer screening program.

55. Data Management Systems (DMS) must be supported by an agreed national minimum dataset that allows regular centralised audit and reporting of key outcome metrics (table 3).

56. DMS have to adhere to information governance (INGV) and General Data Protection Regulation (GDPR) regulations.

3.2 Detailed review and results of technical standards

3.2.1 Capacity and infrastructure requirements

Evidence review

The evidence review for this section was limited to papers which covered capacity and infrastructure requirements. Of 138 full texts reviewed, 30 papers were included, alongside 2 websites[10,17]. These ranged from single site pilot/ trial data to national protocol/consensus statements.

A United States (US) 10-pillar model has also been produced which summarises the elements which are felt to be required to support a successful screening program.[18] The American Thoracic Society / American Lung Association implementation guide (ATS/ALA IG) provides detailed guidance on various aspects of capacity and infrastructure and also gives examples from many sites in the US[9,10]. The National Health Service England Targeted Lung Health Check (NHSE TLHC) Standard Protocol has set out requirements for the capacity and infrastructure needed to run lung cancer screening[12] and there is a Spanish expert consensus statement on how to implement and evaluate screening in Spain.[19] Smaller trials and single site pilot projects have also summarised their individual requirements.[20-23] There were key capacity and infrastructure requirements identified as essential to be able to deliver a CT screening program which are summarised in table 1. The ATS/ALA guide notes that programs may be “centralised” where all of the screening process is coordinated from a centre, “decentralised”, where the program provides the LDCT but with all other elements left with the referred and hybrid programs.

Another aspect which was considered in the literature was how to assess the readiness of a centre to implement LDCT screening. One US study proposed that tools could be employed to assess implementation readiness, with the Diabetes Care Coordination Readiness Assessment given as an example.[24,25] The tool considers five domains: organisational capacity, care coordination, clinical management, quality improvement, and infrastructure. A wide range of other readiness assessment

tools exist which the authors suggest could be adapted for use to assess readiness to start LDCT screening, with suggested metrics for implementation readiness being competing priorities, concurrent activities, ongoing or upcoming systems challenges, and system readiness.[26]

Some small studies have looked at current capacity constraints and what impact LDCT screening may have on this[27,28]. A study by Rodin et al (2016) highlighted inequities in access to radiotherapy machines, radiation oncologists and medical physicists across Europe.[29] Access to CT scanners also varies widely between countries. Data on the number of CT scanners by country and per million population has been produced by the Organisation for Economic Co-operation and Development (OECD) and shows wide geographical variation in availability.[17] A microsimulation model using data from the National Cancer Database has been published to look at the potential increase in treatment demand that screening may pose.[30] This work suggests that full-scale implementation of lung cancer screening would cause a major increase in surgical demand, with a peak within the first 5 years. The authors advise that careful surgical capacity planning is essential for successfully implementing screening. Each country or region will have specific areas which may require focus and investment, considering current infrastructure, the healthcare system and competing priorities. This will also be influenced by screening uptake rates and the proportion of the population who are eligible.

Summary

Although specific capacity requirements and infrastructural considerations will differ between countries there are common key requirements that are felt to be essential for the delivery of LDCT screening which are summarised above.

Capacity and infrastructure standards

1. Prior to commencement, and at regular intervals during the expansion and full implementation of a LCS program, there should be a full assessment of the essential components where the capacity and/or infrastructure could jeopardise the safety and effectiveness of the program. These are shown in Table 1.

3.2.2 Clinical governance, roles and responsibilities

Clinical governance has a central position in the overall organisation and running of a screening program and is a feature of successful screening programs[31,32]. The detail of how clinical governance is organised is likely to be influenced by the way the health services as a whole are organised and funded, the level of funding per capita and the infrastructural and clinical standards of healthcare, especially for lung cancer[33,34]. Nevertheless, adhering to established principles is important in all healthcare systems as it will underpin higher quality despite the constraints that may apply. As LCS develops, governance structures will be required and are best defined and implemented before the start.

Evidence review

A total of 87 full texts were reviewed. Two systematic reviews on LCS commissioned by two German national agencies[35,36], a pilot protocol for the National Cancer Screening Program in South Korea[37], several statement papers by societies and expert groups on the international and national level[3-5,7,38,39] as well as narrative reviews covering aspects of the lung cancer screening pathway[18,19,21,40-58] were reviewed. Whilst these described some elements that could be included in a governance structure, none dealt specifically with topic. Other studies provided experiences and outcome data in lung cancer screening pilots as well as implementation initiatives within national programs [20,25,59-63].

The review of society and national management standards was more informative. The ACR has produced accreditation standards for thoracic radiology since 1987 and have described an accreditation process for the radiology for LCS, essentially supporting quality assurance[64]. Similarly, the Royal College of Radiologists (RCR) and British Society of Thoracic Imaging (BSTI) has recommendations on radiology standards[65]. The ATS/ALA IG provides collated information on locally adopted solutions in the US as examples of how to set up clinical governance and who to involve within LDCT LCS screening programs[9,10]. The NHSE TLHC Standard Protocol has set out requirements for governance, including descriptions of roles and responsibilities in the running and oversight of the local programme[11,12]. National lung cancer screening standards were also identified from Germany[66], and Poland[67,68]. We utilized these publications and documents as available evidence basis to provide a suggested structure and description of the major roles that can be adapted for use in individual national healthcare settings.

The design of the clinical governance structure within a national LCS program depends on whether the program is centralized, decentralized, or a hybrid. A centralized program takes full responsibility for enrolling participants, managing them along the entire pathway including follow-up schedules, whereas a decentralized LCS program is limited to LDCT scanning, reading and reporting to referring providers who are then in charge of organising all subsequent pathway steps.

Figure 1 shows the core roles and their responsibilities that were found in the evidence review, represented is a hierarchical structure. This can be adapted according to the design of the program (central or local). Appendix D shows the roles functions found in the literature review.

Summary

Most, if not all, screening programs and pilots have some form of governance structure although this is often not well-described. Those that document governance arrangements favour a hierarchical structure and create specific roles within that with defined responsibilities. Effective governance will serve to improve the efficiency, efficacy, monitoring and safety of LCS whether at the decentralised level or when overseen by a national structure.

Governance and roles standards

2. LCS programs should have a clearly defined and documented governance structure.
3. There should be a national oversight committee or a collaborative group to ensure a unform approach and appropriate equity in coverage and standards; this should involve capacity considerations.
4. There should be regionally and locally based steering committees to oversee and monitor the screening programs which should report to the national committee.
5. There should be defined roles to which individuals are appointed to take overall responsibility for standards of the assessment and recruitment process, radiology reporting and clinical work-up.
6. There should be documented mechanisms to ensure equity of access to the program.

3.2.3 Participant pathway

The participant pathway is important to define for each program as it will be a clear summary of the process and may be important in ensuring cost effectiveness. There are numerous such pathways in implementation guides but little in the way of evidence to inform an evidence-based pathway (other than that reviewed in this paper for individual steps e.g. invitation method). A sample pathway that was developed for the UK National Screening Committee health economics evaluation that led to the recent recommendation for a UK targeted lung cancer screening program[69] is shown in appendix E.

3.2.4 Invitation methods

Despite the established efficacy of LDCT LCS, participation in programs has been mostly low although variation is seen within and between countries. In the US, where LDCT screening has been funded since 2015, participation rates were 3.3% of the eligible population in 2015 and more recently estimated to be 14-19% in 2018 although only 4-7% in the uninsured[70-73].

Barriers to participation include emotional and practical barriers that reduce engagement and uptake and limit the effectiveness of interventions. Practical barriers include travel, employment and other commitments, costs of screening (especially where there is limited medical insurance)[74] and comorbidity.[75] Among the emotional issues, we include fatalism about risk and survival, low perceived efficacy of treatment, fear of diagnosis, stigma, guilt and misunderstanding[75-80]. There are also practical barriers from the provider perspective such as difficulties in identifying the eligible individuals due to the lack of reliable data on smoking history in the population registries and Electronic Medical Records[77]. Most studies show that older people, females, current smokers and those with a lower socioeconomic status (SES) groups are less likely to participate[75,81-83]. Physical distance and access are also known to be a practical barrier[84], leading to the provision of mobile CT in some programs[12,85-89] with one study showing a preference for this amongst participants[90] and another showing no difference in attendance rates[91].

Evidence review

Of 124 full papers reviewed, 58 were included as providing some details of invitation methods into pilots and programs. Invitation methods described fell broadly into two: a systematic approach where there is an attempt to offer the whole eligible population screening and an unsystematic approach where the strategies did not attempt to provide uniform access.

Systematic approaches

The UKLS[92] and NELSON studies employed a population approach where all people of eligible age were sent an initial letter (NELSON recruited mainly men[93].) This was clearly shown to have very low uptake from the total people contacted (1.6% UKLS and 2.6% NELSON). Similarly, a study in Milan tested the feasibility of recruiting participants via telephone contact. The call recipient was asked if there were any family members who were over the age of 50 and had a greater than 30 pack year smoking history. Those meeting these criteria were contacted and asked to participate in the program. Only 1.9% of a total of 2300 persons were eligible for screening and only 27% of these (0.5% overall) agreed to participate[94]. This contrasts with the targeted systematic approach used in several UK studies[85,86,91,95,96] and the TLHC[12,97] where participation rates are generally over 30% and in some of the TLHC centres, over 60% (unpublished data). These studies and pilot programs all used the NHS primary care record to identify ever smokers in the eligible age range and then either telephone or clinic assessment of eligibility. The invitation method was modelled on both research from other cancer screening programs and from lung cancer screening. The Lung Screen Uptake Trial (LSUT) was primarily designed to test the impact on informed screening uptake of low-burden tailored information in a population with high levels of social deprivation[98]. Although the intervention had little impact, the participation was 52-3%. This may have been because of the efficacy of the invitation method which combined an approach from primary care, the use of pre-invitation letters (information about the program before invitation), reminder letters for non-responders, pre-scheduled appointments and a framing of the invite akin to a 'Lung Health Check' in an opt-put fashion. The reminder letter with a second appointment explained 10% uptake. The NHSE TLHC Protocol recommends ensuring easy access to the LDCT, including obtaining appointments and changing these where desired. It recommends a formal process for contacting non-attenders and feedback from non-attenders to evaluate their reasons[12]. There is little evidence about how to encourage repeated non-attenders to participate.

Unsystematic approaches

Unsystematic invitation methods are the most used of all methods in trials and are also used in some programs. They are necessary because of the absence of a central database of people that contains details of lung cancer risk factors, primarily smoking[99]. In a study from Canada, a primary care administered questionnaire was developed to collect these data, but the uptake was low, and a recommendation made for this to be incorporated into appointments[100]. Recommendations to establish a better primary care record have been made in parts of the US[101,102]. Invitation methods employ advertisements[103], media campaigns, social media[104], telephone contacts[105] and other methods[106,107]. Information about potentially eligible people has been obtained from questionnaires in different settings. For example, one study administered questionnaires to new consults in a department of Radiation Oncology and Otolaryngology and found that of 546 new consults, 528 people completed questionnaires and 104 (20%) met criteria for LCS[108]. A further study incorporated information about CT screening into an information video on smoking cessation and showed that this increased the usage of both CT and LDCT amongst those shown the video[109].

Equality

Disparities have been described in several minority groups including racial[110-114] and sexual orientation[115,116] A study used what is said to be the first mobile CT to screen uninsured people in the US , aged 55-64 years from underprivileged backgrounds. This study found a baseline cancer detection rate of 2.2% (12 of 550) This was despite excluding people over 64 with Medicare cover[117].

Summary

Invitation methods for LCS need to take into account the barriers that prevail in the eligible population. The invitation methods associated with the highest participation rates identify and approach the potentially eligible population via primary care electronic records. They use primary care as the first approach, provide information in a format which has been designed for the demographic and designed to reduce fear (e.g. the “Lung Health Check”). They employ pre-invitation letters, texts, reminders, pre-scheduled appointments and repeat appointments for non-attenders. New programs should have high visibility and person-facing materials need to present balanced information on benefits and harms, tailored to the demographic. The lack of a population-based electronic record containing details of smoking habit means that other approaches need to be taken which are less effective but can include a variety of methods to engage with potential participants. Patient advocacy groups may play an important part in supporting informed decisions about participation.

Invitation Methods Standards

7. Identification of the potentially eligible population should be via electronic records containing data on smoking habit where these exist.
8. National programs should consider creating a population record of individual smoking habits as part of health surveys.
9. Where there is no such national record, invitation methods should be deployed in a variety of settings that may include high-risk geographic locations, smoking cessation clinics, community centres, occupational health clinics and via other screening programs.
10. Materials providing accurate information about LCS should be distributed to high-risk individuals via mail and social media and should include written material and educational videos.
11. Information and invitations should be tailored to account for potential inequity in access and uptake in minority groups

12. The first approach to potential participants should be via primary care, where possible.
13. Invitation methods should include: provision of information in a format sensitively designed for the demographic and designed to reduce fear; pre-invitation letters, texts, reminders, and pre-scheduled appointments; and repeat appointments for non-attenders.
14. There should be easy geographical and physical access to screening and appointments with easy rescheduling for participants.
15. Feedback from non-attenders should be sought and used to improve invitation methods.
16. Patient advocacy groups should be part of the engagement with potential participants.

3.2.5 Risk assessment for entry into screening programs

Screening for lung cancer differs from other established cancer screening programs in that it is targeted to a population at higher risk of developing lung cancer because the benefit is greater[118]. In addition, it may also be a stratified program where an element of the program (for LCS, this is the screen interval) is varied according to level of risk. Definitions of targeted and stratified screening have been published by the UK National screening Committee[119]. In most randomised controlled trials of LCS, eligibility has been determined by age and tobacco smoking criteria[120,121]. A number of multivariable risk prediction models have been developed that are more sensitive and specific, but are still heavily dependent on smoking and age[122,123]. Some have been used successfully in trials and pilot programmes and have yielded higher detection rates, although they may also select people with more comorbidities[8,92,124,125].

Evidence review

Of 137 full text reviews, 58 contained information about entry criteria according to risk. Both NELSON and NLST used age and smoking criteria[93,120] and some later trials used multivariable models[85,96,125-128].

Age and smoking criteria

NLST entry criteria were a minimum of 30 pack years and a quit time within 15 years of entry in people aged 55 to 74[120]. These were later modified to a recommendation to screen people in the wider age range of 55 to 80. Most recently the US Preventive Services Task Force (USPSTF) have widened the criteria considerably to include people 50 to 80 years who have smoked at least 20 pack years and quit within 15 years[129]. However, it has been shown that multivariable models provide a more efficient method to select participants, although they may select some individuals who have greater comorbidity.[130-133]

Multivariable models

In a recent systematic review, 27 studies were identified describing 30 different models that predicted either lung cancer incidence or mortality[134]. Fourteen of 27 studies described external validation. Studies have shown that criteria used in studies based on age and smoking select fewer people who develop lung cancer and a fitter population, mainly by virtue of including younger people[127,135-137]. Models vary in their complexity and most earlier comparative studies show similar performance with the $PLCO_{m2012}$ often achieving the highest discrimination [122,123,138]. However, these comparative studies did not test the latest models[139,140] and performance of any model may be influenced by the population to which they are applied and the quality of the input data[141]. Another suggested approach is to apply a simple "pre-screening" approach where basic criteria are applied to electronic data records to "enrich" the population before more complex models are employed[141,142]. Although most models predict risk, an alternative approach is to predict benefit in terms of life years gained[143].

Risk prediction in selected populations

People with a previous history of cancer have been shown to be at increased risk of lung cancer and led some to suggest these should be included in LCS for example survivors of lymphoma,[144] breast, head and neck and lung cancer[145].

Age and smoking criteria have been shown to be less effective in some East Asian populations because of their reliance on smoking history[146]. Here bespoke multivariable models have been developed, for example in Taiwan where screening is offered to never smokers[146-148]. Newer models have been proposed using blood biomarkers and / or genetic information in both Western and Eastern populations[149-155].

Occupational exposures are included in the National Comprehensive Cancer Network (NCCN) selection criteria. One study showed that when NCCN guidelines were applied in a group of workers exposed to carcinogens the cancer detection rate was 1.6% despite only 45% meeting NLST criteria[156]. Similarly, working for 5 or more years in US construction was found to be equivalent to having a positive family history, a previous history of cancer or a diagnosis of COPD[157]. Several screening programs for workers exposed to asbestos have been described[158-162]. Mortality from lung cancer and all-cause mortality was reduced by 59% and 39% respectively in one retrospective study that compared participants in a screening program with a non-participant control group.[158] Whilst a systematic review of 7 cohort studies concluded that asbestos exposed workers had a similar lung cancer incidence to heavy smokers[161], another study suggested that asbestos exposure alone was not sufficient to make workers eligible for screening and instead other risk factors were required[160]. The LLP models include asbestos exposure as a variable[163,164].

There is little evidence to support simple age and smoking criteria as the preferred method to assess eligibility other than as a way to identify a population that is potentially eligible. Furthermore, risk thresholds can be more precisely defined. Never smokers are unlikely to be eligible for screening unless/until biomarkers become available that can be applied[165]. Combining clinical data with genetic variants has been shown to improve risk prediction in smokers[149] but how this can be cost effective in screening programs is not clear. Novel approaches include using artificial intelligence applied to chest X-rays in prediction of lung cancer[166] .

Stratification

Analyses of both NELSON and NLST showed that the presence of nodules on baseline or subsequent screens increases the risk of lung cancer[167,168] and a lower risk in NLST participants with a negative baseline screen prompted the suggestion of a longer screening interval in this population[169]. More recently, multivariable models have been developed to better define subsequent risk and may offer a risk stratified approach to screening[139,170-173].

Fitness assessment

Participants should have a reasonable chance of benefiting from early detection of lung cancer. This essentially means that there is a high chance of cure.

It is noted that even early detection of lung cancer that is at a later stage can benefit lung cancer patients because their fitness is better, and they may therefore benefit more from systemic anticancer therapy. However, this is not considered further here. A check should be made for any of the exclusion criteria for fitness enough to prevent curative intent treatment. Using this approach, most screening trial and pilots show high treatment rates[85,92,120,121].

Reassessment Method

Reassessment may apply to people who exit the program if risk falls below the baseline criteria, e.g. having quit smoking for more than 15 years or developed a new health problem in USPSTF criteria[129]. Where multivariable models have been used, there can be a repeat risk assessment that could be first completed *in silico* using existing data but with the age changed and assuming there has been no change in smoking status and other model parameters. This can be followed up using confirmed data. The interval between risk assessments may need to vary depending on proximity to risk threshold.

Summary

Selecting a population at high risk of lung cancer is a key factor in ensuring efficiency. Multivariable models are evolving and show superior cancer detection rates compared with simple age and smoking criteria. They can also facilitate variable thresholds according to cost effectiveness and willingness to pay threshold. Newer models and those incorporating biomarkers, genetic factors, AI and applied in specific populations may further improve accuracy.

Risk assessment for entry into screening programs standards

17. Multivariable models that have been externally validated in the local population or one very similar are preferred over age and smoking history alone.
18. Multivariable models or single criteria (e.g. presence of pulmonary nodules) may be used to stratify participants into annual or biennial screening intervals.
19. Participants should be reassessed for eligibility by risk threshold; this can be done *in silico* if using multivariable model(s).
20. Participants should be reassessed for fitness at each screening round to ensure they can still benefit from screening.

Research recommendations

- Multivariable models should be validated in the population in which they will be used.
- Evaluation of novel approaches using additional risk factors and in specific populations should ensure that the impact on prognosis and hence efficacy of screening is included.
- Research into the best multivariable model for individual programs should investigate accuracy, ease of application and potential to increase inequities.
- Evaluation of the best way, and at what interval, risk should be recalculated in individuals previously found to be below the risk threshold

3.2.6 Smoking Cessation

In most populations, LCS is offered to people who have ever smoked tobacco. In most screening trials and pilots, a substantial proportion of those screened were current smokers, typically 35 to 55%[85,92,120,121]. Smoking cessation is a well-established cost-effective intervention that reduces mortality from many conditions including Chronic Obstructive Pulmonary Disease (COPD) and Ischaemic Heart Disease and has been shown to double the impact of LCS on mortality reduction from lung cancer in the NLST[174-176].

Evidence review

Seventy-six full papers were reviewed and 26 contained some details of smoking cessation used in the development of the statements. The majority of LCS trials provided brief advice and referral for smoking cessation. Trials that measured smoking cessation all concluded that the smoking cessation rates were above that observed in the general population[177-181]. The optimal strategy for integrating smoking cessation has been the focus of much research[15,174,179,182-194]. There are limited data around

provision of other services, such as psychological support, within the screening program. There is no consistent evidence of a 'licence to smoke' effect, whereby a normal scan discourages quitting. Indeed, there is some research to suggest that lung cancer screening represents a 'teachable moment' where participants maybe particularly receptive to smoking cessation interventions[189,195-197]. Research published in abstract form from the UK has shown that quit rates of over 30% at one year can be achieved using opt-out, co-located, comprehensive cessation services with follow-up[183]. Of all current smokers attending for screening, 86% took up the initial consultation, with 85% of these agreeing to a 4-week period of smoking cessation support[198]. Another randomised trial showed that immediate telephone-based smoking cessation, including pharmacotherapy, resulted in a 21% self-reported quit rate at 3 months compared with 9% in controls[199].

Smoking cessation is known to be cost effective so in assessing cost effectiveness of screening programs the quit rate needs to be included. From the literature, quit rates vary so a variety of quit rates should be modelled to allow an assessment of how achieving these might influence the overall cost-effectiveness of the screening programme.

In the context of the light-touch intervention in the UK Lung Screen (UKLS) trial, the smoking cessation rate in the intention to treat population at 2 years was 15%[177]. This should be regarded as the worst-case scenario (15% 2-year quit rate) and increments above this should be modelled up to 30%.

Summary

Evidence shows that LCS is an opportunity to markedly increase smoking cessation rates. The most effective method is to use comprehensive smoking cessation services that are located at the site, and provided at the time, of the LDCT.

Smoking cessation standards

21. CT screening programs should include an integrated smoking cessation intervention for participants who are smokers.
22. The smoking cessation service should be comprehensive and include smoking cessation practitioners, availability of pharmacotherapy and regular follow up.
23. Smoking cessation services should be co-located with the screening services, and offered at the same time on an opt-out basis.

Research recommendation

- Research should directly compare co-located services with those at a separate site.
- Research into the optimal strategy to deliver smoking cessation in individual programs should be determined.

3.2.7 Non-attendance and Exiting the Program

Non-attendance may be an issue at the start of the screening process where participants elect not to take up an appointment where this is offered. The factors that influence this, and their mitigations, are reviewed in the section on invitation methods. Attendance at subsequent screening rounds, essential if the full potential of the process is to be realised for participants, is usually termed "adherence". It is variously defined in studies as attendance within a timeframe, for example a study from Colorado, adherence was defined as attendance for the annual screen within 18 months of the baseline scan[200]. In other studies, adherence included attendance for additional imaging and work up.

Evidence review

Of 82 full-text reviews completed a total of 16 had useful information about this topic, including 3 systematic reviews[81,201,202] and 4 additional papers identified from reference lists. As the evidence review found that some studies measured adherence to the next screen, whilst other included adherence to any recommendation, both are included particularly because the findings were very similar.

Participant and program features important in non-attendance

The features of individuals that are less likely to attend are similar to those that characterise people that choose not to participate in screening at baseline[81]. These are people in underprivileged groups,[203-205] current smokers[201], the non-white population in the US[112,202], participants with a lower risk perception[201,204,205] and negative baseline CT[201,206]. Unlike baseline participation, there was no clear relationship with sex and people aged under 60 were least adherent whilst those 60-75 most adherent[201]. Program-related factors associated with adherence are shown in Table 2.

In the meta-analysis by Lam et al, the overall second round non-attendance rate from 12 studies was 28% (95% CI: 20-37%), with a wide range of 5 to 63%. Much of the evidence for both non-attendance and methods employed to improve adherence come for the US, which has the longest western implementation period for a national program. Navigators have been identified as an important way to improve adherence[205,207,208]. It is established that either nurse navigators or lay patient navigators improve baseline participation. In one primary network based randomised controlled trial in the US, patient navigators assessed eligibility, undertook shared decision making and addressed concerns and barriers[209]. Participation amongst eligible people was 94% and of all people approached, 31% in the navigator arm and 17% in the control arm had a CT. A study in Colorado, US showed that a nurse navigator administered reminder achieved reattendance in 63% of partcipants[200]. Both the NHSE TLHC Protocol and the ATS/ALA Implementation Guide recommend the same methods that are applied at the baseline invitation to be applied for ongoing screens[10,12]. In addition, some examples given in the ATS/ALA guide are to schedule a repeat appointment as soon as possible and to provide reminders 30, 60 and 90 days after the screening due date to participants and their physicians. The evidence for the efficacy of this is mainly found in other cancer screening programs[82].

Exiting the program

Most programs have defined eligibility criteria and hence participants are assumed to exit the program when they no longer meet these due to exceeding the age threshold or other exclusion criteria developing such as another life-limiting condition. The NHSE TLHC Protocol states that participants should exit the program when they reach the upper age limit, but should also be assessed for comorbidity and fitness to confirm eligibility and should exit if they are no longer eligible[12]. There is also a recommendation to hand over any ongoing follow up need, specifically nodules under follow up or new nodules on the final screening CT. The ATS/ALA Implementation Guide notes that the ALA do not force people to exit the program if they reach the 15 year smoking quit duration[10].

Summary

Non-attendance is a substantial issue in LCS with high rates seen in trials, pilots, and programs. Similar factors are associated with reduced adherence and baseline participation, so the same methods used to maximise participation seem appropriate, adapted to ongoing screening and follow-up of findings. Exiting the program has little evidence but it is defined in at least one program protocol; participants should understand why they are exiting.

Non-attendance and exiting the program standards

24. Methods effective in increasing baseline participation should be employed to reduce non-attendance (see invitation methods).
25. In addition, appointments for ongoing screening should be made as soon as possible after the previous screen and reminders provided nearer the time of the scan.
26. Information for participants should emphasise the importance of ongoing screening for the individual.
27. Programs should have Navigators (nurse, patient, or both) to support the participants in ongoing screening as well as helping with administration such as reminders, identifying travel needs and facilitating rescheduling.
28. Participants should exit the program once they no longer meet the eligibility criteria; they should be given clear information why they should no longer be screened and information about what to do if they have symptoms that could be due to lung cancer.

Research recommendation

- Future research into the ongoing psychological outcomes of screening and how this might influence adherence is needed[210,211].

3.2.8 LDCT Acquisition, Reading and Reporting

Evidence review

The evidence was taken from trials and protocols for pilot programs as well as the NHSE Protocol and QAS[11], the ACR-STR(Society of Thoracic Radiology) technical statement[212] and the ESTI Standard[213]. A total of 54 full text references were reviewed.

Acquisition

Minimizing radiation dose is important to maximize the benefit-risk ratio (cancer deaths prevented/cancers caused by radiation)[214]. In a recent evaluation, assuming NLST mortality benefit of 20%, the ratio was 10 for women and 25 for men[215]. However, this is likely an underestimate as modeling was from age 50 for eligible lifetime annual screening and with an underestimate of deaths prevented (higher in NELSON). It is also noted that the benefits of screening occur earlier than the risks of cancer caused by screening[215].

Improvement in technology has resulted in a reduction in effective dose[216]. For example, in NLST 4-16 detector row scanners delivered 2.19 to 2.4 mSv[217] compared with NELSON where 16 row scanners were used, to achieve a lower dose for participants <80Kg[218]. ESTI advise the use of at least a 32-row CT scanner, 100-120 kVp for standard-sized participants, 140 kVp for larger participants, a slice thickness of maximum 1.0 mm (preferred ≤ 0.75 mm) and a Volume Computed Tomography Dose Index (CTDIvol) of 0.4 mGy, 0.8 mGy and 1.6 mGy for participants <50 kg, 50–80 kg and >80 kg respectively[213]. The NHSE Protocol and QAS provides the same recommendations as the ESTI Standard. The ACR-STR statement, is less restrictive on number of detectors and slice thickness[212].

Thin slices (0.9 – 1.25mm) are necessary for accurate volumetric assessment of pulmonary nodules[126,218-221]. Changing slice thickness or reconstruction algorithms between screening rounds should be avoided in case volume measurement of lung nodules is affected[222].

With the development of newer radiation dose reduction techniques such as iterative and model-based reconstruction, photon-counting technology, CT with tin filtration and denoising algorithms, dose can be further reduced[223-228]. Thus, scanning protocols with a radiation dose similar to that of a chest radiograph, so-called ‘submillisievert’ or ultra-low dose CT, are possible.

Reading and Reporting

There are no well-defined standards for human and automated reading of imaging, or for documentation of findings. Although double-reading was employed in several trials, this was not replicated in program protocols except for initial training[7,11,12,64,218,229]. Expertise is variously defined by national thoracic radiology societies and in protocols[11,18]. These give minimum requirements for number of CTs reported, attendance at training courses and multidisciplinary meetings. Most LCS programs provide further education tools for those recent to field. ESTI, for example, has a certification course (lung cancer screening [LCS] diploma)[230]. For semi-automated and automated reading, commercially available software should be CE approved. Several structured reporting proforma[11] have been used and can be linked to management guidelines such as ACR Lung-RADS[13].

Decision-making within the LSC program

The management of actionable findings from the screen are not within the scope of this standard as they are the subject of established guidelines. However, it is important to ensure the infrastructural elements described above are in place so that guideline-drive management is implemented efficiently. This often involves a multi-disciplinary teams dedicated to the review and management of findings, although other alert mechanisms are employed. There is evidence to show that MDT management of findings reduces the number of actionable findings[231] compared with no such approach[232].

Imaging acquisition and reporting standards

CT and software

29. The minimum specification is a 16-row multi-detector CT calibrated according to the manufacturer's specifications, capable of delivering low radiation dose protocols (see below). There should be regular checks on the equipment according to local protocol.
30. For volumetric software:

    j. It is the preferred method for assessment of solid pulmonary nodules.
    k. The same software should be used to compare volumes.
    l. Where there are software updates these should be recorded and the supplier provide evidence that:
        i. the upgrade provides the same measurements or;
        ii. ensure that the user is prompted to re-measure nodules from preceding scans.
    m. It must be directly or indirectly integrated into PACS systems, capable of automated image retrieval of historical imaging.
    n. Additional desirable standards for volumetry are provided in appendix F

31. Computer aided detection (CAD) should be used as a concurrent or second reader. A false positive rate of <2 per case is desirable for CAD systems.

CT Image Acquisition Protocol

32. Participants should be comfortably positioned supine, arms above their head and thorax in the midline of the scanner. Maximal inspiration should be rehearsed prior to the scan and imaging should be performed during suspended maximal inspiration. No intravenous contrast material should be administered.
33. Programs should use their standard scanogram to localise the start and end positions of the scan. The frontal localiser should be performed in the PA projection and at the lowest possible setting to minimize breast dose.

34. The lung parenchyma (lung apices to bases) must be scanned in its entirety in a single cranio-caudal acquisition. The 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 (≤1.25mm) will be used.
35. The CTDIvol must be kept as low as possible with the effective radiation dose well below 2 mSv. The kVp and mAs settings are adjusted according to the height and weight of participants. Ultra LDCT should be used where considered to be of equivalent diagnostic sensitivity to LDCT.
36. Image reconstruction should be standardised and used for any follow-up examinations, with particular emphasis on ensuring that slice thickness, reconstruction increment, reconstruction algorithm and field of view are identical. Slice thickness should be ≤ 1.25mm. If iterative reconstruction is used, this should be kept constant at follow up.

Reporting

37. 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 checked visually.
38. All scan data should be archived and retained; a national repository should be considered to facilitate education and research.
39. Readers must report a substantial number of thoracic CTs annually as part of their normal clinical practice (>500), including a significant proportion of lung cancer CTs.
40. Readers must be familiar with the use and limitations of nodule volumetry software and apply agree guidelines for nodule management.
41. A structured reporting proforma must be used to promote consistency and assist audit.

Thoracic CT Reader Quality Assurance

42. Each program should have documented quality assurance mechanisms in place for CT reading. QA for CT reading may include:

    o. Ensuring a minimum level of training and expertise of readers including continuous professional development in LCS.
    p. Ensuring initial CT reads of radiologists without experience of LCS are reviewed by more experienced readers (e.g. first 50 cases).
    q. Periodic review of CT readers reports by expert panels, including referral recommendations.
    r. Evaluation of all readers' recall rates, false positive rates and false negative rates, with identification of outliers. This includes incidental findings.
    s. Evaluation of readers against validated cases.

43. National or regional consortia of expert radiologists may be the best way to address capacity, education and QA.

Research Recommendations

Further research into the impact of lower radiation dose techniques on the quality of images is needed.

3.2.9 CT interval and surveillance

Varying the interval between LDCT is important to ensure that indeterminate findings are properly monitored and in stratifying the screening program according to risk. Surveillance of pulmonary nodules is not within the remit of this technical standard because there are well-established and effective guidelines in existence. These recommend shorter intervals than the next annual screen from the index CT depending on the size of the nodule as measured either by manual diameter or semi-automated volumetry[4,13,14]. However, varying the interval between scheduled screens may also depend on the presence of nodules.

Evidence review

From a total of 43 full text reviews, useful evidence on this topic was obtained from 9. Some trials of CT screening have described different screen intervals but the majority used annual screens. The MILD trial randomized 4099 participants to no-screening, annual or biennial and found after a 5-year follow-up that 36% more cancers were detected in the annual group compared to biennial; the trial was underpowered for mortality outcomes[220]. In an analysis of the NLST, the finding of any non-calcified nodule (4mm or greater) was associated with a 2-fold increased risk of lung cancer between 2 and 5ys, and 5 and 7 years after the screen[233]. The NELSON trial showed that previously indeterminate findings conferred a greater subsequent risk of lung cancer[167]. Participants with a negative screen (no nodules, or nodule <50mm3 or nodule with a volume change of <25% if on follow-up) had a 0.6% chance of lung cancer in the next 2.5 years compared with 3.7% of participants who had at least one indeterminate screen (nodule 50-500mm3, or VDT 400-600 days on follow-up). However, another study found that the risk of developing cancer was also related to the risk as estimated by a multivariable model in people with negative scans. This has led others to develop risk prediction models that use the CT findings and other risk factors to predict risk more accurately which may then be used to define the best screening interval[234]. This study found that compared with the TLHC protocol, where scans with nodules <5mm in diameter prompt a biennial CT, the use of a multivariable model delayed diagnosis in 30% of lung cancers compared with 40% in the simple TLHC approach but referred a similar proportion for biennial CT. The evidence for extending screening beyond 2 years is limited, in the NELSON trial the final screening round was at an interval of 2.5 years and the proportion of interval cancers was higher and with more late stage than the 2-year interval between rounds 2 and 3 leading to the conclusion that this was too long an interval[235].

Simulation health economic models have been used to estimate relative cost effectiveness of annual, biennial and risk stratified screening. Goffin et al., based on the Canadian healthcare system, concluded that over 20 years, biennial screening was associated with the same number of QALYs and was more cost-effective than annual screening[236]. However, in another analysis for the Canadian Government, ten Haaf et al concluded, that annual screening was more cost effective[237]. The analysis for the USPSTF showed that all annual scenarios modelled were more cost effective that biennial[238] whilst a modelling study for the UK was less clear[239]. A further modelling study showed that stratified screening reduced harms whilst maintaining mortality benefit[240]. National protocols and statements recommend annual screening with the exception of the NHSE TLHC where a stratified approach is taken.

Summary

The difference in cost effectiveness between annual and biennial screening is small, although annual screening may prevent more deaths. Based on baseline CT findings and other risk factors, participants may undergo stratified screening to reduce harms whilst maintaining mortality benefit.

Interval and surveillance standards

44. Annual LDCT is the preferred interval if capacity and total economic and health service impact allow.
45. Biennial intervals may be applied for lower risk groups using LDCT findings or multivariable risk prediction models to select participants.
46. Participants should be aware of the reason they have been stratified.
47. Screening intervals should not exceed 2 years.
48. Surveillances scans with a shorter interval that 1 year should follow pulmonary nodule guidelines.

Research recommendations

Do multivariable models incorporating imaging findings improve the clinical and cost effectiveness of LDCT screening through stratifying screening intervals?

3.2.10 Communication of results

Timely and accurate communication of the outcome of the screen is essential to mitigate any anxiety and to ensure prompt management of any actionable findings.

Evidence review

Of 52 full text reviews, detail of communication methods was limited, but informative in 21. Communication may involve patient navigators[20], primary care physicians, pneumologists or others. If letters are used, details on serious findings were not included, but were addressed in face-to-face conversations[12,241]. Support lines were described for patients for contact with an experienced healthcare worker or administrator[12,229] .

Focus on Patients

At the time of results disclosure, patients want to be treated with empathy, have the concerns recognized and addressed and understand the care plan[78,241-243]. Communicating concrete information on the next steps can improve adherence[244].

Timeframe

Half of patients in the NELSON trial reported "dread" while awaiting LCS results [245]. Early communication of results can help alleviate distress [246]. It is important that serious findings are acted on immediately and indeterminate findings followed up as required[247] .

Communication of normal results should be accompanied by information about continued risk of lung cancer (which may be provided as a percentage based on a multivariable model) in order to mitigate possible over-reassurance of patients. Patients who were allocated to follow-up scans or referrals to MDT boards were more likely to experience psychological distress[248]. The importance of not ignoring red flag symptoms and the importance of not smoking should be emphasized. A number of commercially available software tools are available to help generate result notification letters, among other functions[18].

Form of communication

Letters are a commonly used form of informing patients. In the SUMMIT study involving 1900 participants, 82.8% were satisfied with receiving their results by letter. 86.3% stated it was their preferred communication method. Patients from less deprived socio-economic quintiles were more likely to report that the letter contained insufficient information, elderly individuals (>70 years old)

were less likely to do so[249]. A qualitative investigation among patients and healthcare providers involved in lung cancer screening programs revealed that even among patients with normal findings patients would have preferred a conversation over a letter, while physicians thought the letter to be sufficient [241]. There is tension between clinicians' preference for efficiency and patients' strong preference for a conversation. In the setting of incidental nodules, patient-centered communication is associated with lower distress and greater adherence to evaluation [250,251]. Information may also be integrated with smoking cessation advice[109,252].

Summary

Communication of results is a key point in the participant pathway and provides an opportunity for support, education and encouragement to continue with the screening process. Although time and resource-efficient methods are often preferred, these may not be appropriate when communicating indeterminate or unclear results. There appears to be some disparity in the views of participants and HCPs on the method and type of information needed which is the subject of ongoing and future research.[78]

Communication of results technical standard

49. Communication of results for each finding needs to be systematically designed for local populations, with local patient representative input.
50. The outcome should be communicated within a timeframe not exceeding 4 weeks from the LDCT.
51. Communication of negative and indeterminate findings can be via mail with an offer of support via telephone or videocall. Communications should include a reminder of the symptoms of lung cancer and the importance of smoking cessation.
52. Communication of positive findings should be face to face, usually within an urgent clinic.
53. Feedback from participants should be collected via a formal process and the results used to improve the participant experience.

3.2.11 Data Management

Evidence review

The evidence reviewed was limited to data management systems (DMS) which have been used in lung cancer screening trials or programs. Six full papers were reviewed of which 3 were included as they mentioned data management approaches.[12,18,253] They comprised 1 protocol document, 1 expert summary and 1 implementation pilot. Two websites about specific data management systems currently available for lung cancer screening were also accessed as part of this process, alongside 1 Bill (H.R.107 - Lung Cancer Screening Registry and Quality Improvement Act of 2021) which is currently undergoing review in the US Congress, and the website for the Centers for Medicare & Medicaid Services[254-257].

Systems that allow administration, registration of data and monitoring of participants in a screening program in an integrated solution are optimal. A good DMS provides structured and automated data collection which enables participants to be identified and tracked throughout the screening program. Integration with imaging platforms, ideally with an all-in-one, end-to-end software solution is ideal. DMS that collect data in a format that facilitates submission, ideally in real-time, to national datasets for analysis, allow continuous monitoring and mitigation of clinical risks. The DMS must also adhere to information governance (INGV)/ General Data Protection Regulation (GDPR) requirements.

DMS are required to have a minimum mandatory dataset, which is agreed in advance and may be updated. Two publications have suggested data items to be included in a minimum dataset, which are summarised in Appendix G.[12,255] However, the Centers for Medicare and Medicaid Services (CMS) have

subsequently removed the requirement for imaging facilities to participate in a CMS-approved screening registry, along with the minimum required data elements, pending the outcome of Bill H.R.107.

Commercial bespoke data management programs are currently available and many more are in development[256,257]. US Congress Bill H.R.107 seeks to establish grant programs and requirements for registries that collect data from lung cancer screening under Medicare. It aims to provide funding to help establish free registries, with the requirement that these registries are interoperable. The Bill also provides grants to support the development of related quality measures for lung cancer screening[254].

Quality metrics

The DMS must collect data required to provide the performance metrics for the program. A detailed report on quality metrics for US LCS was published in 2021[258]. From 30 suggested metrics, 7 items achieved consensus for inclusion, but performance targets were not agreed for any. A suggested collection of performance metrics is provided in table 3.

Data Management Technical Standards

54. An end-to-end, validated data management system is the optimum system for an organised lung cancer screening program.
55. Data Management Systems (DMS) must be supported by an agreed national minimum dataset that allows regular centralised audit and reporting of key outcome metrics (table 3).
56. DMS have to adhere to information governance (INGV) and General Data Protection Regulation (GDPR) regulations.

3.0. Conclusion

The extensive literature review completed for this collaborative taskforce provided the basis for a technical standard that will be an important reference for lung cancer screening programs at all stages of development. It will help those tasked with implementation to negotiate with policymakers, stakeholders and funders for the best financial and structural environment to achieve a high-quality program. Furthermore, the standard will foster common best practice across Europe and facilitate international comparisons on program performance, with optimisation a likely outcome.

Table 1: Key essential capacity and infrastructure requirements for delivery of a LCS program from literature review

1. Risk assessment and recruitment – administrative team, nurse/ health advisor, primary care or pulmonology requirement to assess eligibility and coordinate shared decision making required in some programs
2. Education resource – all members of the delivery team but especially administration, primary care, radiology and pulmonology
3. Information resource for participants
4. Insurance and reimbursement or funding mechanism
5. LDCT scanning capacity and availability, with mobile/ community sites available if required
6. Radiology scheduling, reporting and quality assurance
7. Multidisciplinary clinical management teams to work up and treat referred participants
8. Management teams responsible for screening implementation and quality assurance
9. Program Coordinator and Patient Navigator
10. Information technology (IT) resources to enrol and track patients accurately, ensure follow-up and monitor the program
11. Integrated smoking cessation support and advice
12. Alignment with local services / support from local leadership

Table 2: Program-related factors Associated with attendance / adherence in LCS programs[201]

Factor	**Impact on attendance / adherence**
Primary care recommendation	Increased
Program navigator	Increased
Mobile LDCT[203,259]	Increased in some settings where access to fixed site limited
Increased distance to service[205]	Decreased
Reminders	Increased
Centre type (Academic vs. community)	No impact
Urban vs rural setting[72]	Unclear
Uninsured[260]	Decreased

Table 3: Key Performance Indicators

Indicator
Invitation and attendance – proportion and total number
Proportion of eligible age range identified as ever smokers from Registry or Questionnaire
Proportion of ever smokers who undergo lung cancer risk assessment
Proportion of ever smokers who are eligible for LDCT and invited
Proportion attending for CT scan if high risk and invited for screening

Smoking cessation (CS)
Proportion of people attending for LDCT and are current smokers who are offered CS advice
Proportion of current smokers meeting Smoking Cessation Practitioner (SCP)
Proportion of current smokers attending screening who report quitting at 12 months
Screening Outcome (all screened)
Proportion of participants screened who receive screening results within four weeks
Proportion of participants screened with indeterminate findings
Proportion of participants screened with referral for incidental finding
Proportion of participants screened recalled for interim surveillance CT (prevalence/incidence)
Proportion of participants undergoing further investigation other that surveillance CT
Proportion of participants screened attending an urgent Cancer Clinic or similar
Proportion of participants with screen detected lung cancer stage I/II
Proportion of participants who have surgery for adenocarcinoma in situ and atypical adenomatous hyperplasia
Proportion of participants who develop interval lung cancers
Proportion of participants with lung cancer undergoing treatment with curative intent
Proportion of participants with suspected lung cancer undergoing invasive test(s) for benign disease
Proportion of participants who have surgery for suspected lung cancer that have lung resections for benign disease
Proportion of participants referred for surgery who undergo surgery within 4 weeks from referral
Proportion of cancers diagnosed after surveillance at stage IB and higher
Ongoing screening
Proportion of participants remaining eligible who attend for next screen within 6 months of intended interval

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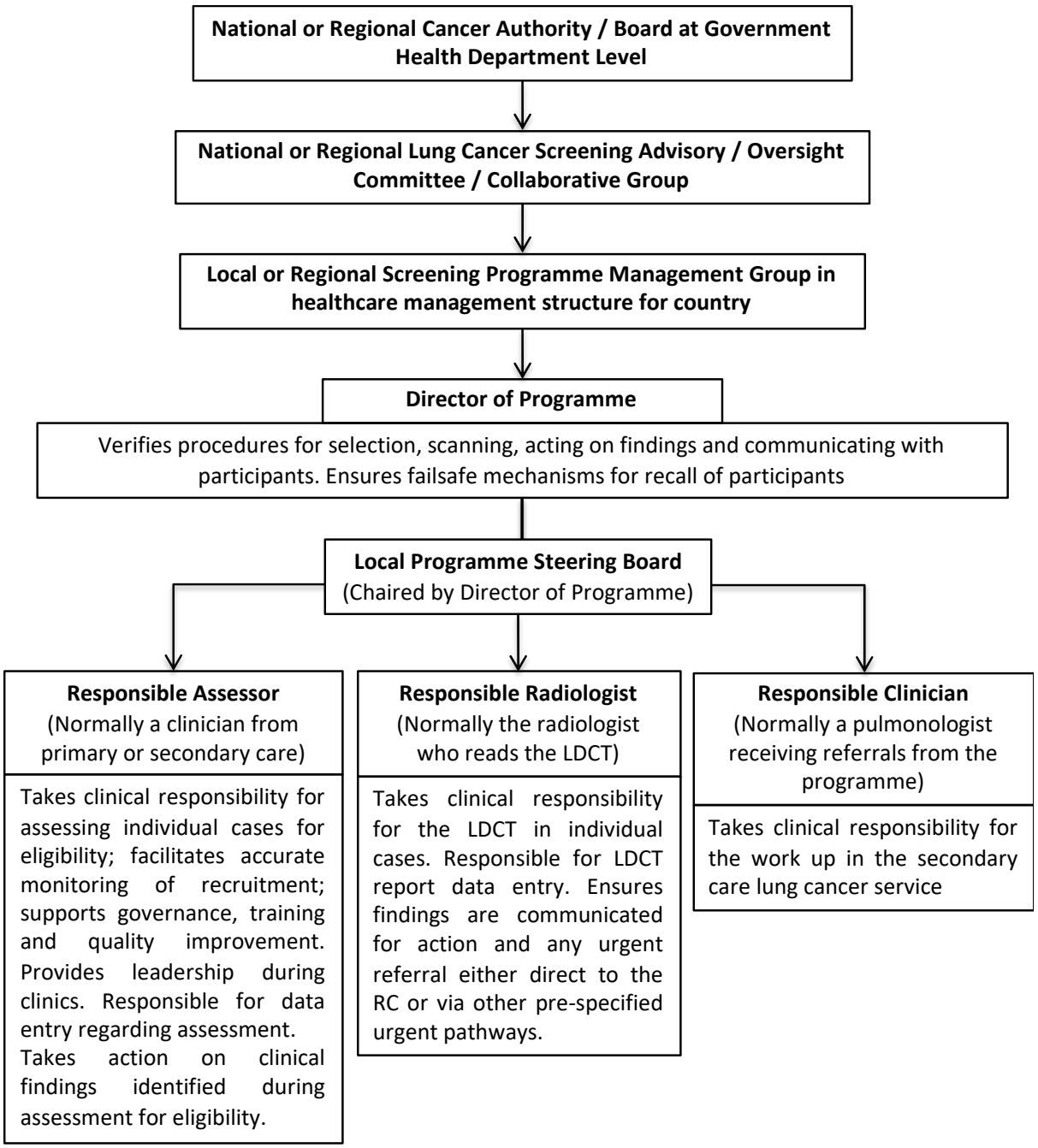
Figure 1: a basic centralized structure with hierarchies, roles and responsibilities.



Developing a Pan-European Technical Standard for a Comprehensive High-quality Lung Cancer CT Screening Program. An ERS Technical Standard

Appendices

Appendix A: Search strategy

SCOPE:

narrative review on pre-defined key steps in LDCT lung cancer screening programmes

a. Capacity and infrastructure requirements
    i. capacity (personnel and equipment)
    ii. infrastructural
b. Clinical governance, roles and responsibilities
    i. clinical governance
c. Invitation methods
    i. invitation methods
d. Participant pathway
    i. pathway
e. Risk assessment for entry into screening programmes
f. Low Dose Computed Tomography Acquisition and Reading
    i. parameters for image acquisition?
    ii. reading of CT imaging?
g. CT interval and surveillance
h. Non-attendance and Exiting the Programme
    i. non-attendance?
    ii. exiting the programme?
i. Communication of results
    i. participants?
    ii. information given on participants?
j. Data management
    i. requirements for data management?

LIMITS:

Systematic Reviews

Cohorts of 50+ cases

Guidelines

Statements

RCTs

Government and Society documents

European languages

SEARCH STRATEGIES:

1. RCTs in LDCT lung cancer screening - DETeCCTS_update_2020 library : large equation with focus on document type, time limit from 2020 (update of previous systematic review by Thierry Berghmans and Valérie Durieux) = 20 new documents (plus previous systematic review(s) accessible for us)

2. Real life publication in LDCT lung cancer screening - DETeCCTS_focus_RL library : large equation with focus on real life, time limit from 2010 = 1340 documents (no time limit: 1663 documents)

3. Risk assessment: DETeCCTS_RA library : equation for risk assessment, time limit from 2015 = 570 documents

1. Information on RCTs in lung cancer screening

(exp mass screening/ or exp early diagnosis/ or screening.tw or early diagnos*.tw) and (lung neoplasms/ or bronchial neoplasms/ or carcinoma, bronchogenic/ or carcinoma, non-small-cell lung/ or small cell lung carcinoma/ or pancoast syndrome/ or lung neoplasm*.tw or lung cancer*.tw or lung carcinoma*.tw or lung tumour*.tw or lung tumor*.tw or pulmonary neoplasm*.tw or pulmonary cancer*.tw or pulmonary carcinoma*.tw or pulmonary tumour*.tw or pulmonary tumor*.tw or bronchial neoplasm*.tw or bronchial cancer*.tw or bronchial carcinoma*.tw or bronchial tumour*.tw or bronchial tumor*.tw or bronchogenic neoplasm*.tw or bronchogenic cancer*.tw or bronchogenic carcinoma*.tw or bronchogenic tumour*.tw or bronchogenic tumor*.tw or pancoast* syndrome*.tw or pancoast* tumor*.tw or pancoast* tumour*.tw) and (exp Tomography, X-Ray/ or Tomography Scanners, X-Ray Computed/ or CT*.tw or Scan*.tw or Tomograph*.tw or Tomodensitometr*.tw) and (smokers/ or exp smoking/ or tobacco/ or exp "Tobacco Use"/ or exp tobacco products/ or smoker*.tw or tobacco smok*.tw or tobacco consumption.tw or cigaret*.tw or high risk*.tw)

AND (comparative study.ti or controlled clinical trial.ti or randomized controlled trial.ti OR rct.ti OR phase iii.ti or clinical trial, phase iii.pt or comparative study.pt or controlled clinical trial.pt or randomized controlled trial.pt)

From 2020 = 20 (25/11/2021)

2. Information on real life publications in lung cancer screening

(exp mass screening/ or exp early diagnosis/ or screening.tw or early diagnos*.tw) and (lung neoplasms/ or bronchial neoplasms/ or carcinoma, bronchogenic/ or carcinoma, non-small-cell lung/ or small cell lung carcinoma/ or pancoast syndrome/ or lung neoplasm*.tw or lung cancer*.tw or lung carcinoma*.tw or lung tumour*.tw or lung tumor*.tw or pulmonary neoplasm*.tw or

pulmonary cancer*.tw or pulmonary carcinoma*.tw or pulmonary tumour*.tw or pulmonary tumor*.tw or bronchial neoplasm*.tw or bronchial cancer*.tw or bronchial carcinoma*.tw or bronchial tumour*.tw or bronchial tumor*.tw or bronchogenic neoplasm*.tw or bronchogenic cancer*.tw or bronchogenic carcinoma*.tw or bronchogenic tumour*.tw or bronchogenic tumor*.tw or pancoast* syndrome*.tw or pancoast* tumor*.tw or pancoast* tumour*.tw) and (exp Tomography, X-Ray/ or Tomography Scanners, X-Ray Computed/ or CT*.tw or Scan*.tw or Tomograph*.tw or Tomodensitometr*.tw) and (smokers/ or exp smoking/ or tobacco/ or exp "Tobacco Use"/ or exp tobacco products/ or smoker*.tw or tobacco smok*.tw or tobacco consumption.tw or cigaret*.tw or high risk*.tw)

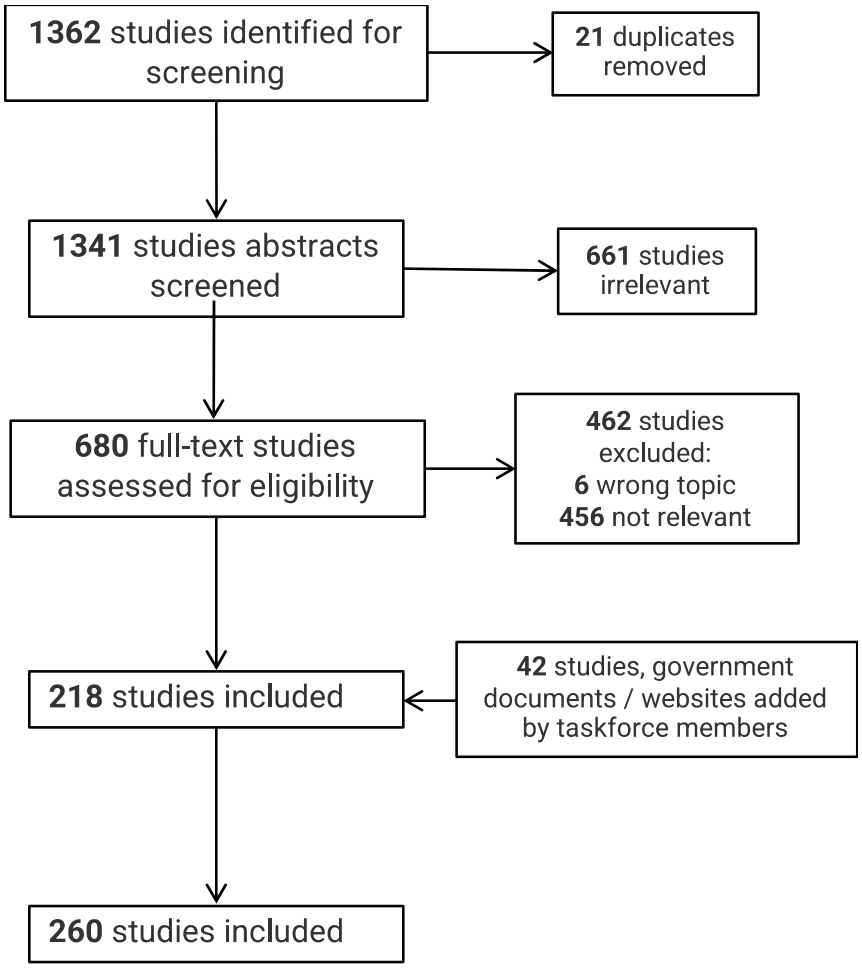
From 2010 = 1340 (25/11/2021)

3. Information on risk assessment

(lung neoplasms/ or bronchial neoplasms/ or carcinoma, bronchogenic/ or carcinoma, non-small-cell lung/ or small cell lung carcinoma/ or pancoast syndrome/ or lung neoplasm*.tw or lung cancer*.tw or lung carcinoma*.tw or lung tumour*.tw or lung tumor*.tw or pulmonary neoplasm*.tw or pulmonary cancer*.tw or pulmonary carcinoma*.tw or pulmonary tumour*.tw or pulmonary tumor*.tw or bronchial neoplasm*.tw or bronchial cancer*.tw or bronchial carcinoma*.tw or bronchial tumour*.tw or bronchial tumor*.tw or bronchogenic neoplasm*.tw or bronchogenic cancer*.tw or bronchogenic carcinoma*.tw or bronchogenic tumour*.tw or bronchogenic tumor*.tw or pancoast* syndrome*.tw or pancoast* tumor*.tw or pancoast* tumour*.tw) and (smokers/ or exp smoking/ or tobacco/ or exp "Tobacco Use"/ or exp tobacco products/ or smoker*.tw or tobacco smok*.tw or tobacco consumption.tw or cigaret*.tw or high risk*.tw) and (risk model*.tw or Risk Assessment/ or Risk assessment*.tw or Risk prediction model.tw or Assessment tool.tw or Prediction score.tw or Bach.tw or Liverpool Lung Project.tw or LLP.tw or Spitz.tw or Two-stage clonal expansion.tw or TSCE.tw or Model for African Americans.tw or Lung cancer in Korean men.tw or Hoggart.tw)

From 2015 = 570 (25/11/2021)

Appendix B: Flow diagram of article screening results



Appendix C:

Topics identified by TF members as essential components of a Lung Cancer Screening program

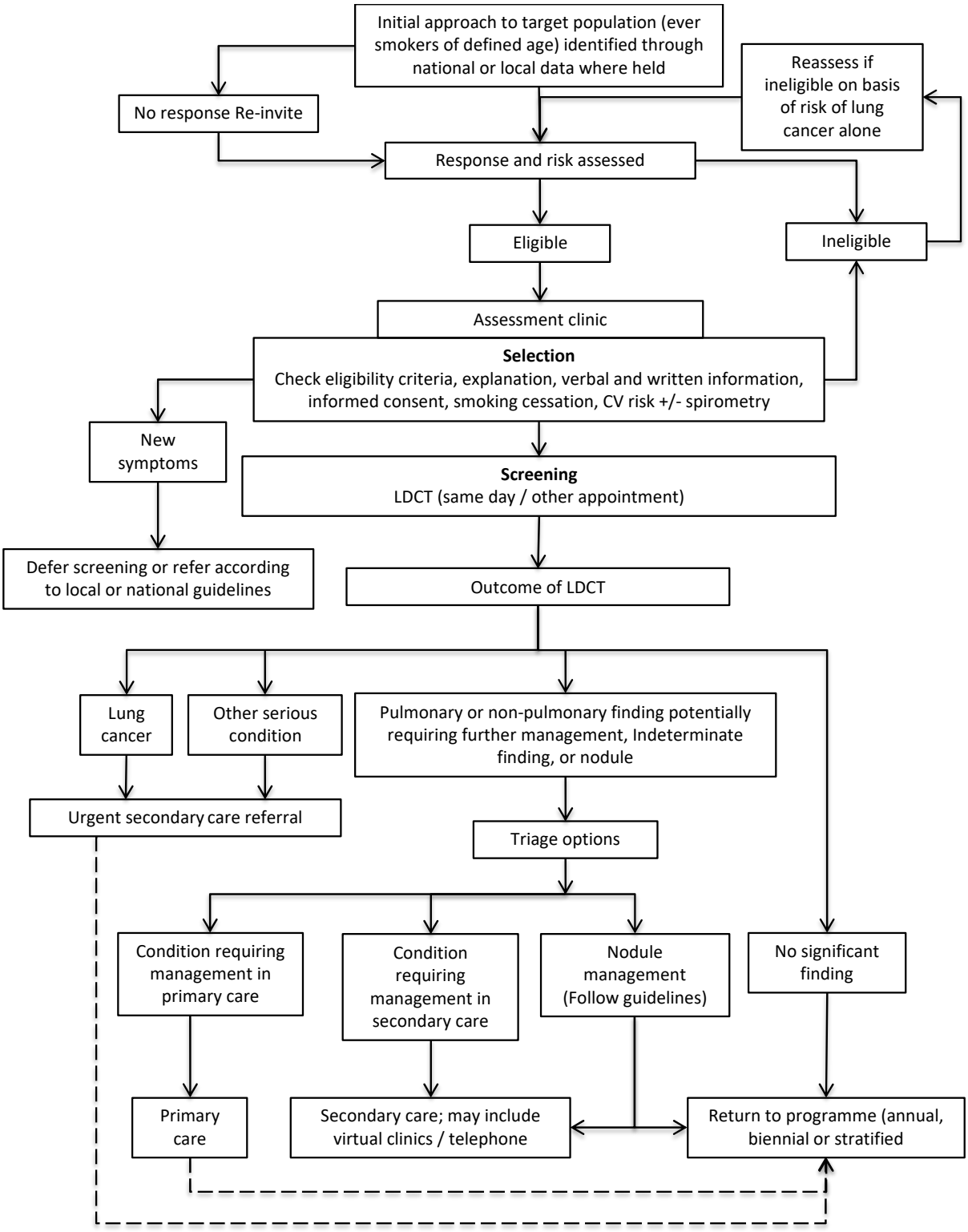
Topic	Questions
Capacity and infrastructure requirements	What are the requirements in terms of capacity (personnel and equipment) in order to deliver a CT screening program for lung cancer? What are the infrastructural considerations that may influence the delivery of a CT screening program for lung cancer? What are additional services within a CT screening program for lung cancer?
Clinical governance, roles and responsibilities	What clinical governance standards apply to CT screening? Which roles form part of clinical governance of programs?
Participant Pathway	What are the components that are included in the participant pathway? What components are regarded as crucial?
Invitation methods	What invitation methods have been used successfully in screening for cancer? Which invitation methods are the most effective?
Risk assessment for entry into screening programs	What methods are used to assess the risk of lung cancer in potential participants? Which risk assessment methods may be applied to select eligible participants?
Smoking cessation	What is the optimum strategy for integration of smoking cessation into LCS programs?
Non-attendance and Exiting the Program	What methods have been applied to address non-attendance? Which methods are most effective What are the options for exiting the program?
LDCT Acquisition, Reading and Reporting	What are the accepted parameters for image acquisition? What are the standards for reading of imaging? What are the standards applied to interpretation and reporting?
CT interval and surveillance	What intervals have been applied between scans? What are the implications of different intervals? What circumstances may influence the choice of interval?

Communication of results	What methods are used to communicate results to participants? What impacts do the methods used, and content of, the information given on participants?
Data management	What are the requirements for data management? What data are collected? How are data analysed? How are data managed and what are the options?

Appendix D: Core roles and responsibilities in the governance of a LCS program.

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

Appendix E: An example lung cancer screening participant pathway



Appendix F: Additional desirable features of semi-automated volumetry

1. Facility to measure nodule volume on nodules not identified by CAD.
2. Facility adjust segmentation in a semi-automated fashion when necessary.
3. Facility to accept or reject CAD identified nodules.
4. Ability to track nodules consistently.
5. Ability to measure and record diameter where segmentation has failed.
6. Provision of percentage volume change and volume doubling time calculations compared to all previous scans.
7. Ability to detect, segment and measure subsolid nodules.

Appendix G: Minimum required dataset items

Centers for Medicare & Medicaid Services[257]		**NHS England Targeted Lung Healthcheck Program[10]**	
Data Type	**Minimum Required Data Elements**	**Data Type**	**Required Data Elements**
Facility	Identifier	Demographic data	Participant ID, LSOA, sex, age, GP Practice code, CCG code, marital status, ethnicity, main language
Radiologist(reading)	National Provider Identifier (NPI)	Co-morbidities	COPD, IHD, Cancer (date of previous cancer diagnosis), other medical diagnoses
Patient	Identifier	Lung Health Check (LHC)	Dates of letters/ telephone contact ID of person contacting participant LHC date LHC assessor ID Symptoms WHO/ECOG Performance Status Height, weight, BMI LDCT consent & ID of person taking consent
Ordering Practitioner	National Provider Identifier (NPI)	Smoking history	Smoking Type, Age started smoking, Date stopped smoking, Total quit period (years), Average number smoked daily, Number of years smoked, Estimated Pack Years,

CT scanner	Manufacturer, Model.	Risk assessment	All LLP v2 variables All PLCOm2021 variables
Indication	Lung cancer LDCT screening absence of signs or symptoms of lung cancer	Exclusion criteria	Unable to lie flat, Weight >200Kg, Previous thoracic CT <12 months ago, does not have capacity to consent to LDCT, Not physically fit, Participant declined
System	Lung nodule identification, classification and reporting system	Smoking cessation	Smoking Cessation Offered, Consent to be referred for smoking cessation. Outcomes of smoking cessation, including quit data at 3 months
Smoking history	Current status (current, former, never). If former smoker, years since quitting. Pack-years as reported by the ordering practitioner. For current smokers, smoking cessation interventions available.	Screening	Date Scanner ID Radiation dose Reader 1 ID/ reader 2 ID CAD used Nodule data/ risk assessment Incidental findings Screening outcome/ recommendation Onward referrals/ reason for these
Effective radiation dose	CT Dose Index (CTDIvol).	Diagnostics	Diagnostic/ staging tests

			Outcome TNM stage if lung cancer Treatment if lung cancer
Screening	Screen date Initial screen or subsequent screen	Outcomes	Death within 30 days of any procedure Date of death Cause of death
LDCT: low-dose computed tomography; LSOA: Lower Super Output Area; GP: General Practitioner; CCG: Clinical commissioning group; COPD: chronic obstructive pulmonary disease; IHD: ischaemic heart disease; WHO/ECOG: World Health Organisation/ Eastern Cooperative Oncology Group; BMI: body mass index; LLP: Liverpool Lung Project; PLCO: Prostate, Lung, Colorectal and Ovarian cancer; CAD: computer-aided detection; TNM: tumour, node, metastasis			