

# How will lung cancer screening and lung nodule management change the diagnostic and surgical lung cancer landscape?

---

**Hardavella, Georgia; Frille, Armin; Chalela, Roberto; Sreter, Katherina B.; Petersen, Rene H.; Novoa, Nuria; de Koning, Harry J.**

*Source / Izvornik:* **European Respiratory Review, 2024, 33**

**Journal article, Published version**

**Rad u časopisu, Objavljena verzija rada (izdavačev PDF)**

<https://doi.org/10.1183/16000617.0232-2023>

*Permanent link / Trajna poveznica:* <https://um.nsk.hr/um:nbn:hr:220:581646>

*Rights / Prava:* [Attribution-NonCommercial 4.0 International/Imenovanje-Nekomercijalno 4.0 međunarodna](#)

*Download date / Datum preuzimanja:* **2024-12-02**



*Repository / Repozitorij:*

[Repository of the Sestre milosrdnice University Hospital Center - KBCSM Repository](#)



# How will lung cancer screening and lung nodule management change the diagnostic and surgical lung cancer landscape?

Georgia Hardavella<sup>1</sup>, Armin Frille <sup>2</sup>, Roberto Chalela<sup>3</sup>, Katherina B. Sreter<sup>4</sup>, Rene H. Petersen<sup>5</sup>, Nuria Novoa<sup>6</sup> and Harry J. de Koning<sup>7</sup>

<sup>1</sup>4th–9th Department of Respiratory Medicine, “Sotiria” Athens’ Chest Diseases Hospital, Athens, Greece. <sup>2</sup>Department of Respiratory Medicine, University of Leipzig, Leipzig, Germany. <sup>3</sup>Department of Respiratory Medicine: Lung Cancer and Endoscopy Unit, Hospital del Mar – Universitat Pompeu Fabra (UPF), Barcelona, Spain. <sup>4</sup>Department of Pulmonology, University Hospital Centre “Sestre Milosrdnice”, Zagreb, Croatia. <sup>5</sup>Department of Cardiothoracic Surgery, University of Copenhagen, Rigshospitalet, Copenhagen, Denmark. <sup>6</sup>Department of Thoracic Surgery, University Hospital Puerta de Hierro-Majadahonda, Madrid, Spain. <sup>7</sup>Department of Public Health, Erasmus University Medical Center, Rotterdam, The Netherlands.

Corresponding author: Georgia Hardavella ([georgiahardavella@hotmail.com](mailto:georgiahardavella@hotmail.com))



Shareable abstract ([@ERSpublications](https://twitter.com/ERSpublications))

**Lung cancer screening implementation and subsequent findings management will change the lung cancer landscape.** <https://bit.ly/3W8xPCA>

**Cite this article as:** Hardavella G, Frille A, Chalela R, *et al.* How will lung cancer screening and lung nodule management change the diagnostic and surgical lung cancer landscape? *Eur Respir Rev* 2024; 33: 230232 [DOI: 10.1183/16000617.0232-2023].

Copyright ©The authors 2024

This version is distributed under the terms of the Creative Commons Attribution Non-Commercial Licence 4.0. For commercial reproduction rights and permissions contact [permissions@ersnet.org](mailto:permissions@ersnet.org)

Received: 9 Nov 2023  
Accepted: 16 April 2024

## Abstract

**Introduction:** Implementation of lung cancer screening, with its subsequent findings, is anticipated to change the current diagnostic and surgical lung cancer landscape. This review aimed to identify and present the most updated expert opinion and discuss relevant evidence regarding the impact of lung cancer screening and lung nodule management on the diagnostic and surgical landscape of lung cancer, as well as summarise points for clinical practice.

**Methods:** This article is based on relevant lectures and talks delivered during the European Society of Thoracic Surgeons–European Respiratory Society Collaborative Course on Thoracic Oncology (February 2023). Original lectures and talks and their relevant references were included. An additional literature search was conducted and peer-reviewed studies in English (December 2022 to June 2023) from the PubMed/Medline databases were evaluated with regards to immediate affinity of the published papers to the original talks presented at the course. An updated literature search was conducted (June 2023 to December 2023) to ensure that updated literature is included within this article.

**Results:** Lung cancer screening suspicious findings are expected to increase the number of diagnostic investigations required therefore impacting on current capacity and resources. Healthcare systems already face a shortage of imaging and diagnostic slots and they are also challenged by the shortage of interventional radiologists. Thoracic surgery will be impacted by the wider lung cancer screening implementation with increased volume and earlier stages of lung cancer. Nonsuspicious findings reported at lung cancer screening will need attention and subsequent referrals where required to ensure participants are appropriately diagnosed and managed and that they are not lost within healthcare systems.

**Conclusions:** Implementation of lung cancer screening requires appropriate mapping of existing resources and infrastructure to ensure a tailored restructuring strategy to ensure that healthcare systems can meet the new needs.

## Introduction

Lung cancer is the most frequent type of malignancy and the leading cause of cancer-related deaths worldwide [1–3]. The majority of lung cancer cases are diagnosed at an advanced stage, where radical treatment is not an option [3]. Lung cancer screening for high-risk populations with low-dose computed tomography (LDCT) is a valid intervention to increase lung cancer diagnosis at an early stage, where radical treatment can be offered and reduce lung cancer mortality [4–10]. However, systematic implementation of LDCT lung cancer screening requires a robust system and process to ensure that



uncertainties are addressed and all relevant findings are managed appropriately. Almost 50% of lung cancer screening LDCTs will report a lung nodule and only 5% of those will be malignant [10, 11]. The detection of lung nodules during lung cancer screening triggers a new diagnostic and treatment pathway that frames a new landscape in the multidisciplinary management of abnormal findings. This article is based on relevant lectures and talks delivered during the successful European Society of Thoracic Surgeons (ESTS)–European Respiratory Society (ERS) Collaborative Course on Thoracic Oncology held in Zurich (Switzerland) in February 2023. Due to the fast-changing field we additionally performed a literature search until December 2023 to ensure we captured recent data. This article aims to present the most updated expert opinion, discuss relevant evidence and further our understanding of the impact of lung cancer screening and lung nodule management on the diagnostic and surgical landscape of lung cancer.

### Search strategy

Original lectures and talks addressing the subject from the ESTS-ERS Collaborative Course on Thoracic Oncology and their relevant references were included. An additional search including the words or variations of “lung nodule”, “diagnosis”, “lung cancer screening” and “thoracic surgery” was conducted, and peer-reviewed studies in English from December 2022 to June 2023 from the PubMed and Medline databases were evaluated with regards to immediate affinity of the published papers to the original talks presented at the course. Letters to the editor, congress abstracts and case reports were excluded. An additional search with the same criteria was conducted from June 2023 to December 2023 to ensure that all latest literature is captured in the rapidly evolving field of lung cancer screening.

### Lung cancer screening in Europe: different gears in various countries

Currently, three European countries run national lung cancer screening programmes (Croatia, Czech Republic, Poland) while the rest run clinical trials and/or implementation studies (table 1). National lung cancer screening programmes in Europe share similarities in the use of quantified inclusion criteria (age and smoking habit cut-offs) rather than risk stratification models. Age as a lung cancer screening inclusion

TABLE 1 Current lung cancer screening situation in various European countries

	National programmes	Implementation studies	Clinical trials
Albania	0	0	0
Austria	0	0	0
Belgium	0	0	1
Bosnia and Herzegovina	0	0	0
Bulgaria	0	0	0
Croatia	1	0	0
Czech Republic	1	1	0
Denmark	0	0	1
Estonia	0	1	0
Finland	0	0	0
France	0	15	0
Germany	0	2	1
Greece	0	0	0
Hungary	0	2	0
Italy	0	9	2
Kosovo	0	0	0
Latvia	0	0	0
Lithuania	0	0	0
The Netherlands	0	2	1
Norway	0	0	0
Poland	1	3	0
Romania	0	0	0
Serbia	0	1	0
Slovakia	0	0	0
Slovenia	0	0	0
Spain	0	6	0
Sweden	0	1	0
Switzerland	0	1	0
United Kingdom	0	16	3
Information from [12].			

criterion is 50–75 years in Croatia, 55–74 years in the Czech Republic and 50–74 years in Poland. Quantification of smoking habit as an inclusion criterion is  $\geq 30$  pack-years in Croatia and  $\geq 20$  pack-years for Poland for current smokers. In Croatia and Poland, ex-smokers are included up to 15 years after quitting. These national lung cancer screening programmes vary in their duration and funding sources [13–15]. Information on recruitment strategies per country is not readily available from the relevant lung cancer screening websites, and a thorough literature search is required to obtain access to detailed information. To date, none of these programmes have publicised specific information on the invitation process, standard operating procedures and obstacles. Another common theme across all countries is the importance of engaging primary healthcare in the recruitment of high-risk individuals who could benefit from lung cancer screening. Ensuring the engagement of family physicians and general practitioners (GPs) remains a significant challenge around Europe and providing training to GPs in lung cancer screening has been recognised as a priority [16, 17].

High-risk individuals around Europe have variable access to lung cancer screening depending on its availability in each country. Variable access implies heterogeneity in processes, structure, quality and provision of service. To address this, the European Society of Radiology and the ERS recommended lung cancer screening in comprehensive, quality-assured, longitudinal programmes within a clinical trial or in routine clinical practice at certified multidisciplinary medical centres [18]. The need for clear algorithms in radiology reporting and further management of findings remained. This has been recently addressed through a technical standard report for a comprehensive high-quality lung cancer screening programme [19] and, in a joint effort, a statement on management of incidental findings from LDCT screening for lung cancer [20]. The management of these findings requires a systematic multidisciplinary approach [21]. In contrast to other cancer screening programmes, LDCT provides much more information than required for lung cancer detection [20]. Incidental findings are detected frequently, and they can potentially trigger further investigations that may benefit or harm the participants while increasing management costs [22–25].

Despite the existing variation of healthcare systems across European countries and their differences in comparison with countries outside Europe, it seems that the national lung cancer screening programmes in Europe share similar underpinning principles with the national lung cancer screening programmes in the United States of America, South Korea and Taiwan [26–31].

The need for clear algorithms in radiology reporting and further management of findings is a common theme which has been addressed in the United States, South Korea and Taiwan through the adoption and implementation of the Lung Imaging Reporting and Data System (Lung-RADS) protocol (<https://acr.org/Clinical-Resources/Reporting-and-Data-Systems/Lung-Rads>). This ensures a systematic approach therefore minimising confusing variation in practice and potential serious incidents.

Similarly to Europe, primary care is a key stakeholder in national lung cancer screening programmes outside Europe, being a main source of identification and referral of high-risk individuals for lung cancer screening [26–31]. Each country adopts the applicability based on existing resources and infrastructure, but they all share similar underpinning principles [32].

### **Impact on lung cancer services of suspicious findings upon lung cancer screening**

Translating lung cancer screening research to real-world programmes has multiple, different challenges across various global healthcare systems [33]. Lung cancer screening impacts on care pathways, in particular clinic appointments and capacity, downstream investigations and interventions towards lung cancer workup, pulmonary function testing (PFT), smoking cessation and costs.

#### ***Impact on clinic appointments and capacity***

Current lung cancer services are inundated; therefore, the implementation of lung cancer screening requires comprehensive planning within relevant healthcare systems as well as involvement of professional organisations to ensure the successful delivery of lung cancer screening programmes. Assessing and planning the health infrastructure capacity for the resources required is needed in advance to ensure that implementation is feasible [33, 34]. Staffing levels, infrastructure, resources and capacity need to be primarily addressed and they should be complemented by governance, quality assurance and programme outcome reporting protocols [33]. Accreditation of screening centres with incorporation of multidisciplinary teams (MDTs) [21] and access to fast-track lung cancer clinical services needs to be in place with a quick turnaround time for diagnostics.

Geography and impaired infrastructure in rural and remote locations may represent a challenge to lung cancer screening provision when compared to urban populations. There is a certain bias towards urban-centric health promotion strategies, which are less effective in rural areas [35].

In these cases, mobile LDCT units have demonstrated potential by reducing travel and improving access to a screening programme outside of a traditional hospital setting which is already overwhelmed by existing clinical services [33]. This method was successfully used for lung cancer screening in rural areas in Japan in the 1990s [36] and its current use in high-risk populations in the United Kingdom and United States continues to expand [37]. Efforts such as the mobile LDCT units appear to be a feasible and acceptable strategy to increase capacity in overstretched radiology departments.

Implementation of a lung cancer screening programme will result in a significant tumour-stage shift, leading to increased workload for thoracic tumour MDTs and theatres, requiring workforce and capacity planning [26]. If curative treatments for screen-detected lung cancers cannot be provided in a timely manner due to lack of capacity, then lung cancer screening cannot benefit the participants [33]. Therefore, treatment capacity will need adaptation over time to meet the increasing demand. Available data suggest that modelling can be utilised in the development of a screening programme by predicting the future clinical problem, assessing the potential impact of different interventions and capacity planning for screening implementation [33, 34, 38, 39]. By these measures, inequalities in access to multidisciplinary lung cancer services may be ameliorated [40].

#### **Impact on imaging and sampling investigations**

If the LDCT screening outcome is suggestive of lung cancer or other suspicious findings, an urgent secondary care referral will be required [21]. In the case of suspicious findings for lung cancer, further investigations follow, including positron emission tomography (PET)/computed tomography (CT), bronchoscopy with endobronchial or transbronchial biopsy, endobronchial ultrasound (EBUS) with transbronchial needle aspiration/biopsy and CT-guided biopsy [41, 42].

These investigations are already in high demand within the existing lung cancer services; therefore, the addition of lung cancer screening participants will further increase waiting times. Decreasing the examination time by using advanced devices is a way to investigate more patients within the same timeframe. The new generation of total-body PET/CT scanners with a long-axial field-of-view offer increased lesion detectability, reduced acquisition time and/or reduced administered dose [43]. These characteristics led to reduced overall time for a single scan, thus allowing a higher number of studies as compared with former generations of PET/CT scanners [44]. The higher number of studies will subsequently increase the workload of nuclear medicine specialists and radiologists in reporting. Suspicious findings will be discussed during thoracic tumour MDT meetings [21] and further investigations will be required for tissue sampling. This can lead to increased referrals to bronchoscopy units for bronchoscopy/EBUS. For those lesions not accessible *via* the endobronchial route, CT-guided transthoracic biopsy demonstrates an alternative approach [45–47]. With the existing shortage of interventional radiologists, significant delays will be anticipated [48, 49].

#### **Impact on PFTs**

PFT is part of the respiratory basic workup delivering functional insight (obstructive or restrictive). Several parameters, such as forced expiratory volume in 1 s or the diffusion capacity of the lung for carbon monoxide, are taken into account when a patient is discussed for thoracic surgery [50]. During the anticipated shift from advanced to early lung cancer stages, the number of PFTs is expected to rise. However, PFT is not necessarily bound to lung cancer service. PFT can be decentralised to outpatient clinics.

#### **Impact on smoking cessation services**

Lung cancer screening and smoking cessation follow a *conditio sine qua non* formula. According to international guidelines and statements, smoking cessation should be integrated in lung cancer screening programmes [16, 18–20, 35, 36, 51]. Geography affects access to smoking cessation services and management protocols may vary depending on the area. Lung cancer screening programmes will presumably increase the number of individuals wishing to quit smoking; hence, an additional smoking cessation infrastructure will be required.

#### **Costs**

In 2014, the United Nations reinforced its political commitment to implement a national and global roadmap towards effective prevention and control of noncommunicable chronic diseases [16]. The main priority is the goal of a 25% relative reduction in overall mortality from noncommunicable chronic

diseases, including cancer. Because most countries struggle with budget and sustainability constraints regarding their national health systems, it is crucial that the most cost-effective health interventions are prioritised, both at the individual and population level [16].

The management of incidental findings detected during lung cancer screening is likely to be a key factor in overall effectiveness and cost-effectiveness of the programme [20].

Data support the notion that lung cancer screening together with smoking cessation efforts can be cost-effective as a population-based measure [39]. With focus on low- and middle-income countries, effectiveness, affordability, feasibility and cost-effectiveness of LDCT screening vary among them due to differences in lung cancer epidemiological patterns and the readiness of their healthcare systems, resulting in a need for country-specific analyses [52, 53].

Region- or country-specific cost-effective analysis would be necessary to estimate individual expenditures. An important question remains unanswered: will lung cancer screening be funded by the community or individually? The answer will impact the number of potential participants in lung cancer screening.

### **Impact of lung cancer screening with nonsuspicious findings on services**

Unlike other screening programmes, lung cancer screening using LDCT encompasses multiple organ systems, making it more complex, but also more interesting, as it may identify multiple abnormalities. In nearly 70% of cases, thoracic and extrathoracic incidental findings unrelated to lung cancer have been reported [23, 54]. Many may not have clinical significance and should not affect the screening process [55, 56]. However, there are significant incidental findings that influence patient prognosis and may call for specific actions [57].

The incidence of incidental findings varies depending on the age and origin of the screened population, the prevalence of active smoking and, most importantly, the significance highlighted by the radiology report. The variability of reporting incidental findings is very high, ranging from 28% in community imaging centres to 67% in university centres [58]. This variation imposes criticism on lung cancer screening reporting, but it is also seen as a significant opportunity for early detection of other pertinent diseases [59–61].

The definition of significant incidental findings and their clinical relevance has been a much-debated topic since screening programmes began. Initial data from the National Lung Screening Trial (NLST) and the Dutch–Belgian lung cancer screening trials (NELSON) have described a relatively low incidence of clinically relevant incidental findings (7.5% and 8.4%, respectively) [4, 56]. Despite this, experts insisted on the need to unify criteria and definitions. In 2014, the American College of Radiology (ACR) introduced the first version of Lung-RADS to recommend a standardisation in lung cancer screening reporting, including the “S” category to define clinically significant or potentially clinically significant incidental findings (<https://acr.org/Clinical-Resources/Reporting-and-Data-Systems/Lung-Rads>). Subsequently, several evidence-based white papers have been published that offer recommendations specific to each organ [62–68]. Recently, the ERS addressed the matter with a joint statement in collaboration with other scientific organisations [20].

According to the published evidence to date, coronary calcifications and emphysema are the most prevalent findings according to most studies [20, 62–68]; however, abnormalities in all organ systems visible on the LDCT are frequently reported.

### **Coronary artery calcification**

Atherosclerotic cardiovascular disease (ASCVD) is a major cause of death, and the presence of coronary artery calcification (CAC) is a well-known specific marker for atherosclerosis. The most common approach to quantify this is the Agatston CAC score, which recognises lesions with an area  $\geq 1$  mm<sup>2</sup> and attenuation  $>130$  HU [69]. The CAC score is clinically significant, as it predicts overall mortality and unfavourable cardiovascular events. When severe, coronary heart disease risk increases nine to 16 times [70, 71], whereas the absence of CAC (CAC=0) confers a very low risk of ASCVD, allowing for reclassification as lower risk, and even deferring specific treatment [72].

In lung cancer screening, the rate of CAC detection is high. Although it is frequently not recorded as a significant incidental finding, its prevalence ranges from 56% to 74% [23, 55, 73]. Cardiac CT and LDCT are technically different, but CAC is detectable and measurable by both, with excellent correlation. CAC evaluation with Agatston scoring or a simple visual assessment of LDCT enables the correct selection of

patients at higher risk of cardiovascular and all-cause mortality [74]. CAC is regularly not reported or underestimated during lung cancer screening, and patients who are mentioned or reported as a significant incidental finding are more likely to receive statin treatment for cardiovascular risk prevention (ORs 1.8 and 4.4, respectively). Depending on the structure of the healthcare system, CAC reporting at lung cancer screening triggers referrals to primary care and/or cardiology services for further investigations and management where required [75–77]. Specific lung cancer mortality is increased in subjects with CAC >400 independent of smoking and traditional risk factors [78]. Multiple large screening cohorts have demonstrated the prognosis impact of incidental CAC detection in LDCTs [79, 80].

In the most recent guidelines, cardiovascular societies in Europe and the United States formally endorse CAC as a strong ASCVD risk modifier and recommend it in specific scenarios. It is worth noting that CAC=0 has been explicitly addressed to reclassify risk downward and avoid statin therapy in some groups [81–84]. A large-scale asymptomatic population-based clinical trial (ROBINSICA) has already randomised 43 447 subjects to investigate whether CAC screening and preventive treatment is effective in reducing cardiovascular and all-cause mortality. Preliminary results show that 16.8% of women and 30.7% of men with a CAC score >100 urgently require preventive treatment [85].

The ROBINSICA trial [85] will answer many of the questions surrounding CAC detection during screening programmes and may potentially change current practice; meanwhile, with existing evidence the CAC score is reported in lung cancer screening LDCT reports. It can identify moderate-to-severe cases of cardiovascular risk, and it can reclassify this risk when a negative CAC (CAC=0) is reported, thus sparing unnecessary clinical appointments.

### **Emphysema**

Emphysema is associated with an increased risk of lung cancer, independent of smoking. The presence of visually detected and automatically quantified emphysema are both linked with an elevated risk of lung cancer, with an overall pooled odds ratio of 2.3 (95% CI 2.0–2.6) [86]. A systematic literature review found the risk of lung cancer to be associated with centrilobular rather than paraseptal emphysema with a higher risk detected in moderate and severe emphysema (ORs 3.7 and 4.5, respectively). The quantification between mild, moderate and severe varies between the different studies, but most agree that the greater the amount of emphysema, the greater the risk [87].

The report of emphysema as an incidental finding in lung cancer screening varies and it depends on whether it is measured automatically using a cut-off value of –950 HU on noise-filtered LDCT or by visual assessment. The percentage low attenuation area used to detect and quantify emphysema has less interobserver variability than visual examination [88–90]. The ITALUNG cohort reported an emphysema prevalence of 32.3%, the SUMMIT cohort 33.4%, the NLST cohorts 45.4%, and the Cleveland Clinic cohort up to 50.6% [3, 23, 55, 91].

We consider it important to report the emphysematous changes as an incidental finding for two reasons. First, its presence is independently related to an increased lung cancer risk and it is a predictor of overall, lung-cancer-related and cardiovascular mortality in lung cancer screening participants [88, 91–93]. Second, emphysema is a highly sensitive and specific biomarker for COPD, and early detection, even if asymptomatic, could improve health status, by offering vaccinations to avoid exacerbations, encouraging regular exercise, managing comorbidities more proactively, and perhaps even starting medication to slow the pace of lung function loss. It is also known that subjects with asymptomatic undiagnosed COPD have an increased risk of pneumonia and exacerbations [94, 95]. Emphysema reporting will increase referrals to primary care/respiratory services and spirometry testing for quantification of lung function and will contribute to earlier diagnosis of COPD.

### **Other pulmonary incidental findings**

Other lung incidental findings include bronchiectasis, interstitial lung abnormalities, tuberculosis and pleural findings such as pleural plaques/thickening and bilateral effusions [20].

Bronchiectasis is usually reported in 7.4–11.6% of patients during lung screening [3, 96]. In the International Early Lung Cancer Action Program cohort, this can reach up to 23% when specifically searched for by skilled radiologists. Bronchiectases are primarily located in the lower lobes, and those who have them experience a higher frequency of respiratory events and symptoms. Although it seems important to report them, bronchiectases are not usually considered a significant incidental finding, and further studies are needed to determine whether early detection could bring prognostic benefits [97, 98].

Interstitial lung abnormalities are incidental CT findings that affect >5% of a lung zone and are potentially compatible with interstitial lung disease (ILD). They include reticulations, ground-glass opacities, nonemphysematous cysts, honeycombing, parenchymal distortions and/or traction bronchiectasis. Interstitial lung abnormalities are classified into three categories: non-subpleural, subpleural nonfibrotic and subpleural fibrotic [99]. The prevalence in general population is 7%, and 2.5–7% in screening cohorts. Mortality risk in subjects with interstitial lung abnormalities detected during screening is increased, particularly for fibrotic interstitial lung abnormalities [93, 100, 101]. ILDs are frequent and potentially serious diseases that require an accurate diagnosis to offer treatments that modify their prognosis. For this reason, interstitial lung abnormalities should be considered as significant incidental findings and consequently reported in lung cancer screening, and patients should be subsequently referred to specialist clinics.

#### ***Osteopenia and osteoporosis***

Treatment for osteoporosis or fragility fractures with osteopenia is strongly recommended, as it reduces fracture rates in real-world studies [102, 103]. Despite this, vertebral fractures and radiological findings suggesting osteopenia or osteoporosis are not usually reported as incidental findings in thoracic CTs [104]. In lung cancer screening subjects, the prevalence of vertebral fractures using the Genant semiquantitative method is 35%, and up to 51% in subjects who died during the screening period. Both vertebral fractures and bone density (measured in vertebral Hounsfield units) are independently associated with overall mortality [105]. The automatic measurement of Hounsfield units using artificial intelligence in LDCTs has demonstrated high diagnostic effectiveness for osteoporosis, and the fact that treatment for established osteoporosis reduces mortality suggests that an opportunistic screening of this condition could have a considerable impact [60, 106].

#### ***Referral implications***

Opportunistic detection of non-lung-cancer-related conditions should bring health benefits to subjects and avoid unnecessary studies, stress and unjustified overcost. Certain significant incidental findings must be reported and generate specific action. Various studies have quantified the workload generated, numbering it between 11.2% and 15% of all screening cases. Most referrals and new diagnoses occurred after first-round screening and <1% required invasive procedures [73, 107].

Determining the clinical significance of incidental findings is a challenge, and a protocolised reporting approach is mandatory to identify relevant nondiagnosed comorbidities. Recently, GAREEN *et al.* [57] re-evaluated the negative screening LDCTs in the NLST and an expert panel classified the incidental findings in specific categories with a unique code. They found 8954 (33.8%) cases with a reported significant incidental finding, most of which were considered reportable to the referring clinician. Similarly, TISI *et al.* [55] published the SUMMIT protocolised incidental findings management protocol, which not only included specific assessment criteria, but also a suggested clinical action for each incidental finding. This approach generated referrals in 9% of screening subjects (5.1% to primary care, 1.1% for pulmonary consultation and 2.8% for cardiology/vascular). It is particularly noteworthy that while moderate, severe or very severe emphysema was described in 11.6% of cases, only 1.1% of cases were referred to a pulmonary consultation, although in all cases a spirometry was recommended.

From a patient-centred approach, two-thirds of lung cancer screening participants consider it very important to receive more information regarding respiratory and cardiovascular incidental findings. Despite 88% having understood the screening report, most prefer direct communication with clinicians, even when results are normal [108]. To minimise heterogeneity in the reports of incidental findings and their subsequent actions, the ACR has published a quick reference guide of incidental findings [109]. In 95% of cases, the lung cancer screening programme navigators found this useful or extremely useful [110].

It is currently unknown whether the reporting and action of incidental findings has a prognosis impact on screening subjects, but data suggest real potential benefits. More research efforts should be directed towards making use of lung cancer screening, and specific additional resources to address incidental findings should be considered.

#### ***The challenge of overdiagnosis***

The concept of overdiagnosis in the context of lung cancer screening has been a matter of debate in the literature for more than two decades [111, 112]. It is important to consider the ongoing controversies related to overdiagnosis through the lens of critical appraisal of the data, taking into account the viewpoints of two diametrically opposed stances (the optimist, who promotes the benefits of lung cancer screening, *versus* the pessimist, who assumes the worst about it) [113, 114]. Given the complexity of this issue, much



discussion has focused on clarifying the meaning of overdiagnosis, ranging from a clinical perspective to an epidemiological definition, and finally, to one with a pathological basis that is commonly used today [111, 115, 116]. Moreover, the extent to which overdiagnosis occurs in the screening population, although widely explored, remains unclear, with variable estimates reported across different clinical trials and screening studies [4, 8, 9, 116–119]. Ascertaining the true magnitude of overdiagnosis in future lung cancer screening programmes remains a major hurdle, although modelling may help derive additional information to extrapolate beyond the time periods of the clinical trials [120]. Conducting research on overdiagnosis, with the aim of reducing its prevalence in order to mitigate any associated harms, is largely hampered by its retrospective nature; that is, it cannot be carried out prospectively, since direct observation in real time in an individual patient is not possible [121].

#### **Definition of overdiagnosis**

Many definitions of overdiagnosis exist in the literature. A consensus on a satisfactory interpretation of this term is essential to prevent and minimise misdiagnosis and overtreatment, with the aim of delivering more effective healthcare [122]. As pertains to cancer screening, a seemingly acceptable and commonly used meaning of overdiagnosis is the discovery of indolent pathology that would not have otherwise progressed to a clinically apparent illness and/or caused death during the lifetime of the individual [116, 123]. Essentially, otherwise asymptomatic people are unnecessarily but “correctly” diagnosed and classified as patients, then subsequently overinvestigated and overtreated, deriving little to no benefit from the diagnosis and treatment, and in the process are thereby harmed [122, 124, 125]. Regarded as the most severe potential harm of lung cancer screening, overdiagnosis has two major causes: over-detection (*i.e.* use of increasingly sensitive tests to identify indolent, nonprogressive or regressive abnormalities) and overdefinition (*i.e.* expanded definitions of disease with lowering of disease thresholds) [122, 125]. Other contributing factors to overdiagnosis have also been identified, such as fear of missing a diagnosis or malpractice suits, public enthusiasm for screening or testing and financial incentives [124, 125]. In addition, overdiagnosis in cancer screening occurs more frequently when there is slow or no growth of cancer pathology and/or high competing risk of death [16, 118].

#### **Estimation of the degree of overdiagnosis of lung cancer in LDCT screening**

The approach to quantifying overdiagnosis is based on a thorough analysis of data collected from long-term observation after screening ends [115, 126]. Research suggests that the magnitude of overdiagnosis at the population level is trivialised with extended post-screening follow-up periods [126]. For instance, overdiagnosis risk (probability that any lung cancer detected by LDCT is an overdiagnosis) was estimated at 18.5% initially (mean follow-up of 4.5 years) *versus* 3% ~9 years after last screen in the NLST [4, 127]. Estimations of the degree of overdiagnosis in the NELSON trial show a similar trend, with 19.7% *versus* 8.9% at 4.5 and 5.5 years after final screening, respectively [5]. However, the exact degree of overdiagnosis in cancer screening trials is unknown due a number of factors: inadequate trial design, varying definitions of overdiagnosis and different methods used to estimate extent of overdiagnosis [120, 128]. Furthermore, due to high risks of bias associated with many randomised trials, the true extent of overdiagnosis is probably underestimated [128]. Microstimulation models may be useful tools to provide more accurate estimates on overdiagnosis for lung cancer screening programmes with designs and populations that differ from those considered in the NLST and other screening trials [120].

#### **Potential harms of overdiagnosis**

The consequences of overdiagnosis can be subdivided into four main domains of harm (physical effects, psychological effects, financial strain and opportunity costs) based on a proposed taxonomy [129]. Other potential downsides of overdiagnosis include the negative effects of receiving a medical (disease) label, side-effects of and quality of life affected by unneeded tests or treatment, large financial burden at an individual and healthcare system level, wasted resources and overmedicalisation of society [124, 125]. The key problem with overdiagnosis is that it may lead to overtreatment, either unnecessary or overaggressive [112, 122]. It is, therefore, imperative to prevent, or at least reduce, overdiagnosis in lung cancer screening.

#### **Potential strategies to reduce overdiagnosis**

Potential strategies to avoid overdiagnosis, thereby minimising overinvestigation and overtreatment, are highlighted by KAUCZOR *et al.* [16] as follows: 1) individualised lung cancer risk calculations and models; 2) conservative nonsurgical management (active surveillance) for ground-glass nodules according to guidelines; 3) volumetry-based management of nodules (calculating volume-doubling time); and 4) biennial LDCT scans (*versus* annual screening) [16, 130–132]. Another important strategy is to develop protocol thresholds during the baseline round of lung cancer screening that define positive results and recommendations for additional workup, thus eliminating unnecessary diagnostic tests [133, 134].

### **The challenge of overinvestigation (overtesting or overutilisation)**

Overinvestigation, also referred to as overtesting or overutilisation, is a growing problem for healthcare practitioners worldwide, given its link not only to overdiagnosis, but also other potential unintended harms, such as misdiagnosis, false positives and false negatives [122, 135]. Although not every instance of overuse leads to overdiagnosis, the risk of the latter is proportionate to the degree of the former [122]. Broadly speaking, overinvestigation consists of the needless medical tests (including diagnostic and screening tests) performed in both asymptomatic and symptomatic individuals, that are not medically necessary for proper clinical decision making or improving health outcomes, and in their absence would present few if any consequences to the patient [135, 136].

#### **Overinvestigation**

False positives are inevitable in screening. False positive rates in lung cancer screening can reach up to 13% and they are affected by a number of patient-specific and site-/radiologist-specific factors [137]. The false positive rate per screening round varies in lung cancer screening trials [138]. A significant concern with false positive results is that the use of finite healthcare resources (*i.e.* already overloaded lung cancer services) prevents their redistribution to patients with true positive results who would have benefited from tests, treatment and other interventions [135].

The mental health impacts of lung cancer screening, including psychological and social aspects, are largely unknown and not yet well understood [139, 140]. Existing evidence on the short- and long-term mental health effects of screening (including false positives and overdiagnosis) is limited [140]. Data in the literature support both the negative and positive effects of cancer screening on mental health [140]. The main issue with false positive results (indicating that the person possibly has the disease when they do not) in screening tests is the psychosocial toll they take on the recipient (*i.e.* generating stress and increasing anxiety, depression, post-traumatic stress disorder and suicide, as well as straining personal relationships) [138, 140, 141]. In the Danish Lung Cancer Screening Trial, an association between more negative short-term psychosocial consequences and false positives was found compared with the control group and true negatives [138]. In the NELSON trial, no negative effects were found in health-related quality of life (HRQoL) among 351 participants up to 6 months after CT scanning [142]; the only discomfort was reported in connection with having to wait for the results of the CT scan and dreading those results. At 2 years follow-up, the HRQoL of 733 screened subjects was similar to that of 733 control subjects; the unfavourable short-term effects of an indeterminate baseline screening result had resolved [143]. Quantification of the psychosocial effects of screening may be carried out using patient-reported outcome measures *via* self-reported questionnaires [139]. Clinicians can help alleviate patients' stress and improve adherence to screening by keeping them well-informed throughout the screening process and after receiving the results [139].

#### **The need for artificial intelligence and imaging biomarkers to reduce false positives and unnecessary investigations**

Artificial intelligence (AI), a term coined by John McCarthy in 1956, is the approach of using computers and technology to simulate human-like intelligent behaviour and critical thinking [144]. In LDCT screening for lung cancer, the application of AI in imaging diagnostics plays a key role in automatic nodule detection using a computer-aided detection system to reduce the burden of radiologists and identify lung structures suspected of malignancy [145, 146]. Effective nodule classification techniques, deep-learning application systems (*e.g.* convolutional neural networks) and radiomics can reduce false positive rates by increasing the sensitivity (accuracy) of screening and supporting the overall diagnosis and management of patients [146, 147]. Further advantages of integrating AI into lung cancer screening include reduction of radiation dose, enabling risk stratification and screening personalisation, and improving time to image interpretation [146]. In addition to AI, ongoing research points to the need for adjunctive testing using liquid biomarkers to complement imaging as a lung cancer screening tool to aid in early diagnosis of disease and risk prediction and decrease false positives [148]. Several biomarkers, such as autoantibodies and blood protein profiling, are currently available for clinical use, but many promising ones (*e.g.* autoantibodies, circulating tumour DNA, complement fragments, microRNA and DNA methylation) still require further validation studies [148]. The use of biomarkers in lung cancer screening will help optimise risk prediction models, improve diagnostic accuracy of indeterminate pulmonary nodules by enriching the screening population, and ultimately curtail the false positivity of LDCT scans and reduce the number of unnecessary referrals [148].

#### **Impact of lung cancer screening on surgical approaches**

Wide implementation of lung cancer screening is expected to increase early-stage lung cancer diagnosis by up to 70%, thereby shifting the stage distribution at the time of diagnosis [4–9]. Earlier lung cancer

stage is projected to increase the total lung cancer surgical volume and the proportion of lung-sparing surgery [149, 150]. Increased surgical volume will increase demand for theatre lists and thoracic surgery beds as well as pre-, peri- and post-operative care. Prolonged lung cancer screening implementation has also shown an upward trend in the incidence of carcinoma *in situ* and its precursor lesions, for which no robust management guidelines exist [149]. Despite the anticipated increasing trend in thoracic surgery volumes, the thoracic surgery workforce is projected to decrease, therefore creating a clear need for new post-surgical appointments [149, 151]. United States data predict a steady decrease of 25% in the number of practicing thoracic surgeons, from ~4000 surgeons in 2000 to ~3000 surgeons in 2050 [150]. Considering continued population growth and increasing life expectancy, the gap will widen further, resulting in the number of practising thoracic surgeons being half the number that is needed [152]. However, this gap is expected to narrow following long-term implementation of lung cancer screening programmes. Mathematical and simulation models have been applied in a Canadian lung cancer screening scenario and they considered lung cancer screening participation rate, clinical volume, retirement estimates and the number of new surgeons entering the workforce [153]. Following an initial increase, a subsequent fall in the surgical volume was predicted after the first 20 years of lung cancer screening implementation owing to a shift in the stages at diagnosis. Considering stages IA–IIIA as “operable lung cancer”, it has been forecast that the incidence of operable lung cancer per surgeon will reach 114 cases in 2030 [153]. Earlier stage at diagnosis in lung cancer screening participants that are asymptomatic and otherwise healthy will result in uneventful surgical resections with decreased hospital length of stay and subsequently increased income for the departments of thoracic surgery, as patients will stay fewer days than prognosticated by the insurance compensation policy, therefore utilising less hospital resources for the same compensation [154].

The technical challenge in early-stage lung cancer resection poses an important question for thoracic surgeons regarding the optimal surgical strategy to treat these patients. Minimally invasive access is preferred where applicable; however, there is an ongoing debate on whether a robotic approach is superior to video-assisted thoracic surgery (VATS) and whether the number of ports can affect clinical outcome (uniportal access *versus* two or three ports) [152, 154–156]. To date, there is no high-quality randomised controlled trial addressing the question of robotic surgery *versus* VATS for early-stage lung cancer, and no major survival or clinical benefit or difference in post-operative pain and recovery has been demonstrated between the various minimally invasive surgical approaches. A question that arises from the wider implementation of lung cancer screening programmes and their subsequent effect on surgical volume and caseload is what the impact of all this will be on thoracic surgery training overall.

#### **Impact of lung cancer screening on oncological treatments**

Lung cancer screening implementation is expected to offer a stage shift and diagnose up to 70% of cases in early-stage disease [4–9], which will impact on systemic and targeted treatments as well as immunotherapy offered in advanced-stage disease [157]. A recent cost-effectiveness analysis showed that earlier lung cancer diagnosis through lung cancer screening subsequently leads to reduced treatment costs. Lung cancer screening could potentially contribute to reducing the escalating costs associated with increasing cancer therapeutic related expenditures [158]. It can be assumed that stage shift at diagnosis will impact on the reduction of oncological workload relating to advanced stage patients and it will change the service delivery models in thoracic oncology to address the increasing needs of early-stage diagnosis. There is lack of real-world data to date regarding the financial and service impact of stage shift due to lung cancer screening. Following the implementation of national lung cancer screening programmes worldwide, it would be interesting for countries to share their data in this area and also present whether the stage shift at diagnosis has led to patient pathway review and redesign as well as to any changes in the delivery of healthcare models in thoracic oncology.

Lung cancer screening is anticipated to have an impact on the study landscape. Current research is mainly focused on therapeutic approaches for the treatment of advanced disease. However, implementation of lung cancer screening will result in a growing number of early-stage patients and a reducing number of advanced-stage patients. Clinical trials studying adjuvant and neoadjuvant treatment options at the early stage will become a priority and they will be even more meaningful in countries with national lung cancer screening programmes [159].

Table 2 summarises the impact of lung cancer screening on lung cancer services, services managing nonsuspicious findings, costs, overdiagnosis and overinvestigation, considerations for policies and procedures, as well as expert consensus advice.

**TABLE 2** Succinct presentation of the impact of lung cancer screening on lung cancer and non-lung cancer services, costs, overdiagnosis and overinvestigation in combination with relevant considerations for the development of policies and procedures, as well as expert consensus advice

	Policy/process considerations	Expert consensus advice
<b>Lung cancer clinic appointments and capacity</b>	Advanced planning across the pathway Encounter distribution and geographic accessibility of the respective healthcare services to patients/participants	1) Prior to implementation, assess staffing levels, infrastructure, resources and capacity 2) Complement with governance, quality assurance and outcome-reporting protocols 3) Accreditation of lung cancer screening centres 4) Adaptation of treatment capacity over time to meet the increasing demand
<b>Imaging/sampling investigations</b>	Increased number of imaging and sampling investigations, which are already in high demand Consider infrastructure and trained personnel	1) Explore the option of advanced devices that will allow more patient scans within the same timeframe 2) Structured radiology reporting to ensure better use of radiology reporting time and decrease serious incidents 3) Plan in advance the training of interventional radiologists and pulmonologists, to ensure that increased biopsy demand is met
<b>PFTs</b>	Consider the potential increase in demand for PFTs	Decentralise in outpatient clinics
<b>Smoking cessation services</b>	Consider the increased demand in combination with geographical variation and access	Plan additional smoking cessation infrastructure
<b>Costs</b>	Consider the variation of effectiveness, affordability, feasibility and cost-effectiveness of LDCT screening among healthcare systems with different readiness	Country-specific cost-effectiveness data prior to implementation and service design
<b>Services with nonsuspicious findings</b>	Increased risk of overloading noncancer services without a clear operating procedure	Establish structured radiology reporting and patient care pathways for nonsuspicious findings, to ensure a streamlined process
<b>Overdiagnosis</b>	Overdiagnosis will utilise further resources	Set up a multidisciplinary diagnostic management team of experts (radiologists, pulmonologists, thoracic surgeons) to discuss and assess cases
<b>Overinvestigation</b>	Overinvestigation will utilise further resources	Set up a multidisciplinary diagnostic management team of experts (radiologists, pulmonologists, thoracic surgeons) to discuss and assess cases and consider the adjuvant use of artificial intelligence where available
<b>Surgical procedures</b>	Reallocation of theatre slots and review of presurgical assessments due to the early-stage shift at diagnosis	Thoracic surgery workforce to train and adopt minimally invasive techniques
<b>Oncological treatments</b>	Reduced workload in advanced-stage patients will affect service delivery and policies need to be updated accordingly	Restructure lung cancer services planning to ensure increased capacity for early-stage <i>versus</i> advanced-stage disease Develop research on early-stage lung cancer

PFTs: pulmonary function tests; LDCT: low-density computed tomography.

### Conclusions

The wider implementation of lung cancer screening programmes is expected to change the landscape of lung cancer and healthcare professionals' perspective of managing the disease. Service capacity, infrastructure and resources need to be carefully studied on a regional and national level prior to wider lung cancer screening implementation. Furthermore, they should be adopted according to projected needs to ensure that lung cancer screening maximises its benefits without causing delays.

### Points for clinical practice

- Careful service mapping is required prior to lung cancer screening implementation.
- Projected needs derived from lung cancer screening should guide service development and inform changes in infrastructure and resources.
- Lung cancer screening participant pathways should be organised on a national/regional level to ensure smooth navigation.
- Flow diagrams for the management of lung cancer screening findings are required to inform meaningful referrals and reduce overdiagnosis, as appropriate.

Provenance: Commissioned article, peer reviewed.

Conflict of interest: All authors have nothing to disclose.

Support statement: A. Frille was supported by the postdoctoral fellowship “MetaRot programme” from the Federal Ministry of Education and Research (BMBF), Germany (FKZ 01EO1501, IFB Adiposity Diseases), a research grant from the “Mitteldeutsche Gesellschaft für Pneumologie (MDGP) e.V.” (2018-MDGP-PA-002), a junior research grant from the Medical Faculty, University of Leipzig (934100-012) and a graduate fellowship of the “Novartis-Stiftung für therapeutische Forschung”.

## References

- 1 Siegel RL, Miller KD, Wagle NS, *et al.* Cancer statistics, 2023. *CA Cancer J Clin* 2023; 73: 17–48.
- 2 International Agency for Research on Cancer. Lung Cancer Factsheet. Available from: <https://gco.iarc.fr/today/data/factsheets/cancers/15-trachea-bronchus-and-lung-fact-sheet.pdf> Date last accessed: 22 October 2023.
- 3 National Disease Registration Service. Cancer Stage at Diagnosis. <https://digital.nhs.uk/ndrs/data/data-outputs/cancer-data-hub/cancer-stage-at-diagnosis> Date last accessed: 28 October 2023.
- 4 The National Lung Screening Trial Research Team, Aberle DR, Adams AM, *et al.* Reduced lung-cancer mortality with low-dose computed tomographic screening. *N Engl J Med* 2011; 365: 395–409.
- 5 de Koning HJ, van der Aalst CM, de Jong PA, *et al.* Reduced lung-cancer mortality with volume CT screening in a randomized trial. *N Engl J Med* 2020; 382: 503–513.
- 6 Field JK, Vulkan D, Davies MPA, *et al.* Lung cancer mortality reduction by LDCT screening: UKLS randomised trial results and international meta-analysis. *Lancet Reg Health Eur* 2021; 10: 100179.
- 7 Becker N, Motsch E, Trotter A, *et al.* Lung cancer mortality reduction by LDCT screening – results from the randomized German LUSI trial. *Int J Cancer* 2020; 146: 1503–1513.
- 8 Infante M, Cavuto S, Lutman FR, *et al.* Long-term follow-up results of the DANTE trial, a randomized study of lung cancer screening with spiral computed tomography. *Am J Respir Crit Care Med* 2015; 191: 1166–1175.
- 9 Paci E, Puliti D, Lopes Pegna A, *et al.* Mortality, survival and incidence rates in the ITALUNG randomised lung cancer screening trial. *Thorax* 2017; 72: 825–831.
- 10 Aberle DR. Implementing lung cancer screening: the US experience. *Clin Radiol* 2017; 72: 401–406.
- 11 Larici AR, Farchione A, Franchi P, *et al.* Lung nodules: size still matters. *Eur Respir Rev* 2017; 26: 170025.
- 12 Lung Cancer Policy Network. Interactive Map of Lung Cancer Screening. 2024. <https://lungcancerpolicy.network.com/interactive-map-of-lung-cancer-screening/> Date last accessed: 12 March 2024.
- 13 Organisation for Economic Co-operation and Development. Croatia: Country Health Profile 2021. [www.oecd.org/countries/croatia/croatia-country-health-profile-2021-717e5510-en.htm](http://www.oecd.org/countries/croatia/croatia-country-health-profile-2021-717e5510-en.htm) Date last accessed: 22 October 2023. Date last updated: 13 December 2021.
- 14 Institute of Health Information and Statistics of the Czech Republic. PrevenceProPlice.cz – Early Detection Programme for Lung Cancer. 2022. <https://prevenceproplce.cz/en/> Date last accessed 22 October 2023.
- 15 Juskanic D, Sandor F, Denkova L, *et al.* Lung cancer screening initiative in Slovakia: guidelines of screening implementation. *Bratisl Lek Listy* 2023; 124: 109–115.
- 16 Kauczor HU, Baird AM, Blum TG, *et al.* ESR/ERS statement paper on lung cancer screening. *Eur Radiol* 2020; 30: 3277–3294.
- 17 Harris M, Thulesius H, Neves AL, *et al.* How European primary care practitioners think the timeliness of cancer diagnosis can be improved: a thematic analysis. *BMJ Open* 2019; 9: e030169.
- 18 Kauczor HU, Bonomo L, Gaga M, *et al.* ESR/ERS white paper on lung cancer screening. *Eur Respir J* 2015; 46: 28–39.
- 19 Baldwin D, O’Dowd E, Tietzova I, *et al.* Developing a pan-European technical standard for a comprehensive high-quality lung cancer CT screening program. An ERS technical standard. *Eur Respir J* 2023; 61: 2300128.
- 20 O’Dowd EL, Tietzova I, Bartlett E, *et al.* ERS/ESTS/ESTRO/ESR/ESTI/EFOMP statement on management of incidental findings from low dose CT screening for lung cancer. *Eur Respir J* 2023; 62: 2300533.
- 21 Hardavella G, Frille A, Theochari C, *et al.* Multidisciplinary care models for patients with lung cancer. *Breathe* 2020; 16: 200076.
- 22 Shemesh J, Henschke CI, Farooqi A, *et al.* Frequency of coronary artery calcification on low-dose computed tomography screening for lung cancer. *Clin Imaging* 2006; 30: 181–185.
- 23 Morgan L, Choi H, Reid M, *et al.* Frequency of incidental findings and subsequent evaluation in low-dose computed tomographic scans for lung cancer screening. *Ann Am Thorac Soc* 2017; 14: 1450–1456.
- 24 Bartlett EC, Belsey J, Derbyshire J, *et al.* Implications of incidental findings from lung screening for primary care: data from a UK pilot. *NPJ Prim Care Respir Med* 2021; 31: 36.
- 25 Muriana P, Rossetti F, Novellis P, *et al.* Lung cancer screening: the European perspective. *Thorac Surg Clin* 2023; 33: 375–383.

- 26 Lam DC, Liam CK, Andarini S, et al. Lung cancer screening in Asia: an expert consensus report. *J Thorac Oncol* 2023; 18: 1303–1322.
- 27 Wolf AMD, Oeffinger KC, Shih TY, et al. Screening for lung cancer: 2023 guideline update from the American Cancer Society. *CA Cancer J Clin* 2024; 74: 50–81.
- 28 Silvestri GA, Goldman L, Tanner NT, et al. Outcomes from more than 1 million people screened for lung cancer with low-dose CT imaging. *Chest* 2023; 164: 241–251.
- 29 Park S, Choi C-M, Hwang S-S, et al. Lung cancer in Korea. *J Thorac Oncol* 2021; 16: 1988–1993.
- 30 Health Promotion Administration, Ministry of Health and Welfare. 2022. The First Country to Provide Lung Cancer Screening for Citizens with a Family History of Lung Cancer or a History of Heavy Smoking: the Lung Cancer Early Detection Program was Launched on July 1, 2022. [www.hpa.gov.tw/EngPages/Detail.aspx?nodeid=1051&pid=16553](http://www.hpa.gov.tw/EngPages/Detail.aspx?nodeid=1051&pid=16553) Date last accessed: 4 June 2024. Date last updated: 13 January 2023.
- 31 Yang P, Chang G, Chiu C, et al. Real-World Data From Taiwan Shows Stage Shift has Improved Lung Cancer Survival Rates. [www.ilcn.org/real-world-data-from-taiwan-shows-stage-shift-has-improved-lung-cancer-survival-rates/](http://www.ilcn.org/real-world-data-from-taiwan-shows-stage-shift-has-improved-lung-cancer-survival-rates/) Date last accessed: 8 March 2024. Date last updated: 7 June 2022.
- 32 Chudgar NP, Stiles BM. Building a lung cancer screening program. *Thorac Surg Clin* 2023; 33: 333–341.
- 33 Rankin NM, McWilliams A, Marshall HM. Lung cancer screening implementation: complexities and priorities. *Respirology* 2020; 25: Suppl. 2, 5–23.
- 34 Blom EF, Ten Haaf K, Arenberg DA, et al. Treatment capacity required for full-scale implementation of lung cancer screening in the United States. *Cancer* 2019; 125: 2039–2048.
- 35 Doogan NJ, Roberts ME, Wewers ME, et al. A growing geographic disparity: rural and urban cigarette smoking trends in the United States. *Prev Med* 2017; 104: 79–85.
- 36 Sone S, Takashima S, Li F, et al. Mass screening for lung cancer with mobile spiral computed tomography scanner. *Lancet* 1998; 351: 1242–1245.
- 37 Raghavan D, Wheeler M, Doege D, et al. Initial results from mobile low-dose computerized tomographic lung cancer screening unit: improved outcomes for underserved populations. *Oncologist* 2020; 25: e777–e781.
- 38 de Koning HJ, Meza R, Plevritis SK, et al. Benefits and harms of computed tomography lung cancer screening strategies: a comparative modeling study for the U.S. Preventive Services Task Force. *Ann Intern Med* 2014; 160: 311–320.
- 39 Ten Haaf K, Tammemägi MC, Bondy SJ, et al. Performance and cost-effectiveness of computed tomography lung cancer screening scenarios in a population-based setting: a microsimulation modeling analysis in Ontario, Canada. *PLoS Med* 2017; 14: e1002225.
- 40 Hardavella G, Charpidou A, Frille A, et al. Lung cancer and inequalities in access to multidisciplinary lung cancer services. In: Sinha IP, Lee A, Katikireddi SV, et al., eds. *Inequalities in Respiratory Health (ERS Monograph)*. Sheffield, European Respiratory Society, 2023; pp. 153–166.
- 41 MacMahon H, Naidich DP, Goo JM, et al. Guidelines for management of incidental pulmonary nodules detected on CT images: from the Fleischner Society 2017. *Radiology* 2017; 284: 228–243.
- 42 Boellaard R, Delgado-Bolton R, Oyen WJ, et al. FDG PET/CT: EANM procedure guidelines for tumour imaging: version 2.0. *Eur J Nucl Med Mol Imaging* 2015; 42: 328–354.
- 43 Nadig V, Herrmann K, Mottaghy FM, et al. Hybrid total-body PET scanners – current status and future perspectives. *Eur J Nucl Med Mol Imaging* 2022; 49: 445–459.
- 44 Alberts I, Sari H, Mingels C, et al. Long-axial field-of-view PET/CT: perspectives and review of a revolutionary development in nuclear medicine based on clinical experience in over 7000 patients. *Cancer Imaging* 2023; 23: 28.
- 45 Cardillo G, Petersen RH, Ricciardi S, et al. European guidelines for the surgical management of pure ground-glass opacities and part-solid nodules: Task Force of the European Association of Cardio-Thoracic Surgery and the European Society of Thoracic Surgeons. *Eur J Cardiothorac Surg* 2023; 64: ezad222.
- 46 Deng CJ, Dai FQ, Qian K, et al. Clinical updates of approaches for biopsy of pulmonary lesions based on systematic review. *BMC Pulm Med* 2018; 18: 146.
- 47 Planchard D, Popat S, Kerr K, et al. Metastatic non-small cell lung cancer: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. *Ann Oncol* 2018; 29: Suppl. 4, iv192–iv237.
- 48 Kalanjeri S, Abbasi A, Luthra M, et al. Invasive modalities for the diagnosis of peripheral lung nodules. *Expert Rev Respir Med* 2021; 15: 781–790.
- 49 Grosu HB, Eapen GA, Jimenez CA, et al. Lung cancer screening: making the transition from research to clinical practice. *Curr Opin Pulm Med* 2012; 18: 295–303.
- 50 Brunelli A, Charloux A, Bolliger CT, et al. ERS/ESTS clinical guidelines on fitness for radical therapy in lung cancer patients (surgery and chemo-radiotherapy). *Eur Respir J* 2009; 34: 17–41.
- 51 Krist AH, Davidson KW, Mangione CM, et al. Screening for lung cancer: US Preventive Services Task Force recommendation statement. *JAMA* 2021; 325: 962–970.
- 52 National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology: Lung Cancer Screening (version 2.2024). 2023. [www.nccn.org/professionals/physician\\_gls/pdf/lung\\_screening.pdf](http://www.nccn.org/professionals/physician_gls/pdf/lung_screening.pdf) Date last updated: 18 October 2023.

- 53 Edelman Saul E, Guerra RB, Edelman Saul M, *et al.* The challenges of implementing low-dose computed tomography for lung cancer screening in low- and middle-income countries. *Nat Cancer* 2020; 1: 1140–1152.
- 54 Tanoue LT, Sather P, Cortopassi I, *et al.* Standardizing the reporting of incidental, non-lung cancer (category S) findings identified on lung cancer screening low-dose CT imaging. *Chest* 2022; 161: 1697–1706.
- 55 Tisi S, Creamer AW, Dickson J, *et al.* Prevalence and clinical characteristics of non-malignant CT detected incidental findings in the SUMMIT lung cancer screening cohort. *BMJ Open Respir Res* 2023; 10: e001664.
- 56 van de Wiel JCM, Wang Y, Xu DM, *et al.* Neglectable benefit of searching for incidental findings in the Dutch–Belgian lung cancer screening trial (NELSON) using low-dose multidetector CT. *Eur Radiol* 2007; 17: 1474–1482.
- 57 Gareen IF, Gutman R, Sicks J, *et al.* Significant incidental findings in the National Lung Screening Trial. *JAMA Intern Med* 2023; 183: 677–684.
- 58 Janssen K, Schertz K, Rubin N, *et al.* Incidental findings in a decentralized lung cancer screening program. *Ann Am Thorac Soc* 2019; 16: 1198–1201.
- 59 Priola AM, Priola SM, Giaj-Levra M, *et al.* Clinical implications and added costs of incidental findings in an early detection study of lung cancer by using low-dose spiral computed tomography. *Clin Lung Cancer* 2013; 14: 139–148.
- 60 Yang J, Liao M, Wang Y, *et al.* Opportunistic osteoporosis screening using chest CT with artificial intelligence. *Osteoporos Int* 2022; 33: 2547–2561.
- 61 Mulshine JL, Aldigé CR, Ambrose LF, *et al.* Emphysema detection in the course of lung cancer screening: optimizing a rare opportunity to impact population health. *Ann Am Thorac Soc* 2023; 20: 499–503.
- 62 Munden RF, Black WC, Hartman TE, *et al.* Managing incidental findings on thoracic CT: lung findings. A white paper of the ACR incidental findings committee. *J Am Coll Radiol* 2021; 18: 1267–1279.
- 63 Munden RF, Carter BW, Chiles C, *et al.* Managing incidental findings on thoracic CT: mediastinal and cardiovascular findings. A white paper of the ACR incidental findings committee. *J Am Coll Radiol* 2018; 15: 1087–1096.
- 64 Herts BR, Silverman SG, Hindman NM, *et al.* Management of the incidental renal mass on CT: a white paper of the ACR incidental findings committee. *J Am Coll Radiol* 2018; 15: 264–273.
- 65 Gore RM, Pickhardt PJ, Morteale KJ, *et al.* Management of incidental liver lesions on CT: a white paper of the ACR incidental findings committee. *J Am Coll Radiol* 2017; 14: 1429–1437.
- 66 Mayo-Smith WW, Song JH, Boland GL, *et al.* Management of incidental adrenal masses: a white paper of the ACR incidental findings committee. *J Am Coll Radiol* 2017; 14: 1038–1044.
- 67 Megibow AJ, Baker ME, Morgan DE, *et al.* Management of incidental pancreatic cysts: a white paper of the ACR incidental findings committee. *J Am Coll Radiol* 2017; 14: 911–923.
- 68 Hoang JK, Langer JE, Middleton WD, *et al.* Managing incidental thyroid nodules detected on imaging: white paper of the ACR incidental thyroid findings committee. *J Am Coll Radiol* 2015; 12: 143–150.
- 69 Agatston AS, Janowitz WR, Hildner FJ, *et al.* Quantification of coronary artery calcium using ultrafast computed tomography. *J Am Coll Cardiol* 1990; 15: 827–832.
- 70 Detrano R, Guerci AD, Carr JJ, *et al.* Coronary calcium as a predictor of coronary events in four racial or ethnic groups. *N Engl J Med* 2008; 358: 1336–1345.
- 71 Erbel R, Möhlenkamp S, Moebus S, *et al.* Coronary risk stratification, discrimination, and reclassification improvement based on quantification of subclinical coronary atherosclerosis: the Heinz Nixdorf Recall study. *J Am Coll Cardiol* 2010; 56: 1397–1406.
- 72 Nasir K, Cainzos-Achirica M. Role of coronary artery calcium score in the primary prevention of cardiovascular disease. *BMJ* 2021; 373: n776.
- 73 Bradley P, Bola BM, Balata H, *et al.* Incidental findings in low dose CT lung cancer screening of high-risk smokers: results from the Manchester Lung Health Check pilot. *Lung Cancer* 2022; 173: 1–4.
- 74 Chiles C, Duan F, Gladish GW, *et al.* Association of coronary artery calcification and mortality in the national lung screening trial: a comparison of three scoring methods. *Radiology* 2015; 276: 82–90.
- 75 Sandhu AT, Rodriguez F, Ngo S, *et al.* Incidental coronary artery calcium: opportunistic screening of previous nongated chest computed tomography scans to improve statin rates (NOTIFY-1 project). *Circulation* 2023; 147: 703–714.
- 76 Yokota S, Mouden M, Ottervanger JP, *et al.* Coronary calcium score influences referral for invasive coronary angiography after normal myocardial perfusion SPECT. *J Nucl Cardiol* 2019; 26: 602–612.
- 77 Sabia F, Balbi M, Ledda RE, *et al.* Fully automated calcium scoring predicts all-cause mortality at 12 years in the MILD lung cancer screening trial. *PLoS One* 2023; 18: e0285593.
- 78 Dzaye O, Berning P, Dardari ZA, *et al.* Coronary artery calcium is associated with long-term mortality from lung cancer: results from the Coronary Artery Calcium Consortium. *Atherosclerosis* 2021; 339: 48–54.
- 79 Gazourian L, Regis SM, Pagura EJ, *et al.* Qualitative coronary artery calcification scores and risk of all cause, COPD and pneumonia hospital admission in a large CT lung cancer screening cohort. *Respir Med* 2021; 186: 106540.

- 80 Mascalchi M, Puliti D, Romei C, *et al.* Moderate-severe coronary calcification predicts long-term cardiovascular death in CT lung cancer screening: the ITALUNG trial. *Eur J Radiol* 2021; 145: 110040.
- 81 Mach F, Baigent C, Catapano AL, *et al.* 2019 ESC/EAS guidelines for the management of dyslipidaemias: lipid modification to reduce cardiovascular risk. *Atherosclerosis* 2019; 290: 140–205.
- 82 Arnett DK, Blumenthal RS, Albert MA, *et al.* 2019 ACC/AHA guideline on the primary prevention of cardiovascular disease: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. *Circulation* 2019; 140: e596–e646.
- 83 Piepoli MF, Abreu A, Albus C, *et al.* Update on cardiovascular prevention in clinical practice: a position paper of the European Association of Preventive Cardiology of the European Society of Cardiology. *Eur J Prev Cardiol* 2020; 27: 181–205.
- 84 Grundy SM, Stone NJ, Bailey AL, *et al.* 2018 AHA/ACC/AACVPR/AAPA/ABC/ACPM/ADA/AGS/APhA/ASPC/NLA/PCNA guideline on the management of blood cholesterol: a report of the American College of Cardiology/American Heart Association task force on clinical practice guidelines. *Circulation* 2019; 139: e1082–e1143.
- 85 Denissen SJAM, van der Aalst CM, Vonder M, *et al.* Screening for coronary artery calcium in a high-risk population: the ROBINSCA trial. *Eur J Prev Cardiol* 2021; 28: 1155–1159.
- 86 Yang X, Wisselink HJ, Vliegenthart R, *et al.* Association between chest CT-defined emphysema and lung cancer: a systematic review and meta-analysis. *Radiology* 2022; 304: 322–330.
- 87 Hunsaker AR. Emphysema as a predictor of lung cancer: implications for lung cancer screening. *Radiology* 2022; 304: 331–332.
- 88 Labaki WW, Xia M, Murray S, *et al.* Quantitative emphysema on low-dose CT imaging of the chest and risk of lung cancer and airflow obstruction: an analysis of the National Lung Screening Trial. *Chest* 2021; 159: 1812–1820.
- 89 Cavigli E, Camiciottoli G, Diciotti S, *et al.* Whole-lung densitometry *versus* visual assessment of emphysema. *Eur Radiol* 2009; 19: 1686–1692.
- 90 Mascalchi M, Camiciottoli G, Diciotti S. Lung densitometry: why, how and when. *J Thorac Dis* 2017; 9: 3319–3345.
- 91 Mascalchi M, Romei C, Marzi C, *et al.* Pulmonary emphysema and coronary artery calcifications at baseline LDCT and long-term mortality in smokers and former smokers of the ITALUNG screening trial. *Eur Radiol* 2023; 33: 3115–3123.
- 92 Henschke CI, Yip R, Boffetta P, *et al.* CT screening for lung cancer: importance of emphysema for never smokers and smokers. *Lung Cancer* 2015; 88: 42–47.
- 93 Lee JE, Jeong WG, Lee HJ, *et al.* Relationship between incidental abnormalities on screening thoracic computed tomography and mortality: a long-term follow-up analysis. *Korean J Radiol* 2022; 23: 998–1008.
- 94 Kaplan A, Thomas M. Screening for COPD: the gap between logic and evidence. *Eur Respir Rev* 2017; 26: 160113.
- 95 Çolak Y, Afzal S, Nordestgaard BG, *et al.* Prognosis of asymptomatic and symptomatic, undiagnosed COPD in the general population in Denmark: a prospective cohort study. *Lancet Respir Med* 2023; 5: 426–434.
- 96 Sanchez-Carpintero Abad M, Sanchez-Salcedo P, de-Torres JP, *et al.* Prevalence and burden of bronchiectasis in a lung cancer screening program. *PLoS One* 2020; 15: e0231204.
- 97 Cai Q, Triphuridat N, Zhu Y, *et al.* Bronchiectasis in low-dose CT screening for lung cancer. *Radiology* 2022; 304: 437–447.
- 98 Verschakelen JA. Reporting bronchiectasis in low-dose CT screening for lung cancer? *Radiology* 2022; 304: 448–449.
- 99 Hatabu H, Hunninghake GM, Richeldi L, *et al.* Interstitial lung abnormalities detected incidentally on CT: a position paper from the Fleischner Society. *Lancet Respir Med* 2020; 8: 726–737.
- 100 Grant-Orser A, Min B, Elmrayed S, *et al.* Prevalence, risk factors, and outcomes of adult interstitial lung abnormalities: a systematic review and meta-analysis. *Am J Respir Crit Care Med* 2023; 208: 695–708.
- 101 Upperton S, Beirne P, Bhartia B, *et al.* Diagnoses and treatments for participants with interstitial lung abnormalities detected in the Yorkshire Lung Screening Trial. *BMJ Open Respir Res* 2023; 10: e001490.
- 102 Camacho PM, Petak SM, Binkley N, *et al.* American Association of Clinical Endocrinologists/American College of Endocrinology Clinical guidelines for the diagnosis and treatment of postmenopausal osteoporosis – 2020 update. Executive summary. *Endocr Pract* 2020; 26: 564–570.
- 103 O’Kelly J, Bartsch R, Kossack N, *et al.* Real-world effectiveness of osteoporosis treatments in Germany. *Arch Osteoporos* 2022; 17: 119.
- 104 Bartalena T, Giannelli G, Rinaldi MF, *et al.* Prevalence of thoracolumbar vertebral fractures on multidetector CT: underreporting by radiologists. *Eur J Radiol* 2009; 69: 555–559.
- 105 Buckens CF, van der Graaf Y, Verkooijen HM, *et al.* Osteoporosis markers on low-dose lung cancer screening chest computed tomography scans predict all-cause mortality. *Eur Radiol* 2015; 25: 132–139.
- 106 Bolland MJ, Grey AB, Gamble GD, *et al.* Effect of osteoporosis treatment on mortality: a meta-analysis. *J Clin Endocrinol Metab* 2010; 95: 1174–1181.



- 107 Chung JH. Shedding light on incidental findings on low-dose lung cancer screening chest computed tomography. *Ann Am Thorac Soc* 2017; 14: 1393–1394.
- 108 Crothers K, Shahrir S, Kross EK, et al. Patient and clinician recommendations to improve communication and understanding of lung cancer screening results. *Chest* 2023; 163: 707–718.
- 109 American College of Radiology. ACR® Lung Cancer Screening CT Incidental Findings Quick Reference Guide. 2022. <https://acr.org/Clinical-Resources/Lung-Cancer-Screening-Resources>
- 110 Dyer DS, White C, Conley Thomson C, et al. A quick reference guide for incidental findings on lung cancer screening CT examinations. *J Am Coll Radiol* 2023; 20: 162–172.
- 111 Yankelevitz DF, Henschke CI. Overdiagnosis in lung cancer screening. *Transl Lung Cancer Res* 2021; 10: 1136–1140.
- 112 Patz EF Jr, Goodman PC, Bepler G. Screening for lung cancer. *N Engl J Med* 2000; 343: 1627–1633.
- 113 Reich JM. A critical appraisal of overdiagnosis: estimates of its magnitude and implications for lung cancer screening. *Thorax* 2008; 63: 377–383.
- 114 Mortani Barbosa EJ Jr. Lung cancer screening overdiagnosis: reports of overdiagnosis in screening for lung cancer are grossly exaggerated. *Acad Radiol* 2015; 22: 976–982.
- 115 Dettlerbeck FC. Overdiagnosis during lung cancer screening: is it an overemphasised, underappreciated, or tangential issue? *Thorax* 2014; 69: 407–408.
- 116 Brodersen J, Schwartz LM, Woloshin S. Overdiagnosis: how cancer screening can turn indolent pathology into illness. *APMIS* 2014; 122: 683–689.
- 117 Veronesi G, Maisonneuve P, Bellomi M, et al. Estimating overdiagnosis in low-dose computed tomography screening for lung cancer: a cohort study. *Ann Intern Med* 2012; 157: 776–784.
- 118 Heleno B, Siersma V, Brodersen J. Estimation of overdiagnosis of lung cancer in low-dose computed tomography screening: a secondary analysis of the Danish Lung Cancer Screening Trial. *JAMA Intern Med* 2018; 178: 1420–1422.
- 119 Amicizia D, Piazza MF, Marchini F, et al. Systematic review of lung cancer screening: advancements and strategies for implementation. *Healthcare* 2023; 11: 2085.
- 120 Ten Haaf K, de Koning HJ. Overdiagnosis in lung cancer screening: why modelling is essential. *J Epidemiol Community Health* 2015; 69: 1035–1039.
- 121 Brodersen J. How to conduct research on overdiagnosis. A keynote paper from the EGPRN May 2016, Tel Aviv. *Eur J Gen Pract* 2017; 23: 78–82.
- 122 Brodersen J, Schwartz LM, Heneghan C, et al. Overdiagnosis: what it is and what it isn't. *BMJ Evid Based Med* 2018; 23: 1–3.
- 123 Marcus PM, Prorok PC, Miller AB, et al. Conceptualizing overdiagnosis in cancer screening. *J Natl Cancer Inst* 2015; 107: djv014.
- 124 Moynihan R, Doust J, Henry D. Preventing overdiagnosis: how to stop harming the healthy. *BMJ* 2012; 344: e3502.
- 125 McCaffery KJ, Jansen J, Scherer LD, et al. Walking the tightrope: communicating overdiagnosis in modern healthcare. *BMJ* 2016; 352: i348.
- 126 Callister MEJ, Sasieni P, Robbins HA. Overdiagnosis in lung cancer screening. *Lancet Respir Med* 2021; 9: 7–9.
- 127 Patz EF Jr, Pinsky P, Gatsonis C, et al. Overdiagnosis in low-dose computed tomography screening for lung cancer. *JAMA Intern Med* 2014; 174: 269–274.
- 128 Voss T, Krag M, Martiny F, et al. Quantification of overdiagnosis in randomised trials of cancer screening: an overview and re-analysis of systematic reviews. *Cancer Epidemiol* 2023; 84: 102352.
- 129 Harris RP, Sheridan SL, Lewis CL, et al. The harms of screening: a proposed taxonomy and application to lung cancer screening. *JAMA Intern Med* 2014; 174: 281–285.
- 130 Katki HA, Kovalchik SA, Berg CD, et al. Development and validation of risk models to select ever-smokers for CT lung cancer screening. *JAMA* 2016; 315: 2300–2311.
- 131 Silva M, Sverzellati N, Manna C, et al. Long-term surveillance of ground-glass nodules: evidence from the MILD trial. *J Thorac Oncol* 2012; 7: 1541–1546.
- 132 Revel MP. Avoiding overdiagnosis in lung cancer screening: the volume doubling time strategy. *Eur Respir J* 2013; 42: 1459–1463.
- 133 Sverzellati N, Silva M, Calareso G, et al. Low-dose computed tomography for lung cancer screening: comparison of performance between annual and biennial screen. *Eur Radiol* 2016; 26: 3821–3829.
- 134 Henschke CI, Yip R, Ma T, et al. CT screening for lung cancer: comparison of three baseline screening protocols. *Eur Radiol* 2019; 29: 5217–5226.
- 135 Lam JH, Pickles K, Stanaway FF, et al. Why clinicians overtest: development of a thematic framework. *BMC Health Serv Res* 2020; 20: 1011.
- 136 Greenberg J, Green JB. Over-testing: why more is not better. *Am J Med* 2014; 127: 362–363.
- 137 Hammer MM, Byrne SC, Kong CY. Factors influencing the false positive rate in CT lung cancer screening. *Acad Radiol* 2022; 29: Suppl. 2, S18–S22.

- 138 Rasmussen JF, Siersma V, Malmqvist J, *et al.* Psychosocial consequences of false positives in the Danish Lung Cancer CT Screening Trial: a nested matched cohort study. *BMJ Open* 2020; 10: e034682.
- 139 Kim A, Chung KC, Keir C, *et al.* Patient-reported outcomes associated with cancer screening: a systematic review. *BMC Cancer* 2022; 22: 223.
- 140 Wadsworth LP, Wessman I, Björnsson AS, *et al.* The half-painted picture: reviewing the mental health impacts of cancer screening. *Medicine* 2022; 101: e30479.
- 141 White T, Algeri S. Estimating the lifetime risk of a false positive screening test result. *PLoS One* 2023; 18: e0281153.
- 142 van den Bergh KA, Essink-Bot ML, Bunge EM, *et al.* Impact of computed tomography screening for lung cancer on participants in a randomized controlled trial (NELSON trial). *Cancer* 2008; 113: 396–404.
- 143 van den Bergh KA, Essink-Bot ML, Borsboom GJ, *et al.* Short-term health-related quality of life consequences in a lung cancer CT screening trial (NELSON). *Br J Cancer* 2010; 102: 27–34.
- 144 Amisha, Malik P, Pathania M, *et al.* Overview of artificial intelligence in medicine. *J Family Med Prim Care* 2019; 8: 2328–2331.
- 145 Joy Mathew C, David AM, Joy Mathew CM. Artificial intelligence and its future potential in lung cancer screening. *EXCLI J* 2020; 19: 1552–1562.
- 146 Cellina M, Cacioppa LM, Cè M, *et al.* Artificial intelligence in lung cancer screening: the future is now. *Cancers* 2023; 15: 4344.
- 147 Ladbury C, Amini A, Govindarajan A, *et al.* Integration of artificial intelligence in lung cancer: rise of the machine. *Cell Rep Med* 2023; 4: 100933.
- 148 Marmor HN, Zorn JT, Deppen SA, *et al.* Biomarkers in lung cancer screening: a narrative review. *Curr Chall Thorac Surg* 2023; 5: 5.
- 149 Hung YC, Tang EK, Wu YJ, *et al.* Impact of low-dose computed tomography for lung cancer screening on lung cancer surgical volume: the urgent need in health workforce education and training. *Medicine* 2021; 100: e26901.
- 150 Dhanasopon AP, Kim AW. Lung cancer screening and its impact on surgical volume. *Surg Clin North Am* 2017; 97: 751–762.
- 151 Williams TE Jr, Satiani B, Thomas A, *et al.* The impending shortage and the estimated cost of training the future surgical workforce. *Ann Surg* 2009; 250: 590–597.
- 152 Perna V, Carvajal AF, Torrecilla JA, *et al.* Uniportal video-assisted thoracoscopic lobectomy versus other video-assisted thoracoscopic lobectomy techniques: a randomized study. *Eur J Cardiothorac Surg* 2016; 50: 411–415.
- 153 Edwards JP, Datta I, Hunt JD, *et al.* The impact of computed tomographic screening for lung cancer on the thoracic surgery workforce. *Ann Thorac Surg* 2014; 98: 447–452.
- 154 Sundaresan S, McLeod R, Irish J, *et al.* Early results after regionalization of thoracic surgical practice in a single-payer system. *Ann Thorac Surg* 2013; 95: 472–478.
- 155 Yang HX, Woo KM, Sima CS, *et al.* Long-term survival based on the surgical approach to lobectomy for clinical stage I nonsmall cell lung cancer: comparison of robotic, video-assisted thoracic surgery, and thoracotomy lobectomy. *Ann Surg* 2017; 265: 431–437.
- 156 AlGhamdi ZM, Lynhiavu L, Moon YK, *et al.* Comparison of non-intubated versus intubated video-assisted thoracoscopic lobectomy for lung cancer. *J Thorac Dis* 2018; 10: 4236–4243.
- 157 Leighl NB, Nirmalakumar S, Ezeife DA, *et al.* An arm and a leg: the rising cost of cancer drugs and impact on access. *Am Soc Clin Oncol Educ Book* 2021; 41: 1–12.
- 158 Pan X, Dvortsin E, Baldwin DR, *et al.* Cost-effectiveness of volume computed tomography in lung cancer screening: a cohort simulation based on Nelson study outcomes. *J Med Econ* 2024; 27: 27–38.
- 159 Kocher F, Pall G. Lung cancer screening from the oncologist's perspective. *Memo* 2019; 12: 175–178.