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# Building the Business Case for a National Lung Cancer Screening Programme

[Country]

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# Introduction and how to use this document

'*Building the Business Case*' provides a flexible, easy-to-use package of carefully researched information and evidence to customise with local data to build the business case for a national lung cancer screening programme in your country. The materials are designed to support you in discussions around developing a national lung cancer screening programme in your country. They bring together the key background information, figures, evidence and protocols for national lung cancer screening programmes to screen people at high-risk for lung cancer in order to diagnose and treat early when the disease is potentially curable.

This package is provided as a word document for you to draw on and adapt to develop your own materials to meet local needs in arguing the case for a national lung cancer screening programme in your country. You can customise the information to the situation to your country by inserting local figures where indicated [shown in blue type in square brackets] or use the figures provided if local data are not available. The *Further Resources* section provides links to additional materials on lung cancer screening.

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# Executive summary: the business case for a national lung cancer screening programme

A national lung cancer screening programme is a key measure to reduce the huge burden that the disease currently imposes on the individuals affected, their families and the country and healthcare system as a whole.

Lung cancer kills more people than any other cancer worldwide (18.0% of all cancer deaths) and causes more deaths than breast and colorectal cancers combined – cancers for which many countries already have population-based screening programmes (IARC 2020; Bray 2018; Field 2016).

Lung cancer has worse survival than most other cancers. The five-year survival rate from lung cancer is only 10-20% in most countries (Sung 2021), which is among the lowest survival rates for all types of cancer (Cancer Research UK 2019). The poor survival is largely due to most people with lung cancer being diagnosed at a late stage.

Lung cancer is associated with higher costs than other cancers due to the relatively high incidence and high mortality.

COVID-19 has dramatically reduced lung cancer referral rates and reduced early diagnosis from incidental findings, driving an urgent need for greater efforts to detect lung cancer earlier.

Lung cancer screening with a non-invasive scan of the lungs (low-dose computed tomography [LDCT]) saves lives by detecting the disease at an early stage when it is potentially curable. A recent large clinical trial of LDCT screening showed a 24% reduction in lung cancer mortality in men and a 33% reduction in women at 10 years of follow-up compared to no screening (de Koning 2020).

Tobacco smoking is, by far, the single biggest risk factor for lung cancer making it simple to identify high-risk people (smokers and ex-smokers) who should be screened for the disease.

Screening high-risk individuals for lung cancer with LDCT is cost-effective. The cost per quality-adjusted life year (QALY) (an estimate that combines years of life with quality of life after a particular health intervention) is within the range considered to be acceptable value for money for public health interventions.

The proposed national lung cancer screening programme will support the early detection of lung cancer by identifying and screening asymptomatic high-risk individuals (smokers and ex-smokers) with LDCT.

In the first 10 years of the lung cancer screening programme in [country] it is estimated that:

- [xxxx] lung cancer deaths would be prevented
- [xx-xx] QALYs would be gained
- [xx] % of all screen-detected lung cancers would be diagnosed at an early stage compared to less than [xx] % of lung cancers currently detected at an early stage in [country]

# The case for a national lung cancer screening programme in [country]

A national lung cancer screening programme is a key measure to reduce the huge burden that lung cancer currently imposes on the individuals affected, their families, the healthcare system and the country as a whole.

## What is lung cancer screening?

Lung cancer screening uses a non-invasive scan of the lungs (low-dose computed tomography [LDCT]) to detect lung cancer at an early stage in apparently healthy people who are at high risk for the disease (smokers and ex-smokers).

- The aim of screening for lung cancer is to diagnose and treat early when the disease is potentially curable

## Why should lung cancer be a high priority for screening?

### Lung cancer is common, deadly and costly …

### Lung cancer is the [second] most commonly diagnosed cancer in [country]

Lung cancer is the second most commonly diagnosed cancer globally, with an estimated 2.2 million new cases each year; it accounts for 11.4% of all cancers diagnosed each year (Sung 2021).

- Lung cancer is the most commonly diagnosed cancer in men in 36 countries across the world while in women it ranks third for incidence after breast and colorectal cancer (Sung 2021)
- In many countries, the number of people being diagnosed with lung cancer is showing an increasing trend, particularly in women, with the number increasing each year (Sung 2021). This increase is predicted to continue to increase over the next few years due to population growth and ageing

[For countries adding national figures]
The number of people diagnosed with lung cancer cases in [year] was [number of cases]: [number of cases] in men and [number of cases] in women. This is [xx]% of all cancers diagnosed each year in [country].

The incidence of lung cancer is about [number of cases per 100 000 people] per 100 000 people.

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## Lung cancer kills more people than any other cancer in [country]

Lung cancer is by far the leading cause of cancer death in [country] and worldwide (accounting for 18.0% of all cancer deaths globally) (Sung 2021).

- Lung cancer causes more deaths than breast and colorectal cancers combined – cancers for which many countries already have population-based screening programmes (Sung 2021; IARC 2020; Bray 2018; Field 2016)

[For countries adding national figures]
Latest figures show that [number of lung cancer deaths each year] people die from lung cancer each year in [country]. This is [xx]% of all cancer-related deaths in [country].

## Lung cancer has worse survival than most other cancers

The five-year survival rate from lung cancer for all stages is only 10-20% in most countries, which means that fewer than one in five people survive for five years or longer after being diagnosed (Sung 2021). This is among the lowest survival rates for all types of cancer (Cancer Research UK 2019).

- The poor survival is largely due to people with lung cancer being diagnosed at a late stage. Around three-quarters of patients with lung cancer present at a late stage at which treatment is used to relieve symptoms and pain (palliative) rather than curative, according to UK figures (Field 2016).

[For countries adding national figures]
The five-year survival rate for lung cancer is only [xx]%, meaning that [xx]% of people survive for five years after diagnosis. This is among the lowest for all types of cancer.

[xx]% of people with lung cancer are diagnosed at Stage IV (advanced disease when cancer has spread from the lungs to other parts of the body).

## Lung cancer is associated with higher costs than other cancers

An EU study showed lung cancer was associated with the highest economic costs of any cancer, based on direct healthcare costs to healthcare systems and costs to the individuals affected including lost earnings and informal care. Figures showed that lung cancer accounted for 15% of overall cancer costs, followed by breast cancer (12%), colorectal cancer (10%) and prostate cancer (7%) (Luengo-Fernandez 2013).

- This reflects the relatively high incidence of lung cancer and the high mortality (Field 2016)

[For countries adding national figures]
The cost of lung cancer to the health care system in [country] has been estimated at [cost] per patient per year. Lung cancer accounts for [xx]% of overall cancer costs.

### COVID-19 has reduced lung cancer referral rates and early diagnosis

COVID-19 has dramatically reduced lung cancer referral rates and reduced early diagnosis from incidental findings, driving an urgent need for organised efforts to detect lung cancer earlier.

- The World Health Organization found that 55% of countries reported disruption to cancer treatment and diagnosis services during the initial peak of the pandemic (WHO 2020). In the UK, some services reported up to a 75% reduction in the number of people being urgently referred with suspected lung cancer during the peak of the pandemic (UK Lung Cancer Coalition 2020)
- Redeployment of staff and resources to the care of patients with COVID-19 may have had a disproportionate impact on treatment for lung cancer

## How screening for lung cancer can help …

### Diagnosing lung cancer at an earlier stage improves survival

Lung cancer screening with LDCT saves lives by detecting the disease at an early stage when it is potentially curable.

- When diagnosed at its earliest stage, almost 60 in 100 (57%) people with lung cancer will survive their disease for five years or more, compared with only five in 100 people (3%) when diagnosed at the latest stage, according to figures for England (CRUK 2021)

Randomised clinical trials of regular screening of high-risk individuals with LDCT have demonstrated its effectiveness in detecting lung cancer at an early stage and in reducing lung cancer mortality (de Koning 2020; NSLT 2019).

- A recent large trial of LDCT screening, the NELSON trial, showed a 24% reduction in lung cancer mortality in men and a 33% reduction in women at 10 years of follow-up compared to no screening (de Koning 2020)
- More than two-thirds (68%) of lung cancers detected in people screened in the NELSON trial were found at an early stage (de Koning 2020)
- The number of people needed to screen with LDCT to prevent one death from lung cancer is around 255 (Tammemägi 2013), which is considerably lower than for other cancer screening programmes. For mammography, the number needed to screen to prevent one breast cancer death is 645-1724 in each age decade from 40 to 79 years

(Canadian Task Force 2019). The number needed to screen to prevent one colorectal cancer death is 850 for flexible sigmoidoscopy (Fitzpatrick-Lewis 2015)

## Smoking history identifies who to screen for lung cancer

Tobacco smoking is, by far, the single biggest risk factor for lung cancer making it simple to identify people who should be screened for the disease.

- Almost 90% of lung cancers in men and 70-80% in women are related to cigarette smoking, according to global figures (Walser 2008)
- Smokers have up to a 30-fold higher risk of developing lung cancer than non-smokers (Walser 2008; CDC 2020)
- People who quit smoking have a lower risk of lung cancer than if they had continued to smoke but their risk is higher than for people who have never smoked (CDC 2020)

[For countries adding national figures]
[xx]% of lung cancers in [country] are related to cigarette smoking.

## Screening high-risk individuals for lung cancer is cost-effective

Screening high-risk individuals for lung cancer with LDCT is cost-effective based on widely used measures of cost-effectiveness used in healthcare.

- The cost per quality-adjusted life year (QALY) (an estimate that combines years of life with quality of life after a particular health intervention) is within the range considered to be acceptable value for money for public health interventions
- Integrating smoking cessation interventions alongside LDCT screening significantly improves cost-effectiveness, potentially preventing an additional 12 lung cancer cases per 1000 smokers screened (Evans 2020)

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# Lung cancer meets the World Health Organization (WHO) criteria for screening programmes to improve public health

The WHO has identified criteria for screening programmes to improve public health. Lung cancer meets these criteria:

- **The disease should be an important health problem.** Lung cancer is the commonest cancer and the leading cause of cancer death in [country]. Most people with lung cancer are currently diagnosed at an advanced stage of the disease, which cannot be cured and is associated with very poor survival

- **There should be a recognisable latent or early symptomatic stage.** Symptoms of lung cancer do not usually appear until the disease is already at a late stage, but LDCT scans of the lungs can detect small abnormal areas in the lungs (nodules) that can be further investigated to see if they are early lung cancer

- **The natural history of the disease should be adequately understood.** Many cases of lung cancer progress relatively slowly over several years, potentially offering opportunities for early detection. The high risk of lung cancer in smokers and ex-smokers enables clear identification of people most likely to benefit from lung cancer screening

## Screening test

- **There should be a suitable test or examination.** LDCT of the chest is the recognised diagnostic test for early diagnosis of lung cancer. It uses X-rays to generate multiple cross-sectional images of the lungs using much less ionizing radiation than a conventional CT scan. Large clinical trials have shown that LDCT of the chest significantly reduces the risk of dying from lung cancer. (National Lung Screening Trial Research Team 2011; De Koning 2020)

- **The test should be acceptable to the population.** A LDCT scan is quick, painless and non-invasive. Individuals lie on their back on the flatbed of a CT scanner which takes multiple images of their lungs. Using LDCT minimises radiation exposure compared to a standard CT scan. (Swedish 2021. Manchester University NHS Trust 2021. Centers for Medicare & Medicaid Services 2021)

## Treatment

- **There should be an accepted treatment for patients with recognised disease.** Evidence-based treatments are available for early lung cancer and are associated with much better survival rates than treatment of advanced lung cancer

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## Screening programme

- **There should be an agreed policy on who to treat.** Large clinical trials and existing lung cancer screening trials have shown that use of protocols provides clear guidance on people who require further investigation and treatment based on scan results

- **Facilities for diagnosis and treatment should be available.** Healthcare systems already have services in place for the diagnosis and treatment of lung cancer

- **The cost of case finding (including diagnosis and treatment of patients diagnosed) should be economically balanced in relation to possible expenditure on medical care as a whole.** Screening high-risk individuals for lung cancer with LDCT is cost-effective with the cost per QALY within the range considered to be acceptable value for money for public health interventions

- **Case finding should be a continuous process and not a 'once and for all' project.** The aim would be to roll out a lung cancer screening programme on an ongoing basis rather than a one-off programme

(WHO 2020)

The purpose of screening is to identify people at higher risk for a health problem or condition or with early disease so that treatment can be offered to reduce the incidence and mortality within the population (WHO 2020).

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# Review of the evidence for the clinical effectiveness of a lung cancer screening programme

## Lung cancer screening detects lung cancer at an earlier stage than waiting for patients to present with symptoms and is associated with better outcomes including lower mortality.

Randomised clinical trials of regular screening of high-risk individuals with LDCT have demonstrated its effectiveness in detecting lung cancer at an early stage and in reducing lung cancer mortality.

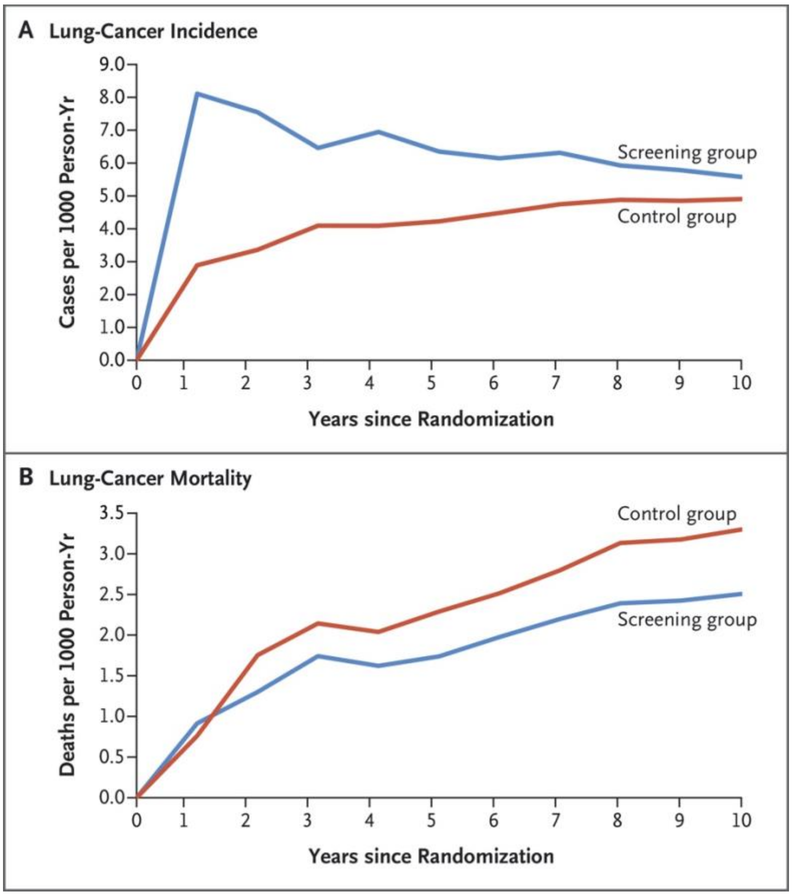
- The two largest trials of LDCT screening, the NELSON trial and the National Lung Screening Trial (NLST), showed a 20-24% reduction in lung cancer mortality (de Koning 2020; NLST 2019)
- More than two-thirds (68%) of lung cancers detected in people screened in the NELSON trial were found at an early stage (de Koning 2020). Seven large randomised controlled trials have shown that lung cancers detected in people undergoing LDCT screening were more likely to be early stage (I and II) than people in control groups not having LDCT screening
- The number needed to screen with LDCT to prevent one death from lung cancer is around 255 (Tammemägi 2013), which is considerably lower than for other cancer screening programmes. For mammography, the number needed to screen to prevent one breast cancer death is 645-1724 in each age decade from 40 to 79 years (Canadian Task Force 2019). The number needed to screen to prevent one colorectal cancer death is 850 for flexible sigmoidoscopy (Fitzpatrick-Lewis 2015)

## The NELSON trial: LDCT screening reduces lung-cancer mortality by 24% at 10 years

The NELSON trial (carried out in the Netherlands and Belgium) randomised 13 195 men and 2594 women aged 50-74, all former or current smokers, to LDCT screening at baseline, 1 year, 3 years and 5.5 years or to a control arm with no screening. The overall referral rate for suspicious nodules was 2.1%. Results showed a significant 24% reduction in lung cancer mortality at 10 years with screening in men (rate ratio for death from lung cancer 0.76, 95% confidence interval 0.61 to 0.94, p=0.01) and a 33% reduction in women (rate ratio 0.67, 95% CI 0.38 to 1.14) (de Koning 2020).

Lung cancers were detected at an early stage (stages I or II) in 68% of the screen-detected cases. Screening detected lung cancers that would otherwise remain undetected, with a higher incidence in people undergoing screening (5.58 cases per 1 000 person years) compared to controls (4.91 cases per 1 000 person years). In total, 203 lung cancers were detected by screening. Overall, 92-133 participants needed to be screened per round of screening to prevent one lung cancer death (Horeweg 2013).

**Figure 1: LDCT screening significantly reduces lung cancer incidence and mortality**

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Panel A shows the cumulative lung-cancer incidence (per 1000 person-years) according to follow-up year since randomization. Panel B shows the cumulative lung-cancer mortality (per 1000 person-years) according to follow-up year since randomization. Cause of death (with known date of lung-cancer diagnosis) was defined by the cause-of-death committee, if available, or by vital-statistics registries (de Koning et al 2020).

### The Lung Screening Trial: LDCT reduces lung-cancer mortality by 20% at 6.5 years

The National Lung Screening Trial (carried out in the US) randomised more than 53, 000 people aged 55-74 years with at least a 30 pack-year smoking history to three annual rounds of screening with either LDCT or chest X-ray (National Lung Screening Trial Research Team 2019). Results showed a 20% reduction in lung cancer mortality after 6.5 years of follow-up in people screened with LDCT (247/100 000 person years) compared to the chest X-ray group (309/100 000 person years). Nearly three-quarters (70%) of the screen-detected lung cancers were at an early stage. The trial also showed a 6.7% reduction in all-cause mortality in people screened with LDCT.

A total of 320 screens were required to prevent one lung cancer death, which is comparable to estimates for breast cancer screening (Richardson 2001; Duffy 2010).

Based on the findings of the trial, the US Preventive Services Task Force have recommended annual lung screening with LDCT for people aged 50-80 years, who have a 20 pack-year smoking history and currently smoke or have quit within the past 15 years in its latest recommendations (US Preventive Services Task Force 2021).

### Several smaller studies have also shown benefits with CT lung cancer screening

The Multicentric Italian Lung Detection (MILD) study compared annual versus biennial CT lung screening versus no screening. The results showed a 39% reduction in lung cancer-related mortality at 10 years in the CT screening groups compared with the control arm (HR 0.42; 95% CI 0.22-0.79) (Pastorino 2019). The LUSI trial reported a 26% reduction in lung cancer mortality overall, which did not reach statistical significance, but found a 69% reduction in lung cancer mortality in women (HR 0.31, 95% CI 0.10-0.96, p=0.04) (Becker 2020), and the ITALUNG study found non-significant reductions in lung cancer and all-cause mortality (Paci 2017). Two other studies (DANTE and DLCST) did not show statistically significant differences in lung cancer or all-cause deaths between LDCT screening and usual care, but the authors acknowledged their limited statistical power (Infante 2015; Wille 2016).

A meta-analysis of the six trials published before the NELSON trial demonstrated that LDCT is associated with a statistically significant 19% reduction in lung cancer mortality (pooled risk ratio 0.81; 95% CI 0.73-0.91) (Canadian Partnership against Cancer 2020).

All of the studies showed that lung cancer detected in the LDCT screening arms were more likely to be early stage (I and II) than those in the control arms.

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## Summary of major randomised trials of LDCT lung cancer screening

**Figure 2: Results of NLST and major European lung cancer screening trials**

| Trial Name | Study Design | Number Recruited | Characteristics of Participants | | | | Year Started | Report Date | LC Baseline Rate (LDCT) | Stage I Cancer at Baseline/Mortality Reduction |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | Age | Sex | Smoker (Pack yrs) | Ex-Smoker (yrs) | | | | |
| NLST | LDCT vs. CXR | 53,454 | 55-74 | M/F | ≥30 | <15 | 2002 | 2011 | 1% | 63% / 20% |
| NELSON | LDCT vs. UC | 15,822 | 50-75 | M/F | ≥15 | <10 | 2003 | 2016 | 0.9% | 63.9% |
| MILD | LDCT vs. UC | 4,099 | ≥49 | M/F | >20 | <10 | 2005 | 2011 | 0.6% | 63% |
| DANTE | LDCT vs. UC | 2,811 | 60-74 | M | ≥20 | <10 | 2001 | 2007 | 2.2% | 57% |
| DEPISCAN | LDCT vs. CXR | 765 | 50-75 | M/F | ≥15 | <15 | 2002 | 2006 | 2.4% | 0.9% |
| ITALUNG | LDCT vs. UC | 3,206 | 55-69 | M/F | ≥20 | <10 | 2004 | N/A | 1.5% | 47.6% |
| DLCST | LDCT vs. UC | 4,104 | 50-70 | M/F | ≥20 | <10 | 2004 | 2016 | 0.8% | 58.8% |
| LUSI | LDCT vs. CXR | 4,052 | 50-69 | M/F | >15 | <10 | 2007 | 2012 | 1.1% | 78.2% |
| UKLS | LDCT vs. UC | 32,000 planned | 50-75 | M/F | N/A | N/A | 2012 | N/A | N/A | N/A |

*LDCT = Low-Dose Computed Tomography; CXR = Chest Radiograph; LC = Lung Cancer; UC = Usual Care*

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*DANTE* = Detection and Screening of Early Lung Cancer by Novel Imaging Technology and Molecular Essays, *DEPISCAN* = French Randomized Pilot Trial of Lung Cancer Screening Comparing Low-Dose CT Scan and Chest X-Ray, *DLCST* = Danish Lung Cancer Screening Trial, *ITALUNG* = Italian Lung Trial, *LUSI* = Lung Cancer Screening Intervention, *MILD* = Multicentric Italian Lung Detection, *NELSON* = Dutch-Belgian Randomized Lung Cancer Screening Trial, *UKLS* = U.K. Lung Cancer Screening Trial (Fintelmann et al, 2015).

## Local pilot study demonstrated feasibility and improved outcomes

*If you have carried out a local pilot study with lung cancer screening add brief details here.*

A local pilot study of LDCT screening in [country] demonstrated feasibility and improved outcomes, including [insert key findings].

# How to optimise benefits and minimise potential harms of screening

As with any intervention, screening for lung cancer can be associated with potential harms but these can be mitigated by following evidence-based protocols that identify high-risk individuals who benefit the most, ensuring any lung nodules identified are managed appropriately and optimising the safety of screening scans. These help to address the potential harms that can result from screening:

## False positive findings

False positive findings are one of the commonest adverse effects of any screening program. These occur when people test positive even though they do not have the condition that is being screened for. Patients with positive screening results may then undergo further diagnostic procedures with additional healthcare costs.

### *What does the evidence show?*

Clinical trials with LDCT screening have shown that the false positive rate is reassuringly low. In the NELSON trial 2.1% of scans (467 of 22 600) were positive. Nearly half (43.5%) of people who were screen-positive were subsequently confirmed to have lung cancer. Only 1.2% (264 of 22 600) of the total scans had a false-positive result. Just under one-quarter of participants with false-positive screen results (67 of 293) underwent an invasive procedure (including transthoracic biopsies) – fewer than 1% (67 of 7582) of all screened participants (Horeweg 2013).

### *How to mitigate this potential harm*

Incorporating a nodule management protocol (such as the British Thoracic Society PN Risk Calculator or Lung-RADS™) into the screening programme minimises the risk of false positives. These protocols set out specific criteria (including nodule size and other characteristics) to define an abnormality as potentially malignant, benign, or indeterminate and can substantially reduce the number of false-positive findings and subsequent additional invasive procedures (American College of Radiology 2019; Tammemägi 2014). Both PanCan and Lung-RADS nodule detection protocols performed well in discriminating between benign and malignant nodules in the Alberta Lung Cancer Screening Study (Tremblay 2019).

## Overdiagnosis

Lung cancer screening aims to detect malignant tumours likely to grow rapidly. However, it can also detect slow-growing tumours that would otherwise have remained silent, regressed or not have led to clinical symptoms and death. This overdiagnosis may result in overtreatment, with possible complications, and incur harms to the patient and costs to the healthcare system.

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### *What does the evidence show?*

In the NSLT the estimated rate of overdiagnosis was 3.1% (20 of 649 participants) (Black 2019). However, the study used a protocol that was less effective in distinguishing between benign and malignant nodules than currently used nodule management protocols (such as the PanCan calculator or Lung-RADS™) (Cancer Partnership Against Cancer 2020).

### *How to mitigate this potential harm*

Incorporating a nodule management protocol (such as the British Thoracic Society PN Risk calculator or Lung-RADS™) into the screening programme minimises the risk of overdiagnosis by discriminating between benign and malignant tumours.

## Exposure to radiation

LDCT uses X-rays to scan the lungs so exposes people to some radiation, but the dose of radiation is less than people typically receive in a year from the natural environment, so the risk of harm is very low (Field 2016; Canadian Business Case 2020).

### *What does the evidence show?*

Modelling based on the dose of radiation delivered in an LDCT scan in the NSLT (about 1.4 millisieverts) indicated minimal long-term health impacts for people undergoing lung cancer screening (Cancer Australia 2020).

### *How to mitigate this potential harm*

Following strict eligibility criteria for identifying people at increased risk for lung cancer limits screening to those who benefit the most at the same time as setting optimal screening frequency and duration. Using LDCT within an organised screening programme, together with routine audit and quality assurance, ensures that people undergoing screening are exposed to low levels of radiation (Canadian Business Case 2020).

## Benefits vs potential risks of LDCT screening for lung cancer

**Table 1: Potential benefits and harms of LDCT screening for lung cancer**

| Potential Benefits | Potential Harms |
|---|---|
| Mortality benefits<br>20% relative decrease in lung cancer death (from 1.66 to 1.33%, or 3 fewer deaths per 1,000 screened)<br>7% relative reduction in all-cause mortality | Harms related to test characteristics<br>Radiation exposure from screening CT<br>False reassurance (aggressive cancers may develop in intervals between screening examinations)<br>Overdiagnosis of clinically insignificant cancers (15–20% of tumors detected) |
| Psychosocial benefits and behavioral changes<br>Reassurance if normal CT<br>Teachable moment for smoking cessation | Harms related to findings of test<br>False positives and other incidental findings<br>Potential harms from downstream evaluation of findings |

*Definition of abbreviation*: CT = computed tomography.

**(Wiener 2015). Reprinted with permission of the American Thoracic Society.**  **For the full reference, please see the reference list on page 28.**

**Summary of key points: optimising benefits and minimising harms associated with lung cancer screening**

- The benefits of LDCT screening for people at high risk for lung cancer outweigh potential harms
- Potential harms are minimised by:
  - Using strict eligibility criteria for identifying high-risk individuals who benefit the most
  - Setting optimal screening frequency and duration
  - LDCT protocols with annual quality assurance to minimise radiation exposure
  - Nodule management protocols to minimise the risk of overdiagnosis

# Review of the evidence for the cost-effectiveness of a lung cancer screening programme

**Screening high-risk individuals for lung cancer with LDCT is cost-effective with the cost per QALY within the range considered to be acceptable value for money for public health interventions.**

Consideration of the cost-effectiveness of lung cancer screening needs to take account of:

- Net costs of screening compared to detection via symptomatic presentation
- Net benefits in terms of additional life expectancy among people screened. People with screen-detected cancers can receive earlier treatments and achieve better health outcomes
- The ratio of net benefit compared to net costs incurred

To be acceptable the ratio must be within the range considered acceptable value for money. In [country] this is [xxxxx] per QALY gained for public health interventions.

### *Cost-effectiveness based on clinical trials of lung cancer screening*

Economic analysis for the UK Lung Cancer Screening trial comparing lung cancer screening against symptomatic presentation gave an estimate for the incremental cost-effectiveness ratio (ICER) of £8,466 per QALY gained for once-only CT screening (Field 2016). Health economic analysis suggested the intervention could be cost-effective; public health interventions associated with costs of £20,000-£30,000 per QALY gained are typically considered acceptable in the UK (Field 2016).

The National Lung Screening Trial in the USA estimated an ICER of US$81,000 per QALY. This was much higher than the UK figure but was explained by the inclusion of multiple screening rounds, higher screening, work up and treatment costs, and inclusion of patient costs (estimated at US$175 per person) (Field 2016). Limiting screening to the highest risk quintile reduced the mean ICER to $32,000.

A Canadian study testing population-based screening in Ontario found an optimal scenario of screening 55–75-year-olds with a smoking history of >40 pack years, with an incremental cost of CAN$41,136 (US$33,835 in 2015 prices) per QALY gained (Canadian Business Case 2020; Ten Haaf 2017). A threshold of CAN$50,000 per QALY gained has been the most commonly used threshold for health interventions in Canada.

### *Modelling studies*

A recent analysis by Cancer Australia found that biennial screening for people aged 55-74 years with a minimum 6-year lung cancer risk of 1.5% (based on PLCOm2012) was the most cost-effective screening programme for the Australian population. The estimated incremental cost-effectiveness ratio was Australian $83,545 per QALY gained (excluding patient costs), which was considered to be cost effective (Cancer Australia 2020).

## Key elements to achieve cost-effectiveness

The major determinants of cost-effectiveness for lung cancer screening are:

### Appropriate selection of high-risk individuals

Lung cancer is most clinically and cost effective when applied to people at high risk. Using lung cancer risk prediction models help to identify these people. The use of an accurate risk prediction model that incorporates risk factors in addition to smoking history and age is more efficient in identifying people who will develop lung cancer and die from the disease and results in more efficient screening (lung cancer deaths averted per screen) (Tammemägi 2014).

### Costs and frequency of LDCT screening

It is important to define the most appropriate screening frequency for individuals according to their screening results. The UK study showed that three consecutive annual screens achieved a better cost-effectiveness ratio than annual, biennial, or one-time scans (Snowsill 2018). The NELSON trial used biennial screening and found no increase in interval cancers (de Koning 2020).

### Use of protocols for management of nodules and incidental findings

Using evidence-based protocols for identifying and managing nodules is essential to ensure optimal use of screening.

### Integrating smoking cessation measures for current smokers.

Integrating smoking cessation therapies alongside LDCT screening significantly improves cost-effectiveness. In addition to early detection of lung cancer, a lung cancer screening programme provides an opportunity to help current smokers quit and to support those who have recently quit as the encounter with the screening programme offers a teachable moment and an opportunity to refer patients for support with smoking cessation. To optimise the benefits, lung cancer screening programmes should incorporate measures to encourage smokers to quit smoking.

A Canadian study showed that smoking cessation in the context of LDCT screening was cost-effective compared to screening alone and could potentially prevent an additional 12 cases of lung cancer and save 200 more life-years per 1000 smokers screened (Evans 2020). Using data from the NLST, researchers estimated that adding 15 years of smoking abstinence to screening would almost double the reduction in mortality risk compared to lung cancer screening alone (Tanner 2016).

**Summary of key points: evidence for the cost-effectiveness of lung cancer screening**

- Screening high-risk individuals for lung cancer with LDCT is cost-effective
- The cost per QALY is within the range considered to be acceptable value for money for public health interventions
- Lung cancer is most cost effective when applied to people at high risk, identified by an accurate risk prediction model
- Integrating smoking cessation interventions alongside LDCT screening significantly improves cost-effectiveness, potentially preventing an additional 12 lung cancer cases per 1000 smokers screened

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# Outline template for proposing a national lung cancer screening programme for [country]

*This section provides an outline template for you use to propose a national lung cancer screening programme for your country, adding locally applicable information (where indicated in blue type) and drawing on the information and resources provided (shown in italics).*

The proposed national lung cancer screening programme will support the early detection of lung cancer by identifying and screening asymptomatic high-risk individuals with LDCT. The aim is to diagnose lung cancer at an earlier stage when the disease is more likely to be curable than waiting until patients present with symptoms.

[Insert a paragraph summarising how the screening programme is tailored to your local situation]

- Brief summary of how the programme will be organised (based at existing hospital units or use of mobile scanning unit etc)
- Short rationale on why this approach fits best with the healthcare system and resources
- How it links to any regional or pilot programmes
- How the programme fits with national cancer plan recommendations relevant to screening/ early diagnosis of cancer/ lung cancer

The screening programme will follow a step-by-step protocol to optimise clinical efficacy, efficiency and safety:

## Risk assessment and recruitment

The programme will offer screening to asymptomatic individuals aged [xx-xx] years who are current smokers or former smokers with [at least a xx-pack-year smoking history, who currently smoke or quit less than 15 years ago OR a x% estimated 6-year risk of developing lung cancer].

- These people are at high risk for lung cancer, with an estimated [x]% risk of developing lung cancer within a [x]-year period
- The estimated number of people eligible for screening each year in [country] is [xxxx]

Participants for screening will:

- Be identified from GP/specialist patient/other records
- Be referred from smoking cessation programmes
- Self-refer for risk assessment following an information campaign

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Awareness campaigns for health professionals and the public will be important to support the launch of the screening programme. People being invited/referred for screening will be provided with clear information on what is involved in taking part in screening.

*See example of information for participants on lung cancer screening:* *https://go2foundation.org/wp-content/uploads/GO2-ALCASE-Trifold_FINAL.pdf*.

## LDCT screening

Target individuals will be screened at [specify screening centres *e.g.* medical imaging units, specialised lung health clinics]. They will be offered:

- An initial LDCT scan at baseline
- Repeat LDCT scans every [x] years (or every year if nodule detected) for a total of [x] rounds of screening

*See recommendations on LDCT scans for screening for lung cancer and parameters:*
*American Society of Physicists in Medicine*
*https://www.aapm.org/pubs/ctprotocols/documents/lungcancerscreeningct.pdf*

## Assessment of CT images

CT images will be assessed by trained radiologists with expertise in early diagnosis of lung cancer using a validated protocol, documenting nodules, enlarged lymph nodes, mediastinal masses, effusions and other abnormalities. Scans will:

- Identify all non-calcified nodules – in baseline and repeat screenings.
- In repeat screenings: identify all new non-calcified nodules and those showing growth (compared to previous scan)

*See recommendations on LDCT scan reporting:*
*ACR-STR practice parameter for the performance and reporting of lung cancer screening thoracic computed tomography. 2019.*
*https://www.acr.org/-/media/ACR/Files/Practice-Parameters/CT-LungCaScr.pdf*
*NHS. Targeted screening for lung cancer with low radiation dose computed tomography. Standard protocol prepared for the Targeted Lung Health Checks Programme. 2019.*
*https://www.england.nhs.uk/wp-content/uploads/2019/02/targeted-lung-health-checks-standard-protocol-v1.pdf*

## Further follow-up based on CT results

Further follow-up will be based on the results of the LDCT scan using a lung nodule management pathway. This will depend on the absence or presence of nodules, their size and shape and whether the size has increased compared to a previous scan.

*Here is an example from the I-ELCAP protocol:*

- *Negative (no nodules) – the individual will return for an annual repeat LDCT scan*
- *Semi-positive (only nonsolid nodules; largest nodule <6.0mm; peri-fissural nodules <10.0mm diameter with smooth margin and lentiform, oval or triangular shape; costal pleural nodules <10.0mm in diameter with smooth margin and regular shape) – the individual will be asked to return for annual repeat scan*
- *Indeterminate (largest solid, part-solid nodule 6.0-14.9mm when follow-up CT scan 3 months after baseline shows growth at non-malignant rate) – the individual will be asked to return 9 months later for first annual repeat scan*
- *Positive (largest solid, part-solid nodule 6.0-14.9mm when follow-up CT scan 3 months after baseline shows growth at malignant rate; largest solid or part-solid nodule ≥ 15.0mm; solid endobronchial nodule) – refer to a multidisciplinary team for diagnostic work-up for lung cancer and management; if lung cancer not diagnosed – the individual will be offered a repeat LDCT scan at 12 months.*

*See also:*
*UK Lung Health Check https://www.england.nhs.uk/wp-content/uploads/2019/02/targeted-lung-health-checks-standard-protocol-v1.pdf*

## Communication of results

The results of the LDCT scan, with recommendations for further action, will be sent to the referring physician and the screened individual (together with a lay summary).

## Smoking cessation

Smoking cessation will be incorporated into the lung cancer screening protocol. CT screening offers a 'teachable moment' for smoking cessation advice not only for current smokers but also for former smokers. Smokers should be given individualised advice and referred to smoking cessation services.

- Incorporating smoking cessation into LDCT screening has been shown to be cost-effective compared to screening alone
- Adding 15 years of smoking abstinence to screening almost doubles the reduction in mortality risk compared to lung cancer screening alone, according to analysis of the LCST (Tanner 2016)
- During COVID, smoking cessation support will be provided virtually (online and by telephone)

## Follow-up of people diagnosed with lung cancer

People diagnosed with lung cancer through the screening programme will be followed up for [xx] years using health records.

- The data will be used to assess outcomes including survival compared with matched non-screen detected cases

## Quality assurance

The lung cancer screening programme will establish and implement quality assurance measures, including the following:

- Quality and safety framework – for operational safety, quality and improvement, overseen by [national quality assurance board]
- Monitoring and evaluation framework – regular monitoring against key performance indicators
- Data governance
- Research programme, to learn from the programme and share best practice

*See, for example:*
*NHS. Targeted screening for lung cancer with low radiation dose computed tomography. Quality assurance standards prepared for the Targeted Lung Health Checks Programme.* *https://www.england.nhs.uk/wp-content/uploads/2019/02/targeted-screening-for-lung-cancer-quality-assurance-standard.pdf*

## Education

The screening programme will include education of all stakeholders, including:

- Healthcare organisations: information for managers and administrators to support allocation of resources
- Clinicians: awareness programmes on the screening programme; information for referring clinicians and those caring for patients requiring further investigation and treatment after screening
- Radiologists and radiology technicians: information on low-CT lung scans, interpretation and reporting of findings
- The public: awareness programmes; information on the benefits and harms of lung cancer screening, selection criteria for screen, what screening involves, the importance of smoking cessation and resources to help quit smoking

*See the following for online education resources on lung cancer screening:*
*Global Lung Cancer Coalition https://www.lungcancercoalition.org/screening-resource/*
*American Cancer Society https://www.cancer.org/cancer/lung-cancer/detection-diagnosis-staging/detection.html*

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**Predicted impact of the lung cancer screening programme in [country]**

In the first 10 years of the lung cancer screening programme in [country], it is estimated that:

- [xxxx] lung cancer deaths would be prevented
- [xx-xx] QALYs would be gained
- [xx] % of all screen-detected lung cancers would be diagnosed at an early stage compared to less than [xx] % of lung cancers currently detected at an early stage in [country]

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# Planning for estimated capacity, infrastructure and workforce requirements

*This section provides an outline guide for you to use in discussions and planning for estimated capacity, infrastructure and workforce requirements associated with developing a national lung cancer screening programme in your country.*

Considering the population age structure in [country] and smoking prevalence an estimated total of approximately [xxxx] individuals may be eligible for lung cancer screening. Based on this number, approximately [xxxx] LDCT scans may be required during the first three years of the screening programme.

The lung cancer screening programme will require the following resources:

## Capacity and workforce

- Screening co-ordinators – to organise and provide administration of the programme, including establishing and maintaining a registry of screened patients, scheduling appointments, follow-up of LDCT results and communication with clinicians and patients
- Health education/promotion time and resources – to plan and run healthcare professional and public awareness campaigns to support launch and roll-out
- Clinician and nurse time and resources – to identify, risk-assess and refer high-risk individuals for screening; provide further evaluation and treatment of referred patients with a positive screen
- Radiologists/radiographer time and resources – to carry out LDCT, interpret results and communicate findings to referring clinicians and patients
- Smoking cessation personnel time and resources – to deliver smoking cessation interventions, support and advice

## Equipment and IT

LDCT scanner time and costs – the programme may use existing equipment or introduce mobile vans. An LDCT scan typically costs around [xxxx] in [country] so to provide lung cancer screening scans for [xxxx] people will cost around [xxxx] per year.

IT systems – to maintain a registry of screened patients; provide structured reporting system; analyse data for audit and quality assurance.

Assessment of workforce and capacity requirement vs current late presentation:

- Most (around 89%) participants will receive a scan every [x] years and no abnormalities will be found – so the most significant impact will be in the recruitment and scanning phases of the screening programme (Cancer Australia 2020)
- Around 11% of people will require further scans or diagnostic interventions and treatment, with impact on secondary care workforce and capacity (Cancer Australia 2020)
- The average detection rate of lung cancer is estimated to be 6-9 cases per 1000 scans (Canadian Business Case 2020), so screening is likely to have low to medium impact on most health professionals and services currently treating lung cancers

## Planning for costs

The following costs should be considered when planning for the resource implications of a national lung cancer screening programme:

| | Per year |
|---|---|
| Estimated eligible (high-risk) population (n) | xxx |
| Total screens (n) | xxx |
| Diagnostic procedures (n) | |
| • Invasive | xxx |
| • Non-invasive | xxx |
| Screen-detected new lung cancers (n) | xxx |
| TOTAL COST | |
| • Screening costs | xxx |
| • Diagnostic work-up costs | xxx |
| • Smoking cessation programme costs | xxx |
| • Incidental finding costs | xxx |
| • Cancer treatment costs | xxx |

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## Figures and tables

**Figure 1: LDCT screening significantly reduces lung cancer incidence and mortality**

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**Figure 2: Results of NLST and major European lung cancer screening trials**

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**Table 1: Potential benefits and harms of LDCT screening for lung cancer**

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# Further resources on lung cancer screening

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