The LungAmbition Alliance

Lung cancer screening: the cost of inaction

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The Health Policy Partnership

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IASLC INTERNATIONAL ASSOCIATION FOR THE STUDY OF LUNG CANCER

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Executive summary

Lung cancer is the leading cause of cancer deaths worldwide, accounting for one in five cancer deaths.[1] Smoking is the major cause of lung cancer, but lung cancer is not just a smokers' disease. Global rates of smoking have been gradually declining in men, but have remained stable, or decreased at a slower rate, in women.[2] Former smokers, however, remain at high risk of lung cancer up to 25 years after quitting.[3] In addition, the prevalence of lung cancer in never-smokers is gradually rising: in the UK and US, around 20% of lung cancers occur in people who have never smoked, and this figure is about 53% in some Asian countries.[4-7] There is also a global shift in the distribution of lung cancer deaths by sex, with mortality rates mostly rising among women in many countries.[8] With all these factors combined, the number of people with lung cancer is likely to remain significant for decades to come.

Governments around the world have committed to reducing the burden of cancer, but few countries are on target to meet their goals. Lung cancer accounts for the greatest economic and public health burden of all cancers.[9] It is responsible for nearly a quarter of productivity losses due to premature mortality from cancer in Europe.[10] Targeted efforts on lung cancer must therefore

Lung cancer accounts for the greatest economic and public health burden of all cancers.

be an integral part of all national cancer control plans if countries wish to achieve their goals and reduce the toll of cancer on their societies.

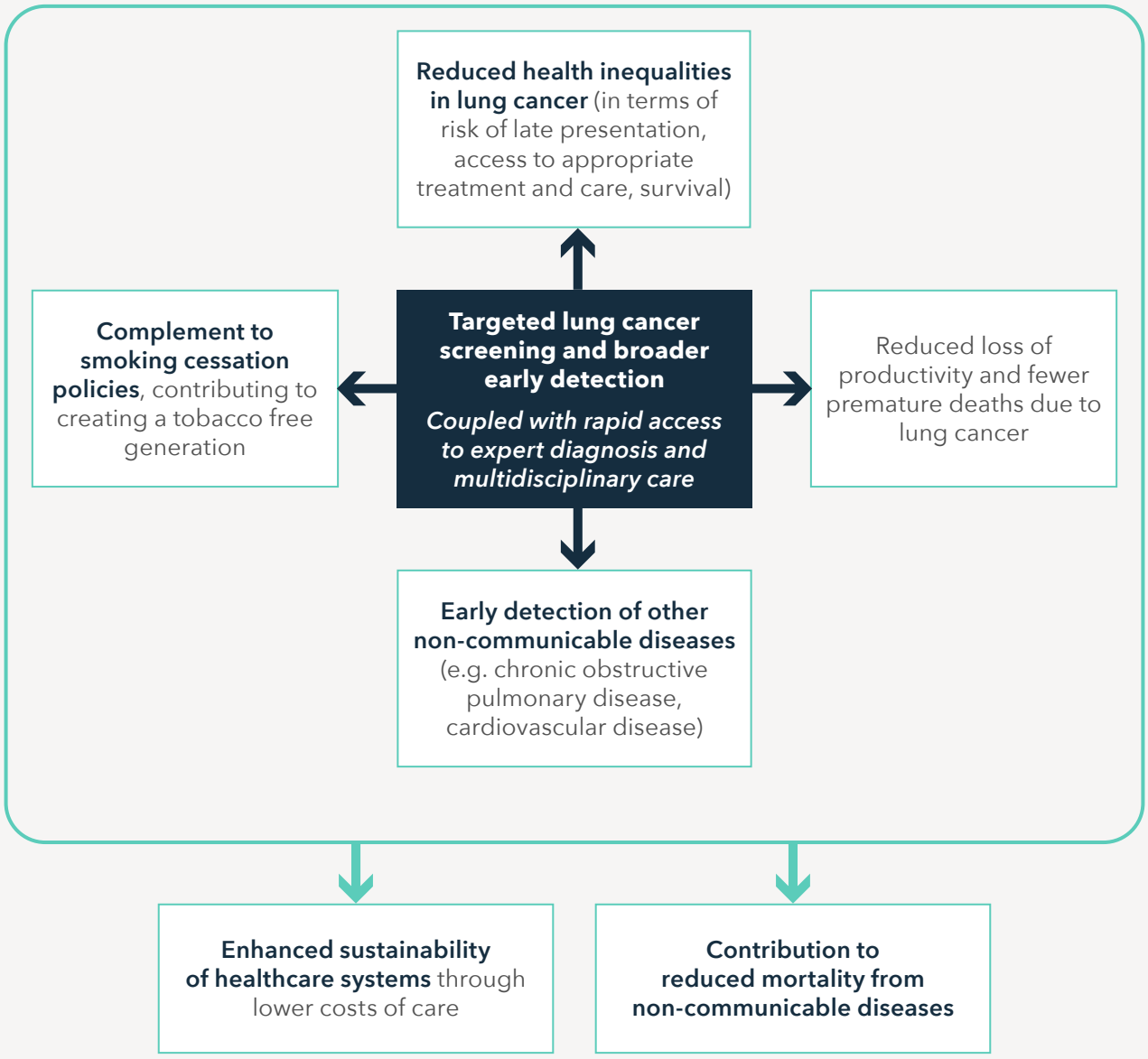
Early detection that allows people rapid access to high-quality diagnosis and care offers the best opportunity to reduce the number of deaths due to lung cancer. Prognosis for lung cancer is poor compared with most other cancers,[11-13] largely due to a high proportion of cases being detected at an advanced stage when treatment options are limited.[14] Around 20% of people with lung cancer are diagnosed at stage I, when their likelihood of surviving 5 years is between 68–92%, compared with more than 40% of people being detected at stage IV, when their likelihood of surviving 5 years is under 10%.[15-17] The proportion of people detected at an advanced stage varies considerably by country. Shifting detection to earlier stages could thus result in a considerable reduction in the number of deaths from lung cancer. This will have a substantial impact on cancer mortality more generally and, in turn, will dramatically decrease the economic toll of cancer on our societies.

Earlier detection through screening may transform lung cancer from a fatal to a treatable condition, with considerable impact on quality of life. The most effective means of achieving this shift is through targeted screening using low-dose computed tomography (LDCT).[18 19] Evidence from large-scale clinical trials has shown that targeted LDCT screening can reduce lung cancer deaths in high risk individuals by nearly a quarter.[18 19] Given that approximately 1.8 million lives are currently lost to lung cancer every year,[1] this would have a considerable public health, economic and societal impact.

In light of this evidence, it is time for national governments to consider large-scale implementation of targeted lung cancer screening. Lung cancer screening should be considered the next big opportunity in cancer screening: experts suggest it compares favourably with other cancer screening programmes in terms of cost-effectiveness and potential benefits,[20] and fewer people need to be screened for lung cancer to prevent one death compared to breast or colorectal cancer screening.[19 21 22] What's more, a decade of implementation research around the world has pointed to factors that can help ensure successful, cost-effective implementation at scale. Of highest importance is the need to secure attendance from people at

Lung cancer screening should be considered the next big opportunity in cancer screening

Figure a. The impact of lung cancer screening extends beyond lung cancer



greatest risk of lung cancer, to optimise the balance of benefits and harms from screening, and to integrate targeted screening programmes into high-quality multidisciplinary care pathways, with early diagnosis and effective treatment options available for all.

The benefits of investing in the early detection of lung cancer extend beyond lung cancer (*Figure a*). Screening presents an opportunity to detect other non-communicable diseases, such as cardiovascular disease and chronic obstructive pulmonary disease, at an early stage in high-risk individuals.[23-25] It can also

The need to invest in early detection has never been more urgent

help reduce health inequalities: people of lower socioeconomic status are at highest risk of lung cancer, of presenting late with symptoms, and of poor survival as a result.[26-28]

Investing in early detection of lung cancer is also an investment in the future sustainability of our health systems and post-pandemic recovery. The COVID-19 pandemic has had a dramatic impact on the entire lung cancer care pathway – including initial presentation, diagnosis and access to treatment – and there is growing evidence that it is undoing some of the progress in lung cancer survival achieved in recent years.[29] Across many countries, screening and urgent referrals have declined sharply, and the backlog of cases the pandemic has created will undoubtedly exacerbate the risk of late presentation for months to come.[29-34] In England, for example, delays in diagnosis due to COVID-19 are expected to result in an 11.2% increase of stage IV diagnoses of lung cancer,[35] and similarly worrying trends are emerging in other countries.[29 36]

Time is everything for people with lung cancer. As systems rebuild following the pandemic, the need to invest in early detection has never been more urgent. Failing to do so condemns lung cancer patients to poor survival and diminished quality of life, and increases the long-term strain on overstretched, under-resourced health systems.

Leadership as we emerge from the pandemic means acting early – the time to act is now. The cost of not doing so is too great, not just for lung cancer patients, but for society as a whole.

1 Introduction

Lung cancer is the leading cause of cancer deaths worldwide. More than 2.2 million people were diagnosed with lung cancer in 2020[i], making it the second most commonly diagnosed cancer worldwide after breast cancer.[1] Approximately one in five cancer deaths globally is due to lung cancer,[37] and the five-year survival rate was just 10–20% in most countries between 2010–2014.[11]

Despite falling smoking rates, the prevalence of lung cancer is expected to remain high for many years. Smoking is the main cause of lung cancer. In most countries, smoking rates have declined among men but remained stable or decreased at a slower rate among women.[2] However, a former heavy smoker remains at three times greater risk of developing lung cancer than a person who has never smoked, and this risk remains for up to 25 years after quitting smoking.[3] In addition, lung cancer is not just a smokers' disease and its frequency among never-smokers is rising globally.[5] In the UK and US, around 20% of lung

i In this report we have used the most recent data available (2020). While it is possible that this number is underestimated due to under-reporting of cases during the COVID-19 pandemic, figures for 2020 are as expected based on current epidemiological trends, and comparable to data from earlier years.

cancers occur in people who have never smoked, and this rate is 53% in some Asian countries.[4-7] There is also a global shift in the distribution of lung cancer deaths by sex, with mortality rates mostly rising among women in many countries.[8] With all these factors combined, lung cancer will remain an important public health problem for decades to come.

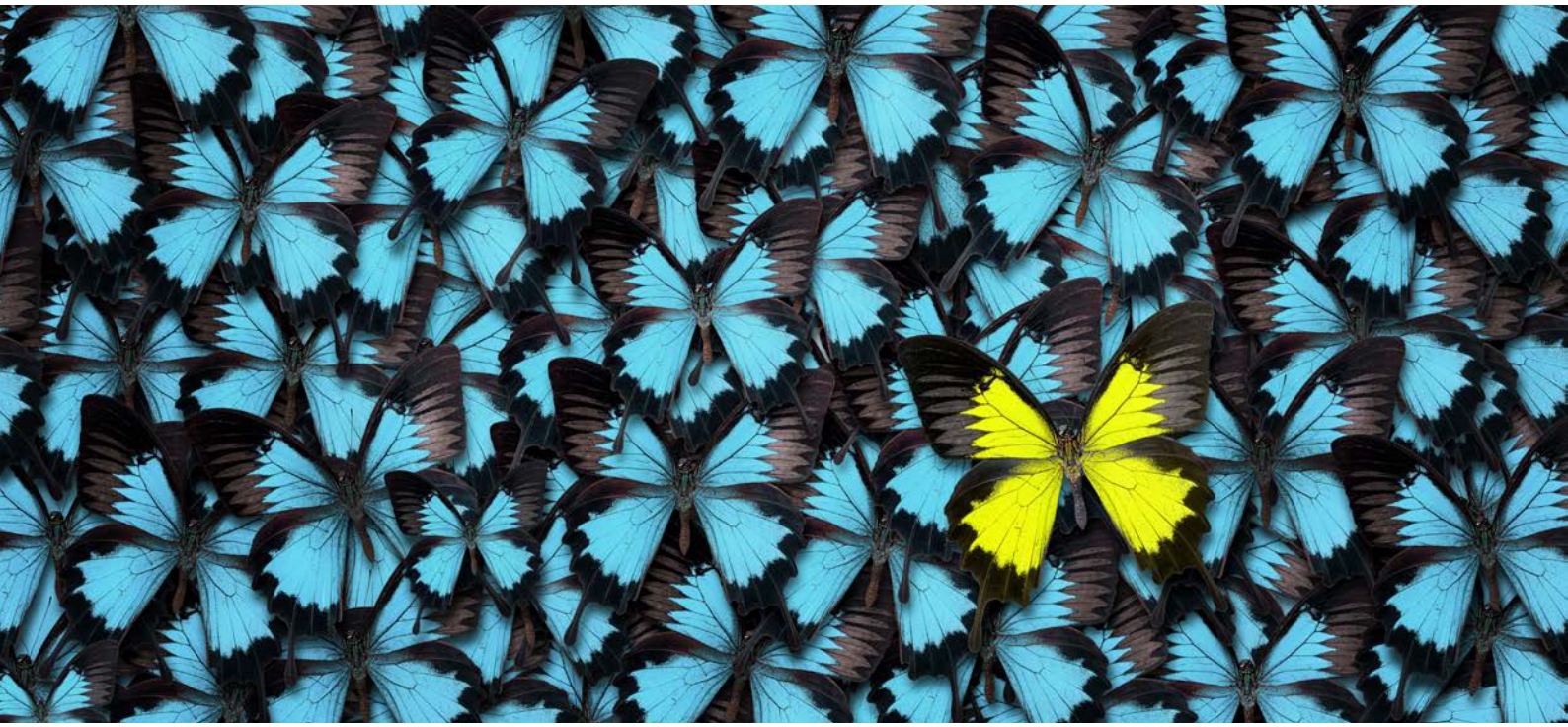
The link with smoking has caused widespread stigma towards people with lung cancer. Such stigma is felt equally by people who do or have smoked and those who have not.[38] Many studies have shown that the emotional burden caused by a lung cancer diagnosis is considered to be significantly higher than for other cancers, and stigma is a big part of this.[38-42] Lung cancer has also traditionally received less attention and funding than other common cancers, despite its overwhelming economic and societal impact.[43]

Many governments have set targets to improve survival from cancer over the next 20 years.[44 45] As lung cancer is the biggest cancer killer, strategies to reduce lung cancer mortality must be part of efforts to achieve those targets.[37] The most effective way to do this is through early detection, specifically screening.

It is recommended that screening for lung cancer take a targeted approach, focusing on people at highest risk of lung cancer. In 2020, the publication of the Dutch–Belgian Randomised Lung Cancer Screening Trial (NELSON) confirmed the findings of the US National Lung Screening Trial (NLST) more than a decade before, that targeted screening of former and current smokers by low-dose computed tomography (LDCT) can significantly reduce deaths from lung cancer.[18 19] Given that lung cancer currently kills approximately 1.8 million people worldwide every year,[1] this impact would be considerable. But the COVID-19 pandemic has halted translation of clinical trial evidence to real-world implementation of screening programmes in many countries. The pandemic has also caused significant disruption to diagnosis and care of people with lung cancer, making the need to reduce the burden of this condition on our societies much more urgent.

As we emerge from the COVID-19 pandemic, we are faced with a unique opportunity: to find the most feasible approach to reducing mortality from lung cancer. Investment in early detection, with screening at its core, must be part of that effort if we are to reduce the devastating costs of lung cancer on people, economies and health systems. This report explores not just why this is something that should be done, but the immense cost to society of not doing so.

2 Lung cancer: a public health priority



Reducing cancer deaths is a global imperative

Cancer is one of the greatest public health issues of our time. Globally, it is responsible for one in six deaths and a third of premature deaths from non-communicable diseases (NCDs) in people aged 30–69.[37] As part of their commitment to reducing mortality from NCDs,[46] many countries around the world have set targets to specifically achieve 10-year survival in three out of four of cancer patients by 2030.[44 45]

Despite these commitments, we are a long way from effectively tackling the global burden of cancer. Fewer than 10% of countries are on track to achieving target reductions in the major NCDs,[46] which include cancer, and only 12 countries worldwide are currently on track to achieving specific targets to reduce cancer mortality.[37] One in five people still faces a cancer diagnosis before the age of 75,[37] and in 2020, 10 million people died from cancer.[47]

Lung cancer presents a considerable public health and economic burden

Lung cancer is the leading cause of cancer deaths globally. One in five cancer deaths is due to lung cancer, and it causes approximately 1.8 million deaths per year (*Table 1*).[1]

Table 1. The public health impact of lung cancer: key facts and figures

Globally, lung cancer is responsible for:

- **2.21 million** new cases per year[1]
- **11.4%** of all new cancer cases[1]
- **45.9 million** disability-adjusted life years (2019)[48]
- **1.8 million** deaths per year[1]
- **18%** of all cancer deaths[1]
- **45.3 million** years of life lost (2019)[48]

Region*	Europe	North America	South America & Caribbean	Africa	Oceania	Asia
New lung cancer cases per year	477,534	253,537	97,601	45,988	16,975	1,315,136
New cases as % of total regional cancer cases	10.9%	9.9%	6.6%	4.1%	6.7%	13.8%
Lung cancer deaths per year	384,176	159,641	86,627	41,171	12,012	1,112,517
Deaths as % of total regional cancer deaths	19.6%	22.8%	12.1%	5.8%	17.3%	19.2%

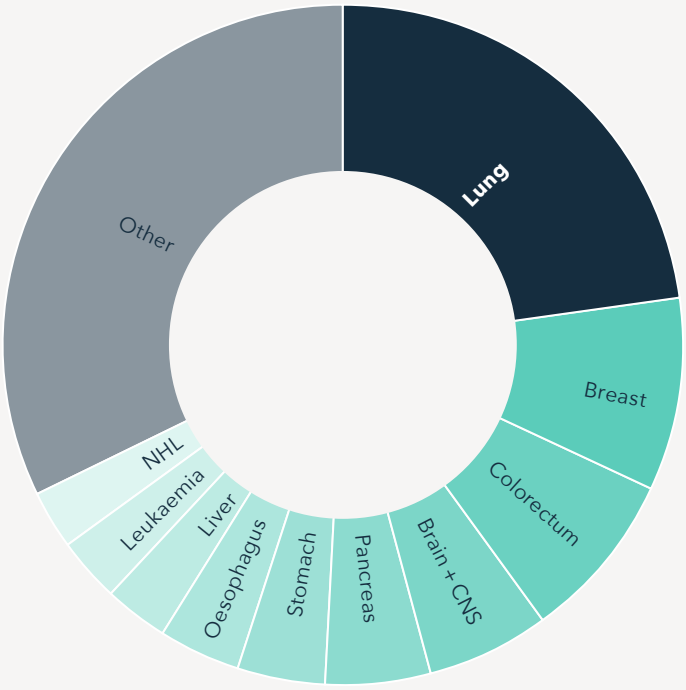
* Continental regional data reported by the World Health Organization Global Cancer Observatory (2020)[47]

Table 2. Lung cancer costs in the European Union (based on 2009 data)[49]

Costs per year	All cancers (billion €)	% of all cancer costs	Costs of lung cancer (billion €)	% of lung cancer costs	Lung cancer as % of all cancer costs
Total costs	**126.2**	**100%**	**18.8**	**100%**	**15%**
Direct healthcare costs	51.0	40.4%	4.2	22.5%	**8%**
Productivity losses (early death)	42.6	33.7%	9.9	52.8%	**23%**
Productivity losses (lost working days)	9.4	7.5%	0.8	4.3%	**9%**
Informal care	23.2	18.4%	3.8	20.3%	**16%**

Lung cancer has the highest economic toll of all cancers. In Europe, the costs of lung cancer are higher than breast, colorectal or prostate cancer[9] and represent 15% of the total economic costs of cancer (*Table 2*).[49] Existing figures date back several years, however, and more up-to-date estimates are needed to understand the full economic toll of lung cancer on our societies.

Figure 1. Lung cancer accounts for nearly a quarter of productivity losses due to premature mortality in Europe, more than any other cancer type[10]



Lung	€17.5bn	(23%)
Breast	€6.9bn	(9%)
Colorectum	€6.3bn	(8%)
Brain + CNS	€4.2bn	(6%)
Pancreas	€3.9bn	(5%)
Stomach	€3.3bn	(4%)
Oesophagus	€2.7bn	(4%)
Liver	€2.4bn	(3%)
Leukaemia	€2.4bn	(3%)
NHL	€1.9bn	(3%)
Other	€23.9bn	(32%)

CNS, central nervous system; NHL, non-Hodgkin's lymphoma

The indirect costs of lung cancer, in terms of productivity losses and informal care, are particularly significant. These costs outweigh direct healthcare costs in published studies.[49 50] Lung cancer's impact on productivity is considerable:[50] it accounts for nearly a quarter (23%) of productivity losses due to premature mortality from cancer in Europe, a higher proportion than any other cancer (*Figure 1*).[10] Many people with lung cancer stop working and do not return, resulting in significant cost of early retirement to individuals, their families and the economy.

In addition to its high financial costs, lung cancer also has a dramatic impact on people's quality of life. In most countries, it is responsible for the most disability-adjusted life years (DALYs) of all cancers.[43] Symptoms like breathlessness and fatigue, along with the need to attend medical appointments or adapt to treatment regimens, may lead to social withdrawal and time off work.[39] The psychological distress, impact of cancer treatment and related side effects substantially affect the mental health and wellbeing of people living with lung cancer and their loved ones.[39 51] The day-to-day impact on loved ones is also significant,[52] with lung cancer accounting for 16% of total costs of all informal cancer care.[49]

3 Earlier detection: the key to reducing the burden of lung cancer

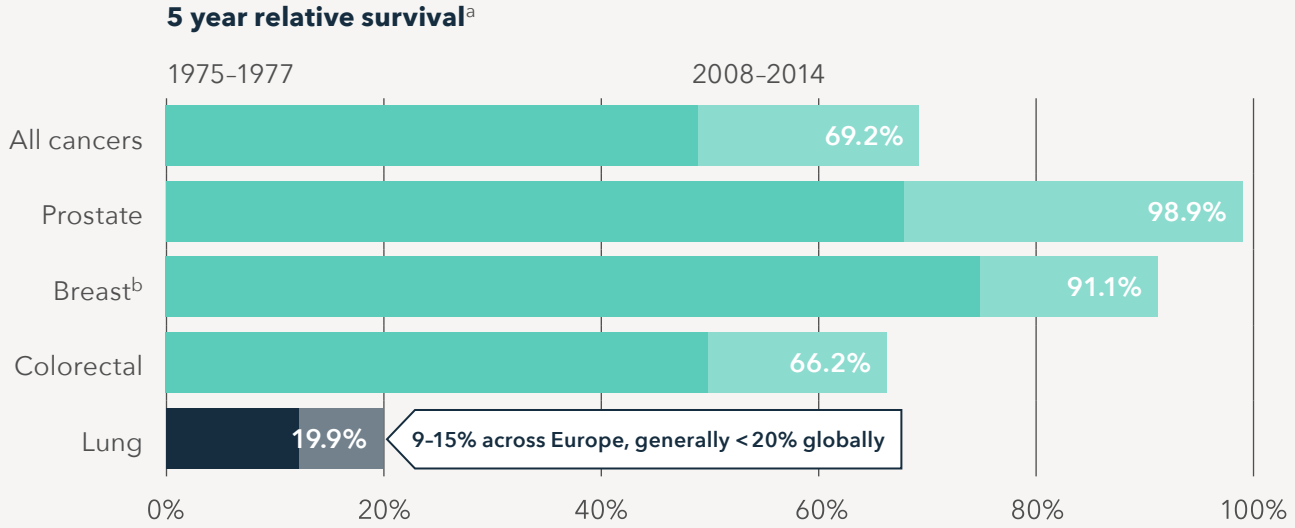
Late presentation is a significant issue in lung cancer

Earlier detection is recognised as the best way to reduce the burden of all cancers – but lung cancer is seldom detected early. Symptoms such as a persistent cough, shortness of breath and repeated lung infections are often difficult for people to recognise as symptoms of lung cancer.[14] As a result, many people present to healthcare professionals only after their cancer has advanced to a stage where treatment options are limited and prognosis is poor.[14 53]

Late presentation in lung cancer has led to poor survival compared with some other common cancers.[11 13] Progress in survival for lung cancer has paled in comparison with that seen in some other cancers (*Figure 2*).[13 54] For example, in England in 2018, half of lung cancers were diagnosed at stage IV (50%), compared to 5% of breast cancers and 25% of colorectal cancers.[16] Although precise estimates vary by country, trends are similar.

Shifting detection to an earlier stage could transform lung cancer from a fatal to a treatable condition. Prognosis for lung cancer is highly dependent on the stage at which the illness is diagnosed (*Figure 3*). A person diagnosed with stage IV lung cancer has less than 10% chance

Figure 2. Improvements in lung cancer survival have lagged-behind those seen in other common cancers (US data)[12 13 54 55]



[a] Five-year relative survival rates show the percentage of people who will be alive five years after diagnosis. This does not include people who die from other diseases. Relative survival rates account for the fact that not all people diagnosed with a certain cancer type will die of that cancer.

[b] Women only.

Data: https://seer.cancer.gov [54]

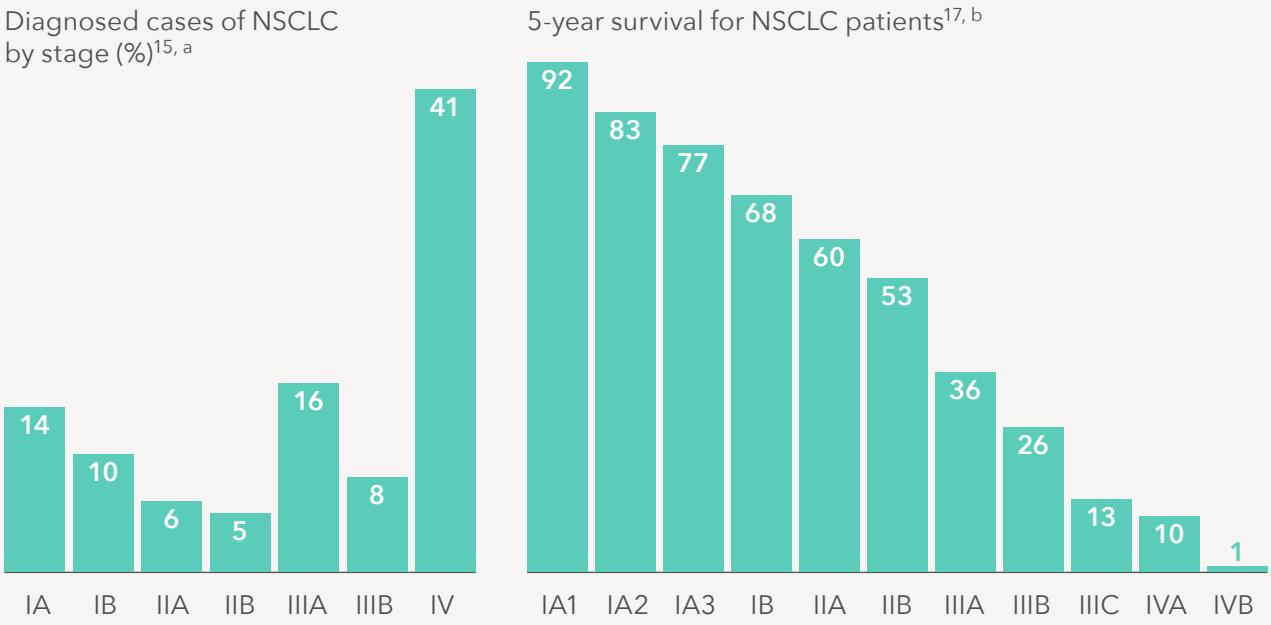
of surviving five years after diagnosis; this increases to between 68–92% if diagnosed at stage I.[17] At stage I, patients can be offered surgical removal (resection) with a high probability of cure,[56] as well as other curative treatments, avoiding the need for more invasive and less effective interventions later on, with considerable impact on quality of life.[57]

Earlier detection of lung cancer would translate into significant benefits for population health. Given its prevalence, a stage shift in lung cancer detection would save countless lives lost to lung cancer every year and would have a dramatic impact on the overall number of deaths from cancer (*Figure 4*).

Early detection of lung cancer would have a significant economic impact

Shifting detection to an earlier stage would significantly reduce the total costs of lung cancer. The costs of treating a person with late-stage lung cancer are higher than for earlier-stage disease due to more complex pathways for clinical management.[14 60 61] With earlier detection, more people will be able to remain active and return to work, therefore reducing the substantial lost productivity costs of lung cancer. For example, people with stage IV lung cancer have been shown to incur higher wage losses and out-of-pocket expenses than those diagnosed at a marginally earlier stage (stage IIIB).[52]

Figure 3. Non-small-cell lung cancer (NSCLC)* is commonly diagnosed at an advanced stage, which is associated with poor prognosis



* Non-small-cell lung cancer accounts for 80–85% of lung cancer cases[58 59]

[a] Estimated from SEER validation data from the 7th edition of the International Association for the Study of Lung Cancer (IASLC) staging project.

[b] Based on the clinical staging data from the 8th edition of the IASLC staging project.

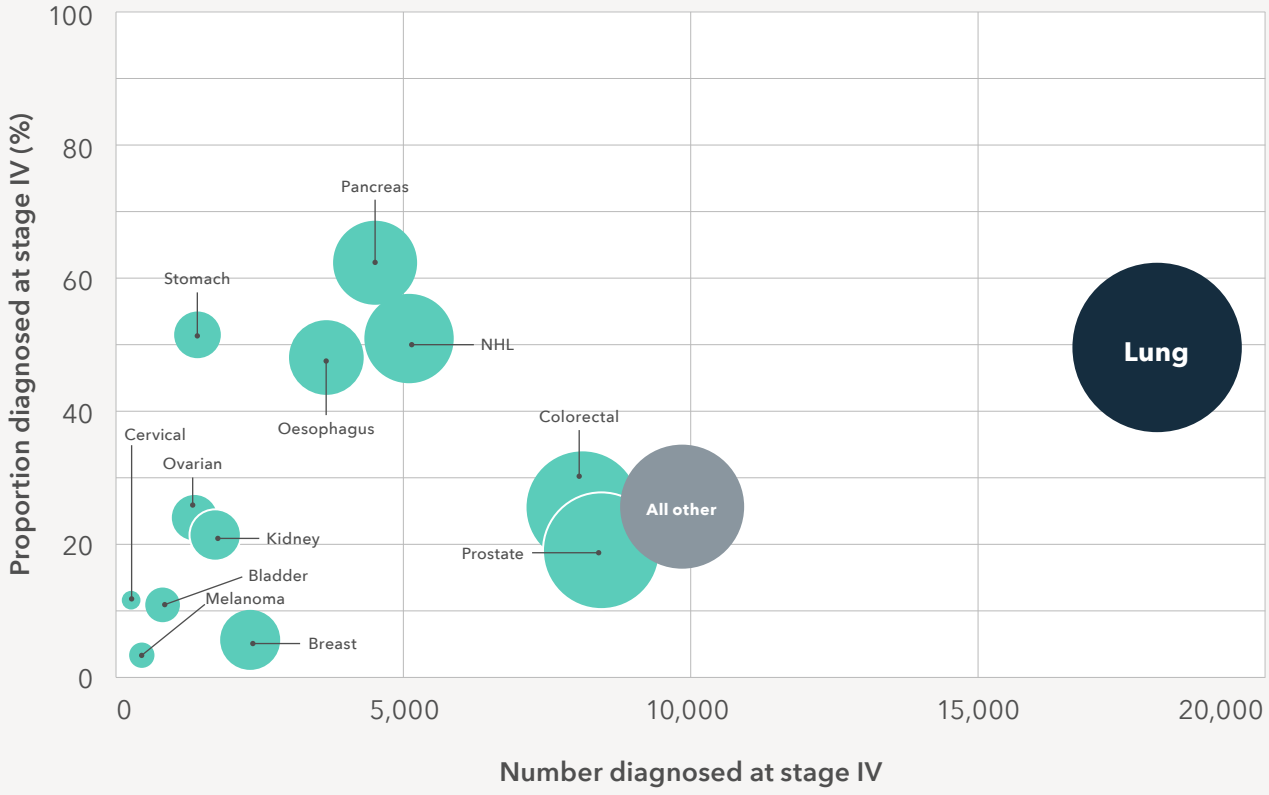
Earlier detection would also significantly reduce the impact of lung cancer on quality of life for patients and their families. Data suggest that people with advanced non-small-cell lung cancer (NSCLC) have worse health-related quality of life than people with other advanced cancer types.[39] Shifting stage of detection can thus reduce the impact on people and their families, including costs linked to informal care.[62]

The risk of late presentation in lung cancer has been exacerbated by the COVID-19 pandemic

The urgency for earlier detection has been enhanced by the COVID-19 pandemic, as late diagnosis is thought to have worsened for all cancers. The World Health Organization reports that 55% of countries experienced disruption to cancer diagnosis and treatment during 2020.[63] Cancer screening programmes were halted in many countries and urgent cancer referrals decreased significantly.[30-33] This situation is likely to lead to an increase in the number of patients presenting with cancer at later stages, when prognosis is worse.[34 64]

A survey of 221 healthcare professionals in Italy, Germany, France, Spain and the UK reported a 52% decline in the number of cancer patients seen per week, and a 63% drop in the number of patients starting

Figure 4. Lung cancer offers the greatest opportunity for early detection (England, 2018)[16]



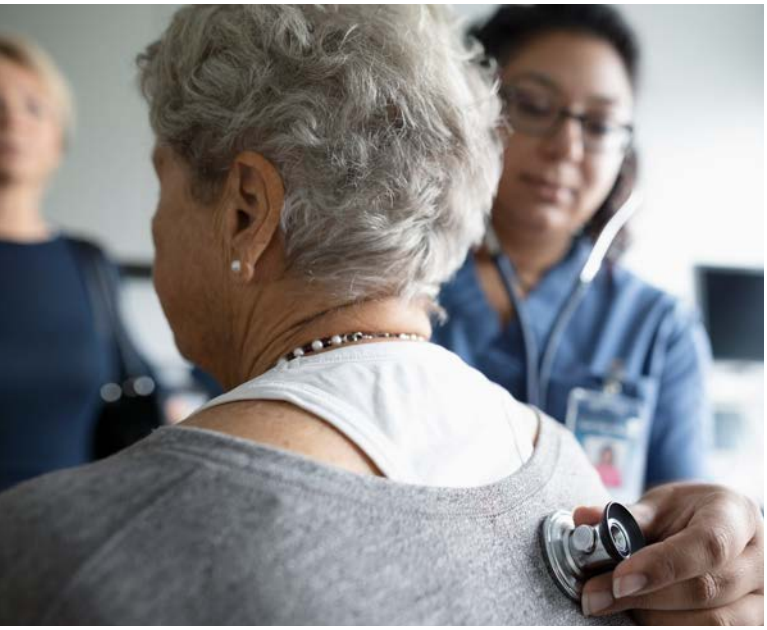
NHL, non-Hodgkin's lymphoma

The size of the circles shows the relative weight of each cancer type in terms of its contribution to the total number of cancers detected at advanced stage.

Update of original figure produced by the United Kingdom Lung Cancer Coalition (UKLCC).[53] Data from Public Health England, 2018.[16]

cancer treatment.[65] At time of writing, only Germany has seen this situation improve.[66]

Lung cancer has been hit particularly hard by the pandemic. The delays for lung cancer diagnoses have been significant due to overlapping symptoms with COVID-19 and specific pressures on respiratory healthcare services.[29 67 68] In Spain, the number of new lung cancer patients fell by 21–32% during the first wave of the pandemic in 2020, compared with the same period the previous year.[69] In the UK, referrals to lung cancer specialists declined by 75% in some areas during the first wave.[68] Reduced access to CT scanners and diagnostic staff have led to further missed opportunities for early detection.[29] Even for those patients diagnosed early enough for surgery to be an option, limited availability of surgery due to competing needs of COVID-19 patients has had a significant effect on prognosis.[64 70] Data for England suggest that a three-month delay in surgery



for bladder, lung, oesophageal, ovarian, liver, pancreatic and stomach cancers would incur 4,755 excess deaths over one year, escalating to 10,760 excess deaths for a six-month delay.[71]

The pandemic has also likely reversed recent progress in lung cancer survival in many countries. Data from England suggest that delays due to missed diagnosis will lead to a 4.8–5.3% increase in lung cancer deaths, equivalent to an additional 1,235–1,372 deaths within five years following diagnosis.[32] In Spain, experts have warned that the pandemic could set back lung cancer survival by 5%, resulting in an additional 1,300 deaths.[69] Also, as healthcare systems emerge from 'crisis mode', they face a significant backlog of cases which may further delay the return to normal service levels[29 34] – and this will inevitably include more people presenting with advanced lung cancer.

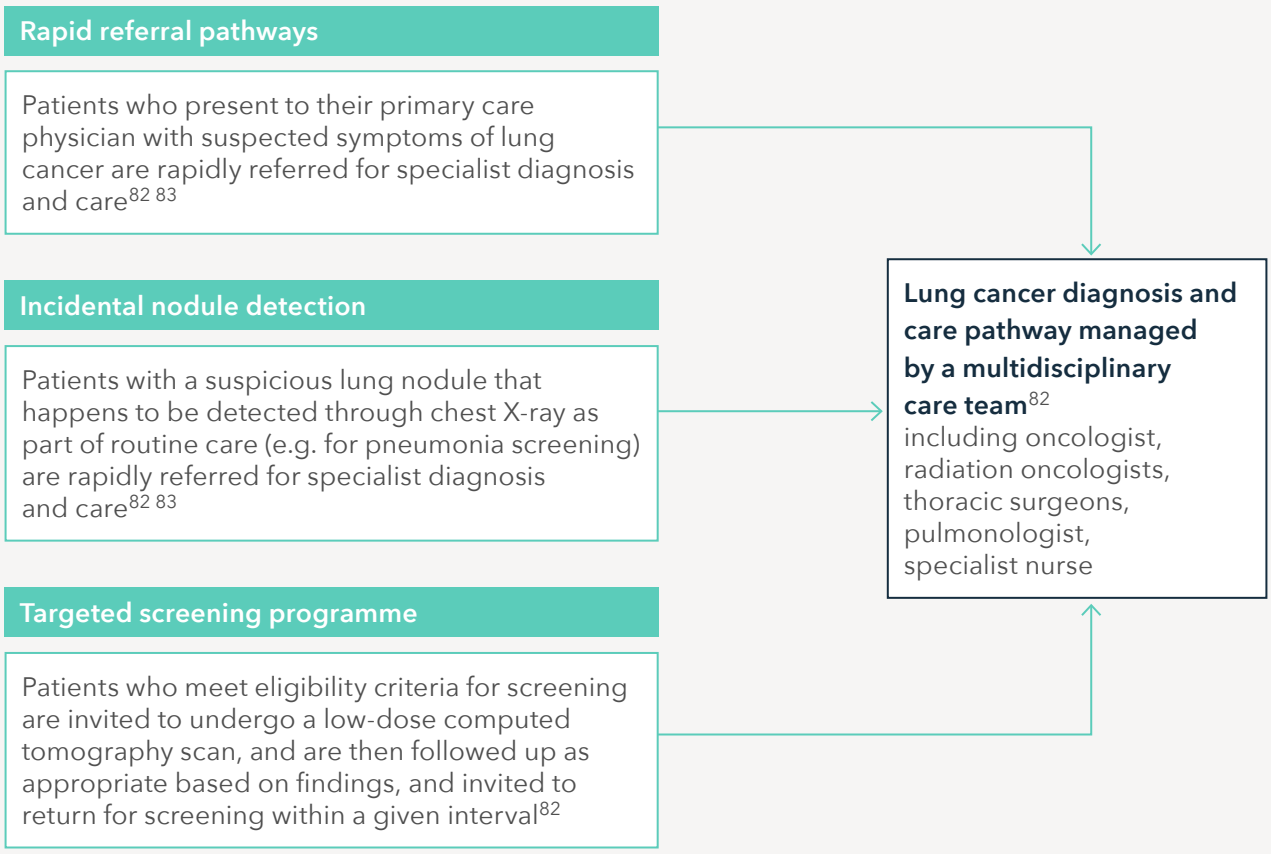
Targeted screening is at the core of early detection for lung cancer

Given the high toll of late presentation in lung cancer, there have been considerable efforts to identify an effective screening tool in recent years. As articulated in Europe's Beating Cancer Plan, screening, coupled with primary prevention, is the most effective way to curb the burden of cancer.[72] Different approaches to screening for lung cancer have been explored, including for example chest X-ray aided by artificial intelligence (AI).[73 74] In particular, LDCT screening has demonstrated statistically significant benefits in large-scale, international clinical trials.[18 19]

It is recommended that lung cancer screening follow a targeted approach and be offered to those considered at highest risk of lung cancer, who are also most likely to benefit. Current recommendations suggest that LDCT screening be offered to current or former heavy smokers within a specific age range.[42 75 76] However, there is growing appreciation that smoking status is insufficient to identify all people at high risk of lung cancer. Individual risk prediction models, which incorporate important risk factors for lung cancer – such as family history of cancer or pneumonia, occupational exposures (e.g. asbestos), race and ethnicity[77] – are recognised as helpful tools to identify high-risk candidates who might be missed by only looking at age and smoking status.[42 78]

The relative importance of smoking compared with other risk factors also varies by country. In Taiwan, for example, 53% of lung cancer deaths

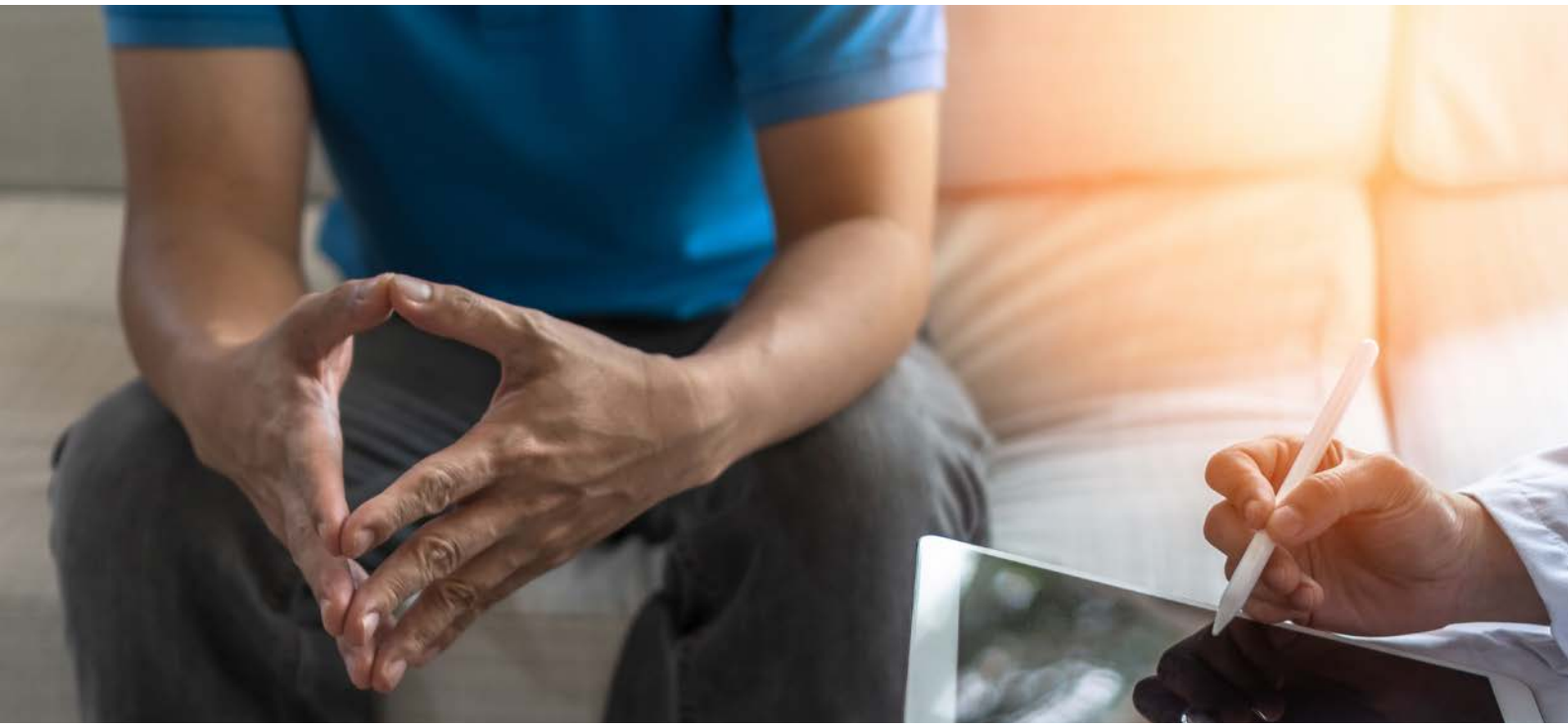
Figure 5. A comprehensive approach to early detection is needed



occur among people who have never smoked,[7] and risk factors such as family history, exposure to cooking fumes, and exposure to environmental carcinogens are increasingly recognised.[79] Similar patterns occur throughout East Asia, leading to recommendations that non-smokers should be included in the target population for lung cancer screening in these countries.[80 81]

In light of the evolving epidemiology of lung cancer, it is important that targeted screening programmes be complemented by other approaches to early detection. Targeted screening programmes can capture people with defined risk factors (such as smoking status and age); however, individuals who do not meet these criteria and present with possible symptoms of lung cancer also need to be referred as quickly as possible for rapid diagnosis by a multidisciplinary care team. A comprehensive approach to early detection should thus include rapid referral pathways for people who present in primary care with possible symptoms, incidental nodule protocols for people who present with a lung nodule while undergoing a routine X-ray for another reason, and targeted screening programmes for those who meet defined screening eligibility criteria (*Figure 5*).

4 LDCT screening for lung cancer: the next big opportunity in cancer detection

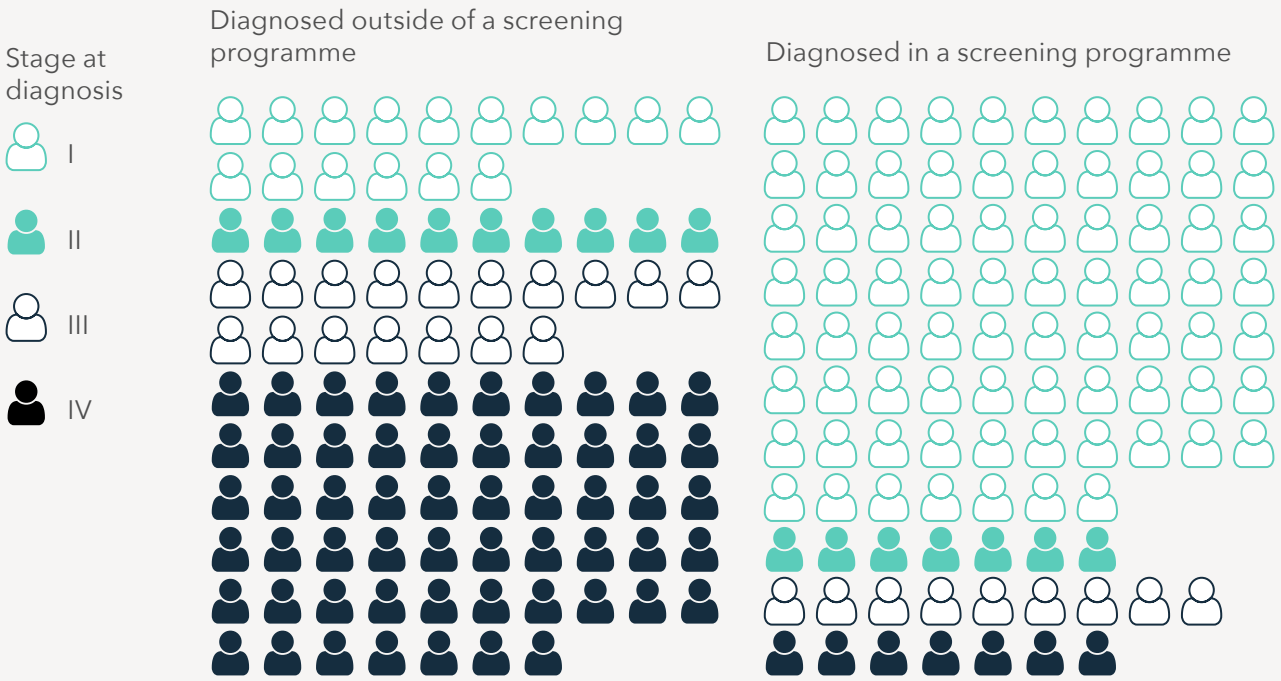


Large-scale clinical trials have shown that LDCT screening is effective at reducing lung cancer mortality

The evidence demonstrating the effectiveness of LDCT screening for lung cancer reached a turning point in 2020. The publication of the NELSON trial[18] showed that LDCT screening in current and former heavy smokers can deliver a significant stage shift to earlier diagnosis in lung cancer (*Figure 6*). In the NELSON trial, 59% of cases among people in the screening arm were early-stage, compared with 14% in the control population who were not offered screening.[18] Similar figures have been found in other settings.[19 84]

LDCT screening also leads to a significant reduction in lung cancer mortality in high-risk patients. In the NELSON trial, 18.4% of 868 deaths in the screening group were due to lung cancer, compared to 24.4% of 860 deaths in the control group.[18] This equates to a reduction in lung cancer mortality in men of 24% over 10 years.[18] A mortality reduction of 33% was found in women, but the number of women participating in the trial was too small for this finding to be statistically significant.[18] These findings have convinced experts around the world that the evidence for LDCT screening to reduce lung cancer mortality is now indisputable.[84 86-88]

Figure 6. Screening programmes allow detection of a much higher proportion of lung cancer cases at an early stage compared to routine care[85]



Adapted from Sands *et al.* (2021). Patient decision-making aid based on combined analysis of existing clinical trials.

Any potential harms caused by LDCT screening are likely outweighed by its benefits

Screening is, by definition, offered to asymptomatic individuals, so it is important to ensure the benefits of screening outweigh any potential risks. With LDCT screening, the main risks are radiation exposure from the scan and misdiagnosis through a false-positive result. Cumulative evidence from randomised clinical trials has shown that LDCT screening presents a negligible risk of radiation exposure.[85] If performed under high-quality standards, LDCT screening does not lead to a large number of false-positive results or subsequent unnecessary procedures or treatments.[85 86]

LDCT screening for lung cancer is expected to meet local cost-effectiveness thresholds when designed appropriately

Based on all published studies, LDCT screening is expected to be a cost-effective investment (*Appendix 1*). Published cost-effectiveness ratios compare well with other population-based screening strategies, including those in place for colorectal, breast and cervical cancers,[89] and are likely to be within accepted economic thresholds.[84] LDCT screening

is also expected to be more efficient than other screening programmes, meaning that fewer people need to be screened for lung cancer to prevent one death compared with breast or colorectal cancer screening (*Box 1*).

Targeted lung cancer screening is expected to offer benefits even greater than those of existing cancer screening programmes

The benefits of LDCT screening are likely to compare favourably to those of existing cancer screening programmes. Globally, the impact of LDCT screening on lung cancer mortality is expected to be significant (*Box 2*). Some experts suggest that, if the highest-risk populations can be reached, lung cancer screening could have a larger absolute impact on cancer mortality than existing cervical or breast cancer screening programmes.[86] This is also seen in cost-effectiveness studies of LDCT screening, where optimal scenarios confer more benefits than any present cancer screening programme.[20]

Box 1. Efficiency of lung cancer screening compared to other cancer screening programmes

Data from different studies suggest fewer screens are required to prevent one lung cancer death compared to breast or colorectal cancer:

- **320** people need to be screened by low-dose computed tomography to prevent one death from lung cancer[19]
- **645–1,724** people need to be screened by mammography to prevent one death from breast cancer[21]
- **864** people need to be screened by flexible sigmoidoscopy to prevent one death from colorectal cancer[22]

Box 2. How many lives could lung cancer screening save?

A summary of current estimates:

- **US:** approximately 12,000 lives saved per year[90]
- **Italy:** 5,000 lives saved per year[91]
- **Australia:** 12,000 lives saved over 10 years[92]
- **Canada:** 5,000–13,000 lives saved over 20 years[93]
- **South Korea:** 14,504 lives saved (91,362 life years gained) over 20 years[94]
- **Japan:** 45,774 lives saved (290,325 life years gained) over 20 years[94]
- **Singapore:** 1,290 lives saved (8,118 life years gained) over 20 years[94]
- **China:** 471,095 lives saved (3,014,215 life years gained) over 20 years[94]

5 An investment in health system sustainability

The benefits of lung cancer screening extend beyond lung cancer

In addition to its impact on lung cancer mortality, lung cancer screening presents an opportunity to detect other NCDs at an early stage. As recently stated by the World Health Organization, investment in NCD prevention and management is 'an insurance policy to improve population health and mitigate the impact of any future crisis'.[95] Retrospective analyses of several LDCT studies found a high rate of incidental findings of cardiovascular disease and respiratory conditions among screening participants.[23-25] There may therefore be value in LDCT screening programmes also focusing on early detection of other pulmonary abnormalities.[96] For example, age and smoking history are the strongest predictors of lung cancer and chronic obstructive pulmonary disease (COPD), therefore it is possible to identify a common target population for screening and detection for both conditions.[25]

Promoting its potential to detect other 'big killers' linked to smoking could make lung cancer screening a more attractive prevention package to high-risk individuals. Experience from existing lung cancer screening programmes has shown that screening can act as a life event that encourages participants to quit smoking and take control of their health

more generally.[97 98] Particularly among former smokers, it is often seen as an opportunity to adopt behavioural changes such as increased physical activity and a healthy diet.[24]

Targeted screening complements the impact of smoking cessation policies

Targeted lung cancer screening should also be seen as a complement to smoking cessation policies, contributing to countries' anti-tobacco agendas. Smoking cessation programmes are the most important preventive measure for lung cancer,[2] but they are not sufficient to decrease the global burden of lung cancer. Targeted screening (and early detection more generally) is needed to protect people who are already at high risk of lung cancer (e.g. former smokers) and for whom prevention has no immediate impact.[42]

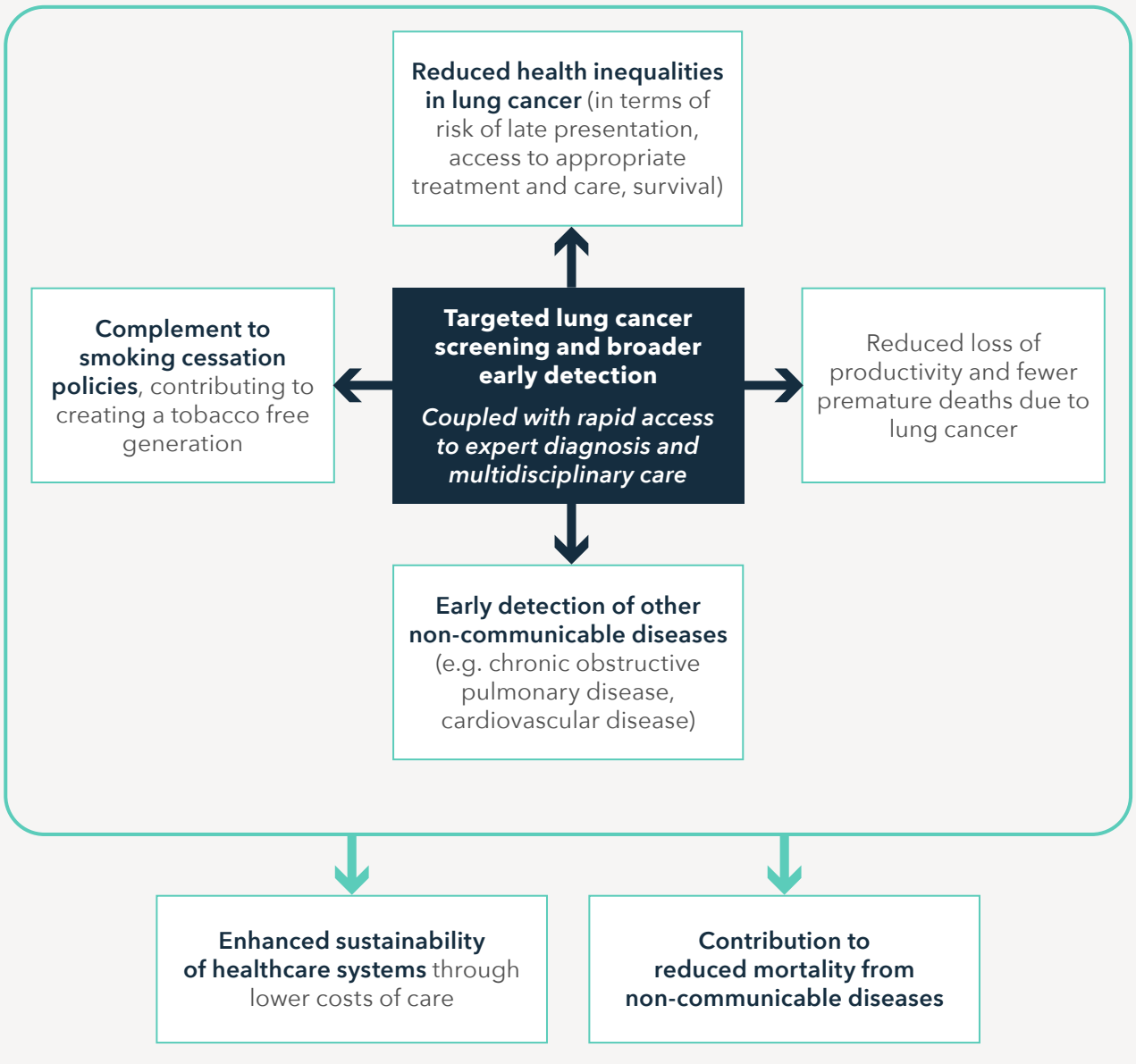
Evidence from clinical trials and pilot studies shows that lung cancer screening amplifies the success of smoking cessation programmes, and vice versa. Experts unanimously recommend that current smokers invited to take part in screening be offered smoking cessation advice and encouraged to quit smoking.[84 99 100] Several studies have shown that a positive or indeterminate screening result in current smokers prompts them to take up smoking cessation and decreases smoking relapse rates.[42 101] Combining the two approaches also increases the cost-effectiveness of lung cancer screening programmes, with a greater impact on reducing mortality.[42 102 103]

Lung cancer screening may help to address growing socioeconomic inequalities in health

Health equity is one of the fundamental tenets of health systems, and it has been threatened by the COVID-19 pandemic. The pandemic has amplified the need to address a decade of widening inequalities due to socioeconomic status and ethnicity.[104] Such inequalities translate to an inequitable gap in life expectancy.[105] For example, in England there is almost a twofold difference in mortality rates between people in the highest and lowest socioeconomic groups.[104 106] And as was recently articulated in Europe's Beating Cancer Plan, 'there should be no first- or second-class cancer patients'.[72]

Social inequalities are highly prevalent in lung cancer. On a global scale, the largest inequalities in cancer mortality rates are found in smoking- and alcohol-related cancers, including lung cancer.[28] People of lower socioeconomic status are at higher risk of lung cancer in all European countries.[28 107] They are also at greatest risk of late presentation, and have the poorest survival.[26-28] Ensuring equitable access to screening programmes is thus essential to address existing health inequalities.[93] Otherwise, disadvantaged groups will continue to experience an unjust share of the health burden.[37 105] These combined benefits are captured in *Figure 7*.

Figure 7. The impact of lung cancer screening extends beyond lung cancer



6 Ensuring successful implementation of lung cancer screening at scale

Governments should chart out a clear roadmap for implementation

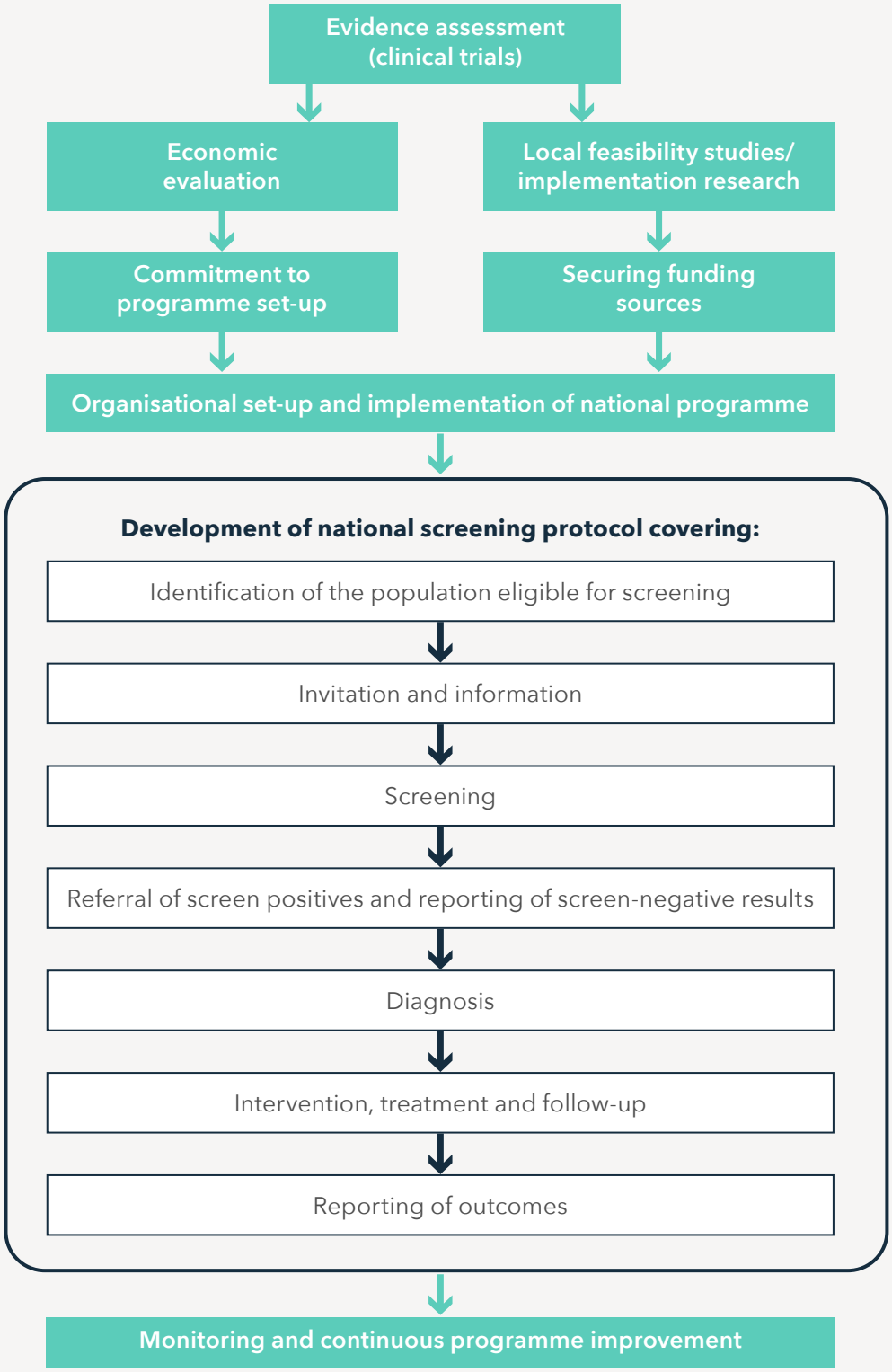
Given the strength of the evidence, it is now time for governments to evaluate the feasibility of lung cancer screening programmes in their specific national contexts. So far, only a few countries – including the US, Japan, South Korea, Poland, Croatia and Australia – have committed to implementing nationwide lung cancer screening programmes. However, pilot projects and local feasibility studies are being conducted in almost every region of the world. Findings from this implementation research should be built into a clear pathway to guide decisions around the most feasible way each country can replicate benefits from screening seen in clinical trials, while minimising potential harms and ensuring the most efficient use of local resources (*Figure 8*).[108]

Findings from existing implementation research should guide the roll-out of lung cancer screening

More than a decade of feasibility and pilot studies has provided a wealth of information, with many lessons learnt to guide implementation in different countries. For example, studies have shown that eligibility criteria used in Europe and North America may not be suitable in China, where there is a high incidence of lung cancer in women and non-smokers.[109] In Taiwan, for example, lung cancer is common in non-smokers, so lung cancer screening is being proposed for other groups at high risk of lung cancer.[110] In Europe, several pilots are exploring the potential to combine LDCT screening with early detection of COPD or other smoking-related conditions.[111 112] The European Commission-funded implementation study 4-IN THE LUNG RUN is looking to identify the best way to individualise screening intervals based on levels of risk.[113]

Based on this considerable research, several key success factors emerge which should be built into the development of large-scale lung cancer screening programmes (*Figure 9*).

Figure 8. A clear roadmap should be followed to guide decisions about local implementation of lung cancer screening



Note: Timing of economic evaluation and feasibility studies varies depending on screening governance framework in each country – as does their impact on choice of national protocol

Figure 9. There are several key factors in the successful implementation of targeted lung cancer screening[84 93 114]

1. **Effective screening requires high-quality, multidisciplinary lung cancer care pathways**
Investment in lung cancer screening is best inscribed in a broader commitment to address lung cancer as a priority. In particular, the success of a screening programme depends on high-quality care pathways.[115] Everyone with a positive result should have rapid access to comprehensive diagnosis and care, led by a multidisciplinary care team.[114] Embedding screening within a broader

focus on early detection, as mentioned previously, is also crucial.

2. Reliable means of identifying people at highest risk of lung cancer are needed

The success of targeted LDCT screening depends on being able to identify the population at highest risk of lung cancer, who are most likely to benefit from screening. A first step to any screening programme is thus to ensure there is a reliable database of the entire population that includes smoking history and other relevant risk factors to determine eligibility. However, most countries do not have such a centralised database,[84] with the exception of those with unified primary care records. Some countries, such as the UK, have found ways to combine data sources, often using a multistep approach where a first outreach is made by a doctor or through a centralised invitation, and then individuals are asked to complete a structured questionnaire to determine smoking levels.[84]

As mentioned previously, eligibility criteria should also be looked at within the context of each country's epidemiology – and adjusted as needed to reduce the potential for inequities in access to screening (*Box 3*).

3. Securing attendance from vulnerable populations is essential to reduce socioeconomic inequalities

Screening programmes must include targeted efforts to engage vulnerable populations, to avoid exacerbating inequalities related to lung cancer. Data from both trial and real-world settings show that people with lower socioeconomic status and other disadvantaged groups are less likely to participate in cancer screening programmes.[114 118 119] Barriers to attending for screening may be physical, financial, informational, social or cultural.[41 78 120] Tailored interventions may help overcome some of these barriers in vulnerable groups, and may also be effective at overcoming barriers to attendance in other groups (*Table 3*).[121-124]

Box 3. The importance of localised eligibility criteria: the US example

The US recently changed its definition of 'heavy smoker' to improve coverage of its LDCT screening programme.[76] The US Preventive Services Task Force found that reducing the pack-year* criterion to 20 pack-years from the 2013 recommendation of 30 pack-years would allow for inclusion of more women and non-Hispanic Black, Hispanic, and American Indian/Alaska Native persons, who were previously left out of screening.[116]

* The National Cancer Institute defines a 'pack-year' as a measure for the amount a person has smoked over a long period of time. It is calculated by multiplying the number of packs of cigarettes smoked per day by the number of years the person has smoked. For example, 1 pack-year is equal to smoking 1 pack per day for 1 year, or 2 packs per day for half a year, and so on.[117]

Table 3. Possible approaches to address barriers to lung cancer screening, particularly among vulnerable populations

Barriers	Approaches to overcome them
Limited information and awareness	
• Insufficient awareness or misinformation about the benefits of participating in lung cancer screening[124 128] • Confusion around screening results or lack of familiar care providers, especially due to language barriers or for people with lower health literacy[124 129] • Difficulty accessing online information services or not being registered with a healthcare service[129]	• Explaining benefits and harms of screening in an accessible format, with language- and literacy-level-appropriate information[42 120] • Providing patient-friendly decision aids such as information brochures, videos and links to electronic resources that people can refer to after an appointment[97 130 131] • Social media campaigns and digitally accessible information on screening to reach underserved or isolated communities[121 132]
Physical and financial barriers to access	
• Distance from screening centres and provision gaps in rural areas[72 133] • Prohibitive transport and parking costs, and difficulty accessing screening centres[93 134] • Difficulty of fitting appointments around work or caregiving commitments[134]	• Linking underserved communities with larger screening centres through emerging digital health tools, to enable community access to multidisciplinary teams[72 97] • Decentralised mobile screening in public spaces like supermarket car parks e.g. Manchester Lung Health Check model[20 126] • Offering assisted travel to imaging units e.g. the 'hub-and-spoke' model[93] • Community pharmacists and other allied health professionals providing information on lung cancer screening to their clients/patients[135]
Psychological and social barriers	
• Forgetting to attend a scheduled appointment or little awareness of the benefits of screening[120] • Social or cultural distrust of healthcare services, or other psychological factors that may undermine motivation to engage in screening e.g. denial, fatalistic health beliefs, embarrassment due to stigma around lung cancer[42 131 134 136]	• Postal, text and telephone reminders after first invitation letter to attend screening[137 138] • Personalised letter encouraging attendance from family physicians[138] (e.g. used for cervical cancer screening in the UK)[121] • Targeted awareness initiatives involving community or faith leaders[28 120] • Co-designing public information and education campaigns with vulnerable groups to ensure suitability and impact of messaging[42 122]

One model of particular interest is to offer screening in public spaces in socioeconomically deprived areas. This model has been developed in some of the Lung Health Check pilots now being rolled out across England.[125-127] Pilot projects in Manchester used mobile units near supermarkets to tackle barriers such as parking and transport costs, inconvenience and location.[87] Three quarters of attendees were from the lowest socioeconomic quintile.[127]

4. Engagement of primary care professionals is essential

Family physicians remain people's most trusted source of health information and play a key role in engaging people to attend for screening. Misinformation about lung cancer and screening can be potential barriers to acceptance of screening.[139 140] Family physicians can help allay people's fears about screening, provide balanced information about risks and benefits, and explain the importance of early detection in lung cancer.

Training of family physicians is essential. Inconsistent levels of awareness around screening guidelines and eligibility, and poor understanding of the risks and benefits of screening, have been evidenced in some countries.[141-143] A recent survey found US healthcare providers with lower knowledge of screening guidelines were less likely to refer patients for LDCT screening.[141] Physicians should also be encouraged to adopt a shared decision-making approach to screening with their patients.[42 97]

Engagement of family physicians should not stop with their role in securing attendance to screening. They should, where feasible depending on the organisation of the health system, play an active role in following-up individuals after their first round of screening, explaining findings and making sure people continue to attend screening.[97 144]

5. Lung cancer screening should be built into overall health promotion messages

Sensitive messaging about lung cancer screening is essential and should tackle stigma related to both lung cancer and smoking. Addressing potential fear and stigma surrounding lung cancer is important.[41 42] Family physicians also need to find the most appropriate way to tackle the need for smoking cessation. In some cultures, some physicians may be reluctant to raise the topic of smoking cessation, and mentioning it in invitations to attend screening may reduce participation.[140] One approach is to present the opportunity to undergo LDCT screening as part of a proactive wellness approach to one's health (*Box 4*).

Box 4. Lung Health Checks in England: taking a wellness approach

The Lung Health Check model adopted across England takes a wellness approach for all respiratory disease rather than focusing on cancer. Individuals are assessed for all lung conditions and offered a CT scan if eligible.

The following approaches have been found to encourage uptake and overcome stigma surrounding smoking and fear of lung cancer:

- Invitations do not mention smoking status or smoking cessation.
- Invitations do not mention lung cancer, so as not to put people off taking part due to fears about cancer.
- Supportive interventions (e.g. psychosocial support) are offered as part of the wellness check.
- Awareness campaigns accompanying the programme offer good-quality information.
- During health checks, information is provided making it clear that lung cancer can be treated if caught early.

Messaging about lung cancer and smoking should be targeted to different groups – for example by gender. Lung cancer incidence has been rising in women, as have rates of smoking – but smoking is not the only factor.[2] [145] [146] Cumulative evidence from lung cancer screening trials also suggests that LDCT screening may have a more beneficial effect in women than men, both in terms of increased early-stage diagnosis and reduced mortality.[18] [84] [147]

6. Clear nodule management protocols and personalised screening intervals can reduce harm and improve programme efficiency

Any screening programme carries risks – and minimising risks is not only an ethical imperative but also a condition for cost-effectiveness. Protocols guided by the most up-to-date evidence[148] [149] are essential to guide healthcare professionals in determining which nodules to refer for further diagnosis and possible treatment, and which to simply monitor.[87] [93] The use of protocols reduces the number of false-positive cases, patient recall and the need for repeat scans and investigative procedures, leading to lower costs overall.[42] [87]

Tailoring follow-up protocols to personal levels of risk may also improve the effectiveness and cost-effectiveness of screening. Both annual and biennial screening programmes have been deemed potentially cost-effective in existing studies.[61] [84] [102] However, personalising screening intervals after baseline screening may minimise the need for potentially unnecessary investigations in people deemed at lower risk. They may be particularly relevant for women, for whom nodules have been shown to have a slower growth rate than for men.[150] [151]

7. The right organisational model and health system resourcing are needed to ensure sufficient staffing and infrastructure

Screening is about more than just the scan itself, and selecting the most appropriate organisational model is key. The logistical aspects of screening – centralising invitations, ensuring systematic follow-up, recording outcomes of screening from cancer registries – require sophisticated information systems and careful coordination,[37] all of which need appropriate resourcing. It may be that structures or resources devoted to existing cancer screening programmes can be leveraged – for example, if all cancer screening is offered by a central coordinating centre.[144]

The most appropriate organisational model should be chosen, balancing the need for outreach and quality assurance. Some countries have chosen to centralise screening in a limited number of specialist centres, which may help ensure high quality of screening.[114] Others locate screening programmes in community settings to foster outreach to vulnerable populations, linking these centres to specialist multidisciplinary teams in a hub-and-spoke approach.[93] Careful consideration of available technical and workforce capacity is also an important factor to consider.

Regardless of the organisational model, building quality assurance and professional training across all centres performing CT scans is essential. This can help ensure CT scans are of consistent quality and that interpretation follows a common approach.[42] Benchmarking CT software and AI may also help improve the reliability of interpretation.[84] These approaches can help to relieve potential capacity shortages in countries where availability of trained radiologists to perform CT scans may be limited.[133 152]

7 Conclusions

Early detection represents the best chance to reduce the number of lives lost to lung cancer. Following similar investments in screening programmes, other common cancers have seen significant improvements in survival, while lung cancer survival remains unacceptably low. Investment in lung cancer screening must be next.

There is now considerable evidence that lung cancer screening using LDCT scans offers a safe, effective and potentially cost-effective tool to deliver significant reductions in lung cancer mortality. A decade of implementation research has provided helpful guidance on how findings from clinical trials can translate into large-scale programmes which can optimise benefits for participants while minimising any potential harms. The onus is now on governments to chart a roadmap to implementation suited to their national context.

In the wake of the COVID-19 pandemic, we have a unique opportunity to take a long-term view and build for a sustainable future. Lung cancer screening is the surest way to shift lung cancer from a fatal to a treatable condition and decrease its toll on the lives of millions of people around the world. Given its prevalence, achieving earlier detection in lung cancer will translate into substantial benefits in overall population health, productivity and societal costs. The benefits of lung cancer screening also extend beyond lung cancer: it can allow the earlier detection of other NCDs linked to smoking and help address growing socioeconomic inequalities in health.

We can no longer afford to neglect lung cancer and its impact on our societies. Focusing on lung cancer must be an integral part of our efforts to build sustainable health systems and strong economies in a post-COVID-19 world. The costs of failing to act now are simply too great.

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Appendix 1.

Synthesis of published cost-effectiveness studies on low-dose computed tomography screening

Study	Key findings
Black *et al*. 2014[152]	In the National Lung Screening Trial study, screening with low-dose computed tomography (LDCT) cost USD $52,000 per life year gained (LYG) and USD $81,000 per quality-adjusted life year (QALY) gained, lower than the USD $100,000/QALY threshold level of reasonable value.
Cressman *et al*. 2017[153]	LDCT would cost CAD $20,724 (at 2015 rates) per QALY gained, which is considered cost-effective by Canadian standards. Cost-effectiveness was driven primarily by non-lung-cancer outcomes.
ten Haaf *et al*. 2017[62]	Microsimulation model results indicate that in Canada, lung cancer screening may be cost-effective, particularly if stringent smoking history eligibility criteria are applied; multiple scenarios indicated a cost per LYG lower than the threshold of CAD $50,000/QALY.
Tomonaga *et al*. 2018[154]	Microsimulation model estimated €24,972 – €48,369 per LYG and €35,674 – €69,099 per QALY gained. Authors conclude screening with LDCT may be cost-effective in Switzerland, which has high smoking prevalence.
Hinde *et al*. 2018[155]	Community-based Lung Health Checks in Manchester, England, report a cost of £10,069 per QALY gained, which is below the National Institute for Health and Care Excellence (NICE) conventional threshold of £20,000 – £30,000/QALY.
Snowsill *et al*. 2018[156]	Systematic review of randomised controlled trials comparing LDCT screening programmes with usual care (no screening) or other imaging screening programmes (CXR), looking at England. The incremental cost-effectiveness ratio (ICER) for a single screen in smokers aged 60–75 years with at least a 3% risk of lung cancer was £28,169 per QALY, below the £30,000 NICE threshold.
Griffin *et al*. 2020[157]	An individual patient model was developed and calibrated against the US National Lung Cancer Screening Trial and costs taken from UK Lung Cancer Screening Trial. Analysis confirmed Snowsill *et al.* findings for single screening and found annual and biennial screening programmes were not predicted to be cost-effective at any cost-effectiveness threshold.

Note: none of these studies include assessment of findings from NELSON trial

The LungAmbition Alliance

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