Increasing the earlier detection of lung cancer: a toolbox for change

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LUNG CANCER POLICY NETWORK

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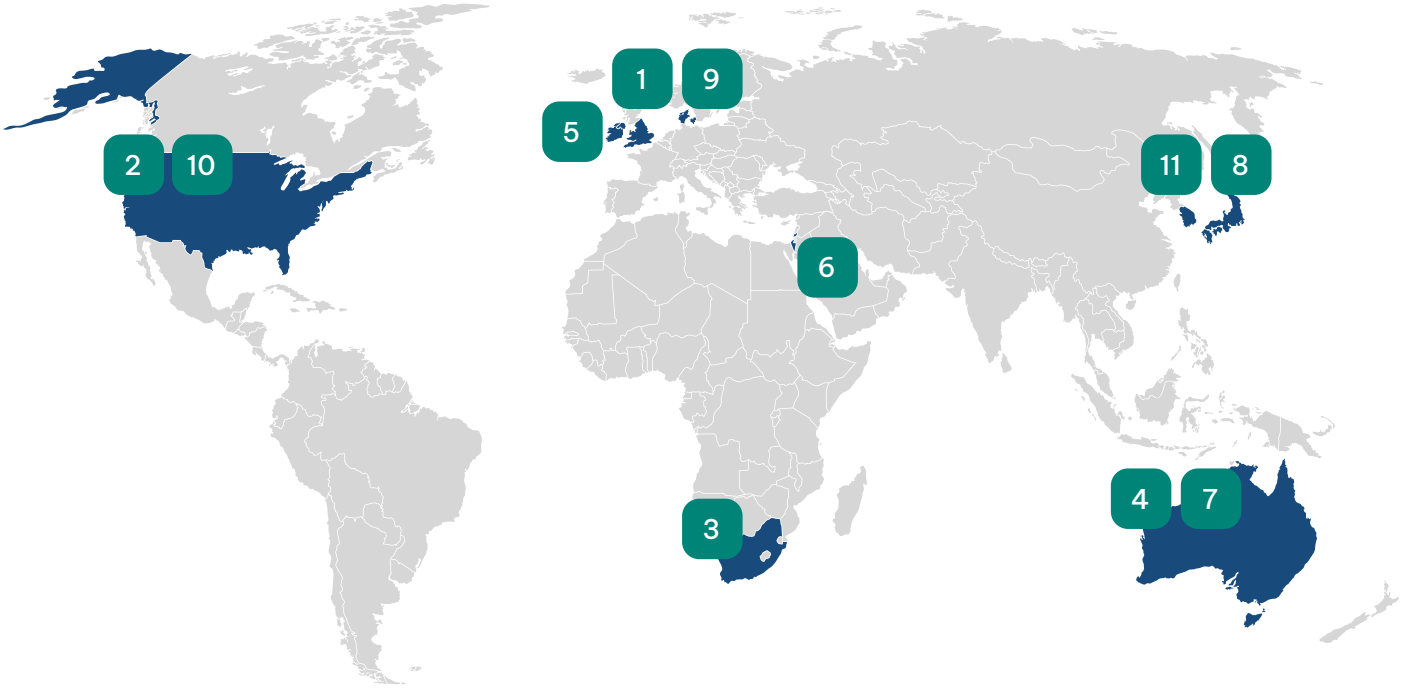

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Executive summary

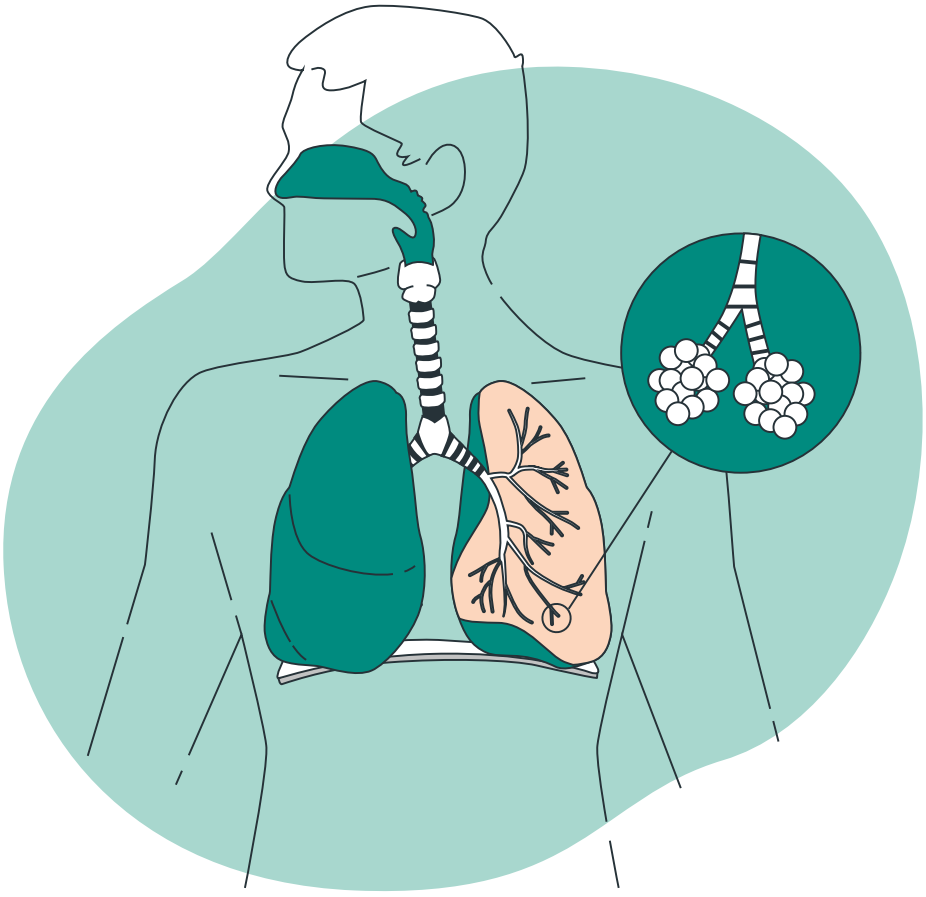
The global burden and mortality rate of lung cancer could be significantly reduced through increased early detection. Most people with lung cancer are currently diagnosed at an advanced stage, which is a major contributor to lung cancer being the leading cause of cancer-related death.[1-3] There is a broad consensus that increasing the earlier detection of lung cancer offers a unique opportunity to shift diagnosis to an earlier stage, thus improving survival rates.[4-6] This is essential to complement ongoing efforts to reduce rates of smoking, currently the leading risk factor for lung cancer.[7] While targeted screening of people at high risk of lung cancer using low-dose computed tomography (LDCT) is the most effective means of detecting lung cancer at an early stage, there are various existing and emerging approaches to early detection.[8-10] These include public awareness campaigns, symptom-based detection, screening, incidental detection, computer-aided detection (CAD) and biomarkers.

The development and implementation of early detection approaches should be prioritised by national decision-makers. Ambitious and practical steps can be made to improve the early detection of lung cancer, using a combination of approaches that reflect a country's current political and health system context.[6] This not only offers the chance to significantly improve lung cancer survival rates, but can also support the achievement of wider cancer and non-communicable disease goals and reduce the current financial burden of the disease.

A strategy for early detection that is tailored to each country's needs is vital to enable effective implementation. National LDCT screening programmes may not currently be feasible in many countries due to the scale of investment and capacity required.[11] Therefore, it is essential to consider local epidemiology, health system capacity and available resources when developing a comprehensive strategy for the early detection of lung cancer across the population. Such a strategy can help address common inequities in lung cancer care and outcomes, and it is important to keep those who could benefit most front of mind.

To support health system leaders and decision-makers in developing and implementing effective and nationally appropriate strategies for the earlier detection of lung cancer, we recommend the following actions:

- **Prioritise and promote** early detection approaches in lung cancer and lung health strategies.
- **Align** early detection approaches within broader national policies such as cancer control plans.
- **Perform** a robust assessment of health system resources and capacity.
- **Involve** communities at highest risks of late presentation of lung cancer to understand the barriers affecting their engagement with care.
- **Explore** the utilisation and integration of technology to improve the effectiveness of detection and diagnostic imaging.
- **Invest** in research to develop new approaches and improve existing approaches to early detection.
- **Conduct** regular monitoring and evaluation of early detection and wider lung cancer metrics.



The opportunity that early detection holds for lung cancer

Increasing the early detection of lung cancer offers a unique opportunity to reduce the disease's significant burden and mortality across the globe. The majority of people with lung cancer are currently diagnosed at an advanced stage (stages III–IV): over 75% for non-small-cell lung cancer (NSCLC) and over 90% for small-cell lung cancer (SCLC).[1] Treatment options are limited for people with advanced lung cancer; for example, they may not be a candidate for potentially curative interventions such as surgery.[12] As a result, people diagnosed at stage IV have a five-year survival rate of less than 10% compared with up to 92% for people diagnosed at stage I.[2 3 13] This is a major contributor to lung cancer being the leading cause of cancer-related death (*Box 1*).

Box 1. The global burden of lung cancer

- Globally, more than 2 million people are diagnosed and almost 1.8 million die from lung cancer each year; it is the cancer with the highest incidence rate and the highest mortality rate.[14]
- If diagnosed at an advanced stage, lung cancer has a lower survival rate as well as incurring greater healthcare costs, due to more complex treatments and care required.[15]
- Lung cancer is often diagnosed at a later stage than other cancers; this contributes to it incurring the highest financial cost of all cancers.
- In 2017, the cost of lung cancer (including tracheal and bronchial cancers) to the global economy was predicted to be USD $3.9 trillion between 2020 and 2050.[16]

Early detection of lung cancer

There are four stages of lung cancer, which indicate its size and whether it has spread.[17] In this report we use the term 'early detection' to refer to detecting lung cancer at stages I and II; this is also often referred to as early-stage cancer. We also use the term 'earlier detection' to refer to shifting the detection of lung cancer from a more advanced stage (such as stage IV) to an earlier stage.

While reducing rates of smoking is key to addressing the burden of lung cancer, early detection is an essential complement to improve outcomes for people whose cancers could not be prevented. Smoking is currently the leading risk factor for lung cancer, and many countries have implemented tobacco control and smoking cessation programmes as recommended by the Framework Convention on Tobacco Control.[18-20] However, tobacco control and smoking cessation alone are not enough to prevent all cases of lung cancer.[7] People who used to smoke remain at a three times greater risk of lung cancer for up to 25 years after stopping, compared with people who have never smoked;[21] lung cancer also affects people who have never smoked.[15] The second leading risk factor for lung cancer is air pollution: lung cancer deaths associated with air pollution have risen by 30% since 2007.[22] Genetic risk factors also account for a significant proportion of lung cancers, and have a higher prevalence in certain regions, such as Asia and Latin America.[23 24]

The earlier detection of lung cancer is vital to achieving the goal of reducing the burden of non-communicable diseases at global and national levels. In the past decade, reducing the burden of cancer has become an international priority, with ambitious targets set at a global level and mirrored at a regional and national level:[25 26]

- United Nations Sustainable Development Goal Target 3.4 – reduce by one third premature mortality from non-communicable diseases through prevention and treatment, and promote mental health and wellbeing.[27]

- World Health Organization – relative reduction of the overall mortality from four non-communicable diseases (cardiovascular diseases, cancer, diabetes and chronic respiratory diseases) by 25%.[28]

Despite these commitments, from 2020 to 2040 it is estimated that the number of deaths from lung cancer could increase by over 60%,[29] rendering these targets unachievable without concerted action at the national level to increase early detection.

To significantly reduce the burden of lung cancer, comprehensive early detection strategies must be developed and implemented. The key principle of early detection is to diagnose a disease at an earlier stage to increase the likelihood of a curative intervention. Although there are many approaches to establishing a strategy for the early detection of lung cancer, there are two cross-cutting components:[6]

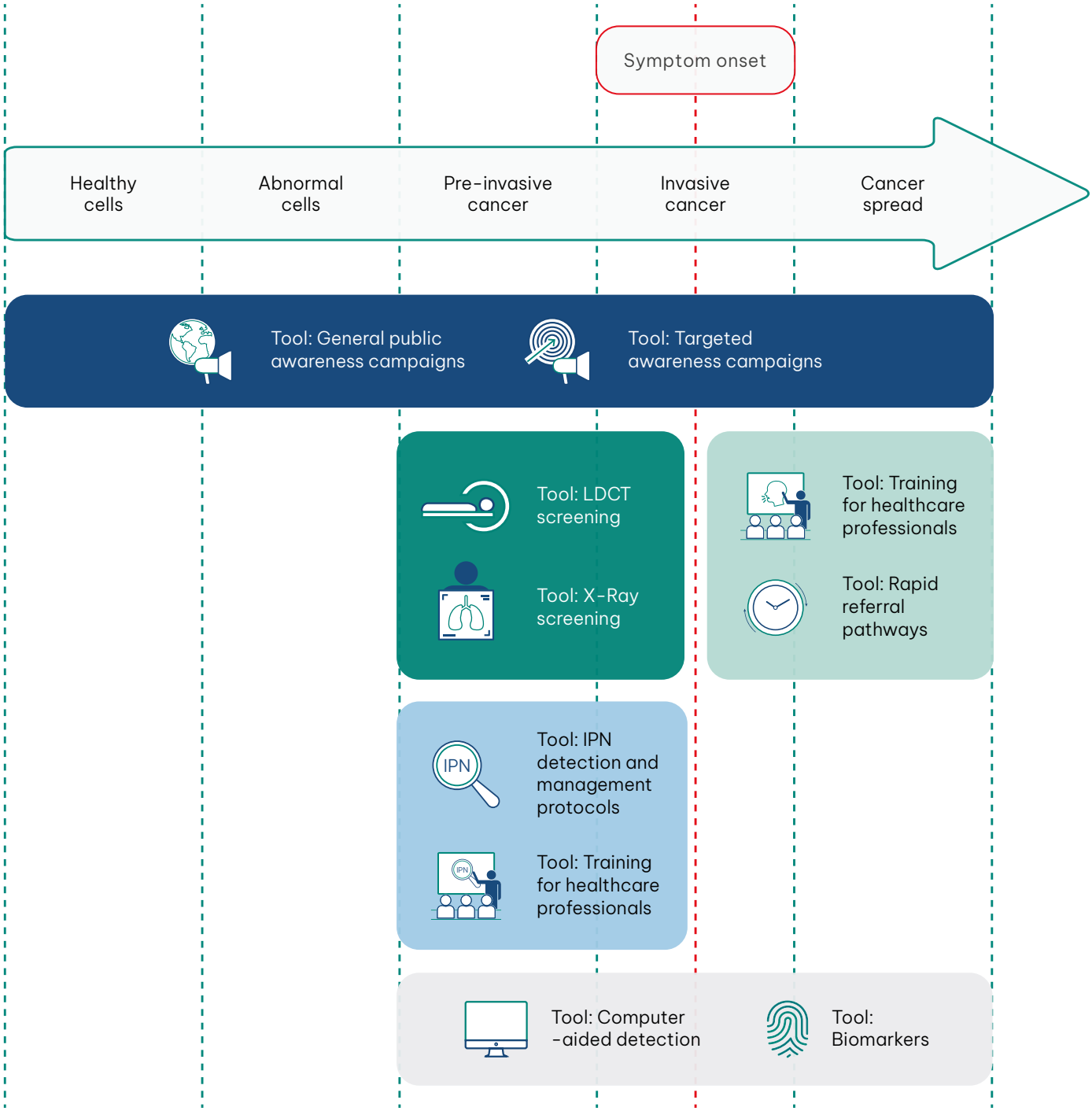
- Detecting people without symptoms (asymptomatic individuals), which can be achieved through early detection approaches such as targeted screening or incidental detection of pulmonary nodules (growths in the lung). This provides the greatest opportunity to diagnose and treat lung cancer at the earliest possible stage.
- Detecting people with symptoms of lung cancer (symptomatic individuals) as early as possible to maximise treatment options and minimise the delay in beginning treatment, to improve disease outcomes.

National cancer control plans, where they exist, do not always include specific lung cancer objectives and can lack a focus on early detection. Despite global recognition that national cancer control plans are a cornerstone of action to address the burden of cancer, almost 20% of countries did not have a national cancer control plan in 2018.[30] Among countries that do have a national cancer control plan, many still do not include or prioritise lung cancer and even fewer specifically prioritise early detection of lung cancer.[31] It is vital that health system leaders and decision-makers address these gaps by ensuring early detection is made an integral feature of national cancer control plans. Ambitious steps must be taken to implement effective and nationally appropriate strategies, making use of existing tools to seize the opportunity to significantly improve survival.

A toolbox for change

Developing an early detection strategy that reflects a country's local epidemiology and national health system is crucial to ensuring its effectiveness and appropriateness. There are various existing and emerging approaches to increase the early detection of lung cancer, which include: public awareness campaigns, symptom-based detection, screening, incidental detection, CAD and biomarkers (*Figure 1*). Targeted screening of people at high risk of lung cancer using LDCT is the most effective means of detecting lung cancer at an early stage.[8 10] However, large-scale implementation of LDCT screening programmes may not be feasible in many countries currently, due to the scale of investment and capacity required.[11] It is therefore necessary to consider the local epidemiology, health system capacity and available resources, using a combination of early detection approaches, to develop a comprehensive strategy to detect lung cancer across the population.

Figure 1. Overview of available approaches to detect lung cancer earlier



Key: Approaches to earlier detection

- Build public awareness
- Implement targeted screening
- Utilise incidental detection
- Incorporate technological innovations
- Enhance symptom-based detection and diagnosis

Build public awareness of lung cancer and the importance of early detection

Low awareness of lung cancer, as well as associated stigma, can cause delays in seeking medical care. Limited lung cancer-related knowledge is a common barrier to people accessing lung cancer screening services and seeking medical attention for symptoms.[32 33] One survey in Scotland found that the average time from a person developing lung cancer symptoms to visiting a physician was 99 days; 75% of people did not realise that their symptoms were suggestive of lung cancer.[34] Additionally, the perception that lung cancer is associated with smoking can cause stigma, which may also lead to people being reluctant to access available services to detect and diagnose the disease.[35] Addressing population-level awareness barriers can improve the earlier detection of lung cancer (*Figure 2*).[36 37]

Figure 2. Population-level awareness barriers to the earlier detection of lung cancer

Limited awareness of risk factors	While smoking is well recognised as a risk factor for lung cancer,[38] other risk factors such as air pollution, family history of lung cancer, exposure to second-hand smoke and exposure to environmental pollutants (such as asbestos) are significantly less well known.[38 39]
Limited awareness of symptoms	In a global survey, over 40% of people were unable to name any symptoms of lung cancer.[40] This could result in people delaying seeking medical attention.[33 41]
Limited awareness of treatment options	There is a misconception that little can be done to treat lung cancer, especially for advanced-stage disease.[35] This can lead to people affected feeling hopeless and reluctant to seek medical advice.[42]
Stigma	The stigma associated with lung cancer can decrease the likelihood of people accepting an invitation for screening or visiting primary care if symptoms begin to emerge.[35]

Tool: Awareness campaigns for the general public

Increasing awareness of lung cancer across the whole population improves recognition of symptoms and challenges misconceptions that contribute to stigma. Public awareness campaigns can be used to communicate key information about lung cancer to a large number of people.[43] A common objective is to improve the awareness of lung cancer symptoms to help reduce delays in people with symptoms seeking medical care (*Case study 1*).[44] In addition, public awareness campaigns can educate people that lung cancer can affect anyone and that everyone is equally worthy of diagnosis and treatment.[35] This can tackle preconceptions and stigma about lung cancer and lead to more people accessing early detection and diagnostic services.[4]

> Too many people **cannot identify** lung cancer symptoms and that is a **major obstacle** to earlier detection.
>
> **– Dr Anne-Marie Baird, Patient Advocate, Europe**

Case study 1.
Increasing public awareness of cancer in England and Wales

The ‘Be Clear on Cancer’ campaign was launched by NHS England and Wales to increase public awareness of the major signs and symptoms of cancer, including lung cancer, and encourage people to see their primary care physician.[45] This was communicated in both Welsh and English across television, radio and online, as well as adverts on buses and posters in pharmacies.[44] Materials were specifically developed to appeal to older adults and people from lower socioeconomic groups, targeted through television and radio scheduling and choosing appropriate locations for advertising.[44] Following the campaign there was a significant increase in urgent primary care referrals for suspected lung cancer.[43]

Tool: Awareness campaigns for people at high risk of lung cancer

Targeted awareness campaigns can deliver relevant information to groups at high risk of lung cancer, increasing knowledge of early detection approaches. There are specific messages that people at high risk of developing lung cancer would benefit from receiving. These include communicating the eligibility criteria and benefits of screening, where available, to support the uptake of a screening invitation (*Case study 2*).[46 47] Targeted campaigns can also be used to support people in navigating the health system through the detection, diagnosis and treatment process; for example, by providing information on healthcare rights (*Case study 3*). Such campaigns can also be used to inform people that there is a wide range of treatment options available, even for advanced lung cancer.

Image used with permission from the American College of Radiology

Case study 2.
Establishing the National Lung Cancer Screening Day in the US

National Lung Cancer Screening Day is an awareness day in November that supports screening centres throughout the US to open outside of their usual working hours (Saturday), allowing people to be screened without needing to take a day off work.[48] The initiative aims to increase awareness of lung cancer screening within the community by creating marketing and instructional materials to be used by facilities and advocacy groups, including promotional flyers (available in Spanish and English), a marketing and communications toolkit and a logistics guide to support Saturday opening.[49] Designing the awareness campaign as a national day means it appears in US calendars, which widens its reach and improves engagement. In 2022, a total of 326 advocates and screening sites signed up, with approximately 560 people screened over the day.[49]

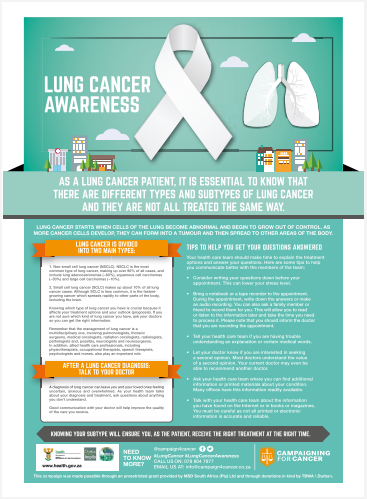
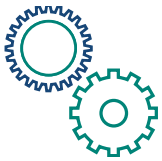


Image used with permission from Campaigning for Cancer

Case study 3.
Empowering people with lung cancer in South Africa

A patient advocacy organisation, Campaigning for Cancer, developed a public awareness campaign in collaboration with South Africa's National Department of Health and clinical experts, to improve people's knowledge of lung cancer and inform people of their rights to healthcare.[50]
A central focus was to support people to navigate through the health system. This included practical advice for people, such as bringing a notebook or tape recorder to appointments, asking for a second opinion if they are not satisfied with their diagnosis or treatment options, and insisting on an explanation if they do not understand.[51]
Materials such as posters and questionnaires were made open source, allowing other organisations such as health centres and charities to add their own branding and use them where and how they chose.[52]



Enhance symptom-based detection and diagnosis of lung cancer

It is important to address the challenges that healthcare professionals face in detecting and diagnosing lung cancer in people with symptoms. Symptom-based detection and diagnosis identifies people with symptoms of lung cancer, often in primary care.[53] It requires symptom recognition from both the individual and the healthcare professional; however, lung cancer symptoms can be challenging to diagnose due to similarities in presentation with other respiratory conditions (*Box 2*).[54] Even in countries with a screening programme, a proportion of people will present with symptoms because eligibility for screening is targeted to a specific population, and because not everyone who is eligible for screening will use the service.[55 56] Therefore, symptom-based detection with appropriate referrals and follow-up diagnostic testing – for example, imaging or biopsy – is an important complement to other early detection approaches.[57 58]

Box 2. Lung cancer symptoms[19 53 54 59]

Chest and respiratory symptoms include:

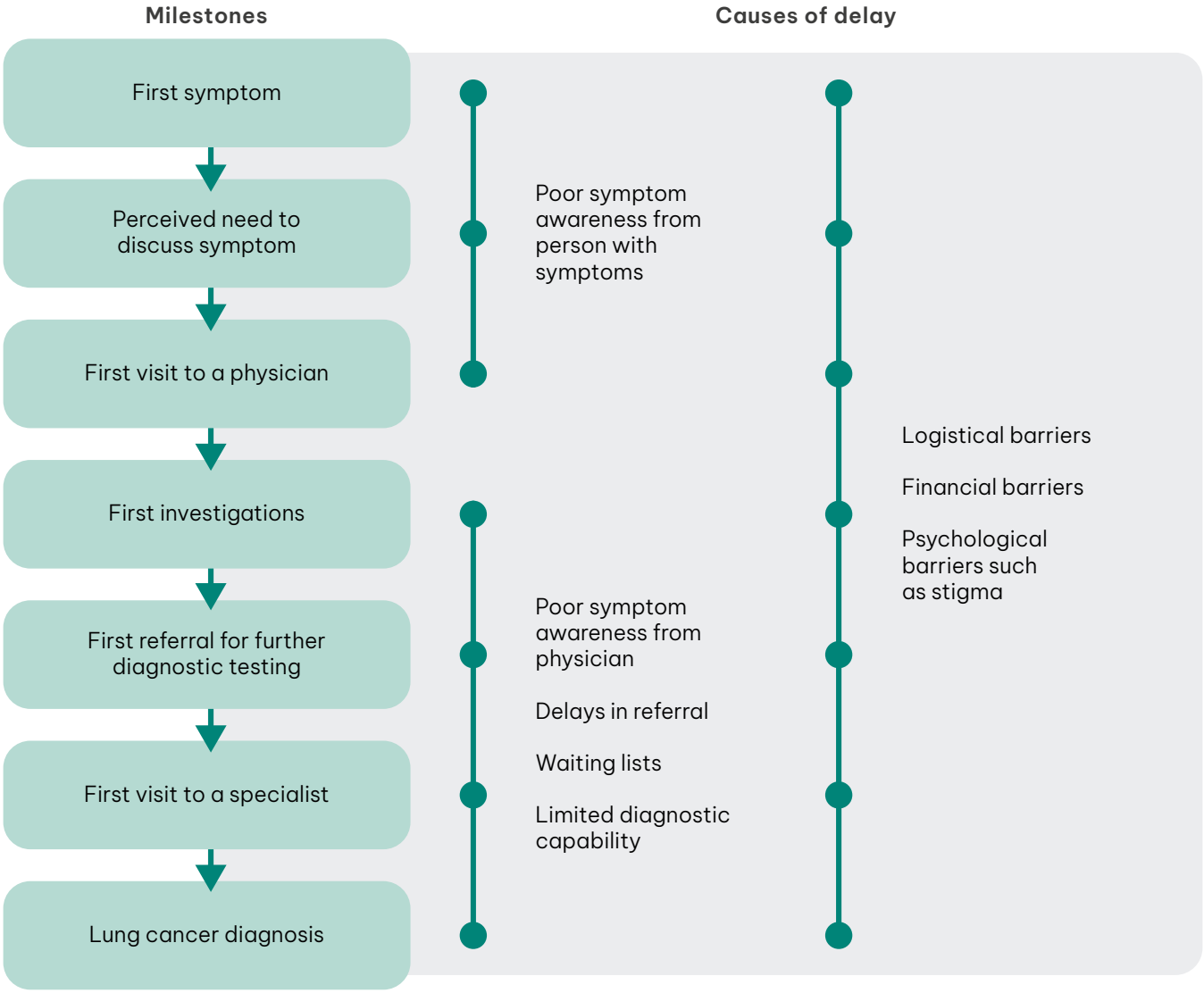
- Chest pain that is often worse with deep breathing, coughing or laughing
- Coughing up blood
- Cough (persistent or worsening)
- Hoarseness
- Shortness of breath
- Wheezing

Systemic symptoms include:

- Decreased appetite and/or weight loss
- Bone pain
- Fatigue, lethargy and weakness

Outcomes of lung cancer could be improved by strengthening training for healthcare professionals and ensuring that rapid referral pathways are available. By the time symptoms become noticeable, lung cancer is often already advanced; urgent action is then required to diagnose and begin treatment as quickly as possible to achieve the best opportunity for survival.[60] There are several factors that can cause delays from first lung cancer symptoms to diagnosis (*Figure 3*). One study from the UK found that 33% of people with lung cancer had visited a primary care physician three or more times before being referred for specialist diagnosis, compared with only 3% of people with breast cancer.[61] Symptom-based detection and diagnosis could be improved by providing training for healthcare professionals to increase recognition of lung cancer symptoms, as well as by implementing rapid referral pathways to reduce delays in accessing specialist diagnostics.[37 62]

Figure 3. Delays and barriers from symptom development to lung cancer diagnosis



Adapted from Hiom (2015) and Olsen (2009).[63 64]

Tool: Symptom awareness training for healthcare professionals

Training for healthcare professionals could increase the earlier detection of lung cancer by improving symptom recognition and timely onward referral. Providing healthcare professionals, particularly primary care physicians, with lung-cancer specific information, resources and guidelines can improve symptom recognition.[65] This can be supported through training programmes such as a free e-learning tool from Lung Foundation Australia and Cancer Australia (*Case study 4*).[66] Training programmes can also develop healthcare professionals' knowledge of lung cancer, which can then be passed on to the public, helping to break down negative beliefs around the disease (for example, Cancer Research UK's Talk Cancer programme).[67] When equipped with relevant information, healthcare professionals can also signpost people at high risk of lung cancer to available early detection interventions such as screening.[68]

Case study 4.
Training healthcare professionals to investigate symptoms of lung cancer in Australia

In 2020, Cancer Australia published *Investigating symptoms of lung cancer: a guide for all health professionals*. This resource provides primary care physicians with a systematic approach to the appropriate investigation and referral of people with symptoms or signs of lung cancer and includes a referral pathway.[69]

Based on this resource, Lung Foundation Australia, in collaboration with Cancer Australia, developed a free, accredited e-learning course for primary care professionals.[66] The course consists of a selection of modules that use clinical scenario-based learning to increase confidence in the recognition of lung cancer symptoms. There is also a specific focus on providing safe and culturally appropriate care for Aboriginal and Torres Strait Islander people.

> One **challenge** we face in Brazil is the **lack of knowledge** about early detection of lung cancer in the medical community. This could be **improved** through **providing resources and training** to healthcare professionals.
>
> **– Professor Ricardo Sales dos Santos, Thoracic Surgeon, Brazil**

Tool: Rapid referral pathways

Rapid referral pathways allow people who present to their primary care physician with symptoms of lung cancer to be urgently referred for specialist diagnosis and care. Several countries, including Canada, New Zealand and the UK, have developed rapid referral pathways to reduce diagnostic delays for people with suspected lung cancer.[70] A common feature of these pathways involves primary care physicians making priority referrals to specialist clinics (*Case study 5*), although their specific design may vary.[70] Most pathways have specific referral criteria and waiting time targets to standardise diagnosis for people with suspected lung cancer within an acceptable time frame.[71]

Case study 5.
Developing Rapid Access Lung Clinics in Ireland

Ireland introduced Rapid Access Lung Clinics in 2009. Primary care physicians refer people with symptoms suggestive of lung cancer to the clinics for prompt diagnostic evaluation, which usually occurs within two weeks.[72] The clinics have specialist staff including respiratory specialists and dedicated lung nurses, and equipment to streamline tests. Lung nurses help individuals navigate through the referral and are available to answer questions at the clinics or on the phone. The target time to receive results is one month after initial consultation. Since implementation, the median time between referral to diagnosis was reduced from 34.5 days to 21 days, with approximately 50% of all cases of lung cancer being diagnosed at the clinics.[73 74]

Implement targeted screening for lung cancer

Screening for lung cancer detects asymptomatic cases through targeted routine examination of people at high risk. Targeted screening, unlike population-based screening, offers screening to groups of people with a higher risk of a specific condition.[75] The two imaging techniques currently used for lung cancer screening are LDCT and X-ray.[75] Alongside screening, the introduction of protocols to evaluate pulmonary nodules by assessing lung cancer risk can inform future care decisions, for example, nodule surveillance, further diagnostic testing or immediate treatment.[76 77]

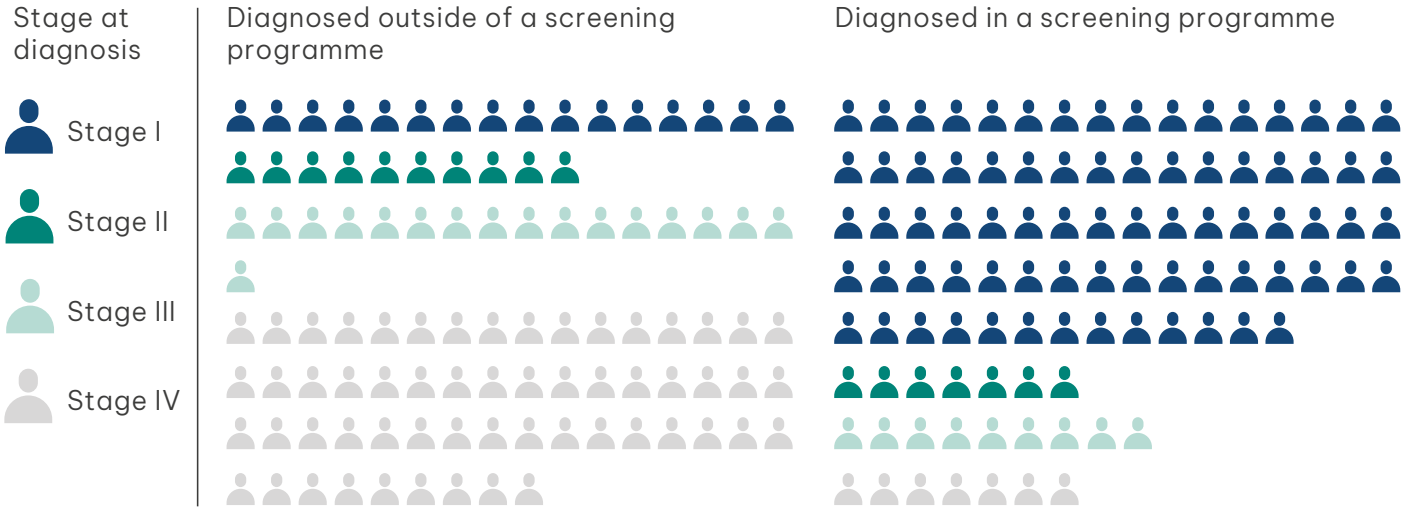
LDCT screening is considered the most effective screening method, and there is growing momentum for its implementation; however, there are challenges that have limited more widespread adoption. Based on the wealth of evidence supporting targeted LDCT screening for lung cancer,[8 9 78] the number of countries with national screening programmes has steadily risen, with more countries making formal commitments for implementation; a small number of countries have also implemented X-ray screening programmes.[79-87] However, in many countries there has been some hesitation to introduce lung cancer screening; this is due to healthcare challenges such as inequitable coverage of services, gaps in timely referrals and limited infrastructure alongside misconceptions of its value, risk and cost-effectiveness.[88-90] In some cases (for example, Colombia), countries have recommended lung cancer screening but have yet to provide resources to implement it.[91]

> Most people seek medical help when they have advanced-stage lung cancer. Therefore, there is a need to implement screening so that the disease can be **detected at an earlier stage**, significantly increasing people's chance of survival.
>
> **– Dr Ros Suzanna Ahmad Bustamam, Oncologist, Malaysia**

Tool: Targeted LDCT screening for people at high risk

LDCT is an accurate, sensitive and effective imaging technique that can be used for the screening of lung cancer. LDCT has a high sensitivity and can detect smaller pulmonary nodules than other imaging techniques such as X-ray, which can lead to an earlier diagnosis of lung cancer.[92] Multiple studies have accumulated robust evidence that targeted LDCT screening can reduce lung cancer deaths by almost one quarter among people at high risk of lung cancer.[8 9] Owing to the targeted nature of LDCT screening, fewer people need to be screened to prevent one death from lung cancer compared with population-based screening programmes for other common cancers.[9 93 94] LDCT screening also contributes to a shift towards diagnosing lung cancer at an early stage (*Figure 4*),[8 95] resulting in improved survival rates.[13] Additionally, it offers an opportunity to detect conditions other than lung cancer during screening, such as chronic obstructive pulmonary disease (COPD), cardiovascular disease and emphysema.[96]

Figure 4. Stage of lung cancer detected in screening programmes compared with routine care



Data from Sands, *et al.* (2021).[95]

> The **cost-effectiveness** of LDCT lung cancer screening beats that of breast and colorectal cancer screening because it is much **more focused** on high-risk people, resulting in a **greater proportion** of detected cancer.
>
> **– Bruce Pyenson, Actuary, US**

Based on robust evidence of the effectiveness of LDCT screening for lung cancer, implementation has become a major ambition in many countries. Countries that have now implemented national LDCT screening programmes include Croatia, Czechia, Poland, the US, South Korea and Taiwan;[79-84] more countries, such as Australia and England, have formally announced the launch of a national programme.[85 87] There are also many ongoing pilots in other countries, aiming to assess the feasibility of LDCT screening at a national level.[31]

Pilots can be an effective starting point for a country to incorporate LDCT screening into an early detection strategy. Pilots can provide data on the feasibility of national-scale implementation of LDCT screening.[97 98] This can be used to guide the design of a national programme, allowing for optimisation of screening processes such as participant recruitment. For example, in Israel, the government has implemented an LDCT screening pilot using different methods of recruitment to ascertain which method produces the highest uptake (*Case study 6*).[99] Screening pilots can act as the basis for a phased approach to building screening into a health system.

Case study 6.

Learning from an LDCT screening pilot in Israel[99]

In 2017, the Ministry of Health (MoH) appointed a multidisciplinary steering committee to develop a plan to implement a national LDCT lung cancer screening programme.[100] Since then, there have been several submissions made to the Health Basket Committee (which approves services and medication included in national health insurance) but all have been rejected. Instead, a pilot programme has been set up to demonstrate that lung cancer screening is feasible in Israel. The pilot will screen 10,000 individuals twice across the country's four healthcare providers. Although there is central coordination by the MoH, each of the four healthcare providers can apply their own recruitment method (such as text or email); data on screening results are reported to the central coordination and will be used to optimise screening going forward. The MoH will decide whether to include lung cancer screening in the health basket on completion of the pilot.

It is important to address practical issues, such as physical infrastructure and health system capacity, to optimise the implementation of LDCT screening. There is a need to develop LDCT screening infrastructure in many parts of the world; common issues include poor availability of LDCT scanners, lack of trained personnel such as radiologists, and under-resourced follow-up diagnostics and care.[101 102] In light of this reality, it may be appropriate for some countries to take a gradual approach to implementing LDCT screening, for example by improving existing early detection schemes alongside building suitable imaging capacity. Technology such as CAD and artificial intelligence (AI) can be used to reduce workforce needs (see Tool: Integrated CAD with chest imaging). Some programmes have been set up to overcome specific challenges such as poor access to scanners in remote regions (*Case study 7*).[103 104]

> A **possible solution** for overcoming inequitable access to screening equipment is by using **mobile screening units**; for example, in the northeast of Brazil, the Propulmão Mobile Project delivers screening in locations far from the major cities.
>
> **– Professor Ricardo Sales dos Santos, Thoracic Surgeon, Brazil**

Case study 7.

Utilising mobile lung cancer screening units in Australia

The Heart of Australia provides mobile health screening, interventions and education programmes for current and former miners at high risk of occupational respiratory diseases such as lung cancer.[105] In 2022, it introduced a new truck fitted with the world's first battery-powered LDCT machine, able to operate in challenging terrain with an unstable power supply. The truck travels to work sites across rural areas of Queensland to perform lung cancer screening. The onboard staff includes a driver, a radiologist, a respiratory specialist and an occupational health nurse. It is expected that the role of mobile units will increase following the government's formal commitment to implement a national LDCT screening programme.[87]

Tool: Targeted screening using chest X-ray

Screening using chest X-ray has demonstrated some effectiveness at detecting earlier-stage lung cancer in real-world settings. Chest X-ray is less effective than LDCT at detecting the earliest stages of cancer but could still be incorporated into an impactful strategy for early detection.[106] A small number of countries currently utilise X-ray screening, including Hungary and Japan. Of people who had lung cancer detected through X-ray screening in Hungary, 32% were diagnosed at stage I.[107] In comparison, only 14% of people who had symptoms of lung cancer were diagnosed at stage I.[107] Additionally, following the implementation of a nationally organised chest X-ray screening programme in Japan, a partial shift in detection from advanced to early-stage lung cancer was observed (*Case study 8*).[108] Evidence suggests that chest X-ray screening for lung cancer is likely to be cost-effective in high-risk populations.[109]

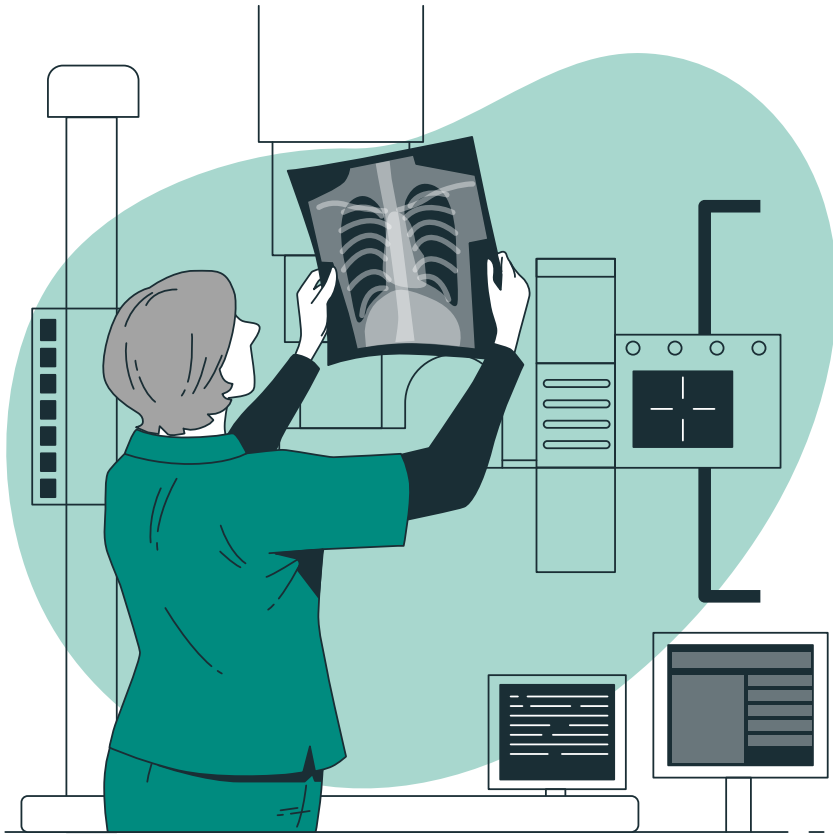
Chest X-ray screening could be used as an alternative where LDCT screening is not currently feasible, utilising existing infrastructure that can be further supported with CAD. Many countries do not have sufficient scanners or workforce capacity for the implementation of LDCT to be imminently feasible.[89 90] However, a lung cancer screening programme using chest X-ray could be established using existing infrastructure.[106] Additionally, as technology continues to develop and with the introduction of CAD (see Tool: Integrated CAD with chest imaging), X-ray screening has become more sensitive to detecting pulmonary nodules.[106] As such, chest X-ray could offer a lower-cost option for lung cancer screening while capacity is built for an LDCT screening programme.

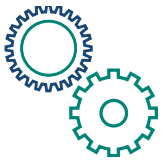
Case study 8.

Implementing a nationwide X-ray screening programme in Japan

Chest X-ray screening was first implemented in Japan in 1972 to detect tuberculosis as part of the Tuberculosis Control Laws.[110] As the Japanese population aged and the prevalence of lung cancer increased, the screening programme was widened in 1987 to include lung cancer.[86] However, formal guidelines for lung cancer screening were not developed until 2003.

Currently, all citizens aged 40 years or over are offered annual chest X-ray screening, with additional sputum cytologic testing available for people at high risk of lung cancer.[111] The implementation of a nationwide screening programme has corresponded with a partial shift in detection from advanced to early-stage lung cancer.[108] Multiple case-control studies conducted in Japan have shown chest X-ray screening to significantly decrease lung cancer mortality.[86 112]





Utilise incidental detection of lung cancer in routine chest care

Another approach for detecting lung cancer is the incidental detection of pulmonary nodules through imaging conducted for other reasons. There is a wealth of chest imaging, including computed tomography (CT) scans and X-rays, routinely conducted in health systems for reasons other than lung cancer detection and diagnosis. Examples include tuberculosis screening, diagnostic chest imaging for other diseases and trauma.[113 114] Pulmonary nodules (growths in the lung) that are detected from these images are known as incidental pulmonary nodules (sometimes referred to as IPNs). Utilising information from incidental findings appropriately is particularly important for people with other respiratory diseases as they are often at elevated risk of developing lung cancer.[115] As with screening, protocols to evaluate incidental pulmonary nodules are needed to enable the identification of suspicious nodules and guide appropriate referral, diagnosis and follow-on care.[77]

Increasing incidental findings of lung cancer will allow otherwise unidentified cases to be detected, diagnosed and treated at an earlier stage either in conjunction with, or independently of, screening. Incidentally detected lung cancer is often identified at an earlier stage than lung cancer detected through symptom-based detection, and this allows treatment to be started earlier.[116] It also enables the detection of lung cancer among people ineligible for screening, while expanding the reach of early detection to underserved populations.[117] Clear protocols and training for healthcare professionals are needed to successfully implement an incidental pulmonary nodule detection and management programme.

> We should be **integrating** the detection of lung cancer into tuberculosis screening. South Africa's health system is built for navigating a person through the tuberculosis care pathway, **so why not lung cancer?**
>
> **– Lauren Pretorius, Patient Advocate, South Africa**

Tool: Incidental pulmonary nodule detection and management protocols

Integrating the detection and management of pulmonary nodules into existing lung health initiatives and chest imaging could be a resource-effective tool to detect potential cases of lung cancer. The design of incidental pulmonary nodule programmes should be compatible with existing lung health initiatives in each country.[76] For example, in many countries, tuberculosis screening is well established; integrating a protocol for tailored incidental detection and management of pulmonary nodules could significantly increase the detection of lung cancer in these countries.[52] Detection and management protocols are also essential to effectively determine follow-up care for people in whom incidental pulmonary nodules are detected (*Case study 9*).[76 77] This would require relatively few resources to implement in comparison with setting up a screening programme, but some infrastructure developments would be needed for detection, assessment and tracking.[118]

Case study 9.

Managing incidental pulmonary nodules to improve the detection of lung cancer in Denmark

The Aarhus University Hospital (AUH) in Denmark has implemented an incidental pulmonary nodule programme using the Fleischner Society guidelines for nodule management.[119] The Fleischner Society has produced one of the most widely used guidelines in addition to the British Thoracic Society guidelines.[77 120] These guidelines provide specific management recommendations based on nodule characteristics (density and size), as well as the number of nodules and overall cancer risk. Between 2018 and 2021 at AUH, 4,181 people with incidental pulmonary nodules had follow-up CT scans and 249 (6%) were diagnosed with lung cancer; of these, 75% had stages I and II lung cancer, and potentially curative treatment was possible for 78%.[119]

Tool: Training for healthcare professionals to incidentally detect lung cancer

It is important to support healthcare professionals to incidentally detect lung cancer and provide assistive technology where available. Healthcare professionals involved in routine chest care vary across the world and, depending on their role, may require specialist training and support to incidentally detect lung cancer (*Case study 10*). They may have other specialisms outside of lung cancer (for example, trauma) and could benefit from training on detecting pulmonary nodules; this could be further supported with CAD.[121] Outside of imaging, healthcare professionals can be given training to identify people not responding to treatment for other diseases and provide further diagnostic testing for lung cancer.[52]

Case study 10.

Supporting healthcare professionals to detect incidental pulmonary nodules in the US[122]

In 2014, Bryan Health, a Nebraska-based health system in the US, developed an incidental pulmonary nodule programme in response to physicians acknowledging that they were missing nodules. The programme is run by an Advanced Practice Registered Nurse-Clinical Nurse Specialist (APRN-CNS) alongside a team of cardiothoracic surgeons, respiratory specialists and radiologists. When developing the programme, training was provided to establish clear roles and responsibilities. Radiology assistants were tasked with reviewing 450–500 identified CT scans with keywords such as 'nodule', 'lesion', 'mass' or 'density' written in their scan reports from across the health system, while the APRN-CNS carried out tasks including reviewing medical records. A report on the incidental pulmonary nodule/s and management recommendations are sent to each person's primary care physician to make a decision regarding follow-up.

Incorporate technological innovations to enhance early detection strategies

As technology has advanced, new approaches for the early detection of lung cancer are emerging. Adapting to technological progress can help detect lung cancer earlier but this requires health systems to be prepared and flexible. New technologies may not be appropriate for all national contexts, and a full assessment of suitability should be performed before implementation. In recent years, two promising areas of development are CAD within chest imaging and biomarker testing as both an independent approach and an opportunity to enhance existing early detection approaches.

Tool: Integrated CAD with chest imaging

CAD has increasingly been used as a tool to enhance screening and incidental pulmonary nodule detection. CAD tools have been developed to assist radiologists in assessing high numbers of scans. They can be integrated into the digital infrastructure of a screening or incidental pulmonary nodule detection programme and act as an additional 'reader'.[123] These tools can increase the accuracy of results, with more cases of lung cancer being correctly detected and fewer false positives (*Case study 11*);[123] this lessens the amount of unnecessary follow-up work and reduces costs.[124 125]

Further development and integration of CAD tools into detection and diagnostic imaging are needed to realise their potential benefits. Although most development of CAD tools has been conducted in high-income countries, these tools have the potential to be universally beneficial.[126] Careful consideration of regional differences in technology, processes and implementation needs is important in the development of an effective CAD tool. In order to implement CAD in more countries, a suitable digital infrastructure must first be established.[127] Additionally, integrating these tools into daily clinical workflow is a prerequisite for them to have practical application.[127]

Case study 11.

Using CAD to improve the detection rate of pulmonary nodules in South Korea[128]

Researchers based in Seoul, South Korea, simulated a real-world setting by embedding an AI-based CAD tool into their hospital's health screening workflow. In a randomised controlled trial, over 10,000 people were recruited to investigate the utility of the CAD tool to improve the detection rate of pulmonary nodules through chest X-ray. Following a health questionnaire, participants had a chest X-ray that was randomly allocated to either a radiologist alone or a radiologist supported with CAD. Pulmonary nodules identified on X-ray were confirmed with a CT scan. The study found that more than double the number of pulmonary nodules that required follow-up were detected by radiologists when supported by CAD while reducing the false-referral rate. This demonstrated the potential of CAD tools to improve the accuracy and effectiveness of imaging to detect lung cancer.

Tool: Preparation for early detection biomarkers

Evidence is building for the potential use of biomarkers in the early detection of lung cancer. There is a growing number of identified biomarkers that could be utilised to detect lung cancer earlier.[129 130] Research is ongoing to develop practical tests that can be used independently or in conjunction with screening.[130] There are various anticipated opportunities for biomarkers to improve the early detection of lung cancer, for example:[75 131 132]

- determining whether pulmonary nodules are malignant
- optimising the selection of high-risk groups for screening
- using independent biomarker screening as an alternative to imaging.

Exploration of early detection biomarker testing is ongoing; however, there are already disparities in access to available tests. At present, biomarkers are mainly used after lung cancer has been detected, to support the diagnosis and categorisation of tumour types to enable the selection of targeted treatments.[129 133] There is significant disparity within and between countries in terms of access to biomarker testing for lung cancer tumours, limiting the potential opportunity for post-detection biomarker testing to help determine the most effective treatment plan.[134 135] As biomarker testing continues to develop, additional resources will be needed to expand sample collection and increase testing facilities to realise its potential positive impact on lung cancer detection.[136]

> There is a vast amount of biomarker research ongoing, **exploring different avenues** for lung cancer early detection. Currently, I see biomarkers as a viable tool to complement the use of LDCT screening.
>
> **– Dr Hilary Robbins, Epidemiologist, International**

Continued investment and research are needed to integrate biomarker testing into early detection strategies for lung cancer. Research programmes are working to establish clear evidence for the effectiveness of using specific biomarkers to help identify people at high risk of lung cancer (*Case study 12*).[131 136] This could be used to refine the eligibility criteria for screening, improving the detection rate. To date, there are no practical examples of biomarker screening as a standalone approach to the early detection of lung cancer. However, current research aims to develop such a biomarker test and even produce a multi-cancer detection test able to assess the probability that someone has one of several cancers, including lung cancer.[137 138] To accelerate future biomarker development, research could be incorporated into existing lung cancer detection strategies to provide real-world evidence of their utility and application.

Case study 12.

The Integrative Analysis of Lung Cancer Etiology and Risk (INTEGRAL) programme[131]

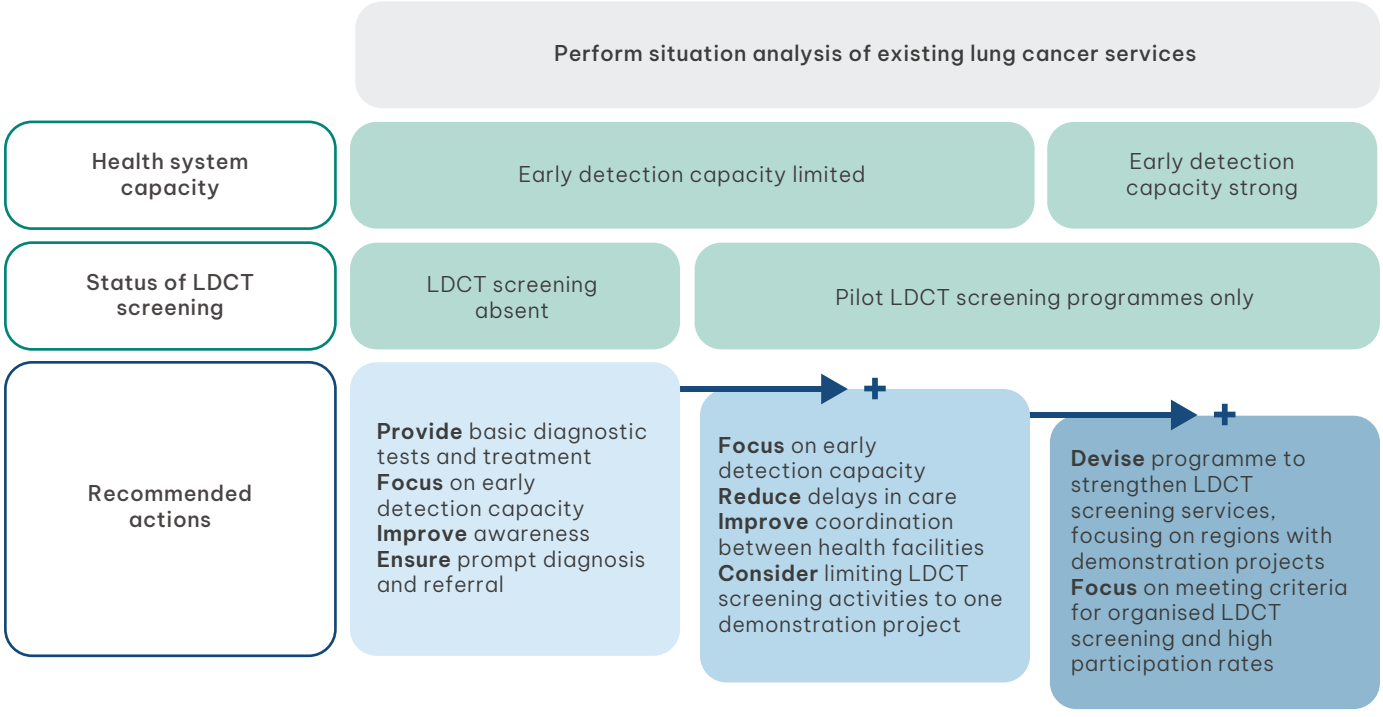
The INTEGRAL programme is a large, international research undertaking funded by the US National Cancer Institute, comprising three projects investigating genetic lung cancer risk, blood biomarkers that indicate lung cancer risk and the use of biomarkers in LDCT screening.

One study in the programme aims to identify and validate a panel of protein markers that can enhance risk prediction among people who currently smoke or used to smoke. This could potentially lead to the ability to better identify and prioritise LDCT screening of high-risk groups. The same panel is also being assessed as a tool to determine whether a pulmonary nodule identified in an LDCT scan is cancerous, which could help reduce missed lung cancers as well as false positives.

Key considerations to successfully implement early detection strategies for lung cancer

National decision-makers should act to reduce mortality from lung cancer through the adoption of early detection approaches. While there is no single approach to detect lung cancer at an early stage, the tools and examples outlined in this report can constitute key components of a comprehensive early detection strategy. This should be adapted to the national context in order to support ambitious and practical steps to improve the earlier detection of lung cancer, regardless of the current situation, ensuring the most efficient use of existing health system resources (*Figure 5*).[6] The chosen approaches should take into account the local epidemiology of lung cancer, tailoring early detection tools to address inequities in access and care with a focus on the people who could benefit most.

Figure 5. Planning early detection and screening according to current capacity



Adapted from WHO (2017).[6]

With these considerations in mind, governments should commit to:

- **Prioritising and promoting early detection approaches in lung cancer and lung health strategies** to ensure that the benefits of earlier detection are identified and fully realised at all opportunities.
- **Aligning early detection approaches within broader national policies,** including cancer control efforts, non-communicable disease plans, research agendas and health system reforms.
- **Performing a robust assessment of health system resources and capacity** to develop contextually appropriate early detection programmes for lung cancer, being mindful of gaps in workforce, resources and infrastructure.
- **Engaging with communities with the highest risks of late presentation of lung cancer and traditionally underserved groups** to understand specific barriers that may affect their engagement with care, and adapt approaches to fit their needs.
- **Exploring the utilisation and integration of technology** such as CAD and AI to improve the effectiveness of detection and diagnostic imaging.
- **Investing in research to develop new approaches and improve existing approaches,** including the opportunity for biomarkers to support early detection.
- **Conducting regular monitoring and evaluation of early detection and wider lung cancer metrics** that can be used to identify areas for improvement and ensure progress.

It is clear that earlier detection has the potential to transform treatment and survival of lung cancer. It is vital that national decision-makers make early detection an integral feature of cancer control plans and take ambitious steps to implement feasible strategies that best serve the needs of their populations and ultimately save lives.

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