Lung cancer screening:
A promising new frontier

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LUNG CANCER is one of the most commonly diagnosed cancers in Australia and is the leading cause of cancer mortality, with 8457 deaths recorded in 2020.[1] In 2022, there were approximately 14,500 new lung cancer diagnoses nationwide.[1] According to the latest statistics from the Australian Institute of Health and Welfare, there were over 21,700 people living with lung cancer between 2013 and 2017.[1] Lung cancer is often asymptomatic in early stages, with 65% of cancers presenting at Stage 3 or 4.[2] As such, many patients are diagnosed with advanced disease, which carries a poor prognosis. The five-year survival rate is highly variable and depends on the stage of presentation: the five-year survival rate for Stage 1 disease is 68%, which declines to 3% for Stage 4 disease.[3] Early detection is therefore desirable and will significantly decrease morbidity and mortality.[4] Low-dose computed tomography (LDCT) has recently emerged as a potential screening tool in asymptomatic, high-risk individuals.[5,6] The Australian government is funding a targeted LDCT screening program for lung cancer, for commencement by 2025.[7] In this article, we highlight the evidence for lung cancer screening using LDCT.

Table 1 summarises the various national lung cancer screening guidelines that have been implemented in the past decade. These guidelines recommend screening in patients ranging from age 50 to 80 years with significant smoking of greater than 20 years. LDCT screening is performed annually to biannually without contrast, with an average radiation dose of 1.5 mSv. By comparison, a conventional diagnostic computed tomography (CT) scan of the chest delivers a radiation dose of 6 mSv, and the background radiation in Australia is 1.7 mSv.[8]

Table 2 summarises the two landmark randomised control trials investigating LDCT lung cancer screening: the National Lung Screening Trial (NLST) in the United States and the Dutch–Belgian Randomized Lung Cancer Screening Trial (NELSON).[5,6] There are significant benefits from screening with LDCT with relative risk reductions in lung cancer-specific mortality of 20% and 24% reported in the NLST and NELSON trials, respectively. These benefits are likely due to

Table 1. Summary of selected international guidelines for low-dose computed tomography for lung cancer screening

Guideline	Year	Recommendation
National Comprehensive Cancer Network[12]	2022	Yearly screening in high-risk individuals (≥20 pack-year smoking history) starting from the age of 50 years with no upper age cut-off
US Preventative Services Task Force[13]	2021	Yearly screening in high-risk individuals (≥20 pack-year history) who either continue to smoke or have quit within the past 15 years from the age of 50–80 years
American Society of Clinical Oncology[14]	2019	Yearly screening in high-risk individuals (≥30 pack-year history) from the age of 55–74 years
American College of Chest Physicians[15]	2018	Yearly screening in high-risk individuals (≥30 pack-year history) who either continue to smoke or have quit within the past 15 years from the age of 55–77 years (Strong recommendation) Yearly screening in high-risk individuals (≥20 pack-year history) who either continue to smoke or have quit within the past 15 years who do not meet the above smoking and/or age criteria from the age of 50–80 years (Weak recommendation)
Canadian Taskforce on Preventative Health Care[4]	2016	Yearly screening in high-risk individuals (≥30 pack-year history) from the age of 55–74 years for three consecutive years only

the diagnosis of lung cancers in earlier stages. In the NLST and NELSON trials, LDCT detected early stage (Ia and Ib) lung cancers in 50% and 58.6% of people screened, respectively, compared with a baseline of 13.5% in the NELSON control group with no screening.[6] Major international screening programs for breast and colorectal cancers have numbers needed to screen (NNS) of 781 and 1250, respectively.[9] The comparatively low NNS of 320 and 130 published in the NLST and NELSON trials further support the initiation of a national screening program for lung cancer in Australia.[5,6]

The NLST study defined a positive screening result as any non-calcific nodule/mass measuring at least 4 mm, or other abnormalities such as lymphadenopathy or effusion.[5] A positive result was seen in 24.2% of the LDCT group and led to further imaging, including follow-up CT scans or invasive procedures.[5] A concern of the NLST was the high false-positive rate, which was 96.4% in the LDCT group. Subsequently, 0.9% of all patients screened were diagnosed with lung cancer.[5] NELSON incorporated an additional indeterminate classification that required follow-up CT scans.[6] Lesions classified as indeterminate could subsequently be upgraded to a positive result upon review of volume and volume doubling time. This resulted in 2.1% of screened patients returning a positive test that required referral to a respiratory physician.[6] Subsequently, 0.9% of all patients screened were diagnosed with lung cancer, with a 43.5% positive predictive value.[6] This shows that a screening program with serial CT imaging for indeterminate nodules can be implemented with low numbers of patients requiring referral.

Early diagnosis of lung cancer confers a significant survival benefit, supporting the introduction of a screening program in Australia. LDCT fulfils the key requirements of a good screening strategy as proposed by the World Health Organization.[10] Lung cancer is a disease of significant mortality and morbidity, with a presymptomatic latent stage that can be detected using LDCT. LDCT is sufficiently sensitive and specific, and is relatively safe for the proposed target population, which itself is well-defined of those with significant smoking history.[10] General practitioners are well placed to identify high-risk individuals who might benefit from screening, as well as to provide counselling and referral in the context of a positive result.[11] With lung cancer screening being recommended across the world, general practitioners will play a significant role when the Australian national lung cancer screening program is initiated.

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Table 2. Summary of the National Lung Screening Trial and Dutch–Belgian Randomized Lung Cancer Screening Trial

Trial	Year	Countries	Sample (n)	Inclusion criteria	Intervention	Follow-up	Findings
NLST[5]	2011	US	53,456	Age 55–74 years >30 pack-years Quit <15 years ago	RCT (LDCT vs CXR) Screening time: 0, 1, 2 years	6.5 years median	20% relative reduction in mortality in screening group (247 vs 309 per 100,000 person-years) NNS: 323 over 6.5 years of follow-up
NELSON[6]	2020	Netherlands, Belgium	13,195	Age 50–74 years >15/day >25 years >10/day >30 years Quit <10 years ago	RCT (LDCT vs no screening) Screening time: 0, 1, 3, 5.5 years	At 10 years	24% relative reduction in mortality in screening group (156 deaths; 2.5 per 1000 person-years) vs control group (206 deaths; 3.3 per 1000 person-years) NNS: 130 over 10 years of follow-up

CXR, chest X-ray; LDCT, low-dose computed tomography; NELSON, Dutch–Belgian Randomized Lung Cancer Screening Trial; NLST, National Lung Screening Trial; NNS, number needed to screen; RCT, randomised control trial.

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