

Low-dose computerised tomography screening for lung cancer in Singapore: Practical challenges of identifying participants

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INTRODUCTION

In March 2022, the European Commission on cancer screening suggested the inclusion of low-dose computerised tomography (LDCT) for lung cancer, targeted at current and former smokers.¹ The aim of LDCT screening is to increase early detection, decrease diagnoses at metastatic stage of the disease and improve overall 5-year survival.² Both China and the US recommend screening with LDCT for lung cancer detection. Currently, the Ministry of Health (MOH) in Singapore recommends individual-level use of LDCT to screen for lung cancer in high-risk populations,³ in line with the College of Radiologists' recommendations.⁴ This policy ought to be reconsidered for population-level screening based on improving prognosis, catering for the unmet need and cost-effectiveness analysis. The key to all this is identifying the right participants.

Lung cancer has traditionally been classified into 2 major categories: non-small cell lung cancer (NSCLC), which is more common and usually associated with smoking; and small cell lung cancer, which is more aggressive and has worse survival rates. Clinical benefit evidence from adequately powered studies such as the National Lung Screening Trial (NLST) in the US and the Dutch-Belgian Randomized Lung Cancer Screening Trial (Nederlands-Leuven Longkanker Screenings Onderzoek [NELSON]) show screening for lung cancer with LDCT to have a mortality benefit.^{5,6} The main reason for this is "stage shift" in diagnosis with increases in early-stage (I–II) and decreases in late-stage (III–IV) lung cancer incidence.

Stage IV diagnosis: Singapore compared with other countries

The stage at diagnosis is an important prognostic factor in explaining international differences in cancer survival and early detection of cancer improves prognosis. The majority of patients in Singapore (>60%) are diagnosed with advanced (or metastatic)

NSCLC, which is higher than international comparative statistics (Fig. 1).

The reason for late diagnosis can be attributed primarily to symptoms being non-specific or more likely asymptomatic. In the US, the 5-year survival rate for early-stage lung cancer was 57% compared with 5% for stage IV disease.⁷

An effective national screening programme may contribute to early detection. The Lung Cancer Policy Model-Asia estimated a 3.8% mortality reduction and 8,118 life-years gained in Singapore through the implementation of LDCT using age and smoking history screening eligibility criteria recommended by the U.S. Centers for Medicare & Medicaid Services.¹⁰ While this appears promising, there are several questions about the practical challenges associated with the implementation of LDCT screening—most notably, how will the healthcare system in Singapore identify and invite high-risk individuals to a national screening programme?

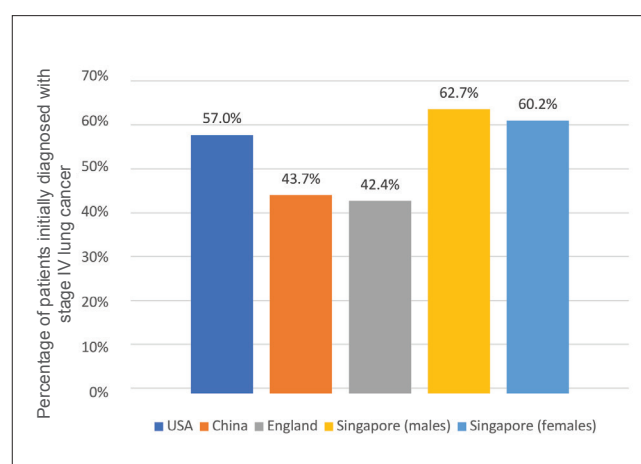


Fig. 1. Percentage of patients diagnosed with American Joint Committee on Cancer (AJCC) stage IV non-small cell lung cancer (NSCLC) in the US,⁷ China² and England,⁸ compared with Singapore.⁹ Superscript numbers: Refer to REFERENCES

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Identifying participants

In the literature, modelling studies focus on smoking history to identify eligible patients for screening, but the definition varies. For example, patient screening eligibility is based upon: “at least 30 pack-years of smoking”, “a maximum of 15 years since quitting”, “20-40 pack-years of smoking” or “between 10 and 20 years since quitting smoking”.^{6,11-13} Risk prediction models also vary with baseline characteristics of age, sex and smoking status¹⁴ or age, smoking history, education, coexisting diagnosis of chronic obstructive pulmonary disorder, family history of lung cancer, and body mass index.¹⁵ The absence of a solitary data source in Singapore that collects the required variables or risk factors discussed above makes it difficult to identify and offer screening to eligible individuals at “high risk” based on pack-years. A strategy based on smoking history would suffice in Singapore. Some possible recruitment strategies in Singapore could be:

- Invite all individuals aged 55–74 years to consider their lung cancer risk and screening eligibility with or without completing a self-administered prostate, lung, colorectal and ovarian (PLCO) cancer screening questionnaire (PLCO_{m2012}) on an annual basis. This would be a large-scale population-based screening but could be inefficient, as invitations would be sent to never-smokers or smokers who would be eventually deemed ineligible.
- Most general practices in Singapore now use some form of patient management system that could potentially be used to identify a target population to invite for screening, based on age and smoking history. This approach would be more focused but will however depend on the access to these patient management systems and on accurate smoking status being captured and updated.
- Targeted case finding where general practitioners conduct a lung cancer risk assessment on individuals who are aged over 55 years and are current or former smokers. The general practitioner will then refer those eligible to go for LDCT screening. The disadvantage of this approach would be that not all eligible individuals aged over 55 years will visit a general practitioner. Also, not all general practitioners may be motivated enough to conduct the lung cancer risk assessment for eligible individuals.

Currently, LDCT screening is widely available in the private healthcare setting in Singapore, suggesting that there is an unmet need. However, the risks of screening include false-positive results leading to follow-up tests and surgeries that are not needed; and overdiagnosis

of cancer cases that may never cause a problem, which again leads to unnecessary treatment. Evaluation of the long-term costs and benefits of vying screening strategies, known as a Health Technology Assessment (HTA), is needed for policymakers within MOH to make recommendations with confidence. Whether validation of the NLST and NELSON trial results for a Singapore population as part of the HTA is needed requires deliberation among clinicians and policymakers.

Implementation of the lung cancer screening programme

Key elements of the programme include customising the inclusion criteria, training of general practitioners and radiologists, targeted recruitment strategy for eligible high-risk participants, integration with existing smoking cessation programmes, and continued research to analyse the uptake and impact of LDCT screening. The successful implementation of a targeted lung cancer screening programme would achieve a stage shift to an increase in stage I/II cancer detection, improved overall prognosis and decreased mortality over time. A recent retrospective audit in a single hospital of Singapore patients (N=126) showed that 85.4% of those presenting at an advanced stage would have benefited from an LDCT based on NLST criteria.¹⁶ However, a trade-off needs to be acknowledged, in that this proposed targeted high-risk screening approach will probably not capture the subpopulation of East Asian non-smoking lung adenocarcinoma cancers.^{16,17} Non-smokers represented a third of patients (33.3%) diagnosed with lung cancer in the hospital audit.¹⁶ Apart from smoking, additional risk factors in Asian populations have been described, including a positive family history¹⁸ and environmental carcinogen signatures,¹⁹ which may need further research as a distinct cohort from the high-risk smoking population. Furthermore, in clinical practice, the Lung Imaging Reporting and Data System (Lung-RADS) classification system of nodules is based on the NLST high-risk smoking population.²⁰ Therefore, if LDCT screening is extended to a low-smoking population cohort, classification and management of lung nodules is also an area for future research.

CONCLUSION

Singapore has a strong smoking cessation and tobacco control public health programme. A national synchronised LDCT screening for lung cancer programme would be complementary. The aim of early intervention and reduction in mortality in high-risk patients would bring

Singapore in line with other countries. Without such a national programme that adheres to predefined principles, ad hoc and discretionary screening of current and former smokers is likely to continue in private healthcare settings. Singapore has the resources necessary to implement a national lung cancer screening programme and a clear incentive to do so from a public health perspective.

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