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Improving selection of individuals into lung cancer screening programmes

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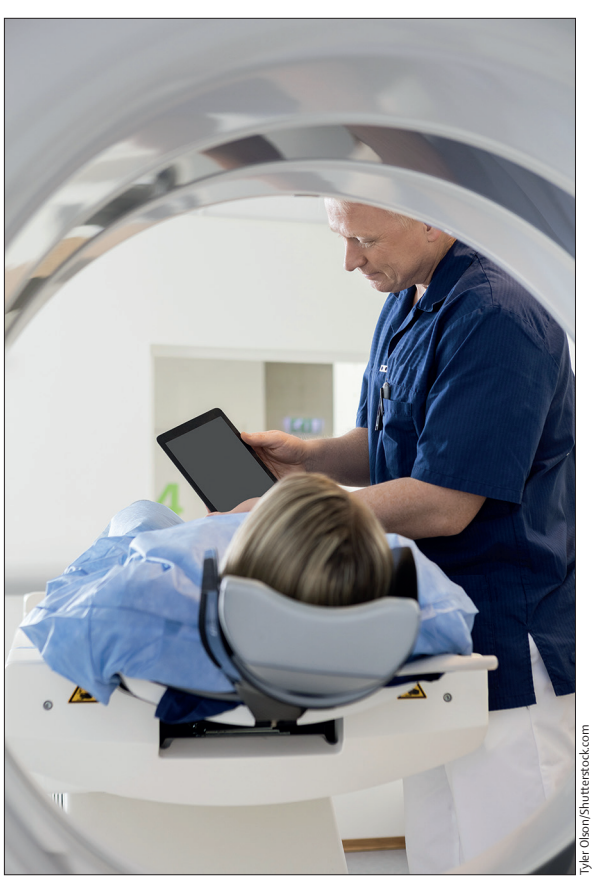
The results of the National Lung Screening Trial (NLST), first announced in November, 2010, showed a 20% decline in mortality with three rounds of screening.[1] The NELSON study was presented at the International Association for the Study of Lung Cancer meeting and confirmed the benefit of screening.[2] Work by James Hanley and colleagues[3] utilised the NLST data and showed that continued annual screening could potentially lower mortality by as much as 30%. Current screening guidelines by the US Preventive Services Task Force (USPSTF), Centers for Medicare and Medicaid Services, and many major US medical organisations follow entry criteria similar to that used for the NLST:[4] age 55–80 years, 30 pack-years of smoking, and, for former smokers, those who quit within the past 15 years. The USPSTF guidelines were based on microsimulation modelling from the Cancer Intervention Surveillance Network and a point on their efficacy frontier that resembled the NLST entry criteria but extended the age cutoff to 80 years.[5] Uptake of lung cancer screening is low according to data from the American College of Radiology.[6]

Many lung cancers in the USA arise in individuals who do not meet current USPSTF entry criteria.[7] The frequency of lung cancer diagnoses varies across the USA because of different demographics such as smoking intensity and socioeconomic and racial diversity. Some of the major medical organisations in the USA, including the National Comprehensive Cancer Network, the American College of Chest Physicians, and the American Association of Thoracic Surgery, call for screening of individuals who do not meet current criteria because of these discrepancies.[4]

In *The Lancet Oncology*, Yung-Hung Luo and colleagues[8] provide comparative information about overall survival in three different subgroups of patients with lung cancer, using prospectively collected long-term data on lung cancer cases at the Mayo Clinic and in Olmstead County, MN, USA. The authors assessed data from patients diagnosed between Jan 1, 1997, to Dec 31, 2017. Although the NLST results were announced in November, 2010, only approximately 1% of patients with lung cancer in the current study had undergone screening. In previous work, this group had shown that in a defined population, aged 50–80 years, with a smoking history of 30 pack-years or more, the most common high-risk



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subgroups for lung cancer outside of the USPSTF criteria were long-term quitters (≥15 years since quitting) aged 55–80 years, and individuals aged 50–54 years. Median overall survival was 16·9 months (95% CI 16·2–17·5) in the present study, and 5-year overall survival in patients with lung cancer was similar in those who met USPSTF guidelines (23% [95% CI 22–24]), those aged 50–54 years (22% [19–25]), and those classified as long-term quitters (27% [25–30]).

The benefit–harm ratio could not be estimated, as the study did not estimate denominators of the populations from which these lung cancer cases were diagnosed. The Mayo Clinic is a tertiary referral centre and 7798 cases from this centre dominated the analysis. Olmstead County contributed 941 cases. The population of Olmstead County is approximately 140 000 people, but the number of individuals in the population who meet these three different criteria of lung cancer risk are not specified. Additionally, to understand the cost-effectiveness of screening, one needs to know the numbers of individuals who will be screened and the risk of lung cancer in the group that undergoes screening. Cost-effectiveness is also driven substantially by costs in the health-care system within which the screening is implemented. The authors only mention a cost-effectiveness analysis from Canada, which has a substantially different health-care system to that in the USA or elsewhere. The authors also call for biomarkers to improve selection of patients for lung cancer screening, but no validated biomarkers are currently available.

How should the lung cancer screening community approach potential changes to screening entry criteria to save more lives? The USPSTF is in the process of updating its lung cancer screening recommendations.[9] The panel is considering whether risk prediction models will improve the balance of benefits and harms compared with existing recommendations. One logical approach is to move to an individualised risk-based modelling approach as opposed to the current microsimulation model. Such an approach has many advantages: more detailed information used in a continual manner allows better risk stratification and as more lung cancer arises outside of existing guidelines, more individuals at risk can be offered screening. Several available models, such as the PLCOm2012, LCRAT, LCDRAT, and Bach models, have shown better utility than the current USPSTF criteria.[10] However, implementation of this approach might be challenging. Should only one risk model be chosen, or should health-care systems choose one that better meets their needs? What risk threshold balances benefits against the costs and harms of screening? How does one pick a threshold and who should set it?

Luo and colleagues[8] have provided additional information for tackling an important public health problem—lung cancer is the leading cause of deaths from cancer globally. The lung cancer screening community needs to improve selection of individuals into screening programmes and, most importantly, the uptake of screening by those who are most likely to benefit.

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