Editorial

Are current lung cancer screening guidelines and programs racially biased?

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Lung cancer screening with low-dose computed tomography (LDCT) is supported by several guidelines and position statements (1-3). It is increasingly becoming available in clinical settings, with Australia and the United Kingdom (UK) being the most recent countries to announce plans for national lung cancer screening programs (4,5). The current proposal in Australia is for a screening program in people aged 50 to 70 years old who are asymptomatic with a smoking history of ≥30 pack-years and are either current smokers or have quit within the last 10 years (6). The UK plans to offer LDCT screening to current or former smokers aged 55 to 74 years old who meet the definition of high-risk for lung cancer on further assessment (5). Other countries with national programs include Korea, with a National Cancer Screening Program offering LDCT screening in people aged 55 to 74 years old with ≥30 pack-year smoking history, who are current smokers or who quit within the past 15 years (7). Similarly the Croatian lung cancer screening program targets those aged 50 to 70 years old who are current smokers or who have quit in the last 15 years (8).

Personal smoking history and age are the key considerations for eligibility in all current lung cancer screening programs, with no obvious consideration of an individual's race in the eligibility algorithms. Age and smoking history were derived from the selection criteria used in the randomised controlled trials (RCTs) which first demonstrated the efficacy of lung cancer screening with LDCT. A meta-analysis of RCTs from 2022 showed that lung cancer screening with LDCT was associated with a 21% reduction in lung cancer-related mortality (9). The two largest RCTs included in the meta-analysis (comprising 76% of analysis participants) were the United States (US) National Lung Screening Trial (NLST) (10) and the Dutch-Belgian Nederlands-Leuvens Longkanker Screenings Onderzoek trial (NELSON) (11) which consisted of 53,454 and 15,789 participants respectively. The NELSON study did not provide details of participant race. 48,549 participants (91%) of the NLST cohort were White, with only 4% Black, 2% Asian, and 2% listed as other (9). There is a clear absence of lung cancer screening RCTs with non-White participants in available literature with long-term data.

As highlighted by Ivic-Pavlicic *et al.* (12), Black Americans have the highest incidence of lung cancer compared to other races in the US (13). Black Americans also have less access to lung cancer treatment compared to White Americans (14) and a lower 5-year lung cancer-related survival rate (15). There are multiple potential contributors to this, including socioeconomic status and

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environmental exposures, with pack-year smoking history being shown to be lower amongst Black Americans with lung cancer compared to White Americans (16). Among smokers of 10 or less cigarettes, White Americans had a relative risk of lung cancer of 0.45 (95% CI: 0.34 to 0.60) compared to Black Americans (17).

Lung cancer screening guidelines' eligibility criteria are based heavily on pack-year history. As such, a retrospective review of lung cancer screening eligibility in people with confirmed lung cancer found that fewer Black Americans would have been eligible compared to White Americans (16). This is despite evidence suggesting that Black participants have a larger reduction in lung cancer-related mortality compared to White participants with LDCT screening in a NLST post hoc analysis (hazard ratio 0.61 *vs.* 0.86 respectively) (18). Consequently, the US Preventative Task Force (USPTF) updated their screening recommendations to lower minimum pack-year and age eligibility criteria to reduced racial disparity in access to screening (19).

However, the current guidelines are working within the constraints of available evidence. There is a need for lung cancer screening studies in more racially diverse populations which can then inform weighting of different risk factors to determine optimal selection of participants and ensure a more equitable benefit from lung cancer screening. Ivic-Pavlicic *et al.* (12) use data from the US National Health and Nutrition Examination Survey (NHANES) to evaluate for racial inequity with the 2021 USPTF lung cancer screening guidelines in an American population. The authors also described the use of urinary cotinine to supplement pack-year history when determining eligibility for lung cancer screening. The results suggest ongoing differences in eligibility between different racial and ethnic groups despite the updated guidelines. This study was limited by its cross-sectional nature and did not capture other relevant lung cancer risk factors. Although, importantly this paper explores other measures of lung cancer risk assessment in a more diverse population. Previous retrospective cross-sectional studies in America have highlighted an increase in eligibility for Black Americans with the updated 2021 USPTF guidelines (20,21). However, a larger cross-sectional study found that the new guidelines still resulted in a significantly lower likelihood of eligibility for Black and Hispanic people compared to White Americans [adjusted odds ratio (OR) 0.39, 95% confidence interval (CI): 0.32–0.47 and adjusted OR 0.15, 95% CI: 0.10–0.23 respectively] (22).

Only one LDCT lung cancer screening RCT published to date, the UK Lung Cancer Screening trial (UKLS), has utilised a risk prediction model (23). However, the Liverpool Lung Project (LLP) version 2 which was utilised did not include race. It does incorporate personal history of pulmonary disease or cancer, family history of lung cancer and occupational exposures, in addition to age and tobacco smoking history (23). Lung cancer is a heterogenous condition, with multiple risk factors contributing to its development and outcome. Whilst age and personal smoking history are the most well-known, other contributors are being increasingly recognised, such as ambient air pollution and genetics (24).

From a practical perspective, not all risk factors can or should contribute to lung cancer screening eligibility, however it must be acknowledged that current screening guidelines are not equitable for the whole population and there is racial bias.

More studies are needed to evaluate optimal lung cancer screening participant selection, such as the International Lung Screen Trial (ILST) (25), which is evaluating risk prediction models, and like Ivic-Pavlicic *et al.*'s which are evaluating biomarkers (12). The ILST is evaluating the USPTF 2013 criteria in comparison to the PLCOm2012 which includes multiple factors including race or ethnicity. LDCT lung cancer screening RCTs in people who have risk factors beyond smoking are also required, and the results of Chinese AME Thoracic Surgery Collaborative Group RCT are much anticipated (26).

Lung cancer screening with LDCT has the potential to be a lifesaving intervention. However, it is vital, as national lung cancer screening programs are being implemented internationally, that governments, healthcare providers and stakeholders recognise how the available evidence applies to their populations, which are often racially diverse and not adequately represented in the trials to date. In failing to do so, we risk exacerbating existing inequities and widening the gap in health outcomes to further disadvantage already vulnerable populations.

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