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COMMENTARY

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# Lung cancer screening—Marching along …

The good news: lung cancer survival is improving worldwide.[1,2] Not so good: lung cancer remains the leading global cause of cancer death (~1.8 million deaths annually).[3] Can lung cancer screening change this?

Lung cancer screening was first recommended in 2013 by the US Preventive Services Task Force (USPSTF). The proportion of diagnosed localised/early-stage lung cancer increased from 17% (mid-2000s) to 28% in 2018, coinciding with declining incidence of advanced-stage diagnoses (Figure 1). Clinical and biological plausibility support this observation. Survival is inversely correlated with lung cancer stage, for instance 5-year relative survival rates of 6% for distant-stage disease, 33% for regional stage and 60% for localized-stage disease.[2]

Given this real-world data which bolsters the increasing and consistent body of evidence from pivotal high-quality randomized trials[4,5] and meta-analyses,[6] why is organized lung cancer screening not more widely implemented worldwide? While lung cancer screening is being evaluated or implemented in several jurisdictions, including Poland, Israel, Spain and Canada, to date, only Korea has a national screening programme.[7]

History teaches us that the implementation of successful cancer screening programmes can take time. Offering an efficacious new screening technology is complex, and to be a successful public health endeavour, must from the outset ensure that high priority groups have equitable access to avoid worsening extant health disparities in lung cancer. Whether in Australia, Asia Pacific or globally, this means planning and implementing a programme that will be accessible by people regardless of whether they live in urban or rural areas; and for people of different ethnicities, Indigenous and First Nations heritage; those disadvantaged by mental or other health problems; and culturally and linguistically diverse (CALD) groups. Notably in 2021, the USPSTF updated its recommendation to expand eligibility for vulnerable populations, lowering the start age for screening from 55 to 50 and reducing smoking history from 30 to 20 pack-years (e.g., Black Americans tend to develop lung cancer at earlier ages with shorter smoking histories).[8]

Alternatively, individualised risk-based lung cancer screening eligibility selection is gaining momentum, demonstrably feasible[6] and apparently more efficient than the $\text{USPSTF}_{2013}$ eligibility criteria ($\text{PLCO}_{\text{m}2012}$ model[9]). Whilst more complex, an individualised approach, accounting for health and sociodemographic risk factors beyond age and smoking, may also help reduce overdiagnosis risk. Overdiagnosis can affect any cancer screening effort and can be particularly significant when screening people at lower risk.[10]

Risk-based selection requires data additional to age and smoking history, arguably the common use of general practice software with such data brings the opportunity for seamless integration into normal work practice and incorporation into regular health check services, potentially helping to accelerate the digital transformation of cancer care. Integrating screening assessment into routine healthcare provides opportunities to discuss important health issues with patients, in particular smoking cessation, but also education to increase lung cancer symptom awareness.[11] Approximately 2.5 million adults smoke daily in Australia. Countries in the diverse Asia-Pacific region may be at different stages of the tobacco epidemic, but nevertheless are still home to one third of the global smoking population. Even though most clinically detected lung cancer cases in Australia now occur in people who no longer smoke, the future risk burden shouldered by people who continue to smoke is extensive. Integrating smoking cessation with screening is not only beneficial for patients, but also a fundamental requirement for all nations to reduce the future burden of disease. Lung cancer screening is undoubtedly a 'teachable moment' for smoking cessation intervention. Backed by strong national Quitline counselling services and subsidized smoking cessation therapy that aligns with national clinical guidelines, screening could be an excellent, long-term vehicle to help people quit smoking. Importantly, positive pro-active messaging surrounding a national screening programme may help combat the prevalent stigma which has shrouded lung cancer and smoking for over half a century.

Continuing the theme of digital transformation, artificial intelligence methodologies are also predicted to help address areas of concern for screening, that of overdiagnosis and incidental findings, through optimal management of pulmonary nodules (radiomics and biomarkers[12]) and by guiding clear and consistent management pathways for incidentally detected comorbidities.[13] The field of deep learning and neural networks is expanding exponentially and is now focussed well beyond simply 'detecting' nodules. These models hold the promise of diagnostics beyond human

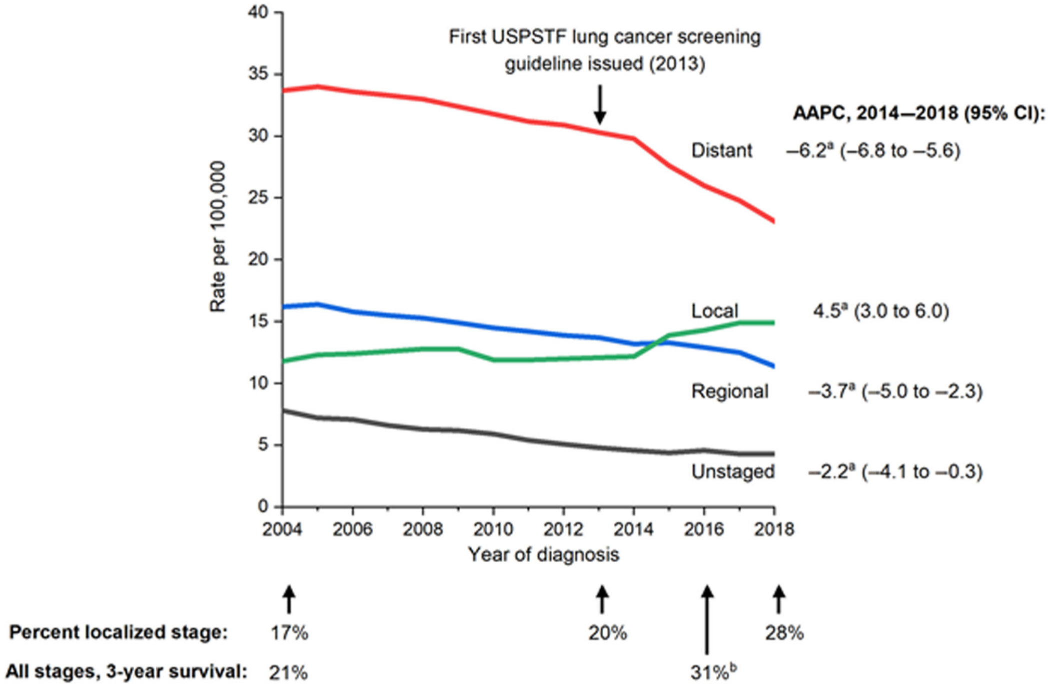


**FIGURE 1** Trends in lung cancer incidence rates by stage at diagnosis, United States, 2004–2018; 3-year relative survival. Incidence rates are age adjusted to the 2000 US standard population. The 3-year relative survival is presented for patients followed through 2018.
[a]The AAPC is significantly different from zero ($p < 0.05$).
[b]Patients were diagnosed from 2015 to 2017.
AAPC, average annual percent change; USPSTF, US Preventive Services Task Force.
Reproduced from Siegel et al.,[2] with permission.

capability through analysis of an entire 3D computed tomography (CT) data set, rather than just a sequence of 2D slices, interrogating the tumour environment, such as blood vessels and other lung structures, and radiomics, the quantitative, rather than visual, analysis of nodule features. The data sets required to train these models are very large, requiring many thousands of annotated CT scans. To this end, large data sets are now publicly available. Screening programmes may be well placed to prospectively curate imaging data sets, or at least contribute to international repositories. This is important because lung cancer is a moving target; we have already witnessed the evolution from predominant central squamous cell carcinomas to more peripheral adenocarcinomas in response to changes in cigarette manufacture and design over the past half-century. Constant product innovation from tobacco companies, not least of which, the increasing use of electronic cigarettes by younger cohorts of people, will no doubt lead to future challenges for lung cancer.

Of course, much more work and knowledge are needed to fully exploit CT to screen for lung cancer, such as how to minimise radiation dose, maximise equitable participation and retention, maintain quality and safety, ensure cost effectiveness and integrate non-stigmatising smoking cessation interventions.

Lung cancer screening is complex. Clearly, as evident across the generality of lung cancer care, effective lung cancer screening must be a team effort, making use of multi- and inter-disciplinary primary care and specialist skills, organized, adequately funded and well governed to enable a programme that will realise the saving of thousands of lives anticipated in Australia (Report on the Lung Cancer Screening Enquiry: © Cancer Australia 2020. ISBN Print: 978-1-74127-355-7) and elsewhere in a timely fashion, lest we miss the window of opportunity for many.

*While each marches to their own drum, time doesn't stop for those at risk … …*

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## KEYWORDS

CT screening, lung cancer, smoking cessation

## CONFLICT OF INTEREST

None declared.

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