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Lung cancer screening implementation: Complexities and priorities

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ABSTRACT

Lung cancer is the number one cause of cancer death worldwide. The benefits of lung cancer screening to reduce mortality and detect early-stage disease are no longer in any doubt based on the results of two landmark trials using LDCT. Lung cancer screening has been implemented in the US and South Korea and is under consideration by other communities. Successful translation of demonstrated research outcomes into the routine clinical setting requires careful implementation and co-ordinated input from multiple stakeholders. Implementation aspects may be specific to different healthcare settings. Important knowledge gaps remain, which must be addressed in order to optimize screening benefits and minimize screening harms. Lung cancer screening differs from all other cancer screening programmes as lung cancer risk is driven by smoking, a highly stigmatized behaviour. Stigma, along with other factors, can impact smokers' engagement with screening, meaning that smokers are generally 'hard to reach'. This review considers critical points along the patient journey. The first steps include selecting a risk threshold at which to screen, successfully engaging the target population and maximizing screening uptake. We review barriers to smoker engagement in lung and other cancer screening programmes. Recruitment strategies used in trials and real-world (clinical) programmes and associated screening uptake are reviewed. To aid cross-study comparisons, we propose a standardized nomenclature for recording and calculating recruitment outcomes. Once participants have engaged with the screening programme, we discuss programme components that are critical to maximize net benefit. A whole-of-programme approach is required including a standardized and multidisciplinary approach to pulmonary nodule management, incorporating probabilistic nodule risk assessment and longitudinal volumetric analysis, to reduce unnecessary downstream investigations and surgery; the integration of smoking cessation; and identification and intervention for other tobacco related diseases, such as coronary artery calcification and chronic obstructive pulmonary disease. National support, integrated with tobacco control programmes, and with appropriate funding, accreditation, data collection, quality assurance and reporting mechanisms will enhance lung cancer screening programme success and reduce the risks associated with opportunistic, ad hoc screening. Finally, implementation research must play a greater role in informing policy change about targeted LDCT screening programmes.

Key words: delivery of health care, implementation science, lung neoplasms, mass screening, smoking.

INTRODUCTION

Lung cancer is the leading global cause of cancer burden and death for both men and women despite the sustained application of tobacco control strategies and reduction in tobacco smoking in many countries.[1] Most people are diagnosed with advanced stage disease and have poor survival outcomes at 5 years.[2] In Australia, lung cancer deaths will continue to rise in the coming decades[3] despite the success of tobacco control measures and reductions in smoking rates.

The mortality benefit of low-dose computed tomography (LDCT) screening is no longer in any doubt. Two large randomized studies, the United States (US) National Lung Screening Trial (NLST) and the Dutch-Belgium Randomized Lung Cancer Screening Trial (NEderlands-Leuvens Longkanker Screenings ONderzoek, NELSON), have shown reduction in lung cancer-specific mortality with the use of LDCT. The reduction in lung cancer-specific mortality was seen

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after only three rounds of screening in both trials.[2,3] The NLST study also showed a reduction in all-cause mortality.

Published results from the NELSON trial of 15 789 participants showed that screening with LDCT screening resulted in 24% reduction in lung cancer mortality over 10 years in men and 33% in a smaller sample of women, suggesting that[4] the mortality benefits from screening may be even greater in women.[4,5] Although comprehensive results for women participants in the NELSON trial are yet to be published, the results reinforce findings from the NLST of 53 454 individuals of a 20% reduction in lung cancer mortality in men and women over a median follow-up of 6.5 years.[6]

The majority of screen-detected lung cancers in both trials were stage I and II (57% NLST and 67.9% NELSON).[4,6] These findings are also reflected in recently initiated clinical programmes. For example, 71% and 80% of lung cancers were stage I or II in an evaluation of eight centres in the Veterans Health Affairs demonstration programme and in the first round Manchester Lung Health Check programme, respectively, indicating that trial results can be reproduced in real-world (clinical) programmes.[7,8]

Implementation of lung cancer screening has now commenced in the US and South Korea and is under consideration in many other countries. In 2013, the United States Preventive Services Task Force (USPSTF) recommended offering LDCT screening for people aged 55–80 years, with a subsequent revision in the stopping age of 77 years by the Centre for Medicare and Medicaid.[9,10] In July 2020, USPSTF released a revised recommendation for public consultation to lower entry age to 50 years and reduce smoking exposure threshold to 20 pack-years. An implementation guide as well as standardization, accreditation and structured reporting for lung cancer screening programmes have been developed for use.[11]

Pilot programmes are underway in countries including China, Canada and the United Kingdom (UK).[8,12,13] In Manchester and Liverpool, the Lung Health Check pilot programme has demonstrated successful implementation in deprived communities using mobile screening vans. The National Health Service has funded a further 10 pilot sites and released a standard protocol to facilitate implementation in 2019.[14]

The focus of future research efforts needs to shift from generating evidence about the mortality benefits of LDCT screening to determining the most effective strategies for implementation. Translating lung cancer screening research to real-world programmes has multiple, different challenges across the various global healthcare systems. Many lessons have been learned over the last 20 years that can be used to maximize the benefit to our respective communities and more will be forthcoming as implementation expands. Broad coverage of the target population is needed to realize the substantial benefits in lung cancer mortality and earlier stage detection as demonstrated in trials.[15,16]

This review considers the core issues that will influence lung cancer screening uptake and the programme elements required to maximize the impact of lung cancer screening. We conclude with a brief overview of implementation research and why it should play a greater role in informing policy change about lung cancer screening programmes.

TARGETED APPROACH TO PARTICIPANT SELECTION

The application of lung cancer screening differs from the broader population-based programmes for breast, cervical and colorectal screening. Most research in lung cancer screening has been conducted in tobacco smokers and both current and proposed clinical programmes are focused on this cohort. Participants at low risk of lung cancer do not benefit from screening and are at risk of harm due to unnecessary downstream investigations. Ongoing research is also needed to expand assessment of lung cancer risk in never smokers.[17,18]

The NLST and NELSON trials used enrolment criteria based on age and smoking history alone and the criteria differed slightly: age ranges were 55–74 and 50–74 years; minimum smoking history was 30 and 15 pack-years; and maximum allowable years since quitting for former smokers were 15 and 10 years, respectively.[4,6] Current smokers comprised 48.2% and 55.5% of the study populations, respectively. Although eligibility requirements based on age and smoking history are undoubtedly important, they oversimplify lung cancer risk, ignoring other well-known risk factors, such as ethnicity and family history.[19] Indeed, use of these limited selection criteria results in lower risk people being screened which is suboptimal for large-scale screening programmes.[20–22]

Recognition of these limitations has led to the development of a targeted approach using validated multivariate risk prediction models such as the one derived from the Prostate, Lung, Colorectal and Ovarian Screening Trial ($PLCO_{m2012}$ model).[20–24] The incorporation of this model for participant selection has been shown to reduce unnecessary screening in low-risk patients without sacrificing detection of lung cancer, and to reduce the overall financial impact of screening.[20–22,25] The PLCO risk prediction model has been utilized prospectively in the Pan Canadian Early Detection of Lung Cancer study (PanCan) and further prospective evaluation is ongoing in Australia, Canada and Hong Kong in the International Lung Screening Trial (ILST).[20,24,25] Future refinement of such a risk prediction model incorporating occupational and environmental carcinogen exposures and biomarkers could further improve risk assessment for lung cancer screening.

RECRUITMENT STRATEGIES USED IN LUNG CANCER SCREENING TRIALS

The recruitment of high-risk individuals from the general population is central to all LDCT screening trials and real-world programmes. The main strategies used to attract participants include direct mailing of

Table 1 Recruitment strategies, response and participation proportions across major European and US trials

		NELSON[4]	ITALUNG[26]	LUSI[27]	NLST[28]	DANTE[29]	DLCST[30]	MILD[31]	UKLS[32]	LSUT[33]
	Recruitment period (years)	2003–2006	2004–2006	2007–2011	2002–2004	2001–2006	2004–2006	2005–2011	2011–2014	2015–2017
	Country	The Netherlands/ Belgium	Italy	Germany	US	Italy	Denmark	Italy	UK	UK
	Recruitment strategy	Direct mail	Direct mail	Direct mail and mass media	Direct mail, mass media and outreach	Direct mail plus mass media	Mass media	Mass media	Direct mail	Direct mail
	Primary care engagement	Yes	Yes	No	In some centres	Yes	No	No	Yes	Yes
Abbreviation	Label									
A	Approached to participate	606 409	71 232	292 440	NR	NR	NR	NR	247 354	2012[†]
R	Responded to the invitation	150 920	17 055	95 797	NR	NR	NR	NR	98 746	1058
X	Did not respond to the invitation	455 489	54 177	196 643	NR	NR	NR	NR	148 608	954
PR	Positive response to the invitation	NR	NR	NR	NR	NR	NR	NR	75 958	1005
RFI	Negative response to the invitation ('refused further involvement')	NR	NR	NR	NR	NR	NR	NR	22 788	53
AFE	Assessed for eligibility (underwent checks to determine eligibility for trial)	150 920	17 055	95 797	53 454	2811	5861	5880	75 958	1005
NAFE	Not assessed for eligibility	NR	0	0	NR	0	0	NR	0	53
AOE	Eligible (assessed outcome 'eligible'): the individual met all the eligibility criteria	30 959	3206	4913	53 439	2532	4443	4099	4868	844
AOI	Not eligible (assessed outcome 'ineligible')	119 961	13 849	90 884	NR	279	1418	1781	71 090	153
EC	Eligible consented: the individual met the eligibility criteria and gave informed consent	15 822	3206	4052	52 486	2532	4104	4099	4061	770
ED	Eligible declined: the individual met the eligibility criteria but did not provide informed consent	15 137	0	861	953	0	339	NR	807	74
S	Scanned (received a CT scan)	7557	1406	2028	26 309	1264	2047	2376	1994	770
DNS	Did not get scanned	343	207	1	49	0	5	0	34	1242
ARP	Approach response proportion (R/A)[‡]	24.89%	23.94%	32.76%	N/A	N/A	N/A	N/A	39.92%	52.58%
ERP		20.51%	18.80%	5.13%	N/A	N/A	N/A	N/A	4.93%	79.77%

Continued

Table 1 Continued

		NELSON[4]	ITALUNG[26]	LUSI[27]	NLST[28]	DANTE[29]	DLCST[30]	MILD[31]	UKLS[32]	LSUT[33]
	Eligible responder proportion (AOE/R)[§]									
RDP	Response decline proportion (ED/R)[¶]	10.03%	0.00%	0.90%	N/A	N/A	N/A	N/A	0.82%	6.99%
EDP	Eligible decline proportion (ED/AOE)[††]	48.89%	0.00%	17.52%	1.78%	0.00%	7.63%	N/A	16.58%	8.77%
EPP	Eligible participation proportion (EC/AOE)[‡‡]	51.11%	100.00%	82.48%	98.22%	100.00%	92.37%	100.00%	83.42%	91.23%
ESP	Eligible scanned proportion (S/AOE)[§§]	24.41%	43.86%	41.28%	49.23%	49.92%	46.07%	57.97%	40.96%	91.23%
SAP	Scanned approach proportion (S/A)[¶¶]	1.25%	1.97%	0.69%	N/A	N/A	N/A	N/A	0.81%	38.27%

[†]147 015 Primary care records were assessed first using a standardized audit search.
[‡]ARP is the proportion of those who responded over those approached (R/A).
[§]ERP is the proportion of those assessed outcome eligible over those who responded (AOE/R).
[¶]RDP is the proportion of those eligible declined over those who responded (ED/R).
[††]EDP is the proportion of those eligible declined over those assessed outcome eligible (ED/AOE).
[‡‡]EPP is the proportion of those eligible consented over those assessed outcome eligible (EC/AOE).
[§§]ESP is the proportion of those people scanned over those assessed outcome eligible (S/AOE).
[¶¶]SAP is the proportion of those people scanned over those approached (S/A).

CT, computed tomography; DANTE, Detection and Screening of Early Lung Cancer by Novel Imaging Technology and Molecular Essays Trial; DLCST, Danish Lung Cancer Screening Trial; ITALUNG, Italian Lung Cancer Screening Trial; LSUT, Lung Screen Uptake Trial; LUSI, Lung Cancer Screening Intervention Trial; MILD, Multi-centric Italian Lung Detection Trial; N/A, not applicable; NELSON, NEderlands-Leuvens Longkanker Screenings ONderzoek; NLST, National Lung Cancer Screening Trial; NR, not reported; UK, United Kingdom; UKLS, United Kingdom Lung Cancer Screening trial; US, United States.

invitation letters, mass media advertisements and community outreach. Table 1 presents a summary of recruitment data for recent European and US LDCT screening trials. Trial publications provide limited information about how recruitment strategies were selected or implemented.[4,6,26,27,29–32] In the NLST, screening centres chose their own recruitment methods and a survey of 22 (of 33) centres found about 77% used direct mailing, either through commercial mailing lists or healthcare system registries, with less frequent use of mass media and community outreach.[34]

Direct mailing uses population-based or primary care registers to select individuals. While these registers are useful for breast and bowel cancer screening containing, for example, data on age and sex, they do not include the important smoking details required such as smoking status and pack-year history. Although primary care registries do include smoking variables, as we discuss later, these data are frequently unreliable. Invitations to participate are therefore accompanied by a self-report questionnaire to collect additional data to determine eligibility. As shown in Table 1, the direct mailing strategy allows for more accurate tracking of potential participants. In contrast, mass media and community awareness activities have a broad reach across the population but are blunt instruments by which to attract eligible participants. There is little evidence about the potential to use social media and direct text alerts to recruit potential participants.[35]

The lack of planning of recruitment strategies indicates a missed opportunity to identify how best to attract the high-risk population.[36] A criticism of recruitment of targeted LDCT screening trials is a bias towards recruiting men, people from higher socioeconomic backgrounds,[37] younger, former smokers, those who are more health conscious and have better access to medical care.[38–41] While direct invitations are most cost-effective in the trial setting,[34] there are few data published about how costs translate to real-world programmes. In the US screening programmes, programme managers report having limited information about people at high risk within the local population and how best to recruit potential participants.[42]

Measuring recruitment: a standard nomenclature for lung cancer screening trials and real-world programmes

A full understanding of the comparative advantages, disadvantages, yield and cost of the various recruitment strategies can only be achieved through consistent data reporting, something that has yet to be achieved. To further this aim, we propose a standardized nomenclature for future implementation studies of lung cancer screening recruitment and to enable calculations of relevant proportions for screening outcomes, as shown in Table 1 for LDCT screening trials and in Table 2 for real-world programmes.

We propose three groups of proportions that are of particular relevance: response, decline and participation proportions. Part of the variability in range of proportions seen across studies is likely to reflect differences in reporting.

Success of the initial invitation to participate in screening: ARP

The approach response proportion (ARP) is defined as the proportion of people who responded (R (responded to invitation)) over the total count of people approached (A (initially approached)). This proportion is calculable for trials and real-world programmes that use direct mailing; the ARP for trials ranges about 25–52%, while in real-world programmes, it is 17–40%. The ARP reflects the success of the initial contact with possible participants. The Lung Screen Uptake Trial (LSUT) may have the highest ARP because all potential invitees, algorithmically selected from primary care databases, were reviewed for suitability by their general practitioner (GP) before the invitation was sent, representing significant tailoring of the approach.

Identifying barriers: EDP—individuals who meet eligibility criteria but decline to have a CT scan

Eligible decline proportions (EDP) reflect the subset of individuals who meet eligibility criteria but decline to participate in screening (ED, eligible declined). EDP can be considered using a denominator of eligible responders (ED/AOE (Assessed outcome 'eligible')) or of all responders (ED/R (responded to invitation)). This group includes people who ultimately do not receive an LDCT scan for reasons such as withdrawal (e.g. claustrophobia and being unable to raise both arms above one's head) or not presenting for an appointment (e.g. unwillingness to travel, loss of interest or lost to follow-up). This proportion is important to understand as it reflects a significant amount of expended effort on the part of potential participants and screening personnel alike; the EDP highlights individuals 'lost' to the programme at some point between determining their eligibility and attending for an LDCT scan. The range of values is wide, pointing to significant heterogeneity across studies and a potentially fruitful area for further investigation. Identifying and addressing pertinent barriers at this process point could improve computed tomography (CT) screening uptake by 14% when EDP is averaged across all relevant studies.

Final arbiters of recruitment strategy success: EPP and ESP

Participation proportions are of particular interest to policymakers to understand the uptake of screening programmes. We propose two relevant proportions: the eligible participation proportion (EPP) and the eligible scanned proportion (ESP). EPP describes the eligible participants who consented (EC) as a proportion of those all individuals who were assessed and found to be eligible (AOE). EPP is the inverse of the EDP and is an intermediate marker of screening uptake success. As shown in Table 1, the EPP range for trials is 51–100% and for real-world programmes is 57–100%.

Table 2 Recruitment strategies, response and participation proportions across real-world programs

		Veterans Health Administration evaluation[7]	LHC Manchester baseline[8]	LHC Liverpool[13]
	Recruitment period (years)	2013–2015	2016–2018	2016–2018
	Country	US	UK	UK
	Recruitment strategy	Electronic database algorithm followed by: (i) nurse review of smoking history; (ii) record review by PCP; and (iii) shared decision-making consultation	GP registers used to generate direct mail invitations	GP registers used to generate direct mail invitations
	Primary care engagement	Yes	Yes	Yes
Abbreviations	Label			
A	Approached to participate	93 033	16 402	11 526
R	Responded to the invitation	NA	2827	4566
X	Did not respond to the invitation	NA	NA	6960
PR	Positive response to the invitation	NA	NA	3591
RFI	Negative response to the invitation ('refused further involvement')	NA	NA	975
AFE	Assessed for eligibility (underwent checks to determine eligibility for trial)	5035	2613	3591
NAFE	Not assessed for eligibility	49 603	214	0
AOE	Eligible (assessed outcome 'eligible'): the individual met all the eligibility criteria	4246	1394	1548
AOI	Not eligible (assessed outcome 'ineligible')	39 184	1219	2043
EC	Eligible consented: the individual met the eligibility criteria and gave informed consent	2452	1384	1318
ED	Eligible declined: the individual met the eligibility criteria but did not provide informed consent	1794	10	230
S	Scanned (received a CT scan)	2106	1384	1318
DNS	Did not get scanned	346	45	NA
ARP	Approach response proportion (R/A)[†]	N/A	17.24%	39.61%
ERP	Eligible responder proportion (AOE/R)[‡]	N/A	49.31%	33.90%
RDP	Response decline proportion (ED/R)[§]	N/A	0.35%	5.04%
EDP	Eligible decline proportion (ED/AOE)[¶]	42.25%	0.72%	14.86%
EPP	Eligible participation proportion (EC/AOE)[††]	57.75%	99.28%	85.14%
ESP	Eligible scanned proportion (S/AOE)[‡‡]	49.60%	99.28%	85.14%
SAP	Scanned approach proportion (S/A)[§§]	2.26%	8.44%	11.44%

[†]ARP is the proportion of those who responded over those approached (R/A).
[‡]ERP is the proportion of those assessed outcome eligible over those who responded (AOE/R).
[§]RDP is the proportion of those eligible declined over those who responded (ED/R).
[¶]EDP is the proportion of those eligible declined over those assessed outcome eligible (ED/AOE).
[††]EPP is the proportion of those eligible consented over those assessed outcome eligible (EC/AOE).
[‡‡]ESP is the proportion of those people scanned over those assessed outcome eligible (S/AOE).
[§§]SAP is the proportion of those people scanned over those approached (S/A).
CT, computed tomography; GP, general practitioner; LHC, Lung Health Check; N/A, not applicable; NR, not reported; PCP, primary care provider; UK, United Kingdom; US, United States.

The ultimate goal of any screening programme is to screen every eligible individual who approaches the programme. The ESP reflects the number of eligible, consented individuals who received a CT scan (S) as a proportion of those who were assessed and found to be eligible (AOE). The gap between EPP and ESP is informative, reflecting attrition of high-risk individuals along the recruitment pathway and should be minimized wherever possible. As shown in Table 1, the average ESP across trials is 49%, whereas for real-world

programmes (as shown in Table 2) using a more targeted approach the average value is 78%. This presents a strong argument to use targeted strategies to attract the relevant population as screening is implemented across new jurisdictions.

Comparison of indicators with existing cancer screening programmes

Bowel, breast and cervical cancer screening programmes use limited indicators of recruitment. This reflects the more easily defined eligibility criteria, and thus simpler recruitment strategies, for population-based programmes (i.e. targeting an age ± sex-defined cohort that does not require additional assessment of behavioural risk factors). A widely used indicator across many programmes is participation rate, defined as the number of people who complete the screening test divided by the number of invitees within a defined period of time.[43] This is most equivalent to the ESP over a defined time period.

UPTAKE IN REAL-WORLD LUNG CANCER SCREENING PROGRAMS

Real-world programmes have sought to address the biases identified for trials by targeting hard-to-reach communities, including the socio-economically deprived communities where smoking rates are higher and uptake of cancer screening is lower. The Lung Health Check approach seeks to overcome known practical and psychological barriers to cancer screening by locating mobile LDCT screening vans in shopping centre car parks with immediate access to CT for eligible participants. The UK LSUT has tested two recruitment strategies, targeted invitation letters and a film about informed decision-making, in order to overcome participation barriers using rigorous randomized controlled trial methods.[33,44] While these strategies increased participant knowledge, neither resulted in a significant difference in screening uptake between intervention and control groups. However, the uptake of 52% in each arm was much higher than in previous studies, indicating that a Lung Health Check approach could represent a minimum standard.

Achieving significant mortality reduction with lung cancer screening will be dependent on uptake by the target population. Lung cancer screening is in an early phase of development and is far less established than other cancer screening programmes. The barriers to successful lung cancer screening uptake will vary within and between countries and healthcare settings. Understanding the local, regional and national barriers will help to design efficient and cohesive programmes. Screening programmes such as breast and colorectal cancer (CRC) have demonstrated that there are many different barriers to uptake of screening, particularly in some minority groups and deprived populations.[38,45,46]

A major concern is the significant underutilization of LDCT screening in the US. From 2010 to 2015, uptake remained low and static (3.3% to 3.9%, respectively).[47] However, as shown in Table 2, the UK Lung Health Check programmes report significantly higher uptake, which ranged from 14% to 29% when calculating the number of completed scans from eligible respondents. Furthermore, results from the LSUT (see above) indicate that much higher engagement could be achieved with the right strategies, specifically, more focused engagement of the relevant target group coupled with provision of tailored resources leading to improvements in informed decision-making.

ATTITUDES AND MOTIVATION

Attitudes towards lung cancer screening vary and will influence screening uptake. Reported attitudes to lung cancer screening are complex and are influenced by multiple factors including practical and emotional barriers, avoidant and fatalistic beliefs, fear, stigmatization, willingness to undergo surgery, low perceived risk of lung cancer and/or benefits of screening, knowledge barriers and dislike of healthcare services .[37,38,48–53] In healthcare systems where screening is not fully funded, costs paid by the screenee also play a role in screening uptake.[52–54]

Relatively few studies have sought to understand individuals' motivation for participating in lung cancer screening.[55] A model to conceptualize the multiple variables that may influence screening uptake is presented in Figure 1 and provides an understanding of how best to encourage screening participation.[56] Screening motivation may be more important in lung cancer than other cancer screening programmes because the target population is current and former smokers, many of whom may be reluctant users of health services, may have poor health literacy and be disinterested in engaging in healthy lifestyle activities.[48,57]

SMOKERS AS A TARGET GROUP ARE 'HARD TO REACH'

Tobacco smoking is the greatest risk factor for lung cancer and an important determinant of LDCT screening eligibility.[54,58–60] Unlike screening programmes for breast, bowel and cervical cancers, LDCT screening takes a targeted approach, where eligibility is defined by age and smoking. Smoking, a highly stigmatized behavioural risk factor, is highly correlated with socio-economic status, ethnicity, education level and geographic remoteness. Differences in smoking rates are seen between urban and rural populations as well as indigenous and non-indigenous communities.[60–62] The equitable delivery of lung cancer screening in countries such as Australia and Canada, where the highest risk rural and indigenous communities have more limited access to healthcare facilities, raises particular challenges.[60–62] When coupled with stigma, the target population for LDCT screening of current and former smokers is widely considered as hard to reach. Several observations illustrate this and are discussed below.

Social disadvantage

Denormalization of smoking has been instrumental in reducing smoking prevalence; however, it has also

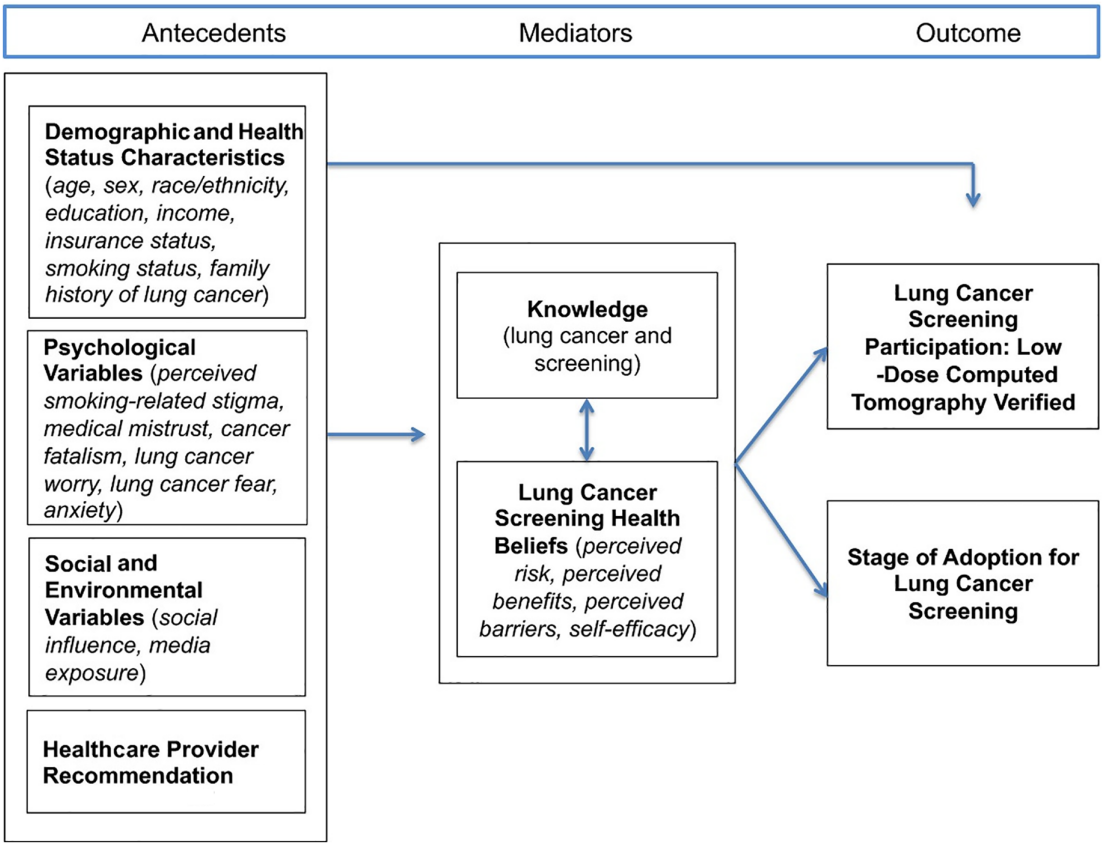

Figure 1 Conceptual model for lung cancer screening participation (Reproduced from Draucker *et al.*,[56] with permission).

meant that smoking is now concentrated in the most vulnerable populations. Smoking rates are higher in socially disadvantaged groups compared to the most affluent groups. For example, in 2012, the rate was four times higher in the most disadvantaged groups compared to the most affluent in the UK (60.7% vs 15.3%).[63] While there have been significant declines in the proportion of smokers across all socio-economic groups since 2014, a significantly higher proportion of people in routine and manual occupations continue to smoke (25.5% compared to 10.2% of those in professional roles).[64] The pattern is similar in the US, where smoking prevalence has differentially declined across population subgroups, widening the gap in smoking rates between disadvantaged and advantaged groups.[65] In Australia, the absolute gap in smoking prevalence between the most and least disadvantaged remained fairly constant for the decade 2004–2013 at about 14%, before narrowing to about 12% in 2016.[66]

In practical terms, disadvantaged smokers have fewer resources and less access to healthcare provision, especially in health systems that rely on private insurance. This may negatively impact their ability to access screening and any follow-up investigations or treatment that may be required. A substantial proportion of smokers are affected; for example, over 50% of current and former smokers who met USPSTF screening criteria were uninsured or Medicaid-insured in one US survey.[67] In the US, the Affordable Care Act requires Medicaid expansion plans and most private health insurance plans to cover, without cost sharing, preventive services given an 'A' or 'B' rating by USPSTF. Medicare and Veterans' Health also cover lung cancer screening. However, standard Medicaid programmes, catering for people with low incomes (approximately 20% of the US population) are not obliged to cover lung cancer screening and thus variably cover screening across different states.[68] Medicaid beneficiaries are a vulnerable group; 26.3% are current smokers compared to 11.1% of individuals with private insurance. As a final consideration, cost-sharing limitations only apply to the screening intervention itself, and not to any follow-up investigations which may result.[68] Successful planning and operationalizing of lung cancer screening programmes cannot ignore the social disadvantage dimension.

Rural and remote locations

Rural location represents a challenge to many aspects of healthcare provision when compared to urban populations. Historically, rural dwellers have suffered worse lung cancer outcomes, have to travel further to access healthcare and have higher smoking prevalence.[69–71] Culturally, rural dwellers may exhibit stoic and self-coping behaviours that manifest as avoidant illness behaviours.[71,72] Differential lung cancer outcomes may be driven by the widening gap in smoking prevalence between rural and urban locations. This smoking disparity is multifactorial, linked to socio-

economic status, but may be contributed to by a bias towards urban-centric health promotion strategies which are less effective in rural areas.[73] Most lung cancer screening trials have been led from academic tertiary centres, targeting urban populations but not necessarily meeting the needs of rural dwellers. Adequate engagement of rural dwellers requires extra effort, but can be achieved using a multicomponent approach as demonstrated in breast, cervical and CRC screening scenarios.[74] Geographic isolation and distance from health care services also presents a barrier to accessing cancer screening. This can be seen in breast cancer screening, where rural-dwelling women are less likely to have ever had a mammogram or to have an up-to-date mammogram than urban women.[75] This is likely to be replicated in lung cancer screening unless models of care that are more disposed towards rural dwellers can be designed and implemented. Currently, the US lung cancer screening centres are geographically maldistributed relative to the rural–urban and regional need.[76]

Reduced engagement and participation in screening

In the US, CRC screening increased significantly during the years 2006–2010 in the general population, but not in smokers. Current smokers had significantly lower odds of CRC screening than never-smokers (OR: 0.71–0.67).[77] Current smokers were less likely to adhere to USPSTF screening guidelines for colonoscopy, mammography or prostate-specific antigen testing compared with never smokers in a nationally representative, cross-sectional study of 83 176 participants.[78] In Australia, smokers and people from disadvantaged groups, including individuals with non-English speaking backgrounds were also less likely to have ever participated in any form of CRC screening.[79]

Current smokers may be less likely to participate in LDCT screening trials and real-world programmes than former smokers. For example, high-risk individuals who declined to participate in the United Kingdom Lung Cancer Screening (UKLS) trial were more likely to be current smokers than former smokers.[49] In the NELSON trial, respondents to an initial eligibility questionnaire were less likely to be current smokers compared to the general population.[80]

STIGMA

Stigma is the experience or anticipation of exclusion, rejection, blame or devaluation resulting from an adverse social judgement about a person or group. It is a social process and medically unwarranted.[81] At the individual level, stigma affects interpersonal relationships and healthcare engagement; at the societal level, it affects public attitudes, policy decisions, media campaigns and research funding. Stigma remains highly prevalent and has downstream effects across the continuum of lung cancer control, from prevention, including in smoking cessation programmes, screening and early detection, diagnosis, treatment and survivorship.[82] Stigma adds complexity to lung cancer screening participation.

The roots of smoking and lung cancer-related stigma can be traced to the tobacco industry's successful counter-litigation strategies since the 1970s. These framed smoking as a 'freedom of choice' issue. Using this argument, smokers, well aware of the health risks of smoking and able to exercise free choice, are to blame for their own illnesses, and industry, compliant with tobacco control legislation, is not responsible. This strategy became the mantra of the industry's public relations campaigns, conveniently ignoring the highly addictive and harmful nature of smoking and the aggressive marketing tactics of the tobacco industry.[83]

Stigma has been unintentionally strengthened by tobacco control measures and the growth of patient advocacy. As disease advocacy has taken on a greater role setting medical research priorities, stigma has become increasingly relevant, contributing to funding disparities that see lung cancer research receive far less funding than for non-stigmatized cancers given the size of the population affected.[84,85] Anti-smoking campaigns reinforce the perception of 'self-inflicted' disease felt by lung cancer patients.[72,86] These measures, highly successful in reducing smoking prevalence, perpetuate stigma by decreasing empathy for smokers. In an international survey, one in five people agreed that they had less sympathy for lung cancer than other forms of cancer, a proportion little changed between 2010 and 2017. In addition, countries with lower smoking prevalence had lower levels of empathy for smokers and lung cancer.[87]

Highly emotive, negative anti-smoking messages may reduce smokers' motivation to quit and increase defensive, smoking-favourable attitudes, especially in lower income smokers.[88,89] Indeed, in the UK and Australia, downward trends in smoking prevalence appear to be driven by increases in never smoking rather than increases in quitting.[63,66] Stigma and shame about lung cancer and smoking are associated with pessimistic and avoidant beliefs about cancer, contributing to high levels of psychological distress, delays in seeking medical help and reduced early-detection behaviour.[72,90–92] In contrast, people with other cancer types are perceived as blameless and deserving of empathy. Stigma is infrequently mentioned as a barrier in the context of non-lung cancer screening.[93–95] Yet, when stigma is present, it is associated with non-compliance in cervical, breast and CRC screening programmes.[96]

Qualitative research has consistently identified stigma as a barrier to lung cancer screening uptake in the UK and the US.[38,57,93,97] In addition to acting as a direct barrier to screening uptake, stigma may contribute to misreporting of smoking status to health professionals, commonly seen in smoking cessation clinical trials.[98] This may indirectly contribute to low screening uptake via the very poor accuracy of smoking status recorded in electronic health records, as discussed below, leading to non-identification of high-risk participants.[99,100]

DOCUMENTATION OF SMOKING HISTORY

Accurate documentation of smoking history is vital to enable appropriate selection of high-risk individuals for LDCT screening participation.[7,101] Inaccurate documentation presents a significant barrier to implementation. For example, in an evaluation of the Veterans Health Administration demonstration project, 39% of patients who met the initial electronic medical record (EMR) screening criteria had missing or incorrectly recorded smoking data, rendering 36 555 people ineligible for further assessment.[7] Other studies have also found EMR records inadequate for determining screening eligibility in 30–50% of patients[99,101–103] and show that nurse-led consultations are an effective strategy for obtaining smoking history. Data mining from hospital electronic health records may be able to mitigate inaccurate current smoking status to a certain extent.[104] Nevertheless, the lack of reliable smoking history documentation is a unique consideration in lung cancer screening and implementation efforts will require parallel improvements in this very basic level of data accuracy.

HEALTHCARE PROVIDER RECOMMENDATIONS

Preventive health care in the community is generally provided by primary care physicians. Successful implementation of lung cancer screening requires knowledge and acceptance by primary care physicians and coordination with screening programmes. The role of healthcare providers in encouraging high-risk individuals to consider participating is central in LDCT screening programmes. The American Academy of Family Physicians does not currently strongly support lung cancer screening and has deemed the evidence insufficient, likely contributing to reduce the uptake of lung cancer screening in the US.[105–108] The UK has a coordinated, universal primary care system that is being utilized in the evaluation of community-based lung cancer screening in a number of ongoing programmes.[109]

The crucial role of primary care clinicians is demonstrated in a retrospective cohort analysis which showed that patient uptake of LDCT screening was more likely if the patient had seen his or her own GP than not (8.5% vs 4.7%, $P < 0.0001$).[110] Qualitative research shows that GP recommendation is a key influence on screening participation.[55,56,111] However, individuals at increased risk of lung cancer may face barriers when seeking medical help; for example, barriers to GP consultations include smoker stigmatization, guilt, fatalism and symptom normalization.[112,113] An Australian study identified a general perceived mistrust of GP for current and former smokers based on previous negative experiences when visiting the GP about their smoking.[112] This indicates another complexity that smoking brings to LDCT screening, but also highlights a targetable GP behaviour by increasing knowledge, awareness and delivery of smoking cessation that may positively impact lung cancer early detection.

The importance of educating healthcare providers about LDCT screening cannot be underestimated. Evidence shows that GP are not necessarily knowledgeable about LDCT screening effectiveness, benefits and harms, or how best to communicate with their patients about eligibility.[36,42] There are no randomized trials to determine the most effective strategies to engage GP in referring high-risk patients to LDCT screening. However, the US programme evaluations have documented successful educational initiatives, including early outreach to GP, education of providers about LDCT screening requirements and eligibility criteria.[114,115]

Outreach education strategies include grand rounds, meetings with primary care clinicians and managers, medical staff meetings and seminars, webinars and information dissemination through health services intranets and web pages.[116] Education sessions about LDCT screening reported as valuable by health professionals include those that detail the LDCT examination procedure, describe LDCT screening as a tool to improve quality of care and outcomes for high-risk individuals and explain how to present ongoing feedback about screening outcomes to patients.[7] Electronic record tools have been developed to supplement GP education.[117] For example, EMR clinical prompts can remind GP to discuss eligibility and engage in shared decision-making and preventive care activities. This could increase provider awareness and referrals, however, further evaluation is needed.[42]

In response to the complex issues of recruitment, smoking and stigma, we highlight a range of implications that should be addressed in future LDCT screening research and practice, as shown in Box 1. In the sections that follow, we address the implementation issues that are important drivers of mortality once a programme has been introduced and we consider the multiple implications for clinical delivery.

INTEGRATION OF SMOKING CESSATION

Participation in a lung cancer screening programme provides a crucial opportunity to engage in smoking cessation counselling with participants. Evaluation of smoking cessation incorporation into a lung cancer screening programme reveals that it has a significant impact on cost-effectiveness.[22,118,119] Improvement of lung cancer screening cost-effectiveness also appears to be driven by improvements in non-lung cancer outcomes for participants without lung cancer, such as mortality reductions or long-term quality of life improvements.[22] Smoking cessation is a low cost intervention that can significantly impact mortality and morbidity from multiple tobacco-related diseases.[120] The combination of smoking cessation and LDCT screening nearly doubles the reduction in lung cancer-specific mortality and overall mortality, highlighting the importance of integrating smoking cessation into lung cancer screening programmes.[120]

The best method of integration into the screening process remains uncertain, but low-intensity strategies such as telephone-based intervention, provision of internet-based resources, tailored written resources or

Box 1. A summary of the implementation issues, knowledge gaps and priorities to increase consumer engagement in lung cancer screening

Target population
- Smoking status, sociodemographic and psychological variables mark smokers as 'hard to reach'
- Out-of-pocket expenses of screening and downstream investigations for participants should be minimized
- Novel strategies to engage rural smokers need to be developed; an urban-centric approach will be less effective in engaging participants

Environment
- Stigma surrounding smoking and lung cancer must be addressed if lung cancer screening is to be successful. As lung cancer screening is a new concept, the impact of future tobacco control messages on the perception and uptake of lung cancer screening should be carefully considered

Program design
- Screening trials and real-world programs should prospectively plan, evaluate and report their recruitment strategies
- A standardized approach to reporting recruitment outcomes will help to identify where interventions are needed to overcome existing barriers to recruitment
- Participation rates in targeted low-dose computed tomography screening (with population specified using eligibility criteria) should not be directly compared with population-based cancer screening programs (i.e. breast, bowel and cervical)
- Primary healthcare providers are pivotal in patient decision-making. The most appropriate and effective methods of educating general practitioner and identifying potentially eligible patients, along with their quantitative impacts on screening uptake and retention, need to be investigated
- Accurate and contemporaneous smoking history is crucial in identifying the target population

single tailored face-to-face intervention do not appear to be more effective than provision of written information pamphlets and/or access to Quitline services.[121–127] In the US, smoking cessation services must be offered by accredited screening facilities for approved reimbursement.[11,120] Internationally, participation in LDCT screening may promote smoking cessation and quit rates have been reported as varying between 12% and 38%.[121,123–131] Reported rates vary across different countries and cultures but higher smoking cessation rates are demonstrated compared to background smoking cessation rates. It is difficult to assess whether this is due to self-selection of participation in screening studies by patients trying to quit or whether it is an effect of being enrolled in the programme. In randomized studies such as the NELSON and Danish Lung Cancer Screening Trial, the effect was not limited to the LDCT intervention arm or the outcome of the screening result.[125,128,129,132] The finding of an abnormality on the LDCT has been reported to increase quit rates in some screening studies but not all.[128–132] In the NLST study, current smoking rates declined over time in all smoking participants even in those with normal LDCT scan results and the smoking cessation rates correlated with LDCT result, that is, higher smoking cessation rates were seen with detected abnormalities and the effect was greatest in those with a suspicious LDCT result. This was a durable effect still observed at 5-year follow-up and a normal LDCT result was not associated with an increased smoking relapse rate.[131,133,134]

Patients with higher nicotine dependency may be less likely to successfully achieve smoking cessation within a screening programme and this is associated with higher lung cancer-specific and all-cause mortality rates.[129,132,135] In a multivariate analysis of an NLST subgroup (Lung Screening Study and American College of Radiology Imaging Network cohorts), factors associated with persistence of smoking in a screening cohort included younger age, lower education, being spouseless, lower BMI, history of heavier smoking intensity, longer smoking duration and exposure to second-hand smoke at home.[131]

More work is needed to improve both the identification of the resistant smoking subgroup and the development of an effective and tailored approach to smoking cessation within a screening programme. It is likely this will need to be developed in collaboration with primary care physicians. Some of these questions may be answered by the ongoing efforts of the Smoking Cessation and Lung Cancer Screening (SCALE) Collaborative.[136,137] This collaborative is supported by the National Cancer Institute in the US and incorporates eight ongoing funded projects at multiple US sites. It includes the evaluation of various smoking cessation interventions within lung cancer screening programmes as well as cost-effectiveness analysis of different strategies. All SCALE collaboration trials use a common core data set and will have the capacity to merge and pool data across the studies.[137]

NODULE MANAGEMENT

One of the largest costs to a lung cancer screening programme are the downstream investigations performed after a finding of a pulmonary nodule on the initial LDCT before the next screening LDCT.[138] Standardization of nodule management is key to reduction in unnecessary investigations and/or surgery. Experience over the last 20 years has shown that although very

small noncalcified pulmonary nodules are often detected, the majority do not require any evaluation before the next screening round.

There has been a large reported variation in 'indeterminate/positive' nodules on the baseline LDCT, which has been influenced by differences in CT technique and differences in definitions in the earlier years of screening research.[4,6,28,139–143] For nodules defined as indeterminate or positive, further evaluation before the next screening round is required. The majority of these investigations consist of a repeat short-term interval LDCT and a smaller number require more expensive or invasive testing such as positron emission tomography (PET) or biopsy (Fig. 2). As screening rounds continue, there is a reduction in indeterminate/positive findings that require additional evaluation. For example, in the NELSON study, 22% of participants required further evaluation after the baseline LDCT and this reduced to 3.9% after the fourth round.[4]

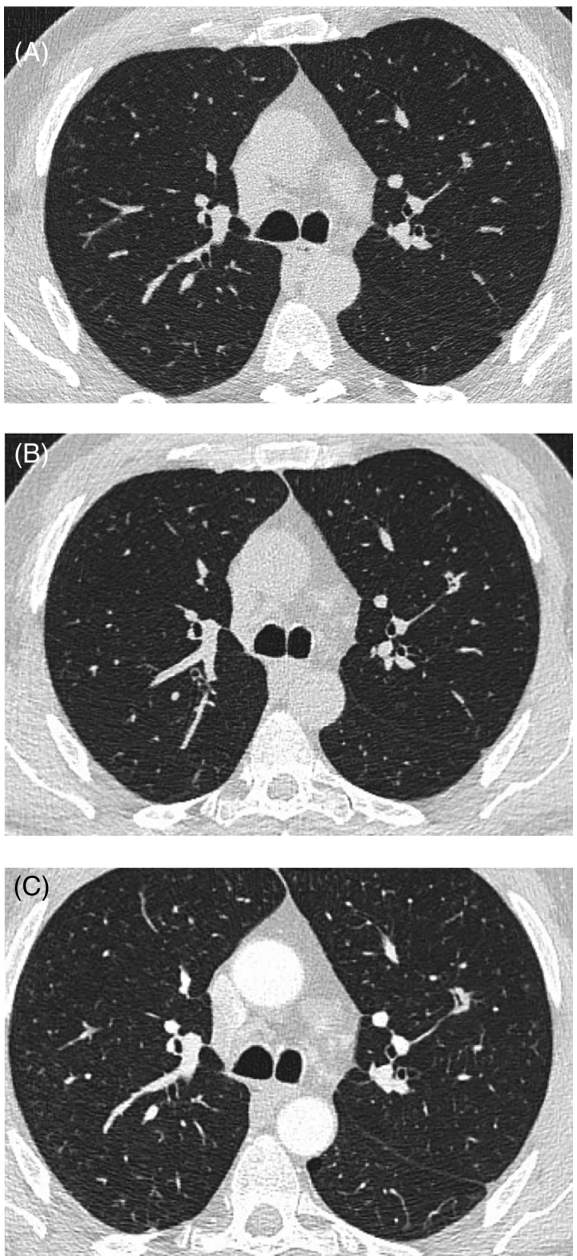

Figure 2 (A) Baseline low-dose computed tomography (LDCT) in a 70-year-old former smoker showing left upper lobe nodule (PanCan (Pan Canadian Early Detection of Lung Cancer study) risk score: 5.9%). (B) 12-Month follow-up LDCT showing some change in the left upper lobe nodule. (C) 15-Month follow-up LDCT showing further change in the left upper lobe nodule, biopsy and resection revealed T1bN0M0 (IA2) adenocarcinoma.

Nodule management algorithms incorporating risk prediction modelling and longitudinal volumetric analysis have been developed.[4,144–149] Nodule risk assessment using a published risk prediction model at the baseline LDCT has been shown to reduce the number of participants that require interval assessment compared to NELSON or LungRADS criteria.[150] This approach is being prospectively validated in the ILST study and has the potential to significantly reduce workload after the baseline LDCT.[25] Volumetric analysis of nodules was used prospectively in the NELSON study and is likely to be a useful tool in the longitudinal assessment of indeterminate nodules requiring surveillance.[4]

OTHER TOBACCO-RELATED COMORBIDITIES

High-risk screening participants are at risk of other comorbidities that contribute to increased mortality such as cardiovascular disease and chronic obstructive pulmonary disease. Coronary artery calcification is commonly detected in lung cancer screened participants and increasing severity of disease is associated with increasing risk of cardiovascular events and all-cause mortality.[151–155] A screening LDCT can also identify the presence of emphysema as well as vertebral fractures and osteoporosis which are independently associated with increased all-cause mortality.[156,157] LDCT chest scans, utilized for lung cancer screening, can therefore be used to evaluate the presence of other undiagnosed comorbidities that are predictive of increased all-cause mortality, providing a potential opportunity to further improve health outcomes. A single screening LDCT could assist in the identification, earlier treatment and promotion of preventive health care across multiple diseases. It remains to be seen whether prospective intervention for these screening detected comorbidities can impact mortality outcomes.

PROGRAM COORDINATION AND DEVELOPMENT

The implementation of lung cancer screening requires comprehensive planning in relevant healthcare systems and with professional organizations including: programme structure and funding, governance, information technology infrastructure and regulation (e.g. database development, data collection and sharing, and website development), recruitment and programme outcome reporting.[114,158–162] Radiological standardization of LDCT scan technique, quality assurance, scan reporting as well as management of LDCT

findings is essential.[159,160] Accreditation of screening centres with incorporation of multidisciplinary teams and access to fast track lung cancer clinical services is needed. Assessing and planning the health infrastructure capacity for the resources required is needed to ensure that implementation is feasible.[163] Lessons learned from implementation of other national screening programmes such as breast, colorectal and cervical screening can be utilized. Ad hoc or opportunistic screening outside an accredited programme may result in screening of low-risk patients, incorrect LDCT technique and incorrect nodule management resulting in unnecessary downstream investigations and/or surgery and the potential for harm.

In the US, initial lung cancer screening implementation began in academic centres with a collaborative or hybrid approach with primary care physicians and community centres.[11] Multiple organizations have worked together to develop accreditation, standardization, guidelines and resources for lung cancer screening.[11,114,159–162] The GO_2 Foundation for Lung Cancer have developed a community-based network of Screening Centers of Excellence (SCOE) to expand lung cancer screening to community centres in addition to academic centres.[114,161] Currently, the distribution of comprehensive lung cancer screening centres, coordinated by the American College of Radiology, includes >3500 facilities across the country.[164] Recent analysis has revealed substantial variation in availability in different states and suboptimal distribution when clinical lung cancer burden was evaluated, but lung cancer screening in the US is still relatively new and is continuing to evolve.[164] In communities planning screening implementation, review of the geographical distribution of lung cancer cases and the at-risk populations across metropolitan, regional and rural areas would improve equity of access to a programme to maximize the benefit.

There is no universal approach to delivering a lung cancer screening programme that will be applicable to all communities; a flexible and multifaceted approach will be required. As described earlier, mobile LDCT units have demonstrated potential in reaching the hard-to-reach populations by reducing travel and improving access to a screening programme outside of a traditional hospital setting. This method was successfully used for lung cancer screening in rural areas in Japan in the 1990s and their use in high-risk populations in the UK and US continues to expand.[8,165–167] It appears to be a feasible and acceptable strategy to reduce barriers to participation. However, in Australia, the utility of mobile CT units needs to be carefully assessed, as infrastructure in rural/regional areas may be inadequate with issues such as poor road conditions, dust and limited power supply creating ongoing access challenges for these high-risk populations. Customized, targeted education programmes and involvement of the primary care team will be needed to allay fears and anxiety and improve screening uptake.[38] LDCT costs will need to be fully covered and multiple access points to LDCT in the community are needed.[52,54] National support and a centrally organized coordinated programme are more likely to result in higher uptakes of screening.

Implementation of a lung cancer screening programme will result in a significant tumour stage shift resulting in changes to workload for thoracic tumour multidisciplinary teams requiring workforce and capacity planning. Treatment capacity modelling has shown that on screening implementation, there is an initial increase in demand for all treatment modalities due to the expected large incidence peak, with the greatest demand for thoracic surgery.[163] Demand for radiotherapy and chemotherapy has a subsequent reduction, whereas thoracic surgery will remain increased compared to no screening.[163] If curative treatments are unable to be provided in a timely fashion for screen-detected lung cancers, due to lack of expertise or availability, the benefits of lung cancer screening will not be maximized. Treatment capacity will need adaptation over time with changes in lung cancer incidence related to evolving population demographics and smoking habits.[3,168] Modelling can be utilized in the development of a screening programme by predicting the future clinical problem, assessing the potential impact of different interventions and capacity planning for screening implementation.[163,169,170]

BUILDING A COLLABORATIVE RESEARCH AGENDA IN IMPLEMENTATION RESEARCH

In response to the complex challenges of lung cancer screening, there is a need to invest in implementation research. Implementation science is 'the scientific study of methods to promote the systematic uptake of research findings and other evidence-based practices into routine practice, and, hence, to improve the quality and effectiveness of health services'.[171] The science is inclusive of using theory-based approaches that link the behavioural and social determinants of health to designing strategies that will enable implementation.[172] Countries that are considering the introduction of a targeted LDCT screening programme need to develop implementation research programmes that take into account unique aspects of healthcare systems and cultural contexts. In the Australian setting, initial efforts must focus on understanding the acceptability and feasibility of LDCT screening implementation with high-risk individuals and hard-to-reach groups such as indigenous and culturally diverse communities. Currently, there are very little Australian data about delivery of LDCT screening outside the trial setting.[173,174] Research into recruitment strategies has commenced through the ILST to compare invitations sent either via the electoral roll compared with those from general practice. Qualitative studies are underway to examine motivation for screening in participants and those who decline, as well as the interaction between smoking, smoking cessation and lung cancer screening uptake. Research into developing interventions that tackle stigma across the continuum is gaining traction[82] and is supported by community advocates such as the Lung Foundation Australia.

Building a collaborative implementation research agenda for a targeted LDCT screening programme requires the partnership of multiple stakeholders across

government, consumer and community organizations, clinical practice, academic researchers and tobacco control experts. Priority must be given to fund research to coordinate efforts and ensure that policymakers resource LDCT screening alongside tobacco control and do not divert resources from one programme to the other.[175]

CONCLUSION

The benefits of lung cancer screening are no longer in doubt. Lung cancer deaths are predicted to continue to rise, particularly in women.[3] LDCT screening will significantly impact lung cancer mortality and should be utilized in tandem with tobacco control strategies. Programme and workforce planning with the development of accreditation and governance structures are needed prior to implementation. Maximal benefits will be achieved by focusing on a planned, targeted recruitment strategy that reaches this hard-to-reach population, use of a standardized probabilistic nodule management protocol by a multidisciplinary team to reduce unnecessary investigations, integration of smoking cessation and identification of other tobacco-related diseases. Issues that require ongoing clarification are the best methods to enhance screening uptake and smoking cessation, particularly in populations at highest risk.[33,176] Investment in implementation research will help to ensure that LDCT screening can deliver programmes to those who will most need them and reap the health benefits so long awaited by our communities.

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Abbreviations: ARP, approach response proportion; BMI, body mass index; CRC, colorectal cancer; CT, computed tomography; EDP, eligible decline proportion; EMR, electronic medical record; EPP, eligible participation proportion; ERP, eligible responder proportion; ESP, eligible scanned proportion; GP, general practitioner; ILST, International Lung Screening Trial; LDCT, low-dose CT; LHC, Lung Health Check; LSUT, Lung Screen Uptake Trial; NELSON, NEderlands-Leuvens Longkanker Screenings ONderzoek; NLST, National Lung Screening Trial; OR, odds ratio; PanCan, Pan Canadian Early Detection of Lung Cancer study; PLCO, Prostate, Lung, Colorectal and Ovarian Screening Trial; RDP, response decline proportion; SAP, scanned approach proportion; SCALE, Smoking Cessation and Lung Cancer Screening; UKLS, United Kingdom Lung Cancer Screening trial; US, United States; USPSTF, United States Preventive Services Task Force

REFERENCES

1 International Agency for Research on Cancer. Lung Cancer: Globocan 2018. [Accessed 2 Mar 2020.] Available from URL: https://gco.iarc.fr/today/data/factsheets/cancers/15-Lung-fact-sheet.pdf
2 Australian Institute of Health and Welfare. Cancer in Australia 2017. Cancer series no. 101. Cat. no. CAN 100. Canberra: AIHW, 2017.
3 Luo Q, Yu XQ, Wade S, Caruana M, Pesola F, Canfell K, O'Connell DL. Lung cancer mortality in Australia: projected outcomes to 2040. *Lung Cancer* 2018; **125**: 68–76.
4 de Koning HJ, van der Aalst CM, de Jong PA, Scholten ET, Nackaerts K, Heuvelmans MA, Lammers JJ, Weenink C, Yousaf-Khan U, Horeweg N *et al.* Reduced lung-cancer mortality with volume CT screening in a randomized trial. *N. Engl. J. Med.* 2020; **382**: 503–13.
5 Pinsky PF, Church TR, Izmirlian G, Kramer BS. The National Lung Screening Trial: results stratified by demographics, smoking history, and lung cancer histology. *Cancer* 2013; **119**: 3976–83.
6 Aberle DR, Adams AM, Berg CD, Black WC, Clapp JD, Fagerstrom RM, Gareen IF, Gatsonis C, Marcus PM, Sicks JD. Reduced lung-cancer mortality with low-dose computed tomographic screening. *N. Engl. J. Med.* 2011; **365**: 395–409.
7 Kinsinger LS, Anderson C, Kim J, Larson M, Chan SH, King HA, Rice KL, Slatore CG, Tanner NT, Pittman K *et al.* Implementation of lung cancer screening in the Veterans Health Administration. *JAMA Intern. Med.* 2017; **177**: 399–406.
8 Crosbie PA, Balata H, Evison M, Atack M, Bayliss-Brideaux V, Colligan D, Duerden R, Eaglesfield J, Edwards T, Elton P *et al.* Implementing lung cancer screening: baseline results from a community-based 'Lung Health Check' pilot in deprived areas of Manchester. *Thorax* 2019; **74**: 405–9.
9 Moyer VA; U.S. Preventive Services Task Force. Screening for lung cancer: U.S. Preventive Services Task Force recommendation statement. *Ann. Intern. Med.* 2014; **160**: 330–8.
10 The Centers for Medicare & Medicaid Services (CMS). Decision memo for screening for lung cancer with low dose computed tomography (LDCT) (CAG-00439N). Baltimore, MD: U.S. Centers for Medicare and Medicaid Services; 2015. [Accessed 1 Mar 2020]. Available from URL: https://www.cms.gov/medicare-coverage-database/details/nca-decisionmemo.aspx?NCAId=274
11 American Thoracic Society, American Lung Association. Implementation guide for lung cancer screening. 2019. [Accessed 4 Oct 2019]. Available from URL: https://www.lungcancer screeningguide.org/
12 Crosbie PA, Balata H, Evison M, Atack M, Bayliss-Brideaux V, Colligan D, Duerden R, Eaglesfield J, Edwards T, Elton P *et al.* Second round results from the Manchester 'Lung Health Check' community-based targeted lung cancer screening pilot. *Thorax* 2019; **74**: 700–4.
13 Ghimire B, Maroni R, Vulkan D, Shah Z, Gaynor E, Timoney M, Jones L, Arvanitis R, Ledson M, Lukehirst L *et al.* Evaluation of a health service adopting proactive approach to reduce high risk of lung cancer: the Liverpool Healthy Lung Programme. *Lung Cancer* 2019; **134**: 66–71.
14 Richards M. *Report of the Independent Review of Adult Screening Programmes in England*. London, NHS England, 2019.

15 Snowsill T, Yang H, Griffin E, Long L, Varley-Campbell J, Coelho H, Robinson S, Hyde C. Low-dose computed tomography for lung cancer screening in high-risk populations: a systematic review and economic evaluation. *Health Technol. Assess.* 2018; **22**: 1–276.
16 Huang KL, Wang SY, Lu WC, Chang YH, Su J, Lu YT. Effects of low-dose computed tomography on lung cancer screening: a systematic review, meta-analysis, and trial sequential analysis. *BMC Pulm. Med.* 2019; **19**: 126.
17 Lam S. Lung cancer screening in never-smokers. *J. Thorac. Oncol.* 2019; **14**: 336–7.
18 Kang HR, Cho JY, Lee SH, Lee YJ, Park JS, Cho YJ, Yoon HI, Lee KW, Lee JH, Lee CT. Role of low-dose computerized tomography in lung cancer screening among never-smokers. *J. Thorac. Oncol.* 2019; **14**: 436–44.
19 Haiman CA, Stram DO, Wilkens LR, Pike MC, Kolonel LN, Henderson BE, Le Marchand L. Ethnic and racial differences in the smoking-related risk of lung cancer. *N. Engl. J. Med.* 2006; **354**: 333–42.
20 Tammemagi MC, Katki HA, Hocking WG, Church TR, Caporaso N, Kvale PA, Chaturvedi AK, Silvestri GA, Riley TL, Commins J *et al*. Selection criteria for lung-cancer screening. *N. Engl. J. Med.* 2013; **368**: 728–36.
21 Kovalchik SA, Tammemagi M, Berg CD, Caporaso NE, Riley TL, Korch M, Silvestri GA, Chaturvedi AK, Katki HA. Targeting of low-dose CT screening according to the risk of lung-cancer death. *N. Engl. J. Med.* 2013; **369**: 245–54.
22 Cressman S, Peacock SJ, Tammemägi MC, Evans WK, Leighl NB, Goffin JR, Tremblay A, Liu G, Manos D, MacEachern P *et al*. The cost-effectiveness of high-risk lung cancer screening and drivers of program efficiency. *J. Thorac. Oncol.* 2017; **12**: 1210–22.
23 Tammemagi MC, Schmidt H, Martel S, McWilliams A, Goffin JR, Johnston MR, Nicholas G, Tremblay A, Bhatia R, Liu G *et al*. Participant selection for lung cancer screening by risk modelling (the Pan-Canadian Early Detection of Lung Cancer [PanCan] study): a single-arm, prospective study. *Lancet Oncol.* 2017; **18**: 1523–31.
24 Weber M, Yap S, Goldsbury D, Manners D, Tammemagi M, Marshall H, Brims F, McWilliams A, Fong K, Kang YJ *et al*. Identifying high risk individuals for targeted lung cancer screening: independent validation of the PLCOm2012 risk prediction tool. *Int. J. Cancer* 2017; **141**: 242–53.
25 Lim KP, Marshall H, Tammemagi M, Brims F, McWilliams A, Stone E, Manser R, Canfell K, Weber M, Connelly L *et al*. Protocol and rationale for the International Lung Screening Trial (ILST). *Ann. Am. Thorac. Soc.* 2020; **17**: 503–12.
26 Paci E, Puliti D, Lopes Pegna A, Picozzi G, Falaschi F, Pistelli F, Aquilini F, Ocello C, Zappa M, Carozzi FM *et al*. Mortality, survival and incidence rates in the ITALUNG randomised lung cancer screening trial. *Thorax* 2017; **72**: 825–31.
27 Becker N, Motsch E, Trotter A, Heussel CP, Dienemann H, Schnabel PA, Kauczor HU, Maldonado SG, Miller AB, Kaaks R *et al*. Lung cancer mortality reduction by LDCT screening – results from the randomized German LUSI trial. *Int. J. Cancer* 2020; **146**: 1503–13.
28 Church TR, Black WC, Aberle DR, Berg CD, Clingan KL, Duan F, Fagerstrom RM, Gareen IF, Gierada DS, Jones GC *et al*. Results of initial low-dose computed tomographic screening for lung cancer. *N. Engl. J. Med.* 2013; **368**: 1980–91.
29 Infante M, Cavuto S, Lutman FR, Passera E, Chiarenza M, Chiesa G, Brambilla G, Angeli E, Aranzulla G, Chiti A. Long-term follow-up results of the DANTE trial, a randomized study of lung cancer screening with spiral computed tomography. *Am. J. Respir. Crit. Care Med.* 2015; **191**: 1166–75.
30 Wille MM, Dirksen A, Ashraf H, Saghir Z, Bach KS, Brodersen J, Clementsen PF, Hansen H, Larsen KR, Mortensen J. Results of the randomized Danish Lung Cancer Screening Trial with focus on high-risk profiling. *Am. J. Respir. Crit. Care Med.* 2016; **193**: 542–51.
31 Pastorino U, Sverzellati N, Sestini S, Silva M, Sabia F, Boeri M, Cantarutti A, Sozzi G, Corrao G, Marchiano A. Ten-year results of the Multicentric Italian Lung Detection trial demonstrate the safety and efficacy of biennial lung cancer screening. *Eur. J. Cancer* 2019; **118**: 142–8.
32 Field JK, Duffy SW, Baldwin DR, Brain KE, Devaraj A, Eisen T, Green BA, Holemans JA, Kavanagh T, Kerr KM *et al*. The UK Lung Cancer Screening Trial: a pilot randomised controlled trial of low-dose computed tomography screening for the early detection of lung cancer. *Health Technol. Assess.* 2016; **20**: 177.
33 Quaife SL, Ruparel M, Dickson JL, Beeken RJ, McEwen A, Baldwin DR, Bhowmik A, Navani N, Sennett K, Duffy SW *et al*. Lung Screen Uptake Trial (LSUT): randomised controlled trial testing targeted invitation materials. *Am. J. Respir. Crit. Care Med.* 2019; **201**: 965–975. https://pubmed.ncbi.nlm.nih.gov/31825647/
34 Marcus PM, Lenz S, Sammons D, Black W, Garg K. Recruitment methods employed in the National Lung Screening Trial. *J. Med. Screen.* 2012; **19**: 94–102.
35 Jessup DL, Glover Iv M, Daye D, Banzi L, Jones P, Choy G, Shepard JAO, Flores EJ. Implementation of digital awareness strategies to engage patients and providers in a lung cancer screening programme: retrospective study. *J. Med. Internet Res.* 2018; **20**: e52.
36 Rankin NM, McGregor D, Donnelly C, Van Dort B, De Abreu Lourenco R, Cust A, Stone E. Lung cancer screening using low-dose computed tomography for high risk populations: investigating effectiveness and screening programme implementation considerations. Sydney: An Evidence Check rapid review brokered by the Sax Institute (www.saxinstitute.org.au) for the Cancer Institute NSW, Eveleigh; 2020.
37 Schutte S, Dietrich D, Montet X, Flahault A. Participation in lung cancer screening programmes: are there gender and social differences? A systematic review. *Public Health Rev.* 2018; **39**: 23.
38 Quaife SL, Marlow LAV, McEwen A, Janes SM, Wardle J. Attitudes towards lung cancer screening in socioeconomically deprived and heavy smoking communities: informing screening communication. *Health Expect.* 2017; **20**: 563–73.
39 McRonald FE, Yadegarfar G, Baldwin DR, Devaraj A, Brain KE, Eisen T, Holemans JA, Ledson M, Screaton N, Rintoul RC *et al*. The UK Lung Screen (UKLS): demographic profile of first 88,897 approaches provides recommendations for population screening. *Cancer Prev. Res.* 2014; **7**: 362–71.
40 Hestbech MS, Siersma V, Dirksen A, Pedersen JH, Brodersen J. Participation bias in a randomised trial of screening for lung cancer. *Lung Cancer* 2011; **73**: 325–31.
41 Aberle DR, Adams AM, Berg CD, Clapp JD, Clingan KL, Gareen IF, Lynch DA, Marcus PM, Pinsky PF. Baseline characteristics of participants in the randomized National Lung Screening Trial. *J. Natl. Cancer Inst.* 2010; **102**: 1771–9.
42 Gesthalter YB, Koppelman E, Bolton R, Slatore CG, Yoon SH, Cain HC, Tanner NT, Au DH, Clark JA, Wiener RS. Evaluations of implementation at early-adopting lung cancer screening programmes: lessons learned. *Chest* 2017; **152**: 70–80.
43 Australian Institute of Health and Welfare. Key performance indicators for the National Bowel Cancer Screening Programme: technical report. Cancer series no. 87. Cat. no. CAN 84. Canberra: Australian Institute of Health and Welfare, 2014.
44 Ruparel M, Quaife SL, Ghimire B, Dickson JL, Bhowmik A, Navani N, Baldwin DR, Duffy S, Waller J, Janes SM. Impact of a lung cancer screening information film on informed decision-making: a randomized trial. *Ann. Am. Thorac. Soc.* 2019; **16**: 744–51.
45 Weller DP, Patnick J, McIntosh HM, Dietrich AJ. Uptake in cancer screening programmes. *Lancet Oncol.* 2009; **10**: 693–9.
46 Szczepura A, Price C, Gumber A. Breast and bowel cancer screening uptake patterns over 15 years for UK South Asian ethnic minority populations, corrected for differences in socio-demographic characteristics. *BMC Public Health* 2008; **8**: 346.
47 Triplette M, Thayer JH, Pipavath SN, Crothers K. Poor uptake of lung cancer screening: opportunities for improvement. *J. Am. Coll. Radiol.* 2019; **16**: 446–50.

48 Patel D, Akporobaro A, Chinyanganya N, Hackshaw A, Seale C, Spiro SG, Griffiths C. Attitudes to participation in a lung cancer screening trial: a qualitative study. *Thorax* 2012; **67**: 418–25.
49 Ali N, Lifford KJ, Carter B, McRonald F, Yadegarfar G, Baldwin DR, Weller D, Hansell DM, Duffy SW, Field JK *et al*. Barriers to uptake among high-risk individuals declining participation in lung cancer screening: a mixed methods analysis of the UK Lung Cancer Screening (UKLS) trial. *BMJ Open* 2015; **5**: e008254.
50 van den Bergh KAM, Essink-Bot ML, van Klaveren RJ, de Koning HJ. Informed participation in a randomised controlled trial of computed tomography screening for lung cancer. *Eur. Respir. J.* 2009; **34**: 711–20.
51 Tanner NT, Egede LE, Shamblin C, Gebregziabher M, Silvestri GA. Attitudes and beliefs toward lung cancer screening among US Veterans. *Chest* 2013; **144**: 1783–7.
52 Jonnalagadda S, Bergamo C, Lin JJ, Lurslurchachai L, Diefenbach M, Smith C, Nelson JE, Wisnivesky JP. Beliefs and attitudes about lung cancer screening among smokers. *Lung Cancer* 2012; **77**: 526–31.
53 Delmerico J, Hyland A, Celestino P, Reid M, Cummings KM. Patient willingness and barriers to receiving a CT scan for lung cancer screening. *Lung Cancer* 2014; **84**: 307–9.
54 Silvestri GA, Nietert PJ, Zoller J, Carter C, Bradford D. Attitudes towards screening for lung cancer among smokers and their non-smoking counterparts. *Thorax* 2007; **62**: 126–30.
55 Roth JA, Carter-Harris L, Brandzel S, Buist DSM, Wernli KJ. A qualitative study exploring patient motivations for screening for lung cancer. *PLoS One* 2018; **13**: e0196758.
56 Draucker CB, Rawl SM, Vode E, Carter-Harris L. Understanding the decision to screen for lung cancer or not: a qualitative analysis. *Health Expect.* 2019; **22**: 1314–21.
57 Tonge JE, Atack M, Crosbie PA, Barber PV, Booton R, Colligan D. "To know or not to know…?" Push and pull in ever smokers lung screening uptake decision-making intentions. *Health Expect.* 2019; **22**: 162–72.
58 David A, Esson K, Perucic AM, Fitzpatrick C. Tobacco use: equity and social determinants. In: Blas E, Kurup A (eds) *Equity, Social Determinants and Public Health Programmes*. Geneva, World Health Organization, 2010.
59 Centers for Disease Control and Prevention. Cigarette smoking and tobacco use among people of low socioeconomic status. 2019. [Accessed 2 Mar 2020.] Available from URL: https://www.cdc.gov/tobacco/disparities/low-ses/index.htm
60 Australian Institute of Health and Welfare. Alcohol, tobacco & other drugs in Australia. 2020. [Accessed 2 Mar 2020.] Available from URL: https://www.aihw.gov.au/reports/alcohol/alcohol-tobacco-other-drugs-australia/contents/drug-types/tobacco
61 Australian Institute of Health and Welfare. Rural & remote health. 2019. [Accessed 2 Mar 2020.] Available from URL: https://www.aihw.gov.au/reports/rural-remote-australians/rural-remote-health/contents/health-status-and-outcomes
62 National Collaborating Center for Aboriginal Health. Tobacco Fact Sheet. 2013. [Accessed 8 Mar 2020.] Available from URL: https://www.nccih.ca/docs/health/FS-Tobacco-EN.pdf
63 Hiscock R, Bauld L, Amos A, Platt S. Smoking and socioeconomic status in England: the rise of the never smoker and the disadvantaged smoker. *J. Public Health* 2012; **34**: 390–6.
64 Office for National Statistics. Adult smoking habits in the UK 2018. London: Office for National Statistics, 2019.
65 Drope J, Liber AC, Cahn Z, Stoklosa M, Kennedy R, Douglas CE, Henson R, Drope J. Who's still smoking? Disparities in adult cigarette smoking prevalence in the United States. *CA Cancer J. Clin.* 2018; **68**: 106–15.
66 Scollo MM, Winstanley MH. *Tobacco in Australia: Facts and Issues*. Cancer Council Victoria, Melbourne, 2019.
67 Jemal A, Fedewa SA. Lung cancer screening with low-dose computed tomography in the United States – 2010 to 2015. *JAMA Oncol.* 2017; **3**: 1278–81.
68 National Academies of Sciences, Engineering, and Medicine. *Implementation of Lung Cancer Screening: Proceedings of a Workshop*. Washington, DC, The National Academies Press, 2017.
69 Singh GK, Siahpush M. Widening rural–urban disparities in all-cause mortality and mortality from major causes of death in the USA, 1969–2009. *J. Urban Health* 2014; **91**: 272–92.
70 Jenkins WD, Matthews AK, Bailey A, Zahnd WE, Watson KS, Mueller-Luckey G, Molina Y, Crumly D, Patera J. Rural areas are disproportionately impacted by smoking and lung cancer. *Prev. Med. Rep.* 2018; **10**: 200–3.
71 Dobson C, Rubin G, Murchie P, Macdonald S, Sharp L. Reconceptualising rural cancer inequalities: time for a new research agenda. *Int. J. Environ. Res. Public Health* 2020; **17**: 1455.
72 Dunn J, Garvey G, Valery PC, Ball D, Fong KM, Vinod S, O'Connell DL, Chambers SK. Barriers to lung cancer care: health professionals' perspectives. *Support. Care Cancer* 2017; **25**: 497–504.
73 Doogan NJ, Roberts ME, Wewers ME, Stanton CA, Keith DR, Gaalema DE, Kurti AN, Redner R, Cepeda-Benito A, Bunn JY *et al*. A growing geographic disparity: rural and urban cigarette smoking trends in the United States. *Prev. Med.* 2017; **104**: 79–85.
74 Rodríguez-Gómez M, Ruiz-Pérez I, Martín-Calderón S, Pastor-Moreno G, Artazcoz L, Escribà-Agüir V. Effectiveness of patient-targeted interventions to increase cancer screening participation in rural areas: a systematic review. *Int. J. Nurs. Stud.* 2020; **101**: 103401.
75 Leung J, McKenzie S, Martin J, McLaughlin D. Effect of rurality on screening for breast cancer: a systematic review and meta-analysis comparing mammography. *Rural Remote Health* 2014; **14**: 2730.
76 Odahowski CL, Zahnd WE, Eberth JM. Challenges and opportunities for lung cancer screening in rural America. *J. Am. Coll. Radiol.* 2019; **16**: 590–5.
77 Oluyemi AO, Welch AR, Yoo LJ, Lehman EB, McGarrity TJ, Chuang CH. Colorectal cancer screening in high-risk groups is increasing, although current smokers fall behind. *Cancer* 2014; **120**: 2106–13.
78 Sanford NN, Sher DJ, Butler S, Xu X, Ahn C, D'Amico AV, Rebbeck T, Aizer AA, Mahal BA. Cancer screening patterns among current, former, and never smokers in the United States, 2010-2015. *JAMA Netw. Open* 2019; **2**: e193759.
79 He E, Lew JB, Egger S, Banks E, Ward RL, Beral V, Canfell K. Factors associated with participation in colorectal cancer screening in Australia: results from the 45 and Up Study cohort. *Prev. Med.* 2018; **106**: 185–93.
80 van der Aalst CM, van Iersel CA, van Klaveren RJ, Frenken FJ, Fracheboud J, Otto SJ, de Jong PA, Oudkerk M, de Koning HJ. Generalisability of the results of the Dutch-Belgian randomised controlled lung cancer CT screening trial (NELSON): does self-selection play a role? *Lung Cancer* 2012; **77**: 51–7.
81 Weiss MG, Ramakrishna J, Somma D. Health-related stigma: rethinking concepts and interventions. *Psychol. Health Med.* 2006; **11**: 277–87.
82 Hamann HA, Ver Hoeve ES, Carter-Harris L, Studts JL, Ostroff JS. Multilevel opportunities to address lung cancer stigma across the cancer control continuum. *J. Thorac. Oncol.* 2018; **13**: 1062–75.
83 Friedman LC, Cheyne A, Givelber D, Gottlieb MA, Daynard RA. Tobacco industry use of personal responsibility rhetoric in public relations and litigation: disguising freedom to blame as freedom of choice. *Am. J. Public Health* 2015; **105**: 250–60.
84 Best RK. Disease politics and medical research funding: three ways advocacy shapes policy. *Am. Sociol. Rev.* 2012; **77**: 780–803.
85 Kamath SD, Kircher SM, Benson AB. Comparison of cancer burden and nonprofit organization funding reveals disparities in funding across cancer types. *J. Natl. Compr. Canc. Netw.* 2019; **17**: 849.
86 Chambers S, Dunn J, Occhipinti S, Hughes S, Baade P, Sinclair S, Aitken J, Youl P, O'Connell D. A systematic review of the impact of stigma and nihilism on lung cancer outcomes. *BMC Cancer* 2012; **12**: 184.

87 Global Lung Cancer Coalition. Global briefing: symptom awareness and attitudes to lung cancer. Findings from a global study. 2017. [Accessed 1 Mar 2020]. Available from URL: http://www.lungcancercoalition.org/uploads/docs/Global%20briefing%20-%20FINAL.pdf

88 Kim J, Cao X, Meczkowski E. Does stigmatization motivate people to quit smoking? Examining the effect of stigmatizing anti-smoking campaigns on cessation intention. *Health Commun.* 2018; **33**: 681–9.

89 Helweg-Larsen M, Sorgen LJ, Pisinger C. Does it help smokers if we stigmatize them? A test of the stigma-induced identity threat model among U.S. and Danish smokers. *Soc. Cogn.* 2019; **37**: 294–313.

90 Park ER, Streck JM, Gareen IF, Ostroff JS, Hyland KA, Rigotti NA, Pajolek H, Nichter M. A qualitative study of lung cancer risk perceptions and smoking beliefs among National Lung Screening Trial participants. *Nicotine Tob. Res.* 2014; **16**: 166–73.

91 Hall MB, Vos P. Comparison of cancer fatalism among rural smokers and nonsmokers. *J. Community Health* 2019; **44**: 215–21.

92 Occhipinti S, Dunn J, O'Connell DL, Garvey G, Valery PC, Ball D, Fong KM, Vinod S, Chambers S. Lung cancer stigma across the social network: patient and caregiver perspectives. *J. Thorac. Oncol.* 2018; **13**: 1443–53.

93 Carter-Harris L, Ceppa DP, Hanna N, Rawl SM. Lung cancer screening: what do long-term smokers know and believe? *Health Expect.* 2017; **20**: 59–68.

94 Long H, Brooks JM, Harvie M, Maxwell A, French DP. How do women experience a false-positive test result from breast screening? A systematic review and thematic synthesis of qualitative studies. *Br. J. Cancer* 2019; **121**: 351–8.

95 Dougherty MK, Brenner AT, Crockett SD, Gupta S, Wheeler SB, Coker-Schwimmer M, Cubillos L, Malo T, Reuland DS. Evaluation of interventions intended to increase colorectal cancer screening rates in the United States: a systematic review and meta-analysis. *JAMA Intern. Med.* 2018; **178**: 1645–58.

96 Vrinten C, Gallagher A, Waller J, Marlow LAV. Cancer stigma and cancer screening attendance: a population based survey in England. *BMC Cancer* 2019; **19**: 566.

97 Prout HC, Barham A, Bongard E, Tudor-Edwards R, Griffiths G, Hamilton W, Harrop E, Hood K, Hurt CN, Nelson R *et al*. Patient understanding and acceptability of an early lung cancer diagnosis trial: a qualitative study. *Trials* 2018; **19**: 419.

98 Benowitz NL, Bernert JT, Foulds J, Hecht SS, Jacob P III, Jarvis MJ, Joseph A, Oncken C, Piper ME. Biochemical verification of tobacco use and abstinence: 2019 update. *Nicotine Tob. Res.* 2020; **22**: 1086–97.

99 Cole AM, Pflugeisen B, Schwartz MR, Miller SC. Cross sectional study to assess the accuracy of electronic health record data to identify patients in need of lung cancer screening. *BMC. Res. Notes* 2018; **11**: 14.

100 Polubriaginof F, Salmasian H, Albert DA, Vawdrey DK. Challenges with collecting smoking status in electronic health records. *AMIA Annu. Symp. Proc.* 2018; **2017**: 1392–400.

101 Begnaud AL, Joseph AM, Lindgren BR. Randomized electronic promotion of lung cancer screening: a pilot. *JCO Clin. Cancer Inform.* 2017; **1**: 1–6.

102 Patel N, Miller DP Jr, Snavely AC, Bellinger C, Foley KL, Case D, McDonald ML, Masmoudi YR, Dharod A. A comparison of smoking history in the electronic health record with self-report. *Am. J. Prev. Med.* 2020; **58**: 591–5.

103 Modin HE, Fathi JT, Gilbert CR, Wilshire CL, Wilson AK, Aye RW, Farivar AS, Louie BE, Vallieres E, Gorden JA. Pack-year cigarette smoking history for determination of lung cancer screening eligibility. Comparison of the electronic medical record versus a shared decision-making conversation. *Ann. Am. Thorac. Soc.* 2017; **14**: 1320–5.

104 Groenhof TKJ, Koers LR, Blasse E, de Groot M, Grobbee DE, Bots ML, Asselbergs FW, Lely AT, Haitjema S, van Solinge W *et al*. Data mining information from electronic health records produced high yield and accuracy for current smoking status. *J. Clin. Epidemiol.* 2020; **118**: 100–6.

105 Rai A, Doria-Rose VP, Silvestri GA, Yabroff KR. Evaluating lung cancer screening uptake, outcomes, and costs in the United States: challenges with existing data and recommendations for improvement. *J. Natl. Cancer Inst.* 2019; **111**: 342–9.

106 Kanodra NM, Pope C, Halbert CH, Silvestri GA, Rice LJ, Tanner NT. Primary care provider and patient perspectives on lung cancer screening. A qualitative study. *Ann. Am. Thorac. Soc.* 2016; **13**: 1977–82.

107 Coughlin JM, Zang Y, Terranella S, Alex G, Karush J, Geissen N, Chmielewski GW, Arndt AT, Liptay MJ, Zimmermann LJ *et al*. Understanding barriers to lung cancer screening in primary care. *J. Thorac. Dis.* 2020; **12**: 2536–44.

108 Schiffelbein JE, Carluzzo KL, Hasson RM, Alford-Teaster JA, Imset I, Onega T. Barriers, facilitators, and suggested interventions for lung cancer screening among a rural screening-eligible population. *J. Prim. Care Community Health* 2020; **11**: 2150132720930544.

109 NHS. Lung Health Checks. 2019. [Accessed 20 July 2020.] Available from URL: https://www.cancerresearchuk.org/about-cancer/lung-cancer/getting-diagnosed/lung-health-checks

110 Li J, Chung S, Wei EK, Luft HS. New recommendation and coverage of low-dose computed tomography for lung cancer screening: uptake has increased but is still low. *BMC Health Serv. Res.* 2018; **18**: 525.

111 Carter-Harris L, Slaven JE Jr, Monahan PO, Shedd-Steele R, Hanna N, Rawl SM. Understanding lung cancer screening behavior: racial, gender, and geographic differences among Indiana long-term smokers. *Prev. Med. Rep.* 2018; **10**: 49–54.

112 Murray SR, Kutzer Y, Habgood E, Murchie P, Walter FM, Mazza D, Shahid S, Emery JD. Reducing barriers to consulting a general practitioner in patients at increased risk of lung cancer: a qualitative evaluation of the CHEST Australia intervention. *Fam. Pract.* 2017; **34**: 740–6.

113 Carter-Harris L, Hermann CP, Schreiber J, Weaver MT, Rawl SM. Lung cancer stigma predicts timing of medical help-seeking behavior. *Oncol. Nurs. Forum* 2014; **41**: E203–10.

114 Copeland A, Criswell A, Ciupek A, King JC. Effectiveness of lung cancer screening implementation in the community setting in the United States. *J. Oncol. Pract.* 2019; **15**: e607–15.

115 Cattaneo SM 2nd, Meisenberg BR, Geronimo MCM, Bhandari B, Maxted JW, Brady-Copertino CJ. Lung cancer screening in the community setting. *Ann. Thorac. Surg.* 2018; **105**: 1627–32.

116 McKee BJ, McKee AB, Flacke S, Lamb CR, Hesketh PJ, Wald C. Initial experience with a free, high-volume, low-dose CT lung cancer screening programme. *J. Am. Coll. Radiol.* 2013; **10**: 586–92.

117 Begnaud A, Hall T, Allen T. Lung cancer screening with low-dose CT: implementation amid changing public policy at one health care system. *Am. Soc. Clin. Oncol. Educ. Book* 2016; **35**: e468–75.

118 Villanti AC, Jiang Y, Abrams DB, Pyenson BS. A cost-utility analysis of lung cancer screening and the additional benefits of incorporating smoking cessation interventions. *PLoS One* 2013; **8**: e71379.

119 McMahon PM, Kong CY, Bouzan C, Weinstein MC, Cipriano LE, Tramontano AC, Johnson BE, Weeks JC, Gazelle GS. Cost-effectiveness of computed tomography screening for lung cancer in the United States. *J. Thorac. Oncol.* 2011; **6**: 1841–8.

120 Tanner NT, Kanodra NM, Gebregziabher M, Payne E, Halbert CH, Warren GW, Egede LE, Silvestri GA. The association between smoking abstinence and mortality in the National Lung Screening Trial. *Am. J. Respir. Crit. Care Med.* 2016; **193**: 534–41.

121 Taylor KL, Cox LS, Zincke N, Mehta L, McGuire C, Gelmann E. Lung cancer screening as a teachable moment for smoking cessation. *Lung Cancer* 2007; **56**: 125–34.

122 Marshall HM, Courtney DA, Passmore LH, McCaul EM, Yang IA, Bowman RV, Fong KM. Brief tailored smoking cessation counseling in a lung cancer screening population is feasible: a pilot randomized controlled trial. *Nicotine Tob. Res.* 2016; **18**: 1665–9.

123 Tremblay A, Taghizadeh N, Huang J, Kasowski D, MacEachern P, Burrowes P, Graham AJ, Dickinson JA, Lam SC, Yang H *et al*. A

randomized controlled study of integrated smoking cessation in a lung cancer screening programme. *J. Thorac. Oncol.* 2019; **14**: 1528–37.
124 Stone E, Marshall H. Tobacco cessation in lung cancer screening—do we have the evidence? *Transl. Lung Cancer Res.* 2018; **7**: S270–4.
125 Pedersen JH, Tonnesen P, Ashraf H. Smoking cessation and lung cancer screening. *Ann. Transl. Med.* 2016; **4**: 157.
126 van der Aalst CM, de Koning HJ, van den Bergh KA, Willemsen MC, van Klaveren RJ. The effectiveness of a computer-tailored smoking cessation intervention for participants in lung cancer screening: a randomised controlled trial. *Lung Cancer* 2012; **76**: 204–10.
127 Clark MM, Cox LS, Jett JR, Patten CA, Schroeder DR, Nirelli LM, Vickers K, Hurt RD, Swensen SJ. Effectiveness of smoking cessation self-help materials in a lung cancer screening population. *Lung Cancer* 2004; **44**: 13–21.
128 van der Aalst CM, van Klaveren RJ, van den Bergh KAM, Willemsen MC, de Koning HJ. The impact of a lung cancer computed tomography screening result on smoking abstinence. *Eur. Respir. J.* 2011; **37**: 1466–73.
129 Ashraf H, Saghir Z, Dirksen A, Pedersen JH, Thomsen LH, Døssing M, Tønnesen P. Smoking habits in the randomised Danish Lung Cancer Screening Trial with low-dose CT: final results after a 5-year screening programme. *Thorax* 2014; **69**: 574–9.
130 Brain K, Carter B, Lifford KJ, Burke O, Devaraj A, Baldwin DR, Duffy S, Field JK. Impact of low-dose CT screening on smoking cessation among high-risk participants in the UK Lung Cancer Screening Trial. *Thorax* 2017; **72**: 912–8.
131 Tammemägi MC, Berg CD, Riley TL, Cunningham CR, Taylor KL. Impact of lung cancer screening results on smoking cessation. *J. Natl. Cancer Inst.* 2014; **106**: dju084.
132 Ashraf H, Tønnesen P, Holst Pedersen J, Dirksen A, Thorsen H, Døssing M. Effect of CT screening on smoking habits at 1-year follow-up in the Danish Lung Cancer Screening Trial (DLCST). *Thorax* 2009; **64**: 388–92.
133 Clark MA, Gorelick JJ, Sicks JD, Park ER, Graham AL, Abrams DB, Gareen IF. The relations between false positive and negative screens and smoking cessation and relapse in the National Lung Screening Trial: implications for public health. *Nicotine Tob. Res.* 2016; **18**: 17–24.
134 Slatore CG, Baumann C, Pappas M, Humphrey LL. Smoking behaviors among patients receiving computed tomography for lung cancer screening. Systematic review in support of the U.S. Preventive Services Task Force. *Ann. Am. Thorac. Soc.* 2014; **11**: 619–27.
135 Rojewski AM, Tanner NT, Dai L, Ravenel JG, Gebregziabher M, Silvestri GA, Toll BA. Tobacco dependence predicts higher lung cancer and mortality rates and lower rates of smoking cessation in the National Lung Screening Trial. *Chest* 2018; **154**: 110–8.
136 Minnix JA, Karam-Hage M, Blalock JA, Cinciripini PM. The importance of incorporating smoking cessation into lung cancer screening. *Transl. Lung Cancer Res.* 2018; **7**: 272–80.
137 Joseph AM, Rothman AJ, Almirall D, Begnaud A, Chiles C, Cinciripini PM, Fu SS, Graham AL, Lindgren BR, Melzer AC *et al.* Lung Cancer Screening and Smoking Cessation Clinical Trials. SCALE (Smoking Cessation within the Context of Lung Cancer Screening) Collaboration. *Am. J. Respir. Crit. Care Med.* 2018; **197**: 172–82.
138 Cressman S, Lam S, Tammemagi MC, Evans WK, Leighl NB, Regier DA, Bolbocean C, Shepherd FA, Tsao MS, Manos D *et al.* Resource utilization and costs during the initial years of lung cancer screening with computed tomography in Canada. *J. Thorac. Oncol.* 2014; **9**: 1449–58.
139 Henschke CI, McCauley DI, Yankelevitz DF, Naidich DP, McGuinness G, Miettinen OS, Libby DM, Pasmantier MW, Koizumi J, Altorki NK *et al.* Early Lung Cancer Action Project: overall design and findings from baseline screening. *Lancet* 1999; **354**: 99–105.
140 Swensen SJ, Jett JR, Hartman TE, Midthun DE, Mandrekar SJ, Hillman SL, Sykes AM, Aughenbaugh GL, Bungum AO, Allen KL. CT screening for lung cancer: five-year prospective experience. *Radiology* 2005; **235**: 259–65.
141 McWilliams AM, Mayo JR, Ahn MI, MacDonald SL, Lam SC. Lung cancer screening using multi-slice thin-section computed tomography and autofluorescence bronchoscopy. *J. Thorac. Oncol.* 2006; **1**: 61–8.
142 Aberle DR, DeMello S, Berg CD, Black WC, Brewer B, Church TR, Clingan KL, Duan F, Fagerstrom RM, Gareen IF *et al.* Results of the two incidence screenings in the National Lung Screening Trial. *N. Engl. J. Med.* 2013; **369**: 920–31.
143 Veronesi G, Maisonneuve P, Spaggiari L, Rampinelli C, Pardolesi A, Bertolotti R, Filippi N, Bellomi M. Diagnostic performance of low-dose computed tomography screening for lung cancer over five years. *J. Thorac. Oncol.* 2014; **9**: 935–9.
144 Tammemagi MC, Lam S. Screening for lung cancer using low dose computed tomography. *BMJ* 2014; **348**: g2253.
145 McWilliams A, Tammemagi MC, Mayo JR, Roberts H, Liu G, Soghrati K, Yasufuku K, Martel S, Laberge F, Gingras M *et al.* Probability of cancer in pulmonary nodules detected on first screening CT. *N. Engl. J. Med.* 2013; **369**: 910–9.
146 Al-Ameri A, Malhotra P, Thygesen H, Plant PK, Vaidyanathan S, Karthik S, Scarsbrook A, Callister ME. Risk of malignancy in pulmonary nodules: a validation study of four prediction models. *Lung Cancer* 2015; **89**: 27–30.
147 Tammemagi M, Ritchie AJ, Atkar-Khattra S, Dougherty B, Sanghera C, Mayo JR, Yuan R, Manos D, McWilliams AM, Schmidt H *et al.* Predicting malignancy risk of screen-detected lung nodules-mean diameter or volume. *J. Thorac. Oncol.* 2019; **14**: 203–11.
148 González Maldonado S, Delorme S, Hüsing A, Motsch E, Kauczor H-U, Heussel C-P, Kaaks R. Evaluation of prediction models for identifying malignancy in pulmonary nodules detected via low-dose computed tomography. *JAMA Netw. Open* 2020; **3**: e1921221.
149 Horeweg N, van Rosmalen J, Heuvelmans MA, van der Aalst CM, Vliegenthart R, Scholten ET, ten Haaf K, Nackaerts K, Lammers JW, Weenink C *et al.* Lung cancer probability in patients with CT-detected pulmonary nodules: a prespecified analysis of data from the NELSON trial of low-dose CT screening. *Lancet Oncol.* 2014; **15**: 1332–41.
150 Myers R, Mayo J, Tammemägi M, Atkar-Khattra S, Yuan R, Yee J, English J, Grant K, Lee A, McGuire A *et al.* MA10.09 evaluation of the clinical utility of the PanCan, EU-NELSON and Lung-RADS protocols for management of screen detected lung nodules at baseline. *J. Thorac. Oncol.* 2019; **14**: S288–9.
151 Ravenel JG, Nance JW. Coronary artery calcification in lung cancer screening. *Transl. Lung Cancer Res.* 2018; **7**: 361–7.
152 Chiles C, Duan F, Gladish GW, Ravenel JG, Baginski SG, Snyder BS, DeMello S, Desjardins SS, Munden RF. Association of coronary artery calcification and mortality in the National Lung Screening Trial: a comparison of three scoring methods. *Radiology* 2015; **276**: 82–90.
153 Sverzellati N, Cademartiri F, Bravi F, Martini C, Gira FA, Maffei E, Marchianò A, La Vecchia C, De Filippo M, Kuhnigk JM *et al.* Relationship and prognostic value of modified coronary artery calcium score, FEV1, and emphysema in lung cancer screening population: the MILD trial. *Radiology* 2012; **262**: 460–7.
154 Mendoza DP, Kako B, Digumarthy SR, Shepard JO, Little BP. Impact of significant coronary artery calcification reported on low-dose computed tomography lung cancer screening. *J. Thorac. Imaging* 2020; **35**: 129–35.
155 Ruparel M, Quaife SL, Dickson JL, Horst C, Burke S, Taylor M, Ahmed A, Shaw P, Soo M-J, Nair A *et al.* Evaluation of cardiovascular risk in a lung cancer screening cohort. *Thorax* 2019; **74**: 1140–6.
156 Regan EA, Lowe KE, Make BJ, Lynch DA, Kinney GL, Budoff MJ, Mao SS, Dyer D, Curtis JL, Bowler RP *et al.* Identifying smoking-related disease on lung cancer screening CT scans: increasing the value. *Chronic Obstr. Pulm. Dis.* 2019; **6**: 233–45.

157 Buckens CF, van der Graaf Y, Verkooijen HM, Mali WP, Isgum I, Mol CP, Verhaar HJ, Vliegenthart R, Oudkerk M, van Aalst CM *et al*. Osteoporosis markers on low-dose lung cancer screening chest computed tomography scans predict all-cause mortality. *Eur. Radiol.* 2015; **25**: 132–9.
158 Carey CT, Andrea BM. American Thoracic Society/American Lung Association lung cancer screening implementation guide. *Am. J. Respir. Crit. Care Med.* 2018; **198**: 1120–1.
159 American College of Radiology. Lung CT screening reporting and data system (Lung-RADS). 2019. [Accessed 2 Mar 2020.] Available from URL: https://www.acr.org/Clinical-Resources/Reporting-and-Data-Systems/Lung-Rads
160 American College of Radiology. ACR designated lung cancer screening center. 2020. [Accessed 8 Mar 2020.] Available from URL: https://www.acraccreditation.org/lung-cancer-screening-center
161 GO_2 Foundation for Lung Cancer. National Screening Framework. 2020. [Accessed 2 Mar 2020.] Available from URL: https://go2foundation.org/for-professionals/national-screening-framework/
162 Renda Soylemez W, Michael KG, Douglas AA, David HA, Kathleen F, Carla RL, Peter JM, David EM, Maryann N, David EO *et al*. An official American Thoracic Society/American College of Chest Physicians Policy statement: implementation of low-dose computed tomography lung cancer screening programmes in clinical practice. *Am. J. Respir. Crit. Care Med.* 2015; **192**: 881–91.
163 Blom EF, Ten Haaf K, Arenberg DA, de Koning HJ. Treatment capacity required for full-scale implementation of lung cancer screening in the United States. *Cancer* 2019; **125**: 2039–48.
164 Kale MS, Wisnivesky J, Taioli E, Liu B. The landscape of US Lung Cancer Screening Services. *Chest* 2019; **155**: 900–7.
165 Sone S, Takashima S, Li F, Yang Z, Honda T, Maruyama Y, Hasegawa M, Yamanda T, Kubo K, Hanamura K *et al*. Mass screening for lung cancer with mobile spiral computed tomography scanner. *Lancet* 1998; **351**: 1242–5.
166 Crosbie PA, Gabe R, Simmonds I, Kennedy M, Rogerson S, Ahmed N, Baldwin DR, Booton R, Cochrane A, Darby M et al. Yorkshire Lung Screening Trial (YLST): protocol for a randomised controlled trial to evaluate invitation to community based low-dose CT screening for lung cancer versus usual care in a targeted population at risk. *BMJ Open*. 2020; **10:** e037075.
167 Raghavan D, Wheeler M, Doege D, Doty JD 2nd, Levy H, Dungan KA, Davis LM, Robinson JM, Kim ES, Mileham KF *et al*. Initial results from mobile low-dose computerized tomographic lung cancer screening unit: improved outcomes for underserved populations. *Oncologist* 2020; **25**: e777–81.
168 Luo Q, Steinberg J, O'Connell DL, Yu XQ, Caruana M, Wade S, Pesola F, Grogan PB, Dessaix A, Freeman B *et al*. Lung cancer mortality in Australia in the twenty-first century: how many lives can be saved with effective tobacco control? *Lung Cancer* 2019; **130**: 208–15.
169 de Koning HJ, Meza R, Plevritis SK, ten Haaf K, Munshi VN, Jeon J, Erdogan SA, Kong CY, Han SS, van Rosmalen J *et al*. Benefits and harms of computed tomography lung cancer screening strategies: a comparative modeling study for the U.S. Preventive Services Task Force. *Ann. Intern. Med.* 2014; **160**: 311–20.
170 Ten Haaf K, Tammemägi MC, Bondy SJ, van der Aalst CM, Gu S, McGregor SE, Nicholas G, de Koning HJ, Paszat LF. Performance and cost-effectiveness of computed tomography lung cancer screening scenarios in a population-based setting: a microsimulation modeling analysis in Ontario, Canada. *PLoS Med.* 2017; **14**: e1002225.
171 Eccles MP, Mittman BS. Welcome to implementation science. *Implement. Sci.* 2006; **1**: 1.
172 Rankin NM, Butow PN, Hack TF, Shaw JM, Shepherd HL, Ugalde A, Sales AE. An implementation science primer for psycho-oncology: translating robust evidence into practice. *J. Psychosoc. Oncol. Res. Pract.* 2019; **1**: e14.
173 Flynn AE, Peters MJ, Morgan LC. Attitudes towards Lung Cancer Screening in an Australian high-risk population. *Lung Cancer Int.* 2013; **2013**: 789057.
174 Marshall HM, Bowman RV, Ayres J, Crossin J, Lau M, Slaughter RE, Redmond S, Passmore L, McCaul E, Courtney D *et al*. Lung cancer screening feasibility in Australia. *Eur. Respir. J.* 2015; **45**: 1734–7.
175 Gritz ER, Sarna L, Dresler C, Healton CG. Building a united front: aligning the agendas for tobacco control, lung cancer research, and policy. *Cancer Epidemiol. Biomarkers Prev.* 2007; **16**: 859–63.
176 Tammemägi M, Hader J, Yu M, Govind K, Svara E, Yurcan M, Miller B, Darling G. P1.03-059 organized high risk lung cancer screening in Ontario, Canada: a multi-centre prospective evaluation: topic: screening. *J. Thorac. Oncol.* 2017; **12**: S579.