



The person behind the nodule: a narrative review of the psychological impact of lung cancer screening

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Abstract: Lung cancer is the leading cause of cancer mortality globally, responsible for an estimated 1.76 million deaths worldwide in 2018 alone. Screening adults at high risk of lung cancer using low-dose computed tomography (LDCT) significantly reduces lung cancer mortality by finding the disease at an early, treatable stage. Many countries are actively considering whether to implement screening for their high-risk populations in light of the recently published Dutch-Belgian trial ‘NELSON’. In deciding whether to implement a national screening programme, policymakers must weigh up the evidence for the relative risks posed to the entire screened population, including the potential psychological burden. This narrative review aimed to critically summarise the evidence for both negative and positive psychological responses experienced throughout the LDCT screening pathway, to describe their magnitude, duration and clinical relevance, and to draw out different aspects of measurement design crucial to their interpretation. A further aim was to discuss the available evidence for individual differences in psychological response, as well as interventions designed to promote psychological well-being. In summary, there was no evidence that the LDCT screening process caused adverse psychological outcomes overall, although those receiving indeterminate and suspicious LDCT results did report clinically raised anxiety and lung cancer-specific distress in the short-term. There was early evidence that demographic factors, smoking status and screening-ineligibility could be associated with individual differences in propensity to experience distress. Qualitative data suggested health beliefs could be modifiable mediators of these individual differences, but their aetiology requires quantitative and prospective research. There was also some evidence of positive psychological responses that could be capitalised on, and of the potential for person-centred communication interventions to achieve this. Further research needs to be embedded in real-world LDCT lung cancer screening services and use condition-specific measures to monitor outcomes and test evidence-based communication interventions in promoting psychological well-being.

Keywords: Anxiety; depression; early detection of cancer; lung neoplasms; quality of life

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Introduction

Decades of clinical trials sought to establish an effective screening test for lung cancer; a disease that can be treated curatively when diagnosed early yet claimed over 1.7 million lives globally in 2018 alone (1). The US National Lung Screening Trial's (NLST) findings were therefore groundbreaking; showing for the first time, a 20% relative risk reduction in lung cancer mortality from screening high-risk adults (due to age and smoking history) annually using low-dose computed tomography (LDCT) compared with chest X-ray (2). This led to its recommendation by several medical bodies in the US, including the US Preventive Services Task Force (USPSTF) (3). Countries elsewhere awaited data from the Dutch-Belgian trial 'NELSON' which recently published a 24% relative risk reduction for high-risk men (4) spurring renewed calls for implementation.

Reduction in mortality is of course not sufficient to warrant the implementation of a population-based screening programme; a benefit that relatively few participants in screening programmes will experience personally. In addition to broader criteria for implementation [such as acceptability, quality assurance, resource, equity (5,6)], policymakers must weigh up evidence for the relative risks posed to the entire screened population. These include the possible psychological costs of participating in screening; most obviously the potential for abnormal screening results and follow-up to cause undue distress. This may be especially important to understand in the context of lung cancer screening because a significant proportion of individuals experience 'indeterminate' pulmonary nodules which are unlikely to be cancer but require surveillance. Two systematic reviews of patient-centred outcomes in 2014 (7) and 2016 (8) found only short-term psychological distress following abnormal screening results but concluded further high quality research is needed, including 'real world' implementation. Since these reviews were published, further trials in different countries have published their psychological outcome data, including a real-world demonstration design. More recent research has also begun to suggest a broader myriad of diverse psychological consequences than those previously reviewed which occur throughout the screening pathway, not just following disclosure of results, and which may include positive effects (9,10).

Any psychological risks or benefits are also important to understand from the individual perspective, to support autonomous informed decision-making and psychological

preparedness, as well as from a system-level perspective, to ensure person-centred services are designed to mitigate potential risk, optimise well-being and capitalise on opportunities for adaptive psychological outcomes and behaviour. The current narrative review aimed to critically summarise state-of-the-art evidence for the psychological impact of LDCT lung cancer screening to-date. The specific objective was to examine the different types of psychological response that have been investigated in terms of their magnitude, duration and clinical relevance, as well as the factors affecting an individual's propensity to experience these psychological responses. A secondary objective was to summarise any available evidence for how lung cancer screening services should be designed to promote psychological well-being. We present the following article in accordance with the narrative review reporting checklist (available at <http://dx.doi.org/10.21037/tlcr-20-1179>).

Methods

A rapid search of two electronic databases (PubMed and PsychInfo) was carried out to identify original research studies of quality of life and psychological outcomes from LDCT lung cancer screening of high-risk adults that had been published in English language on any date up until 30th June 2020 in international peer-reviewed journals. All types of study design were eligible for inclusion. Due to a lack of research examining interventions for improving psychological outcomes from LDCT screening, the search was expanded to include original research studies of person-centred communication in the incidental pulmonary nodule context.

Narrative discussion

Types of psychological outcome

Studies investigating the psychological impact of LDCT lung cancer screening have predominantly focussed on understanding whether the process causes clinically significant psychological morbidity, especially among those receiving abnormal results. However, heterogeneity in the measures used, as well as their timing and sensitivity (i.e., generic- or condition-specific) are critical to interpreting these findings. Therefore, the following sections present the available evidence by the type of outcome measured, with specific reference to these measurement aspects of study design. This is supported by *Table 1* which presents

Table 1 Table of evidence for psychological outcomes extracted from reviewed studies [adapted and expanded from Wu *et al.*, 2016 (8)]

Overall trial design/sample	Sample analysed	Condition-specific measure	Generic measure	Timing	Top-level findings	Publications
DLCST (n=4,104, Denmark)						
<ul style="list-style-type: none"> • Single centre, two-arm RCT • 5 annual LDCT screens vs. no screen • Current/former smokers (quit ≤10 years ago and ≤ age 50) • >20 pack years • Aged 50–70 years 	<ul style="list-style-type: none"> • Screening participants (both arms) vs. no matched community sample (n=521) • Screening arm vs. control arm (n=3,925) 	<ul style="list-style-type: none"> • Consequences of screening in lung cancer (COS-LC) • Consequences of screening in lung cancer (COS-LC) 	<ul style="list-style-type: none"> • Antidepressant and anxiolytic medicine 	<ul style="list-style-type: none"> • Study enrolment • Study enrolment • 1 year after • 3 years after 	<ul style="list-style-type: none"> • Screening participants reported statistically fewer adverse psychosocial aspects than the community sample • Statistically increased negative psychosocial consequences in both arms, but higher in control arm at 1 year • No difference in medication use by trial arm 	<ul style="list-style-type: none"> • Hestbech <i>et al.</i>, 2011 • Aggestrup <i>et al.</i>, 2012 • Kaerlev <i>et al.</i>, 2012
LSUT (n=2,012, UK)						
<ul style="list-style-type: none"> • Real-world demonstration screening pilot • Two centre, two-arm RCT testing invitation materials • Single LDCT screen • Current/former smokers (quit <7 years) • ≥30 pack years or PLCO score ≥1.51% or LLP score ≥2.5% • Aged 60–75 years 	<ul style="list-style-type: none"> • Screening sample (n=787) vs. 'screening unaware' community comparison sample (n=383) • Screening sample (n=28) 	<ul style="list-style-type: none"> • Lung cancer worry (adapted Lerman's Cancer Worry Scale) • In-depth, semi-structured qualitative interviews 	<ul style="list-style-type: none"> • Anxiety and depression (HADS) 	<ul style="list-style-type: none"> • At screening • 1 day after • 3 months after • 4–8 months after 	<ul style="list-style-type: none"> • Statistically higher distress among screening sample, those with abnormal results, and those ineligible for screening. No clinically relevant differences • Diverse positive and negative psychological responses throughout the screening pathway, from invitation to results (e.g., perceived control over respiratory health, reassurance, cancer focus). 	<ul style="list-style-type: none"> • Kummer <i>et al.</i>, 2020a • Kummer <i>et al.</i>, 2020b

Table 1 (continued)

Table 1 (continued)

Overall trial design/sample	Sample analysed	Condition-specific measure	Generic measure	Timing	Top-level findings	Publications
NELSON (n=15,792, Netherlands and Belgium)						
<ul style="list-style-type: none"> Multi centre, two arm RCT 4 LDCT screens at baseline, 1 year, 2 years and 2.5 years vs. no screen 'Current/former smokers (quit ≤10 years) >15 cigarettes daily for >25 years or >10 cigarettes daily for >30 years Aged 50–75 years 	<ul style="list-style-type: none"> Screening arm recruited during 2 months (n=351) Screening arm recruited during 2 months (n=351) 	<ul style="list-style-type: none"> Lung cancer distress (Impact of Event Scale: IES) Affective risk perception Lung cancer distress (IES) Discomfort/dread Lung cancer distress (IES) Lung cancer distress (IES) 	<ul style="list-style-type: none"> HRQoL (SF-12) HRQoL (SF-12, EQ-5D) Anxiety (STAI-6) HRQoL (SF-36) Anxiety (STAI-Y-1) 	<ul style="list-style-type: none"> 1 day before 6 months after 1 day before 1 week after 6 months after Study enrolment Within 1 week before 1 day after 2 months after Study enrolment 2 months after 2 years after 6 months after second screen) Study enrolment 1 month after 6 months after 	<ul style="list-style-type: none"> Clinically higher distress and lower HRQoL among those with a high affective risk perception (vs. low affective risk perception) 1 day before screening, and statistically higher distress only at 6 months Around half reported discomfort or dread while waiting for screening results No adverse effect on HRQoL Statistically lower HRQoL before screening, but no clinically relevant changes in HRQoL or anxiety Clinically elevated distress for indeterminate results and statistically decreased distress for negative results No differences in distress, anxiety or HRQoL at 2 years' follow-up by trial arm or by indeterminate vs. negative results Clinically elevated distress for indeterminate results group at 2 months' follow-up No differences in HRQoL or anxiety by trial arm or type of screening result, except for those with true positive results who had statistically lower HRQoL and higher anxiety at both follow-ups 	<ul style="list-style-type: none"> Bunge et al., 2008 (8) van den Bergh et al., 2008 van den Bergh et al., 2010a van den Bergh et al., 2010b Gareen et al., 2014
NLST (n=53,452, United States)						
<ul style="list-style-type: none"> Multi centre, two arm RCT 3 annual LDCT screens vs. chest X-ray Current/former smokers (quit ≤15 years) ≥30 pack years Aged 55–74 years 	<ul style="list-style-type: none"> Screening arm vs. control arm (n=2,812) 	<ul style="list-style-type: none"> Lung cancer distress (IES) 	<ul style="list-style-type: none"> HRQoL (SF-12, EQ-5D) Anxiety (STAI-6) HRQoL (SF-36) Anxiety (STAI-Y-1) 	<ul style="list-style-type: none"> Study enrolment 6 months after second screen) 	<ul style="list-style-type: none"> Clinically elevated distress for indeterminate results group at 2 months' follow-up 	<ul style="list-style-type: none"> van den Bergh et al., 2010b

Table 1 (continued)

Table 1 (continued)

Overall trial design/sample	Sample analysed	Condition-specific measure	Generic measure	Timing	Top-level findings	Publications
PAN-CAN (n=2,537, Canada)						
<ul style="list-style-type: none"> Multi centre, single arm prospective study 3 LDCT screens at baseline, 1 and 4 years Ever smokers PLCO score ≥2% Aged 50–75 years 	Screening sample (n=1,237)		Anxiety (STAI-Y) HRQoL (SF-12, EQ-5D)	<ul style="list-style-type: none"> Study enrolment 1 month after CT result 1 month after any follow-up scans 12 months after baseline (before annual repeat CT) 	<ul style="list-style-type: none"> No differences in HRQoL over time or for positive screening results A small sub-sample of participants had clinically elevated anxiety at baseline [number needed to harm (NNH) =7] and 12 months (NNH =18) Participants with a positive screening result reported a clinically relevant decrease in anxiety more commonly than an increase 	Taghizadeh et al., 2019
PLUSS (n=3,642, United States)						
<ul style="list-style-type: none"> Single centre, single-arm prospective study Current/former smokers (quit ≤10 years) ≥0.5 cigarette pack for ≥25 years Aged 50–79 years 	Screening sample (n=400)	Fear of lung cancer (adapted from PCQ)	Anxiety (STAI)	<ul style="list-style-type: none"> Study enrolment 1–2 weeks after CT result 6 months after 12 months after 	<ul style="list-style-type: none"> Statistically increased anxiety among those with indeterminate and suspicious results after screening and at 6 months' follow-up Fear of cancer statistically increased for those with suspicious screening at all time points after screening 	Byrne et al., 2008
Stony Brook Cancer Center (n=228, United States)						
<ul style="list-style-type: none"> Single centre, single-arm prospective study Current/former smokers (quit <15 years) Aged ≥55 years and ≥30 pack years Aged ≥50 years and ≥20 pack years and additional risk factor 	Screening sample (n=228)	Distress (NCCN Distress Thermometer)		<ul style="list-style-type: none"> At screening (before CT scan) At screening (after receiving CT result) 	<ul style="list-style-type: none"> Clinically significant distress for 40% of participants before screening and one third of participants after receiving screening results 	Plank and Nemesure, 2015
UKLS (n=4,055, UK)						
<ul style="list-style-type: none"> Two centre, two-arm RCT Single LDCT screen vs. no screening Current/former smokers LLP score ≥5% Aged 50–75 years 	Screening arm vs. control arm (n=4,037)	Lung cancer distress (adapted Lerman's Cancer Worry Scale)	Anxiety and depression (HADS)	<ul style="list-style-type: none"> Study enrolment 2 weeks after CT result/control assignment Up to 2 years after screening 	<ul style="list-style-type: none"> Statistically higher anxiety and depression in the control arm at 2 years' follow-up, but not clinically relevant Statistically higher distress in screening participants with a positive screening result which neared clinically relevant thresholds at 2 weeks' follow-up but this was resolved at 2 years' follow-up 	Brain et al., 2016

an overview of the design and findings of psychological outcome studies in LDCT screening trials.

Health-related quality of life (HRQoL)

Three trials of LDCT lung cancer screening have published the HRQoL outcomes of their participants with all using either the 12 or 36 item version of the Short Form Health Survey (SF-12/SF-36) and the EuroQol questionnaire (EQ-5D). These are generic measures of HRQoL which assess global aspects of both physical and mental functioning and are widely used because they allow comparison across different disease and healthy populations using standardised scores. In doing so, however, they are less sensitive to those aspects of HRQoL that are specific to a particular disease or patient group and could miss important consequences from the individual's perspective. Nevertheless, using these measures, the NLST (11), NELSON (12-14) and Pan-Canadian Early Detection of Lung Cancer Study (PAN-CAN) trials (15) found no evidence of any clinically adverse impact of LDCT lung cancer screening overall on HRQoL across their respective immediate (1 day), short-term (1 and 2 months) and long-term (6 months, 1 year, 2 years) follow-up points. The same was true when comparing HRQoL between the different LDCT result sub-groups, including indeterminate results received at both prevalence and incidence screening rounds (14), although with the exception of those receiving true positive results (11). It is important to note here that the NLST did not distinguish indeterminate results from those which were immediately suspicious for lung cancer. Nevertheless, the consistency of these findings over time, internationally, and with large, statistically powered samples suggests they are likely to be reliable. However, further monitoring within real world screening services is warranted because the 'healthy volunteer' bias observed in trial participation may mean those most likely to experience decline, in physical or mental functioning have been underrepresented to-date (16-19).

Psychological morbidity: depression and anxiety

While generic HRQoL measures include dimensions of psychological and mental functioning, some studies have used measures of clinical psychological morbidity, either instead of or in combination with HRQoL, in order to focus on the psychological consequences of screening specifically. The UK Lung Screening Trial (UKLS) and the

Lung Screen Uptake Trial (LSUT) both used the Hospital Anxiety and Depression Scale (HADS) following a single, one-off screening episode. Neither found clinically relevant differences in anxiety or depression at the one day (LSUT), two weeks (UKLS), 3 months (LSUT) or 2 years (UKLS) follow-up points for their screened cohorts overall. This was the case when compared with UKLS's non-screen control arm (20) and LSUT's 'screening unaware' community comparison sample who had the same age and smoking characteristics as the screening cohort, but were unaware of screening (21). In fact, it was UKLS's control arm and those in LSUT's screening cohort who were ineligible for screening who reported statistically significantly higher anxiety and depression scores, when compared with the intervention arm and community comparison sample, respectively.

The trends in anxiety and depression scores among participants receiving abnormal LDCT results (i.e., indeterminate or incidental) were similar to those observed for HRQoL. Statistically significantly higher anxiety scores were observed at short-term follow-up, but scores remained within the 'normal' clinical range and longer-term follow-up by UKLS (2 years) found any increases in anxiety had diminished. Participants with a suspicious thoracic lesion were more likely to report clinically significant moderate or severe depression scores at 3 months' follow-up within LSUT (21). The extension of findings from UKLS's trial setting to LSUT's 'real world' demonstration service design, supports their external validity and generalisability to high risk, previously underrepresented groups. However, the relatively small number of cases within the abnormal LDCT result sub-groups in LSUT means these findings should be treated cautiously. Future research should aim to embed psychological morbidity measures within real-world services to achieve an ecologically valid and statistically powered assessment for abnormal LDCT result sub-groups.

It could also be argued that distress induced by abnormal results during a one-off screening episode would be expected to have a shorter duration than within a repeat screening programme, because the 'screenee' no longer has the prospect of further screening rounds which could have a cumulative impact. However, a similar pattern of anxiety has been observed among participants of trial and cohort studies undergoing repeat screening intervals using the State Trait Anxiety Inventory (STAI); a measure of transitory anxiety in that moment ('state') and as a stable personal characteristic ('trait'). The NELSON, NLST, PAN-CAN and Pittsburgh Lung Screening Study (PLuSS) found no clinically relevant

changes in STAI scores for their screening samples overall across differing short-term (before screening, next day, post-result, 1 month, 2 months) and long-term (6 months, 1 year, 2 years) time points (11,13,15,22). This was also true when stratified by type of LDCT result, with the exception of those in the true positive group, and for the PLuSS study, those with indeterminate results directly after receiving their results (22). State anxiety in this indeterminate group remained elevated at 6 months' follow-up but decreased over 12 months. In contrast, those in the PAN-CAN study who received a positive screening result more frequently reported a reduction in state anxiety than an increase (15). Taghizadeh and colleagues suggest their personalised method of communicating results could have played a role in reducing anxiety among this group but warn against overinterpreting this finding, given the relatively small absolute number of cases reporting a reduction in anxiety. Furthermore, their 'positive screen' group included both indeterminate findings as well as those needing investigations for lung lesions. Future research should test the effectiveness and feasibility of personalised methods of results communication in improving psychological outcomes, and where possible, analyse the outcomes of different abnormal LDCT result groups separately.

Specific measures of psychological distress

Some trials have also included condition-specific or event-specific measures of distress, because they may be more sensitive to lung cancer screening-induced distress than generic measures of anxiety, depression and HRQoL. For example, while the Danish Lung Cancer Screening Trial (DLCST) found no increase in prescribed anxiolytic or antidepressant medication for their intervention arm over 3 years' follow-up (23), their condition-specific measure of the psychological consequences of lung cancer screening [COS-LC; (24)] did show statistically significant negative psychosocial responses for behaviour (e.g., concentration, withdrawal), dejection (e.g., feeling sad or uneasy) and sleep (e.g., difficulty falling asleep, waking up early) over five annual screening rounds (25). However, it was those in the control arm of the trial (who did not undergo LDCT screening) who reported the most negative psychosocial consequences when compared with the intervention arm across the final 3 years of the five annual screening rounds (25). This is similar to the statistically (but not clinically) higher anxiety and depression scores observed among UKLS's control arm (20), and LSUT's screening-

ineligible participants (21). Together, these findings suggest that the availability of lung cancer screening could cause psychological distress among individuals who feel at high risk of lung cancer, either subjectively (one's own risk perception) or objectively (being eligible for a lung screening trial), if screening is subsequently denied. They also raise the possibility that screening for lung cancer could lower distress among its participants, perhaps by providing a means of proactively managing risk of lung cancer mortality and related concern. Research should seek to inform the design of careful, evidence-based communication about eligibility and ineligibility at both the population and individual level which promotes positive psychological and behavioural outcomes.

With regards to the different LDCT screening results, only one study has reported any impact on those receiving negative results (referred to hereon as 'normal results' to avoid confusion with negative psychological effects). In the NELSON trial, these participants reported a significant decrease in intrusive thoughts [as measured by the Impact of Event Scale (26)] at 2 months' follow-up suggesting a positive psychological effect for this group in the short-term. Instead, studies have more frequently observed that abnormal results induce distress about lung cancer in the immediate and short-term although that this, like with more generic anxiety measures, resolves over time. For example, those receiving positive results (both true and false) within the DLCST reported negative psychosocial effects at one week and 1 month, but these were not sustained at six and 18 months' follow-up (27). Trials have however differed in their conclusions about the clinical relevance of their findings. The NELSON trial found intrusive thoughts about cancer were clinically significantly raised at 2 months' follow-up among those with indeterminate results when compared with their baseline scores, but resolved at 2 years' follow-up (14). The UKLS and LSUT, which used adapted versions of Lerman's Cancer Worry Scale (28), also found raised lung cancer distress among those in the indeterminate as well as the urgent referral results group at their 2 and 3 months' follow-up points, respectively. However, unlike the NELSON trial, both found that the absolute differences were not clinically relevant. For example, in UKLS, cancer distress remained within clinically 'normal' ranges for those in the indeterminate group, although did near clinically relevant thresholds for those receiving urgent referrals for cancer at 2 months' follow-up (20,21). Conversely, the PLuSS study, found no change in lung cancer specific-distress among those with indeterminate results, either

clinically or statistically, when using a measure of lung cancer fear adapted from the Consequences of Screening Questionnaire (22). Fear of cancer was significantly increased among those with suspicious results and remained so at 12 months' follow-up.

There is some evidence that the screening appointment itself and time spent waiting for results may be sources of lung cancer-specific distress. The Stony Brook Cancer Center found that 43% of participants in their cohort study (n=228) experienced raised lung cancer-specific distress immediately before having screening (29), while LSUT found statistically significantly higher reported lung cancer-specific distress at the screening appointment when compared with a matched community comparison sample who were unaware of screening, but the absolute difference in mean scores was small (21). In NELSON, participants reported a statistically significant increase in intrusive thoughts about lung cancer when waiting for their screening results, with half reporting dread or discomfort in a smaller sub-study (n=351) (13). However, at the same time, NELSON participants reported a decline in generic anxiety scores. This suggests that the anticipation of screening results could trigger specific distress about the chances of having lung cancer among some, but that this does not cause more generalised symptoms of anxiety. Nevertheless, it is important to ensure screening results are shared with participants as soon as is practically possible, and that the expected waiting period for results is clearly communicated.

Diverse positive and negative psychological responses

Research has begun to identify diverse cognitive and affective responses to LDCT screening, which move beyond psychological morbidity and distress, to include positive as well as negative dimensions. Qualitative interviews carried out with LSUT participants identified a broad spectrum of responses experienced at every stage of the screening pathway that varied both between different, and within the same, individuals (9). These included, for example, perceived risk of lung cancer (higher, unchanged or lower), perceived control over respiratory health (empowered or fatalistic), focus on cancer (relieved or preoccupied), reassurance (temporary and appropriate or overly reassured) and lung cancer symptom vigilance (attentive to previously unacknowledged symptoms). These more nuanced responses are important to understand because they may mediate individual differences in psychological well-being

following screening and provide modifiable factors for promoting positive psychological outcomes. They might also have important downstream consequences for future early diagnosis and prevention behaviour, including timely symptomatic presentation, adherence to future screening rounds, and smoking abstinence (9).

The most studied of these responses to date is screening participants' perceptions of their risk of lung cancer; particularly among those who remain dependent on tobacco smoking. Harris (2015) warned of the potential 'cognitive harm' screening could cause to some heavy smokers, following qualitative research (30) in which half of the veterans interviewed reported at least one misperception following screening that could undermine motivation to stop smoking. These included the belief that CT screening confers the same benefit as smoking cessation and that a normal screening result means the individual will not suffer harms of smoking. However, there is no quantitative evidence from the trial context that screening causes those who smoke or those who receive a normal LDCT screen to underestimate their risk of lung cancer. In the NLST, which measured both personal and comparative risk perceptions, participants' risk perceptions for lung cancer and other smoking-related disease were unchanged at 1 years' follow-up when compared with those they reported prior to screening (31). This was true across the different LDCT screening result sub-groups, including those who had a normal screen. More generally, it appeared to be former smokers who were the most likely to underestimate their risk of lung cancer, with current smokers who had the highest cigarette consumption reporting the highest risk perceptions (32,33). In PLuSS, while participants' perceived risk of lung cancer did decrease following a normal result, they remained higher than their objective risk regardless of the type of LDCT result they received (22). Future research could use a prospective, longitudinal design to understand how individuals' risk perceptions might change across time in response to multiple screening rounds and the accumulation of different types of LDCT results.

Individual differences in psychological response

While abnormal LDCT results have been an understandable focus of psychological studies, research has begun to implicate sociodemographic factors, smoking history and health beliefs as potential risk factors for explaining individual differences in screening-induced distress.

Sociodemographic characteristics

In UKLS, LSUT, PLSuSS and the Stony Brook Cancer Center study, women reported statistically, but not clinically, higher cancer distress and anxiety scores than men (20-22,29), and in NELSON and PAN-CAN, lower HRQoL (14,15). This trend was observed over time and across both trial arms (screening or no screening) in UKLS, and persisted at 2 years' follow-up. It was also observed at baseline for LSUT and Stony Brook Cancer Center participants, but not at LSUT's 3 months' follow-up after adjusting for baseline lung cancer worry scores. It is possible that enrolment into a screening trial or programme, which prompts conscious comprehension of lung cancer risk, is relatively more anxiety-provoking for women than men. Alternatively, perhaps women who are worried about lung cancer are more motivated to enrol or attend screening whereas worry could instead demotivate attendance among men. Higher reported anxiety among women has been observed outside of the screening context (34), as has cancer fear (35), and so it is also possible that this reflects a broader tendency or even response bias, where women more frequently report symptoms of anxiety and cancer worry.

There is also some evidence that marital status and socioeconomic position (SEP) are associated with psychological outcomes in LDCT lung cancer screening, although this is more mixed. Participants who were not married or cohabiting and had a relatively lower level of education, reported higher anxiety and fear following screening in the PLSuSS study (22), and higher depression scores at baseline in the LSUT (21). In LSUT, education level was also associated with higher anxiety scores at baseline. However, these differences were not clinically significant and were not sustained at 3 months' follow-up after adjusting for baseline scores. In UKLS, those recruited from the relatively more deprived site reported poorer psychological outcomes than those living within the more affluent site, differences which persisted over time although again, the absolute differences were not clinically relevant (20). No studies have yet reported differences by marital status and education in the longer term. Furthermore, and like female gender, low education level has been associated with higher self-reported cancer fear in the general population (35), and both education and marital status with depression (36,37). Further research is needed to understand the origins of these observed gender, SEP and marital status differences to ensure the appropriate support is provided to mitigate

any potential increased propensity to experience screening-induced distress. It will also be important to investigate whether these factors differentiate psychological responses to the type of LDCT result received as to date, research has focussed on differences among the screening cohort overall.

Smoking status

There are mixed findings concerning the impact of smoking status on screening-induced distress. The UKLS, PLSuSS and the Stony Brook Cancer Center studies found current smoking status to be associated with higher worry, fear and distress (respectively) about lung cancer relative to former smokers following screening (20,22,29). However, smoking status did not differentiate any of the psychological outcomes within the LSUT sample (21) nor anxiety within the NELSON and UKLS trials (14,20). In LSUT, the eligibility criteria included very recently quit former smokers (<7 years) which may have made current and former smokers more comparable groups in terms of their emotional response to lung cancer risk. Furthermore, the lack of association with generic measures of anxiety in NELSON and UKLS suggests that the impact of smoking status is limited to lung cancer-specific distress. Indeed, with regards to HRQoL, both current smoking status and number of pack-years were predictive of poorer scores on physical dimensions in the NELSON trial (13), but there were no differences for the mental health dimension. The reasons for current smokers' higher self-reported distress about lung cancer following screening are unknown. It is likely that current smokers experience negative outcomes for lung cancer among their family and social networks relatively more frequently than former smokers (38) and worry more often about their risk of the disease. In support, research has shown that current smokers are more likely to endorse fatalistic and negative beliefs about lung cancer (39-41) and report worrying about lung cancer often (40).

Health beliefs

There is some evidence that pre-existing beliefs about lung cancer and perceptions of personal risk, help to explain individual differences in psychological responses to screening. A qualitative study of individuals who took part in a real-world demonstration pilot of LDCT lung cancer screening as part of LSUT found that the ways in which individuals responded to screening appeared to depend on their perceived risk and health status, perceived

stigmatisation of smoking-related risk, and fatalistic perceptions of lung cancer as a disease (9). Indeed, in the NELSON trial, those with high affective risk perceptions (how one feels about their risk of lung cancer) experienced intrusive thoughts more frequently than those with a low affective risk perception; both the day before screening and 6 months after screening (42). Those with pre-existing lung disease in the Stony Brook Cancer Center study, who may hold more negative perceptions of their health status, also had increased odds of experiencing lung cancer-specific distress following screening (29). The potential role of these beliefs is particularly important for future research to understand because if they are instrumental in explaining sociodemographic and smoking-related differences in psychological response, they could provide modifiable targets for interventions designed to promote positive psychological outcomes for screening.

Intervening to promote psychological well-being

The ways in which individuals respond to screening are potentially modifiable via service design and delivery. It is therefore important to understand any potential positive or negative psychological effects of LDCT lung cancer screening, their aetiology, and the characteristics of potentially vulnerable groups, so that any adverse responses can be minimised and adaptive responses maximised, preemptively. This might include tailored strategies designed for those who may benefit from supportive interventions, including women, those of a lower SEP, current smokers and those with abnormal results.

Person-centred communication throughout the screening pathway: invitation and eligibility

While there have been no interventional or observational studies of effective strategies for promoting psychological well-being in the lung cancer screening setting, there are qualitative data implicating quality, person-centred communication throughout the screening pathway. During interviews with individuals who had undergone LDCT screening, communication appeared to be important from the very outset, including during invitation and risk-based eligibility assessment (9). Indeed, given the evidence for potentially adverse psychological responses among those deemed ineligible for screening, it may also be important to develop strategies for communicating ineligibility at a population as well as individual level. For example,

information about alternative risk management strategies such as smoking cessation and lung symptom awareness should be made available when ineligibility is disclosed to an individual seeking screening, to provide a means of reducing concern about lung cancer without over-reassuring that they are at 'no risk'.

Person-centred communication throughout the screening pathway: results and follow-up

Qualitative data also suggest that feeling informed about, and psychologically prepared for, each of the possible types of LDCT screening result and likelihood of needing surveillance before screening, influence how participants respond to the results they subsequently receive (9). Indeed, in UKLS, participants with a normal screen who had expected to receive an abnormal result were significantly more concerned about their result and perceived the test to be less accurate than those who had expected a normal result (43). Those receiving an abnormal result were most concerned regardless of their prior expectations. Together these findings point to the importance of preparing individuals for the different types of result, including both normal and abnormal findings, and for managing expectations for how frequently they occur and the possibility of surveillance.

Person-centred communication in the context of incidental pulmonary nodules

Useful insight for promoting well-being among individuals with abnormal LDCT findings specifically, may also be drawn from the incidental pulmonary field. A programme of research carried out by Slatore and Wiener (44) also points firmly to the role of evidence-based and person-centred communication in achieving this. Among a cohort of veterans, physician communication styles which emphasised the patient as a person (e.g., expressing interest and a positive partnership approach) significantly reduced self-reported distress (45). Participants reporting a generally higher quality of physician communication about their nodule also had statistically significantly lower distress at baseline and longitudinally (2 years' follow-up) (45,46), as well as improved adherence to recommended follow-up (47). Interestingly, Slatore and colleagues (44) found some physicians avoided mentioning the possibility of cancer as a strategy intended to minimise distress, yet their data showed cancer information was more frequently perceived

as reassuring than distressing (48). Some physicians also believed a certain amount of distress was necessary for motivating individuals to attend scheduled nodule follow-up appointments (49). However, distress appeared to consistently undermine patients' adherence to surveillance, with no evidence for there being any 'optimal' level of distress which motivated adherence (44). This is consistent with findings from other cancer screening settings, such as mammography and colorectal screening, where distress has been associated with poorer subsequent adherence (50).

Summary

Regardless of the type of measure used, studies to-date present no evidence of any adverse psychological impact of the screening process overall. However, those receiving indeterminate and suspicious LDCT findings do report clinically significant increases in anxiety and lung cancer-specific distress in the short-term, which appear to be resolved at long-term follow. Other characteristics for which there was some evidence of statistically raised distress included being female, of a lower SEP, not married or cohabiting, and currently smoking, as well as being ineligible for screening due to lower risk of lung cancer or denied screening following allocation to the control arm of trials. There was also early evidence that pre-existing health perceptions such as perceived risk of lung cancer, fatalism, and stigmatisation of smoking-related risk, could help to explain these individual differences. These may be important modifiable factors when intervening to minimise distress, particularly among potentially vulnerable sub-groups. Indeed, research suggests that evidence-based and person-centred communication throughout the entire screening pathway, from invitation to results, should be developed and used pre-emptively to promote psychological well-being and preparedness for the different types of LDCT result. However, there was also evidence of possible psychological benefit from LDCT lung cancer screening and positive emotional and cognitive responses which deserve further study so that these can be optimised and capitalised upon.

Future research should also seek to examine psychological outcomes longitudinally within real-world LDCT lung cancer screening services for individuals taking part in repeated screening intervals, and compared, if possible, against a matched community sample. These studies should prioritise the use of situation-specific measures which are designed to be sensitive to lung cancer-

specific distress (e.g., cancer worry scale), the screening and results communication 'events' (such as the IES and the COS-LC), as well as those sensitive to clinically significant anxiety (such as the HADS). There would also be benefit in quantitatively understanding the frequency, duration and magnitude of potential positive psychological responses from LDCT screening so that these can be promoted, for which psychometric development studies are needed to reliably measure these different types of response. Exploratory qualitative studies with screening participants and health care professionals are also needed to understand current communication practices, preferences and outcomes in the LDCT lung cancer screening context. This work may be especially important for those under surveillance for pulmonary nodules or undergoing diagnostic work up. This research could be directed by the conceptual model of person-centred communication for incidental pulmonary nodule proposed by Slatore and Wiener (45) in order to systematically build evidence for and test communication interventions aiming to promote psychological well-being and patient benefit.

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