Title: Psychological targets for lung cancer screening uptake: a prospective longitudinal cohort study

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ABSTRACT

Introduction: Low uptake of low-dose computed tomography (LDCT) lung cancer screening by high-risk groups compromises its effectiveness and equity as a population-level early detection strategy. Numerous psychological factors are implicated qualitatively or retrospectively, but prospective data are needed to validate their associations with uptake behaviour and specify psychological targets for intervention.

Methods: A prospective, longitudinal cohort study examining psychological correlates of lung cancer screening uptake. Ever smokers (aged 55-77) were invited to a Lung Health Check at which LDCT screening was offered through the SUMMIT Study; a multi-centre screening implementation trial. One week after their screening invitation, 44,000 invitees were sent the Self-Regulatory Questionnaire for Lung Cancer Screening. Regression analyses examined the constructs' associations with uptake (telephoning for an appointment) and sociodemographic characteristics.

Results: Higher odds of uptake were associated with both positive and negative perceptions. Positive perceptions included lung cancer controllability, benefits of early diagnosis, improved survival when lung cancer is detected early, willingness to be treated, and believing smoking cessation is effective in reducing risk. Negative perceptions included a higher lung cancer risk perception, negative beliefs about the consequences of lung cancer, perceiving lung cancer as stigmatised, and a negative emotional response. While current smokers held the highest risk perceptions, they also reported negative perceptions that could undermine how they behave in response to their risk.

Conclusions: Interventions to improve uptake should focus on changing perceptions that affect how an individual reacts when they believe their risk of lung cancer is high.

KEY WORDS: Lung cancer screening, Uptake, Inequalities, Intervention, Behavioral Sciences

INTRODUCTION

Lung cancer causes almost one in five cancer deaths internationally [1] and contributes significantly to socioeconomic inequalities in premature mortality [2]. While tobacco control strategies remain the cornerstone of lung cancer control, achieving earlier diagnosis would markedly improve survival. Just 27% of patients are diagnosed with early-stage disease [3] for which one-year survival is 88%, compared with 19% for advanced disease [4]. Screening asymptomatic adults at high risk of lung cancer (due primarily to age and smoking history) using low-dose computed tomography (LDCT) detects early-stage disease, and significantly reduces lung cancer mortality [5,6]. It is implemented in the United States (US), Canada, Korea, regions of China, and Croatia, and is actively being considered in the UK and elsewhere.

The effectiveness and equity of LDCT screening implementation depend on a high-risk participant profile, which enriches cases and improves the risk-benefit ratio. Within the US National Lung Screening Trial (NLST), 88% of screen-prevented deaths were for those classified within the three highest-risk quintiles, for whom the false positive rate and number needed to screen were reduced [7]. However, participation has been low, particularly among high-risk groups. Tobacco smoking is the biggest risk factor and most prevalent within socioeconomically deprived communities [8], yet fewer current smokers and lower socioeconomic groups participated across UK [9], European [10] and US trials [11]. The same inequalities are observed in the US service context, where 2% of eligible smokers have been screened since its recommendation in 2013 [12].

It is critical to understand why high-risk groups are less likely to participate in LDCT screening to provide a scientific evidence base for intervention. The Common-Sense Model of Self-Regulation of Health and Illness (known as the Self-Regulation Model; SRM) [13] is a useful framework for conceptualising psychological determinants. According to the SRM, an individual's cognitive and affective perceptions of a health threat and the perceived efficacy of behaviours available to control both the threat and their emotional reaction to it, guide their coping response. When the protection behaviour (e.g., screening) is incongruent with an individual's understanding of the threat (e.g., lung cancer is invariably fatal), an individual may focus on reducing their emotional reaction instead of the threat itself. Indeed, qualitative and cross-sectional studies implicate negative cognitive and affective perceptions in low uptake of LDCT screening, including fatalism about risk and survival, low perceived efficacy of treatment, and fear of diagnosis [14,15]. This is on the basis that they are more frequently reported by high-risk groups [14], retrospectively reported by those declining trial participation [16–18], associated with lower screening intentions [19], and observed during interviews with high-risk individuals deliberating about a hypothetical screening offer [15].

Crucially, these perceptions may provide psychological targets for interventions to improve participation by high-risk groups. However, while studies corroborate similar psychological targets, these are numerous and diverse, and the strength of evidence for their effect on screening behaviour is limited by their small-scale, hypothetical, cross-sectional or retrospective designs. The potential psychological targets should be validated prospectively against behaviour in line with the experimental medicine approach to health behaviour change [20]. Using the SRM as a conceptual framework, we tested for the first time, whether (and which) of these psychological factors are associated with screening uptake behaviour prospectively using a longitudinal cohort design embedded within the SUMMIT Study [21]; a multi-centre LDCT screening implementation trial.

MATERIALS AND METHODS

Study design

A prospective, longitudinal cohort study design examined psychological correlates of LDCT lung cancer screening uptake behaviour across three annual screening rounds. This 'screening uptake and behaviour (SUB) cohort' is embedded within the SUMMIT Study [21], which aims to assess implementation of LDCT lung cancer screening in a high-risk population and to validate a multi-cancer early detection blood test. This paper reports baseline findings from the SUB cohort.

Eligibility criteria

To be eligible for the SUB cohort, individuals had to be eligible for invitation to a Lung Health Check (LHC) which was determined using data from individual primary care records. The inclusion criteria were: i) aged 55-77, and ii) primary care record of smoking tobacco (ever ≤20 years). Individuals were excluded if they had declined research, were receiving palliative care or active cancer treatment, had metastatic cancer, dementia, or were under the gold standards framework (life expectancy <12 months). Those who responded to the Lung Health Check invitation were asked a series of questions over the telephone and in-person at the Lung Health Check appointment, which collected more detailed information (than that in primary care) for determining their eligibility for LDCT lung cancer screening and therefore the SUMMIT Study.

Procedure

Standardised electronic audit searches selected individuals for invitation to a LHC from primary care records. They were mailed the questionnaire and one reminder letter, within the sequence of LHC invitation letters (see Figure 1 for details). The invitation asked individuals to telephone a freephone number if they were interested in an LHC appointment at which LDCT screening may be offered. A prize draw was used to increase questionnaire response rates.

Ethics

An NHS Research Ethics Committee (reference:17/LO/2004) and the UK Health Research Authority's Confidentiality Advisory Group (reference:18CAG0054) granted approval.

Measures

Screening uptake

The primary outcome was uptake of the LHC invitation, defined as telephoning to book an LHC appointment in response to the invitation letter (vs. not telephoning). This is the first active step in participating and we were interested in whether individuals would consider the offer; recognising some may choose not to participate. Data on LHC attendance (among those eligible following the phone screener) and uptake of LDCT screening (among those eligible at their LHC appointment) were descriptive secondary outcomes.

Psychological constructs

The psychometrically validated Self-Regulatory Questionnaire for Lung Cancer Screening (SRQ-LCS, 25) was used to measure psychological constructs hypothesised to be associated

with uptake. The measure was developed using the SRM framework [13] to synthesise and operationalise psychological factors previously implicated in LDCT screening uptake.

The SRQ-LCS measures eleven psychological constructs, defined in Text Box 1 (items published [22]). They include seven three-item sub-scales (consequences, personal control, treatment control, illness control, emotional representation, early diagnosis behavioural response, risk perception) and four single items (response efficacy of smoking cessation, perceived stigma, treatment intention, survival from lung cancer). For the sub-scales, item responses (e.g., 1=strongly disagree, 2=disagree, 3=neither agree/disagree, 4=agree, 5=strongly agree) were summed to create a score (range 3-15), using reverse coding where relevant. Higher scores meant more positive perceptions (of consequences, emotional representation, early diagnosis behavioural response) or higher levels of the construct (perceived personal control, treatment control, coherence, and perceived risk). For the single item measures, responses were dichotomised.

Text box 1 Definitions of SRQ-LCS psychological constructs (for a list of constructs' items see [22])

Construct name	**Definition**
Consequences	Perceived severity of the consequences of lung cancer for the affected person and others close to them.
Personal control	Perceived ability to personally change the course of a lung cancer diagnosis, by making it better or worse.
Treatment control	Perceived effectiveness of treatment in curing or controlling lung cancer.
Illness coherence	Perceived personal knowledge and understanding of lung cancer.
Emotional representation/ response	Extent to which thinking about lung cancer makes the individual feel worried, anxious, or afraid.
Early diagnosis behavioural response	Perceived benefit of early diagnosis and willingness to be tested for lung cancer
Risk perception	Perceived personal risk of, and worry about, getting lung cancer.
Response efficacy of smoking cessation	Perceived efficacy of smoking cessation in reducing risk of lung cancer.
Perceived stigma	Perceived blame directed towards those with lung cancer by other people.
Treatment intention	Willingness to have surgery for a screen-detected early-stage lung cancer.
Survival from lung cancer	Perceived chances of surviving early-stage lung cancer.

Demographic and smoking data

Demographic information was collected from primary care, including age at data extraction, gender, ethnicity, and area-level deprivation (Indices of Multiple Deprivation (IMD) 2015 rank converted from residential postcode and recoded into national quintiles). Individuals' last recorded smoking status by primary care was also collected. The questionnaire collected self-reported smoking status, smoking history, tobacco consumption and tobacco dependence. Plausible thresholds for analysis of tobacco consumption were set (1-80 cigarettes daily) in line with previous research [23]. Self-reported smoking data were used in analyses.

Primary statistical analyses

Chi-square and multiple logistic regression analyses tested for associations between each of the psychological constructs and uptake of screening (telephone response vs. none).

Secondary statistical analyses

Descriptive analyses examined sample characteristics, response rates, and the relationship between screening uptake intentions and behaviour. Descriptive and multiple linear regression analyses were used to determine the distribution of psychological constructs overall, and their sociodemographic and smoking-related correlates. An alpha of 0.01 was used to adjust for multiple testing.

Statistical power

A sample of 1484 participants at the final SUB data collection wave (two years' follow-up) provides 80% statistical power to detect a small effect (OR=1.2 per SD of a continuous independent variable) of the independent variable on screening uptake, with a 5% significance level and two-sided testing [24]. To achieve this, 44,000 individuals were invited, assuming the following: i) 50% attrition (based on cohort retention rates for older adults within the lowest wealth quintile [25] and current smokers [26]), ii) 35% screening uptake rate based on the UK lung screening (UKLS) trial [9], iii) 50% questionnaire response rate from attenders and 25% from non-attenders based on a UKLS non-participant study [16], and iv) halving the final sample receiving annual screening due to (1:1) randomisation within the SUMMIT Study. With our more stringent significance criterion of 0.01, we would need 2,210 participants.

RESULTS

Response rate

Between April and September 2019, the first 44,000 individuals (from 103 primary care practices) invited to an LHC as part of the SUMMIT Study were invited to complete the questionnaire and consent to ongoing follow-up as part of the SUB cohort (Figure 1). Of those invited, 7966 (18.1%) returned the questionnaire, 7730 of which were linked to screening uptake data. Most respondents (n=6921, 89.5%) returned the questionnaire within four weeks, with others taking up to two months (n=394, 5.1%), over two months (n=129, 1.7%) or their time to respond was unknown (n=286, 3.7%).

- Figure 1-

Sample characteristics

Compared with the overall invited group (Table 1), a lower proportion of questionnaire respondents were male (55.0% vs. 58.0%), of a black, Asian or minority ethnic background (18.9% vs. 26.5%), lived in the lowest deprivation quintile (27.8% vs. 33.8%) and reported being current smokers (40.0% vs. 48.9%). There were discrepancies between primary care recorded and self-reported smoking status. For example, 30.1% of respondents self-reported being current daily smokers compared with 40.0% as last recorded by primary care. While all individuals had been recorded by primary care as smoking historically (see Methods), a small proportion were recorded as never having smoked (3.5% self-reported). Respondents starting smoking at a mean age of 18.1 years (SD:5.9) and an average of 15.9 (SD:9.9) cigarettes daily. Amongst current smokers, tobacco dependence was high, with 60.3% smoking within 30 minutes of waking.

- Table 1-

Behavioural intentions and screening uptake behaviour

While 76.8% (5937/7730) intended to telephone to book an LHC (n=3651) or had already done so when completing the questionnaire (n=2286), two thirds (n=5257; 68.0%) actually telephoned to book an LHC. Most (n=2616/2854; 91.6%) underwent LDCT screening if eligible (Supplementary Table 1). The proportion carrying out each uptake behaviour (phone response, attending LHC, undergoing LDCT) varied by intentions as expected (Figure 2): positive intentions more frequently translated to the respective behaviour than negative. Unexpectedly, however, the majority (351/367, 95.6%) of eligible phone responders who had reported being 'very unlikely' to attend an LHC appointment actually attended. The weakest association between positive intentions and behaviour was for phone response, with 69.5% (2537/3651) of those intending to phone doing so.

- Figure 2 -

Psychological correlates of screening uptake

All the SRQ-LCS constructs were statistically significantly associated with uptake in adjusted analyses, except illness coherence and treatment control. Figure 3 presents the adjusted odds ratios indicating (for their interpretation) those relating to unit increases in sub-scale scores and those relating to changes in binary responses.

- Figure 3 -

The odds of uptake were statistically significantly higher for each unit increase in score (range 3-15) for three sub-scales. The strongest positive association was for those who perceived early diagnosis to be more beneficial as a behavioural response (aOR:1.37;1.33,1.41). Those who perceived greater personal control (aOR:1.09; 95% CI:1.05,1.11) or believed their personal risk of lung cancer was high (aOR:1.08;1.05,1.10) were also more likely to respond. However, higher scores on both the consequences (aOR:0.88;0.85-0.91) and emotional representation sub-scales (aOR:0.95;0.93-0.97; indicating more positive perceptions and representations) decreased the odds of uptake.

For the binary responses, the largest increase in odds of uptake was for those who intended to be treated for lung cancer if diagnosed through screening (aOR:1.65;1.45-1.87). Those who perceived smoking cessation as an effective means of reducing lung cancer risk or

thought the chances of surviving early-stage lung cancer were good or fair, also had statistically significantly increased odds of uptake (ps<.01). Similarly, those who perceived lung cancer as stigmatised were more likely to respond (aOR:1.26;1.14,1.40).

Distribution of the psychological constructs

Overall, mean scores for each sub-scale were within the middle range (7.03 to 11.27) of possible scores (3-15), although the consequences of lung cancer were perceived more negatively (M:4.65, SD:1.61) while perceptions of early diagnosis were relatively more positive (M:12.63, SD:2.01; Supplementary Table 2). The majority of respondents perceived the chances of surviving lung cancer as good or fair (65.7%; Supplementary Table 3), thought smoking cessation was moderately or extremely effective in reducing lung cancer risk (67.5%), and intended to have surgery for an early-stage lung cancer if detected through screening (79.3%). Half (50.1%) perceived lung cancer to be stigmatised by other people.

Tables 2 and 3 show the adjusted associations between sociodemographic and smoking characteristics, and each psychological construct. Some of the largest associations seen were between gender and emotional representations (with men relatively more positive), Asian ethnicity and lower personal control, and smoking status and risk perceptions (with current smokers reporting the highest risk perceptions).

- Tables 2 and 3 -

Compared with women, men also reported more positive perceptions of personal and treatment control, and a lower perceived risk of lung cancer (ps<.001). Men were also less likely than women to perceive lung cancer as stigmatised and were more optimistic about survival (ps<.001). However, scores for coherence suggested lower perceived knowledge about lung cancer among men. There were no statistically significant associations with the other constructs.

Increasing age was associated with more positive perceived consequences, greater treatment control, lower perceived stigma and a higher perceived prospect of surviving early-stage lung cancer. However, older adults felt they had less personal control over lung cancer, held lower perceptions of personal risk, and saw less benefit in smoking cessation and early diagnosis (ps<.01). Age was not statistically significantly associated with the other constructs.

Relationship status was only associated with treatment control, treatment intentions, perceived chances of survival, and early diagnosis as a behavioural response. In each case, those who were single, separated, widowed, or divorced reported more negative perceptions than those who were married, in a civil partnership or cohabiting (ps<.01).

Ethnicity was statistically significantly associated with eight of the constructs (ps<.001). Compared with those of a white ethnic background, participants of black and Asian ethnic backgrounds perceived the consequences of lung cancer and the effectiveness of treatment in controlling lung cancer more positively and were less likely to perceive lung cancer to be stigmatised. However, their coherence (knowledge) of lung cancer was lower. Those of a mixed or other ethnic background also held more positive perceptions of treatment control than participants who were white, with participants of other ethnic minority backgrounds holding more negative perceptions of their personal control over lung cancer, the consequences, their coherence, and the benefits of early diagnosis. Participants of Asian

ethnic backgrounds also held more negative perceptions of early diagnosis, as well as the chances of survival and their emotional response to lung cancer.

Area-level deprivation was statistically significantly associated with five of the constructs (ps<.01); specifically, greater affluence was associated with greater perceived personal control and benefit from early diagnosis, but more negative perceptions of the consequences of lung cancer. Participants living in more affluent areas were also more likely to perceive lung cancer to be stigmatised and perceive smoking cessation to be less effective in reducing risk.

Smoking status was statistically significantly associated with nine of the constructs (ps<.01). Current daily smokers tended to report more negative perceptions than former smokers. This included lower personal control over, and higher perceived risk of, lung cancer, as well as lower perceived effectiveness of smoking cessation and higher perceived stigmatisation. Current daily smokers were less willing to be treated for early-stage disease and more pessimistic about survival. Those who smoked occasionally, smoked other types of tobacco, or reported never having smoked at all (despite historical primary care records, see Methods) reported higher perceived risk of lung cancer than former smokers. Participants who smoked other types of tobacco also perceived smoking cessation to be less effective than former smokers.

DISCUSSION

This is the first study to prospectively investigate psychological correlates of LDCT lung cancer screening uptake behaviour using a large, diverse cohort of high-risk adults. Nearly all the psychological constructs were associated with uptake (defined as phoning to book an LHC at which LDCT screening is offered), including perceptions of controllability, survival, mortality risk-reducing behaviours, treatment, and stigmatisation; although not always in the direction expected. These findings pinpoint specific psychological targets for interventions.

Perceptions of personal control over risk of lung cancer mortality and perceived efficacy of risk-reducing behaviours (i.e., early diagnosis, smoking cessation, and surgical treatment) were positively associated with uptake, as was perceived survival from lung cancer. Most of these constructs were also perceived more negatively by current than former smokers; consistent with previous cross-sectional and qualitative research [14–19]. These psychological constructs therefore provide potentially modifiable targets for interventions designed to improve uptake for a high-risk group less likely to attend lung cancer screening. To date, individual-level psychological interventions for cancer screening uptake have had modest success, likely due to the difficulty of changing deep-rooted perceptions with one-off, individual-level communications. The present study suggests prior interventions were ineffective at modifying these psychological targets rather than psychological factors not being important for uptake. Our findings move evidence forward by pinpointing specific psychological targets for intervention design [14–19]. In line with an experimental medicine approach to health behaviour change [20], the next step is to test possible methods, modes and mechanisms for changing these targets; evidence which will inform complex intervention design.

Higher perceived risk of lung cancer was also positively associated with uptake, but with current smokers reporting the highest risk perception scores, at odds with their lower participation in lung screening trials [9–11]. This contradiction may be explained by current smokers also holding more of the negative perceptions associated with lower uptake, which could undermine how they behave in response to their high perceived risk. These included more negative perceptions of lung cancer controllability, early diagnosis and survival, lower willingness to be treated, and believing smoking cessation to be less effective in reducing risk. Indeed, according to the SRM [13], negative perceptions of lung cancer and the efficacy of risk-reducing behaviour, could lower current smokers' motivation to see screening as a way to reduce their risk of lung cancer mortality. Therefore, while perceived risk may be a necessary motivating factor in the main, targeting risk perceptions may be unnecessary for current smokers specifically. Indeed, in the NLST, it appeared to be former smokers who underestimated their risk of lung cancer yet were more likely to attend [27,28]. Furthermore, some studies show the opposite direction of effect, with higher affective risk perceptions retrospectively reported by current smokers declining participation in the UKLS, although there was no comparable attending group [16]. Indeed, systematic reviews of interventions solely targeting risk perceptions show no effect on screening uptake, even when risk information is personalised [29]. The crucial psychological targets for intervention may therefore be those perceptions which optimise behavioural responses to perceived risk rather than risk perceptions themselves.

Associations between the SRQ-LCS constructs and uptake were not always in the direction expected. Perceiving lung cancer to be stigmatised increased the likelihood of uptake; at odds with previous qualitative research [15,18]. Perhaps those most concerned about stigmatisation were less likely to participate and are underrepresented. It might also reflect the present study's measurement of other people's perceptions of stigmatisation [22] rather than personal perceptions. More negative emotional representations of lung cancer similarly increased uptake which was also unexpected. However, it is important to note that the SRM constructs are proposed to be bi-directional [13]. Therefore, if screening is either avoided or attended as a form of emotion-focussed coping, this may feed back into the emotional representation of lung cancer, making it more positive. Future research should investigate how these perceptions might change and interact with uptake behaviour over time and whether combinations of psychological factors better explain uptake.

The measures studied here focussed exclusively on motivational factors and not those affecting capability or opportunity, which may also prevent individuals from realising their intention. Another limitation is the low response rate and possible self-selection bias, although the large sample size and diverse sociodemographic representation strengthen its generalisability. While we oversampled in anticipation of a lower response from those not wishing to be screened, screening uptake was relatively high among questionnaire respondents, indicating bias in response. There is also a possibility that the questionnaire influenced perceptions of lung cancer or prompted uptake by asking about intentions, known as the 'question-behaviour' effect [30]. Last, some participants responded to their LHC invitation before receiving the questionnaire, and so we cannot infer causality. We hope to better understand screening uptake behaviour over time using repeated measures follow-up data from this cohort.

In conclusion, interventions aiming to improve high-risk groups' uptake of LDCT lung cancer screening should target perceptions of lung cancer controllability, survival, and perceived effectiveness of behaviours aimed at reducing the risk of lung cancer mortality, which may

be more effective than trying to change risk perceptions. Experimental studies investigating the methods and mechanisms through which these perceptions could be changed can now inform a complex interventional trial testing these findings. The intervention delivery may demand a multi-level systems strategy, moving beyond one-off, individual-level communications, to more intensive, repeated, and wide-reaching communications.

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TABLE AND FIGURE LEGENDS

Figure 1 Flow diagram to show inclusion of participants

Figure 2 Frequency of each screening uptake behaviour by behavioural intentions of those eligible at each stage

Figure 3 Forest plot of the adjusted associations between each SRQ-LCS psychological construct and screening uptake

Table 1 Characteristics of the sample

Table 2 Adjusted regression coefficients for the associations between demographic factors, smoking status, and sub-scale SRQ-LCS scores

Table 3 Adjusted odds ratios for the associations between demographic factors, smoking status, and single item SRQ-LCS constructs