The UK Lung Screen (UKLS): demographic profile of first 88,897 approaches provides recommendations for population screening.


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Abstract

The UK Lung Cancer Screening trial (UKLS) aims to evaluate low dose computed tomography (LDCT) lung cancer population screening in the UK. In UKLS, a large population sample aged 50-75y is approached with a questionnaire to determine lung cancer risk. Those with an estimated risk of at least 5% of developing lung cancer in the next five years (using the Liverpool Lung project risk model) are invited to participate in the trial. Here we present demographic, risk and response rate data from the first 88,897 individuals approached.

23,794 individuals (26.8% of all approached) responded positively to the initial questionnaire; 12% of these were high risk. Higher socioeconomic status correlated positively with response, but inversely with risk (p<0.001). The 50-55y age group were least likely to participate, and at lowest cancer risk. Only 5% of clinic attendees were aged ≤60y (compared to 47% of all 88,897 approached); this has implications for cost-effectiveness. Among positive responders, there were more ex-smokers than expected from population figures (40% vs. 33%), and fewer current smokers (14% vs. 17.5%). 32.7% of current smokers and 18.4% of ex-smokers were designated high risk. Overall, 1,452 of 23,794 positive responders (6.1%) were deemed high risk and attended a recruitment clinic.

UKLS is the first LDCT population screening trial selecting high risk subjects using a validated individual risk prediction model. Key findings: (a) better recruitment from ex rather than current smokers, (b) few clinic attendees aged early 50s, (c) representative number of socioeconomically deprived people recruited, despite lower response rates.
Introduction

Lung cancer kills more people in the UK than any other cancer. It accounts for over 20% of all deaths from malignancy, and 6% of total deaths; there were over 41,000 lung cancer diagnoses in 2009, and nearly 35,000 lung cancer deaths in 2010 (1). Although improving, the five-year survival rate from lung cancer (all stages) is less than 10% for men and women; amongst the lowest for all cancer types (1). The estimated cost of lung cancer to the NHS is £9071 per patient per year (compared with £2,776 per patient per year for all cancer types) (2), and the total cost of lung cancer to the UK economy is £2.4 billion; more than for any other cancer (2). This reflects the relatively high incidence of lung cancer being compounded by poor survival and high mortality, as most patients present at a late stage when they are unsuitable for curative treatment. Thus survival should be improved by a reduction in smoking, and through initiatives to achieve earlier diagnosis.

Worldwide, a number of screening trials for early detection of lung cancer have been, or are being, conducted (3). These have used both chest x-ray and low dose computed tomography (LDCT) screening; the latter is the superior method (3). The USA National Lung Screening Trial (NLST) randomised over 53,000 people aged 55–74, with a 30 pack year smoking history who had smoked within 15 years, to LDCT or chest X-ray. NLST reported a 20.0% relative reduction in lung cancer mortality in the LDCT arm (4) (5). In Europe, the Dutch-Belgian randomised lung cancer screening trial (NELSON) is currently underway (6). Screening for lung cancer relies firstly upon defining a high risk population; in the UK, criteria for this have been determined through the Liverpool Lung Project (LLP) (7, 8). The LLP risk prediction model incorporates age, sex, family history of lung cancer, smoking, personal history of other cancer and non-malignant respiratory disease, and occupational exposure (7, 8). The LLP model is a robust algorithm that has been validated on two international case-control populations (Harvard and EULC) and one independent cohort (LLP 7500) (9).
The United Kingdom Lung Cancer Screening Trial (UKLS), which has recently completed its pilot phase of recruitment, is a multicentre randomised controlled trial (RCT) of LDCT for the early detection of lung cancer in high-risk subjects (>5% risk over five years, according to the LLP model) aged 50-75 years. The UKLS trial has recruited 4061 high-risk subjects over two discrete time periods in its pilot phase. (The first of these recruitment drives, yielding 1452 high risk participants, is the focus of this report).

The UKLS trial follows the Wald Single-Screen Design (10). Subjects are randomised to receive either one LDCT scan (thus minimising problems with long term compliance), versus standard care. The trial design incorporates a number of elements that are unique to the area of lung cancer RCTs. Firstly, UKLS is a population-based study, which randomly approached people aged 50-75 years through local Primary Care Trust (PCT) records. Secondly, UKLS employs the Liverpool Lung Project (LLP) lung cancer risk prediction model at an individual level (9) to identify high risk subjects; thus targeting resources to those most likely to benefit from screening. Thirdly, UKLS is unique in having a formal care pathway plan, based on categorisation (size, volume and growth) of lung nodules (10). Fourthly, UKLS uses state of the art volumetric analysis of lung nodules identified on LDCT scan: this has only been used consistently by one other trial (the Dutch-Belgian NELSON trial; (11)).

This report details the demographic characteristics of the target population in the UKLS pilot study, with the aim of identifying the factors associated with response or non-response to the study invitation. It is based on the initial round of approaches to 88,897 individuals, and the ensuing recruitment and randomisation of the first 1452 high risk participants for screening. It does not report CT data and outcomes as these data are not yet available. The implications of the findings for the implementation of population screening are discussed.
Materials and Methods

The methods for the UKLS pilot study were derived from an initial feasibility study, and follow the Wald Single Screen Design (10). Other Screening trials have used this design, including the UK Flexisig Trial, the UK Aortic Aneurysm Screening Trial and the Singapore Breast Screening Trial (12-14). UKLS is similar in methodology to NELSON, and this will allow a combined analysis of results to increase the statistical power of both trials. Two main components were used in UKLS: an initial questionnaire-based screen to identify high risk individuals from the population, followed by an RCT with intervention (LDCT) and control arms. Supplementary Figure 1 illustrates the trial recruitment process. The necessary approvals were obtained from the National Research Ethics Service (NRES) and the National Information Governance Board (NIGB). An initial cohort of 88,897 individuals was approached, and it is this cohort that is described here.

Population Approaches

As UKLS is a population study, its starting point was NHS Primary Care Trust (PCT) records covering all UK citizens. From these records, individuals aged 50-75 years of age residing in three Primary Care Trust (PCT) areas around Liverpool, and three PCTs around Cambridgeshire, were randomly selected at the PCT. These data were provided to a third party data management company (DMC), who approached 88,897 individuals by post between August 2011 and March 2012 with an invitation letter (on the respective PCT-headed notepaper) and Questionnaire 1. This questionnaire covered smoking history and duration, personal history of non-malignant lung diseases (e.g. pneumonia) and previous malignancy, exposure to asbestos, and family history of lung and other cancers; in addition, it enquired whether the individual would be interested in participating in a screening study. For those who were unwilling to fill in the entire questionnaire, and who were not interested in participating further, there was a shorter non-participation questionnaire (covering smoking status, lung cancer prior experience and concern, and educational level), which they were asked to return instead. Approached subjects were categorised as follows, based on their response to the first
invitation: Positive Responders: Individuals who returned Questionnaire 1, and agreed to participate in UKLS. Negative Responders: Individuals who declined to participate in UKLS, but supplied some basic information by completing the shorter, non-participation questionnaire. Non-responders: Individuals who did not respond to the first invitation.

Risk Assessment

Completed Questionnaire 1s (from positive responders) were returned to the DMC, scanned, and the data analysed automatically in order to identify individuals at high risk (defined as >5%) of developing lung cancer over the next five years (LLP risk score ≥ 5) (8). (Risk assessment was not carried out for negative responders, as this was not possible from the limited information they supplied). A modified version of the LLP risk algorithm (LLPv2) was utilised for risk calculations. This incorporated additional respiratory parameters (i.e. chronic obstructive pulmonary disease, emphysema, bronchitis and TB) as well as pneumonia, and also included both pipe and cigar usage within the smoking criteria. High risk individuals were contacted with a further questionnaire (Questionnaire 2) to establish eligibility for the RCT (10), and sent a detailed Patient Information Leaflet: these people were also asked to consent to release of their personal information to the UKLS research team. Non-responders to this second invitation were sent a reminder letter.

UKLS Research Clinics

Individuals responding to, and eligible on the basis of, the second questionnaire were invited to one of the recruitment centres (Liverpool Heart and Chest Hospital, or Papworth Hospital, Cambridge). They were shown a DVD outlining the UKLS study (15) and consented by a Research Nurse. Subjects underwent spirometry, and provided blood, buccal swab, nasal, and sputum specimens. Recruits also completed a touch-screen questionnaire; this consisted of follow-up epidemiological and clinical questions, and psychosocial and quality of life questions including the Hospital Anxiety and Depression Scale (HADS) (16) and the Cancer Worry Scale (CWS-R) (17, 18) adapted for lung cancer.
All smokers (both CT screened and non-screened) were offered smoking cessation advice sheets and a list of local NHS Stop Smoking services.

Recruits were randomised into the intervention arm (LDCT scan, screen group) or the control arm (usual care, no screen group) in a ratio of 1:1. Individuals were informed of which group they were in within two weeks of randomisation. Subjects in the intervention group received a thoracic LDCT scan several weeks later.

Follow up

Any lesions identified on LDCT-screening were treated as per the planned care pathway in the study protocol (10) (e.g. follow up scan or referral to multidisciplinary team). Health and mortality outcomes of UKLS participants in both study arms will be followed up for ten years, via the Office for National Statistics (ONS), the Hospital Episode Statistics (HES) database, and the National Cancer Registration Service. The full protocol for the UKLS study is available online (19).

Data storage and analysis

Data were input to and stored on a bespoke system builder database, built by Artex (Netherlands), with data security approved by the National Information Governance Board for Health and Social Care (NIGB). Statistical analysis was undertaken using STATA v12.

Socioeconomic data analysis

Index of Multiple Deprivation (IMD) rank (20) (see legend to figure 3) was obtained from postcode data in an anonymised form for all 88,897 individuals approached (including non-responders). UK IMD data are typically analysed and reported as ranks within quintiles based on England-wide population data: Quintile 1 (Q1; most deprived) = IMD ranks 1-6496; Quintile 2 (Q2; above average...
deprivation) = 6497-12993; Quintile 3 (Q3; average) = 12994-19489; Quintile 4 (Q4; below average deprivation) = 19490-25986; Quintile (Q5; least deprived) = 25987-32482.
Results

Overall Response Rate and Risk

Figure 1 shows the overall response rate, numbers at high risk, and clinic attendance. Out of 88,897 individuals approached in the first round, 56,475 (63.5%) were non-responders (no questionnaire returned), 8,628 (9.7%) were negative responders (non-participation questionnaire returned), and 23,794 (26.8%) were positive responders (Questionnaire 1 returned; willing to participate). Of the positive responders, 2,848 (12.0%) were classified by the LLP risk prediction model to be at high risk (5% or greater over next five years) of developing lung cancer. 1,924/2,848 (67.6%) of the high risk positive responders returned the second questionnaire and agreed to participate in the RCT. 338 individuals were subsequently excluded (as per the protocol criteria; Figure 1), and 134 failed to attend clinic. In total, 1,452 individuals (6.1% of all positive responders, and 51.0% of all high risk positive responders) attended clinic (Figure 1).

Factors influencing response rate and risk

Sex

Men and women were approached in approximately equal numbers (n=44,618 and 44,279 respectively), and were equally likely to respond positively to the first questionnaire (26.7% of males and 26.9% of females were positive responders). However, men were 2.4 times as likely to be classified as at high LLP risk: 2016 (17%) of male and 832 (7%) of female positive responders had a high LLP risk. The frequency of non-responders was similar in men and women (65% of males; 62% of females), and the same was true of negative responders (8.3% of males; 11.1% of females).

Age

Positive response rate generally increased with age, from 23.6% in the 50-55 age group to 31.5% in the 66-70 age group. However, it was lower in the eldest (71-75) age group, at 24.1% (Figure 2a). Amongst the positive responders, age had a major impact upon LLP risk: only 12 out of 6,256
positive responders (0.19%) in the 50-55 age group were classified as high risk, and only five of these attended clinic. Thus, overall in the 50-55 age group, only five of 26,532 individuals originally approached (0.02%) were high risk clinic attendees (Figure 2a). The proportion of positive responders at high LLP risk increased steadily with age: in the 71-75 age group, 997 out of 3550 positive responders (28.1%) were classified as high risk (Figure 2a). The different age profiles of the original approached group versus high risk clinic attendees are shown in Table 1. Almost 95% of high risk clinic attendees were aged 61-75 years (compared with 53% of the 88,897 subjects originally approached).

Considering individual years of age between 55 and 65, there was a slight but steady increase in response rate in older age groups, from 23.4% at age 55, to 35.1% at age 65. The percentage of the positive responders at high LLP risk increased with age, from 1.1% at age 55, to 16.5% at age 65, with a progressive increase starting from age 58 (Figure 2b).

**Socioeconomic Status**

The English Index of Multiple Deprivation (IMD) rank (20) was available on 88,896 individuals. IMD data showed that the social demographics of the two recruitment areas (Liverpool and Cambridgeshire) were markedly different. Almost 50% of the Liverpool area residents approached for UKLS fell into the most deprived quintile of the English population, compared with less than 10% in Cambridgeshire. However, as planned in the pilot study design, the total UKLS approached sample was similar in socioeconomic distribution to the entire English population (Supplementary Figure S2).

Positive response rate increased steadily with higher socioeconomic status: 19.6% of individuals in the lowest (most deprived) IMD quintile gave a positive response compared with 34.2% in the highest quintile (p<0.001; Chi-squared for trend) (Figure 3). Within each IMD quintile, no significant
differences in positive response rate were seen between the Liverpool and Cambridgeshire populations.

The proportion of individuals with a high LLP risk score decreased with higher socioeconomic status; ranging from 17.7% in the most deprived quintile to 8.0% in the least deprived quintile (p<0.001; Chi-squared for trend) (Figure 3). As the social gradient of response and the social gradient of LLP risk were offset by each other, the socio-demographic spectrum of the individuals attending clinic was in proportion to that of the original approached sample (Table 2). People attending clinic therefore spanned all IMD quintiles in roughly equal numbers, including a representative proportion from more deprived postcodes (Figure 3; Table 2). However, of the individuals invited for screening, the clinic attendance rate increased with higher socioeconomic status (Figure 3).

**Smoking**

Of the 23,784 positive responders, 23,562 (99%) gave information about their smoking habits. 45.4% were never-smokers, 14.2% current smokers, and 40.4% ex-smokers (Figure 4). Of the 8628 negative responders, 8163 (95%) provided information about their smoking habits. 54.9% were never-smokers, 9.3% current smokers, and 35.8% ex-smokers (Figure 4). National smoking data (from the Office for National Statistics) for the 50+ age group give an expected distribution of 49.5% never-smokers, 17.5% current smokers, and 33% ex-smokers (21). Thus the observed values in our sample of both positive and negative responders are significantly different from population values (Chi squared test; p<0.0001). Importantly, this suggests that ex-smokers are more likely to respond positively to a screening invitation, with current- and never-smokers being less likely to respond positively. Negative responders are enriched with never-smokers, but comparatively few current smokers respond negatively. From expected population figures (and accounting for known figures from responders) it was possible to estimate the smoking status of the non-responders, of whom approximately 20% are probably current smokers (Figure 4).
Unsurprisingly, smokers and ex-smokers were much more likely than never-smokers to have an LLP risk of >5%. Of the 23,562 positive responders, 1094 (32.7% of 3345) current smokers and 1750 (18.4% of 9520) ex-smokers were designated high risk. However, only four (0.04% of 10,697) never-smokers had a high LLP risk: none of these attended a recruitment clinic, and all were aged at least 73 years. In total, therefore, 22.1% of current and ex-smoking positive responders were high risk, and 11.3% attended clinic and were recruited into UKLS.

Interaction between smoking and socioeconomic status

As people in more deprived socioeconomic groups are more likely to smoke, it is important to control for any possible confounding effects. Data were therefore stratified by both IMD quintile and smoking status. For all IMD national quintiles, the proportion of ex-smokers among positive responders was around 40%. 26.5% of positive responders in the most deprived quintile were current smokers, compared with only 8.6% in the least deprived quintile (Supplementary Table 1). Within all IMD quintiles, there were proportionally more smokers (both current and ex) among positive compared to negative responders, and proportionally more never smokers among negative responders (Supplementary Table 1,2).

Based on known smoking prevalence rates for each IMD quintile, and adjusting for the age distribution of the UKLS sample (22), it was possible to calculate the expected number of smokers in each IMD quintile for the 88,897 approached subjects (Supplementary Table 3). This allowed an estimation of smoking status for non-responders in each IMD quintile, and hence the percentage of current smokers, ex-smokers and never smokers who respond positively to the first screening invitation (Figure 5). The response rate is generally considerably lower among current smokers compared to the overall response rate for the relevant quintile (i.e. there is a smaller proportion of smokers amongst responders than would be expected from quintile-matched population figures).
However, in the most and least deprived quintiles it appears that the response rate among smokers is similar to the overall response rate for that quintile (Figure 5). For ex-smokers and never-smokers, positive response rate increases with socioeconomic status across all IMD quintiles, whereas the positive response rate amongst current smokers only rises in the upper two quintiles of IMD. The group least likely to respond positively are never smokers in the most deprived IMD quintile (calculated as 16.6% positive response rate), followed by current smokers in the three most deprived quintiles (calculated as 17.3-18.3% positive response rate). The highest positive response rate is seen in the ex-smokers from the least deprived IMD quintile (calculated as 37.3% positive response rate). In the highest and lowest IMD quintiles, the calculated hierarchy of response rate is (from the highest): ex-smokers>current smokers>never smokers, whereas for the three middle IMD quintiles, it is: ex-smokers>never smokers>current smokers (Figure 5).
Discussion

This report focuses on the first 88,897 individuals approached for the UKLS pilot study, which utilises the LLPv2 risk model. As clinical outcome data become available, further analysis and validation of this risk algorithm will take place, which may result in further refinement of the LLP model. However, early data suggest that LLPv2 is effective at delineating risk in the UKLS population. Other major models have also been developed for identifying individuals with a high risk of lung cancer: these include Bach (23), Spitz (24), Tammemagi (25), and more recently that of Kovalchik (26). It is of note that two of these models (25, 26) have been used to analyse the NLST data. Tammemagi et al. applied the model derived from the PLCO dataset to the NLST participants; this improved both sensitivity and positive predictive value without loss of specificity, with 41.3 fewer lung cancers missed. The new prediction model referred to in Kovalchik’s recent publication stratified participants into quintiles of five-year risk of lung cancer death; individuals in the highest risk quintile 5 were at >2% risk. The clear correlation between risk quintiles and number of deaths prevented provided further justification for using risk-based selection criteria in lung cancer screening. In comparison to the Kovalchik study, the UKLS criteria are more stringent, in that entry into the trial is offered to those with a >5% risk over five years; this corresponds to a higher level of risk than those included in the fifth quintile of Kovalchik et al. Future studies will consider whether this is a more cost-effective approach.

In the case of the UKLS trial, a number of factors were found to influence recruitment, participation and risk status. The main findings are discussed below.

Sex

Although men and women are equally likely to respond positively to an invitation to take part in UKLS, more men than women are designated as being at high LLP risk (2016 males versus 832 females, giving a gender ratio of 2.4:1). However, national lung cancer incidence figures for the 50-
74 age group in the UK give a male : female ratio of 1.34:1 (1). It will be interesting to consider sex-related outcomes in the UKLS participants in future follow up through ONS, cancer registry and HES.

Age

In general, response rate increased with age, although there was a fall off in the oldest age group (71-75 years), who conceivably are less concerned about their risk of lung cancer, or anticipate more practical difficulties with participating in the study. Nevertheless, as the oldest age group has the greatest percentage at high LLP risk (28% of 71-75y positive responders were high risk) this age group was well represented in terms of clinic attendance (482, or 33.2%, of clinic attendees were aged 71-75y). Thus, despite the sharp fall off in participation rate in the oldest age group, the clinic attendance rate among this group is in proportion to the number of lung cancers expected (around one third of lung cancers in the UKLS age range occur in individuals of 71-75 years (1)).

Only 76 (5.2%) clinic attendees were aged 60 or below, of whom only five (0.3%) were in the 50-55y age group. Thus the youngest (50-55y) age group yielded a clinic attendance of just 0.02% of the 26,532 originally invited to participate in UKLS. This has implications for cost-effectiveness, and, under the LLP model of risk prediction, suggests that it would not be prudent to include this age group in any future lung screening studies or programmes.

In order to determine more accurately when response rate and risk increase to a point where screening is viable from a detection and cost-effectiveness point of view, we analysed by individual year of age within the 55-65 year age groups. The results suggest a fairly sharp increase at 58 years of age in the percentage of positive responders at high LLP risk, from around 1% to 4.3%. This suggests that setting the lower cut-off point for eligibility at 58 years old would be a reasonable strategy for future studies. By considering data only from individuals aged between 58-75 years (n=56,055), this would give an overall positive response rate of 28.5%. Of the 15952 positive
responders in this age group, 2819 (17.7%) are at high LLP risk. The overall clinic attendance rate from the entire sample of 58-75 year olds (n=56,055) is 2.8%.

**Socioeconomic Group**

There was a strong positive correlation between higher socioeconomic group (less deprived quintile of IMD) and positive response to the screening invitation. Similar trends have also been observed in other screening studies, and the lower uptake is considered to relate to barriers including fear and fatalistic beliefs about cancer (27, 28) and poorer self-rated health in people from lower socioeconomic groups (29). Unlike with other cancers (e.g. breast cancer) there are marked socio-demographic differences in lung cancer risk, with individuals from lower socioeconomic groups being at greater risk of developing the disease: this largely relates to disparate tobacco use in different socioeconomic groups. It is therefore not ideal that those at highest risk are the least likely to take up the offer of screening. Our data suggest that this works at two levels: individuals at highest risk of lung cancer (i.e. from the lower socioeconomic groups) are less likely to respond to the initial screening invitation, and also less likely to attend clinic after having been identified as at high risk. Consideration will have to be given to addressing this in any future screening programme.

**Smoking Status**

Analysis suggested that ex-smokers are the most responsive to a screening invitation. It could be argued that consciously deciding to stop smoking and being motivated to participate in screening are related decisions, perhaps made by individuals who are more health aware, or perceive greater risks from smoking. The response rate from current smokers was lower than would be expected based on age matched population figures, possibly suggesting that current smokers are less likely to want to consider their cancer risk, or feel more threatened by the prospect of lung cancer screening. However, it was observed that, if smokers take the trouble to respond, they are more likely in percentage terms to be positive rather than negative responders. The converse is true for never
smokers, who perhaps, correctly, view their own risk as low and hence are over-represented amongst negative responders.

**Interaction between smoking and IMD**

The likelihood of a positive response to a CT screening invitation is lower both in more deprived socioeconomic groups, and in current smokers. As smoking status and socioeconomic status are closely related, it is important to establish whether both independently affect response rate, or whether there is any confounding. Predicted population smoking figures stratified by IMD quintile and age-adjusted to the UKLS sample (22) were therefore compared with the smoking prevalence seen amongst UKLS positive responders in each IMD quintile. This suggests that, in general, socioeconomic deprivation and current smoking status both act independently to lower the positive response rate. However, in the highest and lowest IMD quintiles, the impact of smoking status on response rate is much less marked. In the highest IMD quintile (least deprived), the positive response rate among smokers is slightly higher than the overall positive response rate. In the case of the results from the lowest (most deprived) IMD quintile, this observation partially offsets the trend for high risk individuals being less likely to respond. Across all socioeconomic groups, ex-smokers are the most likely to respond positively. In a possible future UK National lung CT screening programme, strategies may therefore need to be devised to target both current smokers and individuals from lower socioeconomic groups.

**Conclusion**

The data from the first phase (88,897 approaches) of the UKLS pilot trial provide a unique insight into the likely population response to a lung cancer screening trial in the UK. This will enable specific recommendations to be made regarding the implementation of any future UK-wide lung LDCT screening programme, such as initiating screening at age 58. Such a programme would need to give
due consideration to ways to target those most at risk who may be least likely to take up offers of screening (i.e. the most deprived, current smokers, and the over 70s). Possible methods would be to incorporate concurrent advertising, and/or utilise modified invitation materials.

**Acknowledgements**

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References

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2. NCRI, editor. LUNG CANCER UK PRICE TAG ECLIPSES THE COST OF ANY OTHER CANCER. 2012.
### Table 1

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<th>Age (years)</th>
<th>50-55y</th>
<th>56-60y</th>
<th>61-65y</th>
<th>66-70y</th>
<th>71-75y</th>
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<tr>
<td>Total Approached (n=88,897)</td>
<td>26532 (29.8%)</td>
<td>15085 (17.0%)</td>
<td>17370 (19.5%)</td>
<td>15154 (17.0%)</td>
<td>14756 (16.6%)</td>
<td>88897 (100%)</td>
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<tr>
<td>Positive Responders (n=23,794)</td>
<td>6256 (26.3%)</td>
<td>3949 (16.6%)</td>
<td>5263 (22.1%)</td>
<td>4776 (20.0%)</td>
<td>3550 (14.9%)</td>
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<td>High Risk Responders (n=2,848)</td>
<td>12 (0.4%)</td>
<td>150 (5.3%)</td>
<td>670 (23.5%)</td>
<td>1019 (35.8%)</td>
<td>997 (35.0%)</td>
<td>2848 (100%)</td>
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<tr>
<td>High Risk Clinic Attendees (n=1,452)</td>
<td>5 (0.3%)</td>
<td>71 (4.9%)</td>
<td>364 (25.0%)</td>
<td>530 (36.5%)</td>
<td>482 (33.1%)</td>
<td>1452 (100%)</td>
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### Table 2

<table>
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<th>IMD Quintile</th>
<th>Q1: Most Deprived</th>
<th>Q2: Above Average Deprivation</th>
<th>Q3: Average</th>
<th>Q4: Below Average Deprivation</th>
<th>Q5: Least Deprived</th>
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<td>Total Approached (n=88,897)</td>
<td>24138 (27.2%)</td>
<td>13275 (14.9%)</td>
<td>16117 (18.1%)</td>
<td>16973 (19.1%)</td>
<td>18393 (20.7%)</td>
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<td>Positive Responders (n=23,794)</td>
<td>4739 (19.9%)</td>
<td>3291 (13.8%)</td>
<td>4280 (18.0%)</td>
<td>5193 (21.8%)</td>
<td>6291 (26.4%)</td>
<td>23794 (100%)</td>
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<tr>
<td>High Risk Responders (n=2,848)</td>
<td>839 (29.5%)</td>
<td>439 (15.4%)</td>
<td>533 (18.7%)</td>
<td>531 (18.6%)</td>
<td>506 (17.8%)</td>
<td>2848 (100%)</td>
</tr>
<tr>
<td>High Risk Clinic Attendees (n=1,452)</td>
<td>364 (25.1%)</td>
<td>198 (13.6%)</td>
<td>281 (19.4%)</td>
<td>304 (20.9%)</td>
<td>305 (21.0%)</td>
<td>1452 (100%)</td>
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FIGURE LEGENDS

**Figure 1:** Consort Diagram showing response rate and recruitment at each step of the first phase of the UKLS pilot trial. ‘Not eligible’ refers to those people meeting the protocol exclusion criteria: i.e. those who had undergone a CT scan within the previous 12 months or were aged over 75 years. It also incorporates later exclusions made during data-cleaning.

**Figure 2:** Impact of age upon response rate and LLP risk.

(a) Percentage of positive responders at high risk of lung cancer, by five year age band. The box shows positive response rate by age (number and percent of total approached) and clinic attendance rate by age (number and percent of total approached).

(b) UKLS Positive Responders aged 55-65yrs (n=10,009): percentage at High LLP Risk, by individual year of age.

**Figure 3:** Impact of socioeconomic status (IMD)* upon response rate, LLP risk and clinic attendance.

Positive response rate (black line) and percentage of positive responders at high LLP risk (grey bars), by IMD quintile. The box shows clinic attendance by IMD quintile as an absolute number and percentage of the total approached sample (n=88,897 across all IMD quintiles), and as a percentage of all high risk individuals (i.e. those who were invited to clinic; n=2,848 across all IMD quintiles).

*The English Indices of Deprivation 2010 comprise the official measure of deprivation in England. The most commonly used of these ten indices is The Index of Multiple Deprivation (IMD), which is calculated from 38 separate indicators, based on weighted data from the following seven domains: Income Deprivation (22.5%), Employment Deprivation (22.5%), Health Deprivation and Disability (13.5%), Education, Skills and Training Deprivation (13.5%), Barriers to Housing and Services (9.3%),...
Crime (9.3%), and Living Environment Deprivation (9.3%). For the purposes of measuring deprivation, England is divided into 32,482 ‘Lower layer Super Output Areas’ (LSOAs), with each area being carefully defined by its local geography, and containing in the region of 1500 residents (minimum 1000 residents). IMD ranks, which provide a relative measure of deprivation in small areas across England, range from 1 (most deprived LSOA) to 32,482 (least deprived LSOA).

**Figure 4:** Smoking status in positive and negative responders, expected (population) values for the 50+ age group, and estimated distribution in non-responders, calculated from expected numbers less the observed numbers seen in the responders. In this case, ‘non-responders’ (n=57,172) includes 232 positive responders and 465 negative responders who did not disclose their smoking status, as well as the 56,475 true non-responders.

**Figure 5:** Interaction between smoking status and socioeconomic status in determining participation in UKLS.

Calculated positive response rate, percent, by smoking status and IMD Quintile. The purple line (and percentages) denotes the known positive response rate of all individuals within that IMD quintile. Calculations were based on Health Survey for England population smoking figures for each IMD quintile, age matched (in five year bands) to the UKLS sample (See Supplementary Table S1c).
Figure 1

- **88,897 Invitation Letters Sent**
  - **Positive Responses** 23,794
  - **Negative Responses** 8,628
  - **No Reply** 56,475

- **High Risk** 2,848
- **Low Risk** 20,946

- **Positive Responses** 1924
  - **Attended Clinic 1,452**
    - **Screening Arm 731**
    - **Non-Screening Arm 721**
  - **Did not attend clinic 134**
  - **Not eligible 338**
  - **Did not attend clinic 924**

- **Negative or no Reply 924**
Figure 2

a

Percentage of positive responders at high LLP risk

Age group, years

b

Percentage of positive responders at high LLP risk

Age, years

Cancer Research.
Figure 3

<table>
<thead>
<tr>
<th>IMD Quintile</th>
<th>Subjects at high LLP risk, % of positive responders</th>
<th>Overall positive response rate, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Q1: Most Deprived</td>
<td>364 (1.51%)</td>
<td>19.6%</td>
</tr>
<tr>
<td>Q2: Above Average Deprivation</td>
<td>198 (1.49%)</td>
<td>24.8%</td>
</tr>
<tr>
<td>Q3: Average</td>
<td>281 (1.74%)</td>
<td>26.6%</td>
</tr>
<tr>
<td>Q4: Below Average Deprivation</td>
<td>304 (1.79%)</td>
<td>30.6%</td>
</tr>
<tr>
<td>Q5: Least Deprived</td>
<td>305 (1.66%)</td>
<td>34.2%</td>
</tr>
</tbody>
</table>

Number of clinic attendees (percent of total approached):

- Q1: 43.4%
- Q2: 45.1%
- Q3: 52.7%
- Q4: 57.3%
- Q5: 60.3%

Clinic attendance rate among high risk subjects.
Figure 4

<table>
<thead>
<tr>
<th></th>
<th>Positive Responders (n=23,562)</th>
<th>Negative Responders (n=8163)</th>
<th>National Average (age 50+)</th>
<th>Non-Responders (calculated) (n=57,172)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ex-smoker</td>
<td>40.4%</td>
<td>35.8%</td>
<td>33.0%</td>
<td>29.6%</td>
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<tr>
<td>Current Smoker</td>
<td>9.3%</td>
<td>54.9%</td>
<td>49.5%</td>
<td>50.4%</td>
</tr>
<tr>
<td>Never-smoker</td>
<td>54.9%</td>
<td>49.5%</td>
<td>44.5%</td>
<td>20.0%</td>
</tr>
</tbody>
</table>

Positive Responders (n=23,562)

Negative Responders (n=8163)

National Average (age 50+)

Non-Responders (calculated) (n=57,172)
Figure 5

Percentage of Positive Response rate by IMD Quintile:

- Ex-smokers only (calculated)
- Current smokers only (calculated)
- Never smokers only (calculated)
- All approached

Q1: Most Deprived
Q2: Above Average Deprivation
Q3: Average
Q4: Below Average Deprivation
Q5: Least Deprived

IMD Quintile
# The UK Lung Screen (UKLS): demographic profile of first 88,897 approaches provides recommendations for population screening.

Fiona E. McRonald, Ghasem Yadegarfar, David R. Baldwin, et al.

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