Long-term psychosocial outcomes of low-dose CT screening: results of the UK Lung Cancer Screening randomised controlled trial

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ABSTRACT

Background The UK Lung Cancer Screening (UKLS) trial is a randomised pilot trial of low-dose CT (LDCT) screening for individuals at high risk of lung cancer. We assessed the long-term psychosocial impact on individuals participating in the UKLS trial.

Methods A random sample of individuals aged 50–75 years was contacted via primary care. High-risk individuals who completed T0 questionnaires (baseline) were randomised to LDCT screening (intervention) or usual care (no screening control). T1 questionnaires were sent 2 weeks after baseline scan results or control assignment. T2 questionnaires were sent up to 2 years after recruitment. Measures included cancer distress, anxiety, depression and decision satisfaction.

Results A total of 4037 high-risk individuals were randomised and they completed T0 questionnaires (n=2018 intervention, n=2019 control). Cancer distress was higher at T1 in intervention arm participants who received positive screening results (p≤0.001), but not at T2 (p=0.04). T2 anxiety (p≤0.001) and depression (p≤0.01) were higher in the control arm, but the absolute differences were small and not clinically relevant. At both time points, fewer control than screened participants were satisfied with their decision to participate in UKLS (p≤0.001). Regardless of trial allocation, cancer distress was higher in women (p≤0.01), participants aged ≤65 years (p≤0.001), current smokers (p≤0.001), those with lung cancer experience (p≤0.001) and those recruited from the Liverpool area (p≤0.001).

Conclusion Lung cancer screening using LDCT appears to have no clinically significant long-term psychosocial impact on high-risk participants. Strategies for engaging and supporting underserved groups are the key to implement routine lung cancer screening in the UK.

Trial registration number ISRCTN 78513845; results.

INTRODUCTION

Lung cancer is the leading cause of cancer-related mortality in the UK.¹ Although improving, the 5-year survival rate for lung cancer in the UK is approximately 10% and lower than in other countries with comparable healthcare systems.² This is partly due to patients presenting at an advanced disease stage, with over 65% of cases diagnosed at stage III or stage IV² when treatment is usually palliative.
2 months follow-up in recipients of an indeterminate scan result. However, these effects had diminished at 6 months follow-up. Recently, the NLST reported no significant differences between those receiving an abnormal and those receiving normal lung screening result in anxiety and health-related quality of life at 1 and 6 months follow-up.

The UK Lung Cancer Screening (UKLS) pilot trial is the first to assess the feasibility, cost-effectiveness and psychosocial impact of lung cancer screening using a single LDCT screen versus no screening in a UK high-risk population. When considering the impact of lung cancer screening, it is important to understand the moderating role of participant characteristics that could present barriers to successful implementation. For example, smokers may perceive few benefits of screening compared with former or non-smokers. Individuals from poorer backgrounds may be less enthusiastic about screening and face more barriers than those from affluent backgrounds. In earlier UKLS reports, trial participation was less likely in smokers, women, older age groups, those with higher levels of concern about lung cancer and those in lower socioeconomic groups.

We report the effects of UKLS trial participation on short-term and long-term psychosocial outcomes. The primary hypothesis was that intervention arm participants—in particular those with a positive (ie, abnormal) baseline scan result—would report higher short-term cancer distress compared with those in the control arm, but there would be no differential effects of trial arm or screening outcome on long-term distress. In secondary analyses of outcomes adjusted for a range of covariates, it was anticipated that subgroups including smokers and those from socioeconomically deprived areas would report adverse long-term outcomes regardless of trial allocation or result.

METHODS
Participants and procedures
A random sample of 247,354 individuals aged 50–75 years residing in six recruitment centres at two sites (Liverpool, Knowsley and Sefton; Cambridgeshire, Peterborough and Bedfordshire) was sent trial information packs that included a questionnaire regarding lung cancer risk factors. From the questionnaire responders, 8729 patients were identified as having high risk of lung cancer (≥1% over 5 years) using the LLPv2 risk prediction model. Characteristics of trial non-participants are reported elsewhere. In earlier UKLS reports, trial participation was less likely in smokers, women, older age groups, those with higher levels of concern about lung cancer and those in lower socioeconomic groups.

Figure 1 Screening results.
enabled comparison of the short-term responses of participants whose initial screening results were not unequivocally normal/negative. At T2, we distinguished screening outcome for participants with a positive baseline screening result who were free from lung cancer (false-positive) from those who did have lung cancer (true-positive) at long-term follow-up, those with normal results (true-negative) and those with significant abnormalities during baseline or repeat CT scan that were not lung cancer (incidental finding).

Statistical analysis
Analyses were conducted using SPSS (V20; SPSS, Chicago, Illinois, USA). Mean replacement imputation within domains was used and a complete case analysis was carried out. Individuals with missing data >35% within a domain were not included in the analysis. Attrition bias was assessed using $\chi^2$ and independent t tests. During primary analysis, psychosocial outcomes of trial allocation and screening results at T1 and T2 were assessed using analysis of covariance (ANCOVA) adjusted for T0 scores or $\chi^2$ tests. Due to non-normality and heterogeneity of regression slopes for T1 cancer distress scores, analyses of trial allocation effect on the primary outcome were conducted separately for log-transformed (log$_e$) high and low cancer distress thresholds, that is, above or below 12.5. Sensitivity analyses were conducted to assess possible confounding effects of data timing issues and to adjust for missing follow-up data at T1 and T2 using an inverse probability weighting (IPW) approach. The $p$ values $\leq 0.01$ were used to denote statistical significance in the context of multiple testing. Following significant ANCOVA results, post-hoc pairwise comparisons of screening results were performed ($p \leq 0.05$).

A secondary linear mixed-effects risk prediction model was generated to evaluate the impact of trial allocation on the primary outcome of cancer distress at T1 and T2 in (1) univariable regression analyses adjusting for T0 distress scores and (2) multivariable regression analyses adjusting for T0 scores and all other main effects (gender, age group, smoking, deprivation quintile, education, ethnicity, marital group, lung cancer experience, trial site and time since attended recruitment centre). The model fitting process included mechanistically plausible confounders that exhibited independent associations in a forward-stepping method using the likelihood ratio statistic ($p \leq 0.01$), as part of an a priori statistical analysis plan. Since only intervention group participants received a CT scan, trial allocation group was fully nested with the result group.
RESULTS

Trial participation

In total, 4061 individuals (5.3% of 75,958 responders to the risk questionnaire; 46.5% of all high-risk positive responders) attended the recruitment clinic and were consented (see figure 2). Of these, 4037 trial participants completed T0 questionnaires and were randomised (n=2018 intervention, n=2019 control), of whom 3232 completed T1 questionnaires (n=1653/84% intervention, n=1579/78% control). At T2, 2855 participants completed questionnaires (n=1553/82% intervention, n=1302/65% control). The mean time of T2 questionnaire completion was 16 months after attending the recruitment centre (range 10–29 months).

Table 1  Attrition at short-term follow-up: comparison of T1 questionnaire completers and non-completers

|                        | T1 completers (n=3232)* | T1 non-completers (n=749)* | Test statistic (p value) |
|------------------------|--------------------------|-----------------------------|--------------------------|
| Trial allocation       |                          |                             |                          |
| Intervention           | 1653 (51)                | 312 (42)                    | <0.001                   |
| Control                | 1579 (49)                | 437 (58)                    |                          |
| Site                   |                          |                             |                          |
| Liverpool recruitment centre | 1585 (49)          | 420 (56)                    | <0.001                   |
| Cambridge recruitment centre | 1647 (51)          | 329 (44)                    |                          |
| Age (years)            | 67.73 (3.98)             | 67.28 (4.46)                | <0.01                    |
| Gender                 |                          |                             |                          |
| Male                   | 2446 (76)                | 533 (71)                    | <0.01                    |
| Female                 | 786 (24)                 | 216 (29)                    |                          |
| Education†             |                          |                             |                          |
| Up to GCSE/O level     | 1007 (43)                | 334 (57)                    | <0.001                   |
| Beyond GCSE/O level    | 1310 (57)                | 250 (43)                    |                          |
| Ethnicity              |                          |                             |                          |
| White                  | 3190 (99)                | 739 (99)                    | †                        |
| Non-white              | 26 (1)                   | 10 (1)                      |                          |
| Marital group          |                          |                             |                          |
| Married/cohabiting     | 2410 (75)                | 508 (68)                    | <0.001                   |
| Not married/cohabiting | 814 (25)                 | 240 (32)                    |                          |
| IMD                    |                          |                             |                          |
| Quintile 1 (most deprived) | 843 (26)               | 222 (30)                    | <0.001                   |
| Quintile 2             | 367 (11)                 | 109 (15)                    |                          |
| Quintile 3             | 574 (18)                 | 135 (18)                    |                          |
| Quintile 4             | 578 (18)                 | 141 (19)                    |                          |
| Quintile 5 (least deprived) | 870 (27)             | 142 (19)                    |                          |
| Smoking status         |                          |                             |                          |
| Current smoker         | 1194 (37)                | 338 (45)                    | <0.001                   |
| Ex-smoker              | 2037 (63)                | 410 (55)                    |                          |
| Never smoker           | 1 (<1)                   | 1 (<1)                      | †                        |
| Experience of lung cancer (T0) |              |                             |                          |
| No                     | 1870 (58)                | 396 (53)                    | <0.01                    |
| Yes                    | 1355 (42)                | 352 (47)                    |                          |
| Cancer distress (T0)§  | 2.16 (0.28)              | 2.21 (0.31)                 | <0.001                   |
| Anxiety (T0)§          | 8.65                     | 9.16                        |                          |
| Depression (T0)§       | 1.52 (0.71)              | 1.65 (0.71)                 | <0.001                   |
| Decision satisfaction (T0) | 2.56                  | 2.94                        | <0.001                   |
| Not very satisfied     | 1916 (59)                | 428 (57)                    | 0.32                     |
| Very satisfied         | 1308 (41)                | 317 (43)                    |                          |

* Ns vary in each cell due to missing data. Percentages were calculated based on available data.
† A substantial amount of data were missing or uninformative for education.
‡ Data were excluded from analysis due to limited variation.
§ Logn scores are provided in normal text and original scale scores are provided in italics (analyses performed using logn scores).

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Factors associated with study attrition

As shown in tables 1 and 2, intervention participants were statistically significantly more likely than those in the control arm to complete T1 and T2. Questionnaire completers at T1 and T2 were significantly more likely to be older, male, married or cohabiting, more educated, former smokers, resident in the Cambridge area and those who had no experience of lung cancer. Due to missing data for educational level, results for this variable should be interpreted with caution. A significantly greater proportion of questionnaire completers were in the highest IMD quintile at T1 and T2. T1 and T2 completers reported significantly lower baseline (T0) scores on all
psychosocial measures, although the absolute differences were very small and scores were in the low range overall. Differences in decision satisfaction were not statistically significant at either follow-up.

**Baseline sample characteristics**

Most trial participants were male, white, married or cohabiting, former smokers, with an average age of 68 years (see table 3). Of those for whom educational data were available, just over half the participants were educated beyond 16 years. There was a spread of deprivation levels within the sample, with approximately one-quarter in the highest quintile and one-quarter in the lowest quintile. T₀ cancer distress, anxiety and depression scores were equivalent across trial arms. Approximately 40% were very satisfied with their decision to take part. The baseline characteristics of participants who were included in T₁ and T₂ analyses are presented in additional online supplementary tables SI and SII.

**Primary analyses**

Short-term (T₁) outcomes

As shown in table 4, different effects of trial allocation on T₁ cancer distress were found in participants who scored above and below the T₀ distress threshold (12.5). For those with low T₀ cancer distress, anxiety and depression scores were equivalent across trial arms. Approximately 40% were very satisfied with their decision to take part. The baseline characteristics of participants who were included in T₁ and T₂ analyses are presented in additional online supplementary tables SI and SII.

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**Table 2** Attrition at long-term follow-up: comparison of T₂ completers and non-completers

|                                | T₂ completers (n=2855)* | T₂ non-completers (n=1026)* | Test statistic (p value) |
|--------------------------------|--------------------------|-----------------------------|--------------------------|
| **Trial allocation**           |                          |                             |                          |
| Intervention                   | 1553 (54)                | 335 (33)                    | <0.001                   |
| Control                        | 1302 (46)                | 691 (67)                    |                          |
| **Site**                       |                          |                             |                          |
| Liverpool recruitment centre   | 1336 (47)                | 622 (61)                    | <0.001                   |
| Cambridge recruitment centre   | 1519 (53)                | 404 (39)                    |                          |
| **Age (years)**                | 67.79 (3.98)             | 67.19 (4.31)                | <0.001                   |
| **Gender**                     |                          |                             |                          |
| Male                           | 2166 (76)                | 736 (72)                    | <0.01                    |
| Female                         | 689 (24)                 | 290 (28)                    |                          |
| **Education†**                 |                          |                             |                          |
| Up to GCSE/O level             | 940 (44)                 | 367 (53)                    | <0.001                   |
| Beyond GCSE/O level            | 1196 (56)                | 330 (47)                    |                          |
| **Ethnicity**                  |                          |                             |                          |
| White                          | 2825 (99)                | 1004 (99)                   | †                        |
| Non-white                      | 21 (1)                   | 15 (1)                      |                          |
| **Marital group**              |                          |                             |                          |
| Married/cohabiting             | 2174 (76)                | 672 (66)                    | <0.001                   |
| Not married/cohabiting         | 675 (24)                 | 352 (34)                    |                          |
| **IMD**                        |                          |                             |                          |
| Quintile 1 (most deprived)     | 668 (23)                 | 373 (36)                    | <0.001                   |
| Quintile 2                      | 338 (12)                 | 126 (12)                    |                          |
| Quintile 3                      | 523 (18)                 | 170 (17)                    |                          |
| Quintile 4                      | 545 (19)                 | 157 (15)                    |                          |
| Quintile 5 (least deprived)    | 781 (27)                 | 200 (19)                    |                          |
| **Smoking status**             |                          |                             |                          |
| Current smoker                 | 1009 (35)                | 490 (48)                    | <0.001                   |
| Ex-smoker                      | 1845 (65)                | 536 (52)                    |                          |
| Never smoker                   | 1 (<1)                   | 0 (0)                       | †                        |
| **Experience of lung cancer (T₀)**|                          |                             |                          |
| No                             | 1683 (59)                | 522 (51)                    | <0.001                   |
| Yes                            | 1166 (41)                | 503 (49)                    |                          |
| **Cancer distress (T₀)§**      | 2.16 (0.28)              | 2.20 (0.32)                 | <0.001                   |
| Anxiety (T₀)§                  | 1.51 (0.71)              | 1.64 (0.71)                 | 4.17                     |
| Depression (T₀)§               | 1.25 (0.66)              | 1.38 (0.68)                 | <0.001                   |
| Decision satisfaction (T₀)     |                          |                             |                          |
| Not very satisfied             | 1668 (59)                | 612 (60)                    | <0.47                    |
| Very satisfied                 | 1179 (41)                | 410 (40)                    |                          |

* Ns vary in each cell due to missing data. Percentages were calculated based on available data.
† A substantial amount of data were missing or uninformative for education.
‡ Data were excluded from analysis due to limited variation.
§ Logn scores are provided in normal text and original scale scores are provided in italics (analyses performed using logn, scores).
GCSE, General Certificate of Secondary Education; IMD, Index of Multiple Deprivation.
distress (n=2896/3265, 90%), T1 distress scores were significantly higher in the intervention arm, though not to clinical levels and with a very small effect size (logn (Int-Con)=0.03, 95% CI -0.01 to 0.001). Sensitivity analyses to assess the impact of data timing showed no change in statistical significance levels; therefore, further exclusions were not made. Further adjustment for missing data using IPW indicated no change in the direction, magnitude or significance of the difference in cancer distress between intervention and control arms for either low or high scorers.

Intervention participants who were positive for MDT referral at T1 reported statistically significantly higher T1 cancer distress which approached clinical thresholds (p≤0.001) compared with those with negative results (p<0.001), incidental findings (p<0.001) and those positive for a repeat scan (p<0.001). Participants who required a repeat scan at T1 reported significantly higher T1 cancer distress than those with negative results (p<0.001). Statistically significantly greater anxiety was found in participants referred to MDT (p<0.001) compared with those receiving negative results (p<0.001), incidental findings (p=0.02) or positive for repeat scan (p=0.003), although scores were in the low/normal range. The difference in anxiety between those positive for MDT referral and those with incidental findings disappeared when sensitivity analysis accounted for test timing issues. Differences in depression scores were not statistically significant for any screening result group (p=0.35). Intervention participants who were positive for a repeat scan were the least satisfied with their decision (p<0.001).

Long-term (T2) outcomes
The effect of trial allocation on T2 cancer distress was not statistically significant in individuals with low (logn (Int-Con)=0.01, 95% CI -0.01 to 0.02) or high (logn (Int-Con)=-0.02, 95% CI -0.09 to 0.03) T0 distress (see table 5). Although the control group reported significantly higher T2 logn anxiety (logn (Int-Con)=0.08, 95% CI -0.12 to -0.03) and depression (logn (Int-Con)=0.06, 95% CI -0.10 to -0.02), the absolute differences between trial arms were small and not clinically significant. When converted to raw scores, all three measures for both trial arms were within the normal range. Control participants (74%) were significantly less likely than intervention participants (60%) to be very satisfied with their decision to take part (p<0.001).

Differences between screening outcome groups in T2 cancer distress (p=0.04), anxiety (p=0.12), depression (p=0.11) and decision satisfaction (p=0.03) were not statistically significant. The raw scores of all psychosocial variables in all screening outcome groups were within the normal range and not clinically relevant. Sensitivity analyses using IPW to assess the impact of missing data indicated no change in the direction, magnitude or significance of the difference in cancer distress between intervention and control arms, either for low or high baseline scorers.

### Table 3 Baseline psychosocial sample characteristics by trial allocation

|                      | Intervention (n=2018)* | Control (n=2019)* |
|----------------------|-----------------------|-------------------|
|                      | n (%) or mean (SD)    | n (%) or mean (SD) |
| **Site**             |                       |                   |
| Liverpool recruitment centre | 1003 (50)           | 1016 (50)         |
| Cambridgeshire recruitment centre | 1002 (50)           | 1010 (50)         |
| **Age (years)**      | 67.72 (4.04)         | 67.59 (4.13)      |
| **Gender**           |                       |                   |
| Male                 | 1520 (75)            | 1500 (74)         |
| Female               | 498 (25)             | 519 (26)          |
| **Education†**       |                       |                   |
| Up to GCSE/O level or equivalent | 678 (46)           | 683 (46)          |
| Beyond GCSE/O level or equivalent | 788 (54)           | 791 (54)          |
| **Ethnicity**        |                       |                   |
| White                | 1992 (99)            | 1992 (99)         |
| Non-white            | 18 (1)               | 19 (1)            |
| **Marital group**    |                       |                   |
| Married/cohabiting   | 1483 (74)            | 1471 (73)         |
| Not married/cohabiting | 528 (26)            | 545 (27)          |
| **IMD**              |                       |                   |
| Quintile 1 (most deprived) | 545 (27)           | 533 (26)          |
| Quintile 2           | 243 (12)             | 242 (12)          |
| Quintile 3           | 358 (18)             | 361 (18)          |
| Quintile 4           | 353 (18)             | 376 (19)          |
| Quintile 5 (least deprived) | 519 (26)            | 507 (25)          |
| **Smoking status**   |                       |                   |
| Current smoker       | 772 (38)             | 787 (39)          |
| Ex-smoker            | 1244 (62)            | 1232 (61)         |
| Never smoker         | 2 (1)                | 0 (0)             |
| **Experience of lung cancer (T0)** | 1168 (58)        | 1126 (56)         |
| No                   | 846 (42)             | 889 (44)          |
| Yes                  | 217.02 (9)           | 217.02 (9)        |
| **Cancer distress (T0)**† | 8.75                 | 8.74              |
| Anxiety (T0)         | 1.55 (0.71)          | 1.54 (0.71)       |
| Depression (T0)      | 1.30 (0.68)          | 1.28 (0.67)       |
| Decision satisfaction (T0) | 2.66                 | 2.61              |

|                      |                       |                   |
| **Not very satisfied** | 1228 (61)           | 1158 (58)         |
| **Very satisfied**   | 786 (39)             | 853 (42)          |

*Ns vary in each cell due to missing data. Percentages were calculated based on available data.
†A substantial amount of data were missing or uninformative for education. Log scores are provided in normal text and original scale scores are provided in italics (analyses performed using logn scores).
GCSE, General Certificate of Secondary Education; IMD, Index of Multiple Deprivation.
distress scores were back-transformed (95% CI 12% to 17%). Cancer distress scores were statistically significantly higher in women (p≤0.001), younger participants (≤65 years and 66–70 years) compared with those aged over 70 (p<0.001), current smokers compared with ex-smokers (p<0.001), lower socio-economic groups (Q1–Q2 vs Q5 p<0.001, Q3 vs Q5 p<0.01), single or divorced compared with married individuals (p<0.001), those with experience of lung cancer (p<0.001) and participants recruited from the Liverpool area (p<0.001). Education, ethnicity and time since recruitment were not significantly independently associated with cancer distress. Intervention participants who needed a repeat scan or MDT referral reported higher cancer distress than those who received a negative result (p<0.001).

In multivariable analyses adjusting for covariates, the impact of trial allocation on cancer distress was not statistically significant. Higher cancer distress was statistically significantly associated with female gender (p<0.01), younger age group (≤65 vs over 70 years) (p<0.001), current smoking status (p<0.001), lung cancer experience (p<0.001) and Liverpool recruitment site (p<0.001).

Sensitivity analyses to assess the impact of T0 cancer distress level indicated a similar pattern of results for participants with high T0 cancer distress levels.

Table 4 Summary data for short-term psychosocial outcomes (T1) by trial arm and screening result

| Outcome (T1) | Intervention (n=1653) | Control (n=1579) | Intervention arm (n=1653) by screening result† |
|--------------|-----------------------|------------------|-----------------------------------------------|
|              | M (95% CI)            |                  | Negative (n=763)                              |
| Cancer distress‡ | Low T0 scores        | Low T0 scores    | Incidental finding (n=41)                     |
|               | 2.14 (2.13 to 2.16)** | 2.11 (2.10 to 2.12) | 8.54 (8.44 to 8.64)                            |
|               | 8.54 (8.44 to 8.64)   | 8.26 (8.16 to 8.36) | Positive—repeat scan (n=788)                   |
|               | 2.50 (2.46 to 2.53)   | 2.53 (2.50 to 2.57) | Positive—MDT referral (n=48)                  |
| Anxiety‡      | M (95% CI)            |                  |                                              |
|               | 1.54 (1.51 to 1.57)   | 1.56 (1.53 to 1.59) |                                              |
|               | 3.67 (3.54 to 3.80)   | 3.78 (3.64 to 3.92) |                                              |
| Depression‡   | M (95% CI)            |                  |                                              |
|               | 1.26 (1.23 to 1.29)   | 1.34 (1.31 to 1.37)** |                                              |
| Decision satisfaction (n, %) | Not very satisfied | 875 (58) | 378 (54) | 22 (56) | 450 (64)** | 18 (43) |
|               | 624 (42)              | 953 (66)**       |                                              |

* p<0.01, **p<0.001.
†Logn scores are provided in normal text and original scale scores are provided in italics (analyses performed using logn scores). Estimated marginal means are presented. Higher scores denote higher levels of the relevant outcome.
‡Numbers vary in each cell due to missing data.
§Test statistics not calculated due to low variation.

Table 5 Summary data for long-term psychosocial outcomes (T2) by trial arm and screening outcome

| Outcome (T2) | Intervention (n=1553) | Control (n=1302) | Intervention arm (n=1553) by screening outcome† |
|--------------|-----------------------|------------------|-----------------------------------------------|
|              | True-negative (n=740) | Incidental finding (n=76) | False-positive (n=445) | True-positive (n=23) |
| Cancer distress‡ | Low T0 scores        | Low T0 scores    |                                              |                                              |
|               | 2.10 (2.09 to 2.11)   | 2.09 (2.09 to 2.10) | 2.11 (2.09 to 2.12) | 2.14 (2.09 to 2.19) | 2.14 (2.12 to 2.16) | 2.20 (2.10 to 2.30) | 9.01 (8.16 to 9.96) |
| Anxiety‡      | M (95% CI)            |                  |                                              |                                              |
|               | 1.54 (1.51 to 1.57)   | 1.61 (1.58 to 1.65)** | 1.57 (1.53 to 1.62) | 3.82 (3.61 to 4.03) | 3.28 (2.74 to 3.89) | 3.59 (3.34 to 3.85) | 2.94 (2.08 to 4.03) |
| Depression‡   | M (95% CI)            |                  |                                              |                                              |
|               | 1.33 (1.30 to 1.36)   | 1.39 (1.36 to 1.42)** | 1.34 (1.30 to 1.39) | 2.84 (2.68 to 3.00) | 2.38 (1.97 to 2.85) | 2.98 (2.78 to 3.20) | 2.52 (1.79 to 4.34) |
| Decision satisfaction (n, %) | Not very satisfied | 855 (60) | 883 (74)** | 411 (61) | 39 (55) | 239 (59) | 6 (29)§ |
|               | 567 (40)              | 306 (26)         | 267 (39) | 32 (45) | 169 (41) | 15 (71) |

* p<0.01, **p<0.001.
†Logn scores are provided in normal text and original scale scores are provided in italics (analyses performed using logn scores). Estimated marginal means are presented. Higher scores denote higher levels of the relevant outcome.
§Test statistics not calculated due to low variation.
Table 6 Univariable and multivariable analyses of trial allocation effects on cancer distress over T1 and T2

| Cancer distress effect modifiers                  | Log e difference in cancer distress | Estimate (unadjusted), 95% CI | p value | Estimate (adjusted)*, 95% CI | p value |
|------------------------------------------------|-----------------------------------|------------------------------|---------|-----------------------------|---------|
| Trial allocation (Intervention-Control)         |                                   | 0.02 (−0.13 to 0.17)         | 0.42    | 0.03 (−0.20 to 0.26)        | 0.39    |
| Gender (Female-Male)                            |                                   | 0.04 (0.03 to 0.06)          | <0.001  | 0.02 (0.01 to 0.04)         | <0.01   |
| Age group                                       |                                   |                              |         |                             |         |
| Up to 65–over 70                                |                                   | 0.06 (0.05 to 0.08)          | <0.001  | 0.05 (0.03 to 0.07)         | <0.001  |
| 66 to 70–over 70                                |                                   | 0.04 (0.02 to 0.05)          | <0.001  | 0.02 (0.02 to 0.04)         | 0.02    |
| Smoking                                         |                                   |                              |         |                             |         |
| Ex-smoker–Current smoker                        | −0.08 (−0.06 to −0.09)            | <0.001                       | −0.06 (−0.05 to −0.08) | <0.001  |
| Never smoker–Current smoker                     | †                                 |                              | †       |                             |         |
| IMD                                             |                                   |                              |         |                             |         |
| Q1 (most deprived)–Q5 (least deprived)         | 0.09 (0.07 to 0.10)               | <0.001                       | 0.02 (−0.01 to 0.04) | 0.13    |
| Q2–Q5                                          | 0.05 (0.03 to 0.07)               | <0.001                       | 0.01 (−0.02 to 0.03) | 0.66    |
| Q3–Q5                                          | 0.03 (0.01 to 0.04)               | <0.001                       | −0.00 (−0.02 to 0.02) | 0.89    |
| Q4–Q5                                          | 0.02 (0.00 to 0.04)               | 0.029                        | 0.01 (−0.01 to 0.03) | 0.59    |
| Education (Up to GCSE/O level–beyond GCSE/O level) | 0.01 (0.00 to 0.03)               | 0.05                         |         |                             |         |
| Ethnicity (White–non-white)                     | 0.01 (−0.06 to 0.08)              | 0.79                         |         |                             |         |
| Marital group                                   |                                   |                              |         |                             |         |
| Married–Single                                  | −0.04 (−0.02 to −0.07)            | <0.001                       | −        |                             |         |
| Married–Cohabiting                              | 0.01 (−0.02 to 0.04)              | 0.41                         |         |                             |         |
| Married–Widowed                                 | −0.03 (−0.00 to −0.05)            | 0.03                         |         |                             |         |
| Married–Divorced                                | −0.05 (−0.03 to −0.07)            | <0.001                       | −        |                             |         |
| Experience of lung cancer (Yes–No)              | 0.05 (0.03 to 0.06)               | <0.001                       | 0.03 (0.02 to 0.05) | <0.001  |
| Site (Liverpool–Cambridge)                      | 0.07 (0.06 to 0.08)               | <0.001                       | 0.06 (0.04 to 0.07) | <0.001  |
| Time since attended recruitment centre          |                                   |                              |         |                             |         |
| 3 to 6 months–<3 months                         | −0.00 (−0.03 to 0.03)             | 1.00                         | −0.03 (0.00 to −0.05) | 0.09    |
| 6 to 12 months–<3 months                        | −0.05 (−0.09 to −0.01)            | 0.03                         | −0.06 (−0.11 to −0.01) | 0.03    |
| >12 months–<3 months                            | −0.03 (−0.12 to 0.06)             | 0.09                         | −0.05 (−0.10 to 0.00) | 0.05    |
| Screening result                                |                                   |                              |         |                             |         |
| Positive (repeat scan)–Negative                 | 0.09 (0.07 to 0.11)               | <0.001                       | −        |                             |         |
| Positive (referral)–Negative                    | 0.20 (0.15 to 0.24)               | <0.001                       | −        |                             |         |
| Incidental–Negative                             | 0.02 (−0.02 to 0.07)              | 0.33                         | −        |                             |         |

Data are presented for participants with low T0 cancer distress (n=2896/3225, 90%). Base model adjustment factors included: T0 cancer distress, trial allocation, gender, age, smoking, deprivation, education, ethnicity, marital group, time since recruitment, recruitment site and experience of lung cancer.

*Adjusted for T0 cancer distress, trial allocation, gender, age, smoking, deprivation, education, ethnicity, marital group, time since recruitment, recruitment site and experience of lung cancer.

†Data were excluded due to limited variation.

GCSE, General Certificate of Secondary Education; IMD, Index of Multiple Deprivation.

DISCUSSION
The present study is the first to report the long-term psychosocial impact of LDCT screening in a UK high-risk population. Transient negative consequences were observed in individuals allocated to LDCT screening and in those who received unfavourable screening results, but these differences were neither sustained over time nor clinically significant. However, a profile of risk factors emerged for adverse consequences of participating in lung cancer screening.

The overall findings confirm evidence from non-UK controlled trials that allocation to LDCT screening does not appear to produce long-term anxiety or other adverse effects that could potentially deter high-risk individuals from future adherence to lung screening. In studies with repeated screening such as NSLT, the majority of participants returned for further screenings. NELSON and PLCO observed minimal long-term psychosocial effects of LDCT screening. Although UKLS participants who were assigned to the control group reported slightly higher long-term anxiety and depression, the absolute differences were very small and not clinically significant. This finding may reflect unscreened participants’ disappointment or frustration at having been identified as high risk but denied the opportunity to gain reassurance from screening, supported by the finding that a greater proportion were less satisfied with their decision to participate compared with the intervention arm. Similarly, the DLCST reported negative consequences in the unscreened control arm at 1 and 2 years.7

The short-term impact of UKLS participation largely reflected temporary adverse effects of positive screening results, which disappeared by 2 years follow-up. This finding supports previous LDCT trials that indicate long-term resolution of adverse screening effects.8 9 11 Unsurprisingly, participants who were referred due to a suspected major lung abnormality reported higher short-term cancer distress than any other screening result group, with levels close to threshold scores. Those who required a repeat scan reported higher distress than those receiving an immediate ‘all-clear’ result. Higher short-term anxiety was observed in participants with a suspected major lung abnormality, but scores were within the normal range and they were also more at ease with their decision to take part in the trial. The latter finding has been reported in other screening evaluation studies, suggesting decision consolidation and the perception that further diagnostic tests have been carried out thoroughly and for personal benefit.28
Lung cancer

Individual difference variables that predicted higher levels of cancer distress over time, irrespective of trial allocation, included female gender and younger age (under 65 years). Women may feel more worried and less prepared for the prospect of lung cancer screening than men, possibly due to exposure to female cancer screening programmes and perceptions of lung cancer as a traditionally male disease. Smokers and those who had been exposed to lung cancer in their social networks were also more concerned about lung cancer. Perceived stigma and fatalism surrounding a lung cancer diagnosis are important issues, especially for smokers. This may be partly due to adverse vicarious experiences (ie, witnessing poor outcomes in family and friends with lung cancer) that influence the formation of negative beliefs and attitudes towards lung cancer screening. The links between smoking, socioeconomic deprivation and lung cancer incidence and mortality are well known and psychosocial outcomes were indeed poorer in those recruited from the Liverpool area, which is known to have high levels of deprivation and high incidence of lung cancer. Supportive interventions to improve the quality of information and care and minimise potential distress in vulnerable groups, should be implemented alongside routine LDCT lung screening. In addition, individuals with high pre-existing cancer distress could be identified for psychosocial support.

While the overall trend towards minimal psychosocial consequences of UKLS is encouraging, we acknowledge the possibility that sample selection bias may limit external validity. High-risk individuals who were older, female, smokers, from a lower socioeconomic group or more concerned about lung cancer were less likely to participate and continued to be under-represented as the trial progressed. These findings are consistent with barriers to uptake that have been reported in previous lung screening trials. The current findings suggest that women may initially be less aware or convinced of the need for lung screening, compared with breast and cervical cancers where there are well-established screening programmes. In the DLCST, trial participation was similarly associated with deprivation and age, but in contrast to our findings men were under-represented in the DLCST.

We also recognise that sample bias may have led to potential type II error in detecting long-term effects of LDCT screening, due to the relatively small number of participants with true-positive or significant incidental results. Gareen et al reported poorer health-related quality of life and higher state anxiety in NLST participants who received a lung cancer diagnosis. Some participants were excluded from screening outcomes analyses, for example, those referred but in whom lung cancer was not diagnosed. Long-term psychosocial effects in these individuals are unknown. Interestingly, there was no observed difference in distress between participants who had incidental non-lung cancer findings compared with those with negative results. However, the number of significant incidental findings may increase in routine practice compared with a trial setting. The potential for distress caused by unfavourable or unexpected findings of lung screening should not be ruled out. We acknowledge that, in future, the psychosocial consequences of lung cancer screening will need to be examined in the context of a health service (if implemented) and that the single-screen design of the UKLS trial may limit the generalisability of our findings to the context of enrolment in a routine screening programme.

LDCT lung screening is currently recommended in the US, but policy decisions in Europe await pooled data from European trials. There is an ethical imperative to promote informed participation in lung cancer screening prior to its routine implementation in the UK. Public and patient facing information materials should aim to prepare people for informed participation by increasing understanding of the purpose, benefits and risks of lung screening, including the possibility of receiving abnormal results and strategies for coping with associated short-term distress. Interventions that target smokers may improve informed participation in lung screening and provide a platform from which to engage smokers in smoking cessation services.

The present results must be interpreted alongside evidence of feasibility, cost-effectiveness and reach to determine whether LDCT lung cancer screening should become programmatic in the UK. Strategies for engaging and supporting high risk, harder to reach groups should also be trialled if lung cancer screening is to be successfully and equitably rolled out in the community setting.

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