Supplementary document

1. **Invitation and Eligibility criteria**

A letter and information leaflet, were sent to all individuals, aged 55-74, registered at participating GP practices (n=14). This invited ever smokers to book a 'Lung Health Check' (LHC) appointment in a convenient community-based location. Only a single invitation was posted without any reminders. Eligibility criteria for each step of the process are detailed below.

Invitation eligibility criteria
- **Inclusion criteria**
  - Age 55-74 (inclusive)
  - Registered at one of 14 participating General Practices in Manchester
- **Exclusion criteria**
  - Diagnosed with lung cancer within 5 years
  - Listed on a palliative care register (Gold Standards Framework)

Lung Health Check (LHC) appointment eligibility criteria
- **Inclusion criteria**
  - Ever smoker - current or former
- **Exclusion criteria**
  - Never smoker
  - Had CT thorax within 12 months of LHC appointment

Screening eligibility criteria
- **Inclusion**
  - 6-year risk of lung cancer score ≥1.51% (using $PLCO_{M2012}$ risk model)
- **Exclusion**
  - Decline screening
  - Lack capacity to consent to screening
  - Unable to have a CT scan

2. **Lung Health Check (LHC)**

LHCs were run by specialist respiratory nurses and included an assessment of respiratory symptoms, MRC dyspnoea score (range 1-5), performance status (PS, range 0-4), calculation of 6-year lung cancer risk ($PLCO_{M2012}$) (1), smoking cessation advice/signposting to stopping smoking services and measurement of spirometry. PS is a measure of general function which includes activities of daily living and fitness. As a guide, PS 0 refers to people without symptoms who can work and are fully active, whereas PS 3 refers to people who are symptomatic and confined to bed or chair more than 50% of the day. Airflow obstruction was defined as a Forced Expiratory Volume in 1 second (FEV_1) to Forced Vital Capacity (FVC) ratio <0.7. Results of all LHCs were communicated to GPs. Postcodes were recorded to determine Index of Multiple Deprivation 2015 (IMD) rank for England. This is a measure of

relative deprivation in small areas (neighbourhoods) of England; areas are ranked from 1 (most deprived) to 32,844 (least deprived) (2).

3. Lung cancer risk calculation

Variables used to determine lung cancer risk include: age, education level, ethnicity, body mass index (BMI), history of chronic obstructive pulmonary disease (COPD) / emphysema or chronic bronchitis, personal history of cancer, family history of lung cancer and measures of smoking exposure (smoking status, average number of cigarettes/day, duration of smoking and years since quitting). $PLCO_{M2012}$ was derived in the USA and required adaptation for a UK population. Educational level was modified to include 'O' Levels (General Certificate of Educational Ordinary Level) and 'A' Levels (General Certificate of Educational Advanced Level), exams taken at 16 and 18 respectively. The matching of US and UK educational attainment was undertaken in accordance with the International Standard Classification of Education (ISCED) (3).

4. Screening schedule

Annual screening, over two screening rounds, was offered to participants with a lung cancer risk score ≥1.51%, and an immediate LDCT scan, in a co-located mobile CT unit, performed. Those with a lung cancer risk score <1.51% did not qualify for screening but were provided with health promotion advice. The service took place in three separate locations (North, Central and South Manchester), for approximately 20 working days at each site, and moved from one location to another. All LDCT scans (Optima 660, GE Healthcare) used helical acquisition of axial images from lung apices to costophrenic angles, without intravenous contrast, in suspended maximal inspiration, with the patient supine and arms above head (scan time 5-10 seconds). Acquisition parameters (kVp and mAs) varied with body weight (CT dose index <3.0 millisieverts). Images were reconstructed at 1.25mm thickness and 1.25mm increments. Most CT scans were reported within 2 weeks by NHS Consultant Radiologists with an interest in thoracic radiology. Second reads were performed on a random selection of 15% and any discordance resolved at the multi-disciplinary team (MDT) meeting. A structured reporting template was used for quality assurance and to facilitate analysis.

5. Pulmonary nodule management

Pulmonary nodules were managed in accordance with British Thoracic Society (BTS) guidelines adapted for an annual screening programme (4). Nodules were measured using callipers (mean bi-dimensional diameter). Scans were categorised as negative, indeterminate or positive. The definition of a negative scan included: no evidence of malignancy ± small solid pulmonary nodule(s) (<6mm), nodules with benign features or stable pulmonary nodules (over 2-years if solid or 4-years if sub-solid). A negative CT scan was followed by annual LDCT.

Larger nodules not suitable for immediate evaluation (solid [6-7.9mm], sub-solid [≥5mm]), or at low risk of malignancy (solid [≥8mm], <10% risk using the Brock model (5)), were classified indeterminate and required a three-month surveillance scan. A positive scan was defined as any solid nodule ≥8mm with a risk of malignancy ≥10% or any other finding

concerning for malignancy requiring immediate assessment. Participants with a positive scan were assessed in the lung cancer clinic within three working days and managed in accordance with national guidelines (6). All cases with confirmed lung cancer or findings suspicious for lung cancer were reviewed in the lung cancer MDT meeting. The 7th edition of TNM lung cancer staging manual was used. Any significant other findings were communicated to the referring GP, with guidance as required.

6. Statistical analysis

The pilot was designed to screen ≈1,000 individuals and thereby detect ≈20 lung cancers, based on NLST outcomes (7). This was to provide robust information about the implementation of a lung screening service across Manchester. Stage distribution was compared with a similar aged, unscreened population in the same geographical area, the year prior to the start of the pilot. A Chi square test was used, with significance defined as a p value ≤0.05. A false positive was any screened individual referred to the cancer clinic who was not diagnosed with lung cancer. The false positive rate was expressed as either the proportion of all individuals referred from the screening service to the cancer clinic or as a proportion of everyone who had a screening scan. All participants provided written informed consent for their data to be prospectively recorded on an ethically approved database (REC Ref: 16/NW/0013). Participants who did not provide consent for the research database are not included in the analysis.

7. Invitations

In total, 16,402 individuals were sent an invitation. Analysis of smoking status, available in GP databases for 91.9% of invitees (n=15,072), demonstrated that 60.5% were classified as ever smokers. The service had a maximum capacity of 2,827 LHCs. Demand was extremely high and all available LHC appointments were booked within a few days. Almost all those who had a LHC consented to the research database (n=2,541; 99.5%). Although it is not possible to calculate uptake, because demand was much greater than service capacity, we estimate 25.6% of those eligible had a LHC. Details of individuals interested in having a LHC after service capacity was reached were not recorded.

References

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