BMJ Open Respiratory Research

Prevalence and clinical characteristics of non-malignant CT detected incidental findings in the SUMMIT lung cancer screening cohort

Sophie Tisi,[1] Andrew W Creamer ,[1] Jennifer Dickson,[1] Carolyn Horst,[1] Samantha Quaife,[2] Helen Hall,[1] Priyam Verghese,[1] Kylie Gyertson,[3] Vicky Bowyer,[3] Claire Levermore,[3] Anne-Marie Hacker,[4] Jonathon Teague,[4] Laura Farrelly,[4] Arjun Nair,[3] Anand Devaraj,[5,6] Allan Hackshaw,[4] John R Hurst,[7] The SUMMIT Consortium, Samuel Janes[1]

To cite: Tisi S, Creamer AW, Dickson J, *et al*. Prevalence and clinical characteristics of non-malignant CT detected incidental findings in the SUMMIT lung cancer screening cohort. *BMJ Open Respir Res* 2023;**10**:e001664. doi:10.1136/bmjresp-2023-001664

► Additional supplemental material is published online only. To view, please visit the journal online (http://dx.doi.org/10.1136/bmjresp-2023-001664).

Received 8 February 2023
Accepted 26 May 2023

For numbered affiliations see end of article.

Correspondence to
Dr Samuel Janes;
s.janes@ucl.ac.uk

ABSTRACT

Background Pulmonary and extrapulmonary incidental findings are frequently identified on CT scans performed for lung cancer screening. Uncertainty regarding their clinical significance and how and when such findings should be reported back to clinicians and participants persists. We examined the prevalence of non-malignant incidental findings within a lung cancer screening cohort and investigated the morbidity and relevant risk factors associated with incidental findings. We quantified the primary and secondary care referrals generated by our protocol.

Methods The SUMMIT study (NCT03934866) is a prospective observational cohort study to examine the performance of delivering a low-dose CT (LDCT) screening service to a high-risk population. Spirometry, blood pressure, height/weight and respiratory history were assessed as part of a Lung Health Check. Individuals at high risk of lung cancer were offered an LDCT and returned for two further annual visits. This analysis is a prospective evaluation of the standardised reporting and management protocol for incidental findings developed for the study on the baseline LDCT.

Results In 11 115 participants included in this analysis, the most common incidental findings were coronary artery calcification (64.2%) and emphysema (33.4%). From our protocolised management approach, the number of participants requiring review for clinically relevant findings in primary care was 1 in 20, and the number potentially requiring review in secondary care was 1 in 25.

Conclusions Incidental findings are common in lung cancer screening and can be associated with reported symptoms and comorbidities. A standardised reporting protocol allows systematic assessment and standardises onward management.

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ Incidental findings are common in CT scans performed in lung cancer screening.

⇒ Protocolised approaches to incidental findings have recently been developed, but the outcomes of such approaches have not been reported in prospective large-scale screening programmes.

WHAT THIS STUDY ADDS

⇒ Despite incidental findings being identified in over two-thirds of participants, a protocolised approach to non-malignant incidental findings on lung cancer screening CT scans led to review for only 1 in 20 and 1 in 25 participants in primary and secondary care, respectively.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ Protocolised approaches to the reporting of incidental findings in lung cancer screening are essential for the successful implementation of population-level screening in a manner acceptable to participants and demand on downstream primary and secondary care services.

While low-dose CT (LDCT) screening for lung cancer has been demonstrated to reduce lung cancer-associated mortality,[1 2] uncertainty regarding aspects of screening continues to cause hesitancy to widespread implementation.[3] While the primary aim of lung cancer screening (LCS) is to identify pulmonary nodules that may represent early lung cancer, LDCT of the thorax may detect other pulmonary and extrapulmonary abnormalities. For some findings such as renal or adrenal nodules, mediastinal masses or breast lumps, the possibility of an extrapulmonary malignancy may be raised, whereas other findings may be clearly non-malignant, but still be potentially associated with morbidity or mortality. Cardiovascular and non-malignant chronic respiratory disease are known to account for substantial mortality and morbidity in LCS cohorts,[1 2 4 5] and identifying relevant findings on LDCT may offer

scope for opportunities to address underdiagnosis with targeted clinical and behavioural intervention.

The reported prevalence of incidental findings at LCS has been estimated to be between 8% and 40%,[6–8] although published evidence has been confused by varying definitions of what constitutes a 'clinically relevant' finding and a lack of standardised reporting of incidentals.[3] Concerns regarding the financial and workload cost of indiscriminate referrals to primary and secondary care for screen-detected findings have been identified as a potential hurdle to the implementation of population-level screening.[3 9 10] The importance of developing an approach to managing such findings is heightened following the recent decision by the UK National Screening Committee to support the introduction of LDCT screening for lung cancer in the UK[11] While the National Health Service (NHS) targeted lung health check (TLHC) has recently published a protocol covering the management of incidental findings,[12]the outcomes in terms of frequency of findings reported and downstream referrals generated to primary and secondary care of such approaches have not been reported in a prospective large scale screening context.

The SUMMIT study (NCT03934866) is an LCS implementation study, where participants at high risk for lung cancer are invited to three annual LHC with LDCT screening. A protocolised approach to management of non-malignant incidental findings was developed based on a systematic review of existing evidence.[13] Common findings are recorded in a structured manner and a prespecified management approach was developed for each finding.

The aims of this analysis were to (1) examine the prevalence of non-malignant incidental findings within an LCS cohort as assessed by a prespecified, standardised format; (2) explore the characteristics of each incidental finding in terms of association with clinical features and known risk factors for the condition and (3) examine the downstream impact on referrals to primary and secondary care.

METHODS

Summit study design

The SUMMIT study is a prospective observational cohort study to examine the performance of delivering an LDCT screening service to a high-risk population in London and to validate a multicancer early detection blood test. Consented individuals aged 55–77 at high risk of lung cancer, defined as meeting US Preventative Services Task Force 2013 criteria (at least 30 pack year history and if a former smoker has not given up longer than 15 years ago[14] or with Prostate Lung Colorectal Ovarian modified 2012 lung cancer risk of ≥1.3%[15] were offered an LDCT and will return for two further annual visits. This study reports an analysis of all those who attended a baseline study visit from the opening of recruitment in April 2019 to a temporary pause to recruitment in March 2020 following the SARS-CoV-2 pandemic.

Study procedures

LDCT scans were kept below 2 mSv and were non-ECG gated. Scans were performed in the supine position at maximal inspiration. LDCT scans were reported by thoracic radiologists using a bespoke template allowing categorisation of pulmonary nodules and incidental findings (online supplemental appendix 1).

Similar to other LCS studies in the UK,[4 16 17] the SUMMIT screening programme used an LHC model which included spirometry as routine for all participants (unless contraindicated). Prebronchodilator quality-assured spirometry was performed using the Vitalograph Micro spirometer. Subjects prescribed existing bronchodilators were not asked to withhold these. Attendees were encouraged to perform three manoeuvres guided by research practitioners trained to the Association for Respiratory Technology and Physiology standards.[18] The highest value was recorded with measurements and associated reference values (Global Lung Function Initiative[19]) collected for forced expiratory volume in 1 s (FEV1, forced vital capacity (FVC) and the calculated FEV1/FVC ratio.

A targeted consultation was undertaken to screen for the presence of respiratory symptoms and common respiratory comorbidities (online supplemental appendix 2). Detailed data were collected around lung cancer risk factors. Height, weight and blood pressure were measured. Participants additionally completed an electronic questionnaire which contained questions about general health and lifestyle including any previous exposure to relevant occupational exposures. All current smokers were given Very Brief Advice on smoking cessation and offered referral to local smoking cessation services.

Incidental findings management protocol

During the development of the SUMMIT Study, a standardised management approach for common incidental findings was developed, which has been previously published.[13] This protocolised approach to management of non-malignant incidental findings was developed based on a systematic review of existing evidence[13] and relevant clinical guidelines and sought to deliver a pragmatic, evidence-based approach which was practically deliverable by primary and secondary care. Table 1 is adapted from our previous publication (Horst *et al*[13]) and outlines the assessment criteria and subsequent management actions undertaken for each finding.

Statistical analysis

The prevalence of incidental findings among the whole cohort on baseline LDCT was assessed, and individual comparative analyses were undertaken for each incidental

Table 1 SUMMIT protocolised incidental findings management protocol

Incidental finding and assessment criteria		Onward clinical action
Incidental findings of the pulmonary parenchyma:		
Emphysema		
Qualitative grading by visual assessment of extent of lung affected	Mild (>5%–25%)	Research purposes only
	Moderate (>25%–50%)	
	Severe (>50%–75%)	
	Very severe (>75%)	
Bronchiectasis		
Visual grading based on luminal diameter relative to the accompanying artery diameter	Mild (1.5–2×larger)	Research purposes only
	Moderate (2–3×larger)	
	Severe (>3×larger)	PCP to assess patient and consider referral to secondary care
Interstitial lung abnormality		
Visual assessment of extent of interstitial reticulation and presence or absence of fibrotic features	Mild (<10% reticulation)	Research purposes only
	Moderate (>10% reticulation with no fibrosis)	
	Severe (>10% reticulation with fibrotic features present)	PCP to assess patient and consider referral to secondary care
Cardiovascular incidental findings		
Coronary artery calcification (CAC)		
Each territory (the circumflex, the right coronary artery and the left main plus left anterior descending artery) was assigned a score based on its CAC level: none (0 points), mild (1 point), moderate (2 points) or severe (3 points). Combining the score per territory gave a total overall score out of nine for CAC[44 45]	Mild (1–3)	Research purposes only
	Moderate (4–6)	
	Severe (7–9)	
Thoracic aortic aneurysm		
Calliper measurement of the widest diameter of the ascending thoracic aorta[20 46] defined as diameter ≥5.0 cm of the ascending aorta or ≥4.0 cm of the descending aorta[46]	4.0–5.5 cm	PCP to refer to secondary care
	>5.5 cm	Direct referral to vascular surgery
Abdominal aortic aneurysm		
Measurement of widest diameter of the abdominal aorta[47]	≥3–5 cm	PCP to refer non-urgently to vascular surgery
	≥ 5 cm	Direct referral to vascular surgery
Aortic valve calcification		
Radiologist assessment of whether the central or peripheral half of valve commissures had calcification present[48]	Central	Research purposes only
	Peripheral	
	Both	
Other incidental findings		
Osteoporotic wedge fracture		
Visual assessment of extent of loss of vertebral height	≥50%	PCP to refer for bone density assessment
	<50%	Research purposes only
Pleural findings		
Pleural plaques recorded as present or absent Diffuse pleural thickening refers to a diffuse process with no radiological suspicion of malignancy and was recorded as present or absent (unilateral pleural effusions and unilateral or focal pleural thickening were referred to lung MDT for immediate workup as potential cancer)	Bilateral Pleural Effusions[49]	PCP review
	Diffuse pleural thickening	Annual SUMMIT LDCT
	Pleural plaques	Research purposes only
Hiatus hernia		
	Present	Research purposes only

LDCT, low-dose CT; MDT, multi-disciplinary team; PCP, primary care provider.

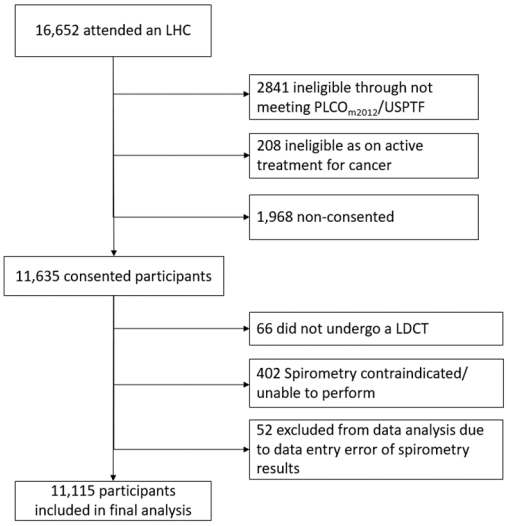

Figure 1 CONSORT (Consolidated Standards of Reporting Trials) diagram. LDCT, low-dose CT; LHC, lung health check; $PLCO_{m2012}$, Prostate Lung Colorectal Ovarian modified 2012; USPSTF, United States Preventive Services Task Force.

finding. Differences between groups (presence and absence of the incidental finding) were assessed using the two-sample independent t-test (parametric data) and Mann-Whitney U test (non-parametric data) for continuous variables, and χ^2 test for categorical data. Statistical significance was defined through p values less than 0.05. Individual univariate and multivariable binary logistic regression analyses were performed to assess the risk of each incidental finding and with adjusted ORs calculated using data on known risk factors associated with that finding. Analysis was performed using SPSS (V.25) and R (V.4.1).

Public and patient involvement

The protocol, study design and supporting documents for this study underwent review by a participant and public involvement group on several occasions. The invitation materials, participant information sheet, consent form and results letters have been reviewed in detail. Invitation letters were reviewed by patient and public representatives for their readability and acceptability. This was an ongoing process and several of the members of this group continue to be involved by being included on the study steering committee.

RESULTS

Baseline characteristics of the cohort

Of 16 6652 attendees to an LHC, 13 633 were eligible for inclusion in the study based on predicted lung cancer risk, of which 11 115 consented to baseline LDCT and underwent spirometry and were included in the final analysis (figure 1).

The demographic characteristics of the total cohort (n=11 115) are outlined in table 2. The mean age of the cohort was 65.35 years (SD 6.11), 57.5% were male and 48.6% were current smokers.

Table 2 Baseline characteristics of cohort

Characteristic	Value
Age (years)	65.35 (±6.11)
% Male	57.5% (n=6386)
Ethnicity	
White	83.8% (n=9259)
Mixed	2.2% (n=250)
Asian	6.7% (n=743)
Black	4.4% (n=484)
Other	3.4% (n=379)
Education level	
Finished school before 16*	39.5% (n=4389)
High school	23.6% (n=2618)
College	10.9% (n=1216)
Further education	8.4% (n=932)
Bachelors degree	12.6% (n=1296)
Further degree	5.1% (n=564)
IMD quintile	
(Most deprived) 1	31.7% (n=3519)
2	28.7% (n=3190)
3	17.6% (n=1961)
4	15.2% (n=1695)
(Least deprived) 5	5.2% (n=574)
Pack years	45.31 (±23.00)
Current smoker? (yes, %)	48.6% (n=5397)
BMI (kg/m^2)	28.14 (±9.50)
Systolic BP (mm Hg)	134.08 (±17.61)
Diastolic BP (mm Hg)	79.97 (±10.40)
Airflow obstruction (%)†	49.5% (n=5497)
Personal history of cancer	13.3% (n=1474)
Family history of cancer	19.0% (n=2107)
Median $PLCO_{m2012}$ score	3.08% (1.87%–5.55%)

*In cases where education level was not given this was recorded as 'finished school before 16'.
†Airflow obstruction defined as prebronchodilator FEV1/FVC ratio of <0.7.
BMI, body mass index; BP, blood pressure; FEV1, forced expiratory volume in 1 s; FVC, forced vital capacity; IMD, index of multiple deprivation; $PLCO_{m2012}$, Prostate Lung Colorectal Ovarian modified 2012.

Frequency of non-malignant incidental findings

Table 3 summarises the prevalence of individual incidental findings within the total cohort and where appropriate a breakdown of the grade of incidental. The most common radiological findings in the cohort were

Table 3 Prevalence of non-malignant incidental findings on baseline LDCT

Incidental finding	LDCT presence (n and % of total cohort)
Emphysema	
TOTAL	3711 (33.4)
Mild	2423 (21.8)
Moderate	900 (8.1)
Severe	331 (3.0)
Very severe	57 (0.5)
Bronchiectasis	
Total	818 (7.4)
Mild	711 (6.4)
Moderate	91 (0.8)
Severe	16 (0.14)
Interstitial lung abnormality	
Total	528 (4.8)
Mild	354 (3.2)
Moderate	62 (0.6)
Severe	112 (1.0)
Coronary artery calcification	
Total	7141 (64.2)
Mild	4035 (36.3)
Moderate	2049 (18.4)
Severe	1057 (9.5)
Thoracic aortic aneurysm	
Total	306 (2.8)
4.0–5.5 cm	301 (2.7)
>5.5 cm	5 (0.1)
Abdominal aortic aneurysm	
Total	2
≥3–5 cm	1
>5 cm	1
Aortic valve calcification	
Total	1808 (16.3)
Central	409 (3.7)
Peripheral	962 (8.7)
Both	437 (3.9)
Osteoporotic wedge fracture	
Total	801 (7.2)
≥50%	132 (1.2)
<50%	669 (6.0)
Pleural findings	
Bilateral pleural effusions	7 (0.06)
Diffuse pleural thickening	92 (0.82)
Pleural plaques	599 (5.4)
Hiatus hernia	
Present	1064 (9.6)

LDCT, low-dose CT.

coronary artery calcification (CAC) (64.2%) and emphysema (33.4%).

Emphysema

Emphysema was present in 33.4% (n=3711) of the total cohort; of which in the majority (65.3%, n=2423) was mild (affecting <25% of the total lung). Participants with emphysema had a higher respiratory symptom burden, being more likely to report persistent cough (28.3% vs 21.9%, p<0.001), sputum production (19.6% vs 13.7%, p<0.001), breathlessness (Medical Research Council (MRC) dyspnoea score >1 70.5% vs 63.9%, p<0.001) and respiratory infection frequency (≥2 exacerbations/year 10.1% vs 6.5%, p<0.001, than those without emphysema, online supplemental table A).

While the prevalence of emphysema was higher in those with airflow obstruction than without (67.3% vs 40.1%, p<0.001), 32.3% of participants with radiological emphysema did not have airflow obstruction. Participants with emphysema were more likely to report an existing diagnosis of chronic obstructive pulmonary disease (COPD) (52.3% vs 31.6%, p<0.001), although 47.7% of participants with radiological emphysema did not report a prior diagnosis of COPD.

Multivariate logistic regression analyses demonstrated that increasing age, increasing pack year history and current smoking status were all significantly associated with increased risk of emphysema on baseline LDCT (table 4).

Bronchiectasis

Bronchiectasis was identified in 7.3% (818) of the total population. 87% of cases were classed as mild (711/818), with 13% (107/818) classed as moderate or severe (severity classifications as defined in table 1). Only 1.7% (n=14) of those with evidence of bronchiectasis on LDCT self-reported a previous diagnosis of bronchiectasis.

Participants with bronchiectasis on LDCT had a higher respiratory symptom burden than those without bronchiectasis, being more likely to report persistent cough (27.6% vs 23.8%, p=0.013) and sputum production (18.8% vs 15.4%, p=0.009, online supplemental table B). Our protocol only reports severe bronchiectasis to primary care providers (PCPs); compared with participants with mild or moderate bronchiectasis this group were more likely to report persistent cough (43.4% vs 27.3%, p=0.24) and sputum production (31.3% vs 18.6% p=0.336), although this did not reach statistical significance.

The association of radiological bronchiectasis and known risk factors were analysed by binary logistic regression analysis (online supplemental table C). Increasing age, increasing number of respiratory infections in the past year, a history of TB and a history of previous pneumonia were all demonstrated to be independent risk factors for bronchiectasis on multivariate analysis.

Table 4 Emphysema: univariate and multivariate binary logistic regression analyses of factors associated with the presence on baseline LDCT

Variable	Unadjusted OR (95% CI)	P value	Adjusted OR (95% CI)	P value
Age				
Per increasing year	1.037 (1.031 to 1.044)	<0.001	1.025 (1.018 to 1.032)	<0.001
Gender				
Female	1		1	
Male	1.074 (0.991 to 1.163)	0.081	1.051 (0.966 to 1.144)	0.245
Smoking status				
Former smoker	1		1	
Current smoker	1.186 (1.096 to 1.283)	<0.001	1.219 (1.120 to 1.326)	<0.001
Pack year history				
Per increasing pack year	1.007 (1.005 to 1.009)	<0.001	1.005 (1.003 to 1.007)	<0.001
Airflow obstruction				
No airflow obstruction	1		1	
Airflow obstruction	3.118 (2.870 to 3.388)	<0.001	2.888 (2.652 to 3.144)	<0.001

LDCT, low-dose CT.

Interstitial lung abnormalities

A total of 528 (4.8%) of the total cohort had evidence of interstitial lung abnormality (ILA) on LDCT with only 6 (1.1%) of these participants reporting a previous diagnosis of an interstitial lung disease (ILD). Participants with ILAs were slightly older (67.52±6.03 vs 65.24±65.24, p<0.001) and were more likely to be male (64.6% vs 57.1%, p=0.001) than those without ILAs (online supplemental table D). There was no difference in levels of current smoking or pack year history between those with and without ILAs on LDCT. There was no difference in respiratory symptoms of persistent cough (26.1% vs 23.9%, p=0.248) or breathlessness (MRC score ≥1 67.4% vs 66.0%, p=0.513).

On univariate and multivariate analyses, the presence of ILAs was independently associated with age, male gender (adjusted odds ratio (AdjOR) 1.272, 95% CI 1.047 to 1.546) and occupational asbestos exposure (adjOR 1.293, 95% CI 1.033 to 1.618) (online supplemental table E).

Other pulmonary incidental findings

Miscellaneous pulmonary incidental findings included suspected mycobacterial infection (tuberculosis or non-tuberculosis mycobacterium in 8 participants (0.07%) and identification of other likely pulmonary conditions in 10 participants (0.09%, including suspected sarcoidosis, pleuroparenchymal fibroelastosis and pulmonary hypertension). Pleural plaques were found in 5.4% (n=599) and diffuse pleural thickening in 0.8% (n=92). Bilateral pleural effusions were found in seven participants (0.06%).

Coronary artery calcification

CAC was present in 64.2% (n=7141) of the total cohort (online supplemental table F); which was mild in 56.5% (N=4035), moderate in 28.7% (2,049) and severe in 14.8% (N=1057). On multivariate logistic regression analysis, increasing age, body mass index (BMI), pack year history, elevated systolic blood pressure and current smoking were all significantly associated with the presence of CAC (table 5).

Aortic aneurysms

Thoracic aortic aneurysms (TAA) were identified in 2.8% (N=306) of participants, of which 301 (2.7%) were 4.0–5.5 cm and 5 (0.04%) were >5 cm in diameter. Participants with aortic aneurysms were more likely to be male (69.9% vs 57.1%, p<0.001) and older (mean age 66.64 years (±9.75) vs 65.32 (±10.0), p<0.001) (online supplemental table G). On logistic regression analysis age, diastolic blood pressure and male gender remained independent risk factors for the presence of TAA on multivariable models (online supplemental table H).

Other cardiovascular incidental findings

Aortic valve calcification was present in 16.3% (N=1808) of participants. Pericardial effusions >2 cm were found in three participants.

Vertebral wedge fractures

Osteoporotic wedge fractures were present in 801 (7.2%) of all individuals (online supplemental table I), with 132 (1.2%) measuring greater than 50% loss and 669 (6.0%) measuring less than 50% loss of vertebral

Table 5 Coronary artery calcification: univariate and multivariate binary logistic analysis assessing the relationship between associated variables and presence on baseline LDCT

Variable	Unadjusted OR (95% CI)	P value	Adjusted OR (95% CI)	P value
BMI				
Per increasing kg/m^2	1.01 (1.00 to 1.01)	0.051	1.01 (1.00 to 1.01)	0.037
Age				
Per increasing year	1.10 (1.09 to 1.10)	<0.001	1.09 (1.09 to 1.10)	<0.001
Gender				
Female	1		1	
Male	2.46 (2.27 to 2.66)	<0.001	2.57 (2.35 to 2.81)	<0.001
Blood pressure				
Systolic BP	1.01 (1.01 to 1.01)	<0.001	1.01 (1.01 to 1.01)	<0.001
Diastolic BP	0.994 (0.990 to 0.997)	0.001	0.99 (0.98 to 0.99)	<0.001
Smoking status				
Current smoker	1		1	
Former smoker	1.15 (1.07 to 1.24)	<0.001	1.11 (1.01 to 1.20)	0.023
Pack year history				
Per increasing pack year	1.01 (1.01 to 1.01)	<0.001	1.00 (1.00 to 1.01)	0.001
Ethnicity				
Other	1		1	
White	1.37 (1.12 to 1.69)	0.003	1.46 (1.17 to 1.82)	0.001
Mixed	0.97 (0.70 to 1.33)	0.832	1.27 (0.90 to 1.79)	0.182
Asian	2.29 (1.76 to 2.97)	<0.001	1.88 (1.42 to 2.48)	<0.001
Black	0.65 (0.50 to 0.87)	0.002	0.69 (0.51 to 0.92)	0.010
Airflow obstruction				
No airflow obstruction	1		1	
Airflow obstruction	1.29 (1.20 to 1.40)	<0.001	1.07 (0.98 to 1.16)	0.138

BMI, body mass index; BP, blood pressure; LDCT, low-dose CT.

height. Known risk factors for osteoporotic fractures were assessed in logistic regression models (online supplemental table J). Increasing age and low BMI remained independent risk factors for the presence of vertebral wedge fractures on multivariate models. Gender, pack year history and personal history of cancer were not found to have a statistically significant association with presence of vertebral fractures. Airflow obstruction was an independent risk factor for the presence of vertebral fracture. (adjusted OR 1.26; 95% CI 1.08 to 1.46, p=0.003).

Hiatus hernia

Hiatus hernias were identified in 9.6% (n=1064) of the cohort (online supplemental table K). Binary logistic regression analysis demonstrated that increasing age, female gender and airflow obstruction remained independent risk factors on multivariate analysis (online supplemental table L).

Implications for primary and secondary care

Our referral policy divided actionable incidental findings into three categories: PCP to manage directly, PCP to assess and consider referral to secondary care, and direct referral to relevant secondary care (table 1). Incidental findings identified on LDCT covered by our management protocol generated a total of 139 (1.3%) referrals for PCP assessment (osteoporotic wedge fractures and bilateral pleural effusions) and 430 (3.6%) referrals for PCP assessment and onward referral (302 referrals for TAA (2.7%) and 128 (1.15%) referrals to respiratory clinics for severe bronchiectasis or ILAs). Six (0.05%) referrals were made directly to secondary care for aortic aneurysms above threshold diameter.

This is in addition to the suspected new pulmonary conditions and pericardial effusions outlined above; these findings were highlighted to physicians working on the study who contacted the participant directly to assess clinical context and arrange appropriate secondary care referral.[20]

DISCUSSION

We report the prevalence of pulmonary, cardiovascular, and other non-malignant incidental findings identified on LDCT in a large LCS cohort as captured by a protocolised approach to identification and management. By interrogating each finding against known risk factors and reported symptoms we provide a clinical context; highlighting associated morbidity and identifying potentially modifiable risk factors. Finally, by having a standardised management protocol, we can quantify the downstream workload created for primary and secondary care, aiming to maximise the benefit of LDCT in LCS. Our results represent the first analysis of outcomes of a prospectively implemented incidental findings protocol in a large, diverse screening cohort. While there are minor divergences between our protocol and that used by the NHS TLHC programme,[12] the extent of overlap means our results are highly translatable to anticipating primary and secondary care referrals generated by the imminent national screening programme.[11]

Comparison to other incidental finding management protocols

Since the SUMMIT study started in early 2019, a number of other management protocols for incidental findings have been published, including the NHS England Quality Assurance standards for the TLHC Programme (V.2, 2022)[12] and the American College of Radiology (ACR) white paper (2021).[21] These follow a similar approach to the SUMMIT protocol in terms of distinguishing between findings, which require no further assessment, those requiring assessment by primary care and those warranting specialist opinion. In keeping with the different audiences (clinical screening rather than a research cohort and in different healthcare systems), there are a number of minor discrepancies between these protocols and the SUMMIT approach in how individual findings should be acted on. Nevertheless, our approaches are similar enough for our results to be of use in both understanding the prevalence of non-malignant incidental findings in a lung cancer cohort and in predicting the downstream demand on primary and secondary care services such an approach will generate. Our protocolised management for common incidental findings generated referrals to primary care for 1 in 20 participants (5.1%), and to secondary care for 1 in 25 (1.1% for pulmonary and 2.8% for cardiology/vascular). This is in addition to referrals made for spirometry indicative of undiagnosed COPD, the universal advice to assess QRISK2, and uncommon miscellaneous pulmonary and extrathoracic findings. It is also in addition to findings suspicious for an extrapulmonary malignancy (eg, liver, breast or thyroid nodules) which are referred directly to the relevant secondary care team for further investigation; an analysis of referrals and subsequent diagnostic yield is a planned future publication.

Clinical significance of radiological incidental findings and opportunities for intervention

Both the SUMMIT protocol and the subsequently published guidelines recognise that there is a distinction between clinically significant incidental findings with established management interventions (such as aortic aneurysms, osteoporotic fractures and bronchiectasis), and findings which may have associated morbidity or prognostic implications, but where at present no evidence exists for specific intervention based purely on radiological findings. Our approach is to report findings in the former category back to PCPs to allow appropriate intervention, while systematically recording the latter for future research purposes without burdening the PCP or participant with knowledge of a finding for which consensus on an evidence-based intervention does not exist.

One area of divergence between the SUMMIT protocol and the ACR white paper and the NHS protocol is the presence of emphysema, with both ACR and the NHS TLHC guidelines advising the finding should prompt 'consideration' of referral to community teams. The diagnosis of COPD is made on airflow obstruction in the context of an appropriate exposure and symptoms,[22] with UK guidelines advising that incidental identification of emphysema on imaging should prompt consideration of spirometry.[23] As spirometry is already part of our LHCs, our protocol was, therefore, not to report emphysema seen on LDCT. While this is in keeping with current UK guidelines and aims to avoid burdening general practitioners and patients with knowledge of a finding for which there is no specific intervention, we acknowledge further research may show benefit in reporting this back. For example, we found that current smoking is a risk factor for the presence of emphysema. Reporting this finding may, therefore, be an opportunity to support those with long-term tobacco dependence with smoking cessation, an approach currently being explored in the Yorkshire Enhanced Stop Smoking trial.[24] It is widely recognised that there is systematic underdiagnosis of COPD,[25] and LCS offers an opportunity to improve diagnosis in a population at risk of this condition. In the UK, the LHC model of delivering LCS with routine spirometry performed for all participants is widely used,[16 17] and is part of the standard protocol for the NHS TLHC programme.[26] However, we recognise that international approaches to LCS may vary, and therefore, agree that in screening programmes where the LHC does not include spirometry, emphysema should be reported back to the PCP with the suggestion to perform spirometry.

Conversely, as the diagnosis of bronchiectasis is made radiologically,[27 28] the combination of this finding with associated symptoms reported at LHC is sufficient to suggest this diagnosis. The correlation with both known risk factors[27 28] and higher rates of symptoms attributable to the condition in our cohort supports that this was a clinically significant finding. With less than 2% of participants with bronchiectasis on LDCT reporting an existing diagnosis, our results suggest significant undiagnosed disease in this cohort, which could be improved by systematic identification at LCS, justifying our approach to reporting this when present. Our approach matches

that of the NHS TLHC protocol, although the NHS TLHC protocol prompts consideration of referral if symptomatic and 'moderate' bronchiectasis is present, rather than just 'severe'.

ILAs refer to specific CT findings potentially compatible with ILD identified in patients without clinical suspicion of the disease.[29] Shared risk factors for ILD and lung cancer make screening cohorts at elevated risk for the condition, and LCS may offer the opportunity for early diagnosis. However, although the presence of ILAs has been demonstrated to be associated with impaired pulmonary function parameters[30] and increased all cause mortality,[31] the natural history and optimal management of these findings remains uncertain.[29] Unlike bronchiectasis and emphysema, we found no difference in respiratory symptoms reported in participants with ILA compared with those without. Our management protocol reflects the increased risk of progression with established fibrosis identified in other studies.[32] Since SUMMIT started Fleichner society guidelines have been published on diagnosis and investigating ILAs[29]; future screening studies may wish to use these recommendations as a basis for management of ILA identified in screening.

While several studies have identified an association of CAC with all-cause mortality and cardiovascular events,[33 34] the evidence is still unclear as to what, if any, specific therapies may be of benefit in this cohort beyond general measures to reduce cardiovascular risk.[35 36] Consistent guidelines are therefore lacking in whether there is any benefit in reporting specific CAC results at LCS.[37] In line with British[36] and US guidelines,[38] SUMMIT radiologists report the presence and severity of CAC. However, we do not feed this back to PCPs or participants; instead, PCPs are informed all participants are likely to be at elevated risk of cardiovascular disease and advised to assess QRISK score.[39] There are several reasons we adopted this approach. First, use of QRISK score to decide on introduction of statin therapy is advocated by national guidelines.[40] Second, previous research has shown that the overwhelming majority (93%–98%)[5 41] of participants in LCS programmes have a QRISK score of ≥10% (the threshold for statin therapy for primary prevention[40]); individualised reporting is therefore arguably superfluous and risks overwhelming PCPs with information. In the ACR guidelines,[20] the presence of CAC gives a recommendation for PCP evaluation of cardiovascular disease risk; the same action that is advised for all of our participants. However, we recognise that this differs to some US guidelines, where the presence of moderate or severe CAC as an incidental finding warrants initiation of statin therapy.[38] Further research is needed to understand the precise role incidentally detected CAC may have in decisions to start lipid-lowering therapy.

Although USPSTF guidelines for osteoporosis screening found insufficient evidence to support this in men,[42] in our population of previous or current smokers there was no difference between genders and risk of vertebral fractures. In the UK, the NICE guidelines advise that all females over 65 and men over 75 should be screened for osteoporosis.[43] While screening in men under the age of 75 is advocated in the presence of risk factors such as smoking and secondary causes of osteoporosis such as COPD, these associations are often unrecognised and many men in these categories may not be assessed for fragility fractures. Eighty-eight per cent of the men in our population who had a vertebral fracture were under the age of 75 and so would not meet routine criteria for osteoporosis screening. Additionally, 29% of women with vertebral fractures were under the age of 65. Therefore, there may be increased utility in vertebral wedge fracture identification in the LCS population particularly in men who would not be identified via routine national osteoporosis screening.

Limitations

While self-reported data were collected on the presence of certain respiratory conditions, participants were not asked about the presence of other comorbidities or current medications, and this self-reported data were not validated against participants hospital or primary care records. While this streamlines the time taken for an LHC appointment to be completed, it limits the ability to determine whether the findings identified were truly incidental or already known about. Consideration must also be given to the potential harms of this approach, particularly psychological; anxiety may be provoked by the identification of unexpected findings and the subsequent diagnostic workup that may follow.

We do not at present have data on how many appointments were made or attended, nor any data on subsequent changes in management. One reason for this is that participants were recruited immediately prior to the COVID-19 pandemic and resulting severe disruption to health services. The time to subsequent healthcare appointments and changes in clinical management during the nationwide lockdown of 2020 are, therefore, unlikely to be representative, and we have, therefore, chosen to present the data in terms of referrals generated, rather than those attended. Data from a UK LCS pilot found that following a referral to primary care for a finding identified at LHC, a change in management was made in 22.6% of participants.[9] However, the proportion of participants who actually attended a primary care appointment following this referral was relatively low, with between 33.3% and 57.1% (depending on the finding in question) not attending. These results, therefore, highlight that consideration needs to be given not only on how incidental findings are fed back to PCPs, but also to the participants themselves.

Future research and feasibility for population level screening

While the data presented here identifies participants who may have potential to benefit from identification of incidental findings and quantifies the downstream impact on primary and secondary care services, a more

fundamental question is whether this leads to any clinical utility. Future work within the SUMMIT Study will enable the collection of longer-term data from primary and secondary care to more accurately assess the downstream clinical impact of our approach. Furthermore, while outside of the scope of this analysis, the impact of identifying potential extrathoracic malignant findings on LDCT screening is an additional important future research outcome from the SUMMIT study.

We acknowledge that since the development of the SUMMIT study protocol guidelines for the management of incidental findings have been developed, which vary between countries based on populations and healthcare systems.[12 21] Nevertheless, our findings report the first large-scale prospective implementation of such a standardised approach, feasible at a large scale, which highlights clinically significant findings while minimising extraneous information. Our results describe the demands on primary and secondary care generated by such an approach, and as such are translatable in predicting likely demand generated by the imminent UK screening programme. Such approaches are an essential component of successfully implementing population-level screening.

Author affiliations
[1]Lungs for Living Research Centre, UCL Respiratory, University College London, London, UK
[2]Wolfson Institute of Population Health, Queen Mary University of London, London, UK
[3]University College London Hospitals NHS Foundation Trust, London, UK
[4]Cancer Research UK and UCL Cancer Trials Centre, University College London, London, UK
[5]National Heart and Lung Institute, Imperial College London, London, UK
[6]Royal Brompton and Harefield NHS Trust, London, UK
[7]UCL Respiratory, University College London, London, UK

Collaborators Sam M Janes, Jennifer L Dickson, Carolyn Horst, Sophie Tisi, Helen Hall, Priyam Verghese, Andrew Creamer, Thomas Callender, Ruth Prendecki, Amyn Bhamani, Mamta Ruparel (Lungs For Living Research Centre, UCL Respiratory, University College London, London), Allan Hackshaw, Laura Farrelly, Jon Teague, Anne-Marie Mullin, Kitty Chan, Rachael Sarpong, Malavika Suresh (CRUK & UCL Cancer Trials Centre, University College London, London), Samantha L Quaife (Centre for Prevention, Detection and Diagnosis, Wolfson Institute of Population Health, Barts and The London School of Medicine and Dentistry, Queen Mary University of London, London), Arjun Nair (University College London Hospitals NHS Foundation Trust, London), Anand Devaraj (Royal Brompton and Harefield NHS Foundation Trust, London. National Heart and Lung Institute, Imperial College, London), Kylie Gyertson, Vicky Bowyer, Ethaar El-Emir, Judy Airebamen, Alice Cotton, Kaylene Phua, Elodie Murali, Simranjit Mehta, Janine Zylstra, Karen Parry-Billings, Columbus Ife, April Neville, Paul Robinson, Laura Green, Zahra Hanif, Helen Kiconco, Ricardo McEwen, Dominique Arancon, Nicholas Beech, Derya Ovayolu, Christine Hosein, Sylvia Patricia Enes, Qin April Neville, Jane Rowlands, Aashna Samson, Urja Patel, Fahmida Hoque, Hina Pervez, Sofia Nnorom, Moksud Miah, Julian McKee, Mark Clark, Jeannie Eng, Fanta Bojang, Claire Levermore (University College London Hospitals NHS Foundation Trust, London), Anant Patel (Royal Free London NHS Foundation Trust, London), Sara Lock (Whittington Health NHS Trust, London), Rajesh Banka (Barking, Havering and Redbridge University Hospitals NHS Trust, Essex), Angshu Bhowmik (Homerton University Hospital Foundation Trust, London), Ugo Ekeowa (The Princess Alexandra Hospital NHS Trust, Essex), Zaheer Mangera (North Middlesex University Hospital NHS Trust, London), William M Ricketts (Barts Health NHS Trust, London), Neal Navani (University College London Hospitals NHS Foundation Trust, London), Terry O'Shaughnessy (Barts Health NHS Trust, London), Charlotte Cash (Royal Free London NHS Foundation Trust, London), Magali Taylor (University College London Hospitals NHS Foundation Trust, London), Samanjit Hare (Royal Free London NHS Foundation Trust, London), Tunku Aziz, Stephen Ellis (Barts Health NHS Trust, London), Anthony Edey (North Bristol NHS Trust, Bristol), Graham Robinson (Royal United Hospitals Bath NHS Foundation Trust, Bath), Alberto Villanueva (Surrey and Sussex Healthcare NHS Trust, Surrey), Hasti Robbie (King's College Hospital NHS Foundation Trust, London), Elena Stefan (The Princess Alexandra Hospital NHS Trust, London), Charlie Sayer (University Hospitals Sussex NHS Foundation Trust, Sussex), Nick Screaton (Royal Papworth Hospital NHS Foundation Trust, Cambridge), Navinah Nundlall, Lyndsey Gallagher, Andrew Crossingham, Thea Buchan, Tanita Limani (University College London Hospitals NHS Foundation Trust, London), Kate Gowers, Kate Davies, John McCabe (Lungs For Living Research Centre, UCL Respiratory, University College London, London), Joseph Jacob (Lungs For Living Research Centre, UCL Respiratory, University College London, London. Centre for Medical Image Computing (CMIC), London), Karen Sennett (Killick Street Health Centre, London), Tania Anastasiadis (Tower Hamlets Clinical Commissioning Group, London), Andrew Perugia (Noclor Research Support, London), James Rusius (Noclor Research Support, London).

Contributors All authors were involved in the design and conduct of the SUMMIT study. ST and AWC drafted the manuscript and analysed data with input from SJ, JRH and AH. All authors contributed to and approved the final manuscript. SJ is responsible for the overall content as guarantor.

Funding The SUMMIT Study is funded by GRAIL Inc. through a research grant awarded to SJ as chief investigator. This work was partly undertaken at UCLH/UCL who received a proportion of funding from the Department of Health's NIHR Biomedical Research Centre's funding scheme. SJ was a Wellcome Trust Senior Fellow in Clinical Science (WT107963AIA). SJ is supported by CRUK programme grant EDDCPGM\100002.

Competing interests ST, AWC, JD, CH, HH and PV are all funded or part-funded through GRAIL as part of the SUMMIT Study. SJ was a Wellcome Trust Senior Fellow in Clinical Science (WT107963AIA). SJ is supported by CRUK programme grant EDDCPGM\100002, the Rosetrees Trust, the Roy Castle Lung Cancer foundation, the Garfield Weston Trust and UCLH Charitable Foundation. SJ's full disclosures are as a Paid Advisory Board member Astra-Zeneca, Bard1 Bioscience, Achilles Therapeutics, Jansen. Assistance for travel to meetings from Astra Zeneca, Takeda, and grant income from GRAIL, Owlstone and share options from Optellum; BARD1 Lifescience. SQ is supported by a Cancer Research UK (CRUK) Population Research Fellowship (C50664/A24460) and Barts Charity (MRC&U0036). AN is part-funded through the UCLH Biomedical Research Centre. AD's disclosures are personal fees from Boehringer Ingelheim, Roche, Galacto Biotech, Galapagos and Vicore. AH's disclosures are consulting fees to Evidera and assistance for travel to meetings from GRAIL. JRH's disclosures are assistance for travel from Astra Zeneca and Boehringer Ingelheim and payment for lectures and presentations from Astra Zeneca, Boehringer Ingelheim, Nutricia and Takeda. There are no disclosures from KG, VB, CL, A-MH, JT and LF.

Patient and public involvement Patients and/or the public were involved in the design, or conduct, or reporting, or dissemination plans of this research. Refer to the Methods section for further details.

Patient consent for publication Not applicable.

Ethics approval This study involves human participants and was approved by an NHS Research Ethics committee (17/LO/2004) and the NHS Health Research Authority's Confidentiality Advisory Group (18/CAG/0054). Participants gave informed consent to participate in the study before taking part.

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement Relevant individual deidentified participant data (including data dictionaries) will be made available on reasonable request via email to SJ (s.janes@ucl.ac.uk) following confirmation by SJ and the Cancer Research UK and UCL Cancer Trials Centre. Data will be available to share after the publication of the study primary and secondary endpoints.

ORCID iD
Andrew W Creamer http://orcid.org/0000-0002-9314-1210

REFERENCES

1 Aberle DR, Adams AM, Berg CD, *et al*. Reduced lung-cancer mortality with low-dose computed tomographic screening. *N Engl J Med* 2011;365:395–409.
2 de Koning HJ, van der Aalst CM, de Jong PA, *et al*. Reduced lung-cancer mortality with volume CT screening in a randomized trial. *N Engl J Med* 2020;382:503–13.
3 Dickson JL, Horst C, Nair A, *et al*. Hesitancy around low-dose CT screening for lung cancer. *Annals of Oncology* 2022;33:34–41.
4 Ruparel M, Quaife SL, Dickson JL, *et al*. Prevalence, symptom burden, and underdiagnosis of chronic obstructive pulmonary disease in a lung cancer screening cohort. *Ann Am Thorac Soc* 2020;17:869–78.
5 Balata H, Blandin Knight S, Barber P, *et al*. Targeted lung cancer screening selects individuals at high risk of cardiovascular disease. *Lung Cancer* 2018;124:148–53.
6 Jacobs PCA, Mali WPTM, Grobbee DE, *et al*. Prevalence of incidental findings in computed tomographic screening of the chest: a systematic review. *J Comput Assist Tomogr* 2008;32:214–21.
7 Nguyen XV, Davies L, Eastwood JD, *et al*. Extrapulmonary findings and malignancies in participants screened with chest CT in the national lung screening trial. *J Am Coll Radiol* 2017;14:324–30.
8 Kinsinger LS, Anderson C, Kim J, *et al*. Implementation of lung cancer screening in the veterans health administration. *JAMA Intern Med* 2017;177:399–406.
9 Bartlett EC, Belsey J, Derbyshire J, *et al*. Implications of incidental findings from lung screening for primary care: data from a UK pilot. *NPJ Prim Care Respir Med* 2021;31:36.
10 van der Aalst CM, Ten Haaf K, de Koning HJ. Implementation of lung cancer screening: what are the main issues *Transl Lung Cancer Res* 2021;10:1050–63.
11 UK National Screening Comittee. Adult screening programme: lung cancer. 2022. Available: https://view-health-screening-recommendations.service.gov.uk/lung-cancer/
12 NHS England. Targeted screening for lung cancer with low radiation dose computed tomography quality assurance standards prepared for the targeted lung health checks programme; 2020.
13 Horst C, Dickson JL, Tisi S, *et al*. Delivering low-dose CT screening for lung cancer: a pragmatic approach. *Thorax* 2020;75:831–2.
14 Humphrey L, Mark M, Miranda M, *et al*. Screening for lung cancer: systematic review to update the U.S. preventive services task force recommendation; 2013.
15 Tammemagi CM, Pinsky PF, Caporaso NE, *et al*. Lung cancer risk prediction: prostate, lung, colorectal and ovarian cancer screening trial models and validation. *J Natl Cancer Inst* 2011;103:1058–68.
16 Crosbie PA, Balata H, Evison M, *et al*. Implementing lung cancer screening: baseline results from a community-based 'lung health check' pilot in deprived areas of manchester. *Thorax* 2019;74:405–9.
17 Crosbie PA, Gabe R, Simmonds I, *et al*. Yorkshire lung screening trial (YLST): protocol for a randomised controlled trial to evaluate invitation to community-based low-dose CT screening for lung cancer versus usual care in a targeted population at risk. *BMJ Open* 2020;10:e037075.
18 A guide to performing quality assured diagnostic Spirometry; 2013.
19 Stanojevic S, Graham BL, Cooper BG, *et al*. Official ERS technical standards: global lung function initiative reference values for the carbon Monoxide transfer factor for Caucasians. *Eur Respir J* 2017;50:1700010.
20 Munden RF, Carter BW, Chiles C, *et al*. Managing incidental findings on thoracic CT: Mediastinal and cardiovascular findings. A white paper of the ACR incidental findings committee. *J Am Coll Radiol* 2018;15:1087–96.
21 Munden RF, Black WC, Hartman TE, *et al*. Managing incidental findings on thoracic CT: lung findings. A white paper of the ACR incidental findings committee. *J Am Coll Radiol* 2021;18:1267–79.
22 Global Initiative for Chronic Obstructive Lung Disease. Global initiative for chronic obstructive lung disease global initiative for chronic obstructive lung disease; 2021.
23 NICE. Chronic obstructive pulmonary disease in over 16S: diagnosis and management NICE guideline; 2018.
24 Murray RL, Brain K, Britton J, *et al*. Yorkshire enhanced stop smoking (YESS) study: a protocol for a randomised controlled trial to evaluate the effect of adding a personalised smoking cessation intervention to a lung cancer screening programme. *BMJ Open* 2020;10:e037086.
25 Diab N, Gershon AS, Sin DD, *et al*. Underdiagnosis and overdiagnosis of chronic obstructive pulmonary disease. *Am J Respir Crit Care Med* 2018;198:1130–9.
26 National Cancer Programme. Targeted screening for lung cancer with low radiation dose computed tomography: standard protocol prepared for the targeted lung health checks programme V1; 2019.
27 Polverino E, Goeminne PC, McDonnell MJ, *et al*. European respiratory society guidelines for the management of adult Bronchiectasis. *Eur Respir J* 2017;50:1700629.
28 Hill AT, Sullivan AL, Chalmers JD, *et al*. British thoracic society guideline for Bronchiectasis in adults. *Thorax* 2019;74:1–69.
29 Hatabu H, Hunninghake GM, Richeldi L, *et al*. Interstitial lung abnormalities detected incidentally on CT: a position paper from the Fleischner society. *Lancet Respir Med* 2020;8:726–37.
30 Hunninghake GM, Hatabu H, Okajima Y, *et al*. Muc5B promoter polymorphism and interstitial lung abnormalities. *N Engl J Med* 2013;368:2192–200.
31 Putman RK, Hatabu H, Araki T, *et al*. Association between interstitial lung abnormalities and all-cause mortality. *JAMA* 2016;315:672–81.
32 Jin GY, Lynch D, Chawla A, *et al*. Interstitial lung abnormalities in a CT lung cancer screening population: prevalence and progression rate. *Radiology* 2013;268:563–71.
33 Jacobs PC, Gondrie MJA, van der Graaf Y, *et al*. Coronary artery calcium can predict all-cause mortality and cardiovascular events on low-dose CT screening for lung cancer. *AJR Am J Roentgenol* 2012;198:505–11.
34 Shemesh J, Henschke CI, Shaham D, *et al*. Ordinal scoring of coronary artery Calcifications on low-dose CT scans of the chest is predictive of death from cardiovascular disease. *Radiology* 2010;257:541–8.
35 Pakdaman MN, Rozanski A, Berman DS. Incidental coronary Calcifications on routine chest CT: clinical implications. *Trends Cardiovasc Med* 2017;27:475–80.
36 Williams MC, Abbas A, Tirr E, *et al*. Reporting incidental coronary, aortic valve and cardiac calcification on non-Gated thoracic computed tomography, a consensus statement from the BSCI/BSCCT and BSTI. *BJR* 2021;94:20200894.
37 Mazzone PJ, Silvestri GA, Patel S, *et al*. Screening for lung cancer: CHEST guideline and expert panel report. *Chest* 2018;153:954–85.
38 Orringer CE, Blaha MJ, Blankstein R, *et al*. The National lipid association scientific statement on coronary artery calcium scoring to guide preventive strategies for ASCVD risk reduction. *J Clin Lipidol* 2021;15:33–60.
39 Hippisley-Cox J, Coupland C, Vinogradova Y, *et al*. Predicting cardiovascular risk in England and Wales: prospective derivation and validation of Qrisk2. *BMJ* 2008;336:1475–82.
40 National Institute for Health and Care Excellence. Cardiovascular disease: risk assessment and reduction, including lipid modification clinical guideline [Cg181]; 2016.
41 Ruparel M, Quaife SL, Dickson JL, *et al*. Evaluation of cardiovascular risk in a lung cancer screening cohort. *Thorax* 2019;74:1140–6.
42 Curry SJ, Krist AH, Owens DK, *et al*. Screening for osteoporosis to prevent fractures: US preventive services task force recommendation statement. *JAMA* 2018;319:2521–31.
43 NICE. *Osteoporosis: assessing the risk of fragility fracture. CG146*. 2012.
44 Chiles C, Duan F, Gladish GW, *et al*. Association of coronary artery calcification and mortality in the National lung screening trial: a comparison of three scoring methods. *Radiology* 2015;276:82–90.
45 Htwe Y, Cham MD, Henschke CI, *et al*. Coronary artery calcification on low-dose computed tomography: comparison of Agatston and ordinal scores. *Clin Imaging* 2015;39:799–802.
46 Hiratzka LF, Bakris GL, Beckman JA, *et al*. 2010 ACCF/AHA/AATS/ACR/ASA/SCA/SCAI/SIR/STS/SVM guidelines for the diagnosis and management of patients with thoracic aortic disease. A report of the American college of cardiology foundation/American heart Association task force on practice guidelines. *J Am Coll Cardiol* 2010;55:e27–129.
47 National Institute for Health and Care Excellence. Guideline scope abdominal aortic aneurysm: diagnosis and management; 2018.
48 Liu F, Coursey CA, Grahame-Clarke C, *et al*. Aortic valve calcification as an incidental finding at CT of the elderly: severity and location as predictors of aortic stenosis. *AJR Am J Roentgenol* 2006;186:342–9.
49 Maskell N, British Thoracic Society Pleural Disease Guideline Group. British Thoracic society pleural disease guidelines--2010 update. *Thorax* 2010;65:667–9.

Appendix 1: Radiology Report proforma for Incidental Findings

9	Emphysema extent	None Unclear Trivial (<5%) Mild (5-25%) Moderate (25-50%) Severe (50-75%) Very severe (>75%)
10	Coronary calcium: LMLAD	None Minimum Mild Moderate Severe Not Reported
11	Coronary calcium: CIR	None Minimum Mild Moderate Severe Not Reported
12	Coronary calcium: RCA	None Minimum Mild Moderate Severe Not Reported
14	Family history of lung cancer	Yes No
15	Please select the applicable pulmonary incidental findings for this patient	None [EXCL] Bronchiectasis Interstitial lung disease Pleural plaques Diffuse pleural thickening Pleural effusion
15a	Bronchiectasis	Mild (1.5-2x artery) Moderate (2-3x artery) Severe- (>3x artery AND >1 segment)
15b	Interstitial lung disease	< 10% reticulation >= 10 % reticulation without fibrotic features >=10% reticulation with fibrotic features
15c	Pleural plaques	Yes No
15d	Diffuse pleural thickening	Yes No

15e	Pleural effusion	Unilateral - Right Unilateral - Left Bilateral
16	Please select the applicable mediastinial and neck incidental findings.	None [EXCL] Thoracic aortic dilatation Anterior mediastinal mass Aortic valve calcification Thyroid nodule
16a	Thoracic aortic dilatation	>= 4 cm and <5.5 cm >= 5.5 cm
16b	Anterior mediastinal mass	< 3 cm, no suspicious features at baseline/no growth on serial imaging < 3 cm, suspicious features or growing on serial imaging >= 3 cm
16c	Aortic valve calcification	Central Peripheral Both
16d	Thyroid nodule	Nodule with fine calcification Nodule associated with local lymphadenopathy Both
17	Please select the applicable subdiaphragmatic incidental findings.	None [EXCL] Adrenal opacity Significant abdominal aortic dilatation Hiatus hernia Osteoporotic wedge fracture
17a	Adrenal opacity	1-4 cm or HU > 10 >4 cm
17b	Significant abdominal aortic dilatation	>=3 cm and <5 cm >=5 cm
17c	Hiatus hernia	Absent Present
17d	Osteoporotic wedge fracture	< 50% >= 50%
18	Are there any other emergency non-cancerous findings?	Yes No
18a	Describe the other emergency non-cancerous findings	
19	Is there a likely non-pulmonary malignancy (not already captured in the structured report)?	Yes No

20	Enter information for suspicious non-pulmonary lesion(s) Site	
20a	Size (in mm)	
20b	MDT recommendation and other comments	
25	Additional comments on the recommendation	

Appendix 2: Lung Health Check questions regarding respiratory symptoms and respiratory co-morbidities

1	Do you currently have a cough?	Yes No
1a	[If 'yes' to Q1] When did the cough start?	Within the last 3 weeks 3 to 6 weeks ago 6 weeks to 6 months ago 6 months to 12 months ago 12 months to 24 months ago Greater than 24 months ago
1b	[If 'yes' to Q1] When you cough, do you usually cough up phlegm (sputum)?	Yes No
2	[Show if Q1a is not equal to "Within 3 weeks"] Have you noticed any change in your normal chest symptoms during the past 3 weeks?	Yes No
2a	[Show If 'yes' to Q2] Have your symptoms improved or deteriorated?	Improved Deteriorated
2b	[Show If answer 'deteriorated' to Q2a] [Show if Q1a is not equal to "Within 3 weeks"] Has the cough worsened in the last three weeks?	Yes No
2c (i)	[Show If answer 'deteriorated' to Q2a or 'within 3 weeks' to Q1a] We would like to ask some more questions about symptoms which may have changed. Fever/ sweats	Yes No
2c (ii)	[Show If answer 'deteriorated' to Q2a or 'within 3 weeks' to Q1a] Increased phlegm (sputum) production/ change in the colour of phlegm	Yes No

2c (iii)	[Show If answer 'deteriorated' to Q2a or 'within 3 weeks' to Q1a] Increased shortness of breath	Yes No
2c (iv)	[Show If answer 'deteriorated' to Q2a or 'within 3 weeks' to Q1a] Increased wheeze (noisy breathing)	Yes No
2c (v)	[Show If answer 'deteriorated' to Q2a or 'within 3 weeks' to Q1a] Sharp chest pain when you take a deep breath (pleuritic pain)	Yes No
3	Are you currently taking antibiotics or steroids prescribed for an acute chest infection?	Yes No
4	How many times in the past 12 months have you used antibiotics or steroids for your chest?	[number input][range 0:50]
9	Have you coughed up blood in the last year?	Yes No
9a	[Show if yes to Q9] Have you coughed up blood within the past two weeks?	Yes No
9b	[Show if yes to Q9] Has the blood been investigated by a doctor?	Yes No
10	Which of these best describes your breathing?	[Only one option can be selected] Only breathless on strenuous exercise Breathless when hurrying on the flat or up a slight hill Slower than peers when walking. Would need to stop after 15 minutes or 1 mile at own pace Would need to stop due to breathlessness after 100 yards on the flat Too breathless to leave house or when washing/dressing

		Unable to answer questions as limited due to other co-morbidity
11	Have you lost weight in the past three months?	Yes No
11a	[Show if 'yes' to Q11] Was the weight loss intentional?	Yes No
11b	[Show if 'yes' to Q11] Do you know how much weight you have lost in the past three months?	Yes No
11c	[Show if 'yes' to Q11b] How much weight have you lost?	[Number input] _____Kg or _____lb
11d	[Show if 'no' to Q11a] Has this unintentional weight loss been investigated by a doctor?	Yes No
	Medical History	
12	Have you ever been told you have any of the following conditions?	
12i	COPD/chronic bronchitis/emphysema	Yes No [Field to auto populate from phone screener Q6, with ability to edit response at LHC]
12ii	Asthma	Yes No
12iii	Atopy - hayfever/eczema/rhinitis	Yes No
12iv	Pulmonary fibrosis	Yes No
12v	Bronchiectasis	Yes No
12vi	Previous Pneumonia	Yes No
12vii	Sarcoidosis	Yes No
12viii	Tuberculosis (TB)	Yes No
12viii a	[show if 'yes' to Q12viii] Did or do you have pulmonary or non-pulmonary Tuberculosis (TB)?	Lung only (Pulmonary) Outside the lung only (extra-pulmonary) Lung and elsewhere in the body I don't know
12viii b	[show if 'yes' to Q12viii] Are you currently receiving treatment for Tuberculosis (TB)?	Yes No

	Family History	
14	Have your parents, brother, sister, or children ever been diagnosed with lung cancer?	Yes No [Field to auto populate from phone screener Q8, with ability to edit response at LHC]
	Demographics	
15	Which of these categories best describes your ethnic group?	White British White Irish Other White White and Black Caribbean White and Black African White and Asian Chinese Other Asian Black Caribbean Black African Other Black Indian Pakistani Bangladeshi Other Mixed Any other ethnic group
16	What is the highest level of education you have achieved?	Finished school at or before the age of fifteen Completed CSEs, O-levels or equivalent Completed A-levels or equivalent Completed further education but not a degree Completed a Bachelor's degree or equivalent Completed a further degree e.g. masters or PhD etc [Field to auto populate from phone screener Q5, with ability to edit response at LHC]
	Smoking History	
17	Have you smoked more than 100 cigarettes in your lifetime?	Yes No [Field to auto populate from phone screener Q1, with ability to edit response at LHC]
17a	[If yes to Q17] Do you currently smoke cigarettes regularly?	Yes No

		[Field to auto populate from phone screener Q3, with ability to edit response at LHC]
17b	At what age did you start smoking cigarettes regularly?	_ years [Field to auto populate from phone screener Q3c, with ability to edit response at LHC] [range 1:78]
17c	[If no to Q17a] At what age did you stop smoking cigarettes regularly?	[number input] _ Years [Field to auto populate from phone screener Q3b, with ability to edit response at LHC] [range 1:78]
17d	[If yes to Q17a] During the time you have smoked cigarettes, have you ever stopped smoking for more than one month?	Yes No [Field to auto populate from phone screener Q3d, with ability to edit response at LHC]
17e	[If yes to 17d] How many months did you stop for in total? [Range 1-500]	Months [Field to auto populate from phone screener Q3d(i), with ability to edit response at LHC]
17f	How many cigarettes do or did you smoke per day on average for the majority of your time as a smoker?	__ number of cigarettes per day or __ grams of tobacco per week [Field to auto populate from phone screener Q3e or Q3f, with ability to edit response at LHC]
18	Have you ever smoked any of the following types of tobacco in addition to or instead of cigarettes?	[Please select all that apply] Cigars Cigarillos Pipe Marijuana Waterpipe None of the above
18a	[show if selects cigars in Q18] How often do or did you smoke cigars?	[please select one option] Occasionally (less than weekly) Regularly (at least once per week)
18b	[Show if select regularly to Q18a] Do you smoke cigars currently?	 Yes No
18c	[Show if select regularly to Q18a] At what age did you start smoking cigars?	[number input]

18d	[Show if select regularly to Q18a and no to Q18b] At what age did you stop smoking cigars?	[number input]
18e	[Show if select regularly to Q18a] How many cigars do or did you smoke per week on average for the majority of your time as a smoker?	[number input] _ per week
18f	[show if selects cigarillos in Q18] How often do or did you smoke cigarillos?	Occasionally (less than weekly) Regularly (at least once per week)
18g	[Show if select regularly to Q18f] Do you smoke cigarillos currently?	Yes No
18h	[Show if select regularly to Q18f] At what age did you start smoking cigarillos?	[number input]
18i	[Show if select regularly to Q18f and no to Q18g] At what age did you stop smoking cigarillos?	[number input]
18j	[Show if select regularly to Q18f] How many cigarillos do or did you smoke per week on average for the majority of your time as a smoker?	[number input] per week
18k	[show if selects pipe in Q18] How often do or did you smoke a pipe?	Occasionally (less than weekly) Regularly (at least once per week)
18l	[Show if select regularly to Q18k] Do you smoke a pipe currently?	Yes No
18m	[Show if select regularly to Q18k] At what age did you start smoking a pipe?	[number input]
18n	[Show if select regularly to Q18k and no to Q18l] At what age did you stop smoking a pipe?	[number input]
18o	[Show if select regularly to Q18k] How many pipe bowls do or did you smoke per week on average for the majority of your time as a smoker?	[number input] per week
18p	[show if selects marijuana in Q18] How often do or did you smoke marijuana?	Occasionally (less than weekly) Regularly (at least once per week) Decline to answer
18q	[Show if select regularly to Q18p] Do you smoke marijuana currently?	Yes No
18r	[Show if select regularly to Q18p] At what age did you start smoking marijuana?	[number input]
18s	[Show if select regularly to Q18p and no to Q18q] At what age did you stop smoking marijuana?	[number input]
18t	[Show if select regularly to Q18p]	[number input] per week

	How many joints of marijuana do or did you smoke per week on average for the majority of your time as a smoker?	
18u	[show if selects waterpipe in Q18] How often do or did you use a waterpipe (20 minute session)?	Occasionally (less than weekly) Regularly (at least once per week)
18v	[Show if select regularly to Q18u] Do you smoke a waterpipe currently?	Yes No
18w	[Show if select regularly to Q18u] At what age did you start smoking a waterpipe?	[number input]
18x	[Show if select regularly to Q18u and no to Q18v] At what age did you stop smoking a waterpipe?	[number input]
18y	[Show if select regularly to Q18u] For how many sessions (20 minutes) do or did you use a waterpipe per week on average for the majority of your time as a smoker?	[number input] per week
	Smoking cessation	
19	[Show if yes to Q17a or 18b or 18g or 18l] Please confirm that Very Brief Advice (VBA) on smoking cessation has been given	Yes No
19a	[Show if 'No' to Q19] If no VBA given, please briefly explain why	[Free text]
20	[if yes to Q17a or 18b or 18g or 18l] Has the participant consented to a smoking cessation referral being made on their behalf? This includes consent to their information being shared with a stop smoking service and to being contacted about the referral by that service.	Yes No, the participant would prefer to self-refer No, the participant does not want support from a stop smoking service No, already in contact with a stop smoking service
	Clinical recordings	
23	Height [range:60-280]	__cm [numerical input to 1.dp]
24	Weight [range:25-350]	__ kg [numerical input to 1.dp]
25	Has the participant had their blood pressure taken?	Yes Declined
25a	[Show if yes to Q25] BP (systolic) [range:30-250]	__ mmHg

25b	[Show if yes to Q25] BP (diastolic) [range:10-250]	__ mmHg
26a	Was spirometry cancelled due to Covid-19 related social distancing guidelines?	Yes No
26b	[show if "No" to 26a] Is spirometry contraindicated?	Yes No
26c	[Show if no to Q26b] FEV1 [Range 0.10L to 9.99L]	__ litres [numerical input to 2. dp]
26d	[Show if no to Q26b] FEV1 % Predicted [Max 250%]	__ % [numerical to 1.dp]
26e	[Show if no to Q26b] FVC [Range 0.1L to 9.99L]	__ litres [numerical input to 2 dp]
26f	[Show if no to Q26b] FVC % Predicted [Max 250%]	__ %
26g	[Show if no to Q26b] FEV1: FVC [Range 0-1]	[Numerical input to 2.dp]
27	BMI [This should be calculated, no need for staff to enter] [Hidden from the nurse/UI]	__ kg/m2
28	USPSTF criteria met? [This should be calculated, no need for staff to enter] [Hidden from Nurse/UI]	Yes No
29	PLCO risk score [This should be calculated, no need for staff to enter] [Hidden from Nurse/UI]	Numeric
30	Smoking pack years [This should be calculated, no need for staff to enter] [Hidden from Nurse/UI]	Numeric

Appendix 3: Supplementary data

	Emphysema (n=3711)	**No emphysema (n=7404)**	**p value**
Age (years)	66.26 (±6.01)	64.90 (±6.11)	<0.001
Male (%)	58.6% (n=2175)	56.9% (n=4211)	0.081
Current smoker (%)	51.4% (n=1907)	47.1% (n=3490)	<0.001

Pack year history (years)	47.84 (±22.72)	44.05 (±23.03)	<0.001
Airflow obstruction? (%)	67.8% (n=2515)	40.3% (n=2982)	<0.001
Cough > 6 weeks (%)	28.3% (n=1052)	21.9% (n=1620)	<0.001
Sputum (%)	19.6% (n=727)	13.7% (n=1012)	<0.001
MRC score ≥1 (%)	70.5% (n=2618)	63.9% (n=4730)	<0.001
≥2 exacerbations per year (%)	10.1% (n=375)	6.5% (n=479)	<0.001
Self-reported diagnosis of COPD	52.3% (n=2126)	31.6% (n=2342)	<0.001

Supplementary Table A: Characteristics of those with emphysema on baseline LDCT compared to those without

	Bronchiectasis (n=818)	**No bronchiectasis (n=10,297)**	**p value**
Age (years)	67.33 (±5.88)	65.20 (±6.10)	<0.001
Male? (%)	59.8% (n=489)	57.3% (n=5897)	0.162
Cough > 6 weeks (%)	27.6% (n=226)	23.8% (n=2448)	0.013
Sputum (%)	18.8% (n=154)	15.4% (n=1585)	0.009
MRC score ≥1 (%)	67.8% (n=555)	66.0% (n=6793)	0.275
Haemoptysis in past year? (%)	2.6% (n=21)	2.3% (n=237)	0.627
Exacerbations in past year (median)	0.00 (0.00-1.00)	0.00 (0.00-0.00)	<0.001
≥2 exacerbations per year (%)	10.1% (n=83)	7.5% (n=771)	0.006
Previous pneumonia (%)	20.8% (n=170)	14.5% (n=1495)	<0.001
Previous TB (%)	4.4% (n=36)	1.9% (n=199)	<0.001
Self-reported bronchiectasis (%)	1.7% (n=14)	0.7% (n=75)	0.002
FEV1% predicted (%)	74.01 (±22.14)	76.16 (±19.58)	0.003
Airflow obstruction (%)	54.5% (n=446)	49.1% (n=5051)	0.003

Supplementary Table B: Characteristics of those with and without bronchiectasis on baseline LDCT

Variable	**Unadjusted OR (95% CI)**	**p**	**Adjusted OR (95% CI)**	**p**
Age				
Per increasing year	1.06 (1.05-1.07)	<0.001	1.05 (1.04-1.07)	<0.001
Gender				

Male	1		1	
Female	0.902 (0.780-1.043)	0.162	0.87 (0.75-1.01)	0.064
Previous TB				
No history of TB	1		1	
Previous TB	2.332 (1.626-3.356)	<0.001	2.20 (1.53-3.12)	<0.001
Pneumonia				
No previous history	1		1	
History of pneumonia	1.545 (1.293-1.845)	<0.001	1.42 (1.19-1.71)	<0.001
Smoking status				
Current smoker	1	<0.001	1	
Former smoker	1.49 (1.29-1.72)		1.22 (1.45-1.54)	<0.001
Exacerbations in past 12 months				
Per increasing exacerbation	1.12 (1.06-1.12)	<0.001	1.10 (1.04-1.17)	0.002
Airflow obstruction				
No airflow obstruction	1		1	
Airflow obstruction	1.25 (1.08-1.44)	0.003	1.08 (0.93-1.25)	0.305

Supplementary Table C: Bronchiectasis: Univariate and multivariate binary logistic analysis assessing the relationship between associated variables and presence on baseline LDCT

	ILD (n=528)	**No ILD (n= 10,587)**	**p value**
Age (years)	67.52 (±6.03)	65.24 (±6.09)	<0.001
Male Sex (%)	64.6% (n=341)	57.1% (n=6045)	0.001
Current smoker (%)	47.5% (n=251)	48.6% (n=5146)	0.631
Pack year history (years)	45.80 (±25.70)	45.29 (±22.86)	0.620
Cough > 6 weeks (%)	26.1% (n=138)	23.9% (n=2534)	0.248
MRC score ≥1 (%)	67.4% (n=356)	66.0% (n=6992)	0.513
Self-reported ILD (%)	1.1% (n=6)	0.3% (n=37)	0.004
FEV1% predicted (%)	77.98 (±18.60)	75.91 (±19.84)	0.019
Emphysema present (%)	37.3% (n=197)	33.2% (n=3541)	0.050
Airflow obstruction (%)	42.8% (n=226)	49.8% (n=5271)	0.002

Supplementary Table D: Characteristics of those with and without ILA on baseline LDCT

Variable	**Unadjusted OR (95% CI)**	**p**	**Adjusted OR (95%CI)**	**p**
Age				
Per increasing year	1.062 (1.049-1.079)	<0.001	1.072 (1.055-1.088)	<0.001
Gender				
Female	1		1	
Male	1.370 (1.142-1.644)	0.001	1.272 (1.047-1.546)	0.016
Pneumonia				

No previous history	1		1	
History of pneumonia	0.952 (0.742-1.221)	0.699	0.942 (0.731-1.214)	0.646
Smoking status				
Current smoker	1		1	
Former smoker	1.044 (0.876-1.243)	0.632	0.878 (0.733-1.052)	0.159
Pack years				
Per increasing year	1.001 (0.997-1.005)	0.620	1.00 (0.996-1.003)	0.852
Occupational Asbestos exposure				
No	1		1	
Yes	1.389 (1.127-1.712)	0.002	1.293 (1.033-1.618)	0.025
Airflow obstruction				
No airflow obstruction	1		1	
Airflow obstruction	0.755 (0.633-0.990)	0.002	0.608 (0.504-0.734)	<0.001

Supplementary Table E: Interstitial Lung Abnormalities: Univariate and multivariate binary logistic analysis assessing the relationship between associated variables and presence on baseline LDCT

	CAC present (n=7141)	No CAC (n=3974)	p value
Age (years)	66.52 (±5.98)	63.26 (±5.78)	<0.001
Male Sex(%)	65.3% (n=4663)	43.4% (n=1723)	<0.001
BMI (kg/m^2)	28.28 (±9.63)	27.90 (±9.24)	0.040
Systolic BP (mmHg)	135.34 (±17.68)	131.83 (±17.23)	<0.001
Systolic BP ≥140mmHg (%)	40.7% (n=2906)	32.1% (n=1275)	<0.001
Systolic BP ≥160mmHg (%)	8.4% (n=598)	5.9% (n=233)	<0.001
Diastolic BP (mmHg)	79.72 (±10.53)	80.41 (±10.15)	0.001
Current smoker (%)	47.3% (n=3378)	50.8% (n=2019)	<0.001
Pack year history (years)	46.67 (±24.19)	42.88 (±20.48)	<0.001
Ethnicity			
White	84.0% (n=5997)	82.1% (n=3262)	<0.001
Mixed	2.0% (n=141)	2.7% (n=109)	
Asian	7.8% (n=560)	4.6% (n=183)	
Black	3.2% (n=226)	6.5% (n=258)	
Other	3.0% (n=217)	4.1% (n=162)	
Airflow obstruction (%)	51.8% (n=3696)	45.3% (n=1801)	<0.001

Supplementary Table F. Baseline characteristics of those with CAC compared to those without CAC on baseline LDCT

	Thoracic aneurysm present (N=306)	No aneurysm present (N=10809)	p value
Age (years)	66.64 (±9.75)	65.32(±10.00)	<0.001
Male Sex(%)	69.9% (n=214)	57.1%(N=6172)	<0.001
BMI (kg/m^2)	28.08 (±5.90)	28.15 (±6.61)	0.810
Systolic BP (mmHg)	135.5 (±22.0)	134.0 (±24.0)	<0.001
Systolic BP ≥140mmHg (%)	38.9% (n=119)	37.6% (n=4062)	0.685
Systolic BP ≥160mmHg (%)	9.5% (n=29)	7.4% (n=802)	0.215
Diastolic BP (mmHg)	83.2 (IQR±14)	79.88 (±14)	<0.001
Current smoker (%)	47.3% (n=3378)	50.8% (n=2019)	<0.001
Pack year history (years)	43.46 (±19.25)	45.36 (±18.75)	0.136
Ethnicity			
White	84.0% (n=5997)	82.1% (n=3262)	<0.001
Mixed	2.0% (n=141)	2.7% (n=109)	
Asian	7.8% (n=560)	4.6% (n=183)	
Black	3.2% (n=226)	6.5% (n=258)	
Other	3.0% (n=217)	4.1% (n=162)	
Airflow obstruction (%)	50.7% (n=155)	49.4% (n=5342)	0.714

Supplementary Table G: Baseline characteristics of those with and without thoracic aortic aneurysm on baseline LDCT

Variable	Unadjusted OR (95% CI)	p	Adjusted OR (95% CI)	p
BMI				
Per increasing kg/m^2	0.998 (0.980-1.008)	0.822	0.998 (0.980-1.007)	0.827
Age				

Per increasing year	1.036 (1.017 – 1.055)	<0.001	1.048 (1.027- 1.069)	<0.001
Gender				
Female	1		1	
Male	1.748 (1.370 – 2.248)	<0.001	1.655 (1.290 – 2.139)	<0.001
Blood pressure				
Systolic BP	1.010 (1.004-1.017)	0.001	0.998 (0.990 – 1.005)	0.537
Diastolic BP	1.030 (1.019 – 1.040)	<0.001	1.032 (1.020 – 1.045)	<0.001
Smoking status				
Former smoker	1		1	
Current smoker	1.019 (0.812-1.279)	0.869	1.126 (0.890 – 1.425)	0.321
Pack year history				
Per increasing pack year	0.996 (0.990 – 1.001)	0.152	0.994 (0.988 – 1.000)	0.044
Airflow obstruction				
No airflow obstruction	1		1	
Airflow obstruction	1.051 (0.837 – 1.319)	0.671	1.000 (0.790-1.263)	0.990

Supplementary Table H: Thoracic Aortic Aneurysm: Univariate and multivariate binary logistic analysis assessing the relationship between associated variables and presence on baseline LDCT

	Vertebral wedge fracture *(n=801)*	**No vertebral wedge fractures *(n=10,314)***	**p value**
Prevalence in males	467/6386 (7.3%)	-	
Prevalence in females	334/4729 (7.1%)	-	
Age (years)	67.24 (±6.15)	65.21 (±6.08)	<0.001
Female (%)	41.7 % (n=334)	42.6% (n=4395)	0.614
BMI (kg/m^2)	27.42 (±5.24)	28.20 (±9.74)	0.026
Pack year history	45.98 (±22.36)	45.26 (±23.05)	0.394
Current smoker (%)	47.7% (n=382)	48.6% (n=5015)	0.611
Personal history of cancer (%)	15.4% (n=123)	13.1% (n=1351)	0.07
IMD rank	12,147.84 (±7660.29)	12068.96 (±7797.61)	0.784
Exacerbations over last year	0.00 (0.00-0.00)	0.00 (0.00-0.00)	0.351
Airflow obstruction (%)	58.1% (n=465)	48.8% (n=5032)	<0.001

Supplementary Table I: Characteristics of those with and without the presence of vertebral wedge fractures on baseline LDCT

Variable	**Unadjusted OR**	**p**	**Adjusted OR**	**p**
BMI				
Per increasing kg/m^2	0.98 (0.97-0.99)	0.004	0.99 (0.97-1.00)	0.043
Age				
Per increasing year	1.06 (1.04-1.07)	<0.001	1.05 (1.04-1.07)	<0.001
Gender				
Male	1		1	
Female	0.96 (0.83-1.11)	0.61	0.95 (082-1.10)	0.505
Smoking status				
Current smoker	1		1	
Former smoker	1.04 (0.90-1.20)	0.611	0.96 (0.82-1.11)	0.957

Pack year history				
Per increasing pack year	1.00 (1.00-1.00)	0.39	1.00 (1.00-1.00)	0.885
Personal history of cancer				
No	1		1	
Yes	1.20 (0.98-1.47)	0.07	1.1 (0.90-1.35)	0.368
Airflow obstruction				
No airflow obstruction	1		1	
Airflow obstruction	1.45 (1.26-1.68)	<0.001	1.26 (1.08-1.46)	0.003

Supplementary Table J: Vertebral wedge fractures: Univariate and multivariate binary logistic analysis assessing the relationship between associated variables and presence on baseline LDCT

	Hiatus Hernia *(n=1068)*	**No hiatus hernia *(n=10,047)***	**p value**
Age (years)	67.59 (±5.92)	65.12 (±6.08)	<0.001
Male (%)	49.3% (n=527)	58.3% (n=5859)	<0.001
BMI (kg/m^2)	28.69 (±5.20)	28.08 (±9.84)	0.046
Current smoker (%)	38.5% (n=411)	49.6% (n=4986)	<0.001
Airflow obstruction (%)	55.9% (n=597)	48.85 (n=4900)	<0.001

Supplementary Table K: Characteristics of participants with and without the presence of a hiatus hernia on baseline LDCT

Variable	**Unadjusted OR (95% CI)**	**p**	**Adjusted OR (95%CI)**	**p**
Age				
Per increasing year	1.069 (1.058-1.080)	<0.001	1.062 (1.050-1.073)	<0.001
Gender				
Female	1		1	
Male	0.696 (0.614-0.790)	<0.001	0.693 (0.610-0.788)	<0.001
BMI				
Per increasing kg/m^2	1.004 (1.000-1.009)	0.061	1.005 (1.000-1.009)	0.059
Smoking status				
Current smoker	1		1	
Former smoker	1.575 (1.384-1.792)	<0.001	1.379 (1.207-1.575)	<0.001
Airflow obstruction				
No	1		1	
Yes	1.331 (1.173-1.512)	<0.001	1.195 (1.049-1.362)	0.007

Supplementary Table L: Hiatus Hernia: Univariate and multivariate binary logistic analysis assessing the relationship between associated variables and presence on baseline LDCT

Appendix 1: Radiology Report proforma for Incidental Findings

9	Emphysema extent	None Unclear Trivial (<5%) Mild (5-25%) Moderate (25-50%) Severe (50-75%) Very severe (>75%)
10	Coronary calcium: LMLAD	None Minimum Mild Moderate Severe Not Reported
11	Coronary calcium: CIR	None Minimum Mild Moderate Severe Not Reported
12	Coronary calcium: RCA	None Minimum Mild Moderate Severe Not Reported
14	Family history of lung cancer	Yes No
15	Please select the applicable pulmonary incidental findings for this patient	None [EXCL] Bronchiectasis Interstitial lung disease Pleural plaques Diffuse pleural thickening Pleural effusion
15a	Bronchiectasis	Mild (1.5-2x artery) Moderate (2-3x artery) Severe- (>3x artery AND >1 segment)
15b	Interstitial lung disease	< 10% reticulation >= 10 % reticulation without fibrotic features >=10% reticulation with fibrotic features
15c	Pleural plaques	Yes No
15d	Diffuse pleural thickening	Yes No

15e	Pleural effusion	Unilateral - Right Unilateral - Left Bilateral
16	Please select the applicable mediastinial and neck incidental findings.	None [EXCL] Thoracic aortic dilatation Anterior mediastinal mass Aortic valve calcification Thyroid nodule
16a	Thoracic aortic dilatation	>= 4 cm and <5.5 cm >= 5.5 cm
16b	Anterior mediastinal mass	< 3 cm, no suspicious features at baseline/no growth on serial imaging < 3 cm, suspicious features or growing on serial imaging >= 3 cm
16c	Aortic valve calcification	Central Peripheral Both
16d	Thyroid nodule	Nodule with fine calcification Nodule associated with local lymphadenopathy Both
17	Please select the applicable subdiaphragmatic incidental findings.	None [EXCL] Adrenal opacity Significant abdominal aortic dilatation Hiatus hernia Osteoporotic wedge fracture
17a	Adrenal opacity	1-4 cm or HU > 10 >4 cm
17b	Significant abdominal aortic dilatation	>=3 cm and <5 cm >=5 cm
17c	Hiatus hernia	Absent Present
17d	Osteoporotic wedge fracture	< 50% >= 50%
18	Are there any other emergency non-cancerous findings?	Yes No
18a	Describe the other emergency non-cancerous findings	
19	Is there a likely non-pulmonary malignancy (not already captured in the structured report)?	Yes No

20	Enter information for suspicious non-pulmonary lesion(s) Site	
20a	Size (in mm)	
20b	MDT recommendation and other comments	
25	Additional comments on the recommendation	

Appendix 2: Lung Health Check questions regarding respiratory symptoms and respiratory co-morbidities

1	Do you currently have a cough?	Yes No
1a	[If 'yes' to Q1] When did the cough start?	Within the last 3 weeks 3 to 6 weeks ago 6 weeks to 6 months ago 6 months to 12 months ago 12 months to 24 months ago Greater than 24 months ago
1b	[If 'yes' to Q1] When you cough, do you usually cough up phlegm (sputum)?	Yes No
2	[Show if Q1a is not equal to "Within 3 weeks"] Have you noticed any change in your normal chest symptoms during the past 3 weeks?	Yes No
2a	[Show If 'yes' to Q2] Have your symptoms improved or deteriorated?	Improved Deteriorated
2b	[Show If answer 'deteriorated' to Q2a] [Show if Q1a is not equal to "Within 3 weeks"] Has the cough worsened in the last three weeks?	Yes No
2c (i)	[Show If answer 'deteriorated' to Q2a or 'within 3 weeks' to Q1a] We would like to ask some more questions about symptoms which may have changed. Fever/ sweats	Yes No
2c (ii)	[Show If answer 'deteriorated' to Q2a or 'within 3 weeks' to Q1a] Increased phlegm (sputum) production/ change in the colour of phlegm	Yes No

2c (iii)	[Show If answer 'deteriorated' to Q2a or 'within 3 weeks' to Q1a] Increased shortness of breath	Yes No
2c (iv)	[Show If answer 'deteriorated' to Q2a or 'within 3 weeks' to Q1a] Increased wheeze (noisy breathing)	Yes No
2c (v)	[Show If answer 'deteriorated' to Q2a or 'within 3 weeks' to Q1a] Sharp chest pain when you take a deep breath (pleuritic pain)	Yes No
3	Are you currently taking antibiotics or steroids prescribed for an acute chest infection?	Yes No
4	How many times in the past 12 months have you used antibiotics or steroids for your chest?	[number input][range 0:50]
9	Have you coughed up blood in the last year?	Yes No
9a	[Show if yes to Q9] Have you coughed up blood within the past two weeks?	Yes No
9b	[Show if yes to Q9] Has the blood been investigated by a doctor?	Yes No
10	Which of these best describes your breathing?	[Only one option can be selected] Only breathless on strenuous exercise Breathless when hurrying on the flat or up a slight hill Slower than peers when walking. Would need to stop after 15 minutes or 1 mile at own pace Would need to stop due to breathlessness after 100 yards on the flat Too breathless to leave house or when washing/dressing

		Unable to answer questions as limited due to other co-morbidity
11	Have you lost weight in the past three months?	Yes No
11a	[Show if 'yes' to Q11] Was the weight loss intentional?	Yes No
11b	[Show if 'yes' to Q11] Do you know how much weight you have lost in the past three months?	Yes No
11c	[Show if 'yes' to Q11b] How much weight have you lost?	[Number input] _____Kg or _____lb
11d	[Show if 'no' to Q11a] Has this unintentional weight loss been investigated by a doctor?	Yes No
	Medical History	
12	Have you ever been told you have any of the following conditions?	
12i	COPD/chronic bronchitis/emphysema	Yes No [Field to auto populate from phone screener Q6, with ability to edit response at LHC]
12ii	Asthma	Yes No
12iii	Atopy - hayfever/eczema/rhinitis	Yes No
12iv	Pulmonary fibrosis	Yes No
12v	Bronchiectasis	Yes No
12vi	Previous Pneumonia	Yes No
12vii	Sarcoidosis	Yes No
12viii	Tuberculosis (TB)	Yes No
12viii a	[show if 'yes' to Q12viii] Did or do you have pulmonary or non-pulmonary Tuberculosis (TB)?	Lung only (Pulmonary) Outside the lung only (extra-pulmonary) Lung and elsewhere in the body I don't know
12viii b	[show if 'yes' to Q12viii] Are you currently receiving treatment for Tuberculosis (TB)?	Yes No

	Family History	
14	Have your parents, brother, sister, or children ever been diagnosed with lung cancer?	Yes No [Field to auto populate from phone screener Q8, with ability to edit response at LHC]
	Demographics	
15	Which of these categories best describes your ethnic group?	White British White Irish Other White White and Black Caribbean White and Black African White and Asian Chinese Other Asian Black Caribbean Black African Other Black Indian Pakistani Bangladeshi Other Mixed Any other ethnic group
16	What is the highest level of education you have achieved?	Finished school at or before the age of fifteen Completed CSEs, O-levels or equivalent Completed A-levels or equivalent Completed further education but not a degree Completed a Bachelor's degree or equivalent Completed a further degree e.g. masters or PhD etc [Field to auto populate from phone screener Q5, with ability to edit response at LHC]
	Smoking History	
17	Have you smoked more than 100 cigarettes in your lifetime?	Yes No [Field to auto populate from phone screener Q1, with ability to edit response at LHC]
17a	[If yes to Q17] Do you currently smoke cigarettes regularly?	Yes No

		[Field to auto populate from phone screener Q3, with ability to edit response at LHC]
17b	At what age did you start smoking cigarettes regularly?	_ years [Field to auto populate from phone screener Q3c, with ability to edit response at LHC] [range 1:78]
17c	[If no to Q17a] At what age did you stop smoking cigarettes regularly?	[number input] _ Years [Field to auto populate from phone screener Q3b, with ability to edit response at LHC] [range 1:78]
17d	[If yes to Q17a] During the time you have smoked cigarettes, have you ever stopped smoking for more than one month?	Yes No [Field to auto populate from phone screener Q3d, with ability to edit response at LHC]
17e	[If yes to 17d] How many months did you stop for in total? [Range 1-500]	Months [Field to auto populate from phone screener Q3d(i), with ability to edit response at LHC]
17f	How many cigarettes do or did you smoke per day on average for the majority of your time as a smoker?	__ number of cigarettes per day or __ grams of tobacco per week [Field to auto populate from phone screener Q3e or Q3f, with ability to edit response at LHC]
18	Have you ever smoked any of the following types of tobacco in addition to or instead of cigarettes?	[Please select all that apply] Cigars Cigarillos Pipe Marijuana Waterpipe None of the above
18a	[show if selects cigars in Q18] How often do or did you smoke cigars?	[please select one option] Occasionally (less than weekly) Regularly (at least once per week)
18b	[Show if select regularly to Q18a] Do you smoke cigars currently?	 Yes No
18c	[Show if select regularly to Q18a] At what age did you start smoking cigars?	[number input]

18d	[Show if select regularly to Q18a and no to Q18b] At what age did you stop smoking cigars?	[number input]
18e	[Show if select regularly to Q18a] How many cigars do or did you smoke per week on average for the majority of your time as a smoker?	[number input] _ per week
18f	[show if selects cigarillos in Q18] How often do or did you smoke cigarillos?	Occasionally (less than weekly) Regularly (at least once per week)
18g	[Show if select regularly to Q18f] Do you smoke cigarillos currently?	Yes No
18h	[Show if select regularly to Q18f] At what age did you start smoking cigarillos?	[number input]
18i	[Show if select regularly to Q18f and no to Q18g] At what age did you stop smoking cigarillos?	[number input]
18j	[Show if select regularly to Q18f] How many cigarillos do or did you smoke per week on average for the majority of your time as a smoker?	[number input] per week
18k	[show if selects pipe in Q18] How often do or did you smoke a pipe?	Occasionally (less than weekly) Regularly (at least once per week)
18l	[Show if select regularly to Q18k] Do you smoke a pipe currently?	Yes No
18m	[Show if select regularly to Q18k] At what age did you start smoking a pipe?	[number input]
18n	[Show if select regularly to Q18k and no to Q18l] At what age did you stop smoking a pipe?	[number input]
18o	[Show if select regularly to Q18k] How many pipe bowls do or did you smoke per week on average for the majority of your time as a smoker?	[number input] per week
18p	[show if selects marijuana in Q18] How often do or did you smoke marijuana?	Occasionally (less than weekly) Regularly (at least once per week) Decline to answer
18q	[Show if select regularly to Q18p] Do you smoke marijuana currently?	Yes No
18r	[Show if select regularly to Q18p] At what age did you start smoking marijuana?	[number input]
18s	[Show if select regularly to Q18p and no to Q18q] At what age did you stop smoking marijuana?	[number input]
18t	[Show if select regularly to Q18p]	[number input] per week

	How many joints of marijuana do or did you smoke per week on average for the majority of your time as a smoker?	
18u	[show if selects waterpipe in Q18] How often do or did you use a waterpipe (20 minute session)?	Occasionally (less than weekly) Regularly (at least once per week)
18v	[Show if select regularly to Q18u] Do you smoke a waterpipe currently?	Yes No
18w	[Show if select regularly to Q18u] At what age did you start smoking a waterpipe?	[number input]
18x	[Show if select regularly to Q18u and no to Q18v] At what age did you stop smoking a waterpipe?	[number input]
18y	[Show if select regularly to Q18u] For how many sessions (20 minutes) do or did you use a waterpipe per week on average for the majority of your time as a smoker?	[number input] per week
	Smoking cessation	
19	[Show if yes to Q17a or 18b or 18g or 18l] Please confirm that Very Brief Advice (VBA) on smoking cessation has been given	Yes No
19a	[Show if 'No' to Q19] If no VBA given, please briefly explain why	[Free text]
20	[if yes to Q17a or 18b or 18g or 18l] Has the participant consented to a smoking cessation referral being made on their behalf? This includes consent to their information being shared with a stop smoking service and to being contacted about the referral by that service.	Yes No, the participant would prefer to self-refer No, the participant does not want support from a stop smoking service No, already in contact with a stop smoking service
	Clinical recordings	
23	Height [range:60-280]	__cm [numerical input to 1.dp]
24	Weight [range:25-350]	__ kg [numerical input to 1.dp]
25	Has the participant had their blood pressure taken?	Yes Declined
25a	[Show if yes to Q25] BP (systolic) [range:30-250]	__ mmHg

25b	[Show if yes to Q25] BP (diastolic) [range:10-250]	__ mmHg
26a	Was spirometry cancelled due to Covid-19 related social distancing guidelines?	Yes No
26b	[show if "No" to 26a] Is spirometry contraindicated?	Yes No
26c	[Show if no to Q26b] FEV1 [Range 0.10L to 9.99L]	__ litres [numerical input to 2. dp]
26d	[Show if no to Q26b] FEV1 % Predicted [Max 250%]	__ % [numerical to 1.dp]
26e	[Show if no to Q26b] FVC [Range 0.1L to 9.99L]	__ litres [numerical input to 2 dp]
26f	[Show if no to Q26b] FVC % Predicted [Max 250%]	__ %
26g	[Show if no to Q26b] FEV1: FVC [Range 0-1]	[Numerical input to 2.dp]
27	BMI [This should be calculated, no need for staff to enter] [Hidden from the nurse/UI]	__ kg/m2
28	USPSTF criteria met? [This should be calculated, no need for staff to enter] [Hidden from Nurse/UI]	Yes No
29	PLCO risk score [This should be calculated, no need for staff to enter] [Hidden from Nurse/UI]	Numeric
30	Smoking pack years [This should be calculated, no need for staff to enter] [Hidden from Nurse/UI]	Numeric

Appendix 3: Supplementary data

	Emphysema (n=3711)	**No emphysema (n=7404)**	**p value**
Age (years)	66.26 (±6.01)	64.90 (±6.11)	<0.001
Male (%)	58.6% (n=2175)	56.9% (n=4211)	0.081
Current smoker (%)	51.4% (n=1907)	47.1% (n=3490)	<0.001

Pack year history (years)	47.84 (±22.72)	44.05 (±23.03)	<0.001
Airflow obstruction? (%)	67.8% (n=2515)	40.3% (n=2982)	<0.001
Cough > 6 weeks (%)	28.3% (n=1052)	21.9% (n=1620)	<0.001
Sputum (%)	19.6% (n=727)	13.7% (n=1012)	<0.001
MRC score ≥1 (%)	70.5% (n=2618)	63.9% (n=4730)	<0.001
≥2 exacerbations per year (%)	10.1% (n=375)	6.5% (n=479)	<0.001
Self-reported diagnosis of COPD	52.3% (n=2126)	31.6% (n=2342)	<0.001

Supplementary Table A: Characteristics of those with emphysema on baseline LDCT compared to those without

	Bronchiectasis (n=818)	**No bronchiectasis (n=10,297)**	**p value**
Age (years)	67.33 (±5.88)	65.20 (±6.10)	<0.001
Male? (%)	59.8% (n=489)	57.3% (n=5897)	0.162
Cough > 6 weeks (%)	27.6% (n=226)	23.8% (n=2448)	0.013
Sputum (%)	18.8% (n=154)	15.4% (n=1585)	0.009
MRC score ≥1 (%)	67.8% (n=555)	66.0% (n=6793)	0.275
Haemoptysis in past year? (%)	2.6% (n=21)	2.3% (n=237)	0.627
Exacerbations in past year (median)	0.00 (0.00-1.00)	0.00 (0.00-0.00)	<0.001
≥2 exacerbations per year (%)	10.1% (n=83)	7.5% (n=771)	0.006
Previous pneumonia (%)	20.8% (n=170)	14.5% (n=1495)	<0.001
Previous TB (%)	4.4% (n=36)	1.9% (n=199)	<0.001
Self-reported bronchiectasis (%)	1.7% (n=14)	0.7% (n=75)	0.002
FEV1% predicted (%)	74.01 (±22.14)	76.16 (±19.58)	0.003
Airflow obstruction (%)	54.5% (n=446)	49.1% (n=5051)	0.003

Supplementary Table B: Characteristics of those with and without bronchiectasis on baseline LDCT

Variable	**Unadjusted OR (95% CI)**	**p**	**Adjusted OR (95% CI)**	**p**
Age				
Per increasing year	1.06 (1.05-1.07)	<0.001	1.05 (1.04-1.07)	<0.001
Gender				

Male	1		1	
Female	0.902 (0.780-1.043)	0.162	0.87 (0.75-1.01)	0.064
Previous TB				
No history of TB	1		1	
Previous TB	2.332 (1.626-3.356)	<0.001	2.20 (1.53-3.12)	<0.001
Pneumonia				
No previous history	1		1	
History of pneumonia	1.545 (1.293-1.845)	<0.001	1.42 (1.19-1.71)	<0.001
Smoking status				
Current smoker	1	<0.001	1	
Former smoker	1.49 (1.29-1.72)		1.22 (1.45-1.54)	<0.001
Exacerbations in past 12 months				
Per increasing exacerbation	1.12 (1.06-1.12)	<0.001	1.10 (1.04-1.17)	0.002
Airflow obstruction				
No airflow obstruction	1		1	
Airflow obstruction	1.25 (1.08-1.44)	0.003	1.08 (0.93-1.25)	0.305

Supplementary Table C: Bronchiectasis: Univariate and multivariate binary logistic analysis assessing the relationship between associated variables and presence on baseline LDCT

	ILD (n=528)	**No ILD (n= 10,587)**	**p value**
Age (years)	67.52 (±6.03)	65.24 (±6.09)	<0.001
Male Sex (%)	64.6% (n=341)	57.1% (n=6045)	0.001
Current smoker (%)	47.5% (n=251)	48.6% (n=5146)	0.631
Pack year history (years)	45.80 (±25.70)	45.29 (±22.86)	0.620
Cough > 6 weeks (%)	26.1% (n=138)	23.9% (n=2534)	0.248
MRC score ≥1 (%)	67.4% (n=356)	66.0% (n=6992)	0.513
Self-reported ILD (%)	1.1% (n=6)	0.3% (n=37)	0.004
FEV1% predicted (%)	77.98 (±18.60)	75.91 (±19.84)	0.019
Emphysema present (%)	37.3% (n=197)	33.2% (n=3541)	0.050
Airflow obstruction (%)	42.8% (n=226)	49.8% (n=5271)	0.002

Supplementary Table D: Characteristics of those with and without ILA on baseline LDCT

Variable	**Unadjusted OR (95% CI)**	**p**	**Adjusted OR (95%CI)**	**p**
Age				
Per increasing year	1.062 (1.049-1.079)	<0.001	1.072 (1.055-1.088)	<0.001
Gender				
Female	1		1	
Male	1.370 (1.142-1.644)	0.001	1.272 (1.047-1.546)	0.016
Pneumonia				

No previous history	1		1	
History of pneumonia	0.952 (0.742-1.221)	0.699	0.942 (0.731-1.214)	0.646
Smoking status				
Current smoker	1		1	
Former smoker	1.044 (0.876-1.243)	0.632	0.878 (0.733-1.052)	0.159
Pack years				
Per increasing year	1.001 (0.997-1.005)	0.620	1.00 (0.996-1.003)	0.852
Occupational Asbestos exposure				
No	1		1	
Yes	1.389 (1.127-1.712)	0.002	1.293 (1.033-1.618)	0.025
Airflow obstruction				
No airflow obstruction	1		1	
Airflow obstruction	0.755 (0.633-0.990)	0.002	0.608 (0.504-0.734)	<0.001

Supplementary Table E: Interstitial Lung Abnormalities: Univariate and multivariate binary logistic analysis assessing the relationship between associated variables and presence on baseline LDCT

	CAC present (n=7141)	No CAC (n=3974)	p value
Age (years)	66.52 (±5.98)	63.26 (±5.78)	<0.001
Male Sex(%)	65.3% (n=4663)	43.4% (n=1723)	<0.001
BMI (kg/m^2)	28.28 (±9.63)	27.90 (±9.24)	0.040
Systolic BP (mmHg)	135.34 (±17.68)	131.83 (±17.23)	<0.001
Systolic BP ≥140mmHg (%)	40.7% (n=2906)	32.1% (n=1275)	<0.001
Systolic BP ≥160mmHg (%)	8.4% (n=598)	5.9% (n=233)	<0.001
Diastolic BP (mmHg)	79.72 (±10.53)	80.41 (±10.15)	0.001
Current smoker (%)	47.3% (n=3378)	50.8% (n=2019)	<0.001
Pack year history (years)	46.67 (±24.19)	42.88 (±20.48)	<0.001
Ethnicity			
White	84.0% (n=5997)	82.1% (n=3262)	<0.001
Mixed	2.0% (n=141)	2.7% (n=109)	
Asian	7.8% (n=560)	4.6% (n=183)	
Black	3.2% (n=226)	6.5% (n=258)	
Other	3.0% (n=217)	4.1% (n=162)	
Airflow obstruction (%)	51.8% (n=3696)	45.3% (n=1801)	<0.001

Supplementary Table F. Baseline characteristics of those with CAC compared to those without CAC on baseline LDCT

	Thoracic aneurysm present (N=306)	No aneurysm present (N=10809)	p value
Age (years)	66.64 (±9.75)	65.32(±10.00)	<0.001
Male Sex(%)	69.9% (n=214)	57.1%(N=6172)	<0.001
BMI (kg/m^2)	28.08 (±5.90)	28.15 (±6.61)	0.810
Systolic BP (mmHg)	135.5 (±22.0)	134.0 (±24.0)	<0.001
Systolic BP ≥140mmHg (%)	38.9% (n=119)	37.6% (n=4062)	0.685
Systolic BP ≥160mmHg (%)	9.5% (n=29)	7.4% (n=802)	0.215
Diastolic BP (mmHg)	83.2 (IQR±14)	79.88 (±14)	<0.001
Current smoker (%)	47.3% (n=3378)	50.8% (n=2019)	<0.001
Pack year history (years)	43.46 (±19.25)	45.36 (±18.75)	0.136
Ethnicity			
White	84.0% (n=5997)	82.1% (n=3262)	<0.001
Mixed	2.0% (n=141)	2.7% (n=109)	
Asian	7.8% (n=560)	4.6% (n=183)	
Black	3.2% (n=226)	6.5% (n=258)	
Other	3.0% (n=217)	4.1% (n=162)	
Airflow obstruction (%)	50.7% (n=155)	49.4% (n=5342)	0.714

Supplementary Table G: Baseline characteristics of those with and without thoracic aortic aneurysm on baseline LDCT

Variable	Unadjusted OR (95% CI)	p	Adjusted OR (95% CI)	p
BMI				
Per increasing kg/m^2	0.998 (0.980-1.008)	0.822	0.998 (0.980-1.007)	0.827
Age				

Per increasing year	1.036 (1.017 – 1.055)	<0.001	1.048 (1.027- 1.069)	<0.001
Gender				
Female	1		1	
Male	1.748 (1.370 – 2.248)	<0.001	1.655 (1.290 – 2.139)	<0.001
Blood pressure				
Systolic BP	1.010 (1.004-1.017)	0.001	0.998 (0.990 – 1.005)	0.537
Diastolic BP	1.030 (1.019 – 1.040)	<0.001	1.032 (1.020 – 1.045)	<0.001
Smoking status				
Former smoker	1		1	
Current smoker	1.019 (0.812-1.279)	0.869	1.126 (0.890 – 1.425)	0.321
Pack year history				
Per increasing pack year	0.996 (0.990 – 1.001)	0.152	0.994 (0.988 – 1.000)	0.044
Airflow obstruction				
No airflow obstruction	1		1	
Airflow obstruction	1.051 (0.837 – 1.319)	0.671	1.000 (0.790-1.263)	0.990

Supplementary Table H: Thoracic Aortic Aneurysm: Univariate and multivariate binary logistic analysis assessing the relationship between associated variables and presence on baseline LDCT

	Vertebral wedge fracture *(n=801)*	**No vertebral wedge fractures *(n=10,314)***	**p value**
Prevalence in males	467/6386 (7.3%)	-	
Prevalence in females	334/4729 (7.1%)	-	
Age (years)	67.24 (±6.15)	65.21 (±6.08)	<0.001
Female (%)	41.7 % (n=334)	42.6% (n=4395)	0.614
BMI (kg/m^2)	27.42 (±5.24)	28.20 (±9.74)	0.026
Pack year history	45.98 (±22.36)	45.26 (±23.05)	0.394
Current smoker (%)	47.7% (n=382)	48.6% (n=5015)	0.611
Personal history of cancer (%)	15.4% (n=123)	13.1% (n=1351)	0.07
IMD rank	12,147.84 (±7660.29)	12068.96 (±7797.61)	0.784
Exacerbations over last year	0.00 (0.00-0.00)	0.00 (0.00-0.00)	0.351
Airflow obstruction (%)	58.1% (n=465)	48.8% (n=5032)	<0.001

Supplementary Table I: Characteristics of those with and without the presence of vertebral wedge fractures on baseline LDCT

Variable	**Unadjusted OR**	**p**	**Adjusted OR**	**p**
BMI				
Per increasing kg/m^2	0.98 (0.97-0.99)	0.004	0.99 (0.97-1.00)	0.043
Age				
Per increasing year	1.06 (1.04-1.07)	<0.001	1.05 (1.04-1.07)	<0.001
Gender				
Male	1		1	
Female	0.96 (0.83-1.11)	0.61	0.95 (082-1.10)	0.505
Smoking status				
Current smoker	1		1	
Former smoker	1.04 (0.90-1.20)	0.611	0.96 (0.82-1.11)	0.957

Pack year history				
Per increasing pack year	1.00 (1.00-1.00)	0.39	1.00 (1.00-1.00)	0.885
Personal history of cancer				
No	1		1	
Yes	1.20 (0.98-1.47)	0.07	1.1 (0.90-1.35)	0.368
Airflow obstruction				
No airflow obstruction	1		1	
Airflow obstruction	1.45 (1.26-1.68)	<0.001	1.26 (1.08-1.46)	0.003

Supplementary Table J: Vertebral wedge fractures: Univariate and multivariate binary logistic analysis assessing the relationship between associated variables and presence on baseline LDCT

	Hiatus Hernia *(n=1068)*	**No hiatus hernia *(n=10,047)***	**p value**
Age (years)	67.59 (±5.92)	65.12 (±6.08)	<0.001
Male (%)	49.3% (n=527)	58.3% (n=5859)	<0.001
BMI (kg/m^2)	28.69 (±5.20)	28.08 (±9.84)	0.046
Current smoker (%)	38.5% (n=411)	49.6% (n=4986)	<0.001
Airflow obstruction (%)	55.9% (n=597)	48.85 (n=4900)	<0.001

Supplementary Table K: Characteristics of participants with and without the presence of a hiatus hernia on baseline LDCT

Variable	**Unadjusted OR (95% CI)**	**p**	**Adjusted OR (95%CI)**	**p**
Age				
Per increasing year	1.069 (1.058-1.080)	<0.001	1.062 (1.050-1.073)	<0.001
Gender				
Female	1		1	
Male	0.696 (0.614-0.790)	<0.001	0.693 (0.610-0.788)	<0.001
BMI				
Per increasing kg/m^2	1.004 (1.000-1.009)	0.061	1.005 (1.000-1.009)	0.059
Smoking status				
Current smoker	1		1	
Former smoker	1.575 (1.384-1.792)	<0.001	1.379 (1.207-1.575)	<0.001
Airflow obstruction				
No	1		1	
Yes	1.331 (1.173-1.512)	<0.001	1.195 (1.049-1.362)	0.007

Supplementary Table L: Hiatus Hernia: Univariate and multivariate binary logistic analysis assessing the relationship between associated variables and presence on baseline LDCT