

Novel Approaches to Lung Cancer Screening

S128 LUNGSEARCH: A RANDOMISED CONTROLLED TRIAL OF SURVEILLANCE FOR THE EARLY DETECTION OF LUNG CANCER IN A HIGH RISK GROUP

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10.1136/thoraxjnl-2016-209333.134

Screening for the early detection of lung cancers should increase the percentage of operable tumours, thus improving cure rates. A large randomised US trial showed that CT screening moderate/heavy smokers is effective but expensive, with a high false-positive rate. We designed LungSEARCH in 2006 to target screening in higher-risk subjects. Because most tumours in the UK were of squamous-histology, we hypothesised that sputum cytology plus cytometry would be an effective initial screen, only offering more intensive/expensive tests to those with abnormal sputum.

Eligibility criteria were: current/former smokers (≥ 20 pack-years and/or smoked ≥ 20 years), GOLD-defined COPD, no prior cancer. Subjects were randomised to surveillance or a control group, and each followed for 5 years. Screened subjects provided sputum for central assessment, and those with abnormal results (cytology: low/high-grade squamous intraepithelial lesions, and/or cytometry: abnormal ploidy) were referred for annual low-dose CT and autofluorescence bronchoscopy (AFB) for the remainder of the trial, with diagnostic investigations when cancer suspected by abnormal CT/AFB. Sputum-negatives provided annual sputum samples only. Control subjects had a chest X-ray when they reached 5 years. Primary objective: to show a higher proportion of early stage cancers using surveillance than controls.

1568 subjects were recruited (target 1300) from GPs or chest clinics around 10 UK centres (August 2007–March 2011): 785 screened, 783 controls. Mean age 63 years; males 52%; current (56%), former (44%) smokers; mild (25%), moderate (75%) COPD; from GPs (79%). $>90\%$ screened subjects provided sputum samples in their first year. After 5 years, the overall sputum-positive rate is 33%; 30% (236/785) had a CT scan and 25% (193/785) had an AFB at any time. Of those who had a CT scan 19% (45/236) were abnormal (lung nodule(s) ≥ 9 mm); and of those who had AFB 3% (5/193) had severe dysplasia or worse.

79 lung cancers have been identified to date via the centres/national registry: 43 surveillance and 36 control. But awaiting staging details for 6 surveillance and 14 control cases. Preliminary results are promising: 57% (surveillance) versus 41% (controls) of cancers were diagnosed with stage I/II non-small-cell-lung cancer or limited disease small-cell-lung cancer. Final data available later in 2016.

S129 WHAT PROPORTION OF PATIENTS WITH LUNG CANCER WOULD HAVE BEEN ELIGIBLE FOR CT SCREENING ACCORDING TO VARIOUS PROPOSED INCLUSION CRITERIA?

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10.1136/thoraxjnl-2016-209333.135

Abstract The US National Lung Screening Trial (NLST) identified persons for lung cancer screening by age (55–74 yrs) and smoking history, but a subsequent analysis of the US SEER database showed that only 26.7% of lung cancer cases would have been eligible for screening according to these criteria.

Strategies to increase the proportion of lung cancer patients who might qualify for screening include increasing the upper age limit to 80 years (endorsed by the US Preventative Services Task Force – USPSTF), and using composite lung cancer risk prediction tools. The UK Lung Screening pilot (UKLS) used the Liverpool Lung Project score (LLP) to identify patients for screening. In a validation cohort from the US Prostate, Lung, Colorectal and Ovarian study, a threshold based on the $PLCO_{M2012}$ score identified more cancers than the NLST criteria. We prospectively compared these criteria for the first time in patients presenting with lung cancer in Yorkshire.

Methods We audited the proportion of patients presenting with lung cancer through fast-track clinics at 4 Yorkshire centres who would have been eligible for screening according to the following

Abstract S129 Table 1 The numbers and proportions of lung cancer patients who would have been eligible for CT screening according to various inclusion criteria

Criteria	Descriptor	Number of eligible patients	Proportion of all lung cancer patients	Proportion of 55–80yrs ever-smoking patients
NLST	Age 55–74, ≥ 30 pack years smoking, quit time < 15 years	71	34.5%	51.1%
USPSTF	Age 55–80, ≥ 30 pack years smoking, quit time < 15 years	89	43.2%	64.0%
UKLS	Age 50–75, $\geq 5\%$ lung cancer risk by LLPv.2	67	32.5%	48.2%
$PLCO \geq 1.51\%$	Age 55–80, $\geq 1.51\%$ lung cancer risk by $PLCO_{M2012}$	111	53.9%	79.9%
$LLP \geq 5\%$	Age 55–80, $\geq 5\%$ lung cancer risk by LLPv.2	94	45.6%	67.6%

criteria: NLST criteria, UKLS criteria, USPSTF criteria, LLP $\geq 5\%$ 55–80 yrs, and PLCO $\geq 1.51\%$ 55–80 yrs.

Results Data was collected for 206 patients presenting between January and July 2016 (Leeds 131, Halifax 26, Bradford 12, Mid-Yorkshire 37). Median age was 72 years and the proportion of cases by age cohort was as follows: <55 yrs 9.2%, 55–60 yrs 9.7%, 61–65 yrs 12.1%, 66–70 yrs 13.6%, 71–75 yrs 18.4%, 76–80 yrs 17.0%, >80 yrs 19.9%. Smoking status was: current smoker 89 (43.2%), ex-smoker 106 (51.5%) and never smoker 11 (5.3%). The number of patients eligible by the various criteria are shown in Table 1.

Conclusion The proportion of lung cancer patients who would have been eligible for screening differs considerably between the various criteria. Only approximately one third of patients would have been eligible according to the criteria used in NLST and UKLS. Increasing the upper age limit for screening to 80yrs substantially increases the proportion of cases that would be eligible. A threshold of 1.51% by the PLCO_{M2012} score included the largest number of lung cancer patients of the criteria assessed.

S130 THE PREVALENCE OF UNDIAGNOSED COPD ON SPIROMETRY AND EMPHYSEMA ON LOW-DOSE CT SCANS IN A LUNG CANCER SCREENING DEMONSTRATION PILOT: A TEACHABLE MOMENT?

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10.1136/thoraxjnl-2016-209333.136

Introduction and objectives Chronic obstructive pulmonary disease (COPD) and emphysema are considerably under-diagnosed

conditions. Low dose CT (LDCT) for lung cancer screening, if implemented, may provide an opportunity for earlier diagnosis of smoking-related conditions, in addition to lung cancer. Data gathered in a lung cancer screening demonstration pilot was analysed to look at COPD-related radiological changes and their relationship with patients' pre-existing diagnoses, spirometry results and smoking status. The aims were to better understand these interlinked conditions and identify the potential for earlier diagnosis and management of smoking cessation interventions for these conditions.

Methods Data were collected as part of the Lung Screen Uptake Trial. Smokers and recent former smokers (quit <5 years) aged 60–75 were invited to a 'lung health check' via their general practitioner (GP). Data on pre-existing diagnoses, smoking status and pre-bronchodilation spirometry, categorised according to the National Institute for Clinical Excellence (NICE) criteria, were collected. Patients who met the eligibility criteria for screening went on to have LDCT. Results were analysed for frequencies, and confidence intervals calculated for the most significant results.

Results 275 patients responded to an invitation to attend a 'lung health check' in the first six months of recruitment. 149 (54.2%) had values consistent with COPD on spirometry. 106 [71.1%, (95% CI: $\pm 7.3\%$)] of these individuals were not aware of a diagnosis of COPD, and 81 (76.4%) were current smokers (Figure 1). Of the 103 individuals who had emphysema and no suspicious lesion on LDCT, 74 [71.8%, (95% CI: $\pm 8.7\%$)] were not aware of a diagnosis of COPD or emphysema. 55 (74.3%) of these were current smokers, and 33 (44.6%) had preserved spirometry (Table 1).

Conclusion Our data demonstrate the considerable burden of undiagnosed COPD in at-risk groups (38.5% of all screened individuals), and show the prevalence of emphysematous change in those patients without a pre-existing, self-reported diagnosis of COPD or with preserved spirometry. Early diagnosis and CT evidence of smoking damage may provide the opportunity to co-implement supportive smoking cessation interventions, earlier

Abstract S130 Table 1 Smoking status and severity of COPD on spirometry and severity of emphysema on LDCT. Shaded columns represent the patients within that category who reported a pre-existing diagnosis of COPD or emphysema.

		Severity of COPD based on NICE criteria for COPD (2004) (3)*									
		Normal		Mild		Moderate		Severe		Totals	
		#	% with PMHx COPD	#	% with PMHx COPD	#	% with PMHx COPD	#	% with PMHx COPD	#	% with PMHx COPD
Cases		Cases		Cases		Cases		Cases		Cases	
Smoking Status	No smoking data	0		0		1	100%	0		1	100%
	Current smoker	76	10.5%	39	12.8%	46	30.4%	18	50.0%	179	20.1%
	Former smoker	43	11.6%	13	23.1%	19	36.8%	5	40.0%	80	21.3%
	Occasional smoker	7	0%	4	0%	2	50.0%	2	50.0%	15	13.3%
Total	126	10.3%	56	14.3%	68	33.8%	25	48%	275	20.4%	
		Severity of Emphysema on CT									
		Not present		Mild		Moderate		Severe		Totals	
		#	% with PMHx COPD	#	% with PMHx COPD	#	% with PMHx COPD	#	% with PMHx COPD	#	% with PMHx COPD
Cases		Cases		Cases		Cases		Cases		Cases	
Smoking Status	Current smoker	37	5.4%	40	17.5%	25	28.0%	8	75.0%	110	20.0%
	Former smoker	28	14.2%	16	31.3%	8	12.5%	3	66.7%	55	21.8%
	Occasional smoker	5	0%	1	0%	0	0%	2	50.0%	8	12.5%
Total	70	8.6%	57	21.1%	33	24.2%	13	69.2%	173	20.2%	

*Spirometry values are pre-bronchodilator results, categorised by severity according to 2004 NICE criteria: National Collaborating Centre for Acute and Chronic Conditions. Chronic obstructive pulmonary disease in over 16s: diagnosis and management. 2010;(June).