

Analysis of the baseline performance of five UK lung cancer screening programmes

Haval Balata^{1+2#}, Mamta Ruparel³, Emma O'Dowd⁴, Martin Ledson⁵, John K. Field⁶,
Stephen W. Duffy⁷, Samantha L Quaife⁷, Anna Sharman¹, Sam Janes³, David Baldwin⁴,
Richard Booton¹, Philip A.J. Crosbie¹⁺².

¹Manchester Thoracic Oncology Centre (MTOC), Wythenshawe Hospital, Manchester University NHS Foundation Trust, Manchester, UK. ²Division of Infection, Immunity and Respiratory Medicine, Faculty of Biology, Medicine and Health, University of Manchester, Manchester, UK. ³Lungs for Living Research Centre, UCL Respiratory, University College London, London, UK. ⁴Department of Respiratory Medicine, Nottingham City Hospital, Nottingham, UK. ⁵Liverpool Heart and Chest Hospital NHS Foundation Trust, Liverpool, UK. ⁶Molecular and Clinical Cancer Medicine, Faculty of Health and Life Sciences, University of Liverpool, Liverpool, UK. ⁷Centre for Cancer Prevention, Wolfson Institute of Preventive Medicine, Queen Mary University of London, London, UK.

#Corresponding author: Dr Haval Balata, Manchester Thoracic Oncology Centre, Manchester University NHS Foundation Trust, Southmoor Road, Wythenshawe, M23 9LT. Tel +44 (0)161 291 3597.
E-mail: haval.balata@mft.nhs.uk

Abstract

Introduction: Low-dose CT (LDCT) screening reduces lung cancer specific mortality. Several countries, including the UK, are evaluating the clinical impact and cost-effectiveness of LDCT screening using the latest evidence. In this paper we report baseline screening performance from five UK-based lung cancer screening programmes.

Methods: Data was collected at baseline from each screening programme. Measures of performance included prevalence of screen detected lung cancer, rate of surveillance imaging for indeterminate findings and surgical resection rates. Screening related harms were assessed by measuring false positive rates, number of invasive tests with associated complications in individuals without lung cancer and benign surgical resection rates.

Results: A total of 11,148 individuals had a baseline LDCT scan during the period of analysis (2011 to 2020). Overall, 84.7% (n=9,440) of baseline LDCT scans were categorised as negative, 11.1% (n=1,239) as indeterminate and 4.2% (n=469) as positive. The prevalence of screen detected lung cancer was 2.2%, ranging between 1.8% and 4.4% for individual programmes. The surgical resection rate was 66% (range 46% to 83%) and post-surgical 90-day mortality for those with lung cancer 1.2% (n=2/165). The false positive rate was 2% (n=219/10,898) and of those with a positive result, one in two had lung cancer diagnosed (53.3%). An invasive test was required in 0.6% (n=61/10,898) of screening attendees without lung cancer; there were no associated major complications or deaths. The benign surgical resection rate was 4.6% (n=8/173), equating to 0.07% of the screened population.

Discussion: The performance of UK-based lung cancer screening programmes, delivered within or aligned to the National Health Service, compares favourably to published clinical trial data. Reported harms, including false positive and benign surgical resection rates are low. Ongoing monitoring of screening performance is vital to ensure standards are maintained and harms minimised.

Introduction

Lung cancer is the world's leading cause of cancer related death¹. In the United Kingdom (UK) there are over 45,000 new cases and 35,000 deaths each year². The symptomatic presentation of lung cancer is characteristically associated with advanced disease when treatments are ineffective and survival is very poor. Screening high-risk smokers and former smokers with LDCT detects early stage disease, prior to the development of symptoms, and reduces lung cancer specific mortality. This has been definitively demonstrated in two large randomised controlled trials (RCT), the National Lung Screening Trial (NLST) and the NELSON trial^{3,4}. Screening with LDCT is being implemented in the United States, Canada, some East Asian countries and is being considered across Europe⁵. In the UK, a number of implementation pilots⁶⁻⁸ and research studies⁹⁻¹¹ have demonstrated that screening can be successfully delivered within or aligned to the National Health Service (NHS). Building on these solid foundations NHS England recently announced funding (£71 million) to undertake an expanded screening programme at a number of sites across the country¹².

A critically important requirement for screening implementation is the minimisation of harms. It is also important for individuals who are considering the offer of screening to support informed decision-making by ensuring benefits and risks are clearly communicated. Harms associated with lung cancer screening are well described. These include overdiagnosis, anxiety or psychological harm related to screening outcomes, radiation exposure, false negatives and the investigation and treatment of false positive findings⁵. Although well described, the extent of harm from lung screening is variably reported. Determining the prevalence and clinical significance of screening related harms, for instance due to investigation or treatment of benign disease, is a key measure of screening quality⁵.

Results from large RCTs are commonly used as a benchmark for screening performance and to quantify the potential risks and benefits. However, data extrapolated from RCTs may not provide an accurate representation of screening performance in a 'real world' setting. This may be due to

important differences in population selection, healthcare setting or pulmonary nodule management protocols. One recent study demonstrated how modern pulmonary nodule management may have reduced harm in the NLST¹³. In this paper we present cumulative data from five UK-based lung cancer screening programmes; focusing on performance and measures that reflect possible screening related harms. This is the first-time screening harms data have been examined in detail within the NHS and out with the confines of a single research trial. We present this data as infographics which, after careful evaluation with the target population first, could be used to communicate the harms of screening to those considering screening participation.

Methods

Aggregate data from five UK lung cancer screening programmes is included in the analysis. This includes two RCTs, the UK Lung Cancer Screening Trial (UKLS)⁹ and the Lung Screen Uptake Trial (LSUT)¹⁰, an observational cohort study, the Nottingham Lung Health MOT¹⁴, and two NHS commissioned screening services: the Manchester Lung Health Check pilot^{6,7} and the Liverpool Healthy Lung Project⁸. All sites performed a baseline screening round, Manchester was the only site to perform a second round. British Thoracic Society (BTS) Guidelines for the Investigation and Management of Pulmonary Nodules¹⁵ were used by all sites except UKLS which used a bespoke nodule management protocol¹⁶.

Screening outcomes were categorised as negative, indeterminate and positive. LDCT scan findings requiring further surveillance imaging, without the need for assessment in a lung cancer clinic, were defined as indeterminate. Surveillance was primarily for small nodules or nodules with a low cancer risk. A positive screening test was defined as a finding or findings concerning for lung cancer requiring immediate investigation, usually in the local fast track cancer diagnostic service. A positive was categorised as a false positive if the eventual diagnosis was not lung cancer. The false positive rate was calculated by dividing the number of false positives by the number of false positives and true negatives combined. A zero false negative rate was assumed for the purpose of analysis. Harms were categorised according to the need for further imaging, invasive investigations and/or surgery. All image-guided biopsies and bronchoscopic procedures were classified as 'invasive' investigations as per previous studies. Complications were categorised into minor, indeterminate and major as defined in NLST³.

Results

A brief overview of each screening programme is provided in Table 1. A total of 11,148 individuals had a baseline LDCT scan and are included in the analysis; ranging from 361 to 6,639 at each site. Overall, 84.7% ($n=9,440/11,148$) were categorised as negative and either returned to annual screening or discharged depending on individual site protocols. 11.1% ($n=1,239/11,148$) had an indeterminate screening outcome and required interval imaging. The proportion classified as positive, including those after a period of surveillance, was 4.2% ($n=469/11,148$). A total of 250 individuals (48.8% female) were diagnosed with screen detected lung cancer, a prevalence of 2.2% ($n=250/11,148$); ranging from 1.8% to 4.4% across the sites. The overall stage distribution of the diagnosed lung cancers was 64% stage I, 17.2% stage II, 10.8% stage III and 8% stage IV. The surgical resection rate was 66% ($n=165/250$), range 46% to 83%. Of those with a confirmed lung cancer diagnosis, 2% ($n=5/250$) had a major complication from invasive investigation/treatment. This included two post-operative deaths within 90-days of surgery. The 90-day mortality rate after surgical resection of screen detected lung cancer in this cohort was therefore 1.2% ($n=2/165$).

Of those with a positive screen result, 53.3% had a diagnosis of lung cancer confirmed. The false positive rate was 2% ($n=219/10,898$). The proportion of individuals without lung cancer who required an invasive test (excluding surgery) was 0.6% ($n=61/10,898$) from which there were no major complications or deaths. The benign surgical resection rate, expressed as a proportion of all surgery, was 4.6% ($n=8/173$), representing 0.07% of the screened population. Details of cumulative reported harms are summarised in Table 2. In the Manchester pilot 1,194 participants also underwent a second round of screening from which 19 (1.6%) participants were diagnosed with lung cancer. In this round of screening the false positive rate was 0.9% ($n=10/1,175$), lower than the equivalent number in the baseline screening round. Invasive investigation for benign disease was similar to the baseline round at 0.6% with no associated major complications or deaths. The false negative rate for Manchester's baseline round was 0.4%.

Based on aggregate baseline data from all sites we designed an infographic to illustrate the proportion of individuals classified as either negative, indeterminate and positive in the baseline round (Figure 1). A second infographic demonstrates the prevalence of reported harms for participants including the risk of a false positive screening result (Figure 2). Due to the low incidence of measured harms, data was extrapolated to harms per 10,000 participants and presented in the context of an image thought to be familiar to the general public, in this case an events stadium. Whilst this would require evaluation with the target population first, this is one potential approach to communicate risks of screening as one part of the informed decision-making process.

Discussion

In this paper we report baseline screening performance from five independent UK-based lung cancer screening programmes including over 11,000 participants. The overall prevalence of lung cancer was 2.2%. This compares to 0.9% and 1% in NELSON and NLST respectively. The higher prevalence observed across the UK programmes may reflect the use of individual risk-based selection criteria and the location of services in areas of high socio-economic deprivation. Only 4.2% of participants had a positive screening scan requiring referral and further assessment in local lung cancer diagnostic services. This is significantly lower than NLST (27.3%) and the majority of European screening trials except NELSON (2.3%). Of those with a positive screening outcome, just over half (53.3%) were diagnosed with lung cancer, higher than NLST (3.8%) and NELSON (38.1%). The baseline false positive rate was 2%, equivalent values being 21% in NLST and 1.4% in NELSON.

Harms from the investigation and treatment of findings that were eventually determined not to be lung cancer was low. The rate of invasive investigations (excluding surgery) in those without lung cancer was 0.6% ($n=61/10,898$) and there were no reports of major complications or deaths. The benign surgical resection rate was 4.6% as a proportion of all surgery or 0.07% of all baseline scans. This is significantly lower than NLST (24.4% of all surgeries) and other large lung cancer screening trials, data historically used to discuss screening harms with participants. In this study we report harms from the baseline screening round. It is important to note that harms associated with subsequent screening rounds are likely to differ. In the Manchester programme the rate of harm was lower in the second round, likely due to having a baseline scan as a comparator. This is in keeping with other published studies suggesting the risk of screen-related harms maybe greatest in the first round¹⁷.

We developed two infographics designed to present data related to screening outcomes and measured screening related harms. This is one suggested approach to support the knowledge exchange component of informed decision making in those considering screening participation and

includes our 'real world' data representative of screening outcomes in the UK. It is important to acknowledge however that not all screening related harms were measured in this analysis, including overdiagnosis or the psychological impact of screening. However, recent studies which explored the psychological impact of screening in participants of the LSUT and UKLS (both cohorts included in this analysis), reported raised psychological distress in individuals undergoing screening but at a level that was not thought to be clinically meaningful or long-term^{18 19}.

In conclusion, our data demonstrate that lung cancer screening delivered in the UK, either by commissioned services or research studies aligned to the NHS, provide outcomes that are comparable to and in some aspects superior to published RCTs. Providing individuals who are considering screening participation with 'real world' data that is more representative of the risks of screening delivered within the NHS may help to improve informed decision making. It is also important that these modern, real-world data are considered when cost effectiveness of CT screening is being evaluated.

Table 1. Characteristics of the five UK screening programmes included in the analysis.

Programme	Design	Dates of screening	Screening selection criteria	Number screened at baseline	Nodule management
UK Lung Cancer Screening (UKLS) Trial	RCT	2011-14	Age 50-75 LLP \geq 5%	1,994	UKLS protocol
Lung Screen Uptake Trial (LSUT)	RCT	2015-17	Age 60-75 NLST [#] criteria or PLCO _{M2012} \geq 1.51% or LLP \geq 2.5%	770	BTS Guidelines
Manchester Lung Health Checks	NHS	2016-18	Age 55-74 PLCO _{M2012} \geq 1.51%	1,384	BTS Guidelines
Liverpool Healthy Lung Project	NHS	2016-20	Age 58-75 LLP \geq 5%	6,639	BTS Guidelines
Nottingham Lung Health MOT	Obs*	2016-2019	Age 60-75 Smoker or ex-smoker Qcancer risk top 5% (0.68% 2-year risk)	361	BTS Guidelines

*Observational cohort study, [#]NLST = \geq 30 packyears and smoked within 15 years.

Table 2. Details of cumulative reported harms

Reported screening related harm	Total % (n)	Per 1,000 screening scans
False positive rate	2% (219)	19.6
Invasive investigation* for benign disease (excluding surgery)	0.6% (61)	5.5
Surgical resection for benign disease	0.07% (8)	0.7
Major complication [†] from invasive investigation / treatment for benign disease	0% (0)	0
Deaths from invasive investigation/treatment for benign disease	0% (0)	0

*image guide biopsies or bronchoscopic procedures; [†]as defined by NLST

Figure Legends

Figure 1. Infographic showing baseline outcomes for every 100 people screened in the UK cohort.

Figure 2. Infographic illustrating the frequency of measured screening related harms after the baseline round in the UK cohort.

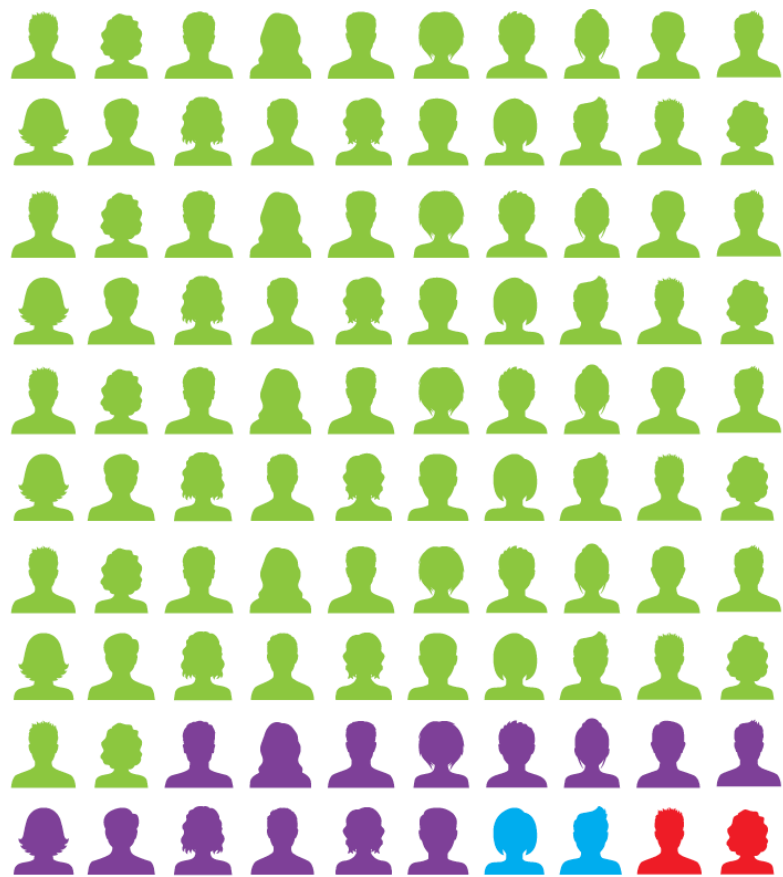
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Figure 1

**For every 100 people who have
a baseline lung screening scan**



82 People
Are likely to have a negative scan, which means there is no sign of lung cancer



2 People
Are likely to be asked to attend the hospital for further tests but will NOT be found to have lung cancer



14 People
Are likely to have a small lung nodule or other minor finding that needs another scan in 3 months. Almost all of these people will NOT have lung cancer on their repeat scans



2 People
Are likely to be diagnosed with lung cancer

Figure 2

Some people need to have further tests after their lung screening scan. This stadium shows how many people are likely to undergo further tests, out of every 10,000 people screened, and the likely outcomes

