Proactive approaches to individuals at high risk of lung cancer

Accelerate, Coordinate, Evaluate (ACE) Programme
An early diagnosis of cancer initiative supported by:
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About the ACE Programme

The Accelerate, Coordinate, Evaluate (ACE) Programme is an early diagnosis of cancer initiative focused on testing innovations that either identify individuals at high risk of cancer earlier or streamline diagnostic pathways. It was set up to accelerate the pace of change in this area by adding to the knowledge base and is delivered with support from: NHS England, Cancer Research UK and Macmillan Cancer Support; with support on evaluation provided by the Department of Health’s Policy Research Units (PRUs).

The first phase of the programme consisted of 60 projects split into various topic-based clusters to facilitate evidence generation and learning. The second phase comprises five projects exploring Multidisciplinary Diagnostic Centre (MDC) based pathways. The learning from ACE is intended to provide ideas and evidence to those seeking to improve local cancer services. The evaluations and findings are produced independently, and are therefore not necessarily endorsed by the three supporting organisations.
Executive Summary

Context
It is well established that poor survival from lung cancer is partly due to the aggression of the disease but also to the fact that it is usually diagnosed at a late stage. [1] With the publication of the US National Lung Screening Trial (NLST), it was identified that reduced lung cancer mortality can be achieved with early detection using low dose computed tomography (CT). [2] The trial showed a 20% mortality reduction for those screened with low dose CT, compared with chest x-ray. As a result, the US Preventative Services Task Force (USPSTF) recommended lung screening in the US for ex-smokers aged 55-80. [3]

The UK National Screening Committee does not currently support a national screening programme as there are still questions around the benefits and potential harms of lung screening as well as how it could best be implemented.

The ACE programme of interventions aimed at improving the pathway to cancer diagnosis and thereby improving cancer outcomes, included a cluster of projects implementing proactive approaches to individuals at high risk of lung cancer.

In this report we focus on projects offering low dose CT scans to subjects at particularly high risk of lung cancer, following a face to face respiratory health consultation. The report also considers the current context and evidence regarding lung cancer screening.

Proactive lung projects
Four projects offering CT scans to subjects at particularly high risk were either in the ACE ‘proactive lung’ cancer cluster or informally associated with it: The Liverpool Healthy Lung Programme (LHLP), The Nottingham Lung Health MOT Pilot, The Manchester Lung Cancer Early Diagnosis Service, and the University College London (UCL) Lung Screen Uptake Trial (LSUT).

We report on the methods of each of these projects, with outcome data from the Nottingham and Liverpool projects up to November 2017. The Manchester and UCL projects plan to evaluate and report their results separately.

Key findings

Engagement and uptake levels
Whilst Liverpool and Nottingham adopted different approaches, both featured targeted awareness raising activities to improve uptake in what is considered a ‘hard to reach’ cohort. Projects used GP records to invite participants meeting specific criteria to a lung health check. It resulted in a 40% uptake for Liverpool, with 55% of those, responding only after a second invitation. The uptake in Nottingham was 27%.

Diagnosis of lung cancer as a result of a low dose CT scan
Based on the currently available outcome data 2-3% of patients receiving a low dose CT scan were diagnosed with lung cancer across the four projects. This is comparable to the results achieved in the UK Lung Cancer Screening Trial (UKLS). [4]

Management of nodules and requirement for further workup
Liverpool and Nottingham projects found a lower rate of nodules requiring further diagnostic workup than observed in the reported randomised trials. This is likely to be due to the management adopted by both projects not to act on nodules smaller than 5 mm in maximum diameter.
Reduction in the stage at diagnosis compared to the general population
The stage at diagnosis of lung cancers detected in the Liverpool, Nottingham and Manchester projects indicates a likely reduction in lung cancer mortality which is consistent with the significant reduction observed in the large US trial of low dose CT screening for lung cancer. \(^5\) The expected reduced mortality in the Liverpool project is 22%. Overall, 80% of lung cancer diagnoses were at early stages (I and II) in all three projects.

Other diagnoses and referral to smoking cessation programmes
Overall Chronic Obstructive Pulmonary Disease (COPD) diagnoses and advice on smoking cessation as well as referrals to smoking cessation programmes were an integral part of project design. For Liverpool and Nottingham an estimated 13% of patients had COPD diagnosed sooner as a result of attending a lung health check than they would otherwise.

Patients express a good level of satisfaction in being invited to attend a respiratory health clinic
Patient satisfaction was high in all three projects and ease of access was reported in Nottingham and Manchester. A need for further or simpler information about the process was reported in Liverpool, reflecting the importance of ensuring all communication is appropriately designed for participants.

Sign of potential economic benefit from respiratory health clinic and CT screening
Taking into account the limitations of the health economic evaluation, the data suggested that evidence exists on the potential of respiratory health and CT screening projects to be cost effective. Based on the diagnoses of lung cancer alone, cost per quality adjusted life-year (QALY) gained are £13,087 for the Liverpool project and £19,453 for the Nottingham project.

Conclusion
The results from the ACE projects suggest that it is feasible to achieve clinical outcome benefits. The respiratory health clinics were a successful element of a targeted approach to high risk individuals, and provided additional benefits such as early diagnosis of COPD and referral to smoking cessation services when appropriate. These results, however, require further confirmation with extended follow-up of lung cancers diagnosed. In addition, further implementation research should be considered to provide guidance to those wishing to put in place similar proactive approaches.
## Contents

Executive Summary ................................................................. i
Introduction ........................................................................ 2
Context .................................................................................. 2
Targeted lung screening published evidence ........................................... 2
ACE proactive lung projects .......................................................... 6
Introduction ........................................................................... 7
Project descriptions and methods ......................................................... 7
Results ................................................................................... 11
Discussion ............................................................................... 16
Conclusions ........................................................................... 16
Abbreviations ......................................................................... 17
References ............................................................................... 18
Resources ............................................................................... 20
Appendix A: Results from Manchester Lung Cancer Early Diagnosis Service ........................................... 21
Appendix B: Economic Evaluation ....................................................... 22
Introduction

It has long been acknowledged that there is considerable room for improvement in survival from lung cancer. Poor survival is partly due to the innate aggression of the disease but also to the fact that it is usually diagnosed at a late stage. [1] With the publication of the US NLST, it was identified that reduced lung cancer mortality can be achieved with early detection using low dose CT. [2] Issues of implementation, diagnostic workup, cost and patient stratification as well as potential over-diagnosis remain. [6][7]

The ACE programme of interventions aimed at improving the pathway to cancer diagnosis and thereby improving cancer outcomes, included a cluster of projects implementing proactive approaches to individuals at high risk of lung cancer. In this report we focus on projects offering low dose CT scans to subjects at particularly high risk of lung cancer, following a face to face respiratory health consultation. We also consider the current context and evidence regarding lung cancer screening.

Context

Following the publication of results from the NLST in 2011 the USPSTF recommended lung screening in the US for ex-smokers aged 55-80. [3] The trial showed a 20% mortality reduction for those screened with low dose CT, compared with chest x-ray.

The UK National Screening Committee does not currently support a national screening programme as there are still questions around the benefits and potential harms of lung screening as well as how it could best be implemented.

Several academic trials aiming to address some of the evidence gaps are currently in development. One example is the Yorkshire Lung Screening Trial which aims to optimise the selection of a lung screening cohort, identifying the most appropriate population, at highest lung cancer risk. Another example is the London based SUMMIT trial, which in collaboration with GRAIL, will investigate the inclusion of lung cancer biomarkers alongside CT screening as an additional early detection tool.

Targeted lung screening is gaining traction and attention. NHS England is encouraging further rollout through its cancer alliances, with several localities receiving funding to develop an approach. Additionally, a recent publication from European experts on lung cancer and low dose CT screening called for European countries to set a timeline for targeted lung cancer screening implementation. [8]

There are a number of important areas to consider with regard to lung cancer screening and the following section provides a brief summary of the published evidence.

Targeted lung screening published evidence

Identification of a suitable targeted cohort

Current evidence suggests that the implementation of lung cancer screening must target a higher risk population in order to deliver a benefit. [9][10]

Earlier trials, such as the American NLST, focused on inviting identified high risk participants straight to a low dose CT scan based on age and smoking history. [5]

Subsequently other trials have used similar criteria in association with a risk algorithm to invite participants to lung health checks. This enables further stratification of the cohort before carrying out low dose CT on those deemed to be at a defined risk level.
LLP (Liverpool Lung Project) and PLCO (Prostate, Lung, Colorectal and Ovarian) Risk algorithm have elements designed specifically for lung cancer and have been used to re-analyse NLST data, which showed the selection criteria were improved. [8][9]

The PANCAN study from Canada found a high incidence of cancers by targeting a high risk population. [11][8]

**Engagement and education**
Following identification of an appropriate screening cohort, engagement is required to promote uptake/educate participants to make an informed choice. Research has been undertaken to understand attitudes toward targeted lung cancer screening, offering insight into effective engagement strategies. These include increasing understanding that lungs are a treatable organ and methods to address fatalistic attitudes. [12]

Importantly, a targeted high risk cohort is likely to include a high proportion of ‘hard to reach’ groups such as those aged over 70 years, smokers and those from the poorest areas. This, therefore, requires an engagement and education approach tailored to meet audience needs. [13]

For example, a trial focusing on smoking cessation (Start2quit) showed that the delivery of personalised risk information alongside an invitation to an introductory session more than doubled the odds of attending the Service Stop Smoking Services compared with a standard generic invitation to contact the service. [14]

**Stage at diagnosis**
Lung cancer screening trials consistently show high proportions of stage I and II diagnosis of lung cancer, often ranging from 70-80%. [11][4] This is considerably better than the UK current distribution of stage at diagnosis for lung cancer, with 72-76% of people being diagnosed at stage III and IV. [15]

However there has not been any data to specifically show a stage shift and increased numbers of early stage diagnoses in the populations targeted for screening as a whole. The lung cancer screening projects are often highly localised and conducted over a short time frame, with limitations in the length of follow up, data collection and data availability.

**Mortality benefit of low dose CT screening for lung cancer**
The American NLST has provided the only data on the mortality benefit as a result of low dose CT screening for lung cancer, showing a 20% reduction in lung cancer mortality when comparing low dose CT screening with chest x-ray screening. [2] This evidence led to the USPSTF recommending a lung cancer screening programme with annual low dose CT for at risk individuals.

Europe is waiting on the publication of the large-scale NELSON trial;[16][17] this is the only trial powered and followed up sufficiently to provide data on mortality in a European population.

All other trials have been too small to be able to show a statistically significant mortality benefit. For some, the data they do have suggest a potential non-significant benefit. [18][19]

**Cost effectiveness assessment of screening for lung cancer**
The UKLS is the only published trial conducted in a UK setting. It suggests that targeted lung screening could be cost effective, giving a cost of £8,466 per QALY gained. [4]

The UKLS analysis pointed out the importance of considering the benefits outside of lung cancer to get the full picture of the cost benefit. This includes the benefits of smoking cessation referrals and earlier diagnosis of cases of other respiratory diseases such as COPD.
Impact of lung cancer screening programme availability on people’s smoking habits

There is ongoing research in this area, following worries that the availability of a lung screening programme may be seen as a safety net for smokers who received a normal result following screening and limit their motivation to quit.\textsuperscript{[20]} A recent publication based on data from the UKLS has shown that lung screening, with smoking cessation referrals incorporated, actually made people more likely to quit successfully than those receiving smoking cessation referrals outside the context of a lung screening programme.\textsuperscript{[21]}

Nodule management protocol to handle potential increased number of lung nodule findings as part of lung screening

The approach taken to nodule management has developed since early lung screening trials as more has been learnt about the potential risk of nodules identified by screening.

The current approach for CT detected nodules recommended by the British Thoracic Society is to use volumetry (rather than manually measuring maximum diameter) to monitor the size and growth of nodules.\textsuperscript{[22]} The use of volume doubling time then helps clinicians to make an informed judgement on whether cancer risk justifies further potentially invasive tests (although it does require a repeat scan). This technique has been used in the more recent lung screening trials, such as NELSON.\textsuperscript{[23]}

False positives as part of a lung screening programme

A false positive result is a case where a participant receives a positive screening test result, but does not go on to receive a cancer diagnosis.

False positive percentages from lung screening trials have been reported in a variety of ways, and the way in which false positives are discussed also varies between different screening programmes so it is difficult to establish a comparison.

In the case of low dose CT screening, following a CT scan it is possible for a participant to follow a number of routes.

1.) Negative result: no further follow up (but potentially remains part of screening programme if applicable)

2.) Indeterminate result: possible follow up CT scan required at 3, 6 or 12 months.

3.) Positive result: referred to clinic and receive further diagnostic tests.

To fully understand the potential impact of false positives in lung screening it is helpful to record the false positive rate for those in group 3 separately from group 2 – particularly as the way indeterminate nodules are being managed is developing with the nodule management protocol improvements. The NLST did not separate these out and gives a false positive rate of 23.2\%,\textsuperscript{[2]} considering all participants who had at least an additional scan as “positive”. NELSON,\textsuperscript{[16]} UKLS\textsuperscript{[4]} and others separated out those referred to clinic or requiring further diagnostic intervention and showed false positive rates of around 3\%.

Over-diagnosis as part of a lung cancer screening programme

Over-diagnosis is a concern for all screening programmes. There will always be cancers diagnosed through screening that never would have presented or caused harm during that patient’s lifetime. However, it is difficult to quantify the scale of over-diagnosis, and balance it against the benefits of screening.

There is limited evidence published on the potential scale of over-diagnosis in lung cancer screening. A publication based on the NLST data suggests a rate of 18.5\%.\textsuperscript{[24]} As yet there has been no better attempt to quantify the rate of over-diagnosis. NLST, and potentially NELSON, are the only trials
currently set up that are large enough and have been followed up for long enough to provide data suitable for estimation of over-diagnosis.

**Definition of optimum screening interval**

Though most trials have focused on annual or just one-off screens, some have carried out research to consider if annual, biennial or even longer might be the optimum screening interval. [17] There is, however, no conclusive decision on what might be best yet.

There are also considerations that the cohort could be further stratified using the results of the baseline screen to keep higher risk people in a more regularly screened group and have the lower risk cohort return for a screen less frequently. [8] [25]

**Management of findings other than lung cancer**

The nature of targeting lung screening on a high risk population group means that a number of respiratory diseases such as COPD and emphysema, along with other atypical findings such as cardiovascular abnormalities, will be picked up in addition to lung cancer. Consequently, it is important to have access to the appropriate clinical expertise to ensure patients are managed effectively. [2] [8]
ACE proactive lung projects

A33 Manchester Lung Cancer Early Diagnosis Service

A91 Nottingham Lung Health MOT

A51 Liverpool Healthy Lung Programme

A90 UCL Lung Screen Uptake Trial
Introduction

Four projects offering CT scans to subjects at particularly high risk were either in the ACE proactive lung cancer cluster or informally associated with it: the Liverpool Healthy Lung Programme, the Nottingham Lung Health MOT Pilot, the Manchester Lung Cancer Early Diagnosis Service, and the University College London Lung Screen Uptake Trial.

We report on the methods of each of these projects, with outcome data from the Nottingham and Liverpool projects up to November 2017. The Manchester and UCL projects are reporting their results separately.

Project descriptions and methods

It is important to note that whilst the project methods described below are correct at the time of writing this report and presenting the available results, in some instances they might have evolved as projects developed further.

Liverpool

Background

The LHLP is an initiative aimed at improving respiratory health and diagnosing respiratory disease at a more treatable stage, undertaken by the Liverpool Clinical Commissioning Group (CCG) working with primary care teams and partner NHS trusts across Liverpool. Liverpool has one of the highest respiratory morbidity rates in England, with double the national lung cancer incidence, particularly in lower socioeconomic groups. The LHLP was initiated in response to both the clinical problem and the health inequality.

The programme had two sequential phases. The first was a series of co-ordinated focused public engagement events throughout the city, starting in areas with the highest lung cancer incidence. The aims were to promote positive messages around lung health, and address the attitudes of fear and fatalism around lung cancer. The second phase (still ongoing) is a programme of individual lung health consultations, risk assessment and referral for CT scans for those at more than 5% risk of lung cancer in the next 5 years.

Participant identification

GP records were used to select ever-smokers and subjects with COPD, aged 58-70 during year one, and 58-75 during year two. The GP practices then sent letters of invitation for a healthy lung check to eligible patients. This was followed by a second letter if the patient did not respond. If the patient did not respond to the second letter, the programme administration team attempted to contact the patient by telephone. Eligible patients were invited for a 40-minute lung health check appointment with a respiratory nurse in a community health hub setting. The lung health checks began in April 2016.

Lung health check

At the appointment, a detailed risk assessment was conducted: height and weight were measured to calculate the body mass index (BMI). Histories and risk factor information were taken, including: emphysema, bronchitis, COPD, tuberculosis, exposure to asbestos, family history of lung cancer, history of malignancy and smoking duration. In those without a pre-existing diagnosis of COPD, spirometry was used to assess lung function (FVC and FEV1 were measured and the ratio FEV1/FVC was calculated). Those with abnormal lung function on spirometry were referred for further investigation, and potentially definitive diagnosis of COPD. In addition, smoking advice and referrals to smoking cessation clinics were provided. 5-year risk of lung cancer was estimated using the...
MyLungRisk calculator, based on the Liverpool Lung Project risk model (LLPv2 as used in the UKLS trial). Those with 5-year lung cancer risk of 5% or more were offered a referral for a low-dose CT scan. Consent was requested from the participating patients to share their data for evaluation purposes.

CT scan and nodule management
CT scans were offered in a hospital setting, and for those with signs of lung cancer or nodules of maximum diameter 10 mm or greater were referred to cancer services. Those with non-calcified nodules of maximum diameter 6.1-9.9 mm were recommended to have a follow-up scan at 3 months. Those with non-calcified nodules of maximum diameter 5-6 mm were recommended to have a follow-up scan at 12 months. No further action was taken for calcified benign nodules and non-calcified nodules of maximum diameter less than 5 mm.

Nottingham
Background
With its high rate of deprivation, Nottingham in general has a higher proportion of smokers than the national average. In response to this, a partnership between Nottingham City CCG, Public Health England and a charity set up by the local MP to improve health and wellbeing in North Nottingham, and Nottingham University Hospitals NHS Trust, set up a lung health test programme using the analogy of the Ministry of Transport roadworthiness test for motor vehicles (MOT), with the aim of reducing mortality and morbidity due to smoking.

The organisers chose a phased introduction of the lung health check service, with the collection of baseline data from a single general practice in the first instance, to determine participation rates prior to community engagement and expansion to further practices. In phase 1, lung health clinics were run between January and February 2016, in Bilborough Medical Centre a single practice in North Nottingham, characterised by high deprivation and smoking rates. In phase 2, clinics were run between March and August 2017, covering a further 5 practices. Phase 2 was funded by the Roy Castle Lung Cancer Foundation.

Amendments following phase 1 included a more comprehensive communication plan to improve uptake rates, trialling hand delivery of invitations to address health inequalities, telephone follow-up of non-responders, and more robust data collection, in particular of health outcomes. In addition, waiting room posters and leaflets were printed as well as some project coverage took place in the local media.

Participant identification
General practice records were used to select current smokers or those with history of smoking in the past 5 years, aged 60-75. The list of potential participants was vetted by a respiratory nurse and the GP – exclusions at this point include those with an existing cancer diagnosis, those with a recent CT scan or any co-morbidity that would prevent screening. This process will also pick up where clinical indicators are not always identifiable by read codes. Once vetted, a letter is sent which includes a copy of a lung health information leaflet, as well as COPD related material. The letter was addressed as from the community respiratory team and the GP practice.

If invitees did not respond to the invitation, a follow up call was made 7-10 days later.

Lung health check
The lung MOT was carried out by a community respiratory nurse and lasted approximately 45 minutes. Similar to the Liverpool programme, the nurse took a detailed history and lung cancer risk assessment and offered additional respiratory health advice and investigations, including: spirometry where appropriate, referral to smoking cessation and other services, and referral for CT if lung cancer risk
was above the stipulated threshold, which differed between phase 1 and 2. In phase 1, those in the highest decile of lung cancer risk (0.37% 2 year risk) as determined by QCancer were offered a CT scan, whereas in phase 2, only the top 5% (0.68% 2 year risk) were offered a scan. Those with abnormal lung function on spirometry were referred for further investigation, and potentially definitive diagnosis of COPD.

**CT scan and nodule management**

CT scans were carried out in mobile units located close to the participating practices as soon as possible following the health checks, ideally within 4 weeks. Following CT scan, the results were provided within 2 weeks. Nodules with a maximum diameter between 5-6 mm were recommended to have a follow up scan at 12 months. Larger nodules were referred for further investigation in accordance with current procedure.

**Manchester**

**Background**

The population of Manchester has very high rates of serious lung disease with many areas of the city having lung cancer incidence rates above the national average. This initiative aimed to reach the ‘hard to reach’ population at high risk of developing lung cancer

A publicity campaign for the project included road shows on a Macmillan bus, appearances on local radio and newspapers and posters in strategic places. “Champions” for the project were also developed to raise awareness in their communities.

**Participant identification**

The local patient booking system was responsible for identifying high risk individuals. In this case, the only criteria used was being aged 55-74. Invitations were sent to all those aged 55-74 from 14 GP practices within North, Central and South Manchester CCGs. People were then asked to book appointments if they currently were or had ever been a smoker. Invitations were carried out in this way as GP records on smoking history were deemed to be incomplete – inviting only those marked as smokers would have missed eligible participants.

Individuals with a lung cancer diagnosed within 5 years or listed on palliative care register were excluded.

**Lung health check**

The lung health checks were carried out in mobile units in community settings. The idea being that the convenient location would be a benefit to uptake. The health checks were carried out by a respiratory nurse, and lasted approximately 20 minutes. As in the other projects, a risk assessment was undertaken as well as a spirometry. Manchester used the PLCO risk algorithm with a threshold of 1.51% lung cancer risk over 6 years.

Those meeting the threshold were referred for a low dose CT scan, with a leaflet on CT available to read.

**CT scan and nodule management**

Low dose CT scans were carried out on the same day, in a mobile unit adjacent to the health check. Participants were sent a leaflet with information about the CT scan with their initial invitation, and had the opportunity to discuss the CT scan during the lung health check. Reports of CT scans to be available within 14 days.
Participants with significant findings were referred to the relevant multidisciplinary team (MDT). 3-month and 12-month follow up scans were also used as necessary.

London

Background
The UCL project (LSUT)\(^{[28]}\) focuses specifically on the fact that uptake of lung cancer screening among the target, high risk group has been poor. Particularly true in smokers and those from socioeconomically deprived backgrounds. The project therefore investigated whether informed uptake in this group can be improved by designing and using a targeted invitation strategy. The project was an academic research study using a randomised controlled trial design. The design of the targeted invitation strategy was informed by extensive reviews of the published literature, as well as the group’s own research on beliefs and attitudes towards lung cancer among heavy smoking and socioeconomically deprived communities in London.\(^{[12]}\) The targeted invitation strategy was designed to be: 1) targeted (attempting to minimise fear, fatalism, blame and stigma of lung cancer), 2) stepped (providing information in stages) and 3) low burden (providing essential information only, followed by further information at the screening appointment).

No community engagement activities were undertaken, as the project was a randomised controlled trial to test the effectiveness of the targeted invitation materials, and so any public-facing campaign may have skewed the results.

Participant identification
GP records were searched by an administrator to select patients recorded as a smoker within the last 5 years aged 60-75. Members of the research team carried out site visits to assist with the process and ensure the protocol was adhered to. The target area covered GP practices across Camden, Islington and Hackney and City CCGs. The aim was to invite 2,000 patients from 16 GP practices who had committed to participating in the study.

Following GP record screening individuals were randomised into the two arms of invitation:

- **Control arm** – invitees were sent a pre-invitation letter notifying patients of the lung health check service and a ‘usual care’ information booklet – mimicking those of existing screening programmes. This was followed by an invitation letter, including a pre-scheduled appointment. Those who missed their appointment without cancelling were then sent a second invitation letter.

- **Intervention arm** – invitees were sent the same stages of invitation as the control group. However, instead of receiving the information booklet, they received a targeted leaflet. Additionally, the invitation and reminder letters used indirect phrasing to explain that smokers and former smokers were being invited.

Lung health check
The lung health checks led by a nurse took place in a hospital and lasted 60 minutes. The nurses undertaking the health checks received training courses based on their existing skill level. Including, the background of lung cancer screening, the purpose of the research, the harms and benefits of CT screening and NCSCT accredited very brief advice on smoking cessation.

As in other projects, a detailed risk assessment was conducted by the nurse including a spirometry test, with a carbon monoxide breath test and referral to smoking cessation and other local health promotion services available as appropriate. This project utilised both the LLP (referral threshold: 2.5% 5-year lung cancer risk) and PLCO (referral threshold: 1.51% 6-year lung cancer risk) risk algorithm
models, with a participant referred for a low dose CT scan if they meet the referral threshold as determined by either model.

**CT scan and nodule management**

CT scans were booked during the lung health check for those accepting referral. Some same day appointments were available – but otherwise as soon as possible and according to each individual’s preference. Scans were carried out in the same hospital as the lung health check. Participants with suspicious findings were referred to the local thoracic (or relevant) MDT. Participants with indeterminate findings were informed of their result by their GP or secondary care as appropriate, with follow up/further investigations arranged as required.

**Results**

**Liverpool**

An earlier report is available online[26] and the purpose of this section below is to update the results following the expansion of LHLP from the first three districts Picton, Speke and Everton to include Norris Green, Croxteth and Anfield.

As reported to the LHLP Steering Group on 9th November 2017, 11,526 people had been invited to a lung health clinic appointment and 4,566 (40%) had attended. To date, permission consent for data use has been given and data processing has been completed for 2,876 appointments (63% of the total) carried out up to 12th September 2017. Of these, 597 (21%) attended following the first invitation letter, 1,582 (55%) after the second letter and 697 (24%) after the telephone call.

**Analysis of lung health checks up to 12th September 2017**

The following data details those participants who attended health checks and consented to share their data (63% of those attending) between April 2016 and 12th September 2017.

Table 1 summarises the attributes of those attending the appointments. The median age was 65 years (range 58-76), 1,473 (51%) of the attenders were male, and 2,321 (81%) were in the most deprived IMD quintile. Based on the recorded data 2,326 (81%) were ever-smokers. The median duration of smoking was 40 years (range 0-61). 674 (23%) subjects had an existing diagnosis of COPD and 437 (15%) had a previous diagnosis of cancer. 948 (33%) subjects had a family history of cancer. The median estimated 5-year risk of lung cancer was 4.4% (range 0.2%-48.9%).

Of the patients attending the health checks, 624 agreed to receive smoking cessation advice. While we did not have data on whether ever-smokers were current or ex-smokers, the post-check patient survey suggested that 29% of ever smokers were current regular or occasional smokers. This would imply that 681 patients were current smokers, so around 90% of current smokers agreed to receive cessation advice. In addition, 109 (16% of estimated current smokers) agreed to be referred to a smoking cessation clinic.

Of those attending health checks, 1,775 (62%) underwent spirometry. Spirometry was abnormal (defined as FEV1/FVC ratio of less than 70%) in 612 (34% of those tested) subjects. While definitive diagnosis of these is ongoing, previous results suggest that 63% would be expected to be diagnosed with COPD, so we anticipate that in this population, 386 subjects will have a diagnosis of COPD, and will have access to treatment earlier than they would otherwise.
Table 1. Demographic and respiratory characteristics of those attending healthy lung health checks.

<table>
<thead>
<tr>
<th>Category</th>
<th>Number (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total number of lung health checks</td>
<td>2,876</td>
</tr>
<tr>
<td>Male</td>
<td>1,473 (51.2%)</td>
</tr>
<tr>
<td>Female</td>
<td>1,403 (48.8%)</td>
</tr>
<tr>
<td>Median age (range)</td>
<td>65 (58-76)*</td>
</tr>
<tr>
<td>Ever smokers</td>
<td>2,326 (81%)</td>
</tr>
<tr>
<td>Previous COPD</td>
<td>674 (23.4%)</td>
</tr>
<tr>
<td>Previous malignancy</td>
<td>437 (15.2%)</td>
</tr>
<tr>
<td>Emphysema</td>
<td>92 (3.2%)</td>
</tr>
<tr>
<td>Pneumonia</td>
<td>502 (17.5%)</td>
</tr>
<tr>
<td>Bronchitis</td>
<td>972 (33.8%)</td>
</tr>
<tr>
<td>Tuberculosis</td>
<td>51 (1.8%)</td>
</tr>
<tr>
<td>Asbestos exposure</td>
<td>997 (34.7%)</td>
</tr>
<tr>
<td>Family history lung cancer</td>
<td>948 (33.0%)</td>
</tr>
<tr>
<td>Median smoking years (range)</td>
<td>40 (0-61)</td>
</tr>
<tr>
<td>Median 5-year lung cancer risk (range)</td>
<td>4.4% (0.2%-48.9%)</td>
</tr>
<tr>
<td>Most deprived IMD quintile</td>
<td>2,321 (80.7%)</td>
</tr>
</tbody>
</table>

* Note the LHLP recruited 58-70 age range until September 2017; from then participants 71-75 years of age were also included.

Table 2 shows the diagnostic cascade of those attending health checks. There were 1,222 (42%) patients with 5-year lung cancer risk greater than or equal to 5% and 1,216 (99.5% of those meeting the 5% risk criterion) were recommended for a CT scan. Of these, 1,046 (36% of total, 86% of those recommended) had a CT scan by the time of close of data collection. 120 (11%) patients who had a CT scan required further investigation (follow-up CT scan at 3 or 12 months, or immediate referral to pathway) and 22 (2.1% of those undergoing CT scan) patients were diagnosed with lung cancer. A further 7 have suspected lung cancer and are undergoing further investigations.

Table 2. Diagnostic cascade of patients attending lung health checks by 12th September 2017

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Numbers</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients attending</td>
<td>2,876</td>
<td></td>
</tr>
<tr>
<td>Spirometry</td>
<td>1,775</td>
<td>62% (of attenders)</td>
</tr>
<tr>
<td>CT scan recommended</td>
<td>1,216</td>
<td>42% (of attenders)</td>
</tr>
<tr>
<td>CT scan carried out</td>
<td>1,046</td>
<td>36% (of attenders), 86% (of recommended)*</td>
</tr>
<tr>
<td>Further investigation</td>
<td>120</td>
<td>11% (of scanned)</td>
</tr>
<tr>
<td>Lung cancer</td>
<td>22</td>
<td>2.1% (of scanned)**</td>
</tr>
<tr>
<td>Suspicious lesion under investigation</td>
<td>7</td>
<td>0.7% (of scanned)</td>
</tr>
</tbody>
</table>

* The percentage of those having a scan may increase slightly; the data are dynamic because the programme is still running, and some people may have subsequently received a healthy lung scan.

** The majority of the patients recruited into the LHLP in this report were selected from the 58-70 year old population, a higher proportion has been reported in the last neighbourhood Croxteth, where 58-75 year old participants were recruited.
Analysis of grouped data up to 9th November 2017

The following section covers grouped data received for all cancer diagnoses up to 9th November 2017 – including those who did not consent to share their individual health check data.

As of November 9th, 2017, 29 lung cancers had been diagnosed in all from 1,542 subjects undergoing CT scans, including those who did not consent to share health check data (no potentially identifiable data from these subjects has been made available to the team) and those for whom complete LHLP data has not been processed yet. This implies a detection rate at the point of CT scan of 2% (1 cancer per 53 people scanned). Table 3 shows the stage distribution of these, with the expected numbers of deaths within 5 years based on national stage specific survival. The table also shows the stage distribution for the general population of lung cancers in the UK following usual care (no screening programme), and the expected 5-year deaths if these 29 cancers had the same stage distribution as the general population.

Table 3. Stage distribution of LHLP CT detected lung cancers and of the UK lung cancer population, with expected numbers of deaths in 5 years predicted from national stage-specific survival rates (one thymoma is included with the stage II cancers)

<table>
<thead>
<tr>
<th>Stage</th>
<th>Usual care stage distribution (%)</th>
<th>Expected 5-year fatality (%)</th>
<th>Predicted deaths (from 29 cancers distributed according to usual care)</th>
<th>LHLP stage distribution (%)</th>
<th>Predicted deaths from LHLP cohort</th>
</tr>
</thead>
<tbody>
<tr>
<td>Not known</td>
<td>11</td>
<td>94</td>
<td>3</td>
<td>3</td>
<td>1</td>
</tr>
<tr>
<td>I</td>
<td>15</td>
<td>65</td>
<td>3</td>
<td>66</td>
<td>12</td>
</tr>
<tr>
<td>II</td>
<td>7</td>
<td>79</td>
<td>2</td>
<td>14</td>
<td>3</td>
</tr>
<tr>
<td>III</td>
<td>19</td>
<td>94</td>
<td>5</td>
<td>10</td>
<td>3</td>
</tr>
<tr>
<td>IV</td>
<td>49</td>
<td>100</td>
<td>14</td>
<td>7</td>
<td>2</td>
</tr>
<tr>
<td>Total</td>
<td>100</td>
<td>90</td>
<td>27</td>
<td>100</td>
<td>21</td>
</tr>
</tbody>
</table>

Stage I and II cancers comprised 80% of the lung cancers diagnosed, as compared with only 22% in the general population. Based on the stage of cancers diagnosed, we would expect 21 deaths from lung cancer in the 5 years following diagnosis. If the LHLP CT-detected cancers had the same stage distribution as the national population of lung cancers, we would have expected 27 deaths. Thus, the programme is expected to have prevented 6 deaths from lung cancer, 1 death prevented per 257 CT scans.

Participants were surveyed after the health check and for those who had a CT scan, after the scan, to obtain patient perspectives and identify information gaps. Of the 109 participants surveyed after the health check, 95% reported feeling better about their lung health after the check, and 90% expressed themselves as satisfied or very satisfied with the process. In terms of information gaps, of the 64 participants surveyed following a CT scan, 31% felt they needed more written information, 52% wanted simpler information and 39% wanted to spend longer talking to the nurse. Overall, 96% of those surveyed following the lung health check reported that they would encourage or strongly encourage a friend to participate, and the same proportion of those surveyed following a CT scan reported that they would encourage or strongly encourage a friend to have a CT scan.
Implications
Phase 2 of the LHLP has now been running since April 2016, and has conducted 4,566 lung health checks to 9th November (40% of the invited population). From data available on 2,876 of these, we found that 81% were ever smokers and 23% had an existing diagnosis of COPD. Following spirometry of those who did not already have a COPD diagnosis, 612 (21%) had abnormal lung function, and from previous clinical experience it is anticipated that 386 (13% of attendees) subjects will in due course be diagnosed with and treated for COPD.

42% of attenders had 5-year lung cancer risk of 5% or more and 86% of those offered a CT scan underwent the scan. Around 2% of those scanned were found to have lung cancer. The stage distribution of lung cancer indicated a reduction in mortality compared to that expected from the general population of around 22% (21 expected deaths vs 27 expected from the general population), similar to that observed in the US randomised trial. This corresponds to an absolute prevention of 1 lung cancer death per 257 CT scans, rather more than observed in the trial, possibly due to the very high risk level required for eligibility for a CT scan in LHLP.

Post health check and post scan surveys indicated a high level of patient satisfaction with the programme. This is likely to be due to the measured and sensitive nature of the lung health check consultations. However, 10-15% felt uninformed about ways of stopping smoking, CT scan process, benefits and risks and 30-50% of those who were referred for CT scan felt they needed more and simpler information. An information gap was identified regarding the process, purpose and outputs of the CT scans.

Nottingham
From January to February 2016 and then March to August 2017 and based on data available so far, 1,208 subjects (54% male, mean age 69, range 52-76 years) were invited to ‘lung MOTs’. All participants were current smokers or had smoked in the last 5 years. Of those invited, 323 (27%) have attended an MOT to date. Of those attending, 166 (51%) met the risk criteria and were referred for a CT scan. Of these 157 (95%) had a scan. As a result, 11 (7% of those scanned) had nodules requiring further investigation, of whom 3 (2% of those scanned) had lung cancer.

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Numbers</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients attending</td>
<td>323</td>
<td></td>
</tr>
<tr>
<td>Spirometry</td>
<td>57</td>
<td>18% (of attenders)</td>
</tr>
<tr>
<td>CT scan recommended</td>
<td>166</td>
<td>51% (of attenders)</td>
</tr>
<tr>
<td>CT scan carried out</td>
<td>157</td>
<td>49% (of attenders), 95% (of recommended)</td>
</tr>
<tr>
<td>Further investigation</td>
<td>11</td>
<td>7% (of scanned)</td>
</tr>
<tr>
<td>Lung cancer</td>
<td>3</td>
<td>2% (of scanned)</td>
</tr>
</tbody>
</table>

Of those attending the MOT, 57 (18%) subjects were referred for spirometry, and 44 were expected to be diagnosed with COPD. There were 9 (3%) referrals to smoking cessation services and 89 (28%) onward referrals to community health services.

Of the 3 lung cancers, 2 were stage I and 1 was stage IV. Two underwent resection.
Implications
Because of the small numbers, no firm conclusions can be drawn from these data in isolation. However, two observations can be made. First, the results are consistent with the LHLP findings, with the majority of diagnoses at stage I. The second, also consistent with the Liverpool results, is the low rate of nodules requiring further diagnostic workup, 7% in this case. This is considerably lower than observed in the randomised trials.[5][4]

Although based on small number, feedback from patients has been very positive. Overall the MOT process and ease of location were valued. All stopped smoking fully or at least reduced a lot as the result of the MOT. Being aware of their diagnoses they are now satisfied to be followed up if applicable. Finally, all the respondents would recommend their friends attend the service should they have any concerns.

Economic evaluation
Taking into account the limitations of the health economic evaluation, the data suggested that evidence exists on the potential of respiratory health and CT screening projects to be cost effective. Based on the diagnoses of lung cancer alone, cost per QALY gained are £13,087 for the Liverpool project and £19,453 for the Nottingham project. Benefit gained from early diagnosis and treatment of COPD as well as referral to smoking cessation services are not included in the current economic model. The full report on this health economic evaluation is given in Appendix B.
**Discussion**

The stage at diagnosis of the lung cancers detected in both the Liverpool and Nottingham ACE projects indicates a likely reduction in lung cancer mortality which is consistent with the significant reduction observed in the large US trial of low dose CT screening for lung cancer.\[^5\] While a definitive economic analysis is not possible without further data on clinical outcomes, preliminary results suggest that the projects have the potential to be cost-effective. This is consistent with findings from the UKLS.\[^4\]

The Liverpool project found encouraging proportions of subjects agreeing to receive smoking cessation advice, and to referral to smoking cessation services.

Both projects observed a rate of around 10% of nodules requiring further workup. This is a considerably lower rate than was observed in the randomised trials.\[^5\]\[^4\] It is at least partly due to the fact that in these projects, nodules smaller than 5 mm in maximum diameter were not acted on. There is a need for further follow-up of all subjects undergoing health checks to assess the extent to which the risk eligibility criteria and the diagnostic algorithm might be causing cancers to be missed.

The LHLP has commissioned further extensive local evaluation which is due to report Spring 2018, and, as noted above, the Manchester and UCL (LSUT) projects will evaluate and publish their findings independently. However, as Manchester has just published its baseline findings and these are relevant to the discussion here, they have given permission for a summary of their results to be included in this report (Appendix A).

It is worth drawing out, that the published findings for the Manchester project indicate similar results to the LHLP, reporting that of 1,384 individuals screened, 3% had lung cancer, 80% of which were early stage.\[^30\] Likewise, a recent abstract from the UCL (LSUT) project also shows similar results, with a lung cancer detection rate of 2.4% and an indeterminate pulmonary nodule rate of 12.5%.\[^31\]

**Conclusions**

In conclusion, the results from the ACE projects suggest that it is feasible to achieve similar clinical outcome benefits to those observed in the US trial of low dose CT screening for lung cancer, with lesser harms in terms of unnecessary diagnostic activity.\[^5\] However, this needs confirmation with extended follow-up, larger numbers of lung cancers diagnosed, and the addition of mortality data. Additional randomised trial results would also add to the precision of estimation of benefits and harms, in particular mortality results from the large European trial, NELSON.\[^32\] It is also of note that the ACE projects indicate that there is considerable potential benefit of proactive approaches to those at high risk of lung cancer in terms of early diagnosis of COPD.
<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>ACE</td>
<td>Accelerate, co-ordinate, evaluate</td>
</tr>
<tr>
<td>BMI</td>
<td>Body mass index</td>
</tr>
<tr>
<td>CCG</td>
<td>Clinical Commissioning Group</td>
</tr>
<tr>
<td>COPD</td>
<td>Chronic Obstructive Pulmonary Disease</td>
</tr>
<tr>
<td>CT</td>
<td>Computed Tomography</td>
</tr>
<tr>
<td>FEV1/FVC</td>
<td>Ratio of the <em>forced expiratory volume</em> in the first one second to the <em>forced vital capacity</em> of the lungs</td>
</tr>
<tr>
<td>IMD</td>
<td>Index of Multiple Deprivation</td>
</tr>
<tr>
<td>LHLP</td>
<td>Liverpool Healthy Lung Programme</td>
</tr>
<tr>
<td>LLP</td>
<td>Liverpool Lung Project</td>
</tr>
<tr>
<td>LOW DOSE CT</td>
<td>Low dose CT scan</td>
</tr>
<tr>
<td>LSUT</td>
<td>Lung Screen Uptake Trial</td>
</tr>
<tr>
<td>MDC</td>
<td>Multidisciplinary Diagnostic Centre</td>
</tr>
<tr>
<td>MDT</td>
<td>Multidisciplinary Team</td>
</tr>
<tr>
<td>NLST</td>
<td>National Lung Screening Trial</td>
</tr>
<tr>
<td>PLCO</td>
<td>Prostate, Lung, Colorectal and Ovarian</td>
</tr>
<tr>
<td>QALY</td>
<td>Quality adjusted life year</td>
</tr>
<tr>
<td>QCancer</td>
<td>Cancer risk algorithms developed by Professor Julia Hippisley-Cox</td>
</tr>
<tr>
<td>UCL</td>
<td>University College London</td>
</tr>
<tr>
<td>UKLS</td>
<td>UK Lung Screening Trial</td>
</tr>
<tr>
<td>USPSTF</td>
<td>US Preventative Services Task Force</td>
</tr>
</tbody>
</table>
References


Resources
The following resources have been used by either the Liverpool or Nottingham projects. They are shared to provide examples to others who are considering implementing a similar initiative.

Public information leaflets:

- Health check general leaflet
- CT scan information
- Lung nodules information
- Referred for a CT scan
- Not referred for a CT Scan

Contact ACE
If you have any queries about ACE, please contact the team at: ACEteam@cancer.org.uk

In addition, you can visit our webpage: www.cruk.org/ace where we will publish news and reports.

The ACE Programme
Accelerate, Coordinate, Evaluate
Appendix A: Results from Manchester Lung Cancer Early Diagnosis Service

The baseline findings from the Manchester lung health check have recently been published which the Manchester team report below: [30]

- 2613 ever smokers aged 50-74 attended a lung health check
- 1384 underwent LDCT scan of which 65 (4.7%) were positive; 176 (12.7%) were intermediate and 1143 (82.6%) were negative
- 5.9% (81) were seen in cancer clinic of which 46 cancers were found in 42 people

The prevalence of lung cancers was 3% (CI 2.3%-4.1%). Cancers were 63% stage I, 17.4% stage 2, 8.7% stage III, and 10.9% stage IV. The represented a significant stage shift (P < 0.0001) compared to the number of cancer diagnosed in the preceding year from the same area. A curative intent treatment was offered for 89.1% of cancers.

Further information is available in the report of the Manchester project, ‘Implementing lung cancer screening: baseline results from a community-based ‘Lung Health Check’ pilot in deprived areas of Manchester. [30]

Appendix B: Economic Evaluation

Follows overleaf.
ACE: Economic Evaluation of the Proactive Lung Cluster

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Date completed: 16th February 2018

About EEPRU
The Policy Research Unit in Economic Evaluation of Health and Care Interventions (EEPRU) is funded by the Department of Health Policy Research Programme. It is a collaboration between the School of Health and Related Research (ScHARR) at the University of Sheffield and the Centre for Health Economics at the University of York. EEPRU is a programme of work extending until 2017. The Unit is led by Professor John Brazier (Director, University of Sheffield) and Professor Mark Sculpher (Deputy Director, University of York). Its aim is to assist policy makers at the Department of Health to improve the allocation of resources in health and social care.

Source of funding
This research was undertaken by the Policy Research Unit in Economic Evaluation of Health and Care Interventions (EEPRU) which is funded by the UK Department of Health Policy Research Programme.

The views expressed in this report are those of the authors and not those of the Department of Health. Any errors are the responsibility of the authors.

Acknowledgements
The authors are grateful for the contributions of the following colleagues: Mark Sculpher (CHE, University of York, and EEPRU), Sophie Whyte (ScHARR, University of Sheffield, and EEPRU), the ACE programme team, and all ACE projects.
Contents
1. Introduction ............................................................................................................................. 4
   2.a. Analytical Plan – short-term analysis ............................................................................... 6
   2.b. Pre-launch community engagement costs ......................................................................... 9
   2.c. Unit costs ......................................................................................................................... 9
   2.d. Short term project resource use ...................................................................................... 11
3. Methods – Long-term analysis ............................................................................................. 12
   3.a. Analytical Plan – long-term analysis ............................................................................. 12
       Lung Cancer ...................................................................................................................... 13
       Wider outcomes ................................................................................................................. 15
4. Results .................................................................................................................................. 18
5. Discussion ............................................................................................................................. 20
6. Conclusion ............................................................................................................................ 22
References .................................................................................................................................. 23
1. Introduction

This chapter reports on economic evaluation in relation to the proactive lung ACE projects by the Department of Health’s Policy Research Unit in Economic Evaluation of Health and Care Interventions (EEPRU). Economic evaluation is concerned with the estimation of the total impact of a specific intervention on population health. Evaluations are structured through the estimation of the short- and long-term incremental cost and health implications (often measured in terms of life-years or quality adjusted life-years (QALYs)) of an intervention, contrasted against other potential management options for the same patients.

A new intervention that is found to be more effective, in terms of population health, than all relevant current alternatives must additionally be evaluated against its incremental cost implications, i.e. how much more or less it costs the NHS than its comparators. A new intervention, found to both increase population health and decrease total costs to the NHS, is said to *dominate* its comparators and is considered to be a worthwhile investment. In contrast, an intervention which increases both health and total costs must be considered against the health benefits of services which could have otherwise been funded, the opportunity cost of the intervention. This comparison is made through the consideration of the incremental cost effectiveness ratio (ICER) of the intervention (the additional total cost to the NHS per gain in health) compared to the cost-effectiveness ‘threshold’. This ‘threshold’ has set between £20,000/QALY and £30,000/QALY based on NICE’s guidance, [1] but this ‘decision rule’ is likely to incorporate more than just opportunity cost (e.g. the value of innovation). Recently health opportunity cost in the NHS has been estimated at approximately £13,000 per QALY (i.e. approximately 77 QALYs forgone per £1,000,000 additional cost of a new service or intervention).[2]

Recent UK research suggests that CT as a screening mechanism to detect lung cancers may be cost effective (the UK Lung Screening Trial, UKLS),[3] finding it to be associated with an incremental cost-effectiveness ratio (ICER) of around £8,500/QALY. The UKLS pilot trial considered the effectiveness of risk prediction modelling and low dose CT screening as a means of identifying lung cancer at an earlier stage in high risk patients than symptomatic presentation. In the pilot, a target population was identified using NHS records and mail questionnaires and classified by their expected risk of developing lung cancer into the future (using the LLP risk algorithm). Only patients identified as being at high risk of lung cancer and eligible for the trial were invited into recruitment centres and for subsequent screening. By solely focussing on the identification of lung cancer, and doing so in a highly targeted manner, the UKLS arguably missed the potential to deliver a broader message of general
respiratory health and to engage with many patients, who while not at high risk of lung cancer, may still have had the potential to have poor respiratory health and may benefit from proactive preventative interventions.

The ACE Proactive Lung cluster projects have sought to implement a broader intervention by combining targeted CT screening for patients at high risk of lung cancer, with face to face respiratory health consultations at which spirometry and brief smoking cessation advice and referrals are available as appropriate. Some of the projects have additionally had a community event component, seeking to improve the local community’s understanding of respiratory health and, as a secondary outcome, to improve uptake of the screening component. By including the respiratory health consultations element alongside the CT screening, the ACE projects have the potential to make and to report impact on a broader range of factors, including COPD diagnosis. Also to identify patients interested in smoking cessation advice, at a potentially lower marginal cost than if such activities were provided independently of screening which the UKLS has indicated is likely to be cost-effective as a standalone intervention. This evaluation will explore what factors could impact the cost-effectiveness of interventions such as those implemented in the ACE projects, and under what conditions an extended intervention, including respiratory health consultations for a wider pool of patients, would have the potential to be cost-effective.

Due to the design of the projects evaluated (primarily their limited size, period of follow up, and lack of robust control), an evaluation of the cost-effectiveness of the ACE projects themselves was not possible. The evaluation conducted here is designed to be illustrative only. The implications of this are that it is not possible directly to compare the effectiveness of the different project designs, nor to comment on the specific merits of each design. Therefore, this evaluation should be seen as primarily an attempt to inform the design - and importantly the evaluation - of future lung cancer screening projects; and to consider the scenarios under which the addition of a respiratory health consultation element to a lung cancer screening intervention may or may not be cost-effective.

Additionally, as the aim of the evaluation is to explore the potential cost-effectiveness of the different project designs should they be incorporated into routine NHS activity, the unit costs are representative of the additional cost burden the NHS would be expected to face from a marginal increase in activity, rather than the cost paid by the commissioner of the projects at the time of funding. This important distinction is most apparent in the consideration of the cost per CT conducted in a mobile CT van. The cost per scan paid by the commissioner during a small, local project would not be a fair indicator of the cost that would be expected if the service was rolled out nationally. As a result, the estimation of the cost of each project is broken into its constituent unit costs and resource use implications.
Of the four ACE proactive lung projects conducted (Nottingham, Liverpool, Manchester, and London), two shared sufficient data on the events observed in the projects to describe them in this report (Nottingham and Liverpool). As a result, this report provides an overview of the design of all four of the projects, but only considers the potential resource implications and health impacts of two of them.

To evaluate the potential impact of the ACE projects, the short-term direct cost to the NHS of each are considered alongside the long-term cost and population health outcomes. Short-term costs are defined here as the direct costs associated with the projects from initial community events and patient identification, to diagnosis of disease at the multi-disciplinary team (MDT). While all four projects are discussed and overviewed, only two of the projects (Liverpool and Nottingham) provided detailed estimates of activity and effectiveness of the intervention, and as such are the only ones to be evaluated in any detail.

2. Methods – short-term analysis
2.a. Analytical Plan – short-term analysis
The key differentiating features of each have been identified and are presented in Table 1. Each of the projects consist of the identification and invitation to a respiratory nurse-led consultation of some population at high risk of poor respiratory health, with spirometry and referral to CT for those deemed high risk of lung cancer using a risk assessment tool. Two of the projects (Liverpool and Manchester) additionally included an element of community engagement and/or pre-health check activity. This was designed to increase uptake of the invited checks and to generate cultural change in how respiratory health was viewed in the population.

The cultural change element of the community engagement activities carried out by Liverpool and Manchester could be expected to impact on outcomes beyond those evaluated here. Discussion with the projects highlighted cases where attendance at the respiratory health check may have increased as a direct result of the untargeted community activities. These activities are discussed further in Section 2b.

Each of the elements presented in Table 1 are costed through the combination of the relevant unit costs for the Liverpool and Nottingham projects, which are presented in Section 2c, and the total relevant resource use, presented in Section 2d, to estimate the total short-term cost of the project. For more details of the elements reported in Table 1 see elsewhere in the ACE Report. As noted in the introduction, this estimated cost is likely to differ from the cost paid by the relevant project commissioners due to the unit costs used being more representative of the
marginal cost of each activity if incorporated as a national NHS service. In addition, a complete case analysis approach, was taken to the 37% of Liverpool patients who opted out of data collection, excluding their costs and outcomes from this analysis.

Due to a lack of suitable data, the short period over which the investigations took place and their non-invasive nature, the assumption was made that there were no short-term quality of life impacts associated with the respiratory health checks. This assumption is reasonable as none of the tests (spirometry, CT, x-ray, etc.) are invasive. Furthermore, recent work has suggested that screening for lung cancer using CT has no significant long-term effect on psychological factors.[4]
### Table 1: Stylised structure of each project

<table>
<thead>
<tr>
<th>Project phase</th>
<th>Nottingham</th>
<th>Liverpool</th>
<th>Manchester</th>
<th>London</th>
</tr>
</thead>
</table>
| 1. Community engagement/pre-launch activity | No pre-launch engagement or advertising material produced in the first phase but some posters and leaflets and media cover for second phase | 1) Construction of well-informed web page  
2) Banners and posters in GP practices  
3) "Breathe Freely" community engagement events  
4) Series of respiratory health drop-in sessions | 1) Macmillan bus roadshows  
2) Local radio and paper participation (61 local engagements)  
3) Posters in participating GP practices, community centres, libraries and pharmacies  
4) Training of community champions | No significant pre-launch activity |
| 2. Patient identification, invitation and booking for Check | Population in in area of high deprivation (age 60-75, AND active smoker in 2010 OR more recently) identified and invited via letter | Population (age 58-70 years – extended to 58-75 during year 2 AND having ever smoked) across CCG identified and invited via letter | Population (age of 55-74 years, with self-selection of ever smokers) identified and invited via letter | Population (age 60 – 75 AND those who had been an active smoker in the last 5 years) identified and invited via letter |
| 3. Health Check | 45 minute face to face consultation with respiratory nurse, including risk assessment (In phase 2: QRisk top 5% (0.68% over 2 years), spirometry for COPD, and brief smoking cessation advice if relevant | 40 minute face to face consultation with respiratory nurse, including risk assessment (LLP 5% over 5 years), spirometry for COPD, and brief smoking cessation advice if relevant | 20 minute face to face consultation with respiratory nurse, including risk assessment (PLCO 1.51% over 6 years), spirometry for COPD, and brief smoking cessation advice if relevant | 60 minute face to face consultation with respiratory nurse, including risk assessment (LLP 2.5% over 5 years OR PLCO 1.51% over 6 years), spirometry for COPD, and brief smoking cessation advice if relevant |
| 4. Post check | CT carried out in mobile unit as soon as possible after check | CT referral using conventional pathways | Same day CT in mobile unit | CT referral using conventional pathways |
| 5. Discussion of suspected cancers at MDT | Suspect CTs referred using conventional pathway | Suspect CTs referred using conventional pathway | Suspect CTs referred using conventional pathway | Suspect CTs referred using conventional pathway |
2.b. Pre-launch community engagement costs
As part of their lung health intervention some of the projects incorporated a community engagement programme, typically focussing on the dissemination of a healthy lung message through websites, posters, etc. and a series of community events rather than as a targeted means of increasing uptake of the screening element of the project, these are detailed in Table 1. Many of the potential health benefits associated with improved lung health public knowledge will not be gathered in the data reported by the projects.

The cost of the community engagement element of each project is based on costs reported directly by project leads for the two projects which provided full data. The Nottingham project did not conduct any community engagement activities in their first phase, but published a range of posters and leaflets at an estimated cost of £500. In contrast, Liverpool conducted a range of activities (see Table 1) at an estimated total cost of £82,556 (£23,434 on lung health leaflets and posters, and £59,122 on events and drop in sessions).

2.c. Unit costs
The first component of the bottom-up short-term costing analysis of the respiratory health checks is the identification of the unit costs relevant to each aspect of the projects, these are presented in Table 2. The cost categories were identified through the consideration of the shared components of the projects, as presented in Table 1. The unit cost estimates were identified through searches of the Department of Health’s National Schedule of Reference Costs 2014/15,[5] the PSSRU’s Unit Costs of Health and Social Care 2015,[6] previous economic evaluations in the area, and the economic returns provided by the projects.

Patient identification and invitation
While each of the projects used slightly different modalities for the identification and invitation of patients (e.g. using private providers or existing staff), we assume that the different modalities would have a similar marginal cost and effect if implemented as usual NHS activity. The unit cost of £10 per invitation sent, including identification of relevant patients, is derived from the UKLS evaluation.[3] While it is possible to derive a unit cost of patient invitation from some of the ACE project returns, the UKLS estimate is considered a better indication of full cost of the activity including the cost of patient identification.

Respiratory health check
The cost per hour of the respiratory nurses’ time, including related costs such as estate, management and administration, is taken from the PSSRU estimates of unit cost.[6] It is assumed that a grade 6 FTE
nurse specialist would conduct the check, resulting in a cost per hour of £65. It is assumed that this time is divisible, such that a half hour check costs half as much as a full hour. Within the check it is assumed that the only additional cost on top of the cost of the nurse is the cost of the spirometry. The cost per spirometry, £9.91, is estimated from the economic evaluation of spirometry for COPD in NICE CG101.[7] In both Nottingham and Liverpool projects the majority of patients suspected of having COPD at the check were required to attend a respiratory service for an additional diagnostic spirometry, costed at the same unit cost as the check spirometry.

Mobile or secondary care based CT and MDT referral

Two modalities of CT investigation are considered, hospital based CT using existing pathways (including cases where radiologists had to be paid out of hour fees), and CT in a mobile vehicle. The hospital based CT unit cost, of £104.87, was taken from the relevant NHS reference cost,[5] while the mobile CT cost, of £340, was provided by the Nottingham project. The mobile CT estimate is a projection of the cost per scan in possible future checks, and is significantly less than the £680 per scan paid by the project for the ACE project mobile CT scans. This estimate is clearly highly uncertain, with other informal estimates suggesting a unit cost closer to £150 per scan for a large-scale screening programme. As the use of mobile CT vans for such interventions does not constitute usual NHS activity, a relevant reference cost does not exist, and the reliance on private companies to provide the scans would suggest that the cost per scan is very variable, dependent on the scale of the intervention and bargaining power of the commissioner.

Finally, the cost per MDT referral, £110.73, is taken from the relevant reference cost.[5]

Table 2: Short term unit costs associated with the conducting of the screening

<table>
<thead>
<tr>
<th>Unit cost</th>
<th>Value</th>
<th>Source</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cost of community engagement and pre-launch activities</td>
<td>Estimated at a project level due to unique nature of activities, reported in the Results section</td>
<td></td>
</tr>
<tr>
<td>Cost of patient identification and invitation</td>
<td>£10.00</td>
<td>UKLS evaluation[3]</td>
</tr>
<tr>
<td>Cost of nurse time, per hour</td>
<td>£65.00</td>
<td>PSSRU 2015 unit cost of a grade 6 FTE nurse specialist, including range of non-salary costs including management, administration and estates staff and non-staff costs[6]</td>
</tr>
<tr>
<td>Cost of spirometry</td>
<td>£9.91</td>
<td>Unit cost estimated for the NICE COPD Guidance CG101[7]</td>
</tr>
<tr>
<td>Cost of hospital based CT</td>
<td>£104.87</td>
<td>Reference cost weighted average (by frequency) of all adult CTs[5]</td>
</tr>
<tr>
<td>Cost of mobile van based CT</td>
<td>£340.00</td>
<td>Estimate of phase 2 project cost per scan, provided by Oliver Simon (Nottingham project)</td>
</tr>
<tr>
<td>Cost of MDT</td>
<td>£110.73</td>
<td>Reference cost cancer MDT meeting (CMDT)[5]</td>
</tr>
</tbody>
</table>
2.d. Short-term project resource use

In addition to the unit cost estimates, evidence is required on the frequency of occurrence of each of the elements of resource consumption. Table 3 reports the frequency and relevant indicators of resource use across the two projects which returned full data. As with the previous section this table only considers the frequency of activities until MDT discussion, the cost of smoking cessation and disease treatment are considered in the next section.

No information was available about the characteristics of the individuals receiving these services, so it is not possible to comment on whether they would be expected to have a similar risk of being diagnosed as a result of the screening. The Liverpool project was not able to provide exact estimates of the number of diagnostic spirometries, nor the number of related MDT discussions. These were estimated, with guidance from the project team, at 45% of the first line spirometries, and 2.7% of those receiving a CT scan. Furthermore, 37% of patients in the Liverpool project declined to consent to data collection and as such are excluded from this analysis. By excluding these patients we are assuming a complete case scenario, such that the patients who consented are assumed to be identical to those who did not. It was not possible with the available evidence to test this assumption.

These resource use estimates are combined with the unit costs in the Results section of this chapter.

*Table 3: Frequency of project resource use*

<table>
<thead>
<tr>
<th></th>
<th>Nottingham</th>
<th>Liverpool (adjusted to reflect 37% non-consent)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of patients invited</td>
<td>1,208</td>
<td>7,261 (11,526 rounded down by 37% to represent those who shared their data)</td>
</tr>
<tr>
<td>Number and duration of respiratory health checks</td>
<td>323 45 minute consultations</td>
<td>2,876 40 minute consultations</td>
</tr>
<tr>
<td>Number of spirometries</td>
<td>57 at health check + 44 diagnostic required to confirm suspected COPD</td>
<td>1775 at health check + 612 diagnostic required to confirm suspected COPD</td>
</tr>
<tr>
<td>Number and modality of CT</td>
<td>157, mobile CT van</td>
<td>1,046 hospital based</td>
</tr>
<tr>
<td>Number of MDT discussions</td>
<td>4</td>
<td>28</td>
</tr>
</tbody>
</table>
6. Methods – Long-term analysis
3.a. Analytical Plan – long-term analysis
The long-term health and cost implications of an intervention is reliant on two key factors. Firstly, the intervention must have a clear causal link to some outcome of interest. In the case of the ACE projects, these outcomes can be considered to be lung cancer, COPD and smoking cessation referrals, as the three outcomes collected and expected to have a clear and definable impact on patient health. Secondly, there must be the ability to link the outcomes with the long-term health of the patient and costs to the NHS. This link can be directly observed within the study being evaluated, or through extrapolation of the outcomes using external sources of evidence, such as previously published trials.

In the case of this evaluation, both the Nottingham and Liverpool projects have been able to record and report the incidence of lung cancer and COPD diagnosis and referrals for smoking cessation services. However, as the projects do not have a control arm, it is not known whether these resulted from the intervention in the project or would have occurred with routine NHS services.

Due to the lack of follow-up of patients in the projects, it is not possible to observe directly the long-term health and cost implications of the respective outcomes. It is, therefore, necessary to investigate the wider literature for estimates of the link between the three outcomes identified and the long-term implications. These searches are detailed in the following section.

The long-term analysis is constructed through a base-case analysis focussing on the diagnoses of lung cancers with additional discursive scenario analyses. The base case analysis takes the UKLS approach alone, as the most robust source of evidence on the cost-effectiveness of lung cancer screening with CT alone. Once the cost-effectiveness of interventions such as the ACE projects as a means of identifying patients with lung cancer has been estimated, additional scenarios are considered as a series of threshold analysis alongside discursive assessment. These scenarios are framed by the potential implications to the intervention’s cost-effectiveness of the inclusion of diagnosis of COPD and referral to smoking cessation in the evaluation. These three areas were chosen due to the a priori expectation by the projects that they represent the primary outcomes of the respiratory health checks.

The short- and long-term costs are consolidated to estimate the total cost to the NHS of each of the packages of care delivered, this is reported alongside the total health implications of each (reported as life years (LYs) and QALYs). Results are reported at a total project level only, as the variation in size and design of the studies makes direct comparison potentially misleading.
The primary perspective of the analysis is that of the NHS and personal social services (PSS), costs are adjusted to 2016 values and, where possible, both costs and outcomes are discounted to net present values at a rate of 3.5% per annum.[1]

3.b. Evidence on the long-term health and cost implications of short-term outcomes

A pragmatic search of the literature was conducted to attempt to identify suitable estimates of the long-term health and cost implications of earlier diagnoses of lung cancer and COPD consistent with the diagnoses made by the ACE projects, as well as the implications of a referral for smoking cessation services.

These searchers were structured around the research team’s prior knowledge of the literature as well as searches of the relevant NICE guidelines. To be deemed relevant, the literature had to be both fully relevant to the decision problem, i.e. the economic evaluation of diagnosis of disease at an earlier stage than symptomatic presentation or referral to smoking cessation services. In addition, it had to have been subject to peer-review or part of formal NICE guidance.

The lead time between diagnosis with and without screening, and thus the benefit of screening, is derived from the literature. Similarly, the lack of available patient-level data from the projects, due to patient anonymity, required the estimation of cost and health outcomes independent on any patient-specific factors, including stage of disease diagnosed, age, gender and smoking history. The implicit assumption is, therefore, that all patients diagnosed with any of the three outcomes of the projects are perfectly characterised by the average patient evaluated in the literature informing the long-term outcome estimation. This assumption is considered in more detail throughout this section and in the Discussion.

This approach further necessitates the assumption that the cost and health implications of treating the three screening outcomes are completely independent. The assumption is also made that there are no additional costs to the NHS or health implications to patients that occur beyond these three outcomes. We are aware of the use of risk assessment tools (including the QRisk tool)[8] during the checks which could inform other diagnoses, and the prescription of statins. However, these elements are beyond the scope of this evaluation.

Lung cancer

The search of the literature concerning screening for lung cancer using CT identified two studies of direct relevance, specifically the UKLS[3] and NLST[9] screening trial evaluations. It was decided that due to it being conducted in the UK, its similarity to the Liverpool screening criteria and accessibility
of the analysis, the UKLS results would be carried forward. Of note, the UKLS economic evaluation did not seek specifically to evaluate the trial, rather it made use of the trial results to inform an evaluation of a CT screening programme for lung cancer in the UK, incorporating, for example, estimates of real word recruitment.

The UKLS evaluation was structured around patient-specific estimates of the survival of each of the 42 lung cancer cases diagnosed, conditional on being diagnosed at screening, compared to diagnosis after symptomatic presentation, consistent with current clinical practice. Stage specific survival estimates for screen-detected cancer were estimated from the US ELCAP CT screening trial and assumptions from the literature, which were contrasted with the survival estimates for patients diagnosed symptomatically in the UK using published evidence. Lead time estimates were informed by the literature as 6, 4, 2, and 0 years for stage 1-4 respectively.

The evaluation further incorporated estimates of the cost and quality of life implications of early diagnosis, estimating ICERs of £6,325 (95% CI £4,109 to £9,430) per life year gained and £8,466 (95% CI £5,516 to £12,634) per QALY gained.

It is possible to derive from the UKLS evaluation an average additional cost and health impact per lung cancer diagnosed by a CT screening programme, such as UKLS and the ACE projects. From the ULKS report[3] we extract the estimated total cost of treatment for all lung cancers diagnosed through the screening programme (£332,534), and the total estimated cost of treating them had they presented symptomatically (i.e. the counterfactual) (£189,379). The significant difference between the two total costs is driven by the UKLS assumptions that, prior to diagnosis, patients do not generate any costs to the NHS, and that patients diagnosed through screening live longer (and as such accrue costs for longer). When considered across the 42 lung cancers diagnosed we can extract an average incremental total discounted cost per cancer diagnosed by the screening programme rather than symptomatically of £3,408 (cost per cancer diagnosed via screening of £7,917 minus symptomatically of £4,509).

Similarly, we can estimate the incremental health effects (both in terms of life years and QALYs) of screen detection. The UKLS report estimated average incremental discounted life year and QALYs gains from screening of 2.1 and 1.6 per lung cancer diagnosed, respectively.

Several assumptions were required in order to use these estimates in our evaluation of the interventions in the ACE projects. While the age range of patients selected in UKLS is similar to the ACE projects (being 50-75), patients are only referred for a CT if they are determined to be at high risk of cancer using the LLP algorithm (>5% risk over 5 years). As different CT referral strategies were used
across the different ACE projects, as shown in Table 1, it is possible that the UKLS set of diagnosed lung cancer patients differs from that which would have been identified using different risk algorithms. However, this bias is expected to be small due to significant similarities in the risk algorithms and the setting of similar threshold risk levels.

Furthermore, the approach taken in this analysis necessitates the assumption that the distribution of lung cancers identified in UKLS is representative of all of the ACE projects, such that the cost and health implications of the average lung cancer patient diagnosed in UKLS are the same as these projects. Similarly, the UKLS is assumed to be representative of all relevant risk factors, including age (as discussed previously), gender, socioeconomic status, and smoking history.

The UKLS analysis did not include the implications of over-diagnosis on the long-term cost-effectiveness of screening, arguing that while the cost-effectiveness would be reduced if there were substantial over-diagnosis, the prevalence of lung cancer was consistent with the expected risk status, and as such over-diagnosis was unlikely. Similarly, while the evaluation of the NLST trial[9] estimated that 18.5% of lung cancers diagnosed with CT were over-diagnosis, they assumed that there was no quality of life or mortality implications of over-diagnosis, but that there was a cost implication.

**Wider outcomes**

Searches for informative evidence on the incremental cost-effectiveness of diagnosing additional cases of COPD and referring attending patients to smoking cessation services were also conducted. In both cases, while the searches produced sources of evidence that, under certain assumptions, were utilisable to inform the analysis, these assumptions were deemed too extreme to inform the base case analysis, and are detailed below.

**COPD**

The search of evidence on the cost and health related implications of COPD diagnoses made as a result of respiratory health checks identified one source of potentially relevant information, the economic evaluation of opportunistic case finding of COPD, conducted as part of NICE guideline CG101.[7] The evaluation was motivated by the Guideline Development Group’s (GDG) desire to know the potential cost-effectiveness of spirometry to diagnose COPD in a population of patients aged 35 and over (using a mean age of 55 for the cohort analysis) who were smokers/ex-smokers with a chronic cough.

The economic evaluation consists of a decision tree structured around the availability or not of a spirometry to this population. In both arms patients can go on to be diagnosed with COPD (but occurring at a later date in the no-spirometry arm), at which point they are offered referral to smoking cessation services which they can accept or reject. Long term health and cost outcomes associated
with each of the different endpoints were incorporated from a range of different estimates in the literature.

The evaluation found that the use of spirometry in this population was associated with incremental costs of £35.49, 0.050 additional years of life, and 0.044 additional QALYs per spirometry conducted. The low incremental cost was due to the low additional cost of spirometry for the entire cohort being offset by the long-term cost saving from a reduction in long term treatment of COPD. These were combined to give an ICER of £814.56/QALY, suggesting the use of spirometry in this population was highly cost effective.

While it is possible to estimate the same sort of evidence as from the UKLS analysis for lung cancer, i.e. the incremental cost and health implications of diagnosing COPD at a potentially earlier stage than without the project, there are two major differences between the NICE CG101 evaluation and the ACE projects which may introduce bias. Firstly, the cohort evaluated is not a good match to those invited to the respiratory health checks evaluated in this study. The NICE evaluation considered all patient aged 35 and over who were smokers/ex-smokers with a chronic cough, in contrast to these studies which took a range of criteria covering patients between 55-75 and ever smokers to active smokers. Secondly, as the NICE evaluation was conducted in 2010 (CG101 was reviewed in 2016 but the evaluation was not updated), and it is clear that several of the assumptions it made and the informative evidence is likely to be outdated. For example, the evaluation discounts future costs and health benefits at a rate of 6% and 1.5% per year respectively, in line with the NICE recommendations at the time of the analysis. However, current recommendations are for discounting at 3.5% for both. Similarly, the evaluation relies on old literature, the analysis being primarily based on lifetables from a 1977 study on COPD, and costs based on treatments used in 2003 that are likely to have changed.

**Smoking Cessation**

A search of the literature relating to the health and cost implications of smoking cessation referral similarly identified one source of potentially relevant evidence, an analysis conducted by the York Health Economics Consortium (YHEC) as part of the NICE guidance on smoking cessation.[10] The evaluation consisted of a cohort analysis of all adult (16+) current smokers accessing 11 forms of smoking cessation services available in the NHS, compared to a scenario of no intervention. The model considers the implications of quitting and relapse rates on a range of related diseases (lung cancer, CHD, COPD, MI, and stroke), and their associated costs and health related implications.

The average incremental cost and health implications per smoker undergoing cessation treatment is reproduced below in Table 4. The table reports the estimated incremental cost and QALY across each of the 12 interventions considered, including no intervention, alongside the modelled cessation rate.
Apart from ‘BA plus self-help material plus NRT’, which was cost-effective with an ICER of £984/QALY, all of the active interventions were found to be more effective but less expensive than ‘no intervention, i.e. dominant’.

Table 4: Results of the YHEC smoking cessation evaluation

<table>
<thead>
<tr>
<th>intervention</th>
<th>cessation rate</th>
<th>cost</th>
<th>QALY</th>
</tr>
</thead>
<tbody>
<tr>
<td>No intervention</td>
<td>2%</td>
<td>£7,232</td>
<td>11.9</td>
</tr>
<tr>
<td>‘Brief advice (BA)’</td>
<td>3%</td>
<td>£7,221</td>
<td>11.91</td>
</tr>
<tr>
<td>BA plus self-help material</td>
<td>4%</td>
<td>£7,206</td>
<td>11.92</td>
</tr>
<tr>
<td>BA plus self help material plus nicotine replacement therapy (NRT)</td>
<td>6%</td>
<td>£7,268</td>
<td>11.94</td>
</tr>
<tr>
<td>BA plus self-help material plus NRT plus specialist clinic</td>
<td>15%</td>
<td>£7,118</td>
<td>12.02</td>
</tr>
<tr>
<td>Less intensive counselling (LIC) and bupropion</td>
<td>24%</td>
<td>£6,920</td>
<td>12.1</td>
</tr>
<tr>
<td>More intensive counselling (MIC) and bupropion</td>
<td>31%</td>
<td>£6,818</td>
<td>12.17</td>
</tr>
<tr>
<td>Nicotine patch plus group counselling</td>
<td>21%</td>
<td>£7,037</td>
<td>12.07</td>
</tr>
<tr>
<td>Nicotine patch plus individual counselling</td>
<td>16%</td>
<td>£7,076</td>
<td>12.03</td>
</tr>
<tr>
<td>Nicotine patch and no counselling</td>
<td>12%</td>
<td>£7,098</td>
<td>11.99</td>
</tr>
<tr>
<td>Nicotine patch plus pharmacist consultation</td>
<td>24%</td>
<td>£7,100</td>
<td>12.1</td>
</tr>
<tr>
<td>Nicotine patch plus pharmacist consultation plus behavioural program</td>
<td>35%</td>
<td>£7,010</td>
<td>12.2</td>
</tr>
<tr>
<td>Average active intervention</td>
<td></td>
<td>£7,079</td>
<td>12.04</td>
</tr>
<tr>
<td>Increment per smoker undergoing cessation</td>
<td></td>
<td>-£153</td>
<td>0.14</td>
</tr>
</tbody>
</table>

However, as with the evidence relating to COPD, the assumptions required directly to incorporate such evidence into the analysis presented here were considered too unrealistic. In the case of this evidence around smoking cessation, neither evidence from the projects nor the YHEC analysis allow us to estimate the difference between the proportions of patients who would receive a smoking cessation intervention as a direct result of attending a respiratory health check compared to the proportion who would have anyway in the absence of that service, nor the proportion of referrals which successfully initiated cessation treatment. As a result, while it would be possible to estimate the cost and health implications to a patient referred to smoking cessation during the ACE project, the benefits associated with it would be hugely overestimated, as such an analysis would implicitly assume that that person would have never received such a referral through other NHS pathways. If a patient is willing to accept such a referral during the project it seems likely that they would receive a referral had they not attended, but just at a later date.
7. Results
As discussed earlier, the results of the analysis are presented as a base-case, where only the long-term health and cost implications of additional lung cancer diagnoses are considered. The potential impacts of additionally including COPD and smoking cessation are considered as scenario analysis. The full set of results, including the short-term costs and three scenarios considered, are presented in Table 5. As discussed above the funding of any project such as those considered here is likely to impose opportunity costs on the NHS, as there is inevitably some other beneficial NHS activity that could have been funded had the ACE projects not been. Using recent research which estimated the marginal cost of a QALY in the NHS and thus the opportunity cost of funding elsewhere,[2] it is possible to comment on whether the projects can be said to have increased or decreased population health. The previous study estimated the marginal cost of a QALY at £13,000, such that any new funding intervention (such as the ACE projects) that imposed an additional cost on the NHS would need to impose this cost at a rate of less than £13,000 per additional QALY of health generated. This allows us to estimate the incremental net health benefit (NHB), i.e. how much additional population health is gained/lost through the funding of such a project.

Table 5: Results for the base case analysis

<table>
<thead>
<tr>
<th>Short term costs of community engagement and screening program</th>
<th>Nottingham</th>
<th>Liverpool</th>
</tr>
</thead>
<tbody>
<tr>
<td>Community engagement</td>
<td>£500</td>
<td>£52,010</td>
</tr>
<tr>
<td>Screening program</td>
<td>£83,150</td>
<td>£333,686</td>
</tr>
<tr>
<td>Diagnoses and referrals</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cases of COPD diagnosed</td>
<td>44</td>
<td>386</td>
</tr>
<tr>
<td>Cases of lung cancer diagnosed</td>
<td>3</td>
<td>22</td>
</tr>
<tr>
<td>Smoking cessation referrals</td>
<td>9</td>
<td>109</td>
</tr>
<tr>
<td>Base case analysis: lung cancer only</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Long-term costs</td>
<td>£10,224</td>
<td>£74,976</td>
</tr>
<tr>
<td>Total cost (short and long-term)</td>
<td>£93,374</td>
<td>£460,672</td>
</tr>
<tr>
<td>Maximum life years gained</td>
<td>6.3 LYs</td>
<td>46.2 LYs</td>
</tr>
<tr>
<td>Maximum QALYs gained</td>
<td>4.8 QALYs</td>
<td>35.2 QALYs</td>
</tr>
<tr>
<td>Cost per life year gained</td>
<td>£14,821/LY</td>
<td>£9,971/LY</td>
</tr>
<tr>
<td>Cost per QALY gained</td>
<td>£19,453/QALY</td>
<td>£13,087/QALY</td>
</tr>
<tr>
<td>Incremental total NHB (using a threshold of £13,000/QALY)[2]</td>
<td>-2.4 QALYs</td>
<td>-0.2 QALYs</td>
</tr>
</tbody>
</table>

The base case analysis considers all of the short-term costs but only the long-term cost and health implications which result for the lung cancer diagnosis made as a direct result of the screening, therefore taking the same approach as the UKLS analysis.
For the Liverpool project this analysis shows that the upfront community engagement costs were £82,556 (scaled down to £52,010 reflect the 37% of patients who did not consent), the costs of running the rest of the project were £333,686, and 22 cases of lung cancer were diagnosed. If these 22 cases would not otherwise have been identified through standard NHS activities, they imply long term additional costs to the NHS, through incremental treatment costs, of £74,976 and a gain of 35.2 QALYs. This results in an incremental cost-effectiveness ratio of £13,087/QALY. When compared against the estimated cost per QALY that could be generated with the same money elsewhere of £13,000,[2] it is clear that in this scenario the Liverpool project is on the margin of what can be considered a cost-effective use of limited NHS resources, if a higher cost-effectiveness threshold of £20,000/QALY were used, as has been historically preferred by decision makers such as NICE, the project would be cost-effective under the modelled scenario.

Using these estimates, it is possible to estimate that, under this scenario, if such a project were funded it would result in a net reduction in population health of 0.2 QALYs, as the same funding (an estimated £460,672) could be used to generate 35.4 QALYs elsewhere in the NHS, rather than the 35.2 QALYs generated by the project.

It is possible to frame the required benefits of the estimated COPD diagnoses and smoking cessation referrals as threshold analysis. Threshold analyses are a simple quantification of the required scale of a variable to change the cost-effectiveness estimate. In this case, such an analysis would ask what net health benefit would have to be achieved through the earlier diagnosis of COPD and additional smoking referrals (or smoking referrals occurring at an earlier time-point than without the projects) to make the projects cost-effective.

For the Nottingham project the total cost of the screening program and cost to the NHS of treating the three lung cancers diagnosed (£93,374) implies that, to be cost-effective, an additional NHB of 2.4 QALYs would have to be achieved as a result of COPD diagnosis or smoking cessation referrals. It is worth noting that this is not the same as generating 2.4 QALYs of additional health, as the NHB estimate additionally takes account of the cost of the diagnosis or referral. For example, if the additional cost to the NHS of the COPD diagnoses was £10,000, to generate a NHB of 2.4 QALYs the program would have to generate at least 3.2 QALYs (2.4QALYs + (£10,000 / £13,000/QALY) = 3.6 NHB). To put this into context, across the 44 cases of COPD diagnoses, each would have to be associated with a NHB of 0.07 QALYs.
8. Discussion
This economic evaluation has sought to estimate the short- and long-term cost and health implications of the ACE proactive lung projects. In doing so, it explores the potential of CT screening approaches for the early diagnosis of lung cancer to be a cost-effective use of limited NHS resources. The analysis has combined the short-term costs and confirmed diagnoses of lung cancer of the Nottingham and Liverpool projects with estimates of the long-term cost and health implications of the diagnoses and referrals. Both projects observed a number of diagnoses of lung cancer, COPD and smoking cessation referrals associated with the respiratory health checks and subsequent CT scans. However, given the lack of control evidence, either historical or contemporaneous, it has not been possible to conclude that these diagnoses and referrals would have not occurred without the ACE projects being in place. Therefore, while the exploratory threshold analyses presented highlight the potential for such projects to be a cost-effective use of limited NHS resources, it is not possible to state that these projects, or ones like them conducted at a national level, are cost-effective.

This study has sought to progress the debate over the cost-effectiveness of CT screening programmes and respiratory health checks by drawing directly from the approach taken in the UKLS economic evaluation, the largest and most recent UK based study in the area, by attempting to consider not only the expected incremental long-term cost and health implications of each additional lung cancer diagnosed with similar estimates from the literature relating to COPD diagnosis and smoking cessation referral.

However, this study has several significant limitations that diminish the robustness of the key finding with the consequence that results should be considered illustrative rather than definitive. The majority of the limitations are intrinsically linked with the nature of the projects which were not designed in an appropriate way to facilitate such an evaluation. Through the lack of comparator data, either longitudinal or contemporaneous, and lack of patient follow-up beyond diagnosis of COPD or lung cancer, or referral for smoking cessation, any evaluation of the projects is intrinsically subject to the risk of bias. As there is no means of robustly determining the counterfactual, nor of validating assumptions made about the long-term implications of the diagnoses and referrals, it is not expected that the quality of evidence presented in this report would be sufficient in isolation to inform national decision makers, such as the National Screening Committee or NICE.

Furthermore, as the two projects that submitted data for evaluation vary in multiple key factors (including risk score algorithm, CT modality, prior community engagement, and greatly on size), it has not been possible to determine the key factors expected to make up an optimal proactive lung screening approach.
Additional limitations of the evaluation include the lack of sensitivity analysis, either through probabilistic sensitivity analysis, nor scenario analysis. Such analyses were not possible as no suitable quantification of the extent of uncertainty around the parameters was possible given the level of data.

The limitations of the evaluation necessitate the careful interpretation of the results. Previous studies in early diagnosis of lung cancer, be it through CT [3] or early awareness campaigns, [11] have demonstrated that, when considering lung cancer alone, early diagnosis strategies are cost-effective but not cost saving. Furthermore, the existing evidence (given their limited direct relevance in this area) around earlier COPD diagnosis and smoking cessation referral, suggests that similar policies are more costly, but cost effective and dominant respectively. Given these previous studies and the evidence from the ACE projects, the case is beginning to emerge that, while not expected to be cost saving overall, projects aiming to capture respiratory disease at an earlier stage and discourage smoking have the potential to be cost-effective.

However, significant future research is required in several key areas. While future trials around CT screening in lung cancer, such as NELSON and the Yorkshire Lung Screening Trial (YLST), will continue to add to the pool of evidence that CT screening is a robust means of delivering stage shift in lung cancer, further research is needed to identify the true benefits of such a stage shift and the associated benefits of earlier COPD diagnosis and smoking cessation referral.
9. Conclusion
This study has sought to use existing evidence on the cost-effectiveness of the individual components of the ACE Proactive Lung CT Screening Projects, i.e. diagnoses of lung cancer, COPD and smoking cessation referrals to comment on the potential for cost-effectiveness. While evidence was identified that allowed for an estimation of the incremental long-term cost and health impact of each component, a number of very significant assumptions would have had to be made to incorporate the estimated implications of COPD diagnosis and smoking cessation referral into the analysis. Most notably these have included, firstly, the transferability of the setting from the published estimates to the projects, which without sufficient evidence on the patient population we have been unable to test. Secondly, the failure to construct historic or contemporaneous comparators for the projects has necessitated the assumption that all of the observed changes in the three components has been caused by the project, and that such diagnoses and referrals would not have occurred without the projects.

Therefore, the conclusion of this analysis must be that evidence exists on the potential of respiratory health and CT screening projects to be cost effective, due to the potential health benefits associated with each of the three factors. However, there is insufficient strength of evidence, both on the ability of the interventions to increase the diagnoses of lung cancer, COPD, and referral for smoking cessation relative to usual NHS activity, and associated with the poor level of evidence relating to the long-term cost and health implications of such diagnoses and referrals. Further evidence is needed in all of these areas before it will be possible to confidently comment on whether such projects represent a cost-effective use of limited NHS resources.
References