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Policy Research Unit in Economic Evaluation
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ACE: Economic Evaluation of the Proactive Lung Cluster

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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.

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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 identify 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^{Error! Reference source not found.} 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

Project phase	Nottingham	Liverpool	Manchester	London
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

Unit cost	Value	Source
Cost of community engagement and pre-launch activities	Estimated at a project level due to unique nature of activities, reported in the Results section	
cost of patient identification and invitation	£10.00	UKLS evaluation [3]
cost of nurse time, per hour	£65.00	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]
cost of spirometry	£9.91	Unit cost estimated for the NICE COPD Guidance CG101 [7]
Cost of hospital based CT	£104.87	Reference cost weighted average (by frequency) of all adult CTs [5]
cost of mobile van based CT	£340.00	Estimate of phase 2 project cost per scan, provided by Oliver Simon (Nottingham project)
cost of MDT	£110.73	Reference cost cancer MDT meeting (CMDT) [5]

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

	Nottingham	Liverpool (adjusted to reflect 37% non-consent)
Number of patients invited	1,208	7,261 (11,526 rounded down by 37% to represent those who shared their data)
Number and duration of respiratory health checks	323 45 minute consultations	2,876 40 minute consultations
Number of spirometries	57 at health check + 44 diagnostic required to confirm suspected COPD	1775 at health check + 612 diagnostic required to confirm suspected COPD
Number and modality of CT	157, mobile CT van	1,046 hospital based
Number of MDT discussions	4	28

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 searches 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 UKLS 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

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

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

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

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 this 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 ($2.4\text{QALYs} + (\pounds 10,000 / \pounds 13,000/\text{QALY}) = 3.6\text{NHB}$). 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.

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