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**Policy Research Unit in Economic Evaluation
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MODELLING THE COST- EFFECTIVENESS OF EARLY AWARENESS INTERVENTIONS FOR THE EARLY DETECTION OF LUNG CANCER

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Summary

Introduction

Five year survival rates in lung cancer in England are significantly lower than in several countries with a similar level of expenditure on healthcare. Furthermore, in the last three decades, the ten year survival rate from lung cancer in England has barely changed (increasing from 4% to 4.6%) compared with some other cancers, which have greatly improved during the same period (for example, breast cancer has seen an increase from 41% to 77% and prostate from 21% to 68%).

This report considers the potential cost effectiveness of a national campaign in England aimed at improving the early awareness of the signs and symptoms of lung cancer. This increased awareness can occur in both the general public (who may be encouraged to present to their GP) and the GPs themselves (who may be more likely to send patients for further investigations). The analysis is framed around the impact of an observed shift in the distribution of the cancer stage at which patients are diagnosed, such that patients are diagnosed at an earlier stage of their disease than they would have prior to the intervention. The recently reported National Awareness and Early Diagnosis Initiative (NAEDI) pilot campaign is used to describe a potential shift in the distribution of stage of clinically identified lung cancer. The impact of such an early awareness campaign is considered using a cost-effectiveness analysis which estimates changes in cost, as well as gains in survival and health related quality of life (HRQoL), associated with a national campaign relative to current practice.

We focus on addressing the limited information available on the natural history of lung cancer in terms of pre-clinical (i.e. before the diagnosis has been made but lung cancer is present) and clinical stages of the disease that is core to the evaluation of an early awareness campaign. An estimate of the relevant parameters that inform this natural history model is presented and these are used, within a decision analytic model, to consider the cost-effectiveness of such a campaign applied at a national level.

We focus on non-small cell lung cancer (NSCLC) because it has the greater prevalence in England as well as being the type in which, based on clinical opinion, the biggest survival gains are to be expected.

Methods

A review of previous models relating to the natural history of the disease highlighted the importance of modelling the impact of an early awareness campaign in lung cancer through calibration methods to estimate the unobservable transitions of pre-clinical disease.

As a result a *de-novo* natural history model was developed that considered patients to be in one of four overarching states: with no disease, pre-clinically identified disease, clinically identified and

diagnosed disease and dead. Within these disease states patients were categorised by the severity of the disease using three alternative stages: (a) I & II; (b) IIIa & IIIb; (c) IV.

The model considers the entire cohort of the English population over the age of 30 and uses a cycle period of one month to allow for the fast progression of NSCLC. The model structure was 'calibrated' to incidence data collected as part of the National Lung Cancer Audit (the LUCADA dataset) to give estimates of the complete set of disease transitions within the model structure subject to a set of initial clinically estimated transition probabilities ('priors'). NSCLC mortality data were provided by the International Cancer Benchmarking Partnership (ICBP) and Cancer Research UK.

A lack of available information on a range of factors necessitates the use of a set of assumptions around the base-case model. All individuals who have NSCLC (pre-clinical or clinical) are subject to HRQoL decrements until death or a period of five years has passed since clinical identification of the disease, at which point they return to the health of a 'normal' individual. Patients in pre-clinical stages of disease are assumed to incur no cost to the NHS, while all of the costs of diagnosis and treatment are accrued within the first year after diagnosis, and only within a hospital setting. In addition, all patients who die as a result of NSCLC are assumed to be clinically identified before dying, while some post-mortem data suggests otherwise it is not of sufficient strength to be used in the analysis.

An underlying shift in the stage of disease at diagnosis was observed in NAEDI pilot study. This was used as the basis of an estimate of the potential long term impact on the severity of disease at diagnosis of a national awareness campaign. This observed shift represented an increase in diagnosis at stages I or II and IIIa (11% and 25%, respectively), and a decrease in stage IIIb or IV (5%). Due to a lack of follow-up data it was assumed that the early awareness campaign was only effective for the period of its funding. The modelling sought to 'smooth out' the short term changes in clinical identification at the beginning and directly after a new campaign, where an initial 'spike' in cases identified might be expected, resulting from a prevalent pool of pre-clinical cases. The cost of such a national early awareness campaign (£2.9 million) was provided by the Department of Health based on the recently completed full NAEDI campaign.

As no data is as yet available on changes in GP attendance of the 'worried well' population, or on shifts in the route of patient presentation with NSCLC, these are considered through two separate scenario analyses. In both scenarios a threshold approach is taken to estimate the size of bias required to change the conclusion of the base-case analysis. The first scenario considers the number of additional GP consultations, not resulting in a diagnosis of NSCLC, required to make the campaign not cost-effective as a result of associated additional costs. The second estimates the required shift towards patient presentation at GP clinics rather than through emergency admission, that would suggest the early awareness campaign was cost-saving.

Results

The calibrated natural history model provides a range of estimates about the incidence and progression of pre-clinical NSCLC in England. It suggests that there is likely to be a significant population in England with early pre-clinical disease (roughly 75,000 with stage I or II who have not

been clinically diagnosed with the disease) who are very unlikely to experience progression to a more severe disease state or to be clinically identified. Furthermore, the model confirms clinical understanding that, in many cases, once early stage NSCLC progresses to a more severe state it can do so very rapidly. This suggests the importance of early clinical identification to enable early treatment before progression.

Application of the observed shift in the stage of disease at diagnosis from the NAEDI pilot (adjusting for the shift in the control area) using base-case assumptions results in an early awareness programme generating additional quality adjusted survival (325 quality-adjusted life years (QALYs)) but at an additional cost to the NHS in terms of diagnostic and treatment costs (£1 million) alongside to the cost of the media campaign (£2.9 million). Taken together, improved outcomes but increased costs results in an incremental cost-effectiveness ratio of £12,192 (i.e. the extra additional cost per quality adjusted life-year gained). This would suggest that, using the National Institute for Health and Clinical Excellence (NICE) cost-effectiveness threshold of between £20,000 and £30,000 per QALY, a national campaign aiming to increase the early awareness of the signs and symptoms of NSCLC would be cost-effective.

The first alternative scenario found that the campaign would no longer be cost-effective if the additional costs of the increase in 'worried well' patients were to be greater than £2.5 million (assuming a cost effectiveness threshold of £20,000 per QALY). Under the assumption that 50% of such patients would be given chest x-rays this would require 35,799 worried well individuals to attend their GP as a result of the campaign for that campaign to cease to be cost effective. The second alternative scenario found that a cost saving of £3.9 million associated with a shift in the route of diagnosis away from emergency admission and towards presentation at GP clinics, would imply a national campaign was both cost-saving to the NHS and health improving.

Discussion

The research shows the potential for current economic evaluation methods to estimate the natural history of diseases that are unobservable. It has also shown that a national campaign to increase the awareness of the signs and symptoms of lung cancer can be cost effective. However, this finding should be treated with caution given the significant uncertainty associated with the available evidence.

The unobservable nature of many of the natural history parameters, as well as the lack of available data to inform the estimation through calibration, results in significant uncertainty in the estimates used to evaluate the early awareness campaign. Additional data could be drawn from lung cancer screening trials to reduce this uncertainty. These data were assessed but their relevance to an English population was considered limited. The ongoing UK Lung Screening (UKLS) trial may generate evidence which can be used alongside LUCADA data on clinically identified lung cancer. This may offer a significant improvement in the predictive capability of the natural history model.

Not only is there uncertainty in the underlying natural history estimates in the model, but there is also significant uncertainty relating to the impact and duration of effect of any national early awareness campaign. The report highlights the range of early awareness campaigns that have been

undertaken in England in the last few years, all of which have reported different outcomes in all of the metrics of interest. The NAEDI pilot was the only one of these to record a significant improvement in the distribution of cancer stage at the time of clinical identification. It is hoped that the national study will provide more definitive estimates of the effectiveness of early awareness campaigns.

Finally, there is potential for an improvement in the cost estimates associated with the diagnosis and treatment of lung cancer based on routinely collected data. This would be achievable through the use of diagnostic and treatment data collected by LUCADA for the English population which routinely collects information on mode of diagnosis of lung cancer, as well as planned treatment for patients.

1. Introduction

The Cancer Reform Strategy was set up by the UK Government in 2007 as a reaction to the poor survival rates for cancers in England relative to those elsewhere in Europe.[1, 2] In particular, the EURO CARE study found that Denmark and the UK have lower all-cancer survival than countries with similar total national expenditure on health. As part of the Government's strategy, a National Awareness and Early Diagnosis Initiative (NAEDI) has been established in England to address issues around the late diagnosis of all cancers.[3] NAEDI consists of four main work streams: (1) raising public awareness of cancer and promoting earlier presentation of symptoms; (2) optimising clinical practice and systems; (3) improving GP access to diagnostics; and (4) research, evaluation and monitoring.

This report focuses on the first stream of this strategy: raising public awareness of cancer and promoting early presentation of symptoms. This area has been highlighted as a potential explanation for England's relatively poor performance in cancer survival relative to the rest of Europe.[4] The focus of this report is on lung cancer, a similar report has been produced by the Economic Evaluation of Health and Care Interventions Policy Research Unit (EEPRU) for colorectal cancer.[5]

Five year survival rates in lung cancer are significantly lower than in several countries with a similar level of expenditure on healthcare. For example, Holmberg *et al.*[6] found that England had lower five year survival rates than Norway and Sweden with age-standardised survival estimates of 6.5%, 9.3% and 11.3% for men and 8.4%, 13.5% and 15.9% for women, respectively. Furthermore, in the last three decades, the ten-year survival rate of lung cancer in England has barely changed (increasing from 4% to 4.6%) compared with other cancers which have greatly improved in the same period (for example, breast cancer has seen an increase from 41% to 77% and prostate from 21% to 68%).[7] The lung cancer type with the greatest prevalence in England is non-small cell lung cancer (NSCLC): the 2011 report from the National Lung Cancer Audit (LUCADA) showed that 11% of diagnosed lung cancers in England and Wales are small cell (SCLC), 5.6% are mesothelioma and 83.3% are confirmed NSCLC or 'other'.[8] NSCLC is also the type which, based on clinical opinion, offers the largest survival gains from early awareness interventions. We therefore focus on NSCLC in this analysis.

This report considers the potential impact of a nationwide campaign in England aimed at improving the early awareness of the signs and symptoms of lung cancer. This increased awareness can occur in both the general public (who may be encouraged to present at their GP) and in GPs (who may be more likely to send patients for further investigations). Specifically, the analysis is centred on the impact of an observed shift in the distribution of stage at which patients' lung cancer is diagnosed, such that patients who, without the intervention, would be diagnosed at a late stage of disease are more likely to be diagnosed earlier following the intervention. The recently reported NAEDI pilot early awareness campaign is used to describe a potential shift in the distribution of stage of clinically identified lung cancer. The impact of such an early awareness campaign is considered using a cost-effectiveness analysis which considers the cost, survival and health related quality of life (HRQoL) gains associated with a national campaign relative to current practice.

The research specifically focuses on addressing the limited information available on the natural history of lung cancer in terms of pre-clinical (i.e. before the diagnosis has been made but lung cancer is present) and clinical stages of the disease that is core to the evaluation of an early awareness campaign. An estimate of the relevant parameters relating to the natural history model is presented and these are used to estimate the cost-effectiveness of a national early awareness campaign. The report emphasises the significant uncertainty in the natural history model, but also assesses the potential impact of any success that a campaign may have in achieving its primary goal of diagnosing patients with lung cancer at an earlier stage of disease.

2. Systematic review

A systematic review was conducted to identify studies which assessed the efficacy of public awareness programmes or interventions in lung cancer. A comprehensive search using terms for 'lung cancer' combined with 'health promotion' or 'awareness' was carried out in December 2011. Key electronic databases and grey literature sources were searched. Studies were selected, data extracted and quality assessed by one reviewer. Sixteen electronic databases were searched including Medline and Medline in Process & Other Non-Indexed Citations; Embase; Cochrane Library comprising the Cochrane Database of Systematic Reviews, Cochrane Central Register of Controlled Trials, NHS Health Economic Evaluation Database, Health Technology Assessment Database, Database of Abstracts of Review of Effects; Web of Science Science Citation Index, Social Science Citation Index and the Conference Proceedings index; Cumulative Index to Nursing and Allied Health Literature; PsycINFO; Health Management Information Consortium; Social Policy and Practice; Dissertation Abstracts. Searches were limited to English language only. Full details are presented in Appendix A, including URL links to programmes or campaigns identified in different countries.

A total of 1,219 references were obtained. Among these, a previously published systematic review on interventions to promote cancer awareness and early presentation of symptoms was identified.[9] This review by Austoker *et al.* included a comprehensive search of the literature from the year 2000 to November 2008 for studies examining the effectiveness of interventions to increase cancer awareness or to promote early presentation. Of the 2,557 abstracts identified in Austoker *et*

al., no studies on lung cancer met the inclusion criteria. Therefore, the systematic review for this report focussed on the period post-2008, which reduced the number of references to 413. These 413 potentially relevant articles were identified and abstracts screened for retrieval. Of these, 64 full text versions of the articles or references were evaluated. The majority were subsequently excluded as either irrelevant or containing little to no further information, as many of the references referred to the same study.

Three main cancer campaigns were subsequently identified in the UK from the literature review findings:

1. The Department of Health regional and local early awareness campaigns, along with the proposed lung cancer signs and symptoms campaign, which was to be piloted in the Midlands before rolling out nationally.
2. The Doncaster Primary Care Trust (PCT) campaign, Early Intervention in Lung Cancer within Doncaster (EICiD). Athey *et al.*[10] presents the findings for the evaluation of the community-based social marketing intervention for the early diagnosis of lung cancer.
3. The Leeds Early Diagnosis of Lung Cancer Campaign. No published articles were obtained but slide sets were available on increasing early detection of lung cancer in Leeds.

These are discussed in detail in the following section.

3. Lung cancer early awareness campaigns

3.1. Introduction to campaigns

Since 2009 England has seen a range of centrally-funded early awareness campaigns designed to promote early diagnosis of a range of cancers including lung cancer. In this report, we consider the four main campaigns related to lung cancer which are part of the wider National Awareness and Early Diagnosis Initiative (NAEDI):

1. A set of local early awareness projects, that ran between October 2010 and October 2011, referred to as the 'NAEDI local projects'.
2. Doncaster Primary Care Trust (PCT) campaign, Early Intervention in Lung Cancer within Doncaster (EICiD), that ran for 6 weeks from March 2008.
3. The Leeds Early Diagnosis of Lung Cancer Campaign (LEDLCC), that initially ran for 12 months from January 2011 but that has been extended to 2013. However, data are only available for the first 12 months.
4. A national early awareness campaign that was piloted in the Midlands (the NAEDI pilot) for six weeks between October and November 2011.

3.2. NAEDI local projects

In 2010 the Department of Health launched a programme of local public health interventions seeking to influence the three cancers responsible for the greatest number of 'avoidable' deaths: breast, bowel and lung cancer.[11] The 'NAEDI local projects' covered 109 Primary Care Trusts (PCTs) across England, with a target population estimated at 13.6 million for all three cancer types. The PCTs ran the interventions over very different time-frames but they all began after 1st October 2010 and most were completed by the 1st November 2011. A few of the campaigns were still running when the first report on the 'NAEDI local projects' was published.

Currently only a first report has been published by the Department of Health (DH) with limited analysis of the results of these campaigns.[11] Therefore, there is not a clear picture of the impact of the campaigns on early diagnosis of the target cancers due to preliminary data only being available.

The different campaigns employed a range of techniques to raise public awareness of cancer within the target population. The majority of the campaigns were focused on raising public awareness of cancer signs and symptoms; however, there were significant differences in the methods used to raise awareness. Most campaigns also aimed to achieve a certain level of GP and other health care professional engagement, with 11 of the 51 PCTs also seeking to achieve a change in the service provided by the local NHS including extended surgery times and direct access to chest x-ray services.

Overall, the first report on the 'NAEDI local projects' acknowledges that the preliminary data have not shown a significant increase in public awareness of the signs and symptoms of cancer between the pre and post intervention surveys. The report suggests that this may indicate a lack of project impact in efficacy or reach, but this may be caused by poor survey techniques or low statistical power. There have been some reported improvements in the confidence of patients in identifying cancer symptoms, the speed in which patients would act upon symptoms, a reduction in barriers to seeing the GP and general attitudes to cancer and early awareness. However, NAEDI emphasises that these are all early results which require further analysis.

The report made use of Two-Week Referral (2WW) data provided by Trent Cancer Registry for the period of analysis. In order to achieve a reliable estimate of the number of cancers diagnosed following a 2WW referral, Trent Cancer Registry recommends a wait of at least four months from the date of interest. As a result, the NAEDI report only presents data on projects which had completed data collection by July 2011. Data are reported on two outcomes: 2WW referrals and cancer diagnoses from 2WW referrals.

The first report presents the following results for lung cancer:

1. Total number of 2WW referrals for suspected lung cancer
2. Number of individuals diagnosed with lung cancer after coming through the 2WW for suspected lung cancer

In all cases two analyses were carried out looking at trends over time and comparing year-on-year changes before and after the intervention.

The campaigns mostly began in 2011. However, there was no uniformity in which month the intervention began and this varied between PCTs. As a result, evaluating any month-on-month difference between the control and intervention areas is very difficult. The report provides a breakdown of the total number of 2WW referrals for suspected lung cancer for January to November 2010 compared with the same period in 2011, these results are presented in Table 1.

Table 1: impact of the campaigns on 2WW referrals for suspected lung cancer

	January to November 2010	January to November 2011	Percent change
Control area (73 PCTs)	16,947	18,064	+7%
Intervention area (76 PCTs)	17,335	18,964	+9%

Source: Department of Health, Promoting early diagnosis of breast, bowel and lung cancers: First report 2010/11 local projects. 2012[11]

The table shows that, from 2010 to 2011, the intervention area recorded a greater increase (9%) in total 2WW referrals for suspected lung cancer than the control area (7%). Formally, this represents only borderline statistical significance (Fisher's test, $p=0.08$) that the number of 2WW referrals increased more in the intervention area than in the control area.

At the PCT level there was strong evidence, on average, of an increase in 2WW referrals for lung cancer during the project period compared with the same period a year earlier (paired t-test $p=0.006$). Twenty-four of the PCT projects saw an increase in the number of 2WW referrals for suspected lung cancer (ranging from 2% to 44% more referrals); 10 projects saw a decrease (ranging from 2% to 17% fewer) and three projects saw no change.

The report also provides information on the absolute number of individuals diagnosed with lung cancer after coming through the 2WW for suspected lung cancer (Table 2).

Table 2: impact of the campaign on lung cancers diagnosed

	January to July 2010	January to July 2011	Percent change
Control area (73 PCTs)	2,560	2,593	+1%
Intervention area (76 PCTs)	2,895	2,985	+4%

Source: Department of Health, Promoting early diagnosis of breast, bowel and lung cancers: First report 2010/11 local projects. 2012[11]

While the percentage change was larger in the intervention group (4%) compared with the control (1%), this difference does not reach statistical significance (Fisher's test, $p=0.43$).

Similarly, at PCT level, there was no evidence of a statistically significant change in the total number of lung cancer diagnoses coming through 2WW referrals in the intervention areas (paired t-test, $p=0.56$). Eight of the projects saw an increase in numbers (ranging from a 2% to 111% increase) and ten saw a decrease (ranging from a 3% to 31% decrease), but many of these projects suffered from a very low number of cases suggesting limited statistical power.

Some PCTs, such as Cumbria and Halton and St Helens, experienced a significant increase in the number of individuals being diagnosed with lung cancer following 2WW (61% and 40% increase, respectively). However, these PCTs had a relatively small increase in the number of 2WW referrals for suspected lung cancer over the same period (6% and 9%, respectively).

Overall, the report on the promotion of early diagnosis of lung cancer in the 'NAEDI local projects' failed to show important and statistically significant results when comparing absolute outcomes for the PCTs that implemented an intervention and control PCTs. There are a number of possible reasons for this including significant differences in the approaches taken amongst PCTs in terms of the intervention and the population selected. This means any method of simple combination of the numbers of referrals and diagnosis in each PCT (that are also likely to represent very different populations) is likely to be misleading.

3.3. Early Lung Cancer Identification in Doncaster, ELCiD

ELCiD ran for 6 weeks from March 2008 in Doncaster after being commissioned by the Public Health Department of the local PCT. The campaign was aimed at men aged over 50 years (and their family members) who had ever smoked and/or worked in heavy industry.[10] The primary endpoints of the study were: self-reported awareness of lung cancer symptoms, intention to seek healthcare for lung cancer symptoms, chest x-ray referral rates in primary care, new lung cancers diagnosed and stage at diagnosis. All endpoints were compared before and after the intervention.

The campaign consisted of two interventions aimed at creating a 'push-pull' approach. The 'push' intervention focussed on raising awareness of the importance of seeing a GP and requesting a chest x-ray with the presence of a persistent cough for 3 weeks or more. A corresponding set of 'pull' interventions were implemented to facilitate health care professionals in supporting and reacting to any increase in GP visits and requests for chest x-rays.

An important feature of the campaign which separates it from others is that no mention was made of the association of persistent coughing with lung cancer in the media strategies used to raise awareness. The impact of the campaign was assessed by a telephone survey of 801 members of the general public before the intervention and 800 after. In addition, chest x-ray data were retrospectively collected from Doncaster Royal Infirmary, recording the number of chest x-rays requested by the priority practices over the 6 weeks before and after the intervention. Doncaster PCT has been recording all cases of lung cancer since 1998 so there was an existing standard of data collection for lung cancer diagnosis.

The outcomes of interest included the self-reported likelihood of visiting the GP with a bad cough and requesting an x-ray, the number and rate of lung cancers diagnosed by stage and the number and rate of chest x-rays requested.

The telephone survey achieved an overall response rate of 76%, with the post-campaign survey indicating that 21% of individuals recalled something about the campaign. Their analysis[10] suggests a small increase in the intervention area in people who indicated they would visit their GP for a persistent cough. The odds ratio of a responder in the intervention group saying that they

would visit for a persistent cough and request a chest x-ray was 1.97 (95% CI 1.18 to 3.31 p=0.01) compared with the control.

In addition, the number of chest x-ray referrals across Doncaster (in both targeted and non-targeted practices) increased by 22% (19% for non-targeted and 27% for targeted), in the six weeks after the campaign compared with the six weeks before. In addition, in the year following the intervention, there continued to be an increase in the number of chest x-ray referrals: 20% increase in the intervention area compared with a 2% decrease in the control area. Importantly, a strong relationship was observed between campaign recall, shifts in attitude and the number of chest x-rays requested.

In terms of lung cancers diagnosed, an increase of 27% was observed in the intervention area when compared with the year prior to the campaign, but fell in the control area by 10%. However, the change in diagnosis rates over time between the intervention and control areas did not reach statistical significance, with an incidence rate ratio of 1.42 (95% CI 0.83 to 2.43, p=0.199). In addition no significant stage shift was found at any of the three time periods considered after the intervention (3 months, 6 months or 1 year).

3.4. Leeds Cancer Early Awareness Project, LEDLCC

To date, no publications are available from the Leeds Cancer Early Awareness Project. However, personal communication with Dr Matthew Callister (Consultant Respiratory Physician, Leeds Teaching Hospital NHS Trust) has provided insight into the campaign as well as access to some initial findings.

The Leeds Project focussed on three activities: a social marketing campaign, a primary care campaign and the creation of a self-referral chest x-ray facility for patients. The main population of interest was people with haemoptysis or an unexplained or a persistent (for three or more weeks) set of symptoms focussing on cough, breathlessness and chest/shoulder pain.

The self-referral chest x-ray part of the campaign consisted of a set of tick-box questions that would lead patients to self-refer if they were over the age of 50 years, had a cough or other respiratory symptoms for over three weeks and had no previous chest x-rays in the previous three months.

The social marketing campaign also focussed on persistent cough or other chest symptoms for three weeks or more, and made use of community health educators, bus advertising boards, media events, beer mats, flyers, posters and pharmacy bags.

The primary outcome was the number of chest x-rays performed in the respective areas in 2009, 2010 (both representing run-in years) and 2011 (representing the campaign). Secondary outcome measures included: public awareness of symptoms of lung cancer, number of lung cancers diagnosed, proportions of stage I and II cancers, proportion of patients receiving radical treatment (curative surgery or radical/stereotactic radiotherapy) and 1-year survival rates.

Initial findings from the campaign suggest a significant increase in community ordered chest x-rays in 2011 (55% increase from the annual average for 2008-10 when compared to 2011) as well as an

increase in the number of weekly referrals to lung cancer clinics. However, no statistically significant change in diagnosed lung cancer was observed (from a per annum average of 499 cases in 2008-10 to 539 cases in 2011, a non-statistically significant 8% increase). Similarly, there was no discernible change in the stage distribution of diagnosed lung cancers.

An important finding of LEDLCC was a significant shift in the route to diagnosis for lung cancer patients during the intervention period. Overall, a 16% relative reduction (from 33% to 28%) was observed in emergency admissions for patients with symptoms, later diagnosed as lung cancer. This was combined with a significant increase in route to diagnosis through a fast-track lung cancer outpatient clinic (24% relative increase). In addition, a reduction in bed days associated with lung cancer patients was observed (636 fewer bed days in 2011 compared to 2008-2010 associated with emergency diagnoses despite 8% more lung cancer diagnoses overall). This reduction in emergency admissions identified by the Leeds Early Lung Cancer Steering Group has resulted in a significant cost saving that may offset some of the costs of the campaign.

3.5. NAEDI pilot and national campaign

The national NAEDI campaign ran from 8th May until 30th June 2012 following a 6-week pilot campaign in the Midlands in October 2011. The results of the full national campaign are not scheduled to be available until Mid-2013; therefore, only the results of the pilot campaign are analysed in this report. The primary endpoints of the pilot campaign related to primary care attendance and referral rates for chest x-ray and chest CT.

Early access was granted to the results of the Midlands pilot by the DH in September 2012. The NAEDI pilot was analysed using data from the lung cancer audit collected by the Health and Social Care Information Centre (HSCIC), which contains data from all trusts in England and Wales.[12] Data were available for 32 trusts within the pilot region (the 'NAEDI trusts') and 141 trusts outside the pilot region (the 'non-NAEDI trusts'). Data provided by HSCIC on relevant indicators were aggregated across October to December 2011 and compared to the same period in the previous year in both NAEDI and non-NAEDI trusts in order to evaluate the impact of the regional campaign. A range of outcomes was considered:

1. Lung cancers diagnosed (excluding mesothelioma)
2. Cell type
3. Age band of diagnosed patients
4. Stage of diagnosed disease (both SCLC and NSCLC)
5. Performance status
6. First definitive treatment
7. Source of referral for further investigation

A number of positive results emerged from the NAEDI pilot. For this report, the primary indicators of interest were the number of lung cancers diagnosed and the stage of diagnosis. The NAEDI trusts saw a 14.0% increase in the number of lung cancer cases diagnosed during the intervention period compared with a 4.7% increase in the non-NAEDI trusts. For NSCLC, the figures were even more

significant with a 15.6% increase in lung cancers diagnosed in the NAEDI trusts compared with a 4.1% increase in the non-NAEDI trusts.

The campaign found a trend of borderline statistical significance ($p=0.06$) towards patients with NSCLC in the NAEDI trusts having a lower stage at diagnosis than those in the non-NAEDI trusts, suggesting that patients in the NAEDI trusts were clinically identified earlier in the progression of the disease. Table 3 provides the staging data for NSCLC diagnosis in NAEDI and non-NAEDI trusts.

Table 3: Staging data for NSCLC

Stage	NAEDI Trusts		Non NAEDI Trusts	
	Oct-Dec 2010	Oct-Dec 2011	Oct-Dec 2010	Oct-Dec 2011
I & II	231 (22.3%)	318 (24.6%)	922 (23.2%)	1038 (23.4%)
IIIA	107 (10.3%)	163 (12.6%)	539 (13.5%)	599 (13.5%)
IIIB & IV	698 (67.4%)	813 (62.8%)	2521 (63.3%)	2801 (63.1%)
Total (I-IV)	1036 (100.0%)	1294 (100.0%)	3982 (100.0%)	4438 (100.0%)

Source: *Be Clear on Cancer, Lung regional pilot – cancers diagnosed and staging (draft). 2012.*[12]

Overall, the results from the pilot campaign are very positive compared with the local NAEDI projects, particularly since much larger numbers of patients were available for analysis, but the precision of some of the intervention effects is relatively limited and the data are not yet complete.

4. Modelling methods

4.1. Overview of existing models in lung cancer

A review of the literature was conducted to identify any previously published studies which modelled the impact of early awareness campaigns in lung cancer or the natural history of the disease. Three reports were identified of relevance: (1) Black *et al.*[13] on the clinical effectiveness and cost-effectiveness of computed tomography screening for lung cancer; (2) the economic modelling project by Frontier Economics on the impact of early diagnosis of cancer on costs and benefits to the NHS;[14] and (3) the modelling approaches by the Cancer Intervention and Surveillance Modelling Network (CISNET) for lung cancer.[15-18] These reports are briefly summarised below.

Black *et al.* The clinical effectiveness and cost-effectiveness of computed tomography screening for lung cancer: systematic reviews[13]

Black *et al.*[13] examines the clinical effectiveness and cost-effectiveness of screening for lung cancer using computed tomography (CT). Although the focus of their report is on screening of lung cancer rather than early awareness interventions, the importance of gaining a full understanding of the natural history of the disease is highlighted, as well as the evidential and data requirements needed for constructing a screening and treatment model for lung cancer. In particular, they note the serious deficiencies in the type and quality of information available from UK sources for this purpose. They conclude that “it is not currently possible to perform a rigorous analysis that could yield useful information to inform decision-making in this important area of public policy” ([13] p.39). The three principal factors leading to this conclusion are:

- Lack of high quality direct evidence of the benefit of screening for lung cancer in terms of extension of life
- High risk of harm related to extensive numbers of false-positive detections
- Currently weak understanding of the origin and development of cancerous lesions amenable to screening

In addition, Black *et al* highlight that the process by which cancerous lesions arise, develop and progress into symptomatic lung cancer is not well understood or described in the literature. In particular, the view that cancerous cells grow exponentially may not be correct (a view concordant with that of Bach[19]). They also discuss the major limitation that any form of human study to directly identify and inform the missing transitions between disease states of a natural history model in lung cancer would be unethical as it would involve withholding treatment from diagnosed patients.

Economic Modelling Project by Frontier Economics[14]

In 2011 Frontier Economics presented a report to the Department of Health on the likely impact of early diagnosis of cancer on costs and benefits to the NHS for five selected cancers (breast, colorectal, lung, prostate and melanoma).

A subsequent unpublished review of the modelling approach taken by Frontier Economics by EEPRU found a range of issues surrounding the modelling approach taken as well as its execution. The main

areas of concern were the absence of a natural history model involving transitions between preclinical and clinical states and the lack of reliable evidence for populating the 'stage-shift' approach used.

More specifically, for the lung cancer model, no consideration was made about the size of the preclinical population (i.e. the incidence of lung cancer in the population that is undiagnosed). This is important as it represents the population of interest for any early awareness campaign that seeks to encourage patients with signs and symptoms potentially indicative of lung cancer to visit their GP. The Frontier economic modelling approach assumes a linear relationship between the number of x-rays performed in the population and the number of lung cancers detected in a population.

In addition, the lung cancer model is based on a set of 'time to progression' parameters instead of a full natural history model. In the absence of suitable data for lung cancer, the model assumes the same expected durations as colorectal cancer. Consequently, the expected development of lung cancer and colorectal cancer are assumed to be identical.

In addition to the assumptions discussed above, Frontier Economics followed a 'stage shift' approach to modelling early awareness interventions. A stage shift model places the focus of the economic evaluation on the current distribution of cancer severity, which is usually measured using the TNM staging criteria condensed into five stages (I, II, IIIa, IIIb and IV). Such a model seeks to evaluate the impact of an intervention (for example, an early awareness campaign) on the stage distribution of clinically identified cancers, and to consider the resulting gains in survival and impact on associated costs. Connor et al.[20] highlights the three main considerations of a stage shift model with reference to the introduction of a screening intervention in lung cancer, these points are transferable to an early awareness campaign:

1. Some cancers are detected at an earlier stage than their usual stage, representing an external shift to a lower stage.
2. Some cancers are detected at their usual stage but at an earlier time, known as an internal shift.
3. Some cancers are not detected earlier as a result of the screening and hence are detected at the same time as without screening.

These three points help to identify the underlying assumptions of a stage shift model, including:

- there is no consideration for lead and length time bias;
- all patients can be diagnosed earlier and receive the corresponding benefits.

These assumptions risk introducing significant biases into the model and, as a result, may lead to unreliable estimates of the impact of an early awareness campaign. While efforts may be made to adjust for these biases, the underlying structure of the stage shift model limits the robustness of any economic model to represent the progression of lung cancer, and therefore to predict accurately the impact of an intervention.

CISNET's Lung Cancer Policy Model (LCPM) and calibration

The Cancer Intervention and Surveillance Modelling Network (CISNET) at the US National Institute of Health has constructed a patient level simulation of the natural history of lung cancer, which models the development and growth of tumours. This model is known as the Lung Cancer Policy Model (LCPM).[15, 18] While a significant literature exists providing a broad overview of the LCPM and its role in policy making in the US,[21] there is little information about the core structure of the model. Along with these published papers and personal communication with Pamela McMahon¹, it is understood that the LCPM is a natural history model structured around calibration of existing US data (for example, from sources such as Surveillance, Epidemiology and End Results (SEER) and the Mayo Clinic). Unfortunately, it was not possible directly to inform policy in the UK based on this model for several reasons:

1. the model focuses on screening interventions and attempts to optimise policy decisions for screening
2. It is based on specific US data, which may not be generalisable to the UK setting

As a result, a *de-novo* economic model is developed to fully assess the impact of an early awareness campaign for lung cancer in the UK.

4.2. Natural history model and calibration

The review outlined in Section 4.1 demonstrates that the most suitable approach for modelling the impact of an early awareness campaign in lung cancer is to construct a natural history model involving transitions between pre-clinical and clinical disease states, and to use calibration methods to estimate the transitions which are unobservable.

Overview of natural history model

A natural history model of lung cancer is developed with a simple structure. A simple structure is justified given the limited data in lung cancer, a general lack of understanding about the growth of cancerous cells, and to maximise the accuracy of any calibration approach used to estimate unobservable parameters.

The schematic of the structure of the natural history model is shown in Figure 1. It is primarily made up of four major health states: no disease (specifically no lung cancer), pre-clinical lung cancer (before diagnosis), clinical lung cancer and mortality. In the schematic the solid black lines represent transitions which can be estimated directly from available data. Dashed grey lines represent transitions which are estimated using calibration techniques as these transitions are unobservable in practice. The model represents a cohort model with the entire cohort starting in the no disease state. The cycle length is one month, after which the patient can either transit to a new disease state or remain in the same disease state. One month was considered appropriate to model the potentially fast development of lung cancer.

¹ The lead author on the majority of relevant papers relating to the LCPM [14,15,17]

There are two states for each cancer stage: pre-clinical and clinical. It was decided² that a three stage description of lung cancer provided the most accurate description of the development of the disease without creating excessive complexity to the model. The three stage description represents what is commonly referred to as 'limited', 'advanced' and 'extensive' disease. For the aggregated TNM staging system these are assumed to represent stages I and II in limited disease, stage IIIa in advanced disease and stages IIIb and IV in extensive disease.

Individuals start in the no disease state and can either stay disease-free or progress to pre-clinical lung cancer stages I or II (stage I and II state). From the pre-clinical states it is possible to transit from an earlier stage to any of the more severe stages of disease. The model permits patients to transit from the limited stages of disease (stages I and II) to extensive (stages IIIb and IV) in a single cycle of the model (i.e. within one month). This was considered necessary due to some cancers being observed to develop to the advanced stages of disease very rapidly. This view was expressed by our clinical advisors as well as by Bach (2008).[19]

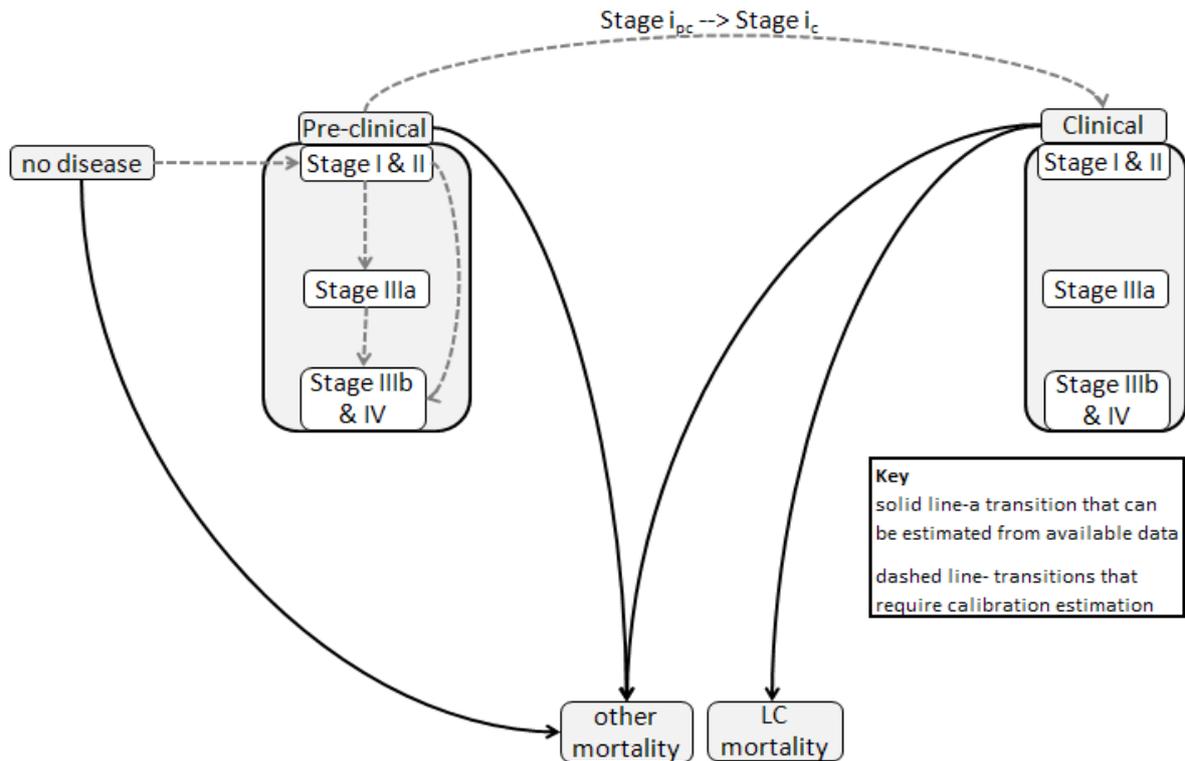
It is possible to be clinically identified from any of the pre-clinical stages of disease. When this occurs, the individual will transit from the pre-clinical stage of disease to the equivalent stage in the clinical state. As this report is concerned with the impact of an early awareness campaign in lung cancer, once individuals are clinically identified the further progression of cancer through clinical stages is not explicitly modelled. However, the impact on costs and HRQoL is incorporated for the remainder of the individual's period of illness.

Individuals in the modelled disease states also face an elevated risk of death. This mortality risk has been split into lung cancer-related deaths and 'other' deaths as shown in Figure 1. All individuals are subject to mortality risk from factors other than lung cancer. Lung cancer mortality is assumed to occur only in the clinical lung cancer stages, under the assumption that all patients would be diagnosed with lung cancer before death. There is currently no evidence available to support this assumption³; however, lung cancer is strongly associated with a range of symptoms which typically become progressively worse and clinical identification is most likely to occur before death. Our clinical advisors indicated that it was not unknown for lung cancer to be diagnosed at post-mortem without clinical identification; however, they agreed that the incidence of this was relatively rare (estimated to be less than 5% of the total incidence).

Figure 1: Schematic of the natural history model

² With clinical input and to represent a consistent approach with the NAEDI UK pilot that will inform the intervention's modelled impact, see Section 3.2

³ This would require an analysis of the specific cause of death in all potential pre-clinical lung cancer cases, and while some data are available from LUCADA about lung cancers diagnosed at post-mortem, these were not considered sufficient to inform the model



Modelled population

The population of interest is the English population over the age of 30 years since lung cancer only very rarely affects those under this age.[22]

The link between smoking and lung cancer has been well established in the literature.[22, 23] However, focussing on this sub-population was deemed to be inappropriate due to issues around the available data as well as the definition of the relevant sub-populations. Therefore, the analysis focuses only on an aggregated population regardless of their smoking characteristics. It is important to note that this approach is not assuming that smoking does not impact on the natural history model. Rather, the typical/average individual is considered in the model and this implicitly takes account of the size of the smoking population and its associated increase lung cancer risk.

Calibration

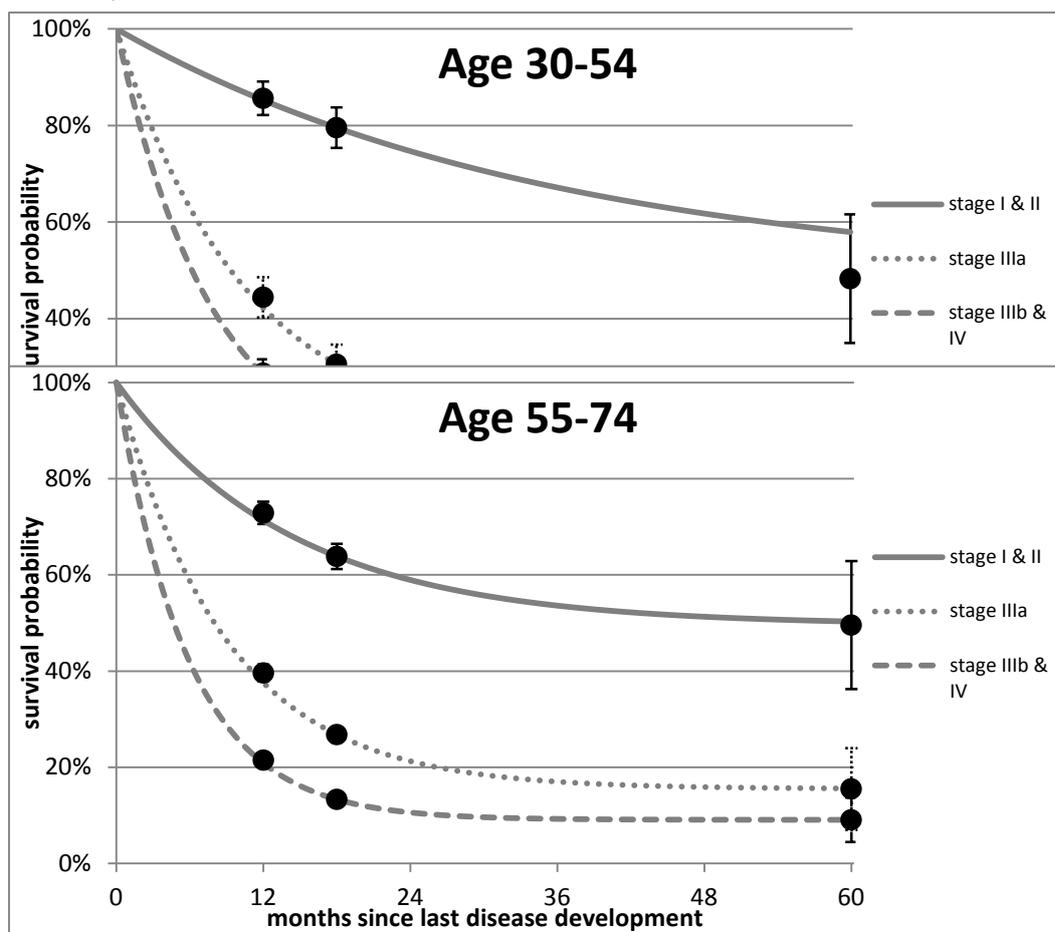
In principle a natural history model would be informed by a set of observed transition probabilities estimated from relevant clinical studies. However, in the absence of observable data, calibration methods can be used to inform transitions. The underlying challenge in a natural history model of lung cancer is the requirement to understand the pre-clinical stages of disease, but it is not possible to conduct clinical trials to observe the impact and development of pre-clinical conditions.[13]

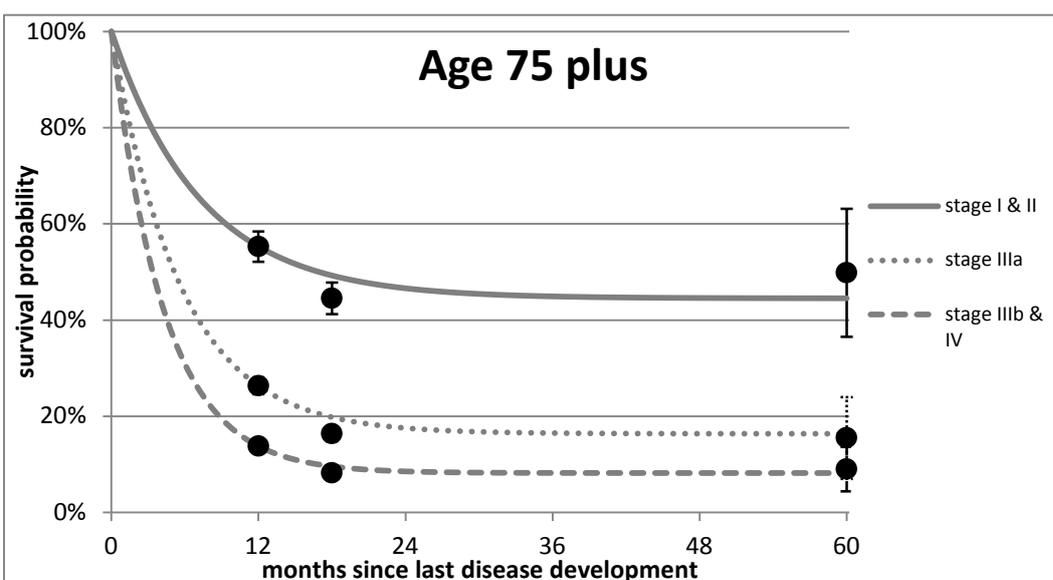
Methods of calibration seek to make use of all available evidence relevant to the disease. This can include expert opinion as a source of 'prior' information, which can be updated using Bayesian statistical methods, or observable data on the prevalence or incidence of cancer, together with a prior expectation about the structure of the natural history of the disease. The use of calibration techniques in the context of cancer modelling has been developed recently in colorectal cancer by Whyte *et al.* [5, 24-26] The approach used in this report follows that of Whyte *et al.*, [24] where the technical details are discussed in full.

Mortality data

Mortality from lung cancer and other causes represents the only set of transitions in the natural history model that can be observed using existing data. Data on lung cancer survival was provided by the International Cancer Benchmarking Partnership (ICBP) and represents an estimate of net survival from lung cancer for the United Kingdom. The ICBP estimates survival probabilities at 12 and 18 months for the various stages of disease and for three different age groups (30-54, 55-75 and 75+ years). In addition, expected long term survival by stage was considered based on Cancer Research UK's five year survival data. [27] These data were not available by age, however, so the confidence intervals for each stage of disease presented in Figures 2, 3 and 4 were assumed to be representative of the age at diagnosis with higher survival assumed indicative of the younger age group. Fitting exponential survival curves to these survival data generated the survival curves shown in Figures 2, 3 and 4 which were used in the model.

Figures 2, 3 and 4: Expected lung cancer survival probabilities over time and the three observed data points with corresponding confidence intervals for different patient age groups (30 to 54, 55 to 74 and 75+ years)





Data on other-cause mortality were taken from Interim Life Tables for 2008-10 for England, from the Office for National Statistics,[28] and adjusted to remove mortality from lung cancer for each age group represented.

Incidence of lung cancer

The incidence of lung cancer in England is available from LUCADA, a dataset including approximately 93%[8] of the expected number of new lung cancer cases in England, Wales and Northern Ireland. The audit collects data on a range of characteristics including stage of cancer, age at clinical identification, treatment received and method of identification.

The NHS Information Centre (IC) provided data on the incidence and stage distribution of NSCLC in England for the year 2010. Data were provided by seven stage classification at diagnosis (stage IA, IB, IIA, IIB, IIIA, IIIB and IV), with all diagnoses presented in a range of age groups (30-54, 55-59, 60-64, 65-69, 70-74, 75-79, 80-84 and 85+ years). In the model, cancer incidence by stage represents the number of patients in England who move from a pre-clinical stage to the corresponding clinical stage of disease.

Informed priors for unobservable data

The model uses a Bayesian approach to calibration, the Metropolis-Hastings algorithm, to estimate transition probabilities which are unobservable.[24] If the model predictions are ‘close’ to the observed data (for example, the incidence of lung cancer), then the parameter set usually represents a good fit. The Bayesian approach allows prior information ('priors'; for example, from expert opinion) about the unobservable data to be updated in the form of a predicted posterior distribution for the parameter of interest. When calibrating a natural history model it is possible to rely on uninformative priors (zero information) about the parameters, but this often results in a ‘poor’ fit to the observed data. A limitation of the model is the lack of any available data on the natural history of lung cancer, with only observed data available on incidence of clinically diagnosed lung cancer from LUCADA. Therefore, expert opinion from clinical advisors was used to provide informed priors for the unobservable parameters, which were subsequently updated in the model. The priors are used to inform the calibration method but they do not act to limit the value that any parameter can take.

Table 4 shows the expected mean values of the priors based on clinical experience, as well as 90% confidence intervals, for the set of unobservable parameters. Any parameter that could not be described with prior information (for example, the transition from no disease to disease stages I and II) was given an uninformative prior (flat distribution giving no information).

Table 4: Priors provided by clinical advisors on natural history transitions

Parameter		Expected monthly transition probability	Confidence interval on same scale
Preclinical development of disease	Stage I & II to IIIa	0.10	0.05-0.7
	Stage I & II to IIIb & IV	0.05	0.03-1.0
	Stage IIIa to IIIb & IV	0.2	0.1-1.0
Probability of being clinically identified given current NHS practice	Stage I & II	0.15	0.003-0.3
	Stage IIIa	0.2	0.1-0.5
	Stage IIIb & IV	0.2	0.1-0.75

In addition to these priors on individual parameter values, clinical understanding of lung cancer suggests the following assumptions to inform the model:

1. The expected probability of developing lung cancer increases with age.
2. The expected probability of an individual with pre-clinical lung cancer being clinically identified increases with the advancement of cancer stage. This assumption can be justified as the advancement of stage of lung cancer represents a spread/enlargement of the disease that, on average, can be expected to be associated with worsening symptoms and illness that in turn would be expected to increase the likelihood of presenting clinically.

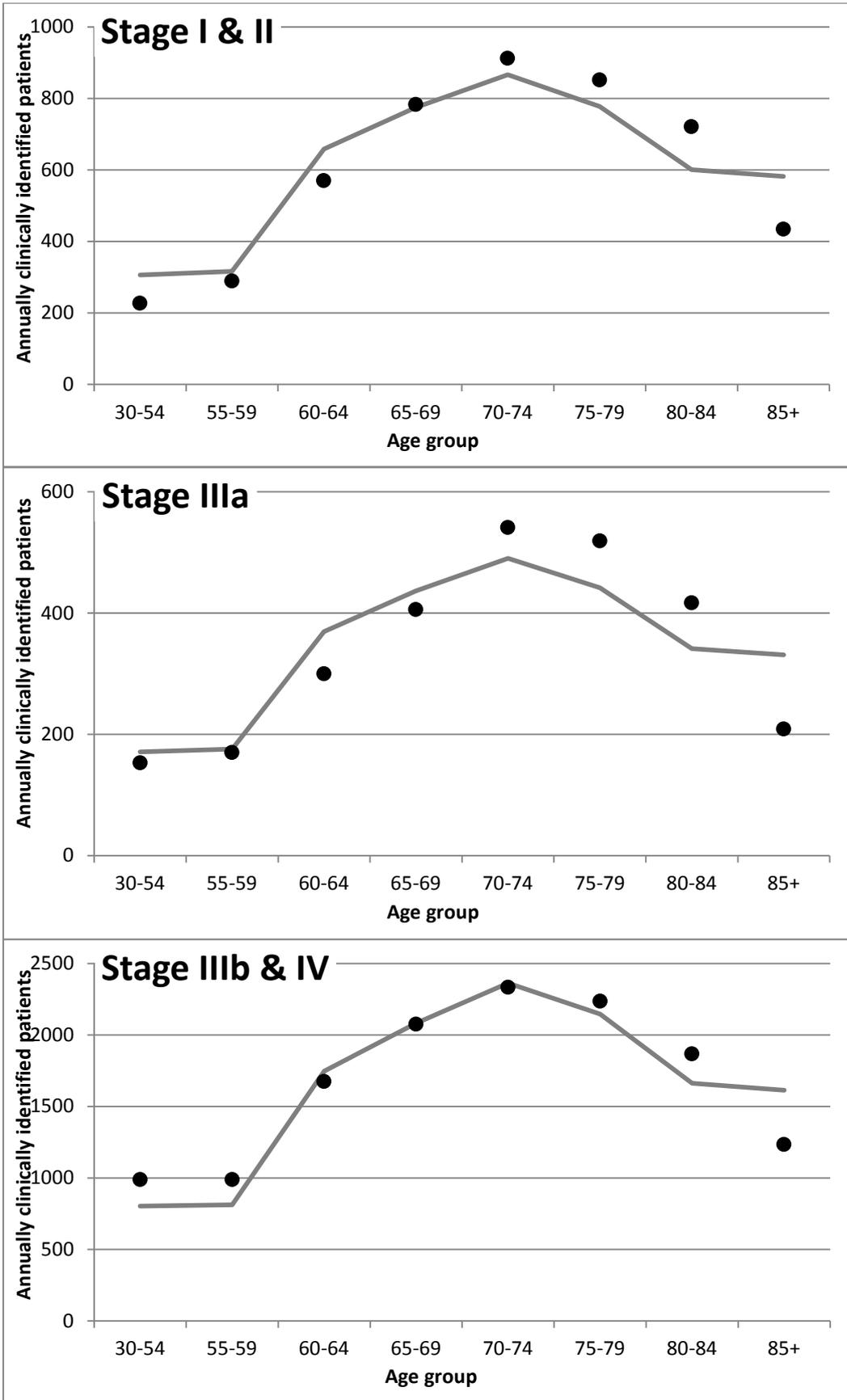
These priors on the transitions were incorporated into the calibration model by subjecting a parameter to an absolute minimum or maximum bound of the current expected probability of the linked parameter. For example, at no point can the model consider a set of parameters in the calibration algorithm whereby the expected probability of clinical identification at stage I and II is greater than that of stage IIIa.

Model calibration results

Model fit

Figures 5, 6 and 7 show how well the set of 'best' fitting parameters, determined by calibration methods, fit the observed data on annual incidence of clinical lung cancer (the number of people diagnosed in a year with NSCLC) in England, for each of the three disease states over a range of age groups. The dots represent the observed incidence data from LUCADA and the lines represent the model predictions.

Figures 5, 6 and 7: graphical representation of the model fit



The figures suggest that the model predictions fit the observed data relatively well. However, in the age group 85+ years, it is clear that, while the model predicts a decrease in the absolute number of

incident clinical cases of lung cancer for all stages, it does not match the observed decrease. This is believed to be due to a lack of flexibility in the model structure in accounting for the increase in the probability of the initial growth of pre-clinical lung cancer in this oldest age group. This may result in an overestimation of the cost-effectiveness of the early awareness campaign due to an overestimate of the effected population size.

Model predictions

In addition to estimating the incidence of clinically identified NSCLC, the model provides an estimate of the annual development of all new pre-clinical NSCLCs in England. Due to the structure of the natural history model, these represent the annual incidence of pre-clinical lung cancers at stages I and II. Table 5 shows how many new NSCLCs the model predicts in previously healthy patients in a year in England, as well as the percentage of the English population that this represents. As shown in Figures 5, 6 and 7, the model does not predict well the incidence of clinical lung cancer in the age group 85+ years and, therefore, this is excluded from the following analyses.

Table 5: Estimated annual incidence of new (pre-clinical) NSCLC in England

Age group	In English population	Proportion
30-54	2,020	0.01%
55-59	2,228	0.07%
60-64	3,710	0.12%
65-69	3,758	0.15%
70-74	3,425	0.17%
75-79	2,423	0.15%
80-84	1,438	0.11%

As far as possible it is important to validate the estimated outputs from the calibration process. Although this is difficult given that the data is unobservable, a quick face validity check suggests that the estimates are not unreasonable: the incidence of clinically diagnosed NSCLC in England is 20,895 from LUCADA, while the model predicts about 19,739 people in England develop stage I or II pre-clinical NSCLC annually. Clearly to maintain face validity we would not expect the annual incidence of clinically diagnosed lung cancer to significantly exceed the annual incidence of new (pre-clinical) lung cancers, as a result their relative similarity suggests a degree of face validity.

It is also possible to estimate the prevalence (the number of people with disease at a given time) of each pre-clinical stage of NSCLC. Table 6 shows the estimates of pre-clinical NSCLC by stage and age for England, again excluding the 85 and over age group.

Table 6: Prevalence of pre-clinical NSCLC in England

Age group	English prevalence			Percentage of population		
	Stage I & II	Stage IIIa	Stage IIIb & IV	Stage I & II	Stage IIIa	Stage IIIb & IV
30-54	5,314	79	284	0.03%	0.00%	0.00%
55-59	5,509	81	288	0.19%	0.00%	0.01%
60-64	11,401	170	615	0.36%	0.01%	0.02%
65-69	13,368	200	731	0.55%	0.01%	0.03%
70-74	14,892	224	826	0.73%	0.01%	0.04%
75-79	13,318	201	747	0.80%	0.01%	0.04%
80-84	10,258	155	577	0.82%	0.01%	0.05%

Table 6 indicates that the model predicts a relatively high prevalence of stage I and II lung cancers in England. The prevalence of Stage IIIa appears low relative to the incident population; however, as Figure 8 below shows, the probability of transiting from the Stage IIIa state is high so people do not spend long in this state resulting in a relatively low level of prevalence.

The other parameters calibrated by the model are based on the progression of pre-clinical lung cancer once it has developed. These can be viewed as either a probability of the disease getting worse or a probability of being clinically identified. The schematic in Figure 8 shows the predicted monthly probability of a patient transiting to the next disease stage either to a more severe pre-clinical stage or to a clinically identified one.

Figure 8: Schematic showing the probability of monthly development between each disease state



Again, it is difficult to establish the validity of these estimates; however, it is possible to consider the associated implications:

1. The probability of transiting from stages I and II to any other stage is very low. This corresponds to the large estimated population of stage I and II pre-clinical patients shown in Table 6. Not only do they have a very low probability of clinical identification (0.49%) but also a low probability of transiting to stages IIIb & IV (0.68% per month) or to stage IIIa (0.94% per month). This suggests that while the model predicts a significant prevalent population with stage I or II pre-clinical lung cancer, their disease is relatively stable and they face a very small risk of it progressing (a combined monthly probability of 2.11%).
2. The probability of transiting from stage IIIa to stages IIIb & IV is high at 44% per month. This may be consistent with the clinical observation that some NSCLCs progress very quickly and, once disease spreads beyond stages I & II, it progresses very rapidly.

From these two observations, the natural history model suggests that there are some individuals who experience very rapid progression of their stage I or II disease to late-stage disease, and others whose disease progresses very slowly or not at all. This finding is consistent with the argument made by Bach[19] that empirical findings suggest that early stage cancer is not necessarily a pre-cursor of advanced cancer.

Uncertainty

It is important to consider uncertainty in the structure of the model, as well as that associated with the estimated parameters. In a 'traditional' natural history model (i.e. one that does not require calibration but makes use of directly observable or elicited parameter values) it is possible to define a probability distribution for each parameter to represent its uncertainty. Monte Carlo simulation methods would be used to obtain probabilistic draws from each parameter to inform overall decision uncertainty. Whyte *et al.*[24] show that parameter uncertainty can be represented in model calibration using the Metropolis Hastings algorithm by considering different parameter sets which are able to match observed data.

The natural history model of lung cancer largely consists of estimates of unobservable parameters. While the analysis estimates the parameter set that is most likely correctly to represent the natural history transitions, there is still a chance that these are not correct. The limited data available to inform the calibration (only the annual incidence of lung cancer in England) and the unsuitability of data from available screening trials, results in the analysis exhibiting significant uncertainty given the use of limited information to estimate a number of parameters. It is, therefore, of importance to consider future data that could reduce this level of uncertainty.

4.3. Costs and health-related quality of life

Systematic reviews were conducted to obtain estimates of both the costs and HRQoL associated with lung cancer. Full details of the search strategies can be found in Appendix B.

Costs

A systematic review of the literature relating to the costs of lung cancer was conducted using NHS EED. The systematic review identified one published study of relevance, Fleming *et al.*[29] which estimated hospital costs relating to lung cancer in Northern Ireland by analysing the case notes of 724 patients diagnosed in 2001 for 12 months following presentation by cell type and extent of disease (limited, advanced and extensive). Since the natural history model considers three separate severity states (limited stage I and II, advanced stage IIIa, and extensive stage IIIb and IV), the severity groupings reported in Fleming *et al.* were assumed representative. Costs were adjusted for inflation to a 2012 price level (Table 7).

Table 7: Mean costs reported in Fleming *et al.*[29] and adjusted for inflation to 2012 prices

Disease severity	Diagnostic costs		Management/treatment costs	
	2001 prices	2012 prices	2001 prices	2012 prices
Stage I and II	£805	£1,035	£6,141	£7,889
Stage IIIa	£814	£1,046	£5,727	£7,358
Stage IIIb and IV	£709	£911	£5,158	£4,954

The use of these costs to inform the analysis assumes that the costs associated with the diagnosis and management of lung cancer in Northern Ireland are generalisable to the English NHS. It is also assumed that the costs of managing a clinically identified lung cancer patient are fully reflected in this 12 months of hospital care.

In addition to the costs of increased diagnosis and treatment, it is important to consider the cost of the campaign itself. The results from the NAEDI full national campaign are used for this purpose. Personal communication with the Department of Health generates a cost estimate for an England-wide NAEDI campaign of £2.9million.

Health Related Quality of Life

The systematic review of literature on HRQoL associated with lung cancer identified 231 papers, an analysis of the titles found 35 to be of relevance, a number reduced to 21 after consideration of the papers' abstracts. These papers were accessed to determine any suitable for the analysis using the following criteria: Meta-analysis of the HRQoL impact of lung cancer

1. Sufficient number of patients for precise estimates
2. Results by stage of lung cancer
3. Suitable age range of individuals surveyed

4. Results independent of treatment received

Only one of the 21 papers was deemed to be suitable, that of Sturza 2010.[30] This HRQoL meta-analysis is used to derive the HRQoL weights presented in Table 8.

Table 8: Health related quality of life estimates used in the model

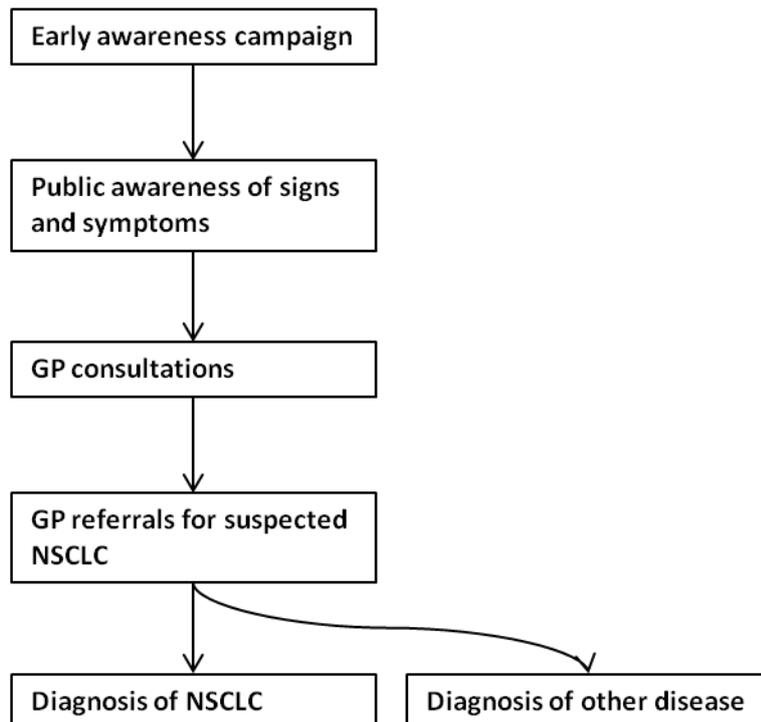
Lung cancer stage	HRQoL weight
Stage I and II	0.825
Stage IIIa	0.772
Stage IIIb and IV	0.573

These HRQoL weights are compared to the age-specific HRQoL weights of the general population from the Health Survey for England[31] to calculate a disease HRQoL decrement for each age. These HRQoL decrements are applied for five years after initial clinical identification. All patients who are long term survivors of the disease (i.e. beyond five years) are assumed to return to the HRQoL level of the general population at that age.

4.4. Modelling the effects of an early awareness campaign

As was outlined in Section 3 there is a range of information available on the impact of early awareness interventions in lung cancer in England. To frame the impact of any early awareness campaign it is useful to consider the schematic in Figure 9 which shows the potential mechanisms by which any campaign can act on the population of interest.

Figure 9: Schematic representing the impact of an of early awareness programme



The model should, therefore, reflect the following:

1. Change in the probability of clinical diagnosis for NSCLC by stage.
2. Change in the number of GP consultations and chest x-rays ordered as a result of the campaign. No data are reported on this from the NAEDI pilot so it is excluded from the base case analysis but considered in scenario analysis in terms of changes in the 'worried well' population.
3. Overall cost of the campaign
4. Possible additional impacts such as the route of diagnosis - these are considered in discussion.

As outlined in Section 3, the NAEDI lung regional pilot conducted in October and November 2011 represents the only analysis of early awareness campaigns in lung cancer to identify a significant increase in the total number of NSCLC cases diagnosed. Initial data provides information on a difference in difference analysis on point 1 outlined above, in addition to a consideration of the cost of a national campaign. However, the NAEDI pilot does not record any information on the change in the number of referrals for chest x-rays or GP clinic hours related to lung cancer as a result of the campaign.

The impact of any campaign to increase the awareness of the symptoms of lung cancer and to encourage patients to visit their GP can be considered in two parts:

1. An initial increase in the incidence of all lung cancers
2. A longer term shift in the stage distribution of cancers diagnosed

The best way of considering these two parts is by framing them around the natural history model described in Figure 1. When an early awareness campaign begins there will be an increase in the probability of clinical identification as people become more aware of the symptoms related to lung cancer and more likely to visit their GP. At the outset of the campaign there will be a relatively large underlying pre-clinical prevalent population, so the increased probability results in a pronounced increase in clinical identification. However, once this initial 'blip' in increased clinical identification has occurred, it would be expected that a shift in the stage distribution of the diagnosis of disease would occur as individuals with early pre-clinical lung cancer are more likely to be clinically identified. This would result in the desired movement in the stage of clinical identification. The base case analysis, therefore, acts to 'smooth out' the initial observed 'blip' in clinical identification from the NAEDI pilot as sufficient data were not available to exclude the run in period of the campaign.

The base case, therefore, makes the assumption that, in the long term, any such campaign would not increase the overall incidence of lung cancer diagnosis but only affect the stage at which disease is diagnosed, i.e. there would be a change in the distribution of stage at the time of clinical identification without an increase in clinically identified lung cancer. In addition, the base-case assumes that the impact is continued throughout the intervention period and any improvements in the probability of clinical identification are lost once the intervention period finishes.

The model focuses on any observed change in the distribution of stage at diagnosis in the available data. This is because, in terms of potential health gain, the primary aim of any early awareness campaign is to create a long term stage shift in the stage of cancer diagnosis, as patients who are diagnosed earlier have a reduced chance of developing late stage disease and, therefore, an improved chance of survival. In contrast, an intervention that only acts to increase the short term

incidence of diagnosis in the population will have a relatively small impact on overall health as patients have already developed advanced stage disease and are, as such, less treatable.

A three month intervention period is considered to provide consistency with the data available from the NAEDI pilot. The impact of such an intervention on the underlying natural history of disease is considered and the costs and health related benefits (in terms of quality-adjusted life-years (QALYs)) associated with it are modelled. The impact of a change in the distribution of stage at clinical identification on long term survival is incorporated into the analysis by assuming that, if a patient survives for five years after initial diagnosis, they return to the age specific levels of HRQoL and mortality risk of the general population from that point.

Change in the probability of clinical diagnosis by stage

Table 9 reports the incidence of clinical identification before and during the NAEDI pilot campaign in both the intervention and control areas. It also shows a representation of the change in distribution of the stage at diagnosis as a result of the intervention, and the results of a simple difference in difference analysis to estimate the change in the distribution of stage at the time of clinical identification. The NAEDI report included a significant number of unstaged incident patients, so it is assumed that these represent late stage disease and are included in the stage IIIb and IV disease state.

Table 9: Change in incidence of clinical identification and observed stage shift from the NAEDI pilot

Stage	NAEDI trusts (intervention)		non-NAEDI trusts (control)		Percentage change in relative size of population		
	Oct-Dec 2010	Oct-Dec 2011	Oct-Dec 2010	Oct-Dec 2011	NAEDI trusts	non- NAEDI trusts	Adjusted change
I and II	231	318	922	1038	19%	8%	11%
IIIa	107	163	539	599	32%	7%	25%
IIIb & IV and unstaged	914	966	3156	3166	-9%	-4%	-5%
Total	1252	1447	4617	4803			

The final column of Table 9 shows the estimated change in the relative size of the population at each stage before and after the intervention. The impact of the campaign is 'smoothed out' by weighting the incidence at each stage of disease by the total observed incidence of disease in the intervention or control area to give an underlying change in the stage at clinical identification.

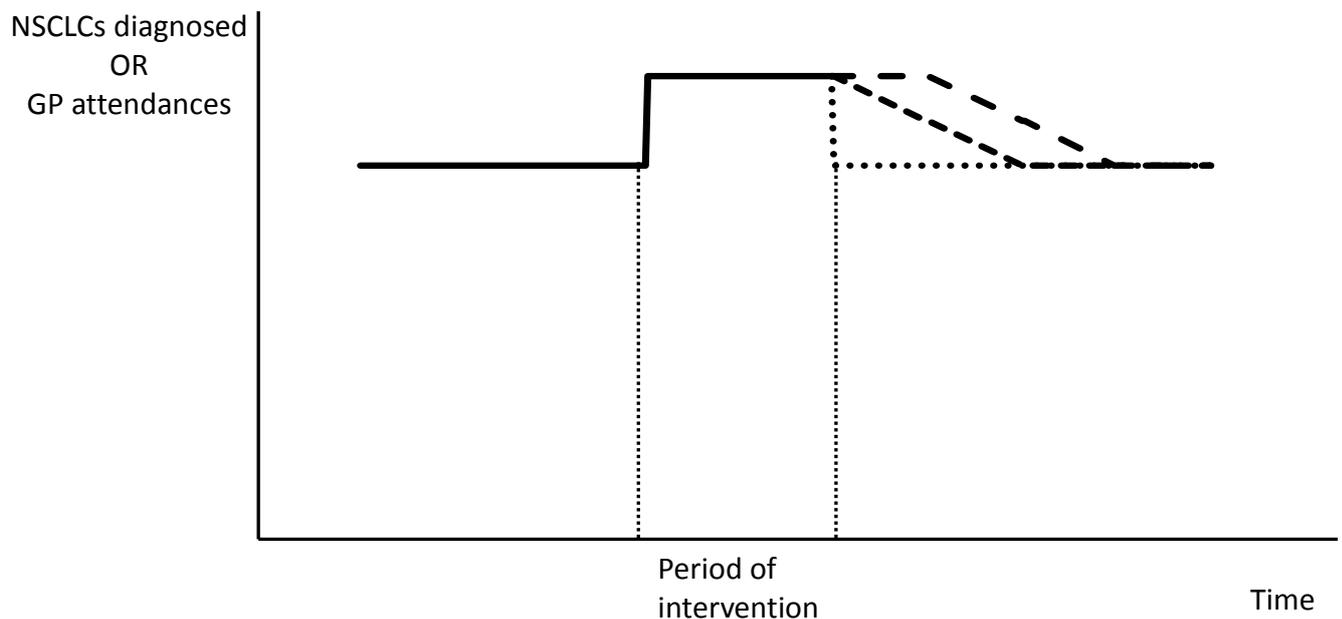
The analysis compares the baseline natural history before the intervention, discussed in Section 4.3, with an altered natural history resulting from a shift away from late stage lung cancer towards early stage induced by the campaign.

Duration of the effect of the campaign

Due to the immaturity of the data being reported from any of the campaigns and a lack of sufficient follow up after the intervention, it is difficult to consider the duration of effect of any early awareness campaign. Data are available from the NAEDI pilot to compare the number of lung cancers diagnosed in October and December 2011 (the period of the intervention) to that of the same period the year before. As a result, as shown in Figure 10, it is not possible to consider the long term effects on individuals' propensity to present with symptoms of lung cancer and, therefore, on the number of lung cancers diagnosed. Three scenarios are possible:

1. The campaign only has an impact on the population for the period of its funding
 - Once the funding stops the propensity to present returns to its pre-intervention levels. This is shown in Figure 10 by the finest dashed line.
2. The campaign has an impact beyond the period of funding but not indefinitely
 - Over a certain period after the intervention the propensity to present returns to pre-intervention periods. This is shown in Figure 10 by the two thicker dashed lines.
3. The campaign has a permanent impact
 - Once the intervention stops the propensity to present stays at its intervention levels. This is not shown in Figure 10.

Figure 10: Alternative scenarios relating to the duration of effect of the campaign



Given this uncertainty in the duration of effect, the base-case analysis assumes that the campaign only has an effect for the period of the intervention. The impact of a 'rebound' in the number of clinically identified patients after the campaign ceases to less than before the campaign was considered implausible and not modelled.

4.5. Cost-effectiveness results

Base-case analysis

The base-case seeks to evaluate the cost-effectiveness of an observed change induced by the campaign in the distribution of cancer stage at clinical identification. The observed change is assumed to occur only for the three months of the intervention. The impact of consequent reductions in mortality risk is calculated for the remainder of patients' life times. The base case analysis does not consider the cost or HRQoL impacts of increases in the 'worried well' population or potential changes in the route of diagnosis. The cost of treatment is assumed to relate to the year after clinical diagnosis.

All costs accrued as a result of lung cancer over the remaining lifetime are considered from an NHS perspective and, together with lifetime QALYs, are discounted at 3.5% per annum in accordance with the NICE Methods Guide.[32]

The application of the costs of the campaign, diagnosis and treatment of lung cancer to the natural history model generated the results shown in Table 10, with all costs scaled up to the English population.

Table 10: Estimated cost impact of the campaign

	Cost of campaign	Cost of diagnoses	Cost of treatment	Total costs
Without campaign	-	£4,999,559	£31,083,815	£36,083,374
During 1 month campaign	£2,900,000	£5,074,439	£32,077,911	£40,052,350
Incremental cost of campaign	£2,900,000	£74,880	£994,097	£3,968,976

Table 10 shows that a 3 month campaign (costing £2,900,000 to run) would result in an estimated increase of £1,068,976 (£74,880+£994,097) in costs associated with increased diagnosis and treatment. Using the HRQoL mortality risk estimates, incremental QALYs resulting from the early awareness campaign are estimated. Since the majority of lung cancer patients die as a direct result of the disease (see Figures 2, 3 and 4) and the probability of long term survival differs significantly between stages, it is important to consider both the short term shifts in HRQoL as a result of improved early diagnosis but also the associated improvement in mortality and, therefore, lifetime QALYs accumulated. The base case analysis estimates the incremental gain in QALYs of a three month national early awareness campaign to be 325 QALYs.

These findings can be combined in the base-case analysis to give an incremental cost-effectiveness ratio (ICER) describing the incremental cost per additional QALY gained. The estimated ICER in the base-case is £12,192 per QALY gained. This ICER can be compared to NICE's threshold range of

£20,000 to £30,000 per QALY.[32] This would suggest that, relative to the current NICE threshold range, a campaign would be cost-effective.

4.6. Scenario analysis

To reflect the uncertainty associated with the assumptions in the base-case, two alternative scenarios are modelled:

1. Size of the 'worried well' population attending their GP and receiving chest x-rays
 - The base-case analysis assumes there is no change in the size of the population visiting their GP with symptoms potentially indicative of lung cancer; this scenario considers the impact of an increase in the size of this group.
2. Route of diagnosis
 - Limited evidence from some of the early awareness campaigns suggests a significant cost saving may arise from people presenting at their GP rather than at an Accident and Emergency department as a result of the campaign. Therefore, a scenario considers the size of the potential cost saving and how it might impact on the cost-effectiveness of the campaign.

The base-case assumes that a three month campaign only impacts the stage of diagnosis for the three months it is funded, but this effect could continue for a longer period. An alternative scenario has not been conducted to explore this further because the base-case assumptions already suggest that a national campaign would be cost effective and such an alternative scenario would simply strengthen this conclusion.

Scenario 1: The impact of any increase in the size of the 'worried well' population

In order to consider the impact of any change in worried well patients, the costs of potential increases in GP attendance and chest x-ray referrals are added to the model. It is assumed that a clinic based consultation by a GP lasts 11.7 minutes and costs £53.00.[33] The unit cost of plain chest x-ray is assumed to be £18.00.[34]

In terms of the change in number of chest x-rays and GP attendances a range of sources of data is considered. Athey *et al.*[10] report changes in the number of x-rays per 100,000 in the control and intervention areas in the Doncaster campaign before and after the campaign. This suggests a 37.5% increase in x-rays ordered (after adjusting for the decrease in the control area this represents an increase from 88 to 121 per 100,000 people). On a similar scale the Leeds campaign saw an increase in community ordered chest x-rays of 56% from one year to the next as a result of the campaign. The Doncaster study does not, however, report the change in GP attendances. Dr. Matthew Callister has provided data from the LEDLCC campaign. These studies give an indication of the possible scale of any change in the worried well population as a result of the campaign. However, it was decided that the significant differences in the approaches and results of these campaigns compared to the NAEDI pilot that informs the base-case cost-effectiveness analysis could make the use of any such data misleading. As an alternative approach a 'threshold analysis' is conducted which considers the

additional cost associated with an increase in the worried well population that would have to be observed to make the campaign no longer cost effective at a threshold of £20,000 per QALY (i.e. what additional cost would change the ICER from £12,192 to £20,000 per QALY gained?).

This additional cost is estimated at £2,541,705 when all other base-case assumptions apply. If it is assumed that a worried well individual visits their GP (at a cost of £53) and receives a chest x-ray (at a cost of £18), it would require an additional 35,799 to be generated by campaign to make the intervention no longer cost-effective. Alternatively, if only every other worried well individual who visits their GP receives a chest x-ray, 40,995 such individuals would be required to visit their GP to move the campaign to not being cost effective.

Scenario 2: The role of the route of diagnosis

The route of symptomatic presentation leading to the diagnosis of lung cancer is another potentially significant cost that is excluded from the base-case analysis. This is important as a patient who presents via emergency admission would be expected to incur significantly higher costs than one who presents via their GP. For this scenario it is assumed that a patient who is diagnosed through their GP has the same long term mortality and HRQoL as one diagnosed through A&E.

The NAEDI pilot found a small but non-significant decrease in the percentage of referrals via the emergency route in the intervention area (15.5% to 13.5%) coupled with a small but significant decrease in the control area (13.6% to 12.1%). These data would suggest that the campaign had no, or a very small, decrease in the percentage of emergency admissions. In contrast, the LEDLCC campaign found no significant increase in the number of lung cancers diagnosed but recorded a statistically significant shift in the route of symptomatic presentation leading to diagnosis. Overall it found a 16% relative reduction in emergency presentations of patients later diagnosed to be lung cancer (an observed reduction of 33% to 28% of all patients), combined with a significant increase in route-to-diagnosis through GPs. In addition, a reduction of 636 bed days associated with lung cancer patients was observed. The cost saving associated with this reduction in bed days (assuming a cost per night of £300) was estimated to be £190,800.

The scenario analysis uses the reported cost per bed day saved of £300 as reported in the LEDLCC campaign to consider how many such bed days would have to be saved to make the campaign cost-saving (in addition to being health improving).

The analysis would require any savings in bed days to offset the additional costs of the campaign, as well as the costs incurred through additional diagnosis and treatment of clinically identified patients, i.e. £3,968,976 as reported earlier in this Section. This would require a national saving in bed days of 13,230 (£3,968,976/£300) as a result of the campaign. Given the saving observed in Leeds as a result of a similar (but less effective) early awareness campaign, it is feasible that this reduction could be observed. However, this simple analysis assumes these patients are identical to those identified at the GP.

5. Discussion

This report investigates the potential impact of a national campaign to improve the early awareness of the signs and symptoms related to NSCLC in England. A set of transition probabilities relating to the natural history of lung cancer has been estimated by considering the development of disease through a set of states of severity as well as through the initial development of the disease. This natural history model was used along with findings from the NAEDI pilot campaign to consider the cost-effectiveness of such a campaign at a national level for a set of base-case assumptions. This analysis found that the campaign would be considered to be cost-effective at NICE cost-effectiveness thresholds, with an ICER of £12,192 per QALY gained. However, the logic of the cost effectiveness threshold is that the NHS would need to displace existing services (outside and/or within oncology) to free-up funding to deliver such a campaign (an estimated cost of £2,900,000 over 3 months).

Significant uncertainty is associated with this estimate. The unobservable nature of the majority of transitions in the natural history model necessitates a calibration approach. An inevitable implication of this approach is the significant difficulty in assessing the validity of the estimated parameters. In addition, there is a lack of suitable data to inform the calibration method, with a reliance on clinical expertise and data collected by the National Lung Cancer Audit (LUCADA).

Additional data could be drawn from lung cancer screening trials because, given estimates of screening accuracy, an estimate of the prevalent population with pre-clinical lung cancer can be made. An investigation was made into the availability of such evidence, but currently available data were considered not to be transferable to the English population. The use of data from the ongoing UKLS[35, 36] alongside those from LUCADA would offer the potential for a significant improvement in the predictive capability of the natural history model.

Not only is there uncertainty in the natural history model but also in the impact of any national early awareness campaign. Section 3 highlighted that a range of early awareness campaigns has been undertaken in England in the last few years, with variable results. The NAEDI pilot in the Midlands was the only study to record a significant change in the distribution of cancer stage. The base-case analysis assumes, therefore, that any national campaign would be able to reproduce the impact of this pilot.

In addition, there is significant potential for an improvement in estimates of the costs associated with the diagnosis and treatment of lung cancer in the English NHS based on routinely collected data. This may be achievable through the use of diagnostic and treatment data routinely collected by LUCADA. As LUCADA routinely collects information on mode of diagnosis of lung cancer, as well as planned treatments, it is possible to analyse such data by age, gender, stage of disease and, in some cases, performance status. Attempts were made to link these data with unit costs and estimates of expected duration of treatment or associated follow up costs. However, it was evident that this required significant understanding of a 'typical' treatment pathway for each of the different treatment categories. With sufficient time and expertise it would be possible to use these data to estimate of the costs of diagnosis and treatment of lung cancer.

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Appendix A: Searches for public awareness programmes in lung cancer

Database/sources searched (December 2011)

1. Medline and Medline in Process & Other Non-Indexed citations (Ovid)
2. Embase (Ovid)
3. Cochrane Database of Systematic Reviews (Cochrane)
4. Cochrane Central Register of Controlled Trials (Cochrane)
5. NHS Health Economic Evaluation Database (Cochrane)
6. Health Technology Assessment Database (Cochrane)
7. Database of Abstracts of Review of Effects (Cochrane)
8. Science Citation Index (Web of Science)
9. Social Science Citation Index (Web of Science)
10. Conference Proceedings index (Web of Science)
11. Cumulative Index to Nursing and Allied Health Literature (EBSCO)
12. PsycINFO (Ovid)
13. Health Management Information Consortium (Ovid)
14. Social Policy and Practice (Ovid)
15. Dissertation Abstracts (ProQuest)
16. UK CRN Portfolio Database (NIHR) -
17. Clinical Trials.gov (NIH)
18. Open Grey
19. American Society of Cancer Oncology
20. European Society for Medical Oncology

Limits applied

Date: None

Language: English only

Study design: None

Country of publication: None

Cancer registers

Search for Other country programmes

Results from Trial Registers

UK Clinical Research Network (UKCRN): NIHR.

<http://public.ukcrn.org.uk/search/>

20th December 2011

Early lung cancer detection in Leeds - Increasing early detection of lung cancer in Inner East and Inner South Leeds		Open	Interventional	No
80745975	Lung-SEARCH - A randomised controlled trial of surveillance for the early detection of lung cancer in a high-risk group.	Closed	Interventional	N/A
22421875	The Chest Study - Reducing time to presentation with symptoms of lung cancer: phase II complex intervention study	Closed	Interventional	N/A

UKLS - UK Lung Cancer Screening Trial (UKLS) - Feasibility study and protocol development	Closed	Observational	N/A
UK Lung Cancer Screening Trial (UKLS) - UK Lung Cancer Screening Trial (UKLS)	Open	Interventional	No

Clinical Trials.gov 0 results **20th December 2011**

metaRegister of Controlled Trials

20th December 2011

0 Results for “Colorectal cancer awareness”

<http://www.controlled-trials.com/mrct/search.html>

GREY LIT SEARCHING

Searched Open Grey

<http://www.opengrey.eu/search/request?q=colon+cancer&b=20>

20th December 2011

Searched for “cancer promotion” to give 14 results when limited to English Language, 4 relevant results below:

1. [Lifestyle and cancer A health promotion programme in the ...](#)
[Hope, A.](#) ; [Kelleher, C.](#) ;
[1995](#) ; I - Miscellaneous
2. [Early cancer detection Possibilities of the systematic early ...](#)
[1983](#) ; I - Miscellaneous
3. [Cancer in the workplace Health promotion and care programmes - a ...](#)
[Ulster Cancer Foundation, Belfast](#) ;
[0000](#) ; I - Miscellaneous
4. [Social representations of cancer and their role in health ...](#)
[Tanner, S.J.](#) ;
[1997](#) ; U - Thesis

American Society of Clinical Oncology (ASCO): <http://www.asco.org/>

20th December 2011

No relevant abstracts

European Society for Medical Oncology (ESMO): <http://www.esmo.org/>

20th December 2011

2008 1st Lung Cancer Conference 1 relevant abstract

Grey literature searching

10th January 2012

Links from the United Kingdom Association of Cancer Registries (<http://www.ukacr.org/content/links>)

Regions of England:

- [Eastern Cancer Registration and Information Centre \(ECRIC\)](#) – No results for “awareness”
- [North West Cancer Intelligence Service \(NWCIS\)](#) – 2 results for “awareness” 1 potentially relevant –
 - http://www.nwcis.nhs.uk/documents/publications/Lung_Cancer_in_the_North_West.pdf
- [Northern & Yorkshire Cancer Registry & Information Service \(NYCRIS\)](#) – 12 results for “awareness” but mostly datasets.
- [Oxford Cancer Intelligence Unit \(OCIU\)](#) – 5 results, 0 on awareness campaigns
- [South West Cancer Intelligence Service \(SWCIS\)](#) – 344 results for “awareness”. Adding “lung cancer awareness” to give 3 results, 2 potentially relevant -
 - Information to support lung cancer awareness month <http://www.swpho.nhs.uk/resource/item.aspx?RID=9300>
 - Lung Cancer Awareness month <http://www.swpho.nhs.uk/resource/item.aspx?RID=9301>
- [Thames Cancer Registry](#) – 35 results with “awareness”, 4 potentially relevant
 - Evidence of effectiveness of interventions to promote cancer awareness and early presentation http://www.thames-cancer-reg.org.uk/bulletin/3_LF_presentation_170211.pdf
 - Improving early diagnosis in NE London – defining the problem, Lung Cancer is included http://www.thames-cancer-reg.org.uk/bulletin/3_LF_presentation_170211.pdf
 - Holmberg L, Sandin F, Bray F, Richards M, Spicer J, Lambe M, Klint A, Peake M, Strand TE, Linklater K, Robinson D, Møller H. National comparisons of lung cancer survival in England, Norway and Sweden 2001-2004: differences occur early in follow-up Thorax (2010) 65, 436-441 <http://www.thames-cancer-reg.org.uk/bulletin/ab240510a.htm>
 - International Studies of Cancer Survival http://www.thames-cancer-reg.org.uk/bulletin/1_HM_presentation_170211.pdf
- [Trent Cancer Registry](#) – 442 results with “awareness”. Searching “lung” within results gave 35 records **similar to the other Cancer Registry**. 0 on awareness campaigns
- [West Midlands Cancer Intelligence Unit \(WMCIU\)](#) – 40 results with “awareness”. 4 results for “lung awareness”, 0 on awareness campaigns.

Ireland, Scotland and Wales:

- [National Cancer Registry, Ireland](#) – 32 results with “awareness”. 29 results for “lung awareness” 1 potentially relevant
 - Survey of public awareness and attitudes towards cancer prevention (<http://www.ncri.ie/research/research.shtml>)
- [Northern Ireland Cancer Registry \(NICR\)](#) – 55 results with “awareness”. 33 results for “lung awareness”, 0 on awareness campaigns
- [Scottish Cancer Registry](#) – 592 results with “awareness” and 8 results for “lung awareness”, 0 on awareness campaigns
- [Welsh Cancer Intelligence & Surveillance Unit \(WCISU\)](#) – 6 results for “awareness”, 0 on awareness campaigns

Other:

- [National Cancer Intelligence Network \(NCIN\)](#) – 20 results for “awareness” and 80 results for “lung awareness”
- Awareness results
 - Filtered result by publication type “Evidence” to give 1 result - Diagnosing Cancer Earlier (2009) British Journal of Cancer 101;S2:S1-S129 <http://www.nature.com/bjc/journal/v101/n2s/index.html>
 - Filtered result by publication type “Guidance” to give 1 result – Local awareness and early diagnosis baseline assessment: a guide to cancer networks and primary care trusts (http://www.ncin.org.uk/publications/guidance_documents/naedi_baseline_guide.aspx).
 - Filtered result by publication type “Presentation” to give one results – “Has awareness changed over the last 20 years?” by Lindsay Forbes (presentation).

- Lung Awareness results
 - Filtered result by publication type “Presentation” to give 32 results – increasing early detection of lung cancer in Leeds <http://www.ncin.org.uk/view.aspx?rid=533>
- [Department of Health - Cancer](#) – 495 results for “awareness”. 26 results for “lung cancer awareness”, 3 potentially relevant.
 - Cancer awareness campaigns announced <http://gp.dh.gov.uk/2011/10/31/cancer-awareness-campaigns-announced/>
 - Local campaigns will target breast, bowel and lung cancer http://www.dh.gov.uk/en/Aboutus/Features/DH_119590
 - New campaign to alert people to early signs of cancer http://www.dh.gov.uk/en/MediaCentre/Pressreleases/DH_119576
- [Northern Ireland Cancer Network](#) – 101 results for “awareness”. 13 results for “lung awareness”, 3 potentially relevant
 - Northern Ireland’s biggest cancer killer – charity marks lung cancer awareness month <http://www.cancerni.net/news/northernireland%E2%80%99sbiggestcancerkillercharitymarkslungcancerawarenessmonth>
 - Lung Cancer Awareness Month Pharmacist toolkit - Northern Ireland <http://www.cancerni.net/publications/lungcancerawarenessmonthpharmacisttoolkitnorthernireland>
 - Lung Cancer Network Group Lung Cancer Awareness Month – November 2010 <http://www.cancerni.net/files/NICaNLungCancerAwarenessMonth2010.pdf>
- [The Scottish Government - Cancer](#) – 15,585 results for “awareness”. 253 results for “lung cancer awareness”, too many to sift through
- [The Welsh Assembly Government - Cancer](#) - 1200 records for “awareness”. 8 results for “lung awareness”, 0 on awareness campaigns

Selected sources of cancer registries (international)

AUSTRALIA - [Australasian Association of Cancer Registries](#)

- New South Wales Central Cancer Registry – approx 360 records in results for “lung cancer awareness”, too many to sift through
- Victorian Cancer Registry – 4 results for “cancer awareness” 0 on awareness campaigns
- Queensland Cancer Registry – Cancer Council Queensland approx 400 records in results for “lung cancer awareness” too many to sift through
- Tasmanian Cancer Registry – 8 results for awareness, 0 relevant.
- New Zealand Cancer Registry - 7 results for “lung awareness” 0 on awareness campaigns

EUROPE - [ENCR Members on the Web](#)

- [International Agency for Research on Cancer \(IARC\)](#) - 443 results for “awareness” and 181 for “lung cancer awareness”. 1 report on “Cancer control knowledge into action WHO guide for effective programmes” <http://screening.iarc.fr/doc/FINAL-Advocacy-Module%206.pdf> .

US

- [North American Association of Central Cancer Registries](#) – 66 results for “awareness”, 24 for lung cancer awareness, 0 on awareness campaigns
- [SEER \(National Cancer Institute, USA\)](#) - 20 results for “awareness”, 0 on awareness campaigns

Programmes/campaigns in raising awareness/early detection of lung cancer in different countries

AUSTRALIA

The Australian Lung Foundation Show us your lungs campaign

<http://www.lungfoundation.com.au/showusyourlungs>

Lung Cancer Awareness Month

<http://www.lungfoundation.com.au/our-initiatives/lung-cancer-national-program/lung-cancer-awareness-month>

AIHW & Cancer Australia 2011. Lung cancer in Australia: an overview. Cat. no. CAN 58. Canberra: AIHW. <http://www.aihw.gov.au/publication-detail/?id=10737420419>

CANADA

Lung Cancer Canada awareness month, free awareness & educational resources

<http://www.lungcancercanada.ca/>

EUROPE

Earlier detection of Lung Cancer Recommendations for workplace interventions: A collaborative awareness-raising project led by the European Men's Health Forum (EMHF) 2009 http://www.emhf.org/resource_images/EMHFlungcancerreport09.pdf

New Survey Reveals Startling Ignorance About Europe's Number One Cancer Killer - Lung Cancer BASEL, Switzerland, October 31

<http://www.prnewswire.co.uk/cgi/news/release?id=182870>

NEW ZEALAND

Middle Cancer Network Early Detection of Lung Cancer

<http://www.midlandcancernet.org.nz/index.aspx?pageid=2145862565>

UK

Local Campaigns will target breast, bowel and lung cancer

http://www.dh.gov.uk/en/Aboutus/Features/DH_119590

Cancer Awareness Campaigns announced October 31 2011

<http://gp.dh.gov.uk/2011/10/31/cancer-awareness-campaigns-announced/>

Regional Lung Cancer Pilot

<http://info.cancerresearchuk.org/spotcancerearly/naedi/lungbeclearoncancer/>

<http://www.bbc.co.uk/news/uk-england-stoke-staffordshire-15242728>

<http://www.uhb.nhs.uk/news/lung-cancer-awareness-campaign-launched.htm>

Symptoms of lung cancer radio advert

http://www.dh.gov.uk/en/MediaCentre/Media/DH_123973

New lung cancer awareness campaign launched in Central Lancashire

http://www.centrallancashire.nhs.uk/your-pct/news/news-releases/lung_cancer_campaign_news.aspx

Cumbria Lung Cancer Awareness Campaign

<http://www.cumbria.nhs.uk/YourHealth/LungCancer/CumbriaLungCancerAwarenessCampaign.aspx>

NAEDI Local Public Awareness Campaigns

http://www.the3ccancernet.org.uk/main_Template.asp?siteID=1&pageID=164
<http://www.the3ccancernet.org.uk/downloads/NAEDI%20Lung%20Cancer%20booklet%20reduced%20size.pdf>

Lung Cancer Awareness Month

<http://www.lunguk.org/media-and-campaigning/campaigns/lungcancerawarenessmonth>
<http://www.rpharms.com/public-health/lung-cancer-awareness-month.asp>

Department of Health Lung Cancer Awareness Month 2007

http://www.dh.gov.uk/en/MediaCentre/DH_080336

UWE Lung Cancer awareness and early detection

<http://www1.uwe.ac.uk/bl/bbs/research/bsmc/bsmcresearchpublications/earlydetectionoflungcancer.aspx>

Royal Pharmaceutical Society The role of pharmacists in early detection

<http://www.rpharms.com/public-health/lung-cancer-awareness-month.asp>

Newham NHS The Small C spotting cancer saves lives

<http://www.smallc.org.uk/assets/Uploads/Documents/Newham.pdf>

USA

<http://www.hellohaveyouheard.com/>

<http://www.prweb.com/releases/lungcancerawarenessmonth/oncimmune/prweb8883244.htm>

<http://www.lungcanceralliance.org/>

<http://www.upstagelungcancer.org/>

Appendix B: Searches for cost and HRQoL in lung cancer

Quality of life

MEDLINE and MEDLINE In-Process

Searched via OVID interface 13/03/12

Database: Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations and Ovid MEDLINE(R) <1946 to Present>

- 1 exp Lung Neoplasms/ (151959)
- 2 exp Carcinoma, Non-Small-Cell Lung/ (25338)
- 3 (lung\$ adj3 (canc\$ or carcinoma\$ or tumo?r\$ or neoplasm\$)).ti,ab. (104506)
- 4 1 or 2 or 3 (178338)
- 5 quality adjusted life year/ (5394)
- 6 quality adjusted life.tw. (4635)
- 7 (qaly\$ or qald\$ or qale\$ or qtime\$).tw. (3875)
- 8 disability adjusted life.tw. (910)
- 9 daly\$.tw. (922)
- 10 (sf6 or sf 6 or short form 6 or shortform 6 or sf six or sfsix or shortform six or short form six).tw. (1182)
- 11 (sf12 or sf 12 or short form 12 or shortform 12 or sf twelve or sftwelve or shortform twelve or short form twelve).tw. (1976)
- 12 (sf16 or sf 16 or short form 16 or shortform 16 or sf sixteen or sfsixteen or shortform sixteen or short form sixteen).tw. (19)
- 13 (sf20 or sf 20 or short form 20 or shortform 20 or sf twenty or sftwenty or shortform twenty or short form twenty).tw. (312)
- 14 (euroqol or euro qol or eq5d or eq 5d).tw. (2746)
- 15 (hql or hqol or h qol or hrqol or hr qol).tw. (5745)
- 16 (hye or hyes).tw. (51)
- 17 health\$ year\$ equivalent\$.tw. (37)
- 18 health utilit\$.tw. (837)
- 19 (hui or hui1 or hui2 or hui3).tw. (740)
- 20 disutili\$.tw. (170)
- 21 rosser.tw. (69)
- 22 quality of wellbeing.tw. (7)
- 23 quality of well being.tw. (296)
- 24 qwb.tw. (150)
- 25 willingness to pay.tw. (1697)
- 26 standard gamble\$.tw. (594)
- 27 time trade off.tw. (617)
- 28 time tradeoff.tw. (192)
- 29 tto.tw. (478)
- 30 or/5-29 (22287)
- 31 4 and 30 (273)

273 results saved to Endnote library marked 'Medline QOL 13/03/12' in Custom 4 field.

Costs

NHSEED

Searched via Cochrane Library 13/03/12

#1 MeSH descriptor Lung Neoplasms explode all trees 4047

#2 (lung* near/3 (canc* or carcinoma* or tumor* or tumour* or neoplasm*)):ti,ab 6061

#3 (#1 OR #2) 6909

#4 (#1 OR #2) 171 (limited to NHSEED only)

171 results saved to Endnote library marked 'NHSEED costs 13/03/12' in Custom 4 field.

After de-duplication of results there were 170 NHSEED and 271 Medline results, so 401 total.