FACTORS INFLUENCING THE DIAGNOSIS AND SUBSEQUENT PROGNOSIS IN PATIENTS WITH LUNG CANCER

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ABSTRACT

Background

The United Kingdom (UK) has poor lung cancer survival rates compared to other countries, and this is partly explained by differences in early mortality. In order to diagnose lung cancer at an earlier stage in the UK there is a pressing need to understand the management process from the recognition of symptoms by people with lung cancer, through the initial interactions with primary care to the referral to secondary care and the choice of the subsequent treatment plan.

Objectives

The aim of this thesis is to use mixed methods to identify some of the factors which may affect the diagnosis and prognosis in patients with lung cancer in the United Kingdom across the whole patient pathway.

Methods

Prospectively collected clinical data were used in conjunction with qualitative methodology. Primary care records were obtained from The Health Improvement Network, alongside data from the National Lung Cancer Audit (NLCA), linked to Hospital Episode Statistics and Office for National Statistics datasets. Case-control and cohort studies were conducted using multivariable logistic regression to look at independent associations with early mortality, likelihood of receiving surgery and place of death. Survival analyses were performed using Kaplan Meier curves and Cox regression and validation studies used area under the receiver operating curves (AUC). The Framework approach

was used to identify themes and sub-themes arising from focus group interviews.

Results

Mixed methods were used to look at barriers to early diagnosis and attitudes towards lung cancer screening in a high risk population. A number of key practical and emotional barriers which may impact on screening uptake were identified, alongside the issue of smoking stigma and blame. Primary care data were used to look at predictors of early (0-90 day) mortality in the UK. Thirty per cent of patients with lung cancer died within 90 days of diagnosis. Increasing age, male sex, socioeconomic deprivation, rural versus urban location and current smoking were all independently associated with early death. Patients who had poorer prognosis did interact with primary care before diagnosis, suggesting missed opportunities to identify them earlier. NLCA data linked to organisational audit data highlighted inequities between Trusts, in particular with regards to variability in the workload of specialists and differences in access to diagnostic and therapeutic modalities. On site access to positron emission computed tomography, stereotactic ablative radiotherapy and video-assisted thoracoscopic lobectomy were independently associated with increased likelihood of receiving surgery for lung cancer. Records for patient who developed brain metastases following radical surgical treatment for lung cancer were reviewed. Those with more advanced disease stage, younger age and adenocarcinoma sub-type were more likely to develop metastases and modelling suggested that 71% may have been visible pre-operatively had magnetic resonance imaging of the brain been performed as

part of the staging process. An internal and external validation was performed to assess the ability of two risk scoring systems to predict 90 day post-operative mortality. AUC values for internal and external validation of the NLCA score and validation of Thoracoscore were 0.68 (95% CI 0.63-0.72), 0.60 (95% CI 0.56-0.65) and 0.60 (95% CI 0.54-0.66) respectively. Post-hoc analysis was performed using NLCA records on 15554 surgical patients to derive summary tables for 30 and 90 day mortality, stratified by procedure type, age and performance status. Linked NLCA data were used to look at place of death from lung cancer. Thirty-five per cent of patients with lung cancer die in acute hospital beds, with male sex, old age (≥ 85 years), socioeconomic deprivation, WHO performance status 4 at diagnosis and emergency route to diagnosis all independently associated with increased likelihood of death in this setting. There is marked geographical variation in place of death, particularly with regard to provision of hospice services.

Conclusions

The studies described in this thesis use prospectively collected data to provide a snapshot of different aspects of the lung cancer patient journey which may impact on prognosis, alongside qualitative methodology to try to determine reasons for diagnostic delay and attitudes towards screening programmes. There remain some important clinical questions about lung cancer care and outcomes which need to be looked at to provide a greater understanding of where the inequities in the lung cancer patient pathway in the UK lie and to try to address modifiable factors with an aim to improve outcomes.

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PUBLICATIONS ARISING FROM THIS THESIS

What characteristics of primary care and patients are associated with early death in patients with lung cancer in the UK?
O'Dowd EL, McKeever TM, Baldwin DR, Anwar S, Powell HA, Gibson JE, Iyen-Omofoman B, Hubbard RB. Thorax. 2015 Feb;70(2):161-8. doi: 10.1136/thoraxjnl-2014-205692

Author's response: What characteristics of primary care and patients are associated with early death in patients with lung cancer in the UK?
O'Dowd EL, McKeever TM, Baldwin DR, Anwar S, Powell HA, Gibson JE, Iyen-Omofoman B, Hubbard RB. Thorax. 2015 Feb;70(2):185. doi: 10.1136/thoraxjnl-2014-206638

Variation in lung cancer resources and workload: results from the first national lung cancer organisational audit
Cusworth K, O'Dowd E, Hubbard R, Beckett P, Peake MD, Woolhouse I. Thorax 06/2015; doi:10.1136/thoraxjnl-2015-207166

Brain metastases following radical surgical treatment of non-small cell lung cancer: is preoperative brain imaging important?
O'Dowd EL, Kumaran M, Anwar S, Palomo B, Baldwin DR. Lung Cancer. 2014 Nov;86(2):185-9. doi: 10.1016/j.lungcan.2014.08.021

Predicting death from surgery for lung cancer: A comparison of two scoring systems in two European countries
O'Dowd E, Lüchtenborg M, Baldwin D, McKeever T, Powell H, Møller H, Jakobsen E, Hubbard R. Lung Cancer 03/2016
doi:10.1016/j.lungcan.2016.03.002

Place of Death in Patients with Lung Cancer: A Retrospective Cohort Study from 2004-2013
O'Dowd EL, McKeever TM, Baldwin DR, Hubbard RB. PLoS One. 2016 Aug 23;11(8):e0161399. doi: 10.1371/journal.pone.0161399. eCollection 2016

LIST OF ABBREVIATIONS

A&E	Accident and emergency
ACCP	American College of Chest Physicians
ACE	Accelerate, Coordinate, Evaluate Programme
AHD	Additional Health Data
ALK	Anaplastic lymphoma kinase
ASA	American Society of Anaesthesiologists
AUC	Area under the curve
BNF	British National Formulary
BTS	British Thoracic Society
CHART	Continuous hyperfractionated accelerated radiation therapy
CI	Confidence interval
CNS	Lung cancer nurse specialist
CPEX	Cardio-pulmonary exercise testing
CRUK	Cancer Research UK
CT	Computed tomography
CXR	Chest x-ray
DCO	Death certificate only
DLCO	Diffusing capacity for carbon monoxide
DLCR	Danish Lung Cancer Registry
DoH	Department of Health
EBUS	Endobronchial ultrasound
ECOG	Eastern Cooperative Oncology Group
ED	Emergency department
EGFR	Epidermal growth factor receptor

ENCR	European Network of Cancer Registries
E-PASS	Estimation of Physiologic Ability and Surgical Stress
EPIC	Epidemiology and Pharmacology Information Core
ERS	European Respiratory Society
ESOS	European Society Objective Score
ESSS	European Society Subjective Score
ESTS	European Society of Thoracic Surgeons
EUS	Endoscopic ultrasound
FDA	Food and Drug Administration
FDG	Fluorodeoxyglucose
FEV1	Forced expiratory volume in 1 second
FVC	Forced vital capacity
GP	General Practitioner
GTSD	General Thoracic Surgery Database
HDU	High-dependency unit
HES	Hospital Episode Statistics
HQIP	Healthcare Quality Improvement Partnership
HR	Hazard ratio
HSCIC	Health and Social Care Information Centre
IASLC	International Association for the Study of Lung Cancer
ICBP	International Cancer Benchmarking Partnership
ICD-10	International Statistical Classification of Diseases and Related Health Problems 10th revision
InPS	In Practice Systems
IQR	Inter-quartile range
LDCT	Low dose computed tomography

LRT	Likelihood ratio testing
LSOA	Lower Layer Super Output Areas
MCCD	Medical Certificate of Cause of Death
MDT	Multi-disciplinary team
MR	Magnetic resonance imaging
MRC	Medical Research Council
NCIN	National Cancer Intelligence Network
NELSON	Nederlands-Leuvens Longkanker Screenings Onderzoek
NHS	National Health Service
NICE	National Institute for Health and Care Excellence
NLCA	National Lung Cancer Audit
NLST	National Lung Screening Trial
NSC	National Screening Committee
NSCLC	Non-small cell lung cancer
NUH	Nottingham University Hospitals NHS Trust
ONS	Office for National Statistics
OPCS-4	Office of Population Censuses and Surveys Classification of Surgical Operations and Procedures version 4
OR	Odds ratio
OSC	Optimal supportive care
PACS	Picture archiving and communication system
PCT	Primary Care Trusts
PD-1	Programmed death receptor 1
PDL-1	Programmed death ligand 1
PET-CT	Positron emission tomography-computed tomography
POSSUM	Physiological and Operative Severity Score for the enumeration of mortality and morbidity

ppo	Predicted post-operative
QALY	Quality-adjusted life years
QOF	Quality and Outcomes Framework
RCP	Royal College of Physicians
RCT	Randomised controlled trials
RFA	Radiofrequency ablation
ROC	Receiver operating curve
SABR	Stereotactic ablative radiotherapy
SCLC	Small cell lung cancer
SEER	Surveillance, epidemiology and end results
SNOMed	Systematised Nomenclature of Medicine
SOA	Super Output Areas
STS	Society of Thoracic Surgeons
THIN	The Health Improvement Network
TKI	Tyrosine kinase inhibitors
TNM	Tumour Node Metastases
UICC	Union for International Cancer Control
UK	United Kingdom
UKLS	UK Lung Cancer Screening Trial
US	United States of America
VALSG	Veteran's Administration Lung Cancer Study Group
VATS	Video-assisted thoracoscopy
WHO	World Health Organisation

CHAPTER 1 : INTRODUCTION

This chapter provides an overview of lung cancer incidence and mortality, summarises the United Kingdom diagnostic pathway and treatment options available and looks at the likely interventions to reduce mortality, including implementation of screening. This will be followed by the thesis justification, objectives and an outline of the subsequent chapters.

1.1 Epidemiology of lung cancer

1.1.1 Worldwide

Lung cancer is the most common cancer worldwide, with 1.8 million new cases diagnosed in 2012 (13% of all cancer cases). The geographical incidence pattern differs between men and women, reflecting historical smoking behaviours largely. (Figure 1-1)

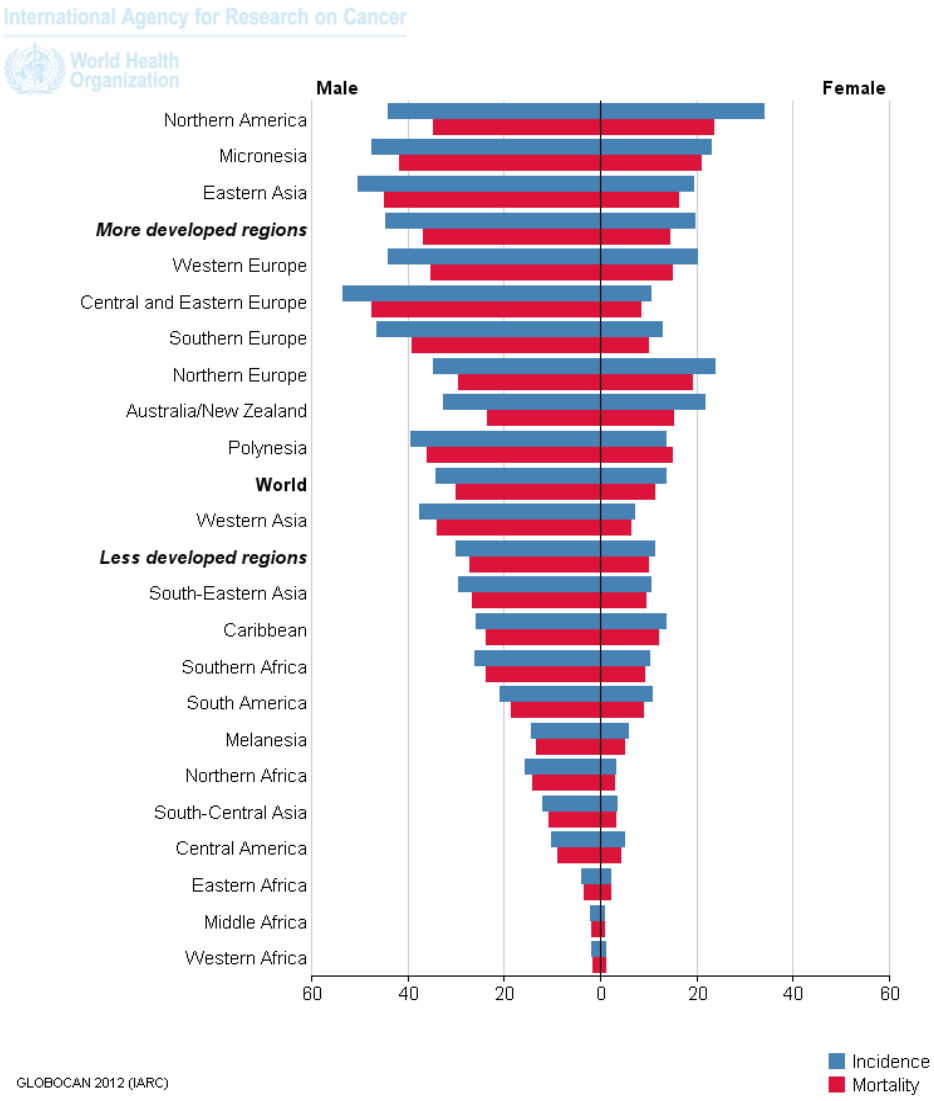


Figure 1-1: Estimated age-standardised rates (World) per 100,000
(Reproduced with permission from (1) Available from: http://globocan.iarc.fr, accessed on 27/10/2016)

Fifty eight per cent of cases occurred in less developed countries, with the highest overall incidence rates in Hungary, followed by Serbia and the Democratic People's Republic of Korea. The highest estimated age-standardised incidence rates for men are in Central and Eastern Europe (53.5 per 100,000) and Eastern Asia (50.4 per 100,000). In women the highest estimated rates are in Northern America (33.8 per 100,000) and Northern Europe (23.7 per 100,000).(1) The lowest rates in both sexes are in Western and Middle Africa. Lung cancer has a high mortality and is responsible for almost 1 in 5 cancer deaths internationally (1.59 million in 2012). There is little geographical variability in survival so incidence mirrors mortality closely.

Tobacco smoking is the main aetiological factor behind the development of lung cancer and is responsible for between 80% and 90% of cases. The landmark *British Doctors Study* conducted by Doll and Hill established the link between smoking and lung cancer in the 1950s.(2) Other agents which have been implicated in the development of lung cancer include exposure to second-hand cigarette smoke (passive smoking), occupational exposure to agents such as asbestos, nickel, chromium, and arsenic, exposure to radiation, including radon gas in homes and mines and exposure to indoor and outdoor air pollution. Some of these agents act synergistically with cigarette smoke to further increase the risk, for example asbestos or radon exposure in combination with smoking may increase lung cancer risk by up to 50 times that of smoking alone.(3) In the past decade there has been a shift in the global burden of lung cancer from high income western countries to low- and middle-income countries, particularly in Asia, which reflects increased uptake in cigarette

smoking in these countries. Absolute numbers of newly diagnosed lung cancers in developing countries now exceed the number in developed countries. The trend of the lung cancer burden becoming increasingly concentrated in the developing world is expected to continue for the foreseeable future.

The 2015 World Health Organisation (WHO) classification categorises lung cancer into 3 main epithelial histological subgroups: adenocarcinoma, squamous cell carcinoma and neuroendocrine tumours (which includes small cell carcinoma).(4) The histologic characteristics of lung cancer in developed countries have changed during the past 50 years. Adenocarcinoma has become more common, whereas squamous cell carcinoma has declined. This is thought to be related to the ageing population, in whom adenocarcinoma is more likely, in combination with a reduction in smoking prevalence.

There is a deprivation gradient with regards to lung cancer incidence which largely reflects increased smoking prevalence in those from more socio-economically deprived backgrounds. This has been seen in the United Kingdom (UK) but also worldwide (5-9) (Figure 1-2 summarises the gradient in England). In addition to higher incidence rates, lower socioeconomic status has also been associated with higher stage at diagnosis and lower survival compared with those from the least deprived groups.(9, 10)

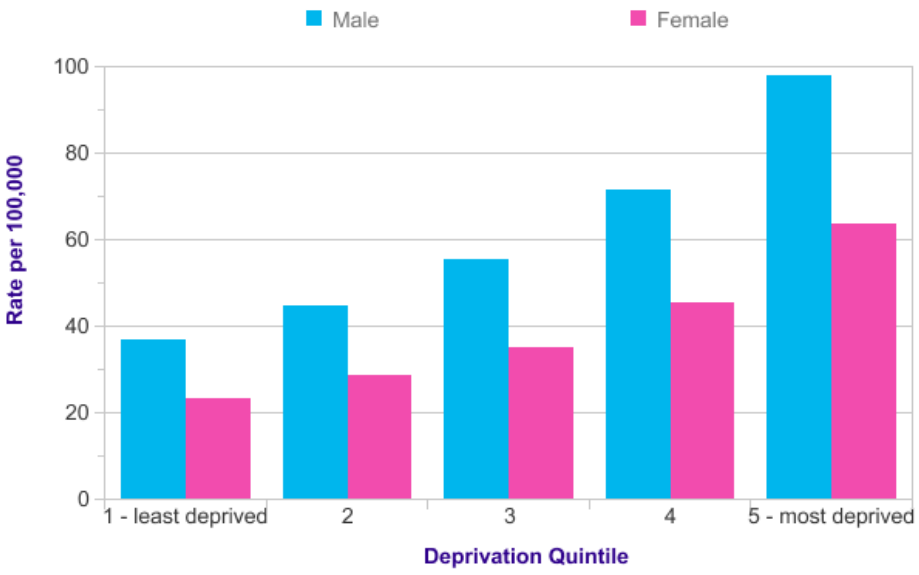


Figure 1-2: Age-Standardised Incidence Rates by Deprivation Quintile, England 2006-2010
(Reproduced with permission from Cancer Research UK)(11)

1.1.2 United Kingdom (UK)

In 2013 in the UK lung cancer was the second most common type of cancer after breast cancer; with over 45500 new cases diagnosed.(11) Although lung cancer remains more common in men, the incidence in women is increasing. This is largely related to changes in smoking behaviours; smoking prevalence in females peaked around 20 years later than that in males (Figure 1-3).

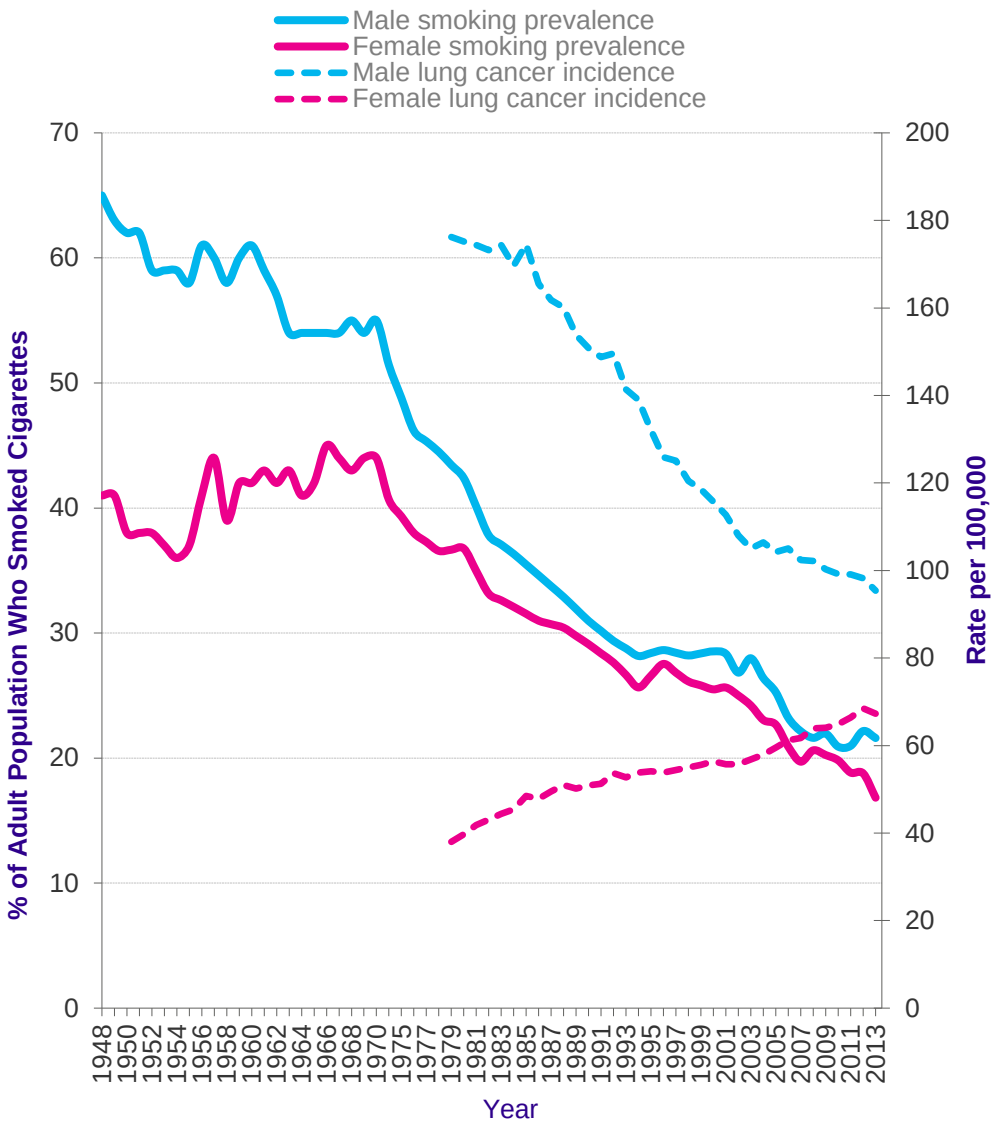


Figure 1-3: Age-Standardised Incidence Rates per 100,000 Population and Smoking Prevalence, by Sex Great Britain 1949-2013
(Reproduced with permission from Cancer Research UK)(11)

Lung cancer mortality has fallen since the 1970s (Figure 1-4). In 2014 35895 people died of lung cancer in the UK which accounts for just over 1 in 5 of all cancer deaths (22%). Age-standardised mortality has fallen by 16% in men but risen by 6% in women (a 6% decrease overall) over the past decade. Survival remains poor for lung cancer patients and the gains in survival have been small;

one year survival figures in the UK were 36% in 2012, with 5 year survival figures of 13%.(12)

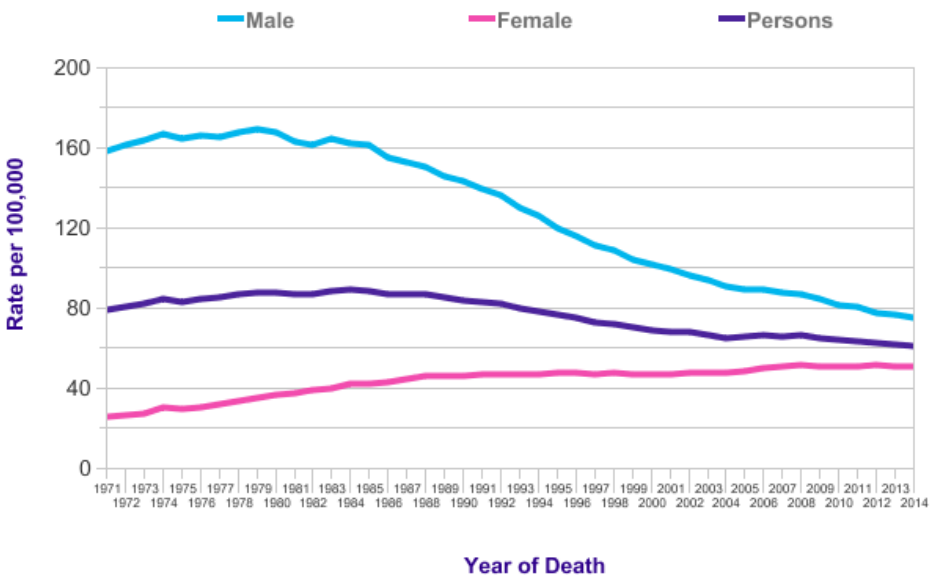


Figure 1-4: Age-Standardised Mortality Rates per 100,000 Population, UK 1971-2014
(Reproduced with permission from Cancer Research UK)(11)

Net survival also varies by stage at diagnosis (Figure 1-5). Of those who were diagnosed with stage 1 disease in England in 2014, 83% survived for 1 year compared with only 17% of those diagnosed with stage IV disease.(13) Almost 50% of patients with lung cancer present with stage IV disease.

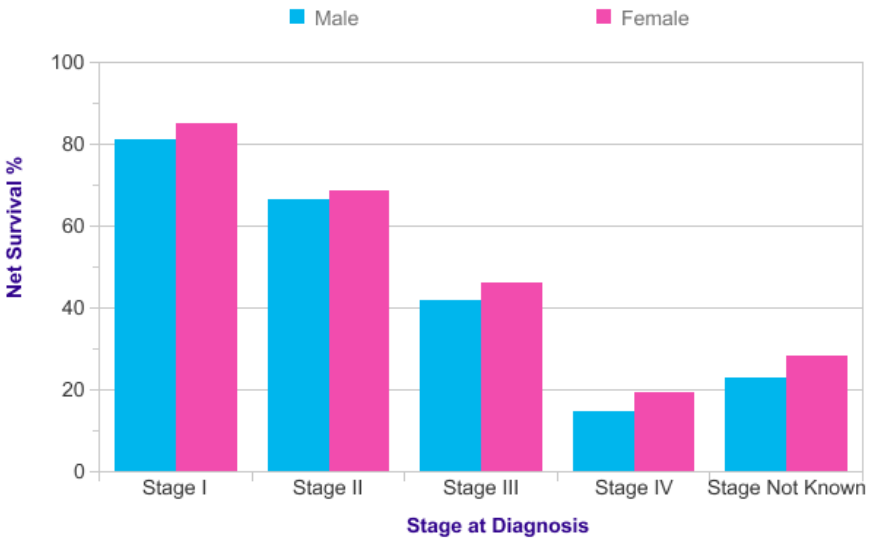


Figure 1-5: One-Year Net Survival (%) by Stage, England 2014
(Reproduced with permission from Cancer Research UK)(11)

1.2 International comparisons

For the past 2 decades the EUROCARE group have used data from population-based cancer registries in 23 European countries to look at outcomes from several common cancers including lung cancer. These studies have suggested that there are inequities in outcomes between countries both in terms of survival and surgical resection rates for lung cancer patients.(14) Following on from this work, the International Cancer Benchmarking Partnership (ICBP) was formed in 2009 to try to compare outcomes between the UK and five other high-income countries which have universal healthcare coverage: Australia, Denmark, Canada, Norway and Sweden. This also highlighted the UK as a country with one of the lowest lung cancer survival rates (14-18). The UK age-standardised 1 year net survival from NSCLC was 30% compared with 46% in Sweden, which in part represents more advanced stage at presentation.(18) However, stage-specific survival was also lower in the UK compared with Canada and Sweden. There seems to be an excess of early deaths, with inequalities particularly in the 0-3 month period post-diagnosis (Figure 1-6).(15, 17) Late diagnosis is thought to contribute to this problem and questions have been raised regarding whether the UK healthcare structure is responsible for this in part, as studies have shown that gatekeeping has been associated with delayed diagnosis and adverse outcomes.(19, 20) The UK had the lowest proportion of patients with early stage disease and one year survival, even for those with stage I lung cancer, was only 72.5% in the UK compared with 86.3% in Canada and 88.4% in Sweden. In the past 5 years there has been some improvement in survival in those with lung cancer in the UK, which is largely

due to increased surgical resection rates in those with early stage disease but despite this prognosis remains worse than in other comparable countries. These poor outcomes are likely to represent a variety of patient and sociodemographic issues alongside late presentation, diagnostic delays and inequities in access to treatment.

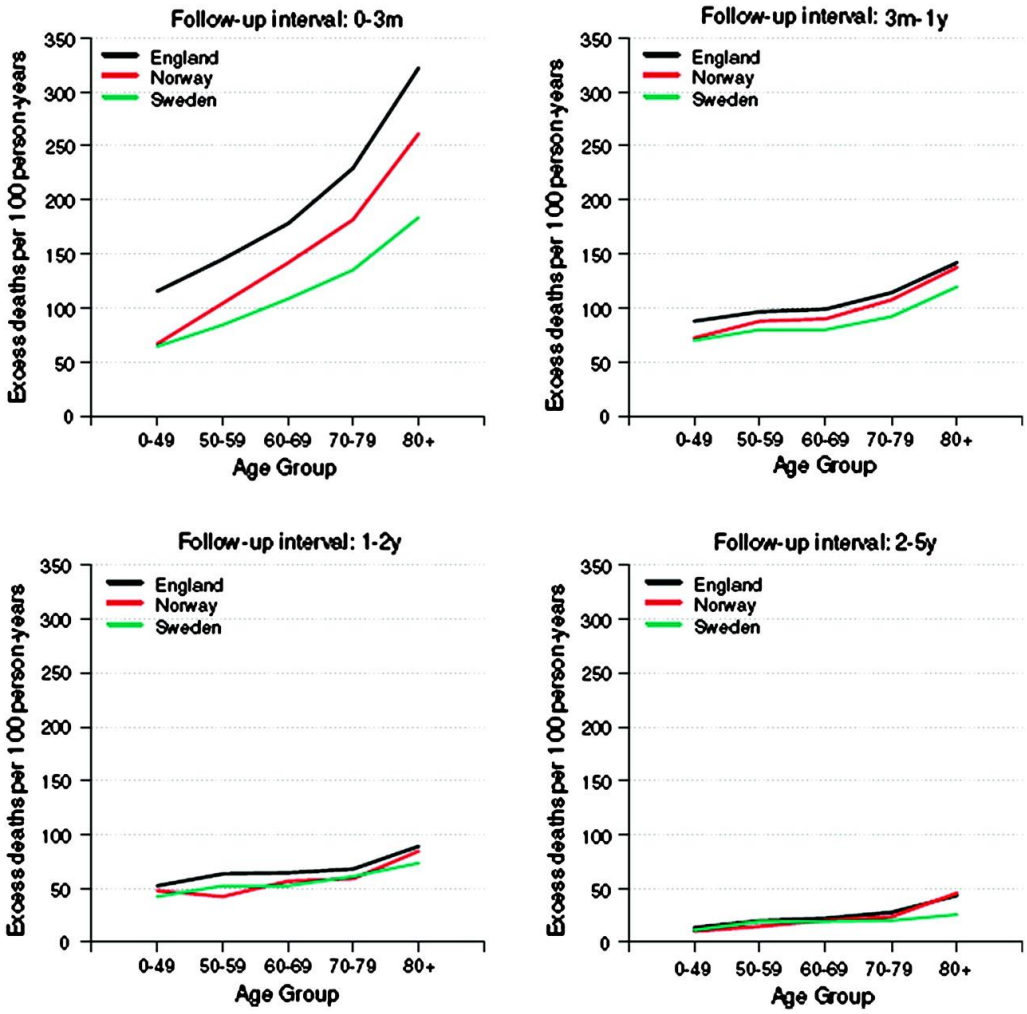


Figure 1-6: Excess deaths/100 person-years by country, age and follow-up interval during the period 2001–2004.

(Reproduced from [Lars Holmberg et al. Thorax 2010;65:436-441, copyright notice 3965951382838 Oct 2016](17) with permission from BMJ Publishing Group Ltd.)

1.3 Diagnosis and patient pathway in the United Kingdom

In the UK most people are registered with a general practitioner (GP) who manages chronic diseases and also organises non-emergency referrals to secondary care. The Routes to Diagnosis project showed that 49% of patients with lung cancer were diagnosed following the "2 week wait" urgent referral pathway or following routine or urgent GP referral.(21) Figure 1-7 summarises the common referral routes and diagnostic pathway that lung cancer patients may encounter in the UK.

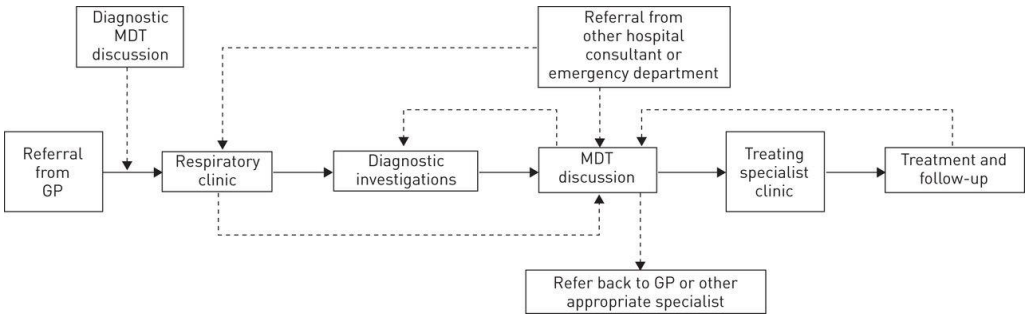


Figure 1-7: Pathway for patients with suspected or confirmed thoracic malignancy
Solid lines represent common routes, dotted lines represent alternative or additional routes. MDT: multidisciplinary team; GP: general practitioner
(Reproduced with permission of the European Respiratory Society ©. European Respiratory Journal Jun 2014, 43 (6) 1776-1786; DOI: 10.1183/09031936.00150813)(22)

1.3.1 NICE criteria

To try to reduce diagnostic delay the National Institute for Health and Care Excellence (NICE) have produced a list of criteria which should prompt timely investigation or referral via the 2 week wait pathway for suspected lung cancer.(23) These are summarised in Table 1-1.

Table 1-1: NICE criteria for investigation and referral for suspected lung cancer (Adapted from NICE Guideline NG12: Suspected cancer: recognition and referral)(23)

Direct referral to 2 week wait service:

- Chest X-ray findings that suggest lung cancer or
- Aged 40 and over with unexplained haemoptysis.

Offer a chest X-ray to assess for lung cancer in people aged 40 and over if they have 2 or more of the following unexplained symptoms, or if they have ever smoked and have 1 or more of the following unexplained symptoms:

- cough
- fatigue
- shortness of breath
- chest pain
- weight loss
- loss of appetite

Consider an urgent chest X-ray (to be performed within 2 weeks) to assess for lung cancer in people aged 40 and over with any of the following:

- persistent or recurrent chest infection
- finger clubbing
- supraclavicular lymphadenopathy or persistent cervical lymphadenopathy
- chest signs consistent with lung cancer
- thrombocytosis

GPs in all areas have access to chest x-ray (CXR) as an initial investigation tool but in some regions direct access to computed tomography (CT) scans in patients who meet specific criteria is being trialled to try to reduce delays in diagnosis. Currently all patients with cancer in the UK should be assessed, diagnosed and commence treatment within 62 days of referral to secondary care but there is an optimal lung cancer pathway which has been proposed with an aim to accelerate this process further as there is evidence that faster pathways improve outcomes.(24, 25)

1.4 Initiatives to try to improve survival

1.4.1 NHS Cancer Plan and Cancer Reform Strategy

There have been several Department of Health (DoH) policy initiatives which have been implemented to try to improve cancer services in England. The NHS Cancer Plan for England (2000) promoted centralisation of services and the use of multi-disciplinary team (MDT) working, alongside tobacco-control strategies and reduction in cancer waiting times.(26) The Cancer Reform Strategy (2007) aimed to build on the recommendations from the Cancer Plan and planned to improve prevention and promote early diagnosis to try to address the inequities in survival between those of different ages, ethnicity, socioeconomic groups and between the UK and other comparable countries. (27)

1.4.2 Routes to diagnosis and early diagnosis initiatives

Work performed as part of the National Cancer Intelligence Network (NCIN) "Routes to Diagnosis" project suggested that 35% of lung cancer patients present via the emergency route and they have a much lower 1 year survival and more advanced stage at presentation (Figure 1-8).(21)

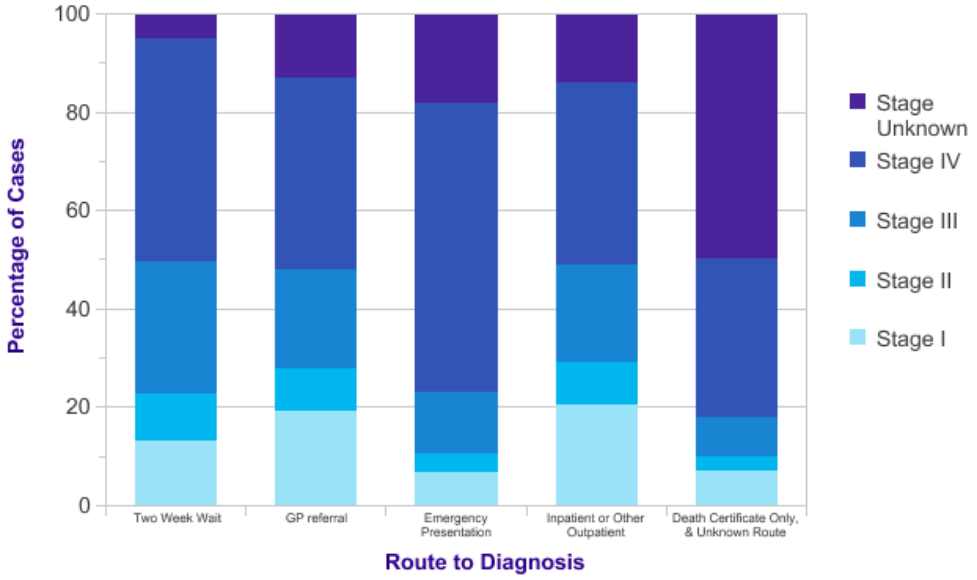


Figure 1-8: Percentage of lung cancer cases by Stage and Route to Diagnosis, England 2012-2013
(Reproduced with permission from Cancer Research UK)(11)

These findings prompted the recent public awareness projects, including the "Be Clear on Cancer" campaign, which ran initially from May to June 2012, with a further initiative taking place in March and April 2014. The results from the initial campaign showed an increase of around 30% in two-week wait referrals for suspected lung cancer, with more lung cancers being diagnosed and a shift towards earlier stage disease.

1.4.3 Screening

Four categories of screening have been studied in lung cancer; imaging, bronchoscopy, sputum analysis and biomarkers in serum and other fluid. To date only CT screening has been shown to be effective in reducing mortality.

Biomarkers and gene technology

The area of biomarker research and identification of genomic abnormalities to try to detect lung cancer at an early stage is a rapidly growing area of cancer research. No specific blood, sputum or exhaled breath test has yet been shown to be effective in clinical trials. It may be that biomarkers will have a place in the risk stratification or identification of patients suitable for entry into screening or who may require more rigorous investigation.(28) A greater appreciation of the different genomic abnormalities in different lung tumours may also allow more targeted and personalised therapies but currently there is no evidence that screening for lung cancer in this way is effective. (29, 30)

Chest x-ray screening

Initial work performed from the 1950s to 1970s focussed on the use of the CXR, with several studies showing that cancers were detected at an earlier stage and suggesting that there was a survival benefit in the screened group. However the Prostate Lung Colorectal and Ovarian (PLCO) screening trial randomised subjects to CXR and showed no reduction in mortality compared to controls.(31)

With the advent and widespread use of CT, recent randomised controlled trials (RCTs) have utilised this as the screening tool of choice for lung cancer.

Key trials in lung cancer screening

There have been several RCTs of screening for lung cancer using low dose CT (LDCT). Many of the European trials, including the largest (NELSON), are still in the follow-up period. These are summarised in Table 1-2.

Table 1-2: Trials of low-dose CT for lung cancer screening

						Participants (baseline), n					
Study	**Country**	**Age range (years)**	**Years of recruitment**	**Completion/ expected completion**	**Inclusion criteria**	**LDCT arm**	**Control arm**	**Total**	**Control arm**	**Screening schedule (Years)**	**Total follow-up period (years)**
Lung Screening Study (LSS) (pilot) (32)	USA	55-74	2000	2001	Current or ex-smokers (>30 pack years, quit < 10 years ago)	1660	1658	3318	CXR	0	1
DANTE (33)	Italy	60-74 (men only)	2001-2006	2010	Current or ex-smokers (>20 pack years)	1276	1196	2472	Annual clinic review (CXR & sputum cytology at baseline)	0, 1, 2, 3, 4	4
National Lung Screening Trial (NLST) (34)	USA	55-74	2002-2004	2009	Current or ex-smokers (> 30 pack years, quit < 15 years ago)	26722	26732	53454	CXR	0, 1, 2	5
Nederlands-Leuvens Longkanker Screenings Onderzoek (NELSON) (35)	Netherlands & Belgium	50-74	2003-2006	2017	Current or ex-smokers (> 15 pack years, quit < 10 years ago)	7915	7907	15822	Usual care	0, 1, 3, 5.5	10
ITALUNG (36)	Italy	55-69	2004-2006	2006	Current or ex-smokers (> 20 pack years, quit < 10 years ago)	1613	1593	3206	Usual care	0, 1, 2, 3	
Danish Lung Cancer Screening Trial (DLCST) (37)	Denmark	50-70	2004-2006	2014	Current or ex-smokers (> 20 pack years, quit < 10 years ago)	2052	2052	4104	Usual care	0, 1, 2, 3, 4	10
Dépiscan (Pilot) (38)	France	50-75	2002-2004	2004	Current or ex-smokers (> 15 pack years, quit < 15 years ago)	336	285	765	CXR	0, 1, 2, 3	2

Multicentric Italian Lung Detection (MILD) (39)	Italy	49-75	2005-2011		Current or ex-smokers (> 20 pack years, quit < 10 years ago)	1190 (annual) 1186 (biennial)	1723	4099	Usual care	Annual/ biennial for 10 years	
Lung Cancer Screening Intervention Study (LUSI) (40)	Germany	50-69	2007		Current or ex-smokers (> 15 pack years, quit < 10 years ago)	2029	2023	4052	Usual care	0, 1, 2, 3, 4	5
UK Lung Cancer Screening Trial (UKLS) (Pilot) (41)	United Kingdom	50-75	2011- 2016	2016	5% risk of developing lung cancer in 5 years using Liverpool Lung Project risk model	2028	2027	4055	Usual care		10

CT Computed tomography

The only trial that has shown a mortality reduction to date is the National Lung Cancer Screening Trial (NLST), performed in the United States of America (US). It recruited almost 53500 people aged between 55 and 74 years who had smoked within the past 15 years and who had a smoking history of at least 30 pack years and randomised them to annual screening by LDCT or CXR. There were 247 deaths from lung cancer per 100000 person years in the LDCT arm compared with 309 deaths per 100000 person years in the CXR group. This trial finished 1 year earlier than planned as it reached its prespecified lung cancer mortality relative reduction of 20% in the LDCT arm. There was also a 6.7% reduction in all-cause mortality rate (1877 deaths in the LDCT arm versus 2000 deaths in the CXR arm).(42)

Based on this study the US Preventative Services Taskforce has recommended that lung cancer screening should be offered to those patients aged between 55 and 80 years who have the same smoking history as those included in NLST.(43) A decision regarding implementation of a screening programme in Europe is pending the results of the largest European study (NELSON), alongside pooled data from all of the European RCTs, and also evidence regarding which selection criteria should be used, associated harms and cost effectiveness analyses.(44)

Harms associated with lung cancer screening

The main harms to consider are radiation exposure from LDCT, adverse events from further invasive investigation of abnormal CT findings, overdiagnosis,

costs incurred by screening and additional diagnostic tests and possible negative effects on smoking cessation rates.

Radiation exposure

The radiation dose in LDCT is around a fifth of that of standard thoracic CT scanning, accounting for less than half of the annual background radiation dose of an individual. Annual screening using LDCT is estimated to cause one radiation-induced lung cancer for every 22 deaths prevented.(45)

Overdiagnosis and false positive results

It is estimated that around 25 benign lesions will be detected for every cancer (false positives). Harm can therefore arise from investigation of these non-cancerous abnormalities. In NLST, across the 3 screening rounds, 96.4% of the LDCT tests were false-positive, with the vast majority of these being due to the detection of benign lymph nodes or granulomata. The majority of these false positive results were confirmed non-invasively using follow-up CT scans. However, 0.2% (59/26722) of those screened underwent CT-guided lung biopsy for a benign lesion, with seven (0.03%) experiencing a major complication. (42)

Overdiagnosis can occur, when an indolent tumour is detected during screening which would not kill the patient. Estimates from NLST suggested that 18.5% (95% confidence interval 5.4%- 30.6%) of cancers were overdiagnosed.(46) These patients do not benefit from the diagnosis and, in addition to the psychological harm associated with a diagnosis of cancer, they are also subject to the harms associated with invasive diagnostic investigations and unnecessary treatment.

False negative results

A false negative result occurs when the test fails to demonstrate the malignancy in an affected individual. In NLST, of the group screened with LDCT, only 44 of the 1060 (0.04%) participants with lung cancer had a negative screening test.(42)

Cost effectiveness

The cost effectiveness of a programme will be strongly influenced by the frequency of screening, duration of screening programme, risk profile of the screened population, uptake of screening in hard to reach groups and smoking cessation. Modelling has been performed, largely based on the results from NLST, with cost-effectiveness estimated at $23000 (£13786), reducing to $17000 when smoking cessation interventions (varenicline and behavioural techniques) were included.(47) In the UK, NICE uses a standard and internationally recognised method to compare treatments and measure their clinical effectiveness: quality-adjusted life years (QALY). A QALY gives an idea of how many extra months or years of life of a reasonable quality a person might gain as a result of treatment. Generally if a treatment costs more than £20000- £30000 per QALY it is not considered cost-effective. UK Lung Screen (UKLS) has modelled data obtained from the pilot study and has shown a cost per (QALY) of £12300. By way of comparison, breast cancer screening cost effectiveness estimates vary widely from £3000 per QALY (48) up to £20000 (49) with less conservative estimates. The best estimate probably comes from the Erasmus group who estimate €12000 (£9700) per QALY for a breast screening programme.(50)

Smoking cessation

There has been some concern that screening would offer false reassurance in those who smoke, leading to continued smoking, new or renewed uptake of the habit. There were somewhat reassuring smoking cessation results from the largest European study (NELSON), with rates of quitting of 14.5% in the screened arm and 19.1% in the control arm. These are substantially higher than the background rate of 6-7%.(51)

Hard to reach groups

An important consideration is uptake rates into a screening programme, as low uptake would render it non-viable.(52) Recruitment into UKLS showed that those who were deemed (using risk stratification tools) to be at highest risk of developing lung cancer were least likely to take up the offer of screening (Figure 1-9).(53) This same finding has been encountered with many other screening programmes,(54-57) with many cultural, social and other demographic reasons postulated as the cause. There are data to suggest that smokers view screening in a nihilistic way and perceive early detection to be of limited use and, as such, are less likely to consider screening participation.(58) Work is ongoing to try to determine how best to target these hard to reach groups to both recruit and retain them in lung cancer screening programmes and this is the basis of the qualitative project described in Chapter 3.

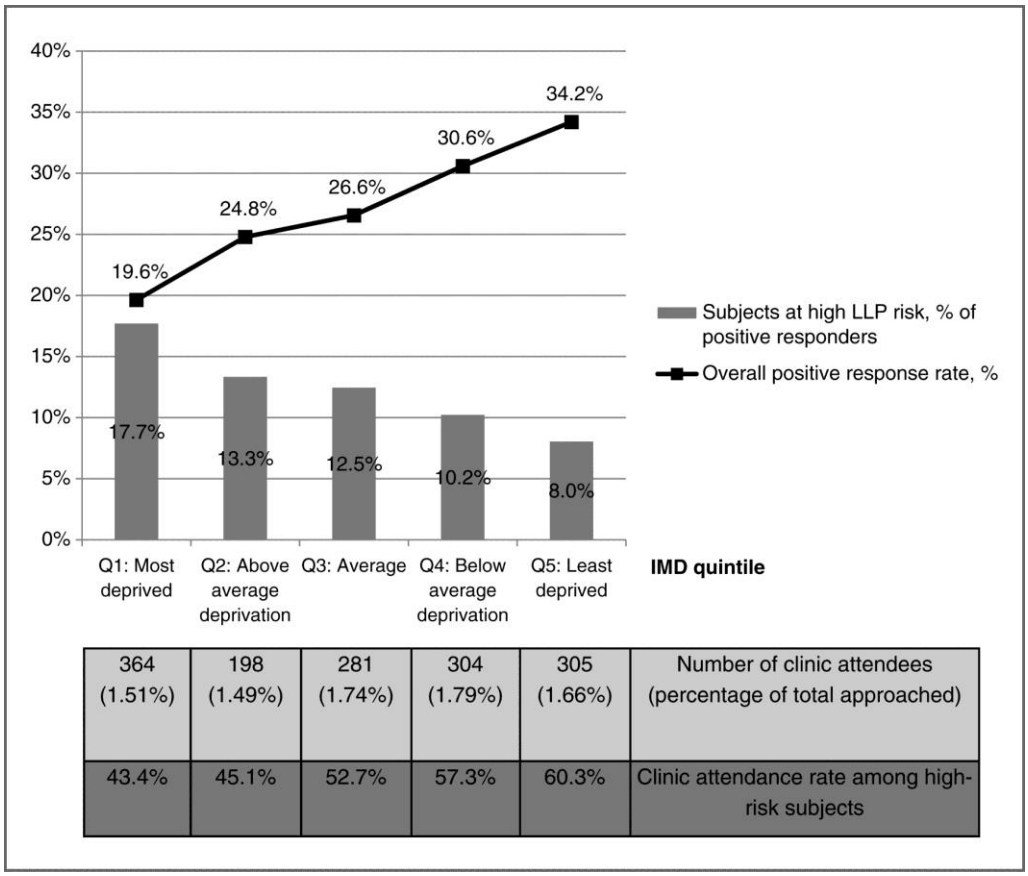


Figure 1-9: Impact of socioeconomic status (IMD) upon response rate, LLP risk, and clinic attendance in the UK Lung Cancer Screening Study (UKLS)
IMD Index of Multiple Deprivation; LLP Liverpool Lung Project
(Reprinted from Cancer Prevention Research, 2014, 7(3), 362-71, McRonald FE et al, The UK Lung Screen (UKLS): Demographic Profile of First 88,897 Approaches Provides Recommendations for Population Screening (53), with permission from AACR- licence number 3987750369159)

What is happening in the United Kingdom?

The UK National Screening Committee (NSC) uses 22 internationally-recognised criteria to establish whether a national screening programme is warranted for a particular condition. Lung cancer screening with LDCT satisfies all of the applicable criteria, in total 19 of 22, and the Department of Health Science and Technology committee have received submissions regarding evidence for screening, alongside a proposal submitted to the UK NSC.

Who, how and when to screen

This is still under consideration in the UK, although the most likely initial implementation regimen is likely to utilise risk stratification tools to identify those who have in excess of 1% per annum risk of lung cancer and offer them annual or biennial screening with LDCT from the age of 60 years, alongside a clear protocol for the investigation and management of abnormal findings and in conjunction with ongoing research into the best methods for selection, recruitment and retention.

1.5 Lung cancer treatment

1.5.1 Smoking cessation

Smoking cessation may seem futile in light of a lung cancer diagnosis but it remains key to highlight the importance and offer support for those wanting to stop. It is of particular significance in those undergoing treatment with curative intent, as it reduces the risk of post-operative and systemic treatment-related complications and in addition reduces the chance of cancer recurrence.(59, 60)

1.5.2 Surgery

Surgery remains the initial treatment option of choice for those with early stage disease NSCLC who are deemed fit enough. However, resection rates in the UK remain lower than many other countries, with inequalities in access to surgical treatment still an issue in some areas. Recent work has shown that patients first seen at a surgical centre were 37% more likely to receive surgery. In addition the largest centres operated on 18% of patients first seen locally, compared to only 12% of those referred to them from peripheral hospitals.(61) As surgical resection offers the greatest chance of cure it is key to try to reduce this variation and increase resection rates if 5 year survival is to improve. Resection rates have doubled in the UK in the past 5 years, largely due to an increased number of procedures performed on older patients. Risk stratification tools are often used to try to give some estimation of post-operative mortality and their use and limitations are discussed in greater detail in Chapter 7. Ideally the procedure of choice should aim to minimise the amount of lung tissue lost whilst still giving the best chance of cure, for example sleeve lobectomy in place of pneumonectomy, in those in whom clear margins can be obtained. Video

assisted thoracoscopy (VATS) is a minimally invasive procedure with a lower incidence of complications, shorter inpatient stay and similar 2 and 5 year survival figures to open surgery and is increasingly being used in preference to open procedures.(62, 63)

1.5.3 Systemic anti-cancer therapy

A sub-set of patients may be offered adjuvant chemotherapy following a surgical resection. Current NICE guidance recommends that patients who have tumours larger than 4cm maximum diameter or N1 or N2 nodal involvement post-operatively should be offered chemotherapy.(64) This has been shown to improve 5-year survival by 4%.(65)

The survival benefit from chemotherapy alone is small and it is therefore predominantly given for the palliative management of lung cancer with a primary aim to improve quality of life or symptoms. Best estimates from a meta-analysis and systematic review suggest that for those with advanced NSCLC there is an absolute improvement in survival of 9% at 1 year compared with best supportive care, which equates to an absolute increase in median survival of 1.5 months (from 4.5 months to six months).(66, 67) However, molecular analysis and stratification of tumour type is a rapidly changing area and there are ever increasing numbers of drugs targeting specific molecular mutations under development. Currently testing for epidermal growth factor receptor (EGFR) mutations is recommended (in those with adenocarcinoma subtype) as tyrosine kinase inhibitors (TKI) are approved as first line therapy in those with advanced NSCLC who have a sensitising mutation. Erlotinib and

gefitinib are the TKIs approved for use in the UK. (68, 69) A large randomised phase 3 trial showed an increase in progression-free survival (9.7 months (95% CI 8.4-12.3) in the erlotinib group, compared with 5.2 months (95% CI 4.5-5.8) in the standard chemotherapy arm).(70) Likewise treatment with gefitinib in those with advanced NSCLC who were never or light smokers from East Asia (where there is a much higher prevalence of EGFR mutations) showed a 12 month progression-free survival of 24.9% compared with 6.7% in those treated with standard chemotherapy regimens.(71) Crizotinib, an anaplastic lymphoma kinase (ALK) and c-ros oncogene 1 (ROS1) inhibitor, has recently been licenced by NICE for the first line treatment of patients with advanced NSCLC who have a mutation in the ALK gene.(72) Rearrangements of the ALK gene are present in 3 to 5% of NSCLC, often in younger patients who have never smoked. A phase 3 study of crizotinib versus conventional chemotherapy showed an increase in median progression-free survival of almost 4 months in the crizotinib arm (10.9 months versus 7 months).(73) Newer targeted treatments include the use of immunological drug therapy in the form of checkpoint inhibitors such as nivolumab and pembrolizumab. These target programmed death receptor 1 (PD-1) which is thought to make tumour cells more aggressive and have been approved by the Food and Drug Administration (FDA) in the US to treat NSCLC. They are currently the focus of NICE technology appraisals.

Those without a sensitising mutation should receive conventional platinum-based regimens first line. Second line chemotherapy, in the form of doxetaxel, erlotinib or pemetrexed, may be offered to those who progress after initial

treatment but are still of good performance status as there is some evidence that this may improve progression-free survival.(74, 75)

1.5.4 Radiotherapy

In those who have early stage NSCLC (stage I or stage II) who are either medically inoperable or decline surgery radical radiotherapy would be the next treatment of choice. This should be delivered in the form of continuous hyperfractionated accelerated radiation therapy (CHART), which has been shown to confer a survival benefit compared with conventional radiotherapy. (76, 77) It offers a similar radiation dose but is given over 12 consecutive days rather than the 6 weeks a conventional regimen takes to complete. In addition those who have stage I peripheral tumours who are not suitable for surgery could be offered a form of highly targeted radiotherapy called stereotactic ablative radiotherapy (SABR). Radiotherapy beams are focussed from many different positions around the body, meeting at the tumour. This means that the tumour receives a high dose of radiation and the tissues around it only receive a low dose, thus lowering the risk of side effects. Small studies suggest SABR may be comparable to surgery in selected patients but a larger trial is ongoing.(78) Palliative radiotherapy has a place in the treatment of thoracic symptoms (for example haemoptysis) and bone metastases.

1.5.5 Brain metastases

The brain is a common site of metastasis in those with NSCLC, particular with adenocarcinoma subtype. Those with a solitary brain metastasis should be

offered resection using radiosurgery or conventional neurosurgery in the first instance, followed by adjuvant radiotherapy, as there is some evidence that this can confer a survival benefit as long as the extracranial disease is controlled.(79, 80) A multicentre randomised trial compared whole brain radiotherapy in combination with optimal supportive care (OSC) (including dexamethasone) with OSC alone. It showed no difference in survival or quality of life between the two groups. (81) Consequently whole brain radiotherapy is no longer recommended for the treatment of multiple cerebral metastases.

1.5.6 Small cell lung cancer

Due to the aggressive nature of small cell lung cancer (SCLC) curative treatment is rarely an option. Surgical resection may be considered in those who have the earliest stage disease (tumours ≤ 3cm with no nodal spread), but only once they have been extensively staged; with resection followed by adjuvant chemotherapy. In all other patients the aim is to commence chemotherapy as soon as possible and to offer prophylactic cranial irradiation to all who do not progress following first-line treatment.

1.5.7 Supportive/ palliative care

Given the advanced stage at diagnosis of many patients with lung cancer, early access to supportive or palliative care is key to help to manage symptoms and also to provide psychological support to patients and relatives. A study by Temel et al (82) compared early palliative care in patients with advanced lung cancer and showed an improvement in median survival in the early palliative care arm (11.9 months versus 8.9 months), alongside improvements in quality

of life, mood and reduction in symptoms. A further study also saw a small survival advantage in those with advanced malignancy who were offered earlier palliative care input.(83) The mechanisms underlying this may be complex and additional research is needed. NHS England is currently piloting enhanced supportive care in some Trusts in the UK to look at the benefits of early palliative care input in those with advanced cancer.

1.7 Thesis rationale and objectives

The aim of this thesis is to study aspects of the lung cancer care pathway, from early pre-diagnostic interactions in primary care and secondary care intervention to final treatment and outcome to try determine why the outlook for lung cancer patients in the UK is so poor.

Specific research questions:

1. To identify barriers to early diagnosis in lung cancer and to look at how best to engage those from hard to reach groups in lung cancer screening programmes.

2. To quantify patient and GP practice factors which are associated with early death (0-90 days post-diagnosis) from lung cancer in the UK, using a primary care dataset (The Health Improvement Network).

3. To identify variation in lung cancer workload and resources between Trusts and to assess whether there is an association with lower surgical resection rates and inequities in access to diagnostic tests/ specialist treatment.

4. To identify factors associated with increased likelihood of developing brain metastases following radical surgical treatment for lung cancer.

5. To validate a surgical score derived by Powell et al (84) to look at ability to predict 90 day mortality following surgical resection for lung cancer.

6. To look at variation in place of death in those with lung cancer and to identify features associated with death in acute hospital beds.

1.8 Thesis overview

A short description of the work contained in each chapter is summarised below:

Chapter 2: Description of databases used

A detailed description of the datasets used during the completion of the thesis, highlighting the limitations and strengths of each, alongside an overview of the variables used.

Chapter 3: An exploration of attitudes to risk of lung cancer and uptake of lung cancer screening in at risk adults

A mixed methods project using focus group interviews alongside questionnaires to address perceived barriers to early diagnosis in lung cancer and the issue of non-engagement in lung cancer screening programmes.

Chapter 4: What characteristics of primary care and patients are associated with early death in patients with lung cancer in the United Kingdom?

A case control study using a primary care dataset looking at predictors of early (0-90 day) mortality from lung cancer in the UK and identifying both patient and primary care features which are associated with poor prognosis.

Chapter 5: Variation in lung cancer resources and workload: results from the first national lung cancer organisational audit

A study using the National Lung Cancer Audit (NLCA) in combination with the results of a national organisational audit to look at inequities in access to

diagnostic and therapeutic interventions and assess what impact this has on surgical resection.

Chapter 6: Brain metastases following radical surgical treatment of non-small cell lung cancer: is preoperative brain imaging important?

A study using the Nottingham University Hospitals lung cancer surgical dataset to look at the incidence of brain metastases post-surgery and risk factors for development of metastases.

Chapter 7: Predicting death from surgery for lung cancer: a comparison of two scoring systems in two European countries

An overview of the risk prediction scores currently available for predicting post-operative mortality following lung cancer surgery followed by an internal and external validation of a surgical predictive score derived using data from the NLCA dataset and a comparison with the currently widely used scoring system (Thoracoscore).

Chapter 8: Place of death in patients with lung cancer: a retrospective cohort study from 2004- 2013

A descriptive study looking at place and cause of death using the NLCA with further work looking at patient, tumour and organisational factors associated with death at home versus in an acute hospital bed.

Chapter 9: Thesis summary and recommendations for future research

A summary of the studies described in the thesis with recommendations for future research/ description of ongoing studies which have arisen as a result of this thesis.

1.9 Chapter summary

This chapter summarised current UK and worldwide incidence and mortality figures for lung cancer and compared outcomes between countries. It also provided an overview of strategies to improve early diagnosis and reviewed the diagnostic pathway and treatment options available for lung cancer in the UK. It provides a background to the studies which will be described in the subsequent chapters of this thesis.

CHAPTER 2 : DATABASES USED IN THE COMPLETION OF THIS THESIS

This chapter summarises the five key datasets which were used in the completion of this thesis:

- The Health Improvement Network (THIN)
- The National Lung Cancer Audit (NLCA)
- Danish Lung Cancer Registry (DLCR)
- Hospital Episode Statistics (HES)
- Office for National Statistics (ONS)

2.1 The Health Improvement Network (THIN)

2.1.1 Background

The Health Improvement Network (THIN) is a computerised, longitudinal, research dataset which contains anonymised data collected from primary care records in the United Kingdom (UK). It was created in 2002 by collaboration between In Practice Systems (InPS) and Epidemiology and Pharmacology Information Core (EPIC), which was subsequently taken over by Cegedim Strategic Data - Medical Research UK (CSD-MR UK). InPS produce the Vision software management system which is currently used by around 2000 general practices in the UK to record all consultations and prescribing information and manage electronic patient records. All symptoms, medical diagnoses, prescriptions, investigations and results are entered into the computer system either during a consultation with a GP or following communication from secondary care. Although prospective data collection began in November 2002 there are computerised records for some patients from 1988 onwards.

2.1.2 Structure of THIN Records

THIN records are supplied in the form of five main files which are summarised in Table 2-1.

Table 2-1: Data files in THIN records

Data file	Information contained within file
Patient	Age, sex, entry date into practice, date of death
Medical	Diagnoses, symptoms, procedures, investigations, hospital referrals
Additional Health Data (AHD)	Lifestyle factors (smoking, weight, height, alcohol consumption), laboratory results and preventative healthcare (immunisations, screening)

Postcode Variable Indicators (PVI)	Information about the sub-postcode area in which the patient lives eg. ethnicity, social deprivation, environmental indices
Therapy	Drug prescriptions

Clinical data in THIN are catalogued using Read codes, which are a standardised clinical terminology used in general practice to record a wide variety of patient findings including diagnoses, procedures, investigations, demographic details and administrative tasks.(85) In addition these codes can be mapped to Office of Population Censuses and Surveys Classification of Surgical Operations and Procedures version 4 (OPCS-4), which is a coding system used to classify procedures performed within National Health Service (NHS) hospitals in the UK, and the International Statistical Classification of Diseases and Related Health Problems 10th revision (ICD-10) coding, a medical classification list from the World Health Organization (WHO). This system is complemented by a set of Additional Health Data (AHD) codes which provide a standardised system for the recording of a wide variety of clinical measurements, and by multiplex drug codes which identify prescribed medications and are linked to chapters in the British National Formulary (BNF). The codes are grouped to form "chapters" (e.g. respiratory system diseases) and include terms relating to symptoms, diagnoses, procedures, and laboratory tests.

2.1.3 Data extraction

The THIN data used for the study presented in Chapter 4 were extracted in May 2013 and contain patient records entered up to the end of January 2013. At the

time of data extraction THIN contained records for over 12.3 million patients; with 3.6 million active patients registered from 587 contributing practices.

A list of 40 Read codes (Appendix A) used to determine diagnoses of lung cancer were compiled by Emma O'Dowd (EOD). These were used by Jack Gibson (Division of Epidemiology and Public Health, University of Nottingham) to extract records for all patients with one or more of these Read codes. Previous validation work using THIN as a source of lung cancer data used an arbitrary earliest date of diagnosis of lung cancer as 1st January 2000 and this was adopted for this thesis also.(86) To ensure that these were incident rather than prevalent cases of lung cancer we excluded patients who registered less than 12 months prior to their diagnosis date. A variety of data cleaning measures were then conducted by EOD to ensure that any patients with missing or incongruous records were excluded. These are described in greater detail in the methods section of Chapter 4.

The extracted THIN dataset contained a total of 39559 incident cases of lung cancer, of which 11778 were excluded as their date of diagnosis was prior to 1st January 2000.

2.1.4 Overview of additional THIN variables and files used in this thesis

Postcode Variable Indicators

Townsend Score

The Townsend deprivation score is a widely adopted measure of social deprivation. It is calculated using four variables obtained from Census records;

number of households without a car, overcrowded households, households not owner-occupied and persons unemployed.(87) These are mapped to Lower Layer Super Output Areas (LSOA) areas, which typically contain a population of around 1500. An individual score is derived for each LSOA which are subsequently divided into quintiles for the purposes of analysis; where 5 is the most deprived and 1 the most affluent grouping.

Urbanrural

This variable uses Rural-Urban data from the Office of National Statistics (ONS) which divides Super Output Areas (SOAs) into three main groupings based on building and population density; urban (population over 10,000), town/ fringe and village, hamlet and isolated dwellings (rural).

Patient file

Famnum

This is a household identifier which can be used to identify individuals living at the same address. The variable refers to a single address rather than a dwelling which means that those living in flats or apartments within the same building may have the same household identifier, despite not actually comprising one household.

Consultation files

These data are linked to medical and AHD records and provide information about the type of consultation (home visit, telephone call, letter/ secondary care result or administrative entry for example), duration of consultation and a staff identifier.

Additional Health Data (AHD)

Smoking records

Read codes and detailed methods to define smoking status and quantity smoked have previously been derived and validated by Barbara Iyen-Omofoman as part of her PhD thesis (86) and were adopted for the study presented in Chapter 4. These codes are summarised in Appendix A. Smoking status was defined as current, ex or never using records prior to the lung cancer diagnosis date. Where there were multiple smoking records the most recent record was used, but excluding the 6 months before the diagnosis date, to exclude changes related to symptomatic disease.

Experian's MOSAIC Public Sector™ variable

These data are provided linked to THIN records. The Mosaic Public Sector™ classification uses over 400 variables to classify households into 11 groups based on demographics, behaviour, consumer values, consumption patterns, lifestyle, education and social and health-related attitudes, which are then further subdivided into 61 subgroups. (88) Data are extracted from a variety of records including the Census, Experian Lifestyle survey, Electoral Register and consumer credit databases. The initial UK version was based at the postcode level, covering around 20 properties with the same code. More recent versions have been developed at an individual household level and offer more accurate classification. Previous studies have used Mosaic Public Sector™ data to look at disparities in lung cancer incidence(89), smoking prevalence (90) and drinking behaviours (91) between different groupings. A summary of the 11 main

groupings from the 2004 classification which were used in this thesis are provided in Table 2-2.

Table 2-2: Mosaic Public Sector™ Groupings

Mosaic Public Sector™ Group	Description	Percentage of UK population
A (Symbols of success)	Career professionals living in sought-after locations	9.62%
B (Happy families)	Younger families living in newer homes	10.76%
C (Suburban comfort)	Older families living in suburbia	15.10%
D (Ties of community)	Close-knit, inner city and manufacturing town communities	16.04%
E (Urban intelligence)	Educated, young, single people living in areas of transient populations	7.19%
F (Welfare borderline)	People living in social housing with uncertain employment in deprived areas	6.43%
G (Municipal dependency)	Low income families living in estate-based social housing	6.71%
H (Blue collar enterprise)	Upwardly mobile families living in homes bought from social landlords	11.01%
I (Twilight subsistence)	Older people living in social housing with high care needs	3.88%
J (Grey perspectives)	Independent older people with relatively active lifestyles	7.88%
K (Rural isolation)	People living in rural areas far from Urbanisation	5.39%

2.1.5 Strengths and limitations

General practice data has a variety of strengths and limitations as a research tool. One main advantage is the size of the database which, even for relatively rare conditions, allows a large number of cases to be identified. Although some studies suggest there is a slight overrepresentation from more affluent practices, THIN has previously been validated for multiple major comorbid

illnesses and exposures. (89, 92-98) In addition work has confirmed that the validity of a lung cancer diagnosis in primary care databases is good and representative of National Cancer Registry data.(89, 99) Data in THIN are prospectively recorded at the time of consultation which minimises reporting and recall bias, however the information relies on accurate coding and timely data entry in primary care. To minimise errors related to this we only used data entered by practices after the practice met the THIN data quality and completeness standard. This comprises a regular audit of the completeness of recording of data related to a group of key conditions and exposures against national figures.(100)

Data recorded in THIN are not collected primarily for research but to allow clinical management of the patient. This may mean that recording, particularly in some areas, is selective rather than comprehensive, (101) as GPs may record only the information that they require or which they consider relevant to the patients' condition at the time of consultation. Since the introduction of the Quality and Outcomes Framework (QOF) as part of the new GP contract in 2004 there are financial incentives to ensure that records are complete and accurate which has reduced the proportion of missing data. Comprehensive records are reliant on patients consulting their GP in the first place however. Additionally detailed information on cancer such as stage at diagnosis are not routinely recorded in primary care records.

Patients are given a unique identifier in THIN which contains a practice identification code and a patient identification code which is unique per

practice. There is no mechanism of identifying patients who transfer from one THIN practice to another so it is possible that some individuals may appear more than once within the database. However, given that the study presented in Chapter 4 concerns incident diagnoses this is unlikely to be a major concern.

2.1.6 Ethical approval

Ethical approval for the study was provided by the Cegedim Strategic Data Medical Research Scientific Review Committee in June 2013 (Ref 13-015).

2.2 The National Lung Cancer Audit (NLCA)

2.2.1 Background

The National Lung Cancer Audit (NLCA) is a prospective database that collates information provided by 157 English NHS hospitals on cases of primary lung cancer and mesothelioma. It is commissioned by the Healthcare Quality Improvement Partnership (HQIP). It was set up in response to concerns about outcomes for patients with lung cancer in the UK and has been collecting data since 2004. Patient data are entered onto an online form at each individual trust and may be entered or updated at any point in the patient pathway by any member of staff. An annual report is produced to summarise outcomes and each trust receives an individual breakdown of performance for a series of predefined targets with the primary aim to drive improvements in care.

Data entry is voluntary rather than mandatory but the case ascertainment from 2009 onwards is thought to be in excess of 97% and the 2014 NLCA annual report suggested that almost 100% of cases of lung cancer presenting to secondary care in England were registered.(102)

At the time these data were extracted NLCA records were collected and held by the Health and Social Care Information Centre (HSCIC) but since January 2015 the new Audit providers are the Royal College of Physicians (RCP).

2.2.2 Data extraction

The data used for the studies presented in Chapters 5, 7 and 8 were extracted in July 2013. This raw data file comprised records for 178 428 patients with

primary lung cancer or mesothelioma who were first seen in England between 1st January 2004 and 31st December 2011. All records were anonymised.

2.2.3 Overview of variables used in this thesis

The NLCA collects information on patient demographics, performance status, lung function, dates of diagnosis, referral and investigations, tumour histology and stage. A summary of the key variables is provided below.

Patient data

Lung function

Lung function is recorded both as percentage predicted forced expiratory volume in 1 second (FEV1) and also FEV1 absolute volume in litres. Previous work using the NLCA excluded any measurements of <10% or >150% as they were felt to represent possible data entry errors and this approach was adopted for the study presented in Chapter 7 also.(103) Although completeness of these fields is improving there remains a substantial proportion of missing data, particularly for earlier years of the NLCA.

Performance status

The NLCA uses the Eastern Cooperative Oncology Group (ECOG) definition of performance status which is summarised in Table 2-3. This is a subjective marker which is used to try to quantify general well-being and ability to carry out activities of daily life and ranges from 0-5. (104)

Table 2-3: Eastern Cooperative Oncology Group performance status

Performance status	Description
0	Asymptomatic; Fully active, able to carry out all pre-disease activities without restriction
1	Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature. For example, light housework, office work
2	Ambulatory and capable of all self-care but unable to carry out any work activities. Up and about more than 50% of waking hours
3	Capable of only limited self-care, confined to bed or chair 50% or more of waking hours
4	Completely disabled. Cannot carry out any self-care. Totally confined to bed or chair
5	Dead

Referral information

Source of referral

This refers to the source of referral to the lung cancer team and comprises two emergency routes (following an emergency admission or following an accident and emergency (A&E) department attendance) and seven semi-elective routes which include GP referral and referral from another secondary care provider or allied health professional.

Diagnosis date (start date)

The NLCA adopts the European Network of Cancer Registries (ENCR) hierarchy for determining date of diagnosis. These rules state that the date of histological/ cytological confirmation is used in the first instance, followed by radiological or clinical diagnosis date, date of death (if malignancy is confirmed) or date of admission to hospital or first outpatient consultation date due to the malignancy if no other information is available. The date of diagnosis, where

present, was used as the start date. Where this field was missing the approach developed by Anna Rich to derive a surrogate diagnosis date as part of her work validating the NLCA was used.(105) An alternative available date (in order of priority) was used and the median difference between this date and the diagnosis date for the whole NLCA cohort was calculated and interpolated to produce a diagnosis date. These dates (in order) were as follows, with the median difference presented in brackets:

- Date of first NHS Trust appointment (+5 days)
- Date of referral to the lung cancer team (+ 18 days)
- Date of multidisciplinary team (MDT) meeting (- 9 days)

Patients in whom a surrogate date of diagnosis could not be ascertained were excluded from further analysis.

End date

In order to conduct survival analyses all patients had to have an end date. This was generated using the date of death or the date that Office of National Statistics (ONS) records were last accessed (18th March 2013) in those in whom there were no death records.

Tumour data

Histological subtype

The NLCA uses the Systematised Nomenclature of Medicine (SNOMed) coding to define histological subtype and these are then categorised as non-small cell lung cancer (NSCLC), small cell lung cancer (SCLC), carcinoid or mesothelioma. This is summarised in Table 2-4.

Table 2-4: Systematised Nomenclature of Medicine (SNOMed) Codes and classification of histology in the NLCA

SNOMed code	Description	NLCA classification
M 8010/2	Carcinoma in situ	NSCLC
M 8041/3	Small cell carcinoma	SCLC
M 8046/3	Non-small cell carcinoma (includes adenosquamous carcinoma)	NSCLC
M 8070/3	Squamous cell carcinoma NOS	NSCLC
M 8140/3	Adenocarcinoma NOS (without alveolar cell features)	NSCLC
M 8250/3	Broncho-alveolar cell carcinoma	NSCLC
M 8012/3	Large cell carcinoma NOS	NSCLC
M 8020/3	Large cell- undifferentiated	NSCLC
M 8013/3	Large cell neuroendocrine	NSCLC
M 8240/3	Carcinoid tumour NOS (includes atypical carcinoid)	Carcinoid
M 8980/3	Carcinosarcoma NOS	NSCLC
M 9050/3	Malignant mesothelioma NOS	Mesothelioma
M 9052/3	Mesothelioma (epithelioid)	Mesothelioma
M 9051/3	Mesothelioma (sarcomatoid)	Mesothelioma
M 8940/3	Mixed tumour (malignant)	NSCLC
M 9999/9	Other	NSCLC

Where there were records for both pre and post-operative histology the pre-operative histology was prioritised over post-operative histology for the studies presented in Chapters 5 and 7 as they focussed on pre-operative assessment and management of the patient. In practice these records rarely differed. As NSCLC is the most common subtype, in the absence of ICD-10 coding for mesothelioma, those with missing histological subtype are presumed to have NSCLC for the purposes of the Audit. This may lead to a small number of patients, with SCLC for instance, being misclassified.

Tumour stage

The NLCA contains records for pre-treatment and, if relevant post-treatment stage. Again for the purpose of the studies presented in Chapters 5 and 7 pre-

treatment stage was used in priority to post-treatment stage, where both were provided, for the same reason discussed above.

- Non-small cell lung cancer (NSCLC)

The Union for International Cancer Control (UICC) Tumour Node Metastases (TNM) classification is used to record stage. (106) Revision 6 and revision 7 produced by the International Association for the Study of Lung Cancer (IASLC) are both used in the NLCA depending on when the data were collected. The 7th revision was published in 2009 and from 2010 onwards Trusts were able to enter stage according to the 7th revision. It is not possible to convert between the 6th or 7th version but a field denoting the staging system used is available and consequently both systems are used for the staging information contained within this thesis.

- Small cell lung cancer (SCLC)

Staging has been traditionally been performed according to a two-stage system developed by the Veteran's Administration Lung Cancer Study Group (VALSG) in the USA which divides patients into limited and extensive disease. The IASLC now advocates use of the 7th version of the UICC TNM staging system for SCLC in addition to NSCLC but the majority of records in the NLCA still use the VALSG classification. For the purposes of this thesis those patients in whom stage was recorded using TNM staging were converted to the VALSG classification; denoted as limited (T1-4, N0-3, M0) or extensive (M1a/b) stage.

Surgical records

Although the NLCA contains several fields recording surgical procedure date and type previous validation work has suggested that these fields may record some patients who did not actually undergo surgery and miss some patients who did. (107) Audit data is provided linked to Hospital Episode Statistics (HES) records (discussed in section 2.4) which are a more accurate method of identifying those who undergo surgery for lung cancer and were used in preference to the NLCA records for this thesis.

2.2.4 Strengths and limitations

One of the key strengths of the NLCA is the size of the database and high levels of case ascertainment. In addition it has previously been validated as a reliable source of UK lung cancer data. (108)

As data entry occurs mostly following lung cancer MDT meetings the NLCA tends to record only those patients who are referred to secondary care, so it may miss a small proportion of patients who are not registered or referred to an MDT or who have a death certificate only diagnosis who may be captured by the Cancer Registry. Unlike Registry data however, functional and physiological information such as performance status and lung function are captured by the NLCA giving a more comprehensive overview.

Missing data remain a problem, although the proportion of fields which are incomplete are decreasing over time. Co-morbidity information in particular is poorly recorded by NLCA, however a link to HES data (section 2.4) allows a measure of co-morbidity to be derived. At the time these data were extracted

all records were entered manually which means that some errors in data entry may have occurred at this point, although these are likely to be random so should not affect the validity of the results.

Each patient record gives a snapshot of a single point in time (usually the time when they are first seen), so the NLCA will not reflect changes in the patient's condition. Although the record may be updated at any point following diagnosis only one performance status or stage may be recorded. This is particularly relevant for the study presented in Chapter 8, as some patients survived for many months or years after diagnosis so their stage and performance status at the end of life is unlikely to be the same as that when initially diagnosed.

2.2.5 Ethics and data sharing agreements

The Healthcare Quality Improvement Partnership (HQIP) approved the use of the National Lung Cancer Audit for this work and a data sharing agreement was completed for use of the data linked to HES and ONS records (reference: RU943-R1).

2.3 Danish Lung Cancer Registry (DLCR)

2.3.1 Background

The Danish Lung Cancer Registry (DLCR) was created in 2000 with an aim to drive improvements in lung cancer care in Denmark. Data describing diagnostic procedures, staging, surgical procedures, complications, oncologic treatment, and survival are registered from the 37 hospital departments which treat lung cancer in Denmark. Since 2005 more than 90% of all Danish lung cancer patients have been included in the database. Data completeness is determined through comparison with the Danish Cancer Registry containing all Danish cancers. DLCR data are linked with data from national databases: demographic information is retrieved from the Central Population Register, pathology information from the National Pathology Registry and comorbidity data from the National Hospital Register.(109)

An annual report comprising a number of key outcome measures is produced but individual departments may check their own information on the online programme each day (the database updates every 24 hours).

2.3.2 Data extraction

These data were only used for the external validation described in Chapter 7. Data extraction was conducted by Margreet Lüchtenborg (ML) (Department of Cancer Epidemiology & Population Health, King's College London). Initial data cleaning was performed by ML and EOD provided statistical analysis files for the study presented in Chapter 7. EOD did not have access to the raw data files as the terms of the data sharing agreement only allowed ML to use these.

2.3.3 Strengths and limitations

A key advantage of the DLCR is the size and level of data completeness and capture. Validation work has confirmed that the data are of high quality and representative.(110) Similar to the NLCA patients are recorded in the DLCR after attending secondary care, so a small proportion of patients who do not follow this route may be missed. Most data entry is automated and so errors are less likely to occur although missing data remain a problem. Data completeness is improving however and in the most recent records is very high.

2.4 Hospital Episode Statistics (HES)

2.4.1 Background

The Hospital Episode Statistics (HES) database records details of all admissions, outpatient appointments and A&E attendances at NHS hospitals in England. Submission of HES records is mandatory, occurs on a monthly basis and allows hospitals to be paid for the care they deliver. Records have been collected since 1987 and are collated by the HSCIC. Those records from 1997 onwards are felt to be of sufficient completeness and quality to be used for research.

Within an admission, the patient stay is divided into episodes. Each episode represents care delivered by a single consultant so one patient may have multiple episodes during a single admission. For each episode, a patient can have up to 20 diagnoses recorded, using ICD-10 diagnostic codes, and up to 24 procedures using OPCS-4 codes. Data are grouped by financial year, so one patient may have many rows of data collected for a single year.

Although HES records A&E and outpatient attendances the linkage process described below only concerns inpatient HES records as the other data were not available.

2.4.2 Data extraction and linkage

The dataset used for the studies presented in Chapters 5, 7 and 8 was extracted in July 2013 and comprises HES data for the financial years 1997/98 to 2011/12 inclusive. Records are linked by staff at the HSCIC to the NLCA using NHS numbers, with a second check to ensure that dates of birth, post codes and sex

match. These data are then pseudonymised to ensure that the researchers do not have access to any identifiable fields.

2.4.3 Variables used in this thesis

Linked NLCA-HES records are used to define two variables for this thesis which are described below.

Charlson co-morbidity score

The Charlson co-morbidity index was derived in 1984 to predict the ten-year mortality for patients with a list of 19 co-morbid conditions.(111) Each condition is assigned a score of 1, 2, 3, or 6, depending on the risk of dying associated with each one. It has been widely adopted as a tool to measure co-morbidity in research studies. An updated version has been produced to reflect the advances in the effectiveness of treatment and chronic disease management, which reassigns weighting of conditions such as HIV and AIDS which are no longer rapidly fatal.(112) This version is less well validated so the original Charlson Index was used for the studies presented in this thesis as the number of patients with lung cancer and HIV is negligible so would be unlikely to materially skew the results. A summary of the weightings and conditions included is provided in Table 2-5.

Clinical coders enter a primary diagnosis or diagnoses and also a list of co-morbidities for each patient episode in HES. ICD-10 codes (Appendix A) were used to identify relevant diagnoses which contribute to the Charlson score and these were given the appropriate weighting (Table 2-5) and summed to produce a single value for each patient. As all patients had lung cancer this was not included in the 'any tumour' section.

Table 2-5: Charlson Co-morbidity Index

Charlson Index weighting	Condition
1	Myocardial infarction Congestive cardiac failure Peripheral vascular disease Cerebrovascular disease Dementia Chronic pulmonary disease Connective tissue disease Ulcer disease Mild liver disease Diabetes
2	Hemiplegia Moderate or severe renal disease Diabetes with end organ damage Any tumour Leukaemia Lymphoma
3	Moderate or severe liver disease
6	Metastatic solid tumour Acquired Immune Deficiency Syndrome

Surgical procedure type

Surgical procedures associated with an inpatient episode are recorded in HES using OPCS-4 codes, alongside a date of procedure. These are required for NHS Trusts to bill Primary Care Trusts (PCTs) for the service provided and validation work has suggested that they are a more reliable source of surgical data than using the NLCA record alone.(107) A list of agreed codes used to define curative surgery for lung cancer which were used in this thesis are summarised in Appendix A. These codes were used to identify any HES records with procedure dates between 1st January 2004 and 31st March 2012. One patient may have multiple procedures during a single episode or multiple episodes and if this were the case the most extensive procedure was given priority, followed by the procedure with the latest date. In order of priority these procedures were

pneumonectomy, bi-lobectomy, lobectomy, segmentectomy/ sleeve/ wedge or other. To try to exclude data entry errors and to ensure that the procedure pertained to the primary lung cancer diagnosis records were excluded if the procedure date was greater than 3 months before or more than 6 months after the NLCA start date in line with the validation work.(107)

2.4.4 Strengths and limitations

Trusts are incentivised to ensure that their HES records are as comprehensive as possible as they are the means by which they charge for service provision. However data are entered by clinical coders manually using clinical notes which are normally inadequate for this purpose in that they are not structured or standardised and consequently errors and omissions may occur.

The HES data used for this thesis rely on a patient having had an admission to hospital prior to their lung cancer diagnosis. Those patients who have never been admitted would have a Charlson co-morbidity score recorded as 0 even though they may have conditions (for example diabetes mellitus) which are managed entirely in primary care, thus resulting in an underestimation of the burden of comorbidity overall.

2.5 Office for National Statistics (ONS)

2.5.1 Background

The Office for National Statistics (ONS) is responsible for collecting and publishing statistics related to the economy, population and society in the UK. As part of this role it collects information on date, cause and place of death from civil registration records.

2.5.2 Data extraction

The HSCIC used NHS numbers and the method described in section 2.4.2 to link ONS records to HES. ONS records were last accessed on 18th March 2013 for the studies included in this thesis. Any patients who did not have a date of death were assumed to be alive, so were censored on this date for the purposes of survival analysis.

2.5.3 Variables used in this thesis

Date of death

This is obtained from the Medical Certificate of Cause of Death (MCCD), completed by a medical practitioner when the death is certified.

Place of death

Individual places of death are recorded by ONS and for the purposes of this thesis were grouped as home, acute hospital, residential/nursing home, hospice, community/rehabilitation hospital or elsewhere (which contained prisons and mental health establishments).

Cause of death

Cause of death is obtained from the MCCD. It is coded by ONS using the criteria set out in the 10th revision of the International classification of diseases (ICD-10) which uses a hierarchical approach to determine a single underlying cause of death.(113) For the majority of deaths the underlying cause is coded automatically using software, while the remainder are coded manually by experienced coders. The accuracy of the coding is checked routinely.

2.5.4 Strengths and limitations

The Births and Deaths Registration Act (1836) made it a legal requirement for all deaths in the UK to be registered so data completeness is high and these data are updated constantly. Deaths in England should be registered within 5 days of the date of death. There are, however, a number of situations when the registration of a death will be delayed; for example, if the death is referred to a coroner which may lead to some patients being incorrectly assumed to be alive on the censor date.

Data are first entered manually and there are validation checks to help ensure the details entered are correct. The registrar will also ask the informant to check that the information entered is correct, before the registration is submitted. Diagnostic tests are then performed by ONS and any issues identified are resolved through contact with individual registrars. Once on the ONS database, data are passed through a series of automatic validation processes which highlight any inconsistencies.

2.6 Statistical Analysis

All statistical analyses were conducted using Stata MP V.12 (StataCorp, Texas, USA). Unless otherwise stated, I conducted all the data management and extraction of the data.

2.7 Funding

Funding was provided by the Roy Castle Lung Cancer Foundation, grant number RB08F1.

2.8 Chapter Summary

In this chapter I have described five sources of routinely collected UK clinical data which have been used to look at diagnosis, management and outcomes for patients with lung cancer. The study presented in Chapter 4 uses primary care data obtained from THIN and Chapters 5, 7 and 8 use the linked NLCA-HES-ONS dataset.

CHAPTER 3 : AN EXPLORATION OF ATTITUDES TO RISK OF LUNG CANCER AND UPTAKE OF LUNG CANCER SCREENING IN AT RISK ADULTS

This chapter summarises the results of a mixed methods study using focus groups and questionnaires to explore barriers to early diagnosis in lung cancer and to understand possible reasons for low participation in a lung cancer screening programme in the United Kingdom.

3.1 Introduction

3.1.1 Background and rationale

As discussed in Chapter 1 uptake rates into a national lung cancer screening programme are an important consideration, as low uptake would render it non-viable.(52) Uptake for breast, cervical and colorectal screening are 73%, 80% and 61% respectively in the United Kingdom (UK).(114-117) However the colorectal screening programme has shown a clear socioeconomic divide in the uptake of screening; with only 35% of those in the most deprived group participating compared to 61% in the least deprived areas.(118) Similar findings have been shown previously in other areas of health care utilisation and screening programme uptake.(119) The reasons for this are complex and likely to be linked to a variety of health beliefs, health literacy, perceived cancer risk, fatalism towards a cancer diagnosis and acceptability of the test.(120-123) Lung cancer screening targets a high risk subgroup of the population, comprising current and ex-smokers, of whom many are from the most socioeconomically deprived groups,(53) so one could postulate that uptake in this group may again be low. There are also data to suggest that smokers view screening in a nihilistic way and perceive early detection to be of limited use and, as such, are less likely to consider screening participation.(58) Recruitment to and participation in lung cancer screening trials to date has tended to comprise more former smokers from more well educated backgrounds.(34, 53, 124) Smoking rates and lung cancer incidence are highest in more socially deprived areas and lung cancer survival is worst in this group. (125) An

understanding of the key barriers to engagement with lung cancer screening is therefore vital prior to implementation of a national screening programme.

3.1.2 Aim of this chapter

The overall aims are to identify perceived barriers to early diagnosis in lung cancer and also to provide knowledge about non-engagement in lung cancer screening programmes. This can be used to improve participation in smokers and ex-smokers when screening is implemented in the UK, with particular focus on those from more deprived backgrounds who are more difficult to engage and recruit.

Specific objectives are:

- To explore current and ex-smokers' perceived barriers towards early diagnosis of lung cancer.
- To explore awareness of and participation in other cancer screening programmes.
- To understand attitudes towards participation in lung cancer screening if it was implemented in the UK and explore reasons for non-participation.

3.2 Methods

3.2.1 Study design and location

The initial plan was to conduct focus groups of eligible participants within deprived communities in Nottingham, although due to problems recruiting the area was extended to include Leicester (a neighbouring city with similar levels of deprivation). Areas with high levels of social deprivation and high smoking prevalence were targeted to try to include participants who may be less likely to engage with traditional research methods. Qualitative research methods were chosen for this study as they allow exploration of perceptions, beliefs and interpretations of individuals that shape decisions and behaviour, rather than attributing cause and effect.(126)

3.2.2 Recruitment strategies

Participants were recruited using community leaders and local contacts in deprived areas of Nottingham City and Leicester. Posters and information leaflets were also distributed to community centres, social clubs and local shops/ meeting rooms. Those who were interested in participating were able to express their interest by contacting the researcher directly (by phone or email listed on the poster), contacting a community leader who would inform the research team or by filling in a response slip and placing it into a post-box in the local community centre or proposed venue with their contact details. They were then contacted to discuss the study in more detail and a participant information sheet was given to them (Appendix B). A suitable date and time for the focus group in the local community was then agreed and an informed consent form was signed immediately before the focus group was conducted.

The research team provided light refreshments (tea, coffee, juice and biscuits) for the participants in the focus groups and in addition remuneration of £20 (shopping voucher) was provided to each participant.

Eligibility criteria for recruitment were any adult aged 40 years or older who was a current or ex-smoker (a pack year history was not required). Although the National Lung Screening Trial (NLST) included those aged 55-75 years(42) and the United Kingdom Lung Screen (UKLS)(41) and Nederlands-Leuvens Longkanker Screenings Onderzoek (NELSON)(127) included those aged 50-75 years only it was felt that it was important to obtain the views of adults who may be eligible for a screening programme in the future should one be implemented.

3.2.3 Data collection

A semi-structured focus group guide was developed to try to elicit participant views on lung cancer, barriers to early diagnosis and attitudes towards cancer screening in general and more specific views around lung cancer screening (Appendix B). Focus groups were conducted face-to-face by two researchers in designated centres in the local community and were digitally audio-recorded. Participants were informed that data would be anonymised, treated confidentially and that they were free to withdraw at any point during the focus group, if they so wished.

3.2.4 Questionnaires

As recruitment to the focus groups proved very difficult the decision was made to adopt a pragmatic mixed-methods approach.(128) Preliminary analysis of the first three focus groups facilitated development of questionnaires to supplement the information already obtained and to check whether it was representative. Purposive sampling was used to try to obtain a maximum number of views from a cross-section of the deprived communities. The same inclusion criteria as the focus groups were used to identify eligible respondents. Using the questionnaires it was possible to target working people, particularly men and also older people (especially those with mobility restrictions) who were less likely to participate in the focus groups. A total of 10 questions were asked; four demographic questions (age, sex, smoking status and quantity smoked), alongside some closed and open ended questions about previous screening programme participation, experiences of lung cancer, feelings about smoking stigma and blame, preferred location of any screening programme and willingness to participate. Some quotations representing themes from the focus groups were provided and participants were asked to indicate agreement with each item to check the representativeness of the themes. The majority of questionnaires were paper-based but some participants requested an email copy preferentially. They were designed to be self-completed at a time convenient to the participant. Community centres and social clubs in deprived areas were again used to promote the questionnaires and community leaders distributed some to local residents. In order to try to maximise the number of responses members of a lunch club in one community in North

Nottinghamshire and also manual workers at a local factory in Derbyshire were also provided with questionnaires and asked to return them. Completed questionnaires were collected in person by community leaders, returned by email to the researcher or placed in a collection box located in community centres/ hubs for collection by the researchers. A copy of the questionnaire is provided in Appendix B.

3.2.5 Data analysis

3.2.5.1 Focus groups

Recordings were transcribed verbatim by an external specialist transcription company, approved by the University of Nottingham. Following receipt of the transcripts all personal identifiers were removed and the transcripts were checked for accuracy. Each participant was assigned a unique code (eg.P4,47,S,F), that identified participant number (P1-13), age, smoking status (S-smoker or Ex-ex-smoker) and sex (M-male, F-female). Data generated from the focus groups were analysed using the Framework approach(129) to examine themes generated. Transcripts were read and re-read several times and annotated where initial codes were generated, resulting in an analytical framework of key themes and sub-themes. Transcripts were double coded by two researchers to ensure the analytical framework was valid. Themes and sub-themes were discussed between the researchers, allowing clarification of the final framework and data were then indexed. Finally, data were charted according to each theme to synthesise the data and aid interpretation. NVivo 11 (QSR International Ltd, Melbourne, Australia) was used as a data management tool.

3.2.5.2 Questionnaires

Data from the questionnaires were analysed once all had been returned to the researchers. Demographic data were charted and the proportion responding positively or negatively to each closed question was determined. The open-ended questions designed to try to glean any additional ideas and opinions were not completed by respondents and therefore additional thematic coding and analysis was not needed.

3.2.6 Research team

The research team comprised myself and two qualitative researchers who conducted the focus groups and also coded the themes and sub-themes; alongside a group of community leaders who assisted in the recruitment to focus groups and distribution of questionnaires.

3.2.7 Ethical approval

Ethical approval for the study was granted by the University of Nottingham School of Medicine ethics committee in August 2014 (reference I14082014 SoM EPH).

3.3 Results

3.3.1 Participant demographics and recruitment

Three focus groups and one interview were conducted over a period of 8 months from February 2015 to October 2015. A total of 13 participants took part. Groups 1, 2 and 4 took place within 3 separate deprived inner city estates in Nottingham with high smoking prevalence (Bulwell, Aspley and Strelley), with group 3 comprising participants from Leicester (approximately 30 miles south of Nottingham). For each focus group between 10 and 12 eligible participants were approached and 8 agreed to take part in each group. Despite multiple reminders prior to the date and remuneration offered to those who agreed to take part only 4 participants turned up to focus groups 1, 2 and 3. In addition, the first focus group was rearranged 3 times prior to taking place. On a further four occasions no one turned up to participate in a focus group despite 6-8 participants agreeing to take part in principle prior to the date and having received telephone/ email reminders. These four failed attempts were from two different deprived inner city estates. Only one participant turned up for focus group 4 and was happy to take part hence a one-to-one interview was conducted. A further 56 people completed questionnaires (of 100 distributed in total). Questionnaires were returned by participants from the two deprived communities in Nottingham in whom focus groups were attempted but did not succeed, a group from Leicester, manual workers from a factory in Derbyshire and also a group from Mansfield (15 miles north of Nottingham). Demographics of those participating in the focus groups and questionnaires is summarised in Table 3-1.

Focus groups lasted between 55 and 79 minutes. Despite conducting fewer focus groups than originally intended saturation of themes was achieved by focus group 4 (interview), with no new subthemes identified. Men were less well represented in the focus groups, with only 3 participating (2 of whom accompanied their female partners). Likewise those from the oldest age group (> 70 years) were more difficult to recruit. Through utilising the questionnaires opinions from more men and those aged over 70 years were obtained. There were also more heavy smokers (> 30 cigarettes/ day) responding to the questionnaires.

Table 3-1: Demographic features of participants

	Focus groups N= 13 n (%)	**Questionnaires** N= 56 n (%)
Sex		
Male	3 (23)	27 (48)
Female	10 (77)	29 (52)
Age group (years)		
<50	8 (62)	15 (27)
51-60	2 (15)	19 (34)
61-70	2 (15)	11 (20)
>70	1 (8)	11 (20)
Smoking status		
Current	9 (69)	34 (61)
Ex	4 (31)	22 (39)
Number smoked in day *		
<10	3 (23)	12 (21)
11-20	9 (69)	29 (52)
21-30	1 (8)	5 (9)
>30	0	8 (14)
Previous screening participation **		
Cervical	6	27
Breast	3	24
Bowel	2	6

* Where answered **Percentages not given as may participate in multiple programmes/ not be eligible for recruitment to screening programme

A discussion of the results from the focus groups will be presented first, with a summary of the supplementary data obtained from the questionnaires described subsequently.

3.3.2 Key themes derived from focus groups

Six core themes with corresponding sub-themes were identified regarding lung cancer screening: accessibility/ practical barriers, perceived positives, perceived negatives, stigma and societal perceptions of smoking, emotional barriers and ideas around education and awareness. These are summarised in Table 3-2.

Table 3-2: Key themes and sub-themes identified from focus groups

Attitudes towards lung cancer screening	Accessibility/ practical barriers	Convenience
		Difficulties accessing healthcare
		Lack of time
		Location of screening
		Method of invitation
		Distrust/ fear of healthcare
	Perceived positives	Experiences of cancer
		Positive experiences of healthcare
		Support for screening
	Perceived negatives	Experiences of cancer
		Lack of perceived benefit
		Perceived dangers of screening
	Stigma and societal perceptions of smoking	
	Emotional barriers	Avoid diagnosis/ fear
		Denial
		"Nanny State"
	Education/ awareness	Awareness campaigns
		Community engagement
		Screening education/ participation

3.3.2.1 Accessibility/ practical barriers

Several participants mentioned that convenience was very important in determining willingness to participate. One community had access to a mobile dentist and another multiple mobile and drop in sessions (dental care, practical

computer sessions and instruction on writing a curriculum vitae for example) in the local community centre, which were well attended. Previous difficulties accessing healthcare and a perceived lack of time were mentioned as reasons for potential non-participation in a screening programme. In addition, waiting times, parking costs and the negative association with healthcare professionals was seen as a reason against a lung cancer screening programme taking place in a hospital setting. Many participants commented on the method of invitation as a key factor in the ability to engage and enrol suitable people in a screening programme. Community workers were viewed as a more trustworthy and non-threatening way of informing participants about the importance of screening and encouraging participation. Several participants mentioned that for some literacy may be an issue and therefore if letters are sent they often get put straight into the bin if no one can read them. One participant mentioned that a bowel screening programme letter was received by a friend but the instructions were too complicated for him to understand so he simply threw it away. If written invitations were to be used the tone and wording of these letters were seen as important factors. In addition distrust and fear of healthcare settings and professionals was cited by some as a reason why they may not consider being screened. There was suspicion that healthcare professionals knew “more than… they let on” (P1, 48, S, F) and even that there was “a medicine out there that's been proven to cure cancer” (P3, 47, Ex, M) but would not be offered because of cost. Quotes summarising the sub-themes around accessibility and practical barriers are presented in Table 3-3.

Table 3-3: Quotes illustrating accessibility/ practical barriers to lung cancer screening

Accessibility/ practical barriers	Participant
Convenience	
"We've got a mobile dentist that comes here and that's what we do, they don't do appointments, everyone just comes"	P2, 55, S, F
"If you've got to access complicated appointments and they do tend to be complicated at GP surgeries these days don't they……. then the impetus goes before it happens, and mixed with the not really wanting to be told off"	P9, 44, Ex, M
"I think it is just more convenience for people. I do think drop in would be better. I think if it's on people's doorsteps they'll use it"	P13, 30, S , F
Difficulties accessing healthcare	
"If I couldn't get through I'm afraid I would be minded to not bother and leave it"	P6, 68, S, F
Lack of time	
"It's just that I've never got five minutes to blinkin' do it!"	P4, 47, S, F
"Family life takes priority"	P1, 48, S, F
"… Not bothered, aint got time, got to do this, got to do that"	P13, 30, S , F
Location of screening	
"I think you'd probably have a greater effect with mobile units. If you set up in certain areas. I think they'd probably be more reluctant to go the hospitals"	P3, 47, Ex, M
"With hospital it's the length of time waiting, the cost of parking. That's why people won't go, waiting and price"	P4, 47, S, F
"I hate waiting. Plus the cost of parking, I mean it's astronomical. That's what puts a lot of people off. Plus if they've got to travel from a distance, buses. If you can come to them or in that community where they live you'll get a lot more response. They're prepared to do that"	P2, 55, S, F
"Somewhere neutral…..like community centre things……..away from the association with all the medical professionals that are pointing the finger"	P11, 43, Ex, F
"If it's there on people's doorsteps I think it would be used more"	P13, 30, S , F
Method of invitation	
It needs to be "done in the right way...in a non-threatening scaremongering way"	P4, 47, S, F
"Explain to the community workers that are out with the community why it's beneficial. Then it's not somebody that's a health professional, because they feel intimidated"	P1, 48, S, F
I have a lot of clients who are dyslexic, can't read, so therefore if you sent something through the post they wouldn't understand it anyway. They won't ask somebody to read it because they feel uncomfortable or they think they're going to be judged"	P4, 47, S, F
"Educate community workers who then can go out and just say in passing do you understand what it is, come along and have a listen to what they've got to say. We're not going to give you loads of forms, we're not going to ask you to read loads of stuff out, just come and have a listen to what it could offer"	P4, 47, S, F
"I think it has got something to do with how it's worded. I don't know if I'm bothered about who it came from"	P5, 58, S, F
"Your GP has to word it right……. because then you wouldn't be thinking 'have I got something wrong with me? Do I really want to go?'"	P6, 68, S, F
"You just get a letter, you just have to go. Nobody has graphic details or pictures or anything. It's just literally a letter"	P12, 44, S, F

Distrust/ fear of healthcare	
"My experience with the hospital has not been good"	P4, 47, S, F
"I've lost trust in doctors"	P2, 55, S, F
"I have lost trust in the GPs. The only one I trust is retired now"	P1, 48, S, F
"This new system stinks"	P4, 47, S, F
"There's a medicine out there that's been proven to cure cancer but the government's reluctant to do it because of cost"	P3, 47, Ex, M
"I think they know certain things that they don't tell the public"	P3, 47, Ex, M
"I think they know more than what they let on"	P1, 48, S, F
"Haven't got much faith. That's my personal experience"	P2, 55, S, F
"I don't think it [screening for lung cancer] should be down for a doctor to decide"	P1, 48, S, F
"Hospitals are scary places"	P2, 55, S, F

3.3.2.2 Perceived positives

Many participants expressed support for the idea of a screening programme for lung cancer and several suggested that they would participate in principle. There were some caveats with regards to how the process would be organised, with one participant stating it needed to be conducted in “a non-threatening scaremongering way” (P4, 47, S, F) and another expressing concerns that they would be less willing to take part if they had “to stand in front of somebody who's not smoked or is judgemental” (P10, 39, S, F). Those who had previous positive experiences of interacting with the healthcare system were more strongly in favour of the idea of a screening programme and willing to take part. Example quotes are summarised in Table 3-4.

Table 3-4: Quotes illustrating perceived positives with regards to lung cancer screening

Perceived positives	Participant
Experiences of cancer	
"I've had cancer of the womb……. I wouldn't have gone to the doctors but I'd got to go for a normal check-up…….and I just mentioned it, and she said we'll get you checked out. So I was lucky"	P2, 55, S, F
Positive experiences of healthcare	
"I can't fault my doctors"	P2, 55, S, F
"I've used the walk-in centre each time really because it's difficult to get an appointment here, and it's a brilliant system. If you need something on that day you need it"	P7, 66, S, F
Support for screening	
I think it should be done now…… same as all the other ones, like cervical, bowel"	P2, 55, S, F
"If you were a smoker that you automatically went into the screening, or there was a history of lung cancer or anything else, I suppose it could be beneficial. But it's about educating people why it's beneficial"	P4, 47, S, F
"I would have one"	P3, 47, Ex, M
"If people were serious about their health then yeah, they would take it up"	P4, 47, S, F
"If it's done in the right way in a non-threatening scaremongering way that is beneficial, then you give the individual the choice. If they don't take that choice then that's their choice"	P4, 47, S, F
"I would love that myself"	P8, 78, Ex, M
"I'd go. It wouldn't bother me"	P7, 66, S, F
"I wouldn't mind being screened at all, but not if I've got to stand in front of somebody who's not smoked or is judgemental and is going to treat me as if I'm stupid for doing it because I already know that"	P10, 39, S, F

3.3.2.3 Perceived negatives

Some participants suggested that there was little point in being screened either because there was little that they could do to change their risk of developing lung cancer or because they did not view themselves as high risk. These views were expressed by both current and ex-smokers. Many expressed a fatalistic view that a diagnosis of lung cancer would "give you no hope" (P12, 44, S, F), with another stating that "99% of lung cancer victims don't survive" (P4, 47, S, F) and a third suggesting that "if I've got anything wrong with my lungs there's nothing I can do to change that" (P9, 44, Ex, M). One suggested that they would wait until they had symptoms and another felt that if they were going to get

lung cancer they would “have it by now” (P9, 44, Ex, M). One participant expressed concerns regarding the radiation dose of the screening and the risks that this may pose to them. Another expressed a distrust of CT scans in general as a result of a negative experience previously (Table 3-5).

Table 3-5: Quotes illustrating perceived negatives with regards to lung cancer screening

Perceived negatives	Participant
Experiences of cancer	
"You never think of your mum or someone close to you dying of cancer…….so it was kind of like a shock in that way"	P3, 47, Ex, M
I don't trust them [CT scans]…..they told my daughter that her cancer had gone to her lungs and she had screening on her lungs……they gave her invasive radio treatment because they thought it had gone onto her lungs, and it hadn't. So the screening to me was a misreading"	P2, 55, S, F
"When my husband was seriously ill the doctor refused to come out to him and I was absolutely furious……..we chose palliative care at home, which wasn't very good"	P7, 66, S, F
Lack of perceived benefit	
"Unless it's life threatening I'll just wait"	P4, 47, S, F
"Oh come on, be honest with you, how many survivors of lung cancer? It's a scary thing, it's a big thing, and 99% of lung cancer victims don't survive more than whatever"	P4, 47, S, F
"They give you no hope"	P12, 44, S, F
"A lot of people know the risks of smoking. So maybe they don't see the benefit in being screened because they already know that they're doing a lot of harm to their body"	P10, 39, S, F
"I don't want to be screened, because I stopped smoking over 10 years ago now, and as far as I'm concerned it's something I used to do, it's in the past……I don't want to know. I don't see that I'm at any more risk"	P9, 44, Ex, M
"What would it mean, I can't stop smoking because I've already stopped. If I've got anything wrong with my lungs there's nothing I can do to change that"	P9, 44, Ex, M
"If I was going to get lung cancer I'd have it by now"	P9, 44, Ex, M
"I wouldn't go….I can't change my risk now. If I'm going to get lung cancer I would start to get symptoms, I don't have symptoms……I mean there might be some merit to screening people who have recently quit. But not like 10 years ago, that's just a waste of money"	P9, 44, Ex, M
Perceived dangers of screening	
"I don't want to have unnecessary x-rays……it will slightly increase your risk of cancer. So why would I want an x-ray which will increase my risk of cancer to screen for a cancer that I probably don't have"	P12, 44, S, F

3.3.2.4 Stigma and societal perceptions of smoking

Almost every participant, whether they were a current or ex-smoker, expressed concerns about the stigma associated with smoking and blame attributed to them as a result of their smoking habit. It was suggested that they were made to feel like “social pariahs” (P6, 68, S, F), were “targeted and picked on” (P6, 68, S, F) and even that they may be “refused treatment because [they] smoke” (P1, 48, S, F). There was concern that they would be made to sit in a “queue of shame” (P11, 43, Ex, F) and might “be preached at” (P11, 43, Ex, F). Several people commented that they felt that if smoking cessation was provided as a part of the screening programme it may put them off attending. Some thought that if they developed lung cancer they would be told that it was their fault for smoking, although conversely others felt that the link between lung cancer and smoking was not proven and that people who had never smoked could still develop lung cancer. One suggested that there were “probably more that die of lung cancer that don't smoke” than smoke (P5, 58, S, F). (Table 3-6).

Table 3-6: Quotes illustrating stigma and blame associated with smoking

Emotional barriers	Participant
Smoking stigma/ blame	
"People that don't smoke have had lung cancer so you know it's not just the smoking. And they say cancer's been proved by smoking, which hasn't"	P1, 48, S, F
"As soon as they know you smoke straightaway that was it"	P2, 55, S, F
"We're going to get refused treatment because we smoke"	P1, 48, S, F
"Being a smoker, and the fact that we are social pariahs now"	P6, 68, S, F
"I don't want Mr Bloggs up the road telling me that I can't smoke"	P6, 68, S, F
"I think if they didn't only aim it [screening] on the smokers, because there is a lot of people that die of lung cancer, in fact probably more that die of lung cancer that don't smoke. But they never show you them figures"	P5, 58, S, F
"I feel that I'm being targeted and picked on"	P6, 68, S, F
"I think it's fear of smokers going, because the general feeling is now that it is very, very bad to smoke, and it's looked down upon"	P9, 44, Ex, M
"I feel personally that if I went to screening they'd be just saying, "Well how many do you smoke a day? Look at the state of your chest, if you hadn't done this your chest wouldn't be looking like this. You've brought this on yourself"	P12, 44, S, F
"I think you need to have an amnesty that you can come and be seen and you won't be judged"	P12, 44, S, F
"I don't want to be preached at"	P11, 43, Ex, F
"They're going to try and make me stop [smoking] and I don't want to"	P12, 44, S, F
"We don't go around with any other group of people and treat them like this do we. "Don't eat so much you're going to die," do we?...But we do it to smokers and it's really horrible"	P12, 44, S, F
"I wouldn't mind being screened at all, but not if I've got to stand in front of somebody who's not smoked or is judgemental and is going to treat me as if I'm stupid for doing it. Because I already know that"	P10, 39, S, F
"The adverts as well, or the information they give, maybe they should concentrate on the benefits of stopping rather than the heinous crime you've committed by doing it in the first place"	P12, 44, S, F
"I think they just need to be a little bit kinder. It's not the brightest thing that we've done, but we haven't killed anybody"	P12, 44, S, F
"You sit there waiting to be told off…"	P10, 39, S, F
"You're sat in the queue of shame"	P11, 43, Ex, F
"I don't know that I want to be sat with lots of smokers, and I don't want to be labelled as a smoker for ….. the stigma and everything when I'm not a smoker anymore"	P9, 44, Ex, M
"I think people will think it's your own fault" [if you have lung cancer]	P12, 44, S, F
"Oh you've got this and that and you've got it because you smoke. So if I didn't smoke what you say it was then?"	P13, 30, S , F

3.3.2.5 Emotional barriers

Fear of diagnosis was expressed by some as a reason to avoid screening, although some participants felt that it would be a driver to make them want to be screened. There were also concerns about the "nanny state" and that screening for lung cancer was an extension of this and another way that control over smokers could be exerted (Table 3-7).

Table 3-7: Quotes illustrating emotional barriers associated with lung cancer screening

Emotional barriers	Participant
Avoid diagnosis/ fear	
"Scared"	P1, 48, S, F
"It is frightening. Very…….This is why I wished I could pack it up. [smoking] I can't"	P2, 55, S, F
"I think it's fear of smokers going, because the general feeling is now that it is very, very bad to smoke, and it's looked down upon"	P9, 44, Ex, M
"I think it's really frightening"	P10, 39, S, F
"I think it's a massive, massive fear. If there's an advert on the television I turn it off"	P12, 44, S, F
"Yeah I'm really scared, I'm honestly really scared. I can't bear to think about what I might have done to myself"	P10, 39, S, F
"Your fear leads you to want to be screened"	P9, 44, Ex, M
Denial	
"Someone's got no symptoms and they're more likely to be believe that it's not going to hit them then"	P3, 47, Ex, M
"Nothing's happened to him so I must be all right"	P3, 47, Ex, M
"I know what's going to happen but if I die, I'll die sooner than you lot, so it will knock the worst years off my life, so it doesn't really matter"	P9, 44, Ex, M
"I don't see that I have an increased risk. Maybe I'm in denial but I don't see what increased risk I have now, it was 10 years ago that I stopped smoking"	P9, 44, Ex, M
"If I'm going to get lung cancer I would start to get symptoms, I don't have symptoms"	P9, 44, Ex, M
"People that don't smoke have had lung cancer so you know it's not just the smoking. And they say cancer's been proved by smoking, which hasn't"	P1, 48, S, F
"Nanny state"	
"I'm sick of being told. I know they've got to fill their papers really but I think they overdo it. Too much of a nanny state"	P6, 68, S, F
"It's very paternalistic the approach to smokers isn't it….And we've made that choice about our own lives and we're adults"	P12, 44, S, F
"I'm sick of the whole thing" [the nanny state]	P6, 68, S, F
"I'm very opposed to being told what to do"	P6, 68, S, F

3.3.2.6 Education/ awareness

One key opinion that was expressed by participants was the importance of community engagement and the use of community workers/ leaders to talk to those who were eligible for screening in a way that they could understand and thus promote it (Table 3-8). There was a feeling that some awareness campaigns were either too graphic or too detailed to be useful. Education about why screening for lung cancer is important was seen as crucial to ensuring participation as long as it was done in the right way, with endorsement of community leaders. Some participants mentioned that plays had been used previously in some community centres to ensure that information and advice about important health conditions was delivered in way that was accessible to all and that these were well received. Face-to-face rather than written information was cited by some as more effective and one group stated that social media had been used as an effective communication and educational tool. Those who had previous negative experiences with other screening programmes were less likely to be positive regarding a lung cancer screening programme.

Table 3-8: Quotes illustrating ideas around education about and awareness of cancer screening

Education/ awareness	Participant
Awareness campaigns	
" I think they do give too much detail when they give the signs"	P2, 55, S, F
"I think if you advertise it on television and say have you got this and have you got that, a hypochondriac will go "oh yeah, I've got all them"! "	P1, 48, S, F
Community engagement	
"Explain to the community workers that are out with the community why it's beneficial. Then it's not somebody that's a health professional, because they feel intimidated"	P1, 48, S, F
"Someone who is a leader in the community who says I've done it, it's fine……..Show them you're not afraid"	P4, 47, S, F
"If you educate community workers who then can go out and just say in passing do you understand what it is, come along and have a listen to what they've got to say"	P4, 47, S, F
"You could have some people who have respect in the community doing it as well couldn't you? Because then I can see that people might be more inclined to go for screening if it was somebody that they respected"	P9, 44, Ex, M
Screening education/ participation	
"You need to educate people as to why they need the screening"	P4, 47, S, F
"It's better to save one that wants to be saved. It is down to personal choice, but it is about educating people"	P4, 47, S, F
"Never ever crossed my mind not to have a cancer smear. Always do it. This bowel thing I haven't"	P7, 66, S, F
"I had it through [bowel screening] but I didn't [do it] …I think I had too much going on at the time"	P7, 66, S, F
"I'd never been for a smear….Got absolutely bullied into it…. I found it the most invasive, crude procedure in the world. The way it was done was horrible, I'm never going back"	P10, 39, S, F

3.3.3 Questionnaire data

In a similar vein to the focus group participants, almost all respondents felt that there was a stigma or blame associated with smoking, which some felt would put them off seeking medical attention. However, almost three quarters of those surveyed said they would definitely or possibly take part in a screening programme were it to be implemented in the future. Around two thirds expressed a preference for drop in sessions rather than appointments, although 43% stated that they may be happy to attend an appointment at the hospital. The majority had no previous experience of lung cancer (Table 3-9).

Table 3-9: Questionnaire responses to questions regarding smoking stigma and screening participation

Questionnaire participants n (%)					
Smoking stigma Do you feel that smokers are blamed for their illnesses	Never 1 (2)	Rarely 3 (5)	Some of the time 30 (54)	Always 22 (39)	
Would fear of smoking stigma put you off seeking medical attention?	Would never put me off 23 (41)	Would rarely put me off 9 (16)	Would sometimes put me off 17 (30)	Would always put me off 7 (13)	
Screening Would you ever take part in lung cancer screening?	Yes definitely 26 (46)	Possibly 15 (27)	Unsure 6 (11)	Probably not 1 (2)	Never 6 (11)
What would be your preferred place for screening to take place?*	Drop in session in the community 20 (36)	Drop in session at the hospital 15 (27)	Appointment for scan in community 8 (14)	Appointment for scan at hospital 24 (43)	
Previous experience of lung cancer?	Yes 16 (29)	No 39 (70)			

* Participants were able to select all options that were applicable to them

Although many respondents felt the idea of lung cancer was frightening, half of those surveyed felt that screening for lung cancer should be offered now. The idea of "an amnesty" for smokers and a non-judgemental approach were also felt to be important in encouraging screening participation. Only a small number felt that there was unlikely to be any benefit or thought that the dangers of screening outweighed the positives (Table 3-10). There was no difference in any of the opinions expressed by smoking status (current versus ex).

Table 3-10: Agreement with example quotations to explore some sub-themes about lung cancer screening from focus groups

Sub-theme example quotation	Participant n (%)
Avoid diagnosis/ fear	
"I don't want to know"	8 (14)
"I think it's really frightening"	15 (27)
Smoking stigma/ blame	
"I feel that I'm being targeted and picked on…." [because I'm a smoker]	5 (9)
"They're going to try and make me stop smoking and I don't want to"	5 (9)
"I think you need to have an amnesty that you can come and be seen and you won't be judged"	16 (29)
"I wouldn't mind being screened, but not if I've got to stand in front of somebody who's not smoked or is judgemental"	20 (36)
Lack of perceived benefit	
"I don't see the benefit"	1 (2)
"Unless it's life threatening I'll just wait"	6 (11)
"If I was going to get lung cancer I'd have it by now"	5 (9)
Denial	
"If I'm going to get lung cancer I would start to get symptoms, I don't have symptoms"	2 (4)
Perceived dangers of screening	
"I don't want to have unnecessary x-rays"	5 (9)
Support for screening	
"I think it should be done now"	28 (50)

3.4 Discussion

3.4.1 Key findings

The results of this mixed-methods study give an insight into some of the ideas and opinions around lung cancer screening and highlight some barriers that need to be addressed prior to implementation of a national screening programme. A combination of practical and emotional barriers, alongside the role of community engagement and education were identified as important. In particular the idea of smoking stigma and blame was almost universal amongst current and ex-smokers and would need to be countered to ensure that a non-judgemental message regarding screening is portrayed. Convenience and accessibility of any given screening programme were stated as key and therefore the practicality of community-based and drop-in sessions may need to be explored to maximise uptake in those at greatest risk.

3.4.2 Previous work in the literature

There has been little work published specifically identifying barriers to participation in a lung cancer screening programme in a "hard-to-reach" population. A study conducted by Quaife et al (130) surveyed 175 individuals and interviewed 21 people from socially deprived communities in London to explore beliefs about lung cancer screening. Similar to this study, smoking stigma and blame were seen as deterrents to participation in a screening programme. Fatalistic views around a diagnosis of lung cancer, alongside a fear of diagnosis were also cited as reasons for non-engagement. Current smokers appeared to express more negative views than ex-smokers in their study, although the association with smoking status was not seen in this work. In a

similar way to participants in this study, the idea of a non-judgemental approach was stated to be key and mentioning smoking cessation at the time was suggested as off-putting. Many participants were positive in principle about the idea of screening, however barriers including fear, stigma and the negative association with a diagnosis of lung cancer in some outweighed this benefit. Patel at al (131) interviewed 60 individuals to look at attitudes towards lung cancer screening. They identified several factors which determined willingness to undertake screening; namely perceived lung cancer risk, accessibility and convenience, perceived benefit/ lack of benefit and knowledge of what screening entailed. Many of these themes and ideas were similar to those that participants in this study expressed as important considerations which would influence their participation. An analysis of those who declined participation in the UK Lung Cancer Screening (UKLS) trial identified several practical and emotional barriers. Key practical barriers cited were travel distance, lack of available public transport and costs of the journey or hospital parking. The most commonly cited emotional barriers were fear and avoidance of lung cancer information.(132) A study interviewing 26 smokers in the United States of America (US) about attitudes towards screening also identified inconvenience, distrust of healthcare professionals and smoking stigma as reasons not to be screened.(133) Furthermore, work surveying women about blame associated with a cancer diagnoses showed that 70% of respondents would consider patients with lung cancer at least partially responsible for their diagnosis, reinforcing this idea of smoking stigma and blame felt by participants in this study.(134)

3.4.3 Strengths and weaknesses

Although the number of people participating in the focus groups were fewer than intended, this group of society is notoriously difficult to engage in research studies and saturation of themes was reached by the final focus group. One strength is that we were able to use the focus groups and questionnaires to obtain opinions from multiple geographically distinct communities. There are however likely to be demographic differences between those who agreed to participate and those who did not. This is a bias that is inherent to qualitative research, although it is recognised that sampling such as this is not designed to be representative of the entire population.(135) Those who were more supportive of lung cancer screening will probably have been more willing to participate and therefore may bias the results in favour of a more positive view of screening. Almost all participants were of Caucasian ethnicity and the age distribution was younger than the population eligible for screening so it is difficult therefore to extrapolate the findings to other ethnic groups or settings outside those inner city communities we sampled. In addition only those who were literate were able to participate due to the need to provide informed, written consent. Some participants may have had help completing the questionnaires and it is therefore also possible that the views of those helping them to fill these in may have unconsciously biased their results. Nonetheless the results of this study are important in identifying barriers which need to be addressed prior to any lung cancer screening programme being instigated. They reinforce options gleaned from other qualitative work on this topic, suggesting that these findings are valid and representative, at least in part, of this section

of the population. These are also more likely to represent a "real-world" population than the results already published from the screening trial population.

3.4.4 Clinical relevance and conclusions

Although many participants were supportive of the idea of a lung cancer screening programme in principle, further discussion elicited many barriers which will need to be overcome in order to maximise uptake when, and if, screening is implemented in the UK. As lung cancer screening will focus on a high-risk group of smokers and ex-smokers their perception of smoking stigma and blame will need to be addressed in a sensitive, non-judgemental way and more novel education and invitation material may need to be developed, in conjunction with community leaders and the target population, to promote screening in a positive light. One randomised controlled trial in London is currently testing targeted invitation material to see if uptake may be improved in this way.(136) Furthermore there needs to be an awareness of the practical barriers and the acceptability and feasibility of community-based or drop-in sessions may need to be explored. Moving forward, it is important to determine to what extent these beliefs are likely to influence participation in a screening programme. There are small screening pilots taking place currently as part of the Accelerate, Coordinate, Evaluate (ACE) Programme, funded by Cancer Research UK (CRUK) to try to understand how best to promote and maximise participation in a screening programme with a focus on deprived communities.(137)

3.5 Chapter summary

This chapter described the results of a mixed methods study using focus groups and questionnaire data to identify barriers to participation in a lung cancer screening programme in “hard to reach” groups in the United Kingdom.

CHAPTER 4 : WHAT CHARACTERISTICS OF PRIMARY CARE AND PATIENTS ARE ASSOCIATED WITH EARLY DEATH IN PATIENTS WITH LUNG CANCER IN THE UNITED KINGDOM?

This chapter describes the use of a primary care dataset derived from THIN to determine features associated with mortality within 30 and 90 days of a lung cancer diagnosis.

4.1 Introduction

4.1.1 Background and rationale

The International Cancer Benchmarking Project (ICBP) and the EUROCARE groups highlighted the United Kingdom (UK) as a country with poor lung cancer survival rates.(14-18) This is partly explained by excess early mortality, with inequalities particularly in the 0-3 month period post-diagnosis.(15, 17)

Almost all patients in the UK are registered with a general practitioner (GP), who acts as a gatekeeper for referrals on to secondary care, and as a first point of contact for any health concerns. Some studies have questioned whether the principle of gatekeeping contributes to poorer overall cancer survival.(19, 138) In order to diagnose lung cancer earlier there is a pressing need to understand the factors in primary care that might lead to late diagnosis and consequent high early mortality from lung cancer.

4.1.2 Aim of this chapter

The aims of this study were:

- To establish the proportion of patients with lung cancer who have a death certificate only (DCO) diagnosis and the proportion who die within 30 and 90 days of diagnosis.
- To identify the demographic features and individual risk factors in patients who died within 0-90 days of diagnosis.
- To assess whether patients are interacting with primary care prior to diagnosis and to determine whether there are any primary care features which may contribute to early mortality.

4.2 Methods

4.2.1 Dataset and study population

This project uses a lung cancer population extracted from THIN which is described in detail in section 2.1. Date of diagnosis and death were used to calculate the proportion of patients who died early (cases). This included people whose date of diagnosis and date of death were the same ("death certificate only diagnoses"), and those who died within 30 or 90 days of diagnosis. Those who survived longer than 90 days were the comparator group.

4.2.2 Covariate descriptions

Smoking status was defined as current, ex, never or missing.(139) Where there were multiple smoking records the most recent record was used, but excluding the 6 months before the diagnosis date, to exclude changes related to symptomatic disease (see section 2.1.4 for more detailed methodology). The presence of co-morbidities before lung cancer diagnosis was identified using Read codes and weighted to calculate a Charlson co-morbidity index, using established methods.(84, 111, 140)

Townsend Index of deprivation, divided into quintiles, was used as a measure of socioeconomic status. Distribution of early deaths by Experian Mosaic Public Sector™ groupings was assessed as previous work has indicated specific groupings in whom lung cancer incidence was high.(89) Social isolation was defined using the household variable in THIN which identifies people living at the same address. Where only one person had a particular household identifier they were defined as living alone. Since individuals living in different flats or

apartments within the same building may be given the same household identifier, if there were greater than 10 people with the same household identifier they were classified as unknown. Urban versus rural residence was defined using the census-derived variable in the dataset (section 2.1.4).

4.2.3 Primary care consultations and chest x-rays

Codes which identified "face-to-face" or telephone consultations (Appendix A) were used to define consultations in the pre-diagnosis period. Multiple entries on the same date were counted as one consultation only. In previous work, the period of 0-4 months from diagnosis date has been identified as the period during which GPs investigate people for lung cancer(139) , so for this analysis the numbers of consultations in this time period were looked at. Patients were then grouped as low (0-5), medium (6-10) and high frequency consulters (>10). All chest x-ray (CXR) requests for cases and controls in the 0-4 months prior to diagnosis were identified. If there were multiple requests for the same person only one was counted. This was combined with consultation frequency to produce a composite variable indicating the number of times an individual had consulted in primary care (low, medium or high as described above) and also whether or not they had a CXR requested by their GP during the 0-4 month time period.

4.2.4 Practice level variables

Annual standardised overall CXR requesting rates for each primary care practice between 1/01/2010 and 31/12/2012 were calculated as a marker of their general propensity to order CXRs. This time period was chosen as all practices

included in the analysis were contributing and the level of data completeness was high. The rate of CXRs was standardised using the THIN population structure on 1/07/2010. Background lung cancer incidence rates were also calculated as proxy markers of exposure/awareness using the same process.

4.2.5 Statistical methods

The proportion of people who died immediately (death certificate only diagnoses), within 30 days and within 90 days of their diagnosis were calculated, within groups according to the demographic covariates, consultations and practice level variables described above. Kaplan-Meier survival curve was plotted for the whole population. Logistic regression was used to calculate odds ratios (OR) for death certificate only diagnosis, 0-30 day mortality (death certificate only + 30) and 0-90 day mortality (death certificate only + 90) within each of the variables described above and listed in Table 4-1. Each variable was looked at individually initially and those which showed an association in the univariate model ($p<0.05$) were included in the multivariate analysis. Likelihood ratio testing was used for all tests of significance.

Since CXR and lung cancer incidence quartiles were grouped by practice the use of Huber's method of robust regression to allow for underestimates in the standard error was explored.(141) There was minimal change in odds ratios and 95% confidence intervals, so the results of the original multivariate analysis are presented.

4.3 Results

4.3.1 Descriptive statistics

There were 39,559 patients with lung cancer in the initial THIN extract. Of these, 11778 with a diagnosis date prior to 01/01/2000 were excluded as discussed in Section 2.1.3. A further 3,035 records with missing demographic data (year of birth, sex or invalid practice registration dates), missing lung cancer diagnosis dates or death dates prior to diagnosis date were also excluded. Standardised CXR rates were plotted and those practices with rates of <1/100 population seemed to be distinct outliers and so all patients registered with any of these 71 practices were excluded from further analysis as it seemed likely that GPs were not routinely coding the CXRs that they were requesting. Thirty eight patients aged less than 30 years were excluded, as lung cancer is rare in this age group and may reflect a slightly different disease process. After these exclusions 20,142 cases of lung cancer from 444 general practices were used for the analysis (Figure 4-1).

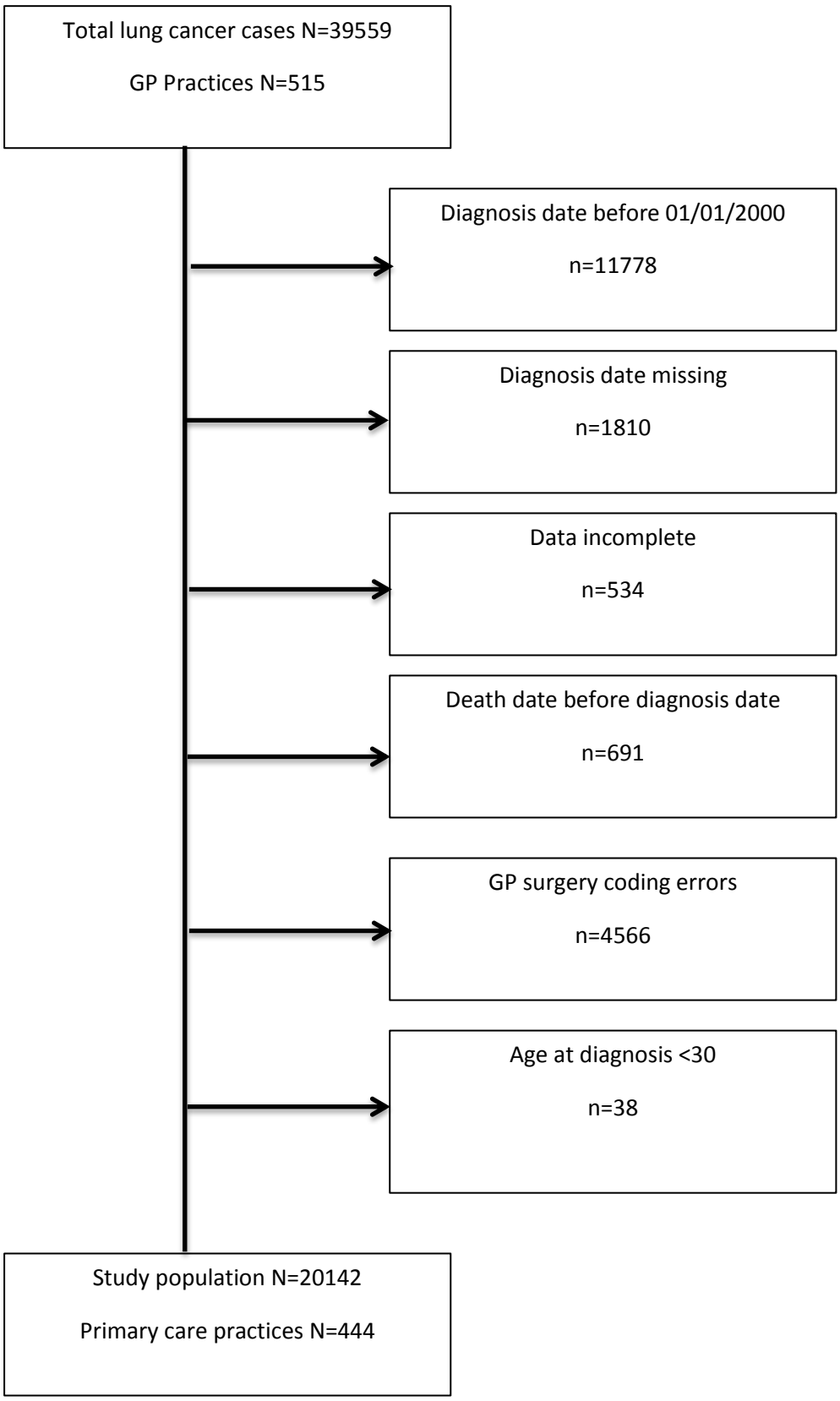


Figure 4-1: Study population and exclusion criteria

Five per cent (1071) of the cohort had death certificate only diagnosis, 10% (2036) died between 1 and 30 days of diagnosis and a further 15% died between 31 and 90 days of diagnosis (Table 4-1).

The Kaplan-Meier survival curve for the whole lung cancer population (truncated at 2 years post-diagnosis) is shown in Figure 4-2.

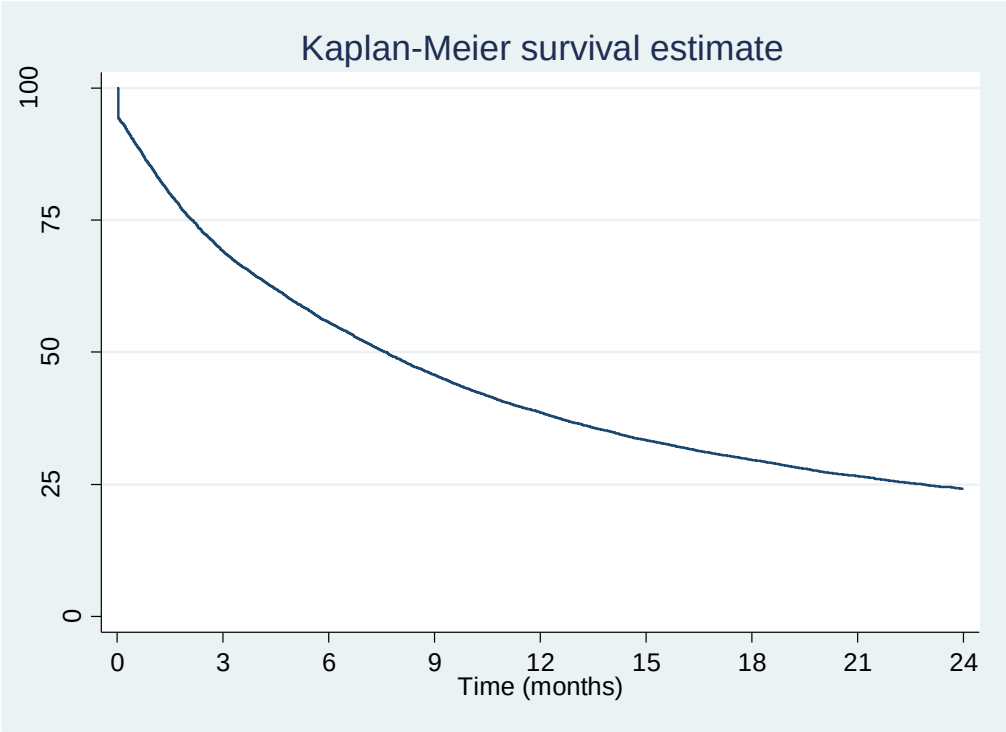


Figure 4-2: Kaplan-Meier survival curve for the lung cancer population

Table 4-1: Demographics of the lung cancer population

		Death certificate only 1071 (%)	Died 1-30 days 2036 (%)	Died 31- 90 days 2976 (%)	Comparator group 14059 (%)
Age at diagnosis (years)	30-39	1 (0.09)	1 (0.10)	4 (0.13)	83 (0.59)
	40-44	8 (0.75)	11 (0.54)	16 (0.54)	138 (0.98)
	45-49	15 (1.40)	22 (1.08)	41 (1.38)	306 (2.18)
	50-54	33 (3.08)	44 (2.16)	77 (2.59)	610 (4.34)
	55-59	45 (4.20)	127 (6.24)	196 (6.59)	1194 (8.49)
	60-64	74 (6.91)	197 (9.68)	335 (11.26)	1868 (13.29)
	65-69	114 (10.64)	294 (14.44)	416 (13.98)	2202 (15.66)
	70-74	173 (16.15)	312 (15.32)	523 (17.57)	2442 (17.37)
	75-79	228 (21.29)	379 (18.61)	612 (20.56)	2410 (17.14)
	>80	380 (35.48)	648 (31.83)	756 (25.40)	1806 (19.96)
Sex	Male	634 (59.20)	1174 (57.66)	1777 (59.71)	7883 (56.07)
	Female	437 (40.80)	862 (42.34)	1199 (40.29)	6176 (43.93)
Townsend deprivation quintile	1	165 (15.41)	356 (17.49)	514 (17.27)	2510 (17.85)
	2	190 (17.74)	392 (19.25)	550 (18.48)	2695 (19.17)
	3	201 (18.77)	428 (21.02)	629 (21.14)	1855 (20.31)
	4	269 (25.12)	435 (21.37)	659 (22.14)	3088 (21.96)
	5	224 (20.92)	382 (18.76)	548 (18.41)	2453 (17.45)
	Missing	22 (2.05)	43 (2.11)	76 (2.55)	458 (3.26)
Smoking status	Never smoker	158 (14.75)	194 (9.53)	226 (7.59)	1356 (9.65)
	Ex-smoker	378 (35.29)	783 (38.46)	1330 (44.69)	7007 (49.84)
	Current smoker	423 (39.50)	874 (42.93)	1272 (42.74)	5149 (36.62)
	Missing	112 (10.46)	185 (9.09)	148 (4.97)	547 (3.89)
Charlson score	0	415 (38.75)	880 (43.22)	1260 (42.34)	6226 (44.28)
	1	264 (24.65)	471 (23.13)	701 (23.56)	3435 (24.43)
	2-3	297 (27.73)	488 (23.97)	768 (25.81)	3385 (24.08)
	>4	95 (8.87)	197 (9.68)	247 (8.30)	1013 (7.21)
Consultations & CXR*	Low, no CXR	396 (36.97)	1032 (33.22)	913 (30.68)	3889 (27.66)
	Medium, no CXR	208 (19.42)	513 (16.51)	404 (13.58)	1317 (9.37)
	High, no CXR	180 (16.81)	478 (15.38)	328 (11.02)	1571 (11.17)
	Low, CXR	111 (10.36)	486 (15.64)	688 (23.12)	4348 (30.93)
	Medium, CXR	98 (9.15)	399 (12.84)	454 (15.26)	1937 (13.78)
	High, CXR	78 (7.28)	199 (6.40)	189 (6.35)	997 (7.09)
No in household	Lives alone	299 (27.92)	609 (29.91)	932 (31.32)	4157 (29.57)
	> 1 person	696 (64.99)	1313 (64.49)	1924 (64.65)	9405 (66.90)
	Unknown	76 (7.10)	114 (5.60)	120 (4.03)	497 (3.54)
Urban vs rural	Urban	750 (70.03)	1437 (70.58)	2035 (68.38)	9468 (67.34)
	Town & fringe	147 (13.73)	205 (10.07)	314 (10.55)	1411 (10.04)
	Rural	74 (6.91)	116 (5.70)	152 (5.11)	684 (4.87)
	Unknown	100 (9.34)	278 (13.65)	475 (15.96)	2496 (17.75)
Practice CXR quartile (Per 100 population)	1-2.73	179 (16.71)	398 (19.55)	600 (20.16)	3108 (22.11)
	2.74-3.84	144 (13.45)	451 (22.15)	661 (22.21)	3201 (22.77)
	3.85-5.33	354 (33.05)	527 (25.88)	778 (26.14)	3635 (25.86)
	≥5.34	394 (36.79)	660 (32.42)	937 (31.49)	4115 (29.27)
Practice lung cancer quartile (Per 100,000 population)	<34.3	191 (17.83)	397 (19.50)	538 (18.08)	2653 (18.86)
	34.3-49.56	262 (24.46)	568 (27.90)	774 (26.01)	3699 (26.31)
	49.57-71.63	298 (27.82)	570 (28.00)	809 (27.18)	3710 (26.39)
	≥ 71.64	320 (29.88)	501 (24.60)	855 (28.73)	3998 (28.44)

* 0-4 months pre-diagnosis

4.3.2 Patient level variables

Overall, 57% (11,468) were male, with a median age at diagnosis of 72 years. Patients who were 80 years and over comprised 35% of the death certificate only group, 32% of the 1-30 day mortality group and 26% of the 31-90 day group. People who died early were more often current smokers (40% in the death certificate only group; 43% in both 1-30 day and 31-90 day mortality groups; and 36% in the control group) but less likely to be ex-smokers (35%, 38%, 45% and 50% respectively). The death certificate only group had the highest proportion of never smokers (15%). More of those who died early were from the most socially deprived Townsend quintile; most marked in the death certificate only group (21% were in Townsend quintile 5 compared to 17% of controls) (Table 4-1).

Odds ratios followed similar trends across each of the 3 early death groups, so the results for the death certificate only + 90 group are reported for the remainder of this section. The univariate analysis for all groups is presented in Table 4-2, with the multivariate analysis results for all groups presented in Table 4-3.

Table 4-2: Univariate odds ratios for Death certificate only, Death certificate +30 day mortality and Death certificate +90 day mortality groups

		Odds Ratios Death certificate Only (95% CI)	p value (LRT)	Odds ratios Death certificate +30 (95% CI)	p value (LRT)	Odds ratios Death certificate +90 (95% CI)	p value (LRT)
Age at diagnosis (years)	30-39	0.23 (0.03-1.69)		0.22 (0.07-0.70)		0.23 (0.10-0.50)	
	40-44	1.12 (0.54-2.34)		0.79 (0.49-1.29)		0.68 (0.46-0.99)	
	45-49	0.95 (0.55-1.64)		0.68 (0.48-0.98)		0.68 (0.52-0.88)	
	50-54	1.04 (0.70-1.56)		0.72 (0.56-0.93)		0.67 (0.56-0.82)	
	55-59	0.73 (0.51-1.04)		0.79 (0.66-0.96)		0.82 (0.71-0.95)	
	60-64	0.77 (0.57-1.03)		0.79 (0.67-0.93)		0.87 (0.77-0.98)	
	65-69	1	<0.001	1	<0.001	1	<0.001
	70-74	1.37 (1.07-1.75)		1.05 (0.91-1.21)		1.10 (0.99-1.23)	
	75-79	1.83 (1.45-2.30)		1.29 (1.13-1.48)		1.35 (1.22-1.50)	
	>80	2.62 (2.11-3.25)		1.85 (1.63-2.10)		1.70 (1.54-1.88)	
Sex	Male	1.14 (1.00-1.29)		1.06 (0.98-1.15)		1.12 (1.06-1.20)	
	Female	1	0.046	1	0.124	1	<0.001
Townsend deprivation quintile	1	1	0.001	1	0.003	1	0.001
	2	1.07 (0.86-1.33)		1.04 (0.92-1.18)		1.02 (0.92-1.13)	
	3	1.07 (0.87-1.32)		1.05 (0.92-1.19)		1.07 (0.97-1.18)	
	4	1.33 (1.08-1.62)		1.09 (0.96-1.23)		1.07 (0.97-1.18)	
	5	1.39 (1.13-1.71)		1.17 (1.03-1.33)		1.14 (1.03-1.26)	
	Missing	0.73 (0.46-1.15)		0.71 (0.54-0.93)		0.75 (0.38-0.44)	
Smoking status	Never smoker	1	<0.001	1	<0.001	1	<0.001
	Ex-smoker	0.46 (0.38-0.56)		0.63 (0.55-0.71)		0.83 (0.75-0.93)	
	Current smoker	0.71 (0.58-0.85)		0.91 (0.80-1.03)		1.17 (1.05-1.30)	
	Missing	1.76 (1.35-2.28)		1.92 (1.61-2.30)		1.91 (1.63-2.24)	
Charlson score	0	1	0.001	1	0.001	1	<0.001
	1	1.15 (0.98-1.36)		1.03 (0.93-1.13)		1.02 (0.94-1.10)	
	2-3	1.32 (1.13-1.54)		1.09 (0.99-1.20)		1.12 (1.04-1.21)	
	>4	1.41 (1.11-1.78)		1.34 (1.16-1.54)		1.30 (1.16-1.45)	
Consultations & CXR *	Low, no CXR	1	< 0.001	1	<0.001	1	<0.001
	Medium, no CXR	1.41 (1.18-1.68)		1.39 (1.23-1.56)		1.39 (1.26-1.54)	
	High, no CXR	1.13 (0.94-1.35)		1.17 (1.04-1.32)		1.03 (0.93-1.13)	
	Low, CXR	0.28 (0.23-0.35)		0.45 (0.40-0.50)		0.54 (0.50-0.59)	
	Medium, CXR	0.50 (0.40-0.63)		0.78 (0.68-0.88)		0.88 (0.80-0.97)	
	High, CXR	0.82 (0.64-1.05)		0.78 (0.66-0.92)		0.78 (0.68-0.89)	
No in household	Lives alone	1	<0.001	1	<0.001	1	<0.001
	> 1 person	1.03 (0.89-1.18)		0.99 (0.91-1.08)		0.94 (0.88-1.01)	
	Unknown	2.13 (1.63-2.78)		1.73 (1.45-2.06)		1.41 (1.21-1.64)	
Urban vs rural	Urban	1	<0.001	1	<0.001	1	<0.001
	Town & fringe	1.32 (1.09-1.58)		1.07 (0.95-1.21)		1.06 (0.96-1.17)	
	Rural	1.37 (1.06-1.76)		1.07 (1.01-1.41)		1.12 (0.98-1.28)	
	Unknown	0.51 (0.41-0.63)		0.67 (0.60-0.75)		0.77 (0.70-0.84)	
Practice CXR quartile (Per 100 population)	1-2.73	1	<0.001	1	<0.001	1	<0.001
	2.74-3.84	0.78 (0.62-0.98)		0.99 (0.88-1.12)		1.04 (0.94-1.14)	
	3.85-5.33	1.69 (1.40-2.04)		1.28 (1.15-1.44)		1.21 (1.01-1.32)	
	≥5.34	1.66 (1.38-2.00)		1.34 (1.20-1.50)		1.28 (1.17-1.39)	
Practice lung cancer quartile (Per 100,000 population)	<34.3	1	0.338	1	0.101	1	0.299
	34.3-49.56	0.98 (0.81-1.19)		1.01 (0.90-1.13)		1.02 (0.93-1.12)	
	49.57-71.63	1.12 (0.92-1.35)		1.04 (0.93-1.17)		1.06 (0.97-1.17)	
	≥ 71.64	1.11 (0.92-1.34)		0.92 (0.82-1.03)		0.99 (0.90-1.08)	

* 0-4 months pre-diagnosis; LRT likelihood ratio testing; 95% CI 95% confidence interval; CXR chest x-ray

Table 4-3: Multivariate odds ratios for Death certificate only, Death certificate +30 day mortality and Death certificate +90 day mortality groups

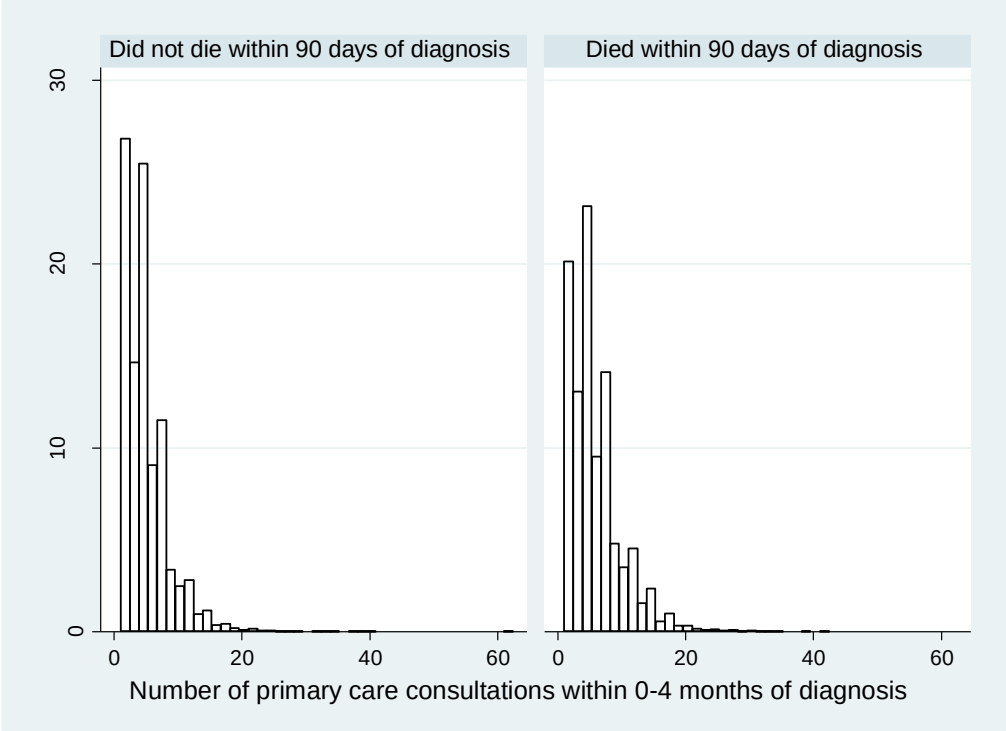
		Odds Ratios Death certificate Only (95% CI)	p value (LRT)	Odds ratios Death certificate +30 (95% CI)	p value (LRT)	Odds ratios Death certificate +90 (95% CI)	p value (LRT)
Age at diagnosis (years)	30-39	0.23 (0.03-1.71)		0.19 (0.06-0.61)		0.20 (0.09-0.45)	
	40-44	1.24 (0.59-2.61)		0.74 (0.45-1.22)		0.64 (0.43-0.94)	
	45-49	0.96 (0.55-1.67)		0.61 (0.43-0.88)		0.62 (0.48-0.81)	
	50-54	1.16 (0.77-1.73)		0.69 (0.53-0.89)		0.64 (0.53-0.78)	
	55-59	0.78 (0.55-1.11)		0.79 (0.65-0.95)		0.81 (0.70-0.94)	
	60-64	0.83 (0.62-1.12)		0.81 (0.69-0.96)		0.88 (0.78-1.00)	
	65-69	1	<0.001	1	<0.001	1	<0.001
	70-74	1.38 (1.08-1.77)		1.07 (0.93-1.24)		1.13 (1.01-1.26)	
	75-79	1.73 (1.37-2.19)		1.30 (1.13-1.50)		1.39 (1.25-1.55)	
	>80	2.28 (1.83-2.85)		1.90 (1.66-2.16)		1.80 (1.62-1.99)	
Sex	Male	1.21 (1.06-1.37)		1.12 (1.04-1.22)		1.17 (1.10-1.24)	
	Female	1	0.004	1	0.005	1	<0.001
Townsend deprivation quintile	1	1	<0.001	1	0.005	1	0.017
	2	1.06 (0.85-1.32)		1.03 (0.90-1.18)		1.00 (0.91-1.11)	
	3	1.12 (0.90-1.39)		1.08 (0.95-1.23)		1.07 (0.96-1.18)	
	4	1.44 (1.17-1.78)		1.14 (1.00-1.30)		1.07 (0.96-1.18)	
	5	1.57 (1.25-1.97)		1.28 (1.11-1.47)		1.16 (1.04-1.30)	
	Missing	1.35 (0.82-2.22)		0.92 (0.68-1.25)		0.86 (0.69-1.08)	
Smoking status	Never smoker	1	<0.001	1	<0.001	1	<0.001
	Ex-smoker	0.48 (0.39-0.58)		0.66 (0.58-0.76)		0.87 (0.78-0.97)	
	Current smoker	0.80 (0.65-0.98)		1.14 (1.00-1.31)		1.43 (1.28-1.61)	
	Missing	1.31 (1.00-1.71)		1.85 (1.53-2.23)		1.89 (1.60-2.23)	
Charlson score	0	1	0.125	1	0.168	1	0.234
	1	1.17 (0.99-1.38)		1.02 (0.92-1.13)		0.96 (0.89-1.05)	
	2-3	1.20 (1.02-1.41)		1.03 (0.93-1.14)		1.02 (0.94-1.11)	
	>4	1.10 (0.87-1.41)		1.19 (1.02-1.38)		1.09 (0.97-1.24)	
Consultations & CXR *	Low, no CXR	1	<0.001	1	<0.001	1	<0.001
	Medium, no CXR	1.43 (1.19-1.71)		1.43 (1.27-1.62)		1.43 (1.29-1.59)	
	High, no CXR	1.05 (0.86-1.27)		1.06 (0.94-1.21)		0.96 (0.86-1.06)	
	Low, CXR	0.28 (0.23-0.35)		0.45 (0.40-0.51)		0.54 (0.49-0.59)	
	Medium, CXR	0.50 (0.40-0.63)		0.80 (0.70-0.91)		0.90 (0.82-1.00)	
	High, CXR	0.88 (0.68-1.13)		0.83 (0.70-0.98)		0.81 (0.71-0.93)	
No in household	Lives alone	1	0.025	1	0.019	1	0.204
	> 1 person	1.17 (1.01-1.36)	0.035**	1.09 (1.00-1.19)	0.057**	1.01 (0.94-1.08)	0.912**
	Unknown	1.39 (1.05-1.84)		1.28 (1.06-1.55)		1.16 (0.98-1.36)	
Urban vs rural	Urban	1	<0.001	1	<0.001	1	<0.001
	Town & fringe	1.60 (1.32-1.95)		1.13 (0.99-1.28)		1.10 (0.99-1.22)	
	Rural	1.69 (1.30-2.20)		1.31 (1.10-1.56)		1.22 (1.06-1.41)	
	Unknown	0.50 (0.40-0.64)		0.68 (0.60-0.78)		0.79 (0.71-0.87)	
Practice CXR quartile (Per 100 population)	1-2.73	1	<0.001	1	<0.001	1	<0.001
	2.74-3.84	0.71 (0.56-0.89)		0.96 (0.84-1.09)		1.03 (0.93-1.14)	
	3.85-5.33	1.72 (1.42-2.09)		1.38 (1.22-1.56)		1.28 (1.16-1.40)	
	≥5.34	1.78 (1.47-2.16)		1.52 (1.35-1.71)		1.41 (1.29-1.55)	
Practice lung cancer quartile (Per 100,000 population)	<34.3	1	0.522	1	0.009	1	0.064
	34.3-49.56	0.92 (0.76-1.12)		0.97 (0.86-1.10)		0.98 (0.89-1.08)	
	49.57-71.63	1.05 (0.86-1.28)		1.02 (0.90-1.15)		1.05 (0.95-1.15)	
	≥ 71.64	1.01 (0.83-1.24)		0.85 (0.75-0.97)		0.93 (0.84-1.03)	

* 0-4 months pre-diagnosis ; ** Excluding unknown; LRT likelihood ratio testing; 95% CI 95% confidence interval; CXR chest x-ray

Increasing age was strongly related to early death, with an adjusted OR of 1.80 (95% CI 1.62-1.99), in people aged ≥ 80 years compared with those aged 65-69 years. Ex-smokers were less likely to die early compared to never smokers; adjusted OR 0.87 (95% CI 0.78-0.97). Current smokers had increased mortality compared with never smokers (adjusted OR 1.43 (95% CI 1.28-1.61)), apart from a small reduction in early deaths in current smokers in the death certificate only group (adjusted OR 0.80(95% CI 0.65-0.98)). Male sex conferred poorer outcomes; OR 1.17 (95% CI 1.10-1.24). Those with greatest levels of socioeconomic deprivation had increased odds of early death compared to more affluent subjects (adjusted OR 1.16 (95% CI 1.04-1.30) for Townsend quintile 5 compared with quintile 1). Rural versus urban location was also associated with poorer prognosis (adjusted OR 1.22 (95% CI 1.06-1.41)). There was no evidence of an independent association between early death and Charlson co-morbidity index or living alone versus in a shared dwelling.

4.3.3 GP consultations & individual CXR requests

Patients who died within 90 days of diagnosis consulted their GP more frequently than controls in the 0-4 months prior to diagnosis, with a median of 5 consultations (Interquartile range (IQR) 3-8) versus 4 (IQR 2-6). Consulting habits were very similar in the 4-12 months prior to diagnosis. Figure 4-3 summarises the consulting frequencies between those who died within 90 days of diagnosis and the control group for each of these time frames.



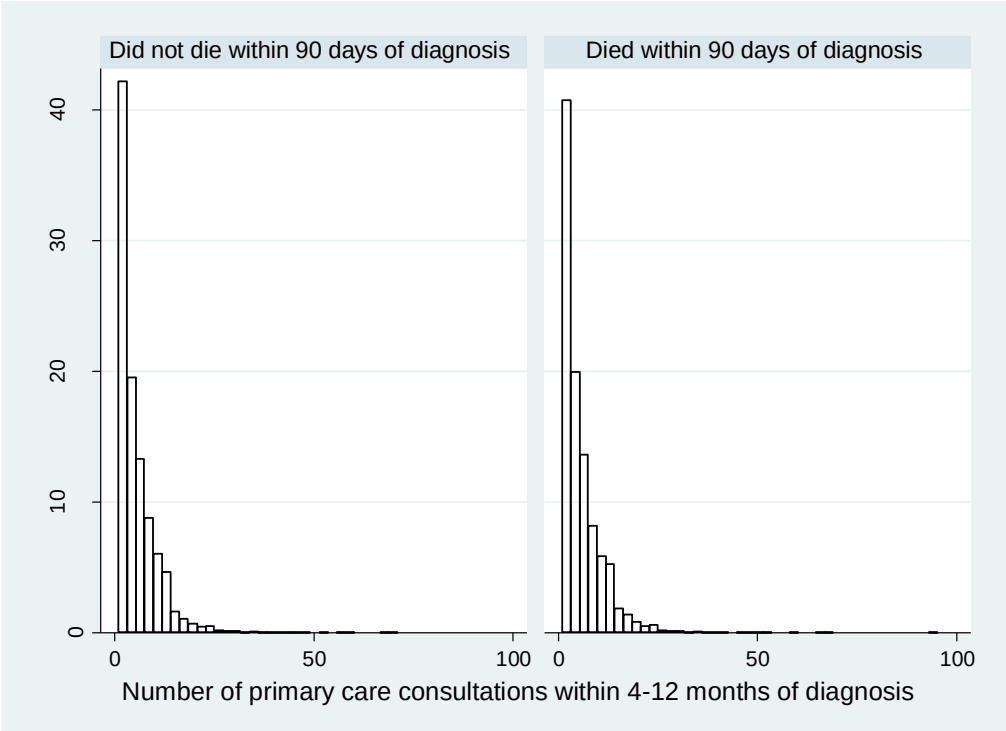


Figure 4-3: Primary care consultations in those who died within 90 days of diagnosis and controls in 0-4 months and 4-12 months prior to lung cancer diagnosis

Those in the death certificate only group were least likely to have had a CXR performed in primary care (27%), compared with 52% of controls. In the

multivariate analysis the odds of early death were lower in people who had a CXR performed in primary care, regardless of the number of times they consulted their GP. Within this group of patients who had a CXR performed, the odds of early death increased as consulting frequency increased. Medium consulters who did not have a CXR performed had greatest overall odds of early death (Table 4-3).

4.3.4 Mosaic Public Sector™ variables

Ninety day mortality in each of the 61 mosaic groups is shown in Figure 4-4. Total numbers in each group dying during this period is presented at the top of each bar. No one group was at greater risk of early death.

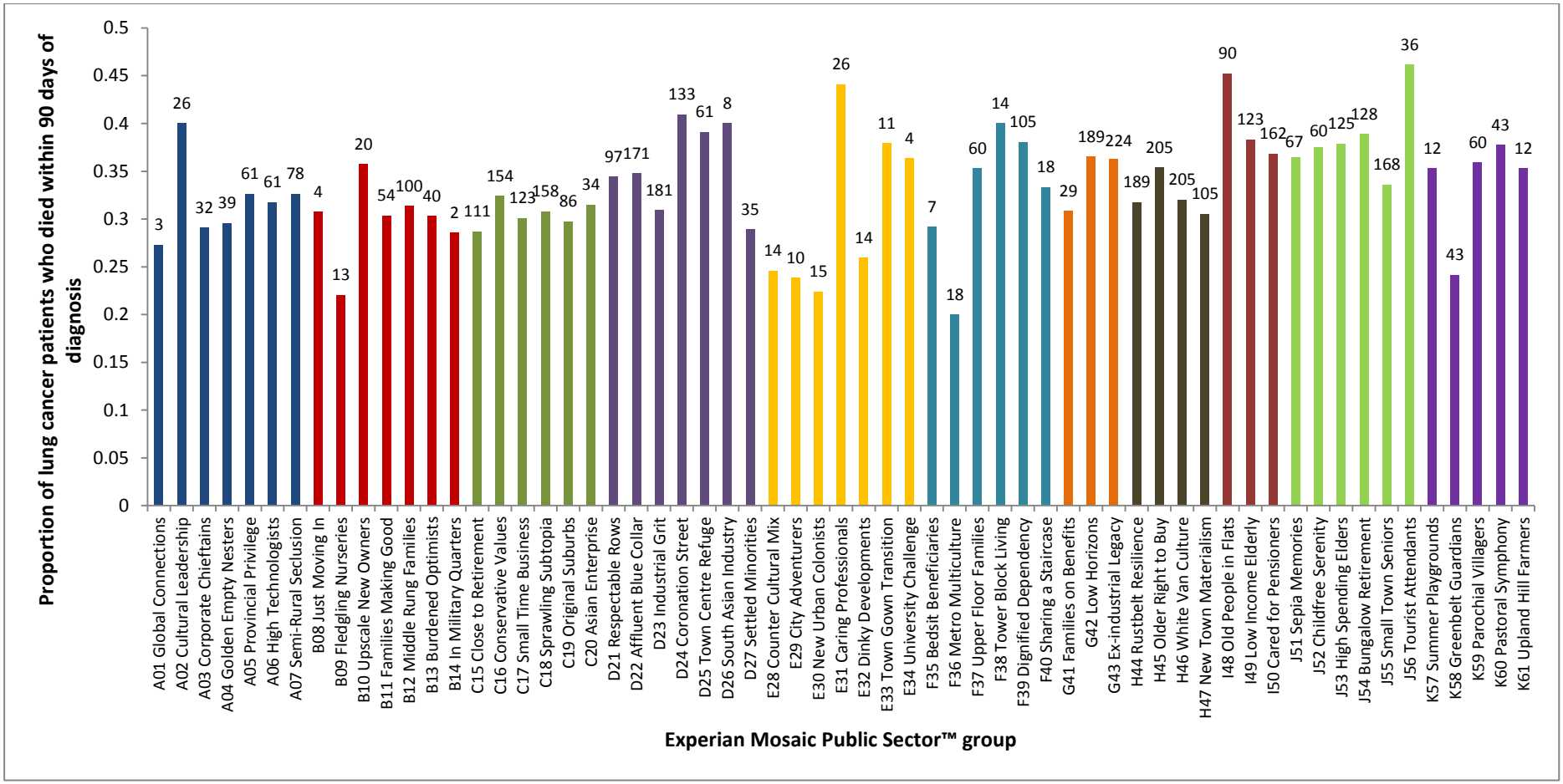


Figure 4-4: Proportion of lung cancer patients dying within 90 days in each Mosaic Public Sector™ group

4.3.5 Practice level variables

Lung cancer rates

Background lung cancer rates varied greatly between regions (Figure 4-5), with a median UK standardised rate of 53/100000 population (IQR 38/100000-74/100000). There was no association between background lung cancer rate at the practice with which the patient was registered and 90 day mortality, although there was a small reduction in 30 day mortality in the group registered at a practice which had the highest background lung cancer rate (OR 0.85 (95% CI0.75-0.97) (Table 4-3).

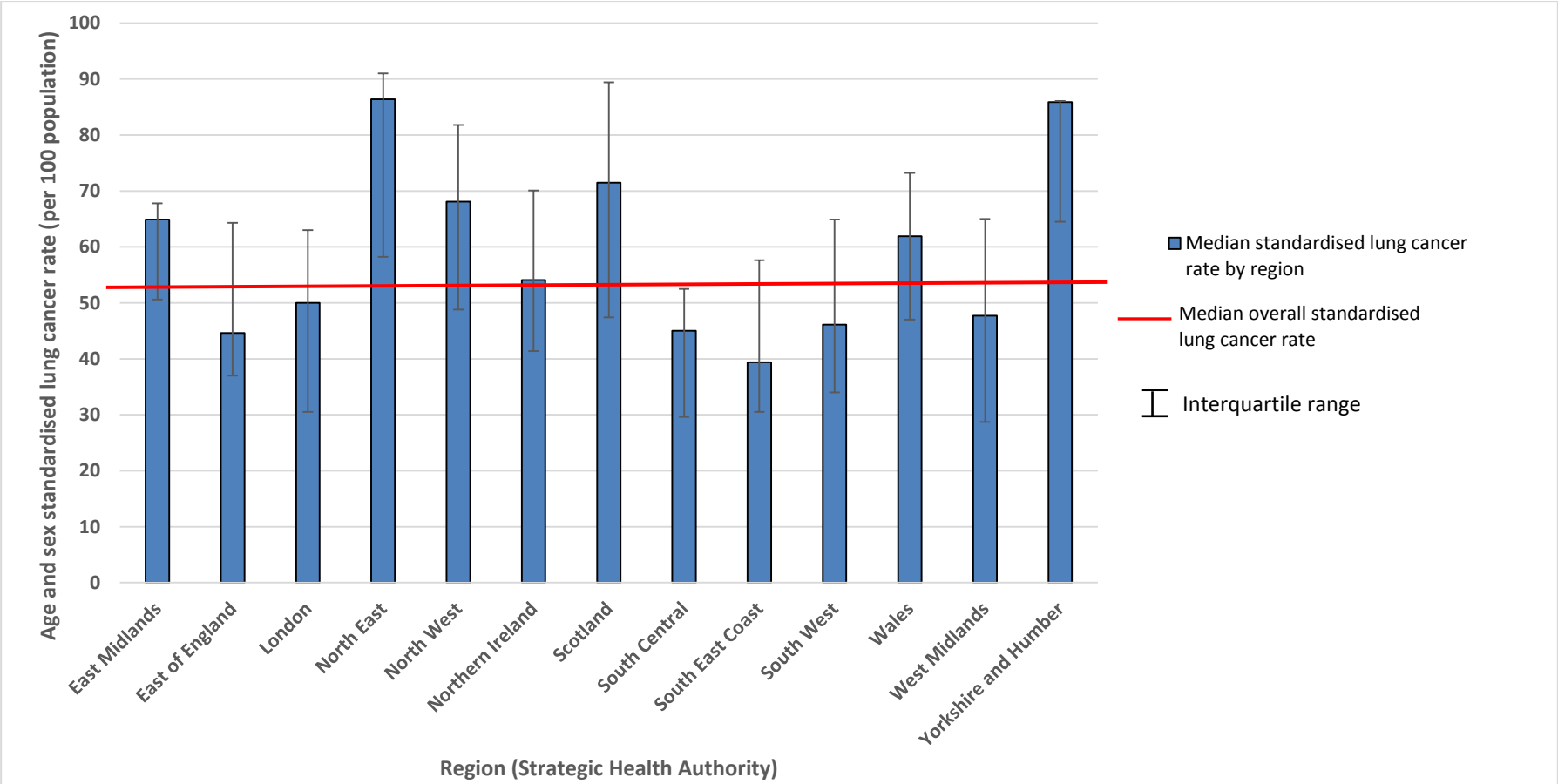


Figure 4-5: Geographic variation in background lung cancer rate (per 100 population)

Practice CXR rates

Age and sex-standardised CXR rates also differed widely between the practices (Figure 4-7); with a median rate of 4 per 100 population per year (IQR 3/100-6/100 population). Odds ratios for early death increased with increasing CXR quartile, even after adjustment for covariates including background lung cancer rate. People registered at a practice with a high propensity to investigate (CXR quartile 4) were 41% more likely to die early than those registered at the lowest quartile practices (death certificate only + 90 day OR 1.41 (1.29-1.55)) (Table 4-3). There was a very weak positive correlation between practices with high background lung cancer rates and high background CXR requesting rates (Figure 4-6), with Pearson's correlation coefficient of 0.25 ($p<0.001$).

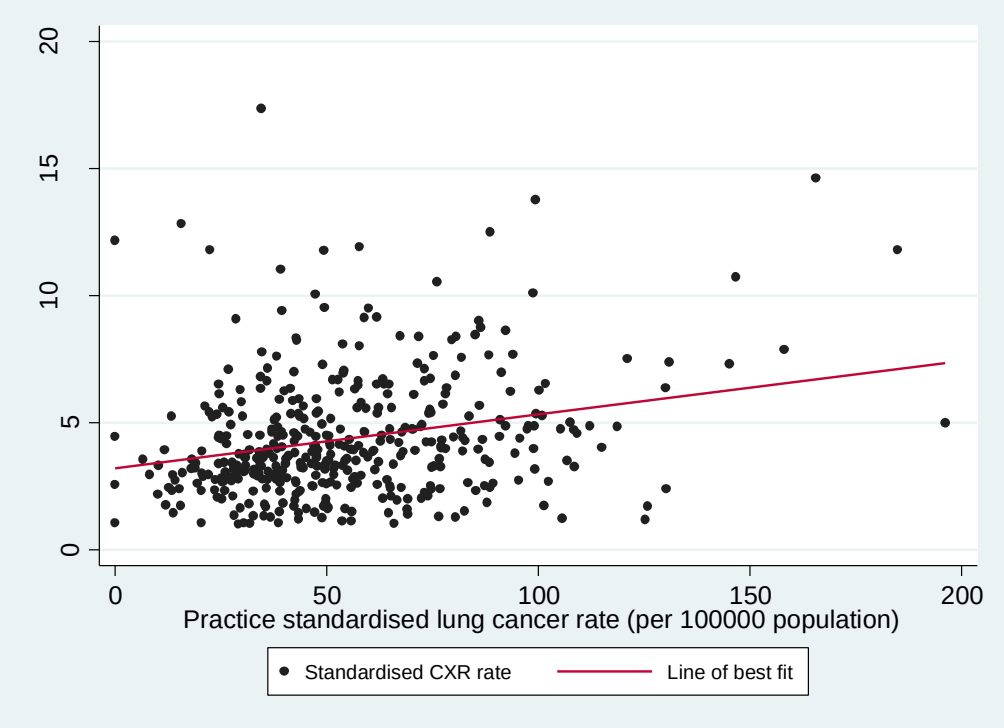


Figure 4-6: Scatter plot showing correlation between practice standardised CXR rate and practice standardised background lung cancer rates

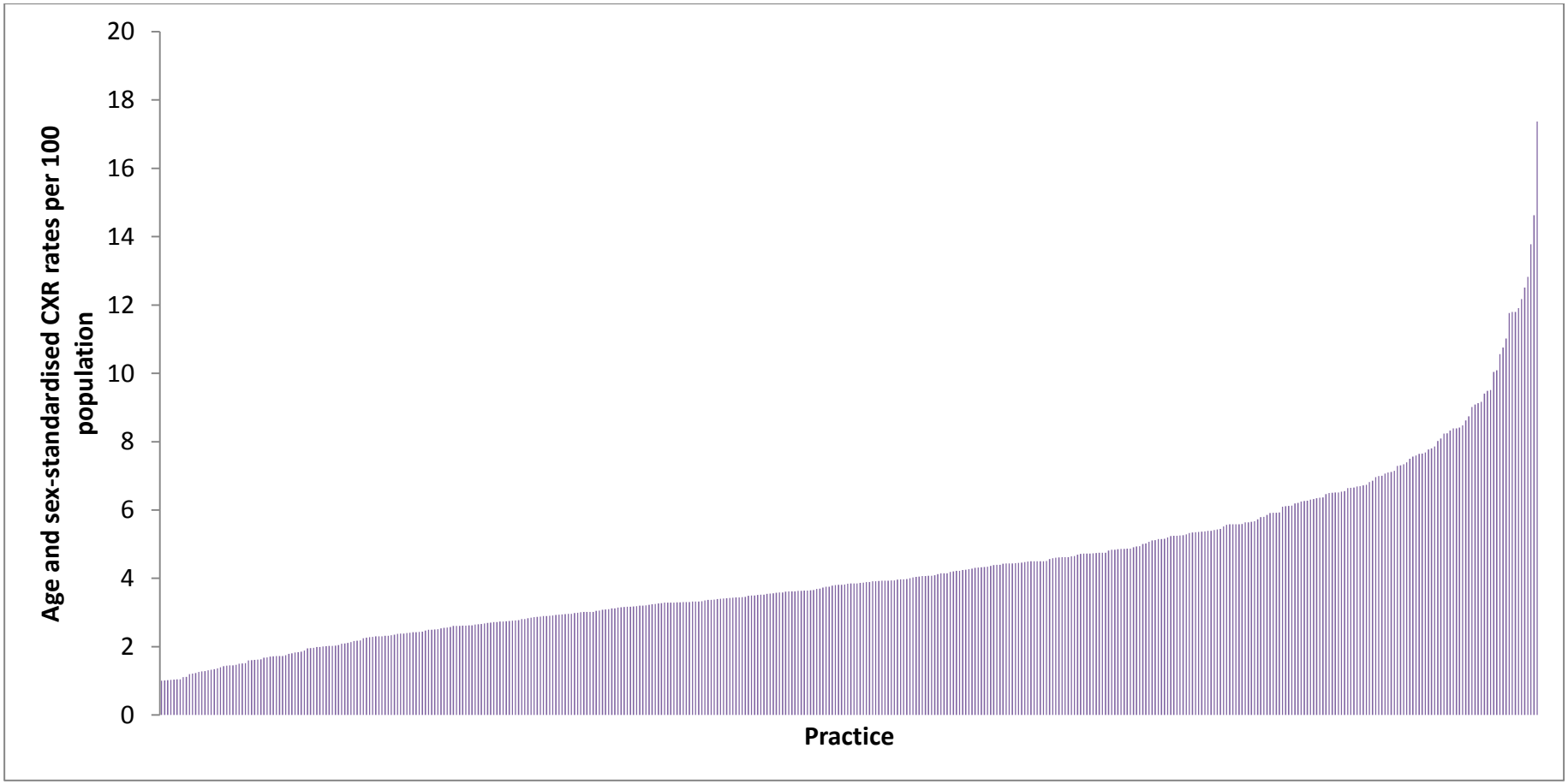


Figure 4-7: Age and sex-standardised CXR rates per 100 population in the GP practices studied

4.4 Discussion

The results show that 30% of patients with lung cancer died within 90 days of their diagnosis. Increasing age, male sex, socioeconomic deprivation, rural versus urban location and current smoking, were all strongly and independently associated with early death, although early death was less likely in ex-smokers compared with never smokers. Those who died early consulted their GP more frequently than those who did not and were less likely to have had a CXR performed by primary care.

At a practice level a higher CXR rate was not associated with a reduction in early deaths; in fact patients seen at these practices were more likely to have died early than those seen at practices with lower CXR rates. Practices with higher background lung cancer rates do not seem to be any more likely to diagnose their patients at an early enough point in the disease process to impact on early mortality.

Socioeconomic class does dominate risk factors for the development of lung cancer (89, 142, 143), but this class gradient vanishes when looking at early mortality from the disease. Previous work has shown peaks in lung cancer incidence in some of the Mosaic Public Sector™(89) groups but, again this does not hold true when it comes to premature mortality. This is likely a reflection of the very poor outcomes across all sectors of society once a diagnosis of lung cancer is made.

4.4.1 Strengths and weaknesses

This work is the first large study looking in detail at how events in primary care relate to early mortality in lung cancer. Previous work has confirmed that the validity of a lung cancer diagnosis in primary care databases is good and representative of National Cancer Registry data.(89, 99) The death certificate only group comprised 5.3% of the lung cancer population, which is broadly similar to death certificate only diagnosis figures from English Registry data,(17) and lends weight to the validity of THIN as a reliable source of lung cancer cases.

Data in THIN are prospectively recorded at the time of consultation in primary care which minimises reporting and recall bias. A detailed discussion of the strengths and weaknesses of the THIN dataset is presented in section 2.1.5.

The principal limitation of this study is the lack of information regarding stage, performance status, histology and interventions in secondary care. We used early deaths as a marker of people in whom lung cancer was diagnosed late, however some of these cases may have had early stage or completely asymptomatic disease and died from other comorbid conditions, although the relatively short interval between lung cancer diagnosis and death means that in the majority underlying malignancy is likely to be the main cause. There are additional limitations with regard to variation in the quality and timeliness of CXR reporting that could have influenced the apparently higher proportion of early deaths in those practices with higher CXR rates. In some practices the number of CXRs requested may be underreported. This is likely to be non-differential (random) misclassification though so it is unlikely to bias the

findings as this will usually lead to an underestimation of the true strength of an association rather than a change in association.

4.4.2 Other work in the literature

The International Cancer Benchmarking Project (ICBP) produced early mortality figures for 4 cancer sites (including lung) for 6 countries.(15, 18) The 30-day mortality from lung cancer in the UK ranged from 21-26% and was substantially higher than in any of the other countries included (apart from Ontario in Canada at 24%).(15) There does appear to be a reduction in 30 day mortality over time, particularly in the UK and Sweden, with mortality in the 2000-2007 cohort falling compared to 1995-1999. This is also the case when the THIN data are stratified by time. A summary of the ICBP data on 30 day mortality compared with THIN is provided in Table 4-4.

Table 4-4: Comparison of data on 30 day mortality from the International Cancer Benchmarking Project and THIN (15)

	ICBP 1995-1999 N (%)	**ICBP 2000-2007** N (%)	**THIN 2000-2007** N (%)	**THIN 2008-2013** N (%)	**ICBP Overall** N (%)	**THIN Overall** N (%)
Alberta	1245(19.1)	2406 (19.4)			3652 (19.3)	
British Columbia	1834 (16.4)	3124 (15.8)			4958 (16.0)	
Manitoba	410 (13.2)	896 (14.9)			1306 (14.3)	
Ontario	7776 (23.9)	13951 (24.5)			21727 (24.3)	
Denmark	-	2499 (15.9)			2499 (15.9)	
Norway	1304 (13.9)	2748 (15.4)			4052 (14.9)	
Sweden	828 (16.2)	1046 (11.1)			1874 (12.8)	
England	37635 (26.3)	53415 (23.1)	1577 (18.3)	986 (14.5)	91050 (24.3)	2563 (16.6)
Northern Ireland	904 (21.6)	1457 (20.5)	70 (19.3)	32 (11.5)	2361 (20.9)	102 (15.9)
Wales	2812 (29.7)	3923 (24.3)	125 (13.4)	78 (9.6)	6735 (26.3)	203 (11.6)
Victoria	1409 (14.4)	2472 (14.5)			3881 (14.5)	

N= total number in group; ICBP International Cancer Benchmarking Project; THIN The Health Improvement Network

The ICBP also showed, as this study did, that increasing age and male sex were associated with early death, and other work has confirmed this survival advantage in women.(144) In addition they suggested that smoking habits may have a role to play, with the UK having a higher prevalence of current smokers

than some of the other counties studied. (15, 17) This is supported by the finding of a higher proportion of early deaths in current smokers compared with never or ex-smokers.

Current smoking at the time of diagnosis has been shown previously to predict poor prognosis. A study published by Tammemagi and colleagues reported an adjusted hazard ratio (HR) for death of 1.26 (95% CI 1.08-1.47) for current smokers versus ex or never smokers.(145) Additionally work looking at health behaviours suggests that ex-smokers are more likely to see themselves as vulnerable to the adverse effects of smoking compared to current smokers (146) and are perhaps more likely to be health-aware leading to presentation earlier in the disease process. This may explain the finding that they are less likely than never smokers to die early.

Research from Leeds, England, looked at primary care CXR referral rates over a 2 year period and showed, in a much smaller sample, that there was marked variation in practice. They found no correlation between practice CXR rates and lung cancer survival (at 1 year).(147)

4.4.3 Interpretation of the results

Evidence presented in the National Cancer Intelligence Network (NCIN) "Routes to Diagnosis" work suggests that 39% of lung cancer patients present via the emergency route, and that these people have a much lower 1 year survival.(21) It is therefore not surprising that the proportion of patients who died early who had a CXR requested by primary care was lower than controls, and it seems likely that these people are diagnosed via an alternative route.

The National Institute for Health and Care Excellence (NICE) referral guidelines(148) give clear advice on specific symptoms which warrant a CXR and urgent referral. However, many patients have a more non-specific presentation, which is often attributed to other comorbid conditions. This may explain the high numbers of consultations for some patients in the 4 months before diagnosis.

Higher CXR rates in general at practice level do not appear to translate to reduction in early deaths from lung cancer; in fact people were more likely to die early from lung cancer if they were registered at a practice that performed more CXRs. This may be due in part to ascertainment bias, as performing more CXRs means you are more likely to detect underlying lung cancer in a terminally ill patient. This in turn highlights that the burden of undiagnosed lung cancer is unknown.

That is not to imply that the CXR is not a useful initial investigation in detection of symptomatic lung cancer. During the Mayo Lung Project mass screening study using CXRs, 90% of peripheral cancers and 70% of central cancers were diagnosed after retrospectively reviewing films.(149) Like any investigation however it needs to be used at an appropriate time, in a selected patient group.

4.4.4 Clinical relevance and conclusions

Patients who die early are interacting with primary care in the run-up to diagnosis, suggesting that there are opportunities to identify them earlier in the disease process. A general increase in CXRs at primary care level is of questionable clinical and cost effectiveness and it is important to establish

which interventions are likely to be useful at which point in the patient pathway. It has been argued that better access to computed tomography (CT) scanning in primary care may be useful in reducing early deaths, however it may be that more timely and appropriate targeting of the CXR remains the key. It seems clear that there needs to be a greater focus on older and socially deprived groups. At an individual GP level lung cancer is rare; with each GP seeing on average 1 new case per annum.(150) For this reason, it is necessary to promote better use of risk assessment tools (139, 151-154) and utilise software prompts to help GPs to identify and investigate those at risk in a timely manner. This has potential to increase the proportion of patients who are diagnosed at an early stage and are therefore suitable for treatment with curative intent.

4.5 Chapter summary

This chapter described the use of a primary care dataset to look at the individual and primary care features associated with death within 90 days from lung cancer.

The work was published in Thorax in October 2014 (155) and was accompanied by an editorial citing this study and further discussing the issues of deprivation, distance and death in lung cancer.(156) The article was also associated with a press release from Thorax which resulted in several local and national newspaper articles and also local and national radio interviews. These are summarised in Appendix C. There was also a summary published in the news section of The Lancet Oncology.(157) The analysis and interpretation of these

data are the work of myself and my co-authors and therefore some may disagree, as demonstrated by correspondence to the journal following publication. (158, 159)

CHAPTER 5 : VARIATION IN LUNG CANCER RESOURCES AND WORKLOAD: RESULTS FROM THE FIRST NATIONAL LUNG CANCER ORGANISATIONAL AUDIT

This chapter summarises the results of a national audit looking at lung cancer workload and access to diagnostic tests and treatment modalities. It also looks at the feasibility of linking these audit data to individual patient data acquired from the National Lung Cancer Audit to try to understand the impact of organisational factors on the likelihood of receiving surgery for lung cancer.

5.1 Introduction

5.1.1 Background and rationale

Reports from the National Lung Cancer Audit (NLCA) have consistently demonstrated variation in diagnostic pathways, treatment rates and lung cancer outcomes that are not wholly explained by case-mix. One hypothesis for this variation is that there is differing access to diagnostic tests, treatment availability and/ or access to specialist expertise between Trusts. Previous studies have shown that patients first seen in a surgical centre are 50% more likely to undergo surgery than those seen in a non-surgical centre and furthermore surgical centres with large catchment populations are less likely to operate on patients from the non-surgical centres they serve, compared with patients presenting to their own centre, despite having more surgeons available.(61, 160) Work using the NLCA to look at chemotherapy in small cell lung cancer (SCLC) also showed that some Trusts delivered more chemotherapy to patients than other Trusts, although this did not seem to translate into a survival benefit.(161) In addition those seen by a lung cancer nurse specialist (CNS) following diagnosis were twice as likely to receive anti-cancer treatment as those who were not.(102) The latest report from the NLCA showed that the proportion of patients receiving some form of anti-cancer treatment varied from 41% to 67% depending on the cancer Network.(162) In order to improve lung cancer outcomes it is essential to ensure that there is equitable access to high quality diagnostics, treatment options and lung cancer care for all and that we understand where the inequalities lie. There is little currently known about the provision of lung cancer services across the United Kingdom (UK).

5.1.2 Aim of this chapter

The aims of this study were:

- To assess the feasibility of conducting a national lung cancer organisational audit.
- To determine whether it was possible to link Trust-level data from this audit to NLCA patient-level data.
- To use this linked dataset to look at the impact of organisational features on likelihood of receiving surgery for lung cancer.

5.2 Methods

5.2.1 Organisational audit

An electronic survey was sent out to all lung cancer lead clinicians in England and Wales in January 2014. This survey included seven questions on service provision, diagnostic and treatment availability. These questions looked at number of patients discussed at each multi-disciplinary team (MDT) meeting, annual numbers of lung cancer patients diagnosed per Trust, access to diagnostic tests (specifically computed tomography (CT) guided lung biopsy, bronchoscopy, mediastinoscopy, video-assisted thoracscopy (VATS) biopsy, positron emission tomography-computed tomography (PET-CT), local anaesthetic (medical) thoracoscopy, endoscopic ultrasound (EUS), endobronchial ultrasound (EBUS), cardio-pulmonary exercise testing (CPEX) and molecular (EGFR and ALK) testing) and number of CNS available at each Trust. Information regarding access to therapeutic procedures- stereotactic ablative radiotherapy (SABR), conventional radiotherapy, thoracic surgery, VATS lobectomy, radiofrequency ablation (RFA), biologic/ targeted therapies, chemotherapy, pulmonary rehabilitation, smoking cessation services and palliative care- was also requested. Three questions were specifically targeted at treatment-only centres- for example those Trusts delivering chemotherapy only or surgery only. These specifically asked about number of surgeons and theatre sessions per week and number of high-dependency (HDU) beds available plus numbers of medical and clinical oncologists. Two electronic reminders were sent to the clinicians and the survey closed in May 2014.

5.2.2 NLCA dataset

This project uses a lung cancer population extracted from linked National Lung Cancer Audit (NLCA) data which is described in detail in Sections 2.2 and 2.4. Patients who underwent curative surgery for non-small cell lung cancer (NSCLC) (using Office of Population Censuses and Surveys Classification of Interventions (OPCS-4) coding) between 1st January 2011 and 31st December 2011 were identified from National Lung Cancer Audit (NLCA) data (Appendix A). This year was chosen as it was the most recent year with complete linked data available. Those who were diagnosed with NSCLC over the same time frame but did not undergo surgery were selected as the comparator group. Data from the survey were linked to NLCA data using the unique identifying code assigned to each Trust. Only those patients who had organisational audit data available were included in this portion of the analysis.

5.2.3 Covariates

Comorbidity was classified according to Charlson index using established methods.(111, 140, 163) Patients were then categorised into five groups based on their Charlson index (0, 1, 2, 3 and ≥ 4). Percentage predicted forced expiratory volume in 1 second (FEV_1) was categorised into five groups (>80%, 61-80%, 40-60%, <40% or missing) and WHO performance status (PS) into five groups (PS: 0, 1, 2, 3 & 4 or missing). Pre-treatment records in NLCA were used for stage (grouped as IA, IB, IIA, IIB, IIIA, IIIB, IV and missing) according to the 7^{th} edition of UICC TNM, with post-treatment stage used if pre-treatment records were missing. Age was categorised into eight groups (<55, 55-59, 60-64, 65-69, 70-74, 75-79, 80-84 and ≥85). Townsend Index of deprivation,

divided into quintiles, was used as a measure of socioeconomic status. Source of referral was coded in 6 groups (emergency admission, GP referral, consultant referral, accident and emergency (A&E), other or unknown).

Trust level data included in this portion of the analysis were access to PET-CT, CPEX, SABR, VATS lobectomy, RFA and pulmonary rehabilitation. These were the variables which seemed to show most inequities in the organisational audit between Trusts. They were categorised as either available on site, off site or not available/ missing.

5.2.4 Statistical analysis

Logistic regression was used to calculate odds ratios (OR) for likelihood of receiving surgery for NSCLC within each of the variables described above. Each variable was looked at individually initially, then those which showed an association in the univariate model ($p<0.05$) were included in the multivariate analysis. Likelihood ratio testing was used for all tests of significance. Individual patient features were analysed initially as part of a multivariable model and then each individual Trust feature was corrected for the patient-level variables but not the other Trust variables. This was because the aim was to look at the impact of each Trust level variable independently when corrected for patient factors rather than to create a multi-level model and assess multiple Trust features.

5.3 Results

A total of 128 records were submitted from 176 Trusts. Once duplicate and empty records were removed 101 were available for analysis. Four Trusts were treatment centres only so were excluded from the service provision and diagnostic portion of the analysis. The proportion of records received from each Strategic Clinical Network is summarised in Figure 5-1.

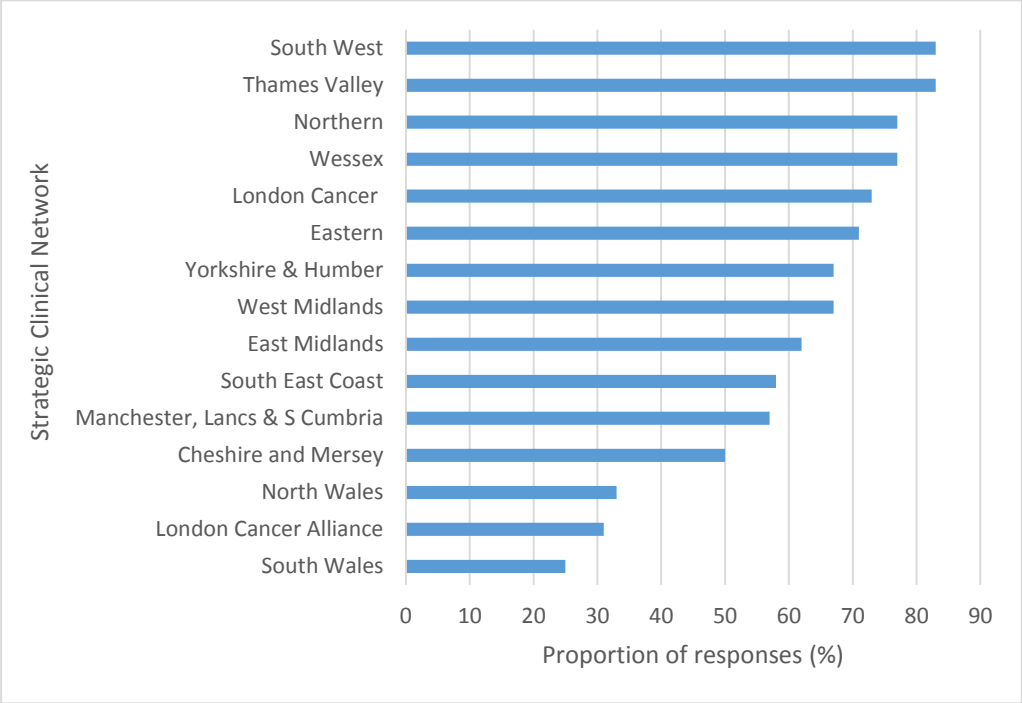


Figure 5-1: Proportion of responses by Strategic Clinical Network

5.3.1 Service provision

The median number of patients discussed per multidisciplinary team (MDT) meeting was 26, with a range of 5-88. Annual numbers of lung cancers diagnosed varied from 41-496, with a median of 189 per Trust (Figure 5-2). This equates to a median of 6 cases discussed at each MDT meeting for each new lung cancer diagnosis. Twenty eight Trusts (28%) have a separate diagnostic/ planning MDT meeting.

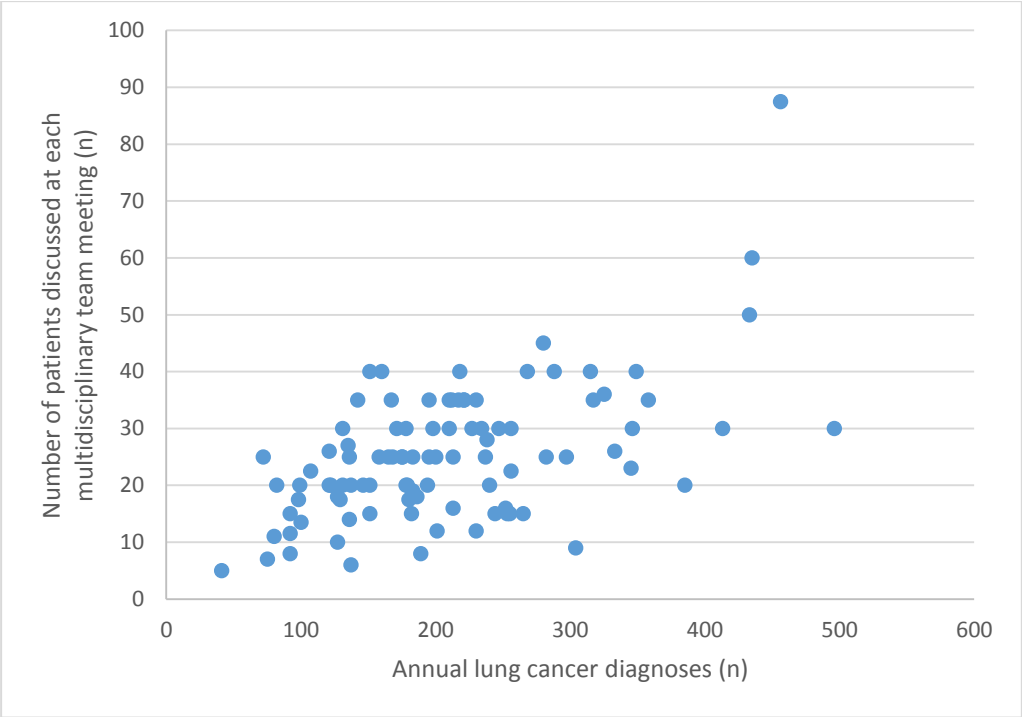


Figure 5-2: Scatter plot of annual number of lung cancers diagnosed at each Trust compared with number of patients discussed at each MDT meeting

Number and workload of lung cancer specialists available to each Trust is summarised in Table 5-1. Some specialists cover multiple Trusts, thus explaining the high workload.

Table 5-1: Number and workload of lung cancer specialists available to each Trust

	Number of whole time equivalents (WTE) median (range)	**Workload- expressed as annual lung cancer diagnoses per WTE specialist** median (range)
Clinical nurse specialists	2 (0.5-10)	90 (10-413)
Thoracic radiologists	2 (0-10)	90 (14-826)
Thoracic pathologists	1 (0-10)	131 (14-716)
Thoracic oncologists	2 (0.3-5)	93 (18-826)
Thoracic surgeons	1 (0-5)	135 (19-1820)

5.3.2 Diagnostic and staging services

Results are presented for 93 Trusts as 8 Trusts did not fully complete this section. All Trusts had access to CT-guided lung biopsy on-site and all, bar one,

had on site bronchoscopy in addition. Overall most Trusts had access to key diagnostic testing either on site or off site. Medical (local anaesthetic) thoracoscopy was not accessible to 13 Trusts (14%), although almost all Trusts had access to surgical VATS biopsy, with only 1 Trust not able to access this procedure. Figure 5-3 summarises the availability of diagnostic procedures by Trust.

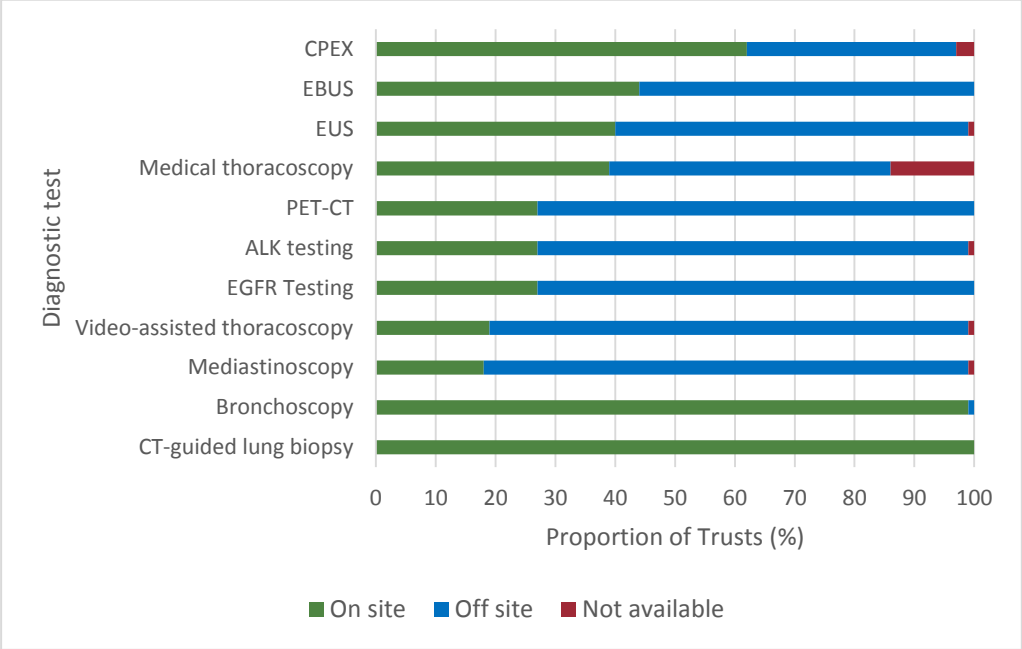


Figure 5-3: Diagnostic test availability by Trust
Results for 93 Trusts as 8 Trusts did not complete this section. PET-CT positron emission tomography-computed tomography; CPEX cardiopulmonary exercise testing; EBUS endobronchial ultrasound; EUS endoscopic ultrasound; ALK anaplastic lymphoma kinase; EGFR epidermal growth factor receptor

5.3.3 Lung cancer treatments

All Trusts had access to palliative care on site. Chemotherapy (including biological therapies), conventional radiotherapy and thoracic surgery are available on site in 89%, 33% and 18% of Trusts respectively. More specialist procedures such as VATS lobectomy, RFA and SABR were not accessible either on or off site in 6%, 10% and 5% of Trusts respectively. Although pulmonary

rehabilitation and smoking cessation services were available to the majority of Trusts on site (80% and 83%) a minority of Trusts still had no access to these services. (Figure 5-4).

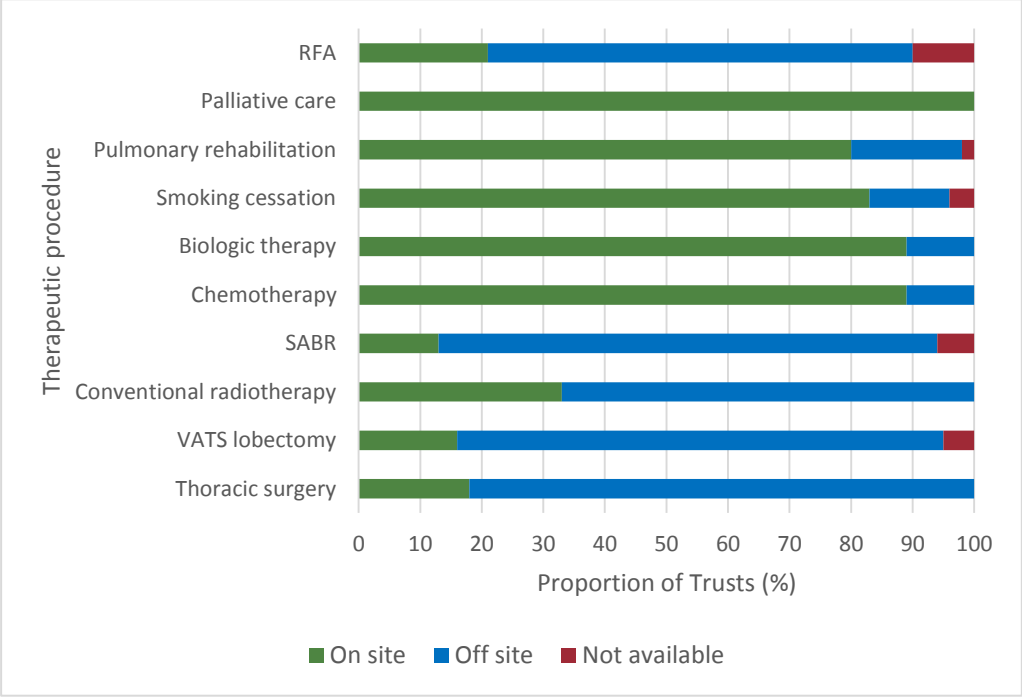


Figure 5-4: Access to therapeutic procedures by Trust
Results for 93 Trusts as 8 Trusts did not complete this section. RFA radiofrequency ablation; SABR stereotactic ablative radiotherapy; VATS video assisted surgery

The thoracic surgical section of the audit was completed by 16 centres (16%). Of these centres 88% also had cardiac surgery on site and 75% had access to on site pulmonary rehabilitation. Table 5-2 summarises the number of surgeons at each centre and also shows the variation in numbers of thoracic theatre sessions available per week and access to high dependency unit beds.

Table 5-2: Thoracic surgery service availability

	Median number (range)
Number of thoracic surgeons	2.25 (0.5-6.0)
Thoracic theatre sessions per week	5.5 (1-18)
Number of thoracic high dependency unit beds	9 (0-24)

The chemotherapy section of the audit was completed by 79 Trusts (75%) and the radiotherapy section was completed by 31 (31%) of Trusts. Service availability is summarised in Table 5-3.

Table 5-3: Service provision and availability at Trusts delivering chemotherapy and radiotherapy

	Chemotherapy Trusts median (range) n=79	Radiotherapy Trusts median (range) n=31
Whole time equivalent (WTE) thoracic oncologists on site	1 (0-4)	2 (0.5-6)
Chemotherapy/ radiotherapy nurses on site (WTE)	4 (0-17)	2 (0-6)
Acute oncology service on site	92%	87%

5.3.4 Multivariable analysis

Data on 24951 patients diagnosed with NSCLC in 2011 were extracted from the NLCA (22148 who did not undergo surgery and 2803 who did). When these data were linked to the Trust organisational audit data there were records available for 15317 patients, of whom 1750 (11.4%) underwent surgery with curative intent. Demographics of those included, alongside Trust variables is summarised in Table 5-4. These data include information from patients from the 8 Trusts who did not fully complete all of the diagnostic and therapeutic portion of the audit and the treatment centres, explaining why there are some

patients recorded as having missing data regarding access to PET-CT for example.

Those in the surgical group were younger (median age 69 years (IQR 63-75 years) compared with 75 years (IQR 68-82 years) in the non-surgical group. They had earlier stage disease at diagnosis (100% were stage IA-IIIA compared with fewer than 25% of the non-surgical group falling into this category) and their PS was better. They were also more likely to have a recorded FEV1 value, with a higher median percentage predicted FEV1 values (78% predicted (IQR 64-92%) compared with 64% (IQR 48-61%)) and they were more likely to have been referred via a GP route. More patients in the surgical group had SABR available on site compared with the non-surgical group (17.8% versus 12.6%). In addition proportionally more surgical patients had access to VATS lobectomy on site (22.5% versus 17.9%).

Table 5-4: Demographic details for patients included in multivariable analysis

		Overall n=15301 n (%)	Surgery n=1750 n (%)	No surgery n=13551 n (%)
Sex	**Female**	6660 (43.5)	790 (45.1)	5870 (43.3)
	Male	8641 (56.5)	960 (54.9)	7681 (56.7)
Age group	**<55**	852 (5.6)	119 (6.8)	733 (5.4)
	55-59	977 (6.4)	141 (8.1)	836 (6.2)
	60-64	1742 (11.4)	265 (15.1)	1477 (10.9)
	65-69	2288 (15)	368 (21)	1920 (14.2)
	70-74	2760 (18)	390 (22.3)	2370 (17.5)
	75-79	2583 (16.9)	307 (17.5)	2276 (16.8)
	80-84	2257 (14.8)	128 (7.3)	2129 (15.7)
	≥85	1842 (12)	32 (1.8)	1810 (13.4)
Performance status	**0**	2865 (18.7)	807 (46.1)	2058 (15.2)
	1	4501 (29.4)	647 (37)	3854 (28.4)
	2	2602 (17)	115 (6.6)	2487 (18.4)
	3&4	3768 (24.6)	19 (1.1)	3749 (27.7)
	Missing	1563 (10.2)	162 (9.3)	1403 (10.4)
Charlson score	**0**	5178 (33.8)	716 (40.9)	4462 (32.9)
	1	3212 (21)	442 (25.3)	2770 (20.4)
	2	2045 (13.4)	285 (16.3)	1760 (13)
	3	1156 (7.6)	132 (7.5)	1024 (7.6)
	≥4	3710 (24.3)	175 (10)	3535 (26.1)
Townsend quintile	**1**	2483 (16.2)	288 (16.5)	2195 (16.2)
	2	2901 (19)	319 (18.2)	2582 (19.1)
	3	3096 (20.2)	373 (21.3)	2723 (20.1)
	4	3404 (22.3)	398 (22.7)	3006 (22.2)
	5	3202 (20.9)	371 (21.2)	2831 (20.9)
	Missing	215 (1.4)	1 (0.1)	214 (1.6)
Stage	**IA**	948 (6.2)	465 (26.6)	483 (3.6)
	IB	846 (5.5)	408 (23.3)	438 (3.2)
	IIA	565 (3.7)	248 (14.1)	317 (2.3)
	IIB	588 (3.8)	216 (12.3)	372 (2.8)
	IIIA	1999 (13.1)	308 (17.6)	1691 (12.5)
	IIIB	1552 (10.1)	0 (0)	1552 (11.5)
	IV	7401 (48.4)	0 (0)	7401 (54.6)
	Missing	1402 (9.2)	105 (6)	1297 (9.6)
FEV1 percentage predicted	**> 80%**	1549 (10.1)	445 (25.4)	1104 (8.2)
	61-80%	1562 (10.2)	323 (18.5)	1239 (9.1)
	40-60%	1289 (8.4)	143 (8.2)	1146 (8.5)
	< 40%	510 (3.3)	22 (1.3)	488 (3.6)
	Missing	10391 (67.9)	817 (46.7)	9574 (70.7)
Source of referral	**Emergency admission**	1959 (12.8)	54 (3.1)	1905 (14.1)
	GP referral	7143 (46.7)	984 (56.2)	6159 (45.5)
	Consultant referral	3375 (22.1)	471 (26.9)	2904 (21.4)
	A&E	1159 (7.6)	41 (2.3)	1118 (8.3)
	Other	1138 (7.4)	136 (7.8)	1002 (7.4)
	Unknown	527 (3.4)	64 (3.7)	463 (3.4)
PET-CT	**Off site**	9832 (64.3)	1069 (61.1)	8763 (64.7)
	On site	4550 (29.7)	562 (32.1)	3988 (29.4)
	Not available/ missing	919 (6)	119 (6.8)	800 (5.9)
CPEX	**Off site**	4766 (31.2)	496 (28.3)	4270 (31.5)
	On site	9464 (61.9)	1115 (63.7)	8349 (61.6)
	Not available/ missing	1071 (7)	139 (7.9)	932 (6.9)
SABR	**Off site**	11644 (76.1)	1239 (70.8)	10405 (76.8)
	On site	2021 (13.2)	311 (17.8)	1710 (12.6)
	Not available/ missing	1636 (10.7)	200 (11.4)	1436 (10.6)
VATS lobectomy	**Off site**	10846 (70.9)	1146 (65.5)	9700 (71.6)
	On site	2822 (18.4)	393 (22.5)	2429 (17.9)
	Not available/ missing	1633 (10.7)	211 (12.1)	1422 (10.5)
RFA	**Off site**	9437 (61.7)	1027 (58.7)	8410 (62.1)
	On site	3646 (23.8)	417 (23.8)	3229 (23.8)
	Not available/ missing	2218 (14.5)	306 (17.5)	1912 (14.1)
Pulmonary rehabilitation	**Off site**	2230 (14.6)	203 (11.6)	2027 (15)
	On site	11801 (77.1)	1369 (78.2)	10432 (77)
	Not available/ missing	1270 (8.3)	178 (10.2)	1092 (8)

FEV1 forced expiratory volume in 1 second; GP general practitioner; PET-CT positron emission tomography-computed tomography; CPEX cardiopulmonary exercise testing; SABR stereotactic ablative radiotherapy; VATS lobectomy video-assisted thoracoscopy lobectomy; RFA radiofrequency ablation

In the multivariable analysis, individual factors associated with decreased likelihood of receiving surgery were older age (OR 0.12 (95% CI 0.07-0.18) in those aged ≥85 years compared with those aged 70-74 years), poorer PS (OR 0.06 (95% CI 0.03-0.09) for those PS 3 and 4 compared with PS 0), higher stage disease (OR 0.09 (95% CI 0.07-0.11) for those with stage IIIA disease compared with stage IA), poorer lung function (OR 0.13 (95% CI 0.08-0.23) for those with FEV1 percentage predicted <40% compared with >80% predicted) and emergency route to diagnosis (OR 0.58 (95% CI 0.40-0.85) for those diagnosed via an emergency route compared with GP referral) (Table 5-5).

Table 5-5: Results of univariable and multivariable analysis looking at likelihood of receiving surgery for non-small cell lung cancer by individual patient features

		Univariate analysis Odds of receiving surgery OR (95% CI)	p value	Multivariate analysis Odds of receiving surgery OR (95% CI)	p value
Sex	**Female**	1	0.18	1	0.61
	Male	0.93 (0.83-1.04)		1.04 (0.89-1.21)	
Age group	**<55**	1.33 (1.02-1.72)		1.24 (0.89-1.73)	
	55-59	1.43 (1.12-1.83)		1.09 (0.78-1.51)	
	60-64	1.26 (1.04-1.53)		0.99 (0.77-1.28)	
	65-69	1.38 (1.16-1.66)		1.08 (0.86-1.37)	
	70-74	1	<0.001	1	<0.001
	75-79	0.76 (0.64-0.91)		0.77 (0.61-0.98)	
	80-84	0.31 (0.24-0.38)		0.33 (0.25-0.44)	
	≥85	0.08 (0.06-0.12)		0.12 (0.07-0.18)	
Performance status	**0**	1	<0.001	1	<0.001
	1	0.43 (0.36- 0.49)		0.51 (0.43-0.61)	
	2	0.12 (0.10-0.16)		0.21 (0.16-0.27)	
	3&4	0.02 (0.01- 0.02)		0.06 (0.03-0.09)	
	Missing	0.22 (0.18-0.26)		0.75 (0.57-0.98)	
Charlson score	**0**	1	<0.001	1	<0.001
	1	0.78 (0.67-0.90)		0.94 (0.77-1.14)	
	2	0.74 (0.63-0.88)		0.82 (0.65-1.03)	
	3	0.54 (0.44-0.67)		0.78 (0.58-1.05)	
	≥4	0.36 (0.30-0.43)		0.51 (0.42-0.70)	
Townsend quintile	**1**	1	<0.001	1	<0.001
	2	0.89 (0.74-1.08)	0.59*	0.82 (0.64-1.06)	0.37*
	3	1.02 (0.85-1.23)		0.89 (0.69-1.13)	
	4	0.97 (0.81-1.16)		0.84 (0.66-1.06)	
	5	0.93 (0.78-1.12)		0.78 (0.61-1.00)	
	Missing	0.04 (0.00-0.10)		0.01 (0.00-0.08)	
Stage	**IA**	1	<0.001	1	<0.001
	IB	0.97 (0.80-1.16)		0.78 (0.61-1.01)	
	IIA	0.81 (0.66-1.00)		0.62 (0.46-0.82)	
	IIB	0.60 (0.48-0.74)		0.38 (0.28-0.50)	
	IIIA	0.19 (0.16-0.23)		0.09 (0.07-0.11)	
	Missing	0.08 (0.07-0.11)		0.07 (0.05-0.09)	
FEV1 percentage predicted	**> 80%**	1	<0.001	1	<0.001
	61-80%	0.7 (0.58-0.85)		0.8 (0.62-1.03)	
	40-60%	0.32 (0.25-0.40)		0.39 (0.29-0.52)	
	< 40%	0.09 (0.06-0.14)		0.13 (0.08-0.23)	
	Missing	0.26 (0.22-0.30)		0.51 (0.41-0.63)	
Source of referral	**Emergency admission**	0.25 (0.19-0.34)		0.58 (0.40-0.85)	
	GP referral	1	<0.001	1	0.01
	Consultant referral	0.93 (0.81-1.06)		1.04 (0.87-1.25)	
	A&E	0.27 (0.19-0.38)		0.61 (0.40-0.94)	
	Other	0.75 (0.61-0.92)		1.03 (0.78-1.36)	
	Unknown	0.65 (0.49-0.87)		0.81 (0.55-1.19)	

*when missing excluded. FEV1 forced expiratory volume in 1 second; GP general practitioner; OR odds ratio; 95%CI 95% confidence interval

Table 5-6 summarises the results of the analysis looking at the impact of on site availability of diagnostic/ treatment modalities on likelihood of receiving surgery. These are corrected for the individual patient features listed in Table 5-5. Patients who were seen in a Trust which had a PET-CT scanner on site were more likely to receive surgery (OR 1.20 (95% CI 1.01-1.41) compared with a Trust with off site access). Patients seen at Trusts which had SABR and VATS

lobectomy available on site were also more likely to receive lung cancer surgery than those seen at Trusts with no on site access (OR 1.55 (95% CI 1.26-1.92) and OR 1.28 (95% CI 1.06-1.56) respectively). On site availability of CPEX testing, RFA and pulmonary rehabilitation made no difference to likelihood of receiving surgery.

Table 5-6: Results of univariable and multivariable analysis looking at likelihood of receiving surgery for non-small cell lung cancer depending on availability of diagnostic and therapeutic treatments (corrected for patient features)

		Univariate analysis Odds of receiving surgery OR (95% CI)	p value	Multivariate analysis * Odds of receiving surgery OR (95% CI)	p value
PET-CT	**Off site**	1	0.09	1	0.09
	On site	1.14 (1.01-1.29)		1.20 (1.01-1.41)	
	Not available/ missing	1.08 (0.87-1.36)		1 (0.75-1.34)	
CPEX	**Off site**	1	0.09	1	0.82
	On site	1.15 (1.01-1.30)		1.05 (0.89-1.25)	
	Not available/ missing	1.1 (0.88-1.37)		1.02 (0.75-1.37)	
SABR	**Off site**	1	<0.001	1	<0.001
	On site	1.53 (1.32-1.78)		1.55 (1.26-1.92)	
	Not available/ missing	1.14 (0.96-1.36)		1 (0.79-1.26)	
VATS lobectomy	**Off site**	1	<0.001	1	0.04
	On site	1.45 (1.26-1.66)		1.28 (1.06-1.56)	
	Not available/ missing	1.23 (1.03-1.47)		1.16 (0.91-1.46)	
RFA	**Off site**	1	0.01	1	0.28
	On site	1.12 (0.98-1.28)		1.09 (0.90-1.31)	
	Not available/ missing	1.24 (1.07-1.45)		1.18 (0.95-1.47)	
Pulmonary rehabilitation	**Off site**	1	<0.001	1	0.38
	On site	1.39 (1.18-1.65)		1.17 (0.93-1.46)	
	Not available/ missing	1.67 (1.32-2.12)		1.2 (0.87-1.65)	

*Variables are corrected for individual features (Table 5-5) but not for each other. PET-CT positron emission tomography-computed tomography; CPEX cardiopulmonary exercise testing; SABR stereotactic ablative radiotherapy; VATS lobectomy video-assisted thoracoscopic lobectomy; RFA radiofrequency ablation; OR odds ratio; 95%CI 95% confidence interval

5.4 Discussion

Although there have been substantial improvements in treatment rates and outcomes for lung cancer in the UK, the NLCA continues to show unexplained variation in care. This audit demonstrates similar variation in the availability and workload of lung cancer specialists, diagnostic and treatment services and also suggests that on site availability of key staging and treatment modalities influences how likely an individual is to receive surgery for lung cancer.

5.4.1 Key findings and previous work

Whilst there remain areas of service provision for which there are no clearly defined standards or recommendations, the wide variation between some Trusts is concerning. For most patients with lung cancer key decisions regarding treatment are made at the MDT meeting, however in nearly a quarter of Trusts, 35 or more cases are discussed per meeting, equating to only 7 minutes (or less) per patient (assuming a 4 hour meeting, which in many Trusts is not practical). It is difficult to maintain focus for that duration of time and it is conceivable that patients discussed towards the end of the meeting may not receive the same high-quality discussion as those discussed at the beginning. One solution might be to have a separate diagnostic and treatment MDT, however only a third of Trusts currently do this.

There is also marked variation in the workload of key members of the MDT. The recommended caseload for a lung cancer CNS is suggested to be approximately 80 cases per annum, (164) however the audit data show that in some Trusts they have a caseload of up to five times this. A report from Macmillan Cancer

Support showed that the ratio of new lung cancer diagnoses in England to lung cancer nurse specialists is far greater than for other cancer types.(165) There is also an association between being assessed by a lung cancer CNS and receiving anti-cancer treatment.(166) In addition a piece of work looking at who was reviewed by a lung cancer CNS suggested that there was an unmet need in some Trusts, with older patients with poor performance status, early stage disease and co-morbidities being less likely to be assessed, particularly in Trusts with a large caseload.(167) The NICE guidance state that every patient diagnosed with lung cancer should have access to a lung cancer CNS and therefore it is essential to reduce the inequity in order to provide high quality care for all patients. (64)

Equally there is variation in the workload of diagnostic specialists, including radiologists and pathologists. Increasingly patients may be offered more targeted therapies for their lung cancer, requiring optimal tissue sampling and expert interpretation and therefore all MDTs should have access to a full range of diagnostic tests and prompt pathology input. Access to local anaesthetic thoracoscopy in particular is an issue for 14% of Trusts. There is also a move towards an accelerated patient pathway as there is evidence that short diagnostic pathways improve outcomes.(24, 25) Unavailability of diagnostic modalities and high specialist workloads may negatively impact on time to diagnosis, treatment rates and outcomes.

Although most Trusts have on-site chemotherapy services (89%) and all have access to surgery or conventional radiotherapy either on or off site, the

provision of newer, more specialist treatment modalities is more variable. For a proportion of Trusts there is no access to VATS lobectomy, SABR or RFA. The number of older patients being diagnosed with lung cancer (>80 years) is increasing and it is crucial that less invasive radical treatment options are available to all patients to provide them with the best chance of survival.(162) In a similar way there should be equitable access to surgeons and oncologists yet these data also suggest that access to and workload of these specialists varies, which in some Trusts may lead to delays in treatment and consequently less favourable outcomes for those patients.

A study by Khakwani et al showed that individual features independently associated with likelihood of receiving surgery for lung cancer were age, sex, stage, PS and co-morbidity, which is similar to those in our study.(61) They also showed that surgical centres were more likely to operate on patients first seen at the surgical centre rather than those referred to them from other hospitals. The association with increased likelihood of surgical resection in Trusts with on site access to the most up-to-date staging and more specialist treatment modalities is supportive of the findings that patients first seen in surgical centres are more likely to receive surgery, as Trusts with on site PET-CT, VATS lobectomy and SABR are likely to be more specialist larger tertiary centres.

5.4.2 Strengths and limitations

This is the first national audit of Trust organisational features and workload and has shown that it is feasible to link organisational level data to individual patient data collected as part of the National Lung Cancer Audit. There were no

responses from some Trusts which does limit the interpretation of the results to some extent and this audit has not been validated but nevertheless this study provides an insight into inequities in service provision nationally. Further work is needed with a more complete dataset to both validate and confirm these findings and also to assess the associations between other aspects of service provision. Multi-level modelling could also be used to look at the impact of multiple Trust features on a variety of patient outcomes and provide a more comprehensive overview.

5.4.3 Clinical relevance and conclusions

These data provide an overview of lung cancer services in England and Wales and suggest how variations in service provision may impact on patient outcomes. Although the majority of lung cancer MDTs have access to all basic diagnostic, staging and treatment modalities, there is variation in the workload of key members of the MDT, alongside gaps in the availability of some more specialised treatment modalities. An understanding of where the gaps and inequalities lie is important to try to ensure equitable access for all and improve outcomes. There is a plan to repeat the audit in 2 years with more detailed links to process, outcomes and patient experience to see whether things have improved.

5.5 Chapter summary

This chapter provides a summary of a study looking at specialist workload, availability of diagnostic tests and access to treatment modalities. It also linked these data to individual patient data to look at likelihood of receiving surgery for lung cancer. This study was published in Thorax in 2015.(168)

CHAPTER 6 : BRAIN METASTASES FOLLOWING RADICAL SURGICAL TREATMENT OF NON-SMALL CELL LUNG CANCER: IS PREOPERATIVE BRAIN IMAGING IMPORTANT?

This chapter describes a study using a dataset which contained all patients who underwent potentially curative surgery for NSCLC at Nottingham University Hospitals NHS Trust. It looks at the incidence of brain metastases following the surgery and describes demographic and tumour features of these patients and assesses the possibility of pre-operative detectability.

6.1 Introduction

6.1.1 Background

Positron emission tomography-computed tomography (PET-CT) plays an important role in the staging of patients with lung cancer prior to radical treatment. The brain is a common site of metastasis in non-small cell lung cancer (NSCLC) and the incidence of brain metastases is reported to be around 20% at the time of diagnosis.(169, 170) The widespread use of integrated PET-CT preoperatively, which often includes head computed tomography (CT), may detect a proportion of brain metastases but its use is limited as lesions are often small or obscured by the high glucose uptake of the surrounding brain parenchyma.

6.1.2 Rationale for the study

American College of Chest Physicians (ACCP) guidelines recommend magnetic resonance imaging (MR) of the brain in those with clinical stage III or IV disease even if neurologically asymptomatic,(171) whilst National Institute for Health and Care Excellence (NICE) and British Thoracic Society (BTS) guidelines recommend consideration of MR or contrast-enhanced CT of the head in patients selected for treatment with curative intent, particularly in stage III disease.(148, 172) The level of evidence to support these recommendations is low, owing to there being no large study to definitively support this guidance or a clear consensus of opinion. Thus the potential gain from the addition of more sensitive brain imaging such as MR or contrast-enhanced CT of the brain to the staging process prior to radical treatment is uncertain.

6.1.3 Aim of this chapter

The aims of this study were:

- To establish the proportion of patients who developed brain metastases following curative surgery and to describe the features of these patients.
- To identify factors associated with development of brain metastases.
- To estimate how many may have been detected by pre-operative MR brain using growth curves.

6.2 Methods

6.2.1 Study Population

A retrospective study of all patients who underwent surgery for lung cancer with curative intent at Nottingham University Hospitals (NUH), a regional thoracic surgical centre, between 2006 and 2011 was performed. All patients had a preoperative PET-CT from vertex to mid-thigh. CT was performed without contrast and CT parameters used for attenuation correction. The fluorodeoxyglucose (FDG) dose was 400 MBq and dose to scan time was one hour. Electronic patient records and radiological imaging were used to identify those who developed brain metastases in the postoperative period. Radiology and patient records were also accessed at the referring district general hospital to ensure that complete follow-up data on each patient were obtained.

6.2.2 Covariate definitions

Age at the time of surgery was obtained from patient records and was grouped as <50, 50-59, 60-69, and ≥70 years. Pathology reports and patient records were used to define post-operative stage according to the 7th edition of UICC TNM classification (section 2.2.3). Post-operative histology was obtained from pathological reports and was grouped into 3 categories (adenocarcinoma (which included non-small cell NOS), squamous cell carcinoma and adenosquamous). Those with histology which was not in keeping with NSCLC were excluded. Procedure type was coded as segmentectomy/wedge resection, lobectomy/bilobectomy (which included video-assisted thoracoscopic (VATS) resection), pneumonectomy/ sleeve pneumonectomy, sleeve resection +/- lobectomy, or any resection with chest wall resection.

6.2.3 Data organisation and analysis

All CT, MR and PET-CT images were imported to the NUH picture archiving and communication system (PACS). They were independently reviewed by a consultant radiologist to ensure that there was no visible cerebral metastasis on the preoperative PET-CT and to confirm the presence of postoperative metastases. The maximum diameter of the largest metastasis was measured for each patient and the number of metastatic deposits on the diagnostic scan were counted and recorded as 1, 2 or multiple (if there were greater than 2 separate deposits). Patient records were then reviewed to look at subsequent management and date of death (if applicable) was obtained. Follow-up data and death records were last updated and censored on 31st August 2012 to ensure that there was at least 12 months complete follow-up on each patient. Twelve months was chosen as it was felt that it was reasonable to expect a brain metastasis to have been potentially visible pre-operatively if it was detected within this time frame.

6.2.4 Statistical analysis

Kaplan-Meier survival curves were plotted for those with and without brain metastases and median survival was calculated from the date of surgery until death or the censor date for those who developed metastases. Cox regression was used to look at whether patients developed brain metastases or not. Hazard ratios were calculated adjusting for age, sex, histological subtype, surgical procedure and post-operative stage. The proportional hazards assumption was checked by inspecting Nelson-Aalen plots and performing Schoenfeld testing.

6.2.5 Determination of preoperative detectability

A further aim was to determine if the brain metastasis might have been visible on a preoperative MR brain. In order to do this an estimation of how large a metastasis would have been at the time of surgery was performed. This was calculated by using the measurements of the largest metastasis and the time from the date of surgery. A paper by Yoo et al(173) looked at metastatic brain tumour growth rates in NSCLC and found a median volume doubling time of 58.48 days (IQR 32.33-98.48 days). The change in diameter of lesions over time was calculated using this volume doubling time (rounded to 60 days), assuming the metastases were spherical. Change in diameter over time of 2mm and 5mm diameter lesions were plotted. These represent the detection limits for optimally performed MR and a more generous "real world" threshold respectively. Then the maximum tumour diameter measured on the diagnostic scan was plotted against the number of days after surgery that the imaging was performed. The date of surgery was defined as time 0. The lesions that fell above the detection limit curves were classified as likely visible had a preoperative MR been performed and reported optimally or in "real world".

6.3 Results

6.3.1 Study population

From the records 891 patients who underwent surgery with curative intent over this time period were identified. Of these, 159 who had resection of a solitary secondary lung deposit, 3 who were diagnosed with a brain metastasis in the pre-operative period, 1 who did not undergo curative resection as extensive pleural disease was found at the time of the procedure and 2 with incomplete follow-up data/ missing staging information were excluded. A further 20 duplicate records were excluded, alongside 61 patients who had non-lung histology, small cell lung cancer (SCLC), carcinoid or benign disease. Forty patients who died within 60 days of surgery (of early complications relating to the surgery) were also excluded (Figure 6-1). This left a population of 604 patients in total. All had pre-operative PET-CT confirming no distant metastases.

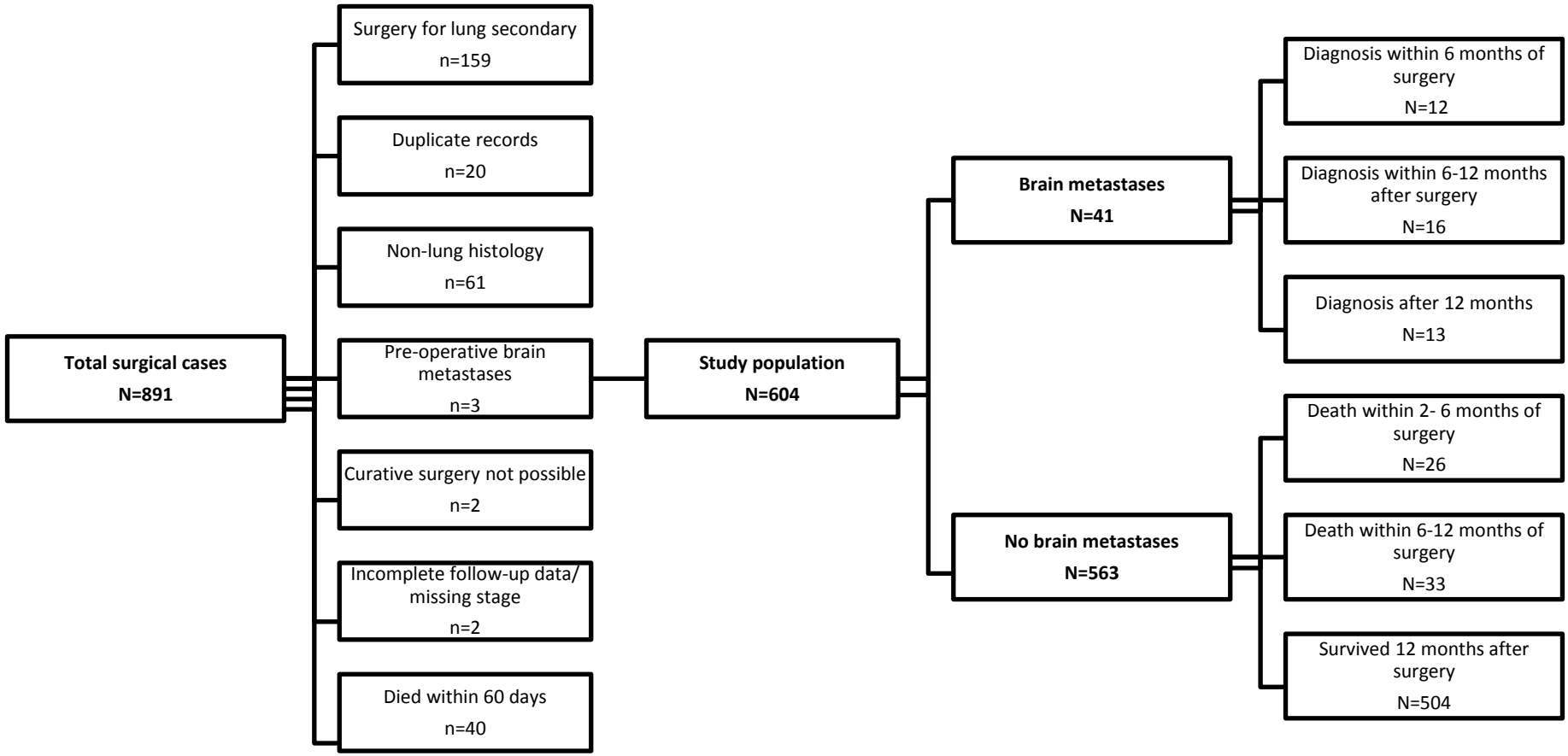


Figure 6-1: Flowchart of inclusion and exclusion criteria and results

Patients were more likely to be male (58%) and to have squamous cell carcinoma (51%) in the surgical population overall. Median age at the time of surgery was 69 years (interquartile range (IQR) 63- 75 years) and the most common procedure type performed was lobectomy/ bilobectomy (64%), which included 40 VATS procedures. Twenty six patients (4%) died within 2-6 months of surgery. Of these, 3 were diagnosed with brain metastases and the others died of surgical complications, other metastatic complications or co-morbid conditions.

6.3.2 Brain metastases patient demographics

Overall 41 (6.8%) patients developed brain metastases during the follow-up period. All of these patients were neurologically asymptomatic at the time of their surgery. Twelve were diagnosed with brain metastases within 6 months of surgery (2.0%) and 16 (2.6%) were diagnosed within 6-12 months. Demographics of those who developed brain metastases compared to those who did not is summarised in Table 6-1. Those with cerebral metastases were more likely to have adenocarcinoma sub-type (56%). In the surgical population overall, 5% with stage I disease developed brain metastases (16/343), which rose to 8% of those with stage II disease (13/153) and 10% of those with stage III disease (11/108).

Table 6-1: Demographics of those with and without brain metastases

	Brain metastases 41 (%)	No brain metastases 564 (%)
Age at time of surgery (years)		
<50	3 (7.32)	12 (2.13)
50-59	7 (17.07)	66 (11.72)
60-69	21 (51.22)	224 (39.79)
≥70	10 (24.39)	261 (46.36)
Sex		
Male	21 (51.22)	330 (58.61)
Female	20 (48.78)	330 (41.39)
Histology		
Adenocarcinoma	23 (56.10)	228 (40.50)
Squamous cell carcinoma	12(29.27)	293 (52.04)
Adenosquamous	6(14.63)	42 (7.46)
Stage		
Stage 1A	6 (14.63)	120(21.31)
Stage 1B	10(24.39)	207(36.77)
Stage IIA	11(26.83)	94(16.70)
Stage IIB	3(7.32)	45(7.99)
Stage IIIA	10(24.39)	95(16.87)
Stage IIIB	1(2.44)	2(0.36)
Procedure type		
Segmentectomy/ wedge resection	2 (4.88)	85(15.10)
Lobectomy/ bilobectomy (including VATS)	26(63.41)	361(64.12)
Pneumonectomy/ sleeve pneumonectomy	9(21.95)	69(12.26)
Sleeve resection +/- lobectomy	1(2.44)	26(4.62)
Any resection with chest wall resection	3(7.32)	22(3.91)

VATS video-assisted thoracoscopic resection

Eighteen patients (44%) had solitary metastases, 6 (15%) had 2 deposits visible and 17 (41%) had multiple metastases at the time of diagnosis. Median maximum diameter of brain metastasis at diagnosis was 25mm (IQR 16-33mm). Ninety per cent (37) who developed brain metastases died during the study period, with a median survival of 100 days following diagnosis of the metastasis (IQR 29-160 days).

6.3.3 Survival analysis

Kaplan-Meier survival curve for the entire surgical population is presented in Figure 6-2 stratified into those who developed brain metastases versus those who didn't. Median survival from the date of surgery in those who developed brain metastases was 453 days (95% CI 289-710 days).

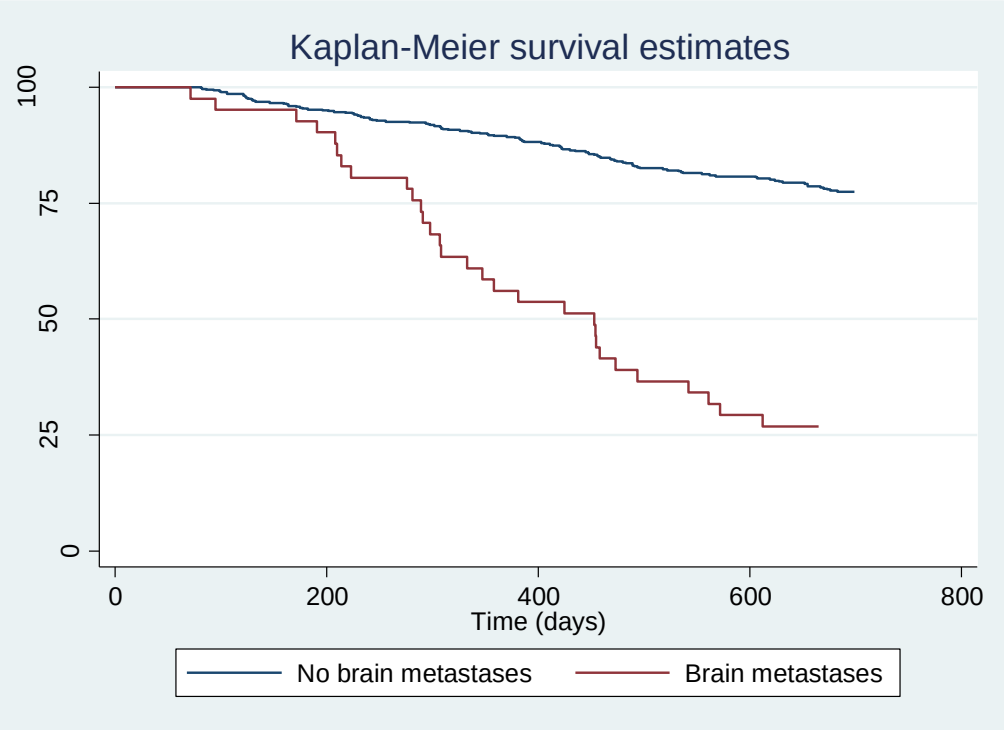


Figure 6-2: Kaplan-Meier plot for the surgical population according to whether they developed brain metastases or not (excluding those who died within 60 days of surgery)

6.3.4 Factors associated with developing brain metastases

Cox regression analysis showed that patients with squamous cell carcinoma subtype were 70% less likely to develop brain metastases than those with an adenocarcinoma subtype (adjusted HR 0.30; 95% CI 0.14-0.64). Also those in the oldest age category (≥70 years) were less likely to develop brain metastases compared to younger age groups (adjusted HR 0.20; 95% CI 0.05-0.79). There was a trend towards higher stage increasing the likelihood of developing brain

metastases, although this did not reach significance once adjusted for other covariates. There was no evidence that sex or procedure type affected the likelihood of metastases developing and no reason to reject the proportional hazards assumption.

Table 6-2: Hazard ratios for developing brain metastases in those who underwent surgery (excluding those who died within 60 days of surgery)

	Hazard ratio (HR)	95% CI	Adjusted HR *	95% CI
Age at time of surgery (years)				
<50	1.00		1.00	
50-59	0.44	0.11-1.68	0.53	0.13-2.17
60-69	0.39	0.12-1.32	0.55	0.15-1.96
≥70	0.17	0.05-0.63	0.20	0.05-0.79
Sex				
Male	0.81	0.44-1.49	1.34	0.69-2.63
Female	1.00		1.00	
Histology				
Adenocarcinoma	1.00		1.00	
Squamous cell carcinoma	0.41	0.20-0.83	0.30	0.14-0.64
Adenosquamous	1.44	0.59-3.54	1.47	0.57-3.78
Stage				
Stage 1A	1.00		1.00	
Stage 1B	0.97	0.35-2.67	1.01	0.37-2.81
Stage IIA	2.33	0.86-6.29	2.18	0.76-6.22
Stage IIB	1.54	0.39-6.18	1.23	0.28-5.40
Stage IIIA	2.41	0.88-6.65	2.17	0.73-6.47
Stage IIIB	13.35	1.59-111.93	8.86	0.80-98.58
Procedure type				
Segmentectomy/ wedge resection	1.00		1.00	
Lobectomy/ Bilobectomy (including VATS)	2.96	0.70-12.49	2.85	0.67-12.18
Pneumonectomy/ sleeve pneumonectomy	5.67	1.22-2.25	3.84	0.74-19.92
Sleeve resection +/- lobectomy	1.79	0.16-19.80	2.09	0.17-25.07
Any resection with chest wall resection	6.08	1.01-36.41	4.72	0.68-32.84

* Adjusted for age, sex, histology, stage and procedure type
HR hazard ratio; 95% CI 95% confidence interval

6.3.5 Detection by MR brain

Three patients who developed metastases at over 2 years post-surgery were excluded from this portion of the analysis as it was felt that these could not reasonably have been detected with a pre-surgery MR brain. Figure 6-3 shows the plot of the remaining 38 patients with curves to show both 2mm and 5mm detection thresholds.

Using a 5mm detection threshold 29 (71%) of brain metastases should have been of at least 5mm maximum diameter at time 0. Using a 2mm detection threshold 34 (83%) would have been at least 2mm in maximum diameter at time 0. These would be potentially detectable had MR brain been performed as part of the staging process. This means that 4.8% (29/605) of patients who underwent surgery may have had their brain metastases detected by preoperative MR and this might have been as high as 5.6% (34/605) with optimal MR detection limits.

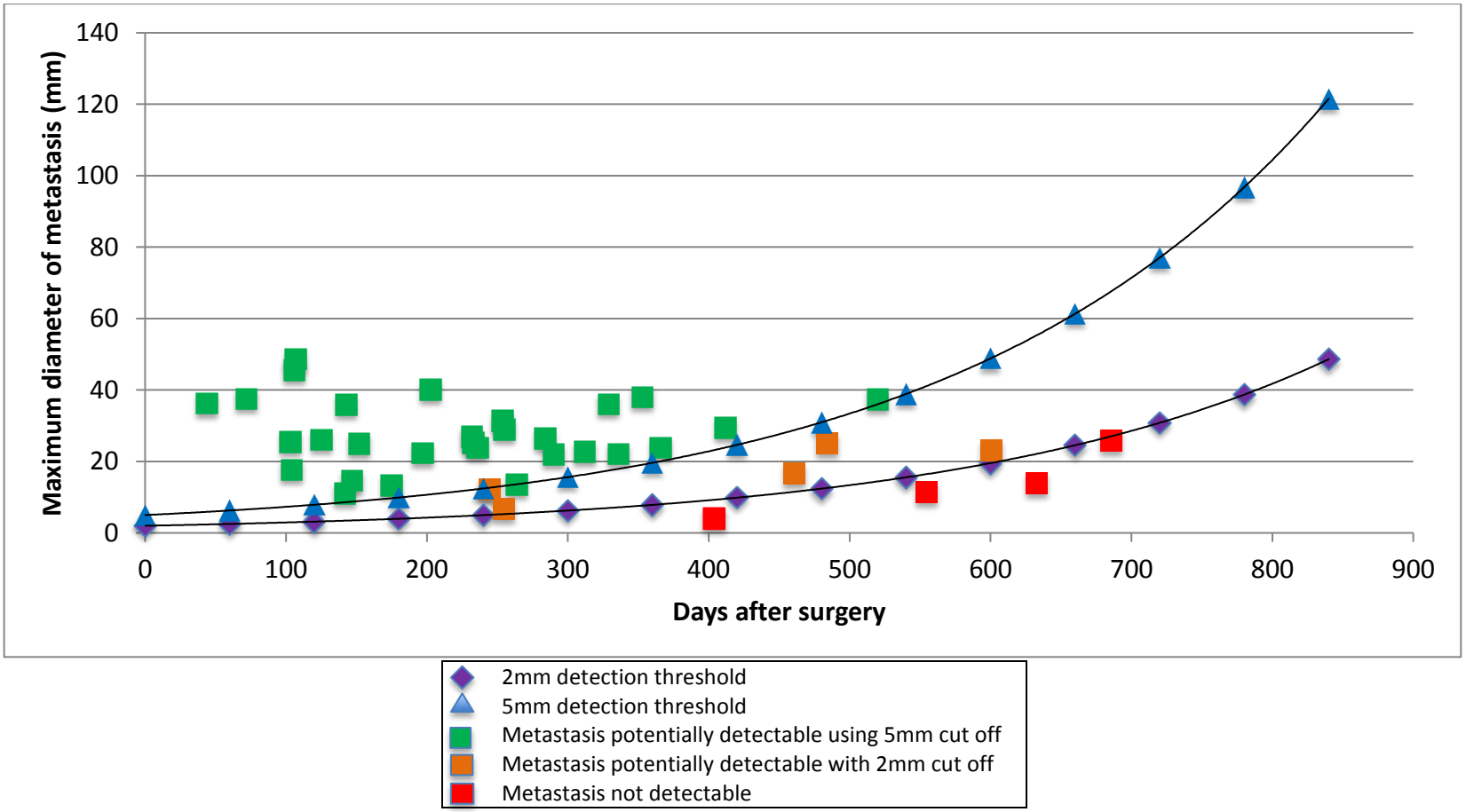


Figure 6-3: Plot of size of brain metastases and time of diagnosis after surgery with 2mm and 5mm MR detection thresholds

6.4 Discussion

In this large series of 604 patients there was a 6.8% incidence of post-operative brain metastases, with the majority (4.6%) occurring within 12 months of surgical resection. Those who subsequently developed metastases were more likely to have had an adenocarcinoma resected and the majority had early stage malignancy (73% had stage I or stage II disease). ACCP, BTS and NICE guidelines recommend considering additional brain imaging, especially in those with stage III disease. Whilst proportionally more stage III patients developed brain metastases, these data argue that preoperative brain imaging should be applied irrespective of stage.

These data suggest that 71% of those who developed cerebral metastases might have been detected preoperatively had they undergone MR brain as part of their staging (assuming a 5mm detection threshold), potentially avoiding futile surgery in 4.8% of patients or providing an opportunity to treat oligometastatic disease.

6.4.1 Strengths and weaknesses

This is the first large study of its kind to address this question in detail. There was a very high level of data completeness and full follow-up information for all patients included, suggesting high validity for the results.

The calculation of growth curves is a potential limitation of this study. The volume doubling time estimate was based on the best evidence in the literature but we have assumed exponential growth. As tumours become very large they may out-grow their blood supply and so increase the volume doubling time.

However, Figure 6-3 shows that most of the larger tumours were well above the detection limits and that there are only 4 patients with relatively large tumours (>25mm) that are close to the calculated detection limit. A second related limitation is the assumption that the metastases were spherical. This is clearly not the case and metastases may grow more in one dimension than another, although when the radiology was reviewed, the majority of metastases in this study were approximately spherical. A further limitation is inability to make adjustments for the effect that adjuvant chemotherapy or different histological subtypes may have made to the tumour growth rate. However it is unlikely that these limitations would substantially alter the conclusions because many of the metastases were in excess of 20 or 30mm at the time of diagnosis, falling well above the 5mm detection growth rate curve, suggesting that even with a change in doubling time or lower scan resolution most should have been visible had MR brain been performed at time 0. In addition a large proportion of patients had early stage disease so would not have been offered adjuvant chemotherapy in any case.

Although the MR scan cuts offs of 2mm and 5mm are arbitrary and some centres may be able to detect lesions below this threshold these numbers were chosen following discussion with consultant neuroradiologists based at NUH. Given optimal MR scanning facilities and optimal patient factors it was agreed that a lesion detection threshold of 2mm would be appropriate. It is acknowledged that in the “real-world” there are often factors which make performing an optimal scan impossible which is why, again following consultation, it was decided that a 5mm detection threshold was appropriate.

MR may detect small false positive lesions which are below the spatial resolution of PET-CT or contrast-enhanced CT brain and care needs to be taken in the interpretation of these smaller lesions should pre-operative MR be routinely used.

6.4.2 Other work in the literature

Previous studies have also shown that those with adenocarcinoma are more likely to develop brain metastases than other non-small cell histological sub-types and in addition these metastases are more frequently neurologically asymptomatic.(174-176) In this series younger age (< 70 years) was associated with an increased likelihood of developing brain metastases and several other studies have reported similar findings.(177-179) A comparison between this study and the previously published data on brain metastases following curative surgery for lung cancer is presented in Table 6-2.

The majority of these studies were conducted in the East Asian population who we know tend to have a higher prevalence of mutation-driven adenocarcinomas (30% versus 7%) and a better prognosis after a diagnosis of NSCLC.(180-182) This may explain their much longer survival following a diagnosis of brain metastases compared with the predominantly Caucasian population in this surgical group. Certainly in the East Asian studies the proportion with adenocarcinoma subtype is higher than in this cohort or the cohorts from the USA.(177, 183) Additionally, in the study by Sakamoto(184) et al 38% of the patients developing brain metastases were treated with epidermal growth factor- tyrosine kinase inhibitors (EGRF-TKI) and 18% in the

Kanou (185) study received EGFR-TKIs. A difference in tumour biology may also explain the longer median time to recurrence.

Three of the studies showed a very similar incidence of brain metastases to this study (6.7-6.9%)(183, 184, 186) and the study by Bae et al (187), which reported an incidence of 4.3%, excluded any patients diagnosed within the immediate 2 months following surgery.

In addition to post-operative imaging, Yokoi et al(186)used pre-operative MR brain in 177 patients planned to undergo curative resection for NSCLC who were neurologically asymptomatic. This MR brain (performed 2 weeks before surgery) detected asymptomatic metastases in 6 out of 17 patients (3.4%).

A study by Lee et al(188) showed that the addition of contrast-enhanced MR brain to PET-CT detected an additional 7% of brain metastases in their patient cohort compared with PET-CT alone. This is slightly higher than the estimated detection proportion in this study but their cohort included only those with adenocarcinoma and also was not limited to those with surgically resectable disease. Fifty-three per cent of their patients with brain metastases had stage I or stage II disease at the time of diagnosis, which further suggests that the current NICE, ACCP and BTS recommendations that emphasise stage III disease would miss a substantial proportion of brain metastases.

Table 6-3: Features and survival from the published series of patients who developed brain metastases following surgery for lung cancer

	Current study	**Sakamoto (184)**	**Bae (187)**	**Kanou (185)**	**Yokoi (186)**	**Hubbs (177)**	**Figlin (183)**
Country	United Kingdom	Japan	Rep of Korea	Japan	Japan	United States of America	United States of America
Dates of study	2006-2011	2004-2009	1992-2012	2002-2008	1989-1995	1995-2005	1977- 1986
Total cases	604	967	2832	1091	332	975	1532
Number of brain metastases (%)	41 (6.8%)	65 (6.7%)	86 (4.3%) #	40 (3.6%)	23 (6.9%)	60 (6.2%) **	104 (6.8%)
Males (%)*	51	66	40	63	-	63	-
Median age (age range)*	65 (38-80)	64 (35-88)	60 (34-80)	65 (49-79)	-	64 (43-77)	-
Adenocarcinoma (%)*	56	71	63	60	61	48	52
Proportion of solitary brain metastases (%)	44	-	42	65	52	43	-
Stage (at time of surgery)*	Stage 1- 39% Stage 2- 34%	Stage 1- 28% Stage 2- 31%	Stage 1- 19% Stage 2- 31%	Stage 1- 33% Stage 2- 48%	Stage 1- 26% Stage2- 22%	Stage 1- 64%** Stage 2-36%	-
Median time to recurrence in months (range)	8.5 (1.5- 47.7)	17.8 (1.9-100.8)	10	10.2 (2.1- 32.3)	-	10 (1-55)	-
Median survival after brain metastases diagnosed (months)	3.3	16.3	-	20.6	CT detected- 10 MR detected- 17	-	-

* In the brain metastasis subgroup # Excluding the initial 2 months post-surgery ** Limited to those who underwent surgery for Stage I & stage II disease only

6.4.3 Interpretation of the results

The early detection of asymptomatic brain metastases may, in some, change the treatment paradigm from one of curative resection of the primary lesion to palliative management and therefore would avoid unnecessary surgery that is not without morbidity and mortality. Eighteen patients (44%) had a solitary cerebral metastasis which, in those with good performance status, would usually be treated radically by either surgical resection or stereotactic radiosurgery. The use of MR brain to detect occult brain metastases provides not only an opportunity to treat oligometastatic disease but studies have also reported improved survival in those in good neurological condition at the time of diagnosis.(189, 190) Prognosis in those who develop symptomatic brain metastases is extremely poor, which is confirmed by our study, and early and accurate diagnosis is crucial to allow early palliative care and advance care planning in those affected and in addition the opportunity to offer treatment before the onset of neurological sequelae to allow extended high quality survival.

6.4.4 Clinical relevance and conclusions

These findings suggest that patients should have preoperative MR brain before undergoing surgery with curative intent in NSCLC regardless of preoperative stage, but especially in those with adenocarcinoma histology. MR brain has been shown to be superior to CT both in the detection of small (sub-1cm) metastases, posterior fossa lesions and multiple metastases. This study provides evidence to change the current recommendations to ensure that patients receive optimal staging before planning radical treatment. A detailed

cost-effectiveness analysis is outside the remit of this work and might be the focus of a separate analysis prior to implementation in routine clinical practice.

6.5 Chapter Summary

This chapter described the use of a surgical dataset to look at the incidence of brain metastases following radical surgical treatment of NSCLC and looked at factors associated with their development. Growth curves to try to determine whether MR brain performed prior to surgery may have allowed pre-operative detection were also produced. This work was published in Lung Cancer in 2014. (191)

CHAPTER 7 : PREDICTING DEATH FROM SURGERY FOR LUNG CANCER: A COMPARISON OF TWO SCORING SYSTEMS IN TWO EUROPEAN COUNTRIES

This chapter provides an overview of the current risk scores available to stratify patients undergoing thoracic surgery. It also uses data from the National Lung Cancer Audit and Danish Lung Cancer Registry to validate a new risk score derived from the National Lung Cancer Audit data to predict 90 day mortality and compares its predictive ability with that of Thoracoscore (the most widely adopted risk stratification tool in the United Kingdom).

7.1 Introduction

7.1.1 Background

Surgery remains the first line curative treatment in lung cancer but a key factor when considering whether to offer a patient surgery for lung cancer is the ability to survive the procedure. Resection rates for lung cancer have almost doubled over the past 10 years from 8.8% in 1998 to 15.4% in 2014 and this is largely due to an increase in the number of resections in older patients (> 75 years).(162, 192) However these patients often have a greater burden of comorbid disease and thus are at higher risk of post-operative morbidity and mortality. Some communication of post-operative morbidity and mortality should be provided to allow informed decision making however there is no international consensus regarding risk stratification prior to lung cancer surgery.

The American College of Chest Physicians (ACCP) guidelines (171) recommend physiological testing to risk stratify patients prior to surgical resection rather than the use of risk scores. They suggest that all patients should have forced expiratory volume in 1 second (FEV1) and diffusing capacity for carbon monoxide (DLCO) measured, with predicted post-operative (ppo) FEV1 and ppo DLCO estimated and additional testing guided by these measurements.

The European Respiratory Society/ European Society of Thoracic Surgeons (ERS/ ESTS) (193) also recommend initial assessment of FEV1 and DLCO for all patients and then subsequent physiological testing if required depending on these values. They reviewed risk scores available to predict post-operative

mortality and concluded that current scoring systems scoring systems do not provide an adequate assessment for individual patients. However, they suggest that risk scores could be utilised for benchmarking and risk stratification among groups of surgical candidates.

Measurement of DLCO pre-operatively for all patients is also recommended in current British Thoracic Society (BTS) guidelines. In contrast to the ERS/ESTS guideline however, the BTS also advocate the use of a risk prediction score such as Thoracoscore to estimate, prior to surgery, the risk of death following radical surgical management.(172)

7.1.2 Rationale for the study

Most risk stratification tools use in-hospital mortality or 30 day mortality as their end-point but recent work has suggested that this may underestimate the risk of early death following surgery for lung cancer.(194, 195) In addition, five studies have validated Thoracoscore, the most widely utilised, but found it to be of limited discriminative ability to predict mortality in lung cancer patients.(196-200) Despite this some surgical centres in the United Kingdom (UK) use this score routinely pre-surgery to provide an estimation of risk. Powell et al(84) used the National Lung Cancer Audit (NLCA) linked to Hospital Episode Statistics (HES) to produce a new score to predict 90 day mortality after surgery in those with lung cancer.

7.1.3 Aim of this chapter

The aims of this chapter are:

- To provide an overview of the current scoring systems available for risk stratification prior to thoracic surgery.
- To validate the risk score derived from the NLCA, henceforth called the NLCA score, and compare its performance with Thoracoscore in patients with lung cancer using an updated NLCA dataset and the Danish Lung Cancer Registry (DLCR).

7.2 Summary of current thoracic surgical risk scores

7.2.1 Search strategy

Medline (1946 to present) and Embase (1974 to latest) were searched systematically for all studies with reference to surgical risk prediction score derivation or validation. There were no language restrictions applied. This search was supplemented using the Google search engine and also by screening reference lists of the selected articles, as well as any review articles identified. These results were then refined to identify those with applicability to thoracic surgery and lung cancer surgery in particular.

Physiological and Operative Severity Score for the enumeration of mortality and morbidity (POSSUM)

The POSSUM score was originally devised as a tool to facilitate general surgical audit. It was derived from a cohort of 1372 general surgical patients from a single UK centre.(201) It consists of 12 physiological features (physiologic score (PS)) and an operative severity score (OSS) which comprises 6 variables associated with the surgical procedure. These are summarised in Table 7-1.

Brunelli et al(202) used an Italian cohort of 250 lung cancer patients to validate POSSUM as a tool for thoracic surgery. They substituted peritoneal soiling with pleural soiling and assigned a score of 8 to extended resection (chest wall resection, lymph node dissection and resection of other mediastinal structures), 4 to lobectomy and pneumonectomy and 2 to atypical resection and segmentectomy. The authors assessed two models, one using the original POSSUM score and the second adding a number of preoperative predictive

factors from their logistic regression analysis- sex, smoking history, type of resection, FEV1, FVC, FEV1/FVC ratio, predicted postoperative FEV1, arterial carbon dioxide level, serum albumin, total lymphocyte count, neoadjuvant chemotherapy and radiotherapy and diabetes- to POSSUM. In their cohort there were only 5 deaths (2%) so an assessment of mortality prediction was not possible. A composite end point of morbidity which included mortality was used and both models showed moderate discriminative ability (area under ROC curve of 0.66 and 0.67). In order to calculate POSSUM both the PS (scored at the time of surgery) and OSS (scored post-operatively) are required to be complete which renders this less useful in providing patients with an estimation of pre-operative risk.

Table 7-1: POSSUM Score

Variable	Score			
	1	**2**	**3**	**4**
Physiologic Score (PS)				
Age (years)	≤60	61-70	≥71	
Cardiac signs	No failure	Diuretic, digoxin, antianginal or hypertensive therapy	Peripheral oedema; warfarin therapy	Raised jugulo-venous pressure
Chest radiograph			Borderline cardiomegaly	Cardiomegaly
Respiratory history	No dyspnoea	Dyspnoea on exertion	Limiting dyspnoea (1 flight)	Dyspnoea at rest (rate ≥ 30/min)
Chest radiograph		Mild COPD	Moderate COPD	Fibrosis/ consolidation
Systolic blood pressure (mmHg)	110-130	131-170 or 100-109	≥171 or 90-99	≤89
Pulse (beats/min)	50-80	81-100 or 40-49	101-120	≥121 or ≤39
Glasgow Coma Score	15	12-14	9-11	≤8
Haemoglobin (g/100ml)	13-16	11.5-12.9 or 16.1-17.0	10.0-11.4 or 17.1-18.0	≤9.9 or ≥18.1
White cell count (x 10^{12}/l)	4-10	10.1-20.0 or 3.1-4.0	≥20.1 or ≤3.0	
Urea (mmol/l)	≤7.5	7.6-10.0	10.1-15.0	≥15.1
Sodium (mmol/l)	≥136	131-135	126-130	≤125
Potassium (mmol/l)	3.5-5.0	3.2-3.4 or 5.1-5.3	2.9-3.1 or 5.4-5.9	≤2.8 or ≥6.0
Electrocardiogram	Normal		Atrial fibrillation (rate 60-90)	Any other abnormal rhythm; Q waves; ST/T wave changes
	Score			
Operative Severity Score (OSS)	**1**	**2**	**4**	**8**
Operative severity	Minor	Moderate	Major*	Major +*
Multiple procedures	1		2	>2
Total blood loss (ml)	≤100	101-500	501-999	≥1000
Peritoneal soiling	None	Minor (serous fluid)	Local pus	Free bowel content, pus or blood
Mode of surgery	Elective		Emergency (resuscitation of > 2 hours possible) Operation < 24 hours after admission	Emergency (immediate surgery < 2 hours needed)
Malignancy	None	Primary only	Nodal metastases	Distant metastases

*COPD chronic obstructive pulmonary disease * Major surgery includes any laparotomy, bowel resection, cholecystectomy with choledochotomy, peripheral vascular procedure or major amputation; major+ includes any aortic procedure, abdominoperitoneal resection, pancreatic or liver resection, oesophagogastrectomy*

Ln R/1-R = -7.04 + (0.13 x physiological score) + (0.16 x operative severity score)- where R= post-operative mortality

Estimation of Physiologic Ability and Surgical Stress (E-PASS)

The Estimation of Physiologic Ability and Surgical Stress (E-PASS) score was originally derived to assess the surgical risk in patients undergoing gastrointestinal surgery in Japan.(203) Yamashita et al(204) used a thoracic surgical population to determine whether a modified version of E-PASS would be useful in determining operative mortality following elective thoracic surgery. The score comprises 6 preoperative factors (preoperative risk score (PRS)) and 3 surgical factors (surgical stress score (SSS)) which are then combined to generate the comprehensive risk score (CRS). The coefficients and equation for generating these scores are summarised in Table 7-2.

Table 7-2: Estimation of Physiologic Ability and Surgical Stress (E-PASS) score

Variable	Subgroup	β coefficient
Preoperative Risk Score (PRS)		
Age (years)	Age in years	0.00345
Severe heart disease (NYHA Class III/IV; arrhythmia requiring mechanical support)	Yes = 1 No = 0	0.323
Severe pulmonary disease (VC <60%; FEV1 <50%)	Yes = 1 No 0	0.205
Diabetes mellitus	Yes = 1 No = 0	0.153
Performance status (Japanese Society for Cancer Therapy)	0-4	0.148
American Society of Anaesthesiologists score	1-5	0.0666
Constant		-0.0686
Surgical Stress Score (SSS)		
Blood loss/ body weight (g/kg)		0.0139
Operation time (hours)		0.0392
Extent of skin incision	Laparoscopic/Thoracoscopic=0 Thoracotomy or laparotomy=1 Both =2	0.352
Constant		-0.342
Comprehensive Risk Score (CRS)		
-0.328 + 0.936(PRS) + 0.976(SSS)		

NYHA New York Heart Association; VC vital capacity; FEV1 forced expiratory volume in 1 second
*PRS & SSS both calculated =sum ((subgroup*coefficient) +constant)*

The validation cohort comprised 731 patients and seemed to show a good correlation between E-PASS and morbidity (R 0.985 ($p<0.03$)) however the in-hospital mortality was only 0.7% (5 patients) which meant that assessment of mortality prediction was not possible. These studies were conducted in the East Asian population who we know have a better prognosis after a diagnosis of NSCLC(180-182) which may in part explain this, however the cohort also had a low lung cancer prevalence (51%). Thus applicability of this score, in particular to the UK lung cancer population, is unclear.

European Society Subjective Score (ESSS) and European Society Objective Score (ESOS)

Data from 27 thoracic surgical units from 14 countries collected for the European Thoracic Surgery Database were used to derive two risk models for in-hospital mortality following thoracic surgery.(205) The first, the European Society Subjective Score (ESSS), used data from 2056 patients who underwent thoracic surgery for any reason (85% for malignancy). Age, American Society of Anaesthesiologists (ASA) score, procedure type and dyspnoea score were shown to be independent predictors of in-hospital mortality. Table 7-3 summarises the key components of ESSS.

Table 7-3: European Society Subjective Score (ESSS)

Variable	Subgroup	β coefficient
Age (years)	Age in years	0.036
American Society of Anaesthesiologists score	1	-0.63
	2	-0.13
	3	1.04
	4	-0.28
Medical Research Council (MRC) dyspnoea score	1	-1.25
	2	-1.14
	3	-0.54
	4	2.94
Procedure class	Lung volume reduction	-3.62
	Wedge and segments	0.23
	Lobectomy	1.30
	Pneumonectomy	2.08
Constant		-6.68

*Odds = sum of coefficients +constant (where age is age in years*β coefficient); Probability of in-hospital mortality= exp(odds)/(1+exp(odds))*

When ESSS was internally validated it performed well for patients at low risk but underestimated mortality in the medium risk group and overestimated mortality in the highest risk cohort. Subsequently the authors decided that the patient population may have been too heterogeneous to produce a useful risk score so used 1694 patients with lung cancer from the dataset to produce a score for in-hospital mortality within this subgroup, termed the European Society Objective Score (ESOS). ESOS comprises two variables- age and post-operative predicted FEV1 (ppoFEV1) and the coefficients are summarised in Table 7-4.

Table 7-4: European Society Objective Score (ESOS)

Variable	β coefficient
Age (years)	0.0501
Post operative predicted FEV1 (%) (ppoFEV1)	0.0218
Constant	-5.8858

*Odds = constant+ (β coefficient*age)-(β coefficient*ppoFEV1); Probability of in-hospital mortality= exp(odds)/(1+exp(odds))*

ESOS has been externally validated in four studies. (197-199, 206) Three studies provided area under the ROC curve values which ranged from 0.70-0.80 indicating moderate discriminative ability. ESOS was derived from a solely malignant population however two of the validation studies included all surgical patients, with lung cancer prevalence in their cohorts of 80% and 89%.(198, 199)

Thoracoscore

Falcoz et al(207) used a French database (Epithor) of 15183 patients who underwent thoracic surgery between 2002 and 2005 to derive a score to predict in-hospital mortality. The coefficients and variables comprising the score are summarised in Table 7-5. Five studies have externally validated Thoracoscore and have shown it to be of only moderate discriminatory value (area under the receiver operating curves (ROC) of between 0.44 and 0.71).(196-200) Thoracoscore was not derived from a population with solely malignant disease but included patients undergoing thoracic surgery for a range of indications from the relatively minor spontaneous pneumothorax to complicated pneumonectomy for lung cancer. Applicability to the lung cancer population is therefore unclear.

Table 7-5: Thoracoscore

Variable	Subgroup	β coefficient
Age (years)	< 55	-
	55-65	0.7679
	≥ 65	1.0073
Sex	Female	-
	Male	0.4505
American Society of Anaesthesiologists score	≤ 2	-
	≥ 3	0.6057
Performance status	≤ 2	-
	≥ 3	0.689
Dyspnoea score	≤ 2	-
	≥ 3	0.9075
Priority of surgery	Elective	-
	Urgent or emergency	0.8443
Procedure class	Other	-
	Pneumonectomy	1.2176
Diagnosis group	Benign	-
	Malignant	1.2423
Comorbidity score	0	-
	≤ 2	0.7447
	≥ 3	0.9065
Constant		-7.3737

Odds = exp(sum of coefficients +constant); Probability of in-hospital mortality= odds(1+odds)

Chamogeorgakis et al(208) used a modified version of Thoracoscore (excluding dyspnoea score) again to look at in-hospital mortality and externally validated this. Although the area under the ROC curve was 0.95 in the external validation this was a population with a very low prevalence of malignancy (45%) so applicability to the lung cancer population is uncertain.

Epithor

Bernard et al(209) used an updated version of the Epithor dataset (used to derive Thoracoscore) to develop and perform an internal validation of a score to predict in-hospital mortality following surgery for lung cancer. The authors devised two models- one in which co-morbidities were listed individually and one in which the number of comorbidities per patient were counted and

grouped as a ranked variable (Table 7-6). Internal validation for both models was performed using bootstrap resampling (random selection of individuals from the derivation dataset) which showed moderate discriminative ability for both scores (area under ROC of 0.78). This score has not been externally validated and furthermore is quite complex, including coefficients which take into account three interaction variables (Table 7-6), predominantly related to the different weighting that pre-procedure forced expiratory volume (FEV) had depending on whether the patient underwent a limited or more extensive resection. This may be the reason why this model has not been adopted in routine clinical practice.

Table 7-6: Epithor Model 1 and Model 2

Variable	Subgroup	β coefficient Model 1	Variable *	Subgroup *	β coefficient Model 2
Age	Increasing years	0.048			0.045
Sex	Female	-0.74			-0.745
	Male	-			-
Side	Left vs right	-0.43			-0.42
American Association Of Anaesthesiologists score	Increasing units	0.39			0.39
Performance Status	Increasing units	0.31			0.30
Body mass index (kg/m2)	≤ 17	-			-
	18-21	-0.87			-0.89
	22-26	-1.15			-1.18
	> 26	-1.46			-1.53
FEV	Increasing %	-0.011			-0.01
Lobectomy	Yes vs no	0.63			0.56
Pneumonectomy	Yes vs no	1.07			1.09
Pneumonectomy · FEV	Interaction	0.01			0.01
Side · pneumonectomy	Interaction	-0.47			-0.485
Extended resection	Yes vs no	-0.92			-0.9
Extended resection · FEV	Interaction	0.018			0.018
Stage	III vs I or II vs IV	0.49			0.47
Stage	IV vs I or II vs III	0.53			0.50
Chronic bronchitis	Yes vs no	0.2	Number of	0	-
Cardiac arrhythmia	Yes vs no	0.38	comorbidities	1	0.50
Coronary artery disease	Yes vs no	0.44		2	0.81
Congestive cardiac failure	Yes vs no	0.52		3 or 4	0.95
Peripheral vascular disease	Yes vs no	0.39			
Alcoholism	Yes vs no	0.645			
History of malignant disease	Yes vs no	0.36			
Prior thoracic surgery	Yes vs no	0.82			
Constant		-6.7			-6.64

*FEV forced expiratory volume; * Where different from model 1*

Society of Thoracic Surgeons (STS) Score

The Society of Thoracic Surgeons (STS) General Thoracic Surgery Database (GTSD) was set up in the US to provide information for research and to allow benchmarking between institutions. Kozower et al(210) used data on 18800 patient who underwent surgery for lung cancer between 2002 and 2008 to derive a prediction score for in-hospital/ 30 day mortality. In their multivariable

analysis 12 variables were shown to be independent predictors- age, sex, performance status, ASA score, pneumonectomy, bilobectomy, renal dysfunction, induction chemoradiotherapy, steroid use, urgent procedure, FEV1 and BMI- although no β coefficients are provided. Internal validation using bootstrap sampling was conducted by the authors with area under the ROC curve value of 0.77, indicating moderate discriminative ability. Poullis et al(197) performed an external validation in a UK cohort with lung cancer and the STS score showed poor discriminative ability in this population with area under the ROC curve of 0.61.

National Lung Cancer Audit (NLCA) Score

The NLCA was used to produce a score to predict 90 day mortality following surgery for lung cancer.(84) Data from 10991 patients who underwent surgery between 2004 and 2010 in England were obtained and formed the derivation dataset. The coefficients and equation for generating these scores are summarised in Table 7-7. To date this is the only risk score to assess 90 day mortality as most focus on in-hospital or 30 day mortality.

Table 7-7: National Lung Cancer Audit (NLCA) Score

Variable	Subgroup	β coefficient
Age (years)	<55	-
	55-65	0.31
	66-75	0.97
	> 75	1.40
Sex	Female	-
	Male	0.23
Performance status	0	-
	1-2	0.68
	≥3	0.21
FEV1 (% predicted)	>80	-
	61-80	0.20
	40-60	0.69
	<40	0.95
Procedure type	(Bi-)lobectomy, wedge or segmentectomy	-
	Other*	0.07
	Pneumonectomy	1.16
Charlson comorbidity score	0-1	-
	≥2	0.33
Stage	IA	-
	IB	0.42
	IIA or IIB	0.51
	IIIA	0.84
Constant		-5.28

*FEV1 forced expiratory volume in 1 second * Chest wall resection, codes for "open operation of lung"*
Odds = exp(sum of coefficients +constant); Probability of 90 day mortality= odds(1+odds)

An internal and external validation of the NLCA score has been performed as part of this thesis and the results are presented in section 7.4.

Other risk scores

Damhuis et al(211) used data from The Netherlands and UK to derive and perform an internal validation on a score to predict death in-hospital or within 30 days of surgery. Four variables were found to be predictive and these are summarised in Table 7-8. Internal validation was performed with area under the ROC curve of 0.71; however this score has not been externally validated.

Table 7-8: Damhuis et al risk score

Variable	Subgroup	β coefficient
Age (years)	<60	-
	60-64	0.54
	65-69	0.96
	70-74	1.29
	75-79	1.55
	≥80	1.84
Sex	Female	-
	Male	0.36
Procedure type	(Bi)lobectomy	-
	Left pneumonectomy	0.73
	Right pneumonectomy	1.28
Histology	Adenocarcinoma	-
	Squamous cell carcinoma	0.40
	Other	0.55
Constant		-5.01

Total risk score= ln(probability/1-probability)

Poullis et al(197) used data on 2574 patients who underwent surgery for lung cancer at a single UK centre between 2001 and 2011. Six variables were shown to be predictors of in-hospital mortality (Table 7-9) and bootstrap resampling was used to validate this score. Area under the ROC curve values of 0.81 and 0.82 were obtained indicating good discriminative ability in this population however this score has not been externally validated.

Table 7-9: Poullis et al risk score

Variable	Subgroup	β coefficient
Age (years)	Age in years	0.098315
Sex	Male	-
	Female	-1.066924
Predicted post-operative FEV1	FEV1 %	-0.036763
Alcohol consumption	Units	0.015209
Emphysema	Yes	1.167361
	No	-
Pre-existing renal disease	Yes	1.449695
(creatinine > 180µmol/l)	No	-
Constant		-8.225937

FEV1 Forced expiratory volume in 1 second; Predicted mortality (%)= 100 x ((exp(sum of coefficients + constant))/(1+ (exp sum of coefficients + constant)))

A German cohort of pneumonectomy patients was used by Safi et al(212) to derive a score to predict in-hospital mortality specifically following this procedure. Five variables were shown to be predictive (Table 7-10) and the model performed well in internal validation (area under ROC 0.85) but again has not been externally validated.

Table 7-10: Safi et al risk score for mortality following pneumonectomy

Variable	**Subgroup**	**β coefficient**
Age (years)	Age in years	0.039
Palliative indication	Yes	1.138
	No	-
Current alcohol use	Yes	1.318
	No	-
Leucocyte count > 13000/µl	Yes	1.276
	No	-
Coronary artery disease	Yes	1.039
	No	-
Constant		-6.152

Risk= sum of coefficients +constant

A summary table which allows comparison of the derivation and validation studies for all of the risk scores discussed is provided in Table 7-11.

Table 7-11: Summary of derivation and validation studies assessing mortality following thoracic surgery

Authors	Score/ scores	Years of data collection	Validation or derivation	Number of patients	Proportion with malignancy (%)	Study setting	Age (mean/ median in years)	Time of mortality assessment (days)	Mortality	Predictive variables	AUC (95% CI)
Brunelli et al(202)	POSSUM	1993-1996	External validation	250	100	Italy	Not given	In-hospital/ 30 day	5 (2%)	*Table 7-1* *Model 1:* PSS + OSS *Model 2:* PSS +OSS + sex, smoking, FEV1, FVC, FEV1/FVC, ppoFEV1, PaC02, lymphocyte count, albumin, diabetes, chemotherapy, radiotherapy	Model 1: 0.66 ## Model 2: 0.67 ##
Yamashita et al(204)	Estimation of physiologic ability and surgical stress (E-PASS)	1995-2000	External validation	282 (retrospective) 458 (prospective)	61	Japan	65 (29-79) 65 (14-85)	In-hospital		Table 7-2	Not given
Yamashita et al (213)	E-PASS	2001-2003	External validation	731	51	Japan	64 (10-89)	In-hospital	5 (0.7%)	Table 7-2	Not given
Berrisford et al(205)	European Society Subjective Score (ESSS)	2001-2003	Derivation Internal validation	2056 1370	85	Europe (multicentre)	62 (IQR 53-70)	In-hospital	66 (1.9%)	Table 7-3	Not given
Berrisford et al(205)	European Society Objective Score (ESOS)	2001-2003	Derivation Internal validation	1694 1128	100	Europe (multicentre)	Not given	In-hospital	33 (1.9%)	Table 7-4	Not given
Brunelli et al(206)	ESOS	2004-2006	External validation	695	100	Europe (3 centres)	64.5 66.4 64.6	In-hospital	6 (2.3%) 7 (2.6%) 7 (4.1%)	Table 7-4	Not given

Falcoz et al (207)	Thoracoscore	2002-2005	Derivation Internal validation	10122 5061	57	France	54.7 +/- 17.4	In-hospital	338 (2.2%)	Table 7-5	0.86 (0.83-0.89)
Bradley et al(196)	Thoracoscore	2007-2010	External validation	703	91	UK	68 (14-89)	In-hospital	16 (2%)	Table 7-5	0.68 (0.56-0.80)
Qadri et al(200)	Thoracoscore	1998-2008	External validation *	243	96	UK	64 +/- 9	In-hospital	11 (4.5%)	Table 7-5	0.44
Chamogeorgakis et al(214)	Modified Thoracoscore	2002-2006	Derivation Internal validation	1675	48	USA	53.5 +/- 18.4	In-hospital	54 (3.2%)	Table 7-5 (excluding dyspnoea score)	0.84 (0.79-0.88)
Chamogeorgakis et al(208)	Modified Thoracoscore	2006-2008	External validation	155	45	Greece	60.3 +/- 15.7	In-hospital	8 (5.2%)	Table 7-5 (excluding dyspnoea score)	0.95 (0.91-0.99)
Bernard et al(209)	Epithor (Model 1)	2003-2008	Derivation Internal validation	18049	100	France	62.5 survivors 66.9 mortality group	In-hospital	690 (3.8%)	Table 7-6	0.78 (0.76-0.8)
Bernard et al(209)	Epithor (Model 2)	2003-2008	Derivation Internal validation	18049	100	France	62.5 survivors 66.9 mortality group	In-hospital	690 (3.8%)	Table 7-6	0.78 (0.76-0.8)
Kozower et al(210)	Society of Thoracic Surgeons (STS)	2002-2008	Derivation Internal validation	18800	100	USA	Not given	In-hospital/ 30 day	413 (2.2%)	Age; Sex; PS; ASA score; Pneumonectomy; Bilobectomy; Renal dysfunction; Induction chemoradiotherapy Steroids; Urgent procedure; FEV1; BMI	0.85
Powell et al(84)	NLCA score	2004-2010	Derivation	10991	100	UK	67 +/- 9.3	90 day	647 (5.9%)	Table 7-7	NA

Damhuis et al(211)	New score	1993-2002	Derivation Internal validation	6110	100	The Netherlands UK	Not given	In-hospital/ 30 day	257 (4.2%)	Table 7-8	0.71
Poullis et al(197)	New score Thoracoscore ESOS STS	2001-2011	Derivation Internal validation External validation External validation External validation	2574	100	UK	67.3 (66.9-67.7)	In-hospital	2.3%	Table 7-9 Table 7-5 Table 7-4 See Kozower et al	0.81 (0.79-0.83) 0.82 (0.80-0.84) 0.69 (0.67-0.71) 0.70 (0.68-0.71) 0.61 (0.59-0.63)
Safi et al(212)	New score	2003-2010	Derivation * Internal validation	542 232	97	Germany	61	In-hospital	35 (6.5%)	Table 7-10	0.85
Barua et al(198)	Thoracoscore ESOS	2008-2011	External validation External validation	290	89	UK	68 (37-91)	In-hospital	9 (3.1%)	Table 7-5 Table 7-4	0.6 0.8
Sharkey et al(199)	Thoracoscore ESOS	2011-2012	External validation External validation	2245 1912 **	80	UK	64.4 +/- 12.9	In-hospital	31 (1.4%) 28 (1.5%)	Table 7-5 Table 7-4	0.71 (0.64-0.72) 0.74 (0.65-0.83)

PS performance status; ASA American Association of Anesthesiologists; FEV1 % percentage predicted forced expiratory volume in 1 second; IQR interquartile range; FEV forced expiratory volume; BMI body mass index; CCF congestive cardiac failure; PSS physiological severity score; OSS operative severity score; GCS Glasgow coma score; ppoFEV1 post-operative predicted FEV1; $PaCO_2$ arterial carbon dioxide level; *Pneumomectomy patients only; # post-operative complications including mortality but not exclusively; ** subgroup with complete data to allow score calculation; ## Composite variable of morbidity which includes mortality

7.3 Methods

7.3.1 Internal validation

Patient population and data source

This project uses a lung cancer population extracted from linked National Lung Cancer Audit (NLCA) data which is described in detail in Sections 2.2 and 2.4. Patients who underwent curative surgery for NSCLC (using Office of Population Censuses and Surveys Classification of Interventions (OPCS-4) coding) between 1st January 2004 and 31st March 2012 were identified from National Lung Cancer Audit (NLCA) data. (Appendix A) Those with stage 3b or stage 4 lung cancer were excluded, as were those with International Classification of Diseases- revision 10 (ICD-10) codes for metastases recorded prior to the procedure date. The original predictive score was derived from NLCA patient data for operations performed between 1st January 2004 and 31st March 2010 so the internal validation cohort was limited to those who underwent surgery between 1st April 2010 and 31st March 2012 to ensure that this was an independent population.

7.3.2 External validation

Data source and patient population

All patients who underwent curative surgery for NSCLC between 2005 and 2011 were identified from the Danish Lung Cancer Registry (DLCR) to form our external validation cohort. Key features of this dataset are summarised in Section 2-3.

7.3.3 Covariates

For the purposes of validation procedure type was classified as pneumonectomy, bi-lobectomy/lobectomy/wedge/segmentectomy, or other. Where there were multiple procedure codes for an individual the most extensive procedure type was included and the most recent procedure date was included if there was more than one for any individual. Comorbidity was classified according to Charlson index using established methods.(111, 140, 163) Patients were then categorised into two groups based on their Charlson index (0-1 and ≥ 2). Percentage predicted forced expiratory volume in 1 second (FEV_1) was categorised into four groups (>80%, 61-80%, 40-60% and <40%) and WHO performance status into three groups (PS: 0, 1-2, ≥3). Pre-treatment records in NLCA and DLCR records linked to National Pathology Registry were used for stage (grouped as IA, IB, IIA/IIB and IIIA) according to the 7th edition of UICC TNM, with post-treatment stage used if pre-treatment records were missing. Age was categorised into four groups (<55, 55-65, 66-85 and >75). Those with missing data from any of the covariates listed were excluded from the validation.

7.3.4 Statistical analysis

All patients in the NLCA and DLCR datasets were assigned a risk score using the coefficients and constants from the multivariable model in the NLCA score (84) (Table 7-7) using the equation: risk score = constant + sum of β coefficients at different values of each covariate. Those who died within 90 days of surgery were then identified.

The NLCA dataset only was then used to assign each patient a risk score based on Thoracoscore in the same way using the β coefficients and constant derived for Thoracoscore.(207) (Table 7-5) Since the NLCA dataset does not contain fields for American Society of Anesthesiologists (ASA) score or Medical Research Council (MRC) dyspnoea score which are required to generate Thoracoscore, data that were available to estimate these scores for the purposes of validation were used as follows; patients are given a coefficient in Thoracoscore if their ASA grade is ≥ 3; which refers to severe systemic disturbance from any cause. It is not possible to state an absolute measure of severity, as this is a matter of clinical judgement. A combination of Charlson co-morbidity score and performance status (as a measure of functional capacity) were therefore used to derive the ASA grade. Those with a Charlson score of ≥ 2 and performance status ≥ 2 were given an ASA grade of 3 for the purposes of this analysis. Patients with MRC dyspnoea score of ≥ 3 are allocated a coefficient in Thoracoscore. This refers to those with some limitation of activity due to breathlessness during daily life. Those who had FEV1 < 60% predicted were assigned MRC dyspnoea score of ≥ 3. A sensitivity analysis was performed using various thresholds of Charlson score, performance status and FEV1 to assign MRC dyspnoea score and ASA grade to the population, all of which produced very similar results in the validation. Once all patients had been assigned a coefficient for all covariates all those who died in hospital (date of death prior to or the same as discharge date for their surgical procedure) were identified.

The discriminatory power of each score to predict mortality was assessed by means of a receiver operating characteristic (ROC) curve and an area under the curve (AUC) calculation. The validation in the NLCA dataset was also repeated using multiple imputation to create substituted values for the missing data fields for FEV1, performance status and stage.

7.4 Results

7.4.1 NLCA patients

There were records for 17687 patients in the NLCA who received curative surgery for NSCLC between 1st January 2004 and 31st March 2012. Of these 670 patients who had an ICD-10 code for metastases prior to their operation date, 612 patients who had missing or incongruous diagnosis dates and 851 in whom the procedure date was >3 months before or >6 months after the NLCA diagnosis date were excluded. This left 15554 patients of which 6080 had a procedure date between 1st April 2010 and 31st March 2012. A further 3222 with incomplete data on FEV1, missing performance status or missing stage were also excluded leaving a final validation cohort of 2858 patients. (Figure 7-1)

7.4.2 Multiple imputation

Due to the amount of missing data in the NLCA multiple imputation was performed to create substituted values for the missing variables. The analysis was repeated for the entire 6080 patients using the imputed values for FEV1, performance status and stage, where these were missing. There was minimal change in the area under the ROC curve, so the results of the original validation, restricted to those with complete data are reported.

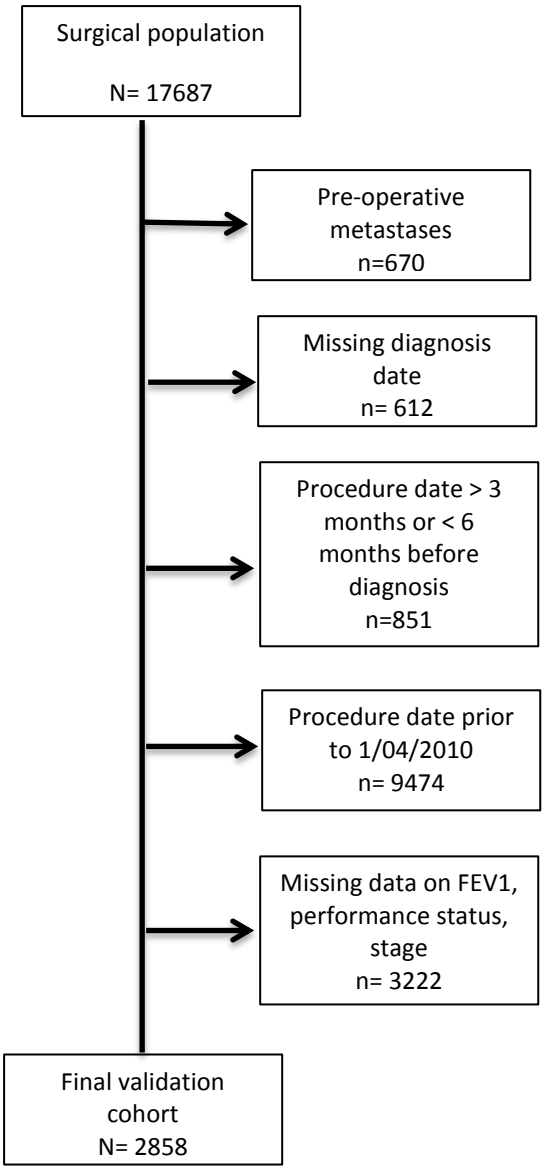


Figure 7-1: Study population and exclusion criteria for National Lung Cancer Audit data

7.4.3 DLCR patients

The DLCR cohort comprised 4234 patients who underwent curative surgery from 2005 onwards. Of these, 1043 patients with missing data on FEV1, performance status or stage were excluded, giving a validation cohort of 3191 patients.

7.4.4 Demographic features

Those in the NLCA validation cohort were older than those in DLCR, with a median age of 69 years (interquartile range (IQR) 63-75 years) versus 66 years (interquartile range (IQR) 60-73 years) in the DLCR. There were proportionally more women in the DLCR group (49% versus 46%) and their cohort also had a greater proportion of patients who were classified as WHO performance status 0 (54% compared with 43%). Pneumonectomy was infrequent in both groups with 9% of those in DLCR and 8% in NLCA undergoing that procedure. Despite these differences, both groups had a similar 90 day mortality of 5% (288 patients died within 90 days of surgery in NLCA and 204 patients in DLCR overall). Features of the NLCA and DLCR groups are summarised in Table 7-12.

Table 7-12: Demographics of NLCA and DLCR validation cohorts

	NLCA - N=6080		DLCR - N=4234	
	n	%	n	%
Age				
<55	415	6.83	490	11.6
55-65	1660	27.3	1331	31.4
66-75	2589	42.58	1643	38.8
>75	1416	23.29	770	18.2
Sex				
Male	3291	54.13	2155	50.9
Female	2789	45.87	2079	49.1
Performance status				
0	2618	43.06	2279	53.8
1-2	2624	43.16	1224	28.9
≥3	48	0.79	31	0.7
Missing	790	12.99	700	16.5
Predicted FEV1%				
>80%	1453	23.9	2413	57
61-80%	1064	17.5	1056	24.9
40-60%	504	8.29	588	13.9
<40%	88	1.45	83	2
Missing	2971	48.87	94	2.2
Procedure type				
(Bi-)lobectomy, wedge or segmentectomy	5333	87.71	3837	90.6
Pneumonectomy	475	7.81	397	9.4
Other	475	7.81	-	-
Charlson score				
0-1	4020	66.12	3107	73.4
≥2	2060	33.88	1127	26.6
Stage				
IA	1747	28.73	1248	29.5
IB	1478	24.31	1135	26.8
IIA or IIB	1499	24.65	712	16.8
IIIA	871	14.33	331	7.8
Missing	485	7.98	808	19.1

7.4.5 Validation of NLCA score

The ROC curve generated from the application of the NLCA score to the NLCA validation cohort is shown in Figure 7-2 (internal validation) and application to the DLCR cohort in Figure 7-3 (external validation). Area under the ROC curve

was 0.68 (95% confidence interval (CI) 0.63-0.72) and 0.60 (95% CI 0.56-0.65) respectively.

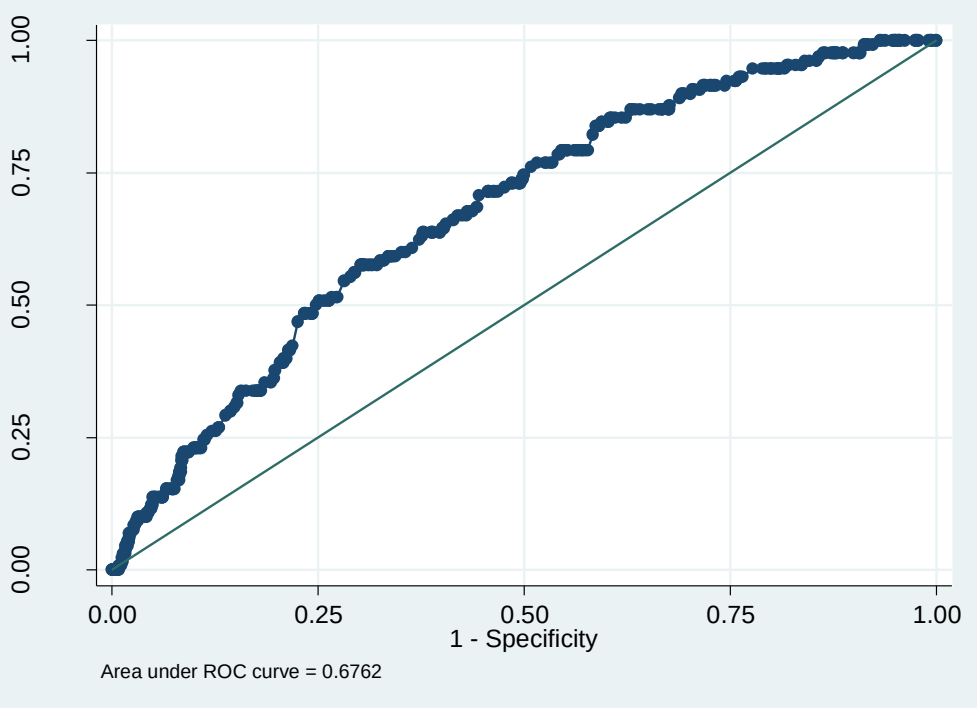


Figure 7-2: Receiver operating characteristic (ROC) curve for 90 day mortality for the NLCA score (Internal validation using 2010- 2012 data)

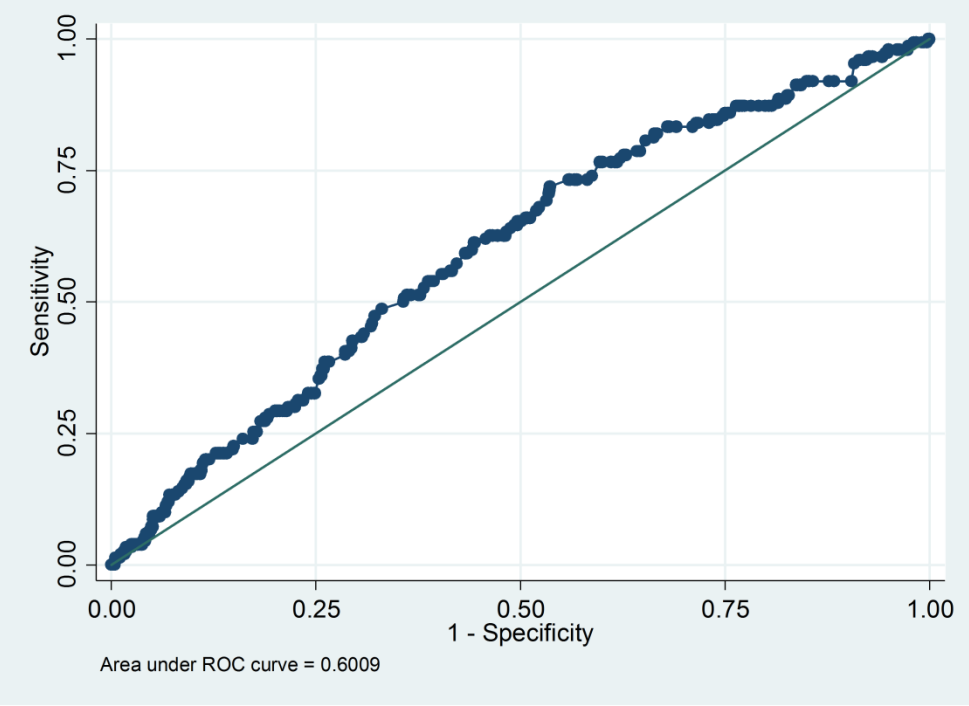


Figure 7-3: ROC curve for 90 day mortality for the NLCA score (External validation using the Danish Lung Cancer Register)

7.4.6 Validation of Thoracoscore

When the coefficients derived from Thoracoscore were used to compute risk probability scores in the NLCA validation cohort the area under the curve was 0.60 (95% CI 0.54-0.66). The ROC curve is presented in Figure 7-4.

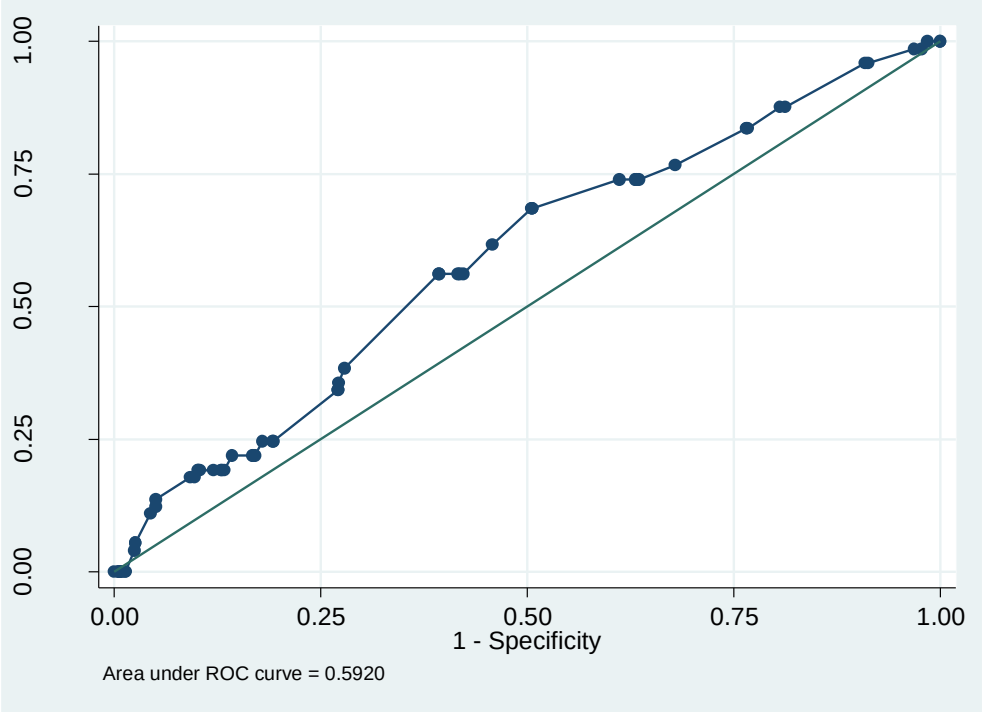


Figure 7-4: ROC curve for in-hospital mortality for Thoracoscore using NLCA data 2010- 2012

7.4.7 Post-hoc analysis: Summary tables

Neither Thoracoscore nor the NLCA score performed well enough to be advocated for routine use to predict surgical mortality in lung cancer patients. In the work by Powell et al(84) age, procedure type and performance status were identified as the major drivers of post-operative mortality. A post hoc analysis was therefore performed using data from the NLCA on all 15554 patients who underwent curative surgery for NSCLC between 1st January 2004 and 31st March 2012 to derive summary tables for 30 and 90 day mortality,

stratified by procedure type, age and performance status. Those sub groups which contained fewer than 50 patients were excluded as it was impossible to provide accurate estimations of mortality due to the small numbers. Results for 30 day mortality are summarised in Table 7-13 and for 90 day in Table 7-14. In general, these show increasing risks of mortality with increasing age and worsening performance status regardless of procedure type, however those undergoing pneumonectomy have higher predicted post-operative mortality than the lobectomy group for each age and performance status sub group.

Table 7-13: Summary table for 30 day mortality for those undergoing lobectomy (Table 7-13a) and pneumonectomy (Table 7-13b)

Table 7-13a: 30 day mortality following lobectomy

	Performance status		
Age (years)	**0**	**1**	**2**
< 70	**1%** (0-1%) 2534	**2%** (1-2%) 1467	**3%** (1-5%) 222
70-80	**2%** (1-3%) 1361	**3%** (2-4%) 1420	**5%** (2-8%) 219
>80	**3%** (1-5%) 263	**4%** (2-6%) 377	**8%** (2-15%) 72

Table 7-13b: 30 day mortality following pneumonectomy

	Performance status		
Age (years)	**0**	**1**	**2**
< 70	**5%** (3-7%) 436	**6%** (3-8%) 289	-
70-80	**11%** (6-16%) 143	**6%** (3-10%) 154	-

The 95% confidence intervals are presented in brackets below the risk %, with the total number in this group underneath

Table 7-14: Summary table for 90 day mortality for those undergoing lobectomy (Table 7-14a) and pneumonectomy (Table 7-14b)

Table 7-14a: 90 day mortality following lobectomy

Age (years)	Performance status 0	1	2
< 70	**2%** (1-2%) 2534	**3%** (2-4%) 1467	**7%** (3-10%) 222
70-80	**4%** (3-6%) 1361	**6%** (5-7%) 1420	**8%** (5-12%) 219
>80	**6%** (3-9%) 263	**7%** (5-10%) 377	**17%** (8-25%) 72

Table 7-14b: 90 day mortality following pneumonectomy

Age (years)	Performance status 0	1	2
< 70	**7%** (5-10%) 436	**12%** (8-16%) 289	-
70-80	**18%** (12-25%) 143	**12%** (7-18%) 154	-

The 95% confidence intervals are presented in brackets below the risk %, with the total number in this group underneath

7.5 Discussion

Two independent datasets were used to compare the performance of the recently derived NLCA score (84) with the currently recommended scoring system (Thoracoscore) for predicting early mortality after lung cancer surgery. There are several scales which are used for AUC value interpretation but, in general, ROC curves with an AUC < 0.75 are not considered to be clinically useful. These results suggest therefore, that neither of these scoring systems has sufficient predictive or discriminative ability to be advocated for use in predicting risk of mortality for individual patients prior to surgery for NSCLC.

7.5.1 Strengths and limitations

The strength of this study is that both an internal and external validation were performed using large UK and non-UK lung cancer populations to fully explore the performance of these risk scoring systems. The NLCA has previously been shown to be representative of the UK lung cancer population (108) and likewise the DLCR contains high quality data (110). However both datasets are made up of a predominantly white population so extrapolation of these results to different ethnic groups is difficult. A specific assessment of model calibration using, for example the Hosmer-Lemeshow test for logistic regression fit, was not conducted given the poor performance of the model in validation.

Although data completeness is improving in the NLCA, missing data are still a challenge. A substantial proportion of patients do not have data on FEV1 (49% in our validation cohort). This is likely to represent data that were unavailable to the administrators at the time of data entry as all patients will have had some

measure of their lung function performed prior to undergoing surgical resection. Likewise the DLCR has some fields which have a lot of missing data, namely performance status (17% missing) and stage (19%) although their recording of FEV1 is complete in 98% of records. Even after those with missing data fields were excluded sample sizes remained large and our multiple imputation analysis did not change any of the results substantially suggesting that the missing data did not affect the validity of the findings.

In order to validate Thoracoscore two covariates (MRC dyspnoea score and ASA grade) were derived as these fields were not available in the NLCA. A sensitivity analysis performed using different cut offs to assign ASA grade and MRC dyspnoea score did not change the results of the validation which suggests that this is not an important limitation. ASA grade is allocated based on clinician judgement and studies have shown that there is only moderate agreement between anaesthetists regarding allocation of a score to an individual (215-217), suggesting that even in datasets where this is included, patients with similar co-morbidities and functional capacity may be assigned different ASA grades.

7.5.2 Comparison with other studies

Five studies have validated Thoracoscore and these are summarised in Table 7-11 and Section 7-2. (196-200) These studies suggest that Thoracoscore tends to under-estimate mortality in those at low-risk and over-estimate risk in high-risk cases. They confirm the findings of this study showing that Thoracoscore has at best moderate discriminative ability in the lung cancer population.

7.5.3 Clinical relevance

The question is raised regarding what clinicians should use to inform pre-operative conversations about surgical risk with patients; by using scoring systems which do not predict individual mortality accurately patients may be misled. Communicating a range of risk, such as that described in the summary tables (Tables 7-13 and 7-14), taking into account performance status, age and procedure type, may be the simplest and most appropriate method of exploring the concept of procedural risk with patients. Individual risk assessment may be possible in the future if improved risk prediction models are developed incorporating physiological measurements. Ensuring that risk assessment and scoring systems are validated and robust is equally important with the proposal that thoracic surgeons should publish surgeon specific outcome data.

7.5.4 Conclusions

These results suggest that although the recently derived NLCA score performs slightly better than Thoracoscore in this UK population, neither performs well enough to be advocated for routine use prior to lung cancer surgery. It may be that either the addition of physiological parameters to demographic and procedural data or risk stratification using physiological measurements alone is needed to better predict individual mortality; and this should form the basis of further research. In the interim the summary tables provide clinicians and patients with easy-access to the actual range of post-operative mortality in the UK for lobectomy and pneumonectomy according to performance status and age.

7.6 Chapter Summary

This chapter described the use of two independent datasets to perform an internal and external validation of a new risk score for 90 day mortality following lung cancer surgery.

These data were presented in poster form at the British Thoracic Oncology Group meeting in Dublin in January 2015 (218) and formed the basis of an oral presentation at the 16th World Conference on Lung Cancer in Denver in September 2015. The results were published in Lung Cancer in 2016.(219)

CHAPTER 8 : PLACE OF DEATH IN PATIENTS WITH LUNG CANCER: A RETROSPECTIVE COHORT STUDY FROM 2004- 2013

This chapter describes the use of data from the National Lung Cancer Audit linked to Hospital Episode Statistics and Office for National Statistics to look at place and cause of death in patients with lung cancer.

8.1 Introduction

8.1.1 Background and rationale

Many patients with cancer die in an acute hospital bed although this may be the location they prefer the least.(220) Those who die in acute hospital beds have been shown to have a worse quality of life compared to those who die in hospices or at home.(221) In addition their caregivers are at increased risk of psychiatric problems after the bereavement.(221, 222) There are also cost implications; research has shown that end of life care in hospital costs three times more than that delivered in the community.(223, 224) The National Health Service (NHS) implemented the National End of Life Care Programme in 2004 with the aim of allowing more patients to receive end of life care in their preferred location. Since then the proportion of patients dying at home or in hospices in many cancer types has increased but in lung cancer this does not seem to be the case.(225)

8.1.2 Aim of this chapter

The aims of this study were:

- To identify place and cause of death in patients with lung cancer to determine which features are associated with dying in an acute hospital bed versus at home.
- To assess geographical variation in place of death in England.

8.2 Methods

8.2.1 Dataset and study population

This project uses a lung cancer population extracted from linked National Lung Cancer Audit (NLCA) data which is described in detail in Sections 2.2, 2.4 and 2.5. All patients diagnosed with non-small cell (NSCLC) or small cell lung cancer (SCLC) who were recorded in the NLCA between 1st January 2004 and 31st December 2011 inclusive were identified. Those who did not have a date of death recorded on the final date that ONS records were updated (March 2013- 14 months after the last patient entry into the dataset) were presumed to still be alive and therefore excluded from further analysis.

8.2.2 Covariate descriptions

Comorbidity was classified according to Charlson score; using inpatient data from HES and established methods.(111, 140) Patients were then categorised into five groups based on their Charlson index score (0, 1, 2, 3 and ≥ 4). Townsend Index of deprivation, divided into quintiles, was used as a measure of socioeconomic status**.** Pre-treatment records in NLCA were used for stage (grouped as IA/IB, IIA/IIB, IIIA, IIIB, IV, SCLC limited or SCLC extensive) according to the 7th edition of UICC TNM, with post-treatment stage used if pre-treatment records were missing. Pre-treatment recording of histology and again post-treatment records were used if this was missing. Performance status (PS) was categorised as per World Health Organisation (WHO) definition into five groups (PS: 0-4). Age at the time of diagnosis was used to categorise patients into eight groups (<55, 55-59, 60-64, 65-69, 70-74, 75-79, 80-84 and ≥85 years).

ONS records were used to characterise place of death as home, acute hospital, residential/nursing home, hospice, community/rehabilitation hospital or elsewhere. Cause of death was defined by ONS using the criteria set out in the 10th revision of the "International classification of diseases" (ICD-10) to determine a single underlying cause of death.(113) England was divided into 28 cancer networks at the time these data were collected so these were used to assess geographical variation in place of death. The proportion of patients dying in each location was calculated and stratified by cancer network. Changes in place of death over the duration of the NLCA were assessed in addition. Four groups were created based on year of death (2004-2006, 2007-2008, 2009-2010 and 2011-2013) and the proportion of patients dying in each place was determined, as described previously, for each year grouping. In addition those who died within 6 months of diagnosis were compared with those who died more than 6 months after diagnosis.

8.2.3 Statistical methods

In order to compare the factors influencing death in the least preferred location (acute hospital) with home, which is frequently reported to be the desired place of death, those who died in other locations were excluded from this part of the analysis. Logistic regression was used to calculate odds ratios (OR) for death within an acute hospital bed within each of the variables described above. Each variable was looked at individually initially, then those which showed an association in the univariate model ($p<0.05$) were included in the multivariate analysis. Likelihood ratio testing was used for all tests of significance.

8.3 Results

8.3.1 Patient population and data source

Records were identified for 178,178 patients in the NLCA. Of these 24150 were excluded as they were still alive at the time ONS records were last accessed for dates of death and a further 8702 patients with carcinoid or mesothelioma histological subtypes, 1417 with dates of diagnosis after their date of death and 282 with missing information on place of death were also excluded. This left a final cohort of 143,627 patients.

8.3.2 Demographic features

Overall 58% were male, with a median age at diagnosis of 73 years (interquartile range (IQR) 65-79 years). The majority had NSCLC (88%) and most patients had advanced disease at presentation; 39% had stage IV NSCLC, 12% stage IIIB, with stages IA to IIA NSCLC comprising 18% collectively. A large proportion of patients were from the most deprived socioeconomic groups (40% from Townsend quintiles 4 and 5), with a median Charlson co-morbidity score of 1 (IQR 0-3).

8.3.3 Place of death

Forty per cent of patients (57678) died in acute hospital beds, 29% (41957) in their own home, 17% (24108) in hospice beds, 8% (12099) died in residential or nursing homes, 4% (5517) in community or rehabilitation hospitals and 2% (2268) “elsewhere”; which contained those dying within prisons and mental health institutions. A summary of the demographics of those dying in each location is provided in Table 8-1. Those dying in residential or nursing homes

were older than the other localities and had worse WHO performance status at diagnosis (33% PS 3 or 4). Proportionally more of the younger age groups died within hospices. Those from the most affluent socioeconomic groups (Townsend quintiles 1 and 2) were most likely to die either in a hospice or at home.

Table 8-1: Demographics of patients stratified by place of death

		Home N=41957		Acute hospital N=57678		Residential/ nursing home N=12099		Hospice N=24108		Community/ rehab hospital N=5517		Elsewhere N=2268	
		n	%	n	%	n	%	n	%	n	%	n	%
Sex	**Female**	17794	42.4	22820	39.6	5926	49	10851	45	2341	42.4	1208	53.3
	Male	24163	57.6	34858	60.4	6173	51	13257	55	3176	57.6	1060	46.7
Age group	**<55**	2593	6.2	3562	6.2	151	1.3	2022	8.4	199	3.6	173	7.6
	55-59	3161	7.5	4173	7.2	300	2.5	2103	8.7	264	4.8	162	7.1
	60-64	5276	12.6	6895	12	621	5.1	3292	13.7	470	8.5	239	10.5
	65-69	6570	15.7	8780	15.2	1013	8.4	3802	15.8	701	12.7	333	14.7
	70-74	7609	18.1	10347	17.9	1576	13	4144	17.2	903	16.4	357	15.7
	75-79	7791	18.6	10401	18	2369	19.6	4048	16.8	1111	20.1	394	17.4
	80-84	5732	13.7	8066	14	2830	23.4	2994	12.4	1096	19.9	360	15.9
	85+	3225	7.7	5454	9.5	3239	26.8	1703	7.1	773	14	250	11
Performance status	**0**	5513	13.1	6874	11.9	820	6.8	3264	13.5	547	9.9	255	11.2
	1	10513	25.1	13229	22.9	1942	16.1	6187	25.7	1180	21.4	514	22.7
	2	7512	17.9	9446	16.4	2099	17.4	4084	16.9	899	16.3	432	19.1
	3	6341	15.1	8625	15	2910	24.1	3148	13.1	910	16.5	372	16.4
	4	1451	3.5	3657	6.3	1128	9.3	794	3.3	278	5	81	3.6
	Missing	10627	25.3	15847	27.5	3200	26.5	6631	27.5	1703	30.9	614	27.1
Charlson score	**0**	16627	39.6	21170	37.6	4158	34.4	10121	42	2164	39.2	965	42.6
	1	8553	20.4	12162	21.1	2594	21.4	4623	19.2	1120	20.3	466	20.6
	2	5039	12	7124	12.4	1641	13.6	2674	11.1	631	11.4	253	11.2
	3	2605	6.2	3944	6.8	1026	8.5	1358	5.6	368	6.7	120	5.3
	≥4	9133	21.8	12738	22.1	2680	22.2	5332	22.1	1234	22.4	464	20.5
Townsend quintile	**1**	6000	14.3	7029	12.2	1766	14.6	3456	14.3	748	13.6	307	13.5
	2	7262	17.3	8531	14.8	2111	17.5	4129	17.1	1096	19.9	376	16.6
	3	7277	17.3	9641	16.7	2452	20.3	4282	17.8	1151	20.9	359	15.8
	4	8002	20.6	11175	19.4	2400	19.8	4362	18.1	1031	18.7	459	20.2
	5	8647	20.6	13358	23.2	2046	16.9	4807	19.9	606	11	516	22.8
	Missing	4769	11.4	7944	13.8	1324	10.9	3072	12.7	885	16	251	11.1

		Home N=41957		Acute hospital N=57678		Residential/ nursing home N=12099		Hospice N=24108		Community/ rehab hospital N=5517		Elsewhere N=2268	
		n	%	n	%	n	%	n	%	n	%	n	%
Histology	**Adenocarcinoma**	6790	16.2	9248	16	1348	11.1	4506	18.7	748	13.6	377	16.6
	Squamous cell	7313	17.4	9433	16.4	1615	13.4	3772	15.7	837	15.2	380	16.8
	NSCLC NOS	7746	18.5	10155	17.6	1549	12.8	4653	19.3	993	18	383	16.9
	SCLC	5384	12.8	6954	12.1	928	7.7	3037	12.6	604	11	282	12.4
	Other	1721	4.1	2205	3.8	444	3.7	1055	4.4	193	3.5	89	3.9
	Missing	13003	31	19683	34.1	6215	51.4	7085	29.4	2412	38.8	757	33.4
Stage	**IA/ IB**	2325	5.5	3904	6.8	990	8.2	1140	4.7	288	5.2	110	4.9
	IIA/ IIB	1589	3.8	2262	3.9	587	4.9	820	3.4	175	3.2	83	3.7
	IIIA	3351	8	4156	7.2	1020	8.4	1833	7.6	370	6.7	160	7.1
	IIIB	5356	12.8	7013	12.2	1305	10.8	2935	12.2	654	11.9	290	12.8
	IV	16773	40	21605	37.5	4414	36.5	9928	41.2	2036	36.9	920	40.6
	SCLC Limited	448	1.1	536	0.9	75	0.6	225	0.9	48	0.9	14	0.6
	SCLC Extensive	1047	2.5	1502	2.6	152	1.3	635	2.6	149	2.7	58	2.6
	Missing	11068	26.4	16700	29	3556	29.4	6592	27.3	1797	32.6	633	27.9
Source of referral	**Emergency admission**	5012	12	9096	15.8	2243	18.5	2708	11.2	951	17.2	308	13.6
	GP referral	21255	50.7	25453	44.1	4809	39.8	11651	48.3	2607	47.3	1018	44.9
	Consultant referral	8092	19.3	11287	19.6	2495	20.6	4719	19.6	928	16.8	456	20.1
	A&E	2514	6	4485	7.8	1077	8.9	1534	604	353	6.4	183	8.1
	Other	2787	6.6	4032	7	814	6.7	1807	7.5	283	5.1	186	8.2
	Unknown	2297	5.5	3325	5.8	661	5.5	1695	7	395	7.2	117	5.2

8.3.4 Multivariable analysis

In order to compare the odds of death in an acute hospital with home the 43992 patients who died in the other locations were excluded, which left a cohort of 99635 patients for the univariable and multivariable analyses. The results are presented in Table 8-2. Males were more likely than females to die in acute hospital beds compared with home (adjusted odds ratio (OR) 1.14; 95% confidence interval (95% CI) 1.12-1.17). Those in the oldest age bracket (85 years and older) were at increased odds of dying in acute hospital beds (adjusted OR 1.16; 95% CI 1.08-1.24) compared with all of the younger age groups. There was no real difference between the other age brackets and likelihood of death within an acute hospital bed. Patients who presented at WHO performance status 4 (bed bound) were more likely to die in acute hospitals compared with those who were fitter (adjusted OR 1.73; 95% CI 1.61-1.87 for WHO PS 4 compared to WHO PS 0). Again there was only an impact on likelihood of dying with an acute hospital in the least fit group (WHO PS 4), with no difference between the other classes in the multivariable analysis. There were increasing odds of death within acute hospitals with increasing levels of socioeconomic deprivation (adjusted OR 1.31; 95% CI 1.25-1.37) for Townsend quintile 5 versus quintile 1). Compared with diagnosis via a general practitioner (GP) referral via all other routes was associated with an increased chance of dying within an acute hospital bed. This was most marked for the emergency admission route (adjusted OR 1.45; 95% CI 1.39-1.51) and in those diagnosed following attendance at accident and emergency (A&E) departments (adjusted OR 1.43; 95% CI 1.35-1.51). Those with highest stage disease (stage IV) at

diagnosis were less likely to die in acute hospital beds when compared with those with earlier stage disease at presentation (adjusted OR 0.74; 95% CI 0.70-0.79). In fact those with stage IA and IB NSCLC were more likely to die in acute hospital beds than all other stages of NSCLC and also than those with limited and extensive stage SCLC.

Table 8-2: Univariable and multivariable analysis comparing death in an acute hospital versus death at home

		Univariable analysis Death in acute hospital		p value	Multivariable analysis Death in acute hospital		p value
		OR	95% CI	(LRT)	OR	95% CI	(LRT)
Sex	**Female**	1		p<0.01	1		p<0.01
	Male	1.28	1.26-1.31		1.14	1.12-1.17	
Age group	**<55**	0.96	0.90-1.03		0.97	0.91-1.04	
	55-59	0.95	0.89-1.01		0.97	0.91-1.03	
	60-64	0.97	0.92-1.03		0.98	0.92-1.02	
	65-69	0.99	0.93-1.05		0.98	0.93-1.04	
	70-74	1		p<0.01	1		p<0.01
	75-79	0.97	0.92-1.03		0.95	0.90-1.01	
	80-84	1.02	0.96-1.09		0.99	0.93-1.06	
	85+	1.23	1.15-1.32		1.16	1.08-1.24	
Performance status	**0**	1		p<0.01	1		p<0.01
	1	1.01	0.97-1.05		0.99	0.95-1.03	
	2	1.01	0.96-1.06		0.95	0.90-0.99	
	3	1.09	1.04-1.14		0.97	0.93-1.03	
	4	2.02	1.88-2.17		1.73	1.61-1.87	
	Missing	1.2	1.15-1.25		1.08	1.03-1.13	
Charlson score	**0**	1		p<0.01	1		p=0.251
	1	1.09	1.05-1.13		1.04	1.00-1.08	
	2	1.08	1.04-1.13		1.02	0.98-1.06	
	3	1.16	1.10-1.22		1.06	1.01-1.12	
	≥4	1.07	1.03-1.10		0.99	0.96-1.03	
Townsend quintile	**1 more affluent**	1		p<0.01	1		p<0.01
	2	1	0.96-1.05		1.01	0.96-1.06	
	3	1.13	1.08-1.18		1.13	1.08-1.18	
	4	1.19	1.14-1.25		1.19	1.13-1.24	
	5 less affluent	1.32	1.26-1.38		1.31	1.25-1.37	
	Missing	1.42	1.35-1.49		1.38	1.31-1.46	
Histology	**Adenocarcinoma**	1		p<0.01	1		p=0.026
	Squamous cell	0.95	0.91-0.99		0.92	0.88-0.97	
	NSCLC NOS	0.96	0.92-1.00		0.97	0.93-1.01	
	SCLC	0.95	0.90-0.99		0.92	0.88-0.98	
	Other	0.94	0.88-1.01		0.92	0.86-0.99	
	Missing	1.11	1.07-1.15		0.97	0.94-1.01	
Stage	**IA/ IB**	1		p<0.01	1		p<0.01
	IIA/ IIB	0.85	0.78-0.92		0.86	0.79-0.94	
	IIIA	0.74	0.69-0.79		0.76	0.71-0.82	
	IIIB	0.78	0.73-0.83		0.79	0.74-0.84	
	IV	0.77	0.73-0.81		0.74	0.70-0.79	
	SCLC Limited	0.71	0.62-0.82		0.76	0.66-0.87	
	SCLC Extensive	0.85	0.78-0.94		0.86	0.77-0.95	
	Missing	0.9	0.85-0.95		0.84	0.79-0.89	
Source of referral	**Emergency admission**	1.52	1.46-1.58		1.45	1.39-1.51	
	GP referral	1		p<0.01	1		p<0.01
	Consultant referral	1.16	1.13-1.20		1.13	1.09-1.17	
	A&E	1.49	1.41-1.57		1.43	1.35-1.51	
	Other	1.21	1.15-1.27		1.16	1.10-1.23	
	Unknown	1.21	1.14-1.28		1.16	1.09-1.23	

OR odds ratio; 95%CI 95% confidence interval; LRT likelihood ratio testing; GP general practitioner; A&E accident and emergency; SCLC small cell lung cancer; NSCLC non-small cell lung cancer

8.3.5 Geographical variation in place of death

There was evidence of marked variation in place of death when the analysis was stratified by each of the 28 cancer networks (Figure 8-1). These regional inequalities were most marked in the proportion of patients dying within hospices, with only 9% in the lowest network dying within this setting compared with 33% in the highest. There was a 20% difference in the proportion dying in acute hospital beds between the lowest and highest cancer network (28% to 48%). There was similar variation in the proportion of patients dying in their own home (22% versus 34% in the highest and lowest networks respectively).

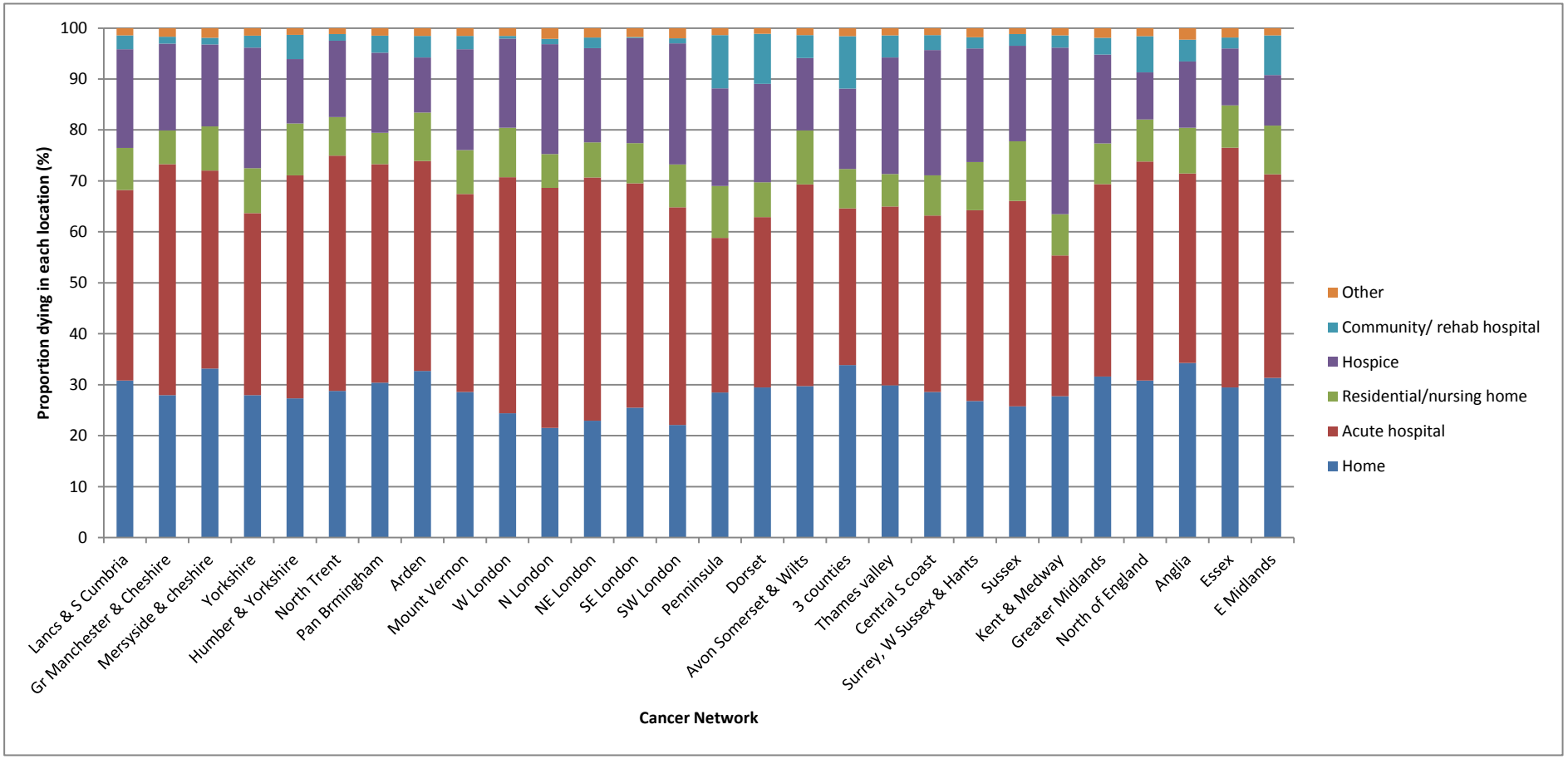


Figure 8-1: Place of death stratified by Cancer Network

8.3.6 Changes over time

Changes in place of death between 2004 and 2013 were also assessed (Figure 8-2), showing a decrease in the proportion of patients dying in acute hospital beds from 45% in 2004-2006 to 35% in 2011-2013. There has been a corresponding increase in the proportion dying at home (26% in 2004-2006 compared to 32% in 2011-2013) but only a very small increase (from 16% to 18%) in the proportion dying within hospice beds. An increase in those dying within residential and nursing home beds has been mirrored by a reduction in the number of community hospital beds and corresponding decrease in the proportion dying within that setting.

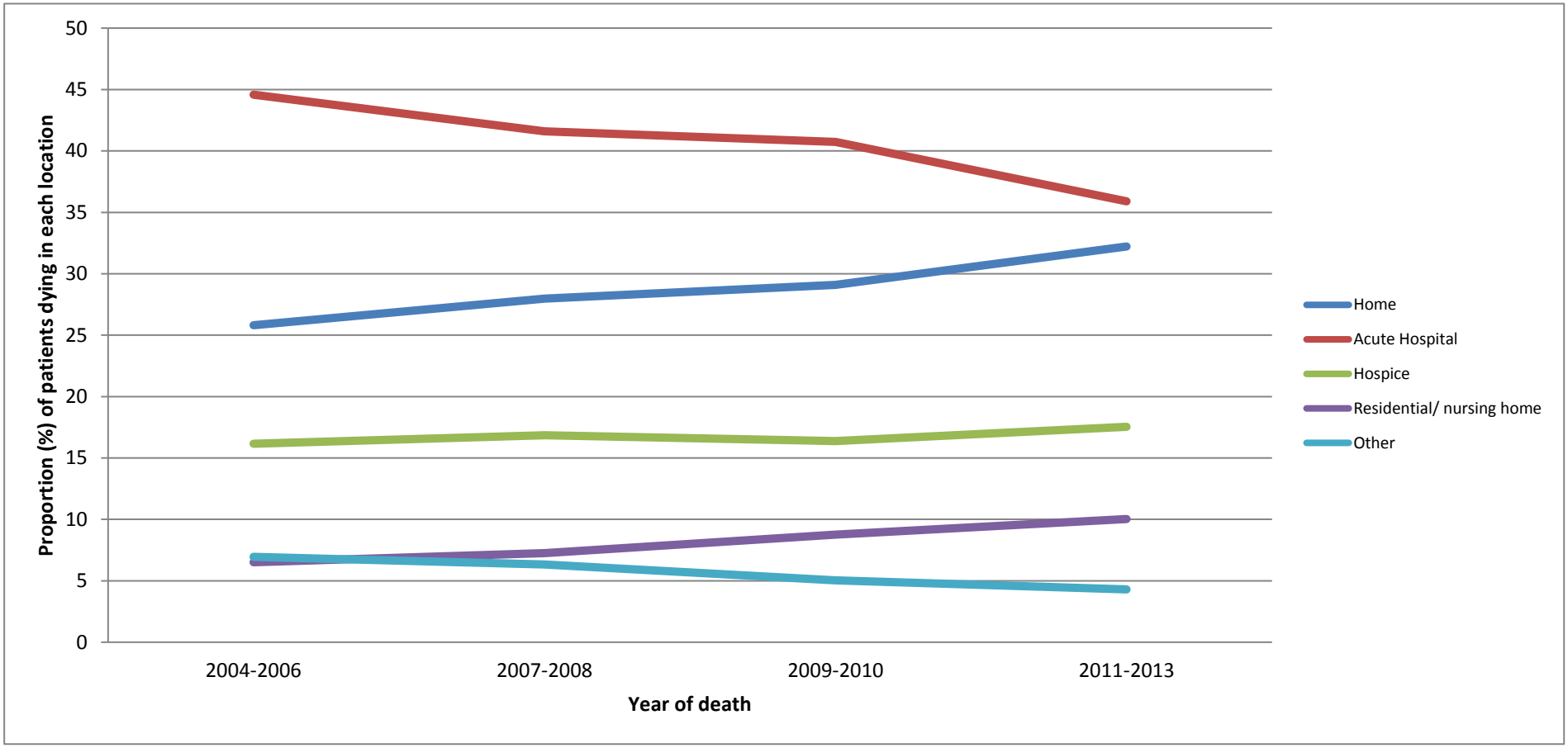


Figure 8-2: Changes in place of death over the duration of the National Lung Cancer Audit (NLCA)

8.3.7 Death within the first 6 months of diagnosis

Finally place of death in those who died in the 6 months following the lung cancer diagnosis was assessed and compared with those who survived for more than 6 months. Fifty six per cent of the cohort died within the 0-6 month time frame. Proportionally more of these patients died in acute hospital beds (44% compared to 35% of those who lived for over 6 months). Patients who survived for over 6 months after their diagnosis were more likely to die at home (32% versus 27%) or in a hospice setting (19% versus 15%) than those who died in the first 6 month window (Figure 8-3). Those who died within the initial 6 months after diagnosis were older (median age at diagnosis of 74 years (IQR 66-80) compared with median age at diagnosis of 71 years (IQR 63-78) in the group who lived for longer than 6 months). There were similar proportions of males and females between the 2 groups (58% males in the group who died within 6 months of diagnosis versus 56% in the group who survived for longer). There was a marked difference in the distribution of performance status when comparing the 2 groups; 50% of those in the group who survived more than 6 months were deemed to be WHO PS 0 or 1 at diagnosis compared with only 23% of those in the group who died within 0-6 month time frame. There were proportionally more patients who were felt to be WHO PS 3 or 4 in the cohort who died within 6 months (30% versus 8%). Seventeen per cent of those in the group who lived for longer than 6 months presented with lung cancer that was stage IA-IIB compared with only 5% in the group who died within 6 months, whilst 48% of the group who died within 6 months had stage IV disease at presentation versus 27% in the group who survived for longer. The group who

died within 6 months were also proportionally more likely to be diagnosed via an emergency admission route (28% versus 12%), with only 40% referred from their GP compared with 55% in the group who lived for longer than 6 months.

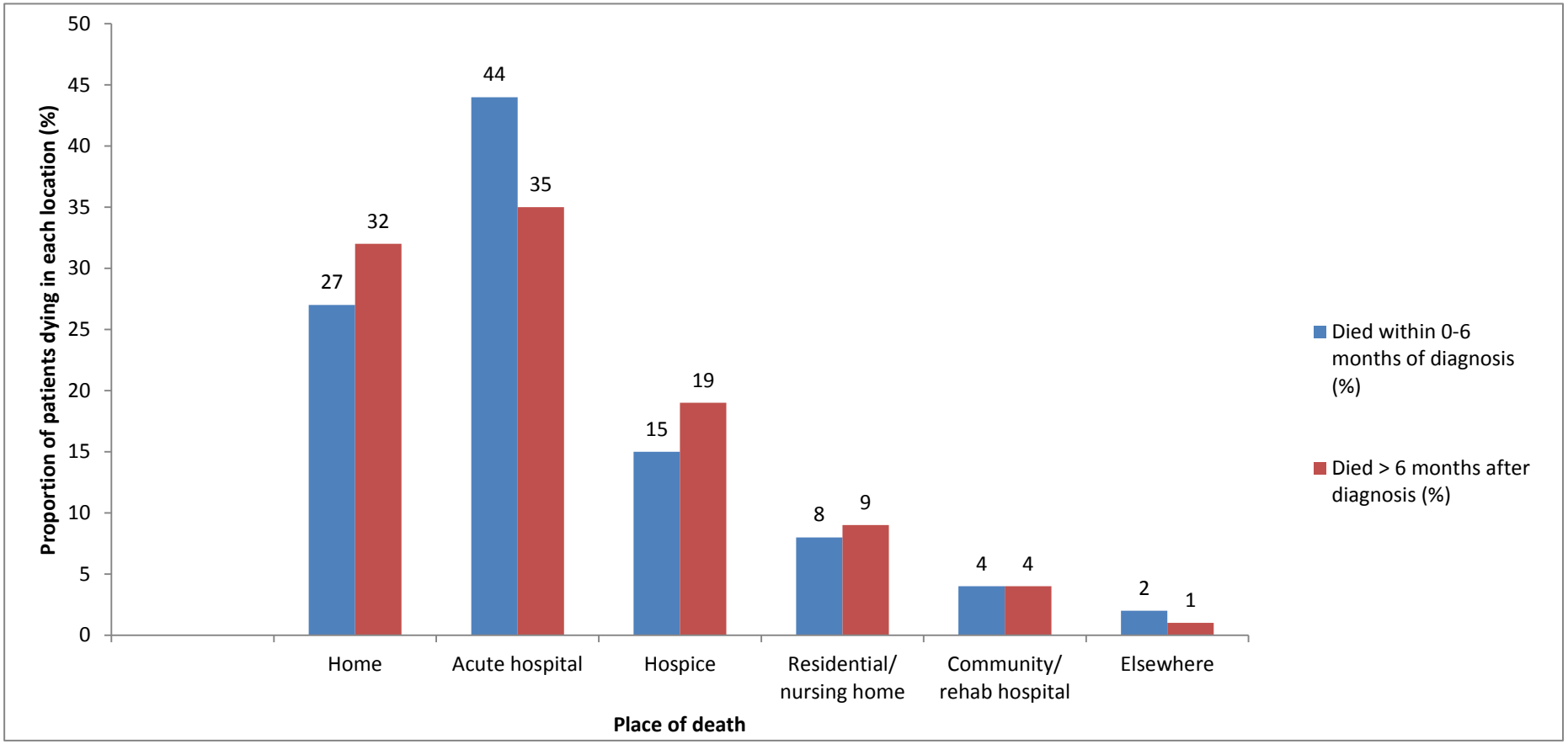


Figure 8-3: Proportion of patients dying in each location stratified by time of death (0-6 months versus >6 months post-diagnosis)

8.3.8 Cause of death

Cause of death was recorded as lung cancer in 86% (123147) of patients. Death was attributed to other malignancies in 6% (8996) of cases, chronic obstructive pulmonary disease (COPD) in 1.4% (2021) and ischaemic heart disease (IHD) in 1.5% (2172), with a variety of other conditions comprising the remaining 5% (Table 8-3).

Table 8-3: Cause of death (as defined by Office for National Statistics)

Cause of death	**Number of patients**	**%**
Lung cancer	123147	85.7
Chronic obstructive pulmonary disease	2021	1.4
Ischaemic heart disease	2172	1.5
Other malignancy	8996	6.3
Mesothelioma	838	0.6
Sepsis/ infection	950	0.7
Pneumonia	565	0.4
Other	4934	3.4
Unknown	4	0

8.4 Discussion

The results show that although there has been a small reduction in the proportion of patients with lung cancer dying in acute hospital beds between 2004 and 2013 overall 35% still die within that setting. Old age (≥ 85 years), male sex, socioeconomic deprivation, WHO performance status 4 at diagnosis and emergency route to diagnosis are all strongly and independently associated with increased likelihood of death within acute hospitals, although death in this location is less likely with more advanced stage disease at presentation. In additional there is evidence of geographical variation in place of death, particularly with regard to provision of hospice services. Given the often advanced stage of disease at presentation and poor prognosis it is unsurprising that the majority of patients with a diagnosis of lung cancer are recorded as having died of the underlying disease.

8.4.1 Strengths and limitations

This is the first study to look in detail at both place and cause of death in lung cancer patients specifically and the large number of patients and representative nature of the population is a particular strength. The NLCA has previously been validated as a reliable source of the UK lung cancer data and currently has in excess of 90% case ascertainment. (108) The population in NLCA is predominantly white which does make extrapolation of these results to other ethnic groupings difficult. In addition work by Gao et al (225) has suggested that marital status may be relevant to place of death; with those who are single, widowed or divorced being more likely to die in the hospital setting. These data are not routinely recorded in these datasets so there may be

confounding due to inability to adjust for this. It was also not possible to take into account patient preference in place of death or assess whether this might change when faced with worsening symptoms in the terminal phase of the illness. However, although not all patients will choose to die at home existing evidence suggests that this is the preference for most. (220)

8.4.2 Other work in the literature

Gao and colleagues used ONS data to look at changes in place of death for all cancer deaths in England between 1993 and 2010.(225) They also looked at some features associated with death at home or in a hospice. Although there was a decrease in the overall proportion of cancer patients dying in hospital over this time frame there was little change in the lung cancer group. Similar to this study they found that male sex, increasing age, social deprivation and in addition marital status were independently associated with increased likelihood of dying in acute hospitals. A further piece of work by Gomes et al (226) looked at changes in place of death between 2004 and 2010 for both cancer and non-cancer patients and showed that there has been a small rise in the proportion of patients overall dying at home over this time period; with 27% of all cancer patients dying in their own home in 2010. This is very similar to the 29% observed in the lung cancer population for the years 2009-2010 in this study. In addition Davies et al (227) assessed changes in place of death for cancer patients in the Thames Cancer Registry over a 17 year period (1985-2002), showing a decrease in the proportion of patients dying within acute hospital beds from 67% to 47% by 2002. They also showed that those who were older (> 75 years) were more likely to die in acute hospital beds. A randomised

controlled trial conducted by Brumley et al (228) assigned patients with a terminal prognosis to usual care or in-home palliative care, which comprised not only pain and symptom relief, but a variety of educational, medical and social support services. They looked at visits to the emergency department (ED) and also place of death in both groups and showed that the group receiving palliative care support had fewer visits to the ED and also were 20% more likely to die at home compared to the usual care arm. This highlights the key role that early and effective palliative care has to play in ensuring that wherever possible patients are able to achieve their preferred place of death. Studies consistently show that patients with lung cancer are more likely to die in acute hospital beds than patients with many other solid organ tumours and there is a suggestion that this is due to late discussions about end-of-life care (229) in combination with a rapidly progressive disease. There is evidence that patients who discuss end of life care preferences are more likely to die within home or hospice settings however we did not have the data available to know what extent these factors contributed to death within acute hospital settings in our cohort.(230, 231) It may be that those patients who survived for more than 6 months after diagnosis had more time to plan and discuss preferences for end of life care than those who died earlier in the disease process possibly explaining in part the smaller proportion of patients in this group who died in acute hospital beds when compared with those who died in the 6 months immediately following their diagnosis. A variety of patient and tumour features also contribute to mortality within the initial 6 months following diagnosis which may make discharge from acute hospital beds more difficult to facilitate. Work from the

National Cancer Intelligence Network (NCIN) “Routes to Diagnosis” work has shown that lung cancer patients who present via the emergency route have a much lower 1 year survival(21) which explains why proportionally more patients in the group who died within 0-6 months were diagnosed via an emergency admission route. In addition performance status has been previously shown to be an independent predictor for overall survival in lung cancer, with the differences in performance status marked between those who died within 6 months and those who lived for longer in our cohort.(232) Work performed in South East England has suggested that those from ethnic minority groups were more likely to die in hospital beds and less likely to access hospice services than white patients, which suggests there may be an additional need to look in more detail at the ethnicity of patients and the part it has to play in place of death.(233) The wide geographic variations in place of death are likely to represent service availability and accessibility. A study by Gatrell et al (234) looked at variations in geographic access to hospices in England and Wales and showed that there are inequities in provision of beds between regions, with the lowest numbers of beds per 1000 cancer deaths in the North East and East Midlands; which corresponds to the two cancer Networks with the lowest proportion of patients dying within hospice beds in this study (North of England and East Midlands).

8.4.3 Interpretation of the results

The fact that those with higher stage disease at presentation are less likely to die within an acute hospital setting was an unexpected finding, however it may indicate that clinicians are better at offering early palliative care to patients

with non-curative disease to try to ensure that they achieve their preference in place of death compared with those who undergo surgery or aggressive systemic anti-cancer treatment; where the focus is on management with curative intent rather than end of life care. Those with higher stage disease would also therefore be less likely to suffer morbidity and mortality related to treatment side effects which may necessitate hospitalisation in the latter days of life. It may also be the case that recognition that the patient has reached the terminal phase of the disease, with a shift in the treatment paradigm from curative to palliative, may occur too late to allow the preference in place of death to be met. There is no study which has specifically addressed this question however. It is difficult to suggest what the optimal proportion of patients dying in acute hospital settings should be as many patients develop distressing symptoms in the latter days of life which necessitate hospitalisation. Only 28% of patients in the lowest cancer network died in acute hospital beds (due principally to a large number of in-hospice deaths in this region) so it is not unreasonable to suggest that this could be the gold standard given optimal service provision and resource allocation, although there are differing social and patient demographic features which also may influence this between regions. Another option may be to optimise palliative services for these patients on site at acute hospitals or provide a more integrated community and acute hospital service than many regions currently have to facilitate discharge to a more appropriate setting. A pilot project looking at the impact of early palliative care in those with advanced cancer in the UK is ongoing.

8.4.4 Clinical relevance and conclusions

A substantial proportion of patients with lung cancer die in acute hospital beds and this is more likely in the most elderly (≥85 years), males, those who are socially deprived, those diagnosed via an emergency admission route and in those with the worst performance status (WHO PS 4). There is marked geographical variation, suggesting a need to improve end-of-life planning in those at greatest risk, and to review the allocation of resources to provide more hospice beds, enhanced community support and ensure equal access. Increasing the proportion of patients dying in the community would undoubtedly offer cost savings in addition to psychological benefits.

8.5 Chapter summary

This chapter described the use of linked NLCA data to look in detail at place and cause of death in patients with lung cancer in England. These data were presented in oral and poster form at the British Thoracic Oncology Group meeting in Dublin in January 2015(235) and formed the basis of a poster presentation at the 16th World Conference on Lung Cancer in Denver in September 2015. This work was published in PLOS ONE in 2016.(236)

CHAPTER 9 : THESIS SUMMARY AND RECOMMENDATIONS FOR FUTURE RESEARCH

This Chapter summarises the key findings in this thesis and makes some suggestions for future research.

9.1 Summary of main findings and clinical relevance

This thesis has looked at a variety of factors which may affect the diagnosis and prognosis in patients with lung cancer in the United Kingdom across the whole patient pathway. The key findings from the thesis are summarised below:

- Qualitative and quantitative methods were used to identify barriers to early diagnosis in lung cancer and also to look at how best to engage those from hard-to-reach groups. Smoking stigma, alongside practical barriers such as location of screening, transportation costs and accessibility were identified as key. The results from this study can be used to inform screening pilots and to ensure that uptake into and engagement with any future lung cancer screening programme are maximised to ensure that it is both viable and cost-effective. Public awareness campaigns also need to try to address and counter the issue of stigma and negative societal perceptions of smoking to ensure that individuals at high risk of lung cancer do not feel victimised.

- In order to try to look at possible reasons for the excess early (0-90 days) mortality in the United Kingdom (UK) primary care data were used to identify patient and GP features which predict death within 90 days of diagnosis and to try to determine if the gatekeeper role of the GP may contribute to this. Almost a third of patients die within 90 days of diagnosis and that these are more likely to be men from deprived, rural environments and current smokers. These patients do interact with primary care prior to diagnosis suggesting missed opportunities to identify them earlier.

- The first organisational audit of lung cancer service availability and provision was performed and this was linked to individual patient data from the National Lung Cancer Audit (NLCA). Through this a variety of Trust and patient-level features were identified that are associated with increased likelihood of receiving surgery for lung cancer. The variation in workload and access to diagnostic and therapeutic interventions between centres was also described. A future audit is planned with further links to process and outcomes which will allow more in-depth assessment of inequities and to see whether things are improving.

- I looked at development of brain metastases following radical surgical management of lung cancer to try to determine whether further staging investigations should be performed pre-operatively to ensure that patients will benefit from treatment with curative intent. This study suggests that magnetic resonance imaging (MR) may have a place in more accurately staging the brain prior to this treatment and may in the future lead to a change in guidelines and clinical practice.

- This thesis used linked NLCA data in combination with data from the Danish Lung Cancer Registry (DLCR) to perform an external validation of two lung cancer surgical mortality prediction scores. This work suggests that the scoring systems currently available are not able to provide accurate individual risk prediction and therefore more appropriate summary tables were developed, based on the NLCA, that can be used to explore the concept of thoracic surgical risk with patients.

- Using linked NLCA data, I found variations in place of death and individual features which were associated with increased likelihood of death in acute hospital beds compared with home. These results may enable clinicians to improve end-of-life planning by identifying those at greatest risk earlier.

9.2 Suggestions for future research

9.2.1 Pre-diagnostic interactions in primary care

The finding that patients who die within the first 90 days of diagnosis are interacting with primary care prior to their diagnosis suggests that there may be an opportunity to diagnose them earlier. Using primary care data it will be possible to look in more detail at what is happening during consultations in the 12 months prior to diagnosis to understand what lung cancer patients are presenting with, and when, to determine if there are indeed avoidable delays. It is also important to try to unpick the finding that practices that performed more chest x-rays (CXR) had a higher proportion of patients who died early. Understanding what specifically triggers a CXR request in primary care is important and may shed some light on this, either using primary care alone or with linkage to the diagnostic imaging dataset. It may not be easy to determine the answer to this question using quantitative methods alone so a qualitative methodology using semi-structured interviews may also need to be utilised. Furthermore it may be possible to identify the features of a CXR request that are associated with a more favourable outcome for example.

9.2.2 Linked primary care dataset

One of the projects that I aimed to complete during this thesis was to try to map the whole lung cancer patient pathway; from early pre-diagnostic interactions in primary care, to the referral process and secondary care intervention to final treatment and outcome to try to determine why the outlook for patients in the UK is so poor. Problems with data linkage and data sharing agreements with the Health and Social Care Information Centre meant

that this project was not possible during my research time. Linkage of primary care data to Cancer Registry data and the NLCA should be possible now and therefore a study looking at different parts of the diagnostic process to see where delays to diagnosis in particular may lie could be performed. Other questions that it may be possible to answer using this linked dataset may be:

1. Do patients who have potentially curative interventions differ from those who do not in terms of their early interaction with primary care?

2. To what extent are patients who are admitted and diagnosed with lung cancer as part of an acute admission seen in primary care in the last year before diagnosis?

9.2.3 Surgical risk prediction

The finding that current lung cancer surgical risk prediction tools do not seem to provide accurate individual mortality prediction is important. It is essential to communicate an accurate risk to patients in a way that they can understand so that they can make an informed decision. Further work to try to refine risk prediction scores and to understand the key drivers of post-operative mortality is therefore important. It may be that other patient factors have a role to play such as haemoglobin, serum albumin, serum creatinine, or that intra-operative factors (estimated blood loss or duration of procedure) or Trust features such as high dependency unit (HDU) bed availability may all be relevant. In order to assess this I have collected data at Nottingham University Hospitals NHS Trust (NUH) on detailed patient, procedural and trust features as part of a pilot study. The intention will also be to perform a multi-centre study to collect more data

to try to look into this in more depth in order to determine whether producing a more accurate risk prediction tool is feasible. It may be that providing an individual assessment of mortality is not possible as intra-operative and post-operative factors may have a larger role to play.

9.2.4 Organisational audit linked dataset

The pilot project showed that it is feasible to collect data on Trust features including information on workload of cancer specialists and also that it is possible to link these data to individual patient data. A repeat audit of organisational features is planned and a linked dataset could be used to look at the impact that different Trust features have on specific patient outcomes. Other proposed linkages could be to patient experience data to try to determine if organisational features have an impact on this in addition to outcomes such as survival and likelihood of receiving radical and palliative treatment for lung cancer. Multi-level modelling could be employed to look at the effect of multiple organisational factors alongside multiple patient features.

9.2.5 Using the SEER-Medicare dataset to answer key questions about lung cancer care

The CONCORD study compared cancer survival in 5 continents for breast, colorectal and prostate cancers and showed more favourable outcomes in the United States (US).(237) Work published in the CONCORD-2 study showed lung cancer 5 year survival figures of 18.7% in the US compared with 9.6% in the UK between 2005 and 2009.(238) Most of the International comparative data on lung cancer do not include the US and it will be interesting to compare outcomes from the US with the UK as the healthcare provision is very different

between the two countries. The SEER-Medicare dataset is a national cancer registry dataset linked to insurance data (containing all hospital admissions and treatments received and billed for). It is possible look in detail at provision of lung cancer care in the US and compare this with data already obtained from the NLCA about care in the UK. Specific questions which it may be possible to answer are:

1. To identify all cases of non-small cell lung cancer, small cell lung cancer and carcinoid and look at overall survival and healthcare utilisation prior to diagnosis.

2. To determine what treatment options are offered to patients and look at morbidity and mortality associated with this.

3. What are the characteristics of people with lung cancer who die early (within 30 and 90 days) with and without treatment?

a. For all people in the dataset

b. For those who receive chemotherapy

c. For those who have surgery with curative intent

d. For those who receive radical or palliative radiotherapy

e. To what extent can multivariate scores predict this mortality for patients in groups a-d in the dataset?

4. To what extent do organisations vary in the use of active and palliative treatments (surgery, chemotherapy and radiotherapy) and can we identify factors which explain this?

a. For all people in the dataset, and how does this affect overall survival.

b. For people with stage I & II disease and good performance status.

5. What is the utilisation of hospice resources in the US and what are patterns of care in the last 6 months of life?

6. To compare access and availability of treatments for lung cancer and outcomes in the US with data already analysed using a UK lung cancer dataset (NLCA) for the above parameters.

9.3 Conclusions

The studies described in this thesis use prospectively collected data to provide a snapshot of different aspects of the lung cancer patient journey which may impact on prognosis, alongside qualitative methodology to try to determine reasons for diagnostic delay and attitudes towards screening programmes. There are questions which cannot be addressed using large datasets like those described in this thesis, however there remain some important clinical questions about lung cancer care and outcomes for which these datasets provide valuable information. In particular linkage of primary and secondary care datasets to Cancer Registry data, organisational data and newer datasets such as the Systemic Anti-Cancer Therapy dataset, diagnostic imaging dataset and radiotherapy dataset will allow a much greater understanding about where inequities lie in lung cancer care in the UK and may provide some insight into why there is apparent excess mortality compared with other countries. Ultimately the aim is to modify and streamline the patient pathway and identify inequalities so that all patients receive high quality care with a view to maximising survival where possible.

REFERENCES

1. Ferlay J, Soerjomataram I, Ervik M, Dikshit R, Eser S, Mathers C, et al. GLOBOCAN 2012 v1.0, Cancer Incidence and Mortality Worldwide: IARC cancerbase No. 11 [Internet]. Lyon, France: International Agency for Research on Cancer2013 [cited 2016 Oct]; Available from: http://globocan.iarc.fr.
2. Doll R, Hill AB. Lung cancer and other causes of death in relation to smoking - a 2nd report on the mortality of british doctors. British Medical Journal. 1956;2(NOV10):1071-81.
3. Lee PN. Relation between exposure to asbestos and smoking jointly and the risk of lung cancer. Occupational and Environmental Medicine. 2001;58(3):145-53.
4. Travis WD, Brambilla E, Nicholson AG, Yatabe Y, Austin JHM, Beasley MB, et al. The 2015 World Health Organization Classification of Lung Tumors Impact of Genetic, Clinical and Radiologic Advances Since the 2004 Classification. Journal of Thoracic Oncology. 2015;10(9):1243-60.
5. Li XJ, Sundquist J, Zoller B, Sundquist K. Neighborhood Deprivation and Lung Cancer Incidence and Mortality A Multilevel Analysis from Sweden. Journal of Thoracic Oncology. 2015;10(2):256-63.
6. Devesa SS, Diamond EL. Socioeconomic and racial-differences in lung-cancer incidence. American Journal of Epidemiology. 1983;118(6):818-31.
7. Mao Y, Hu JF, Ugnat AM, Semenciw R, Fincham S, Canadian Canc Registries E. Socioeconomic status and lung cancer risk in Canada. International Journal of Epidemiology. 2001;30(4):809-17.
8. Vanloon AJM, Goldbohm RA, Kant I, Swaen GMH, Kremer AM, vandenbrandt PA. Socioeconomic status and lung cancer incidence in men in The Netherlands: Is there a role for occupational exposure? Journal of Epidemiology and Community Health. 1997;51(1):24-9.
9. Schwartz KL, Crossley-May H, Vigneau FD, Brown K, Banerjee M. Race, socioeconomic status and stage at diagnosis for five common malignancies. Cancer Causes & Control. 2003;14(8):761-6.
10. Booth CM, Li G, Zhang-Salomons J, Mackillop WJ. The Impact of Socioeconomic Status on Stage of Cancer at Diagnosis and Survival A Population-Based Study in Ontario, Canada. Cancer. 2010;116(17):4160-7.
11. Cancer Research UK. [cited 2016 September]; Available from: http://www.cancerresearchuk.org/health-professional/cancer-statistics/statistics-by-cancer-type/lung-cancer.
12. Walters S, Benitez-Majano S, Muller P, Coleman MP, Allemani C, Butler J, et al. Is England closing the international gap in cancer survival? British Journal of Cancer. 2015;113(5):848-60.

13. Office for National Statistics. Cancer survival by stage at diagnosis for England (experimental statistics): Adults diagnosed 2012, 2013 and 2014 and followed up to 2015. 2016.
14. Berrino F, De Angelis R, Sant M. Survival for eight major cancers and all cancers combined for European adults diagnosed in 1995-99: results of the EUROCARE-4 study (vol 8, pg 773, 2007). Lancet Oncology. 2007;8(10):868-.
15. Coleman MP, Forman D, Bryant H, Butler J, Rachet B, Maringe C, et al. Cancer survival in Australia, Canada, Denmark, Norway, Sweden, and the UK, 1995-2007 (the International Cancer Benchmarking Partnership): an analysis of population-based cancer registry data. Lancet. 2011;377(9760):127-38.
16. Verdecchia A, Guzzinati S, Francisci S, De Angelis R, Bray F, Allemani C, et al. Survival trends in European cancer patients diagnosed from 1988 to 1999. European Journal of Cancer. 2009;45(6):1042-66.
17. Holmberg L, Sandin F, Bray F, Richards M, Spicer J, Lambe M, et al. National comparisons of lung cancer survival in England, Norway and Sweden 2001-2004: differences occur early in follow-up. Thorax. 2010;65(5):436-41.
18. Walters S, Maringe C, Coleman MP, Peake MD, Butler J, Young N, et al. Lung cancer survival and stage at diagnosis in Australia, Canada, Denmark, Norway, Sweden and the UK: a population-based study, 2004-2007. Thorax. 2013;68(6):551-64.
19. Vedsted P, Olesen F. Are the serious problems in cancer survival partly rooted in gatekeeper principles? An ecological study. British Journal of General Practice. 2011;61(589).
20. Young GP, Lowe RA. Adverse outcomes of managed care gatekeeping. Academic Emergency Medicine. 1997;4(12):1129-36.
21. Elliss-Brookes L, mcphail S, Ives A, Greenslade M, Shelton J, Hiom S, et al. Routes to diagnosis for cancer - determining the patient journey using multiple routine data sets. British Journal of Cancer. 2012;107(8):1220-6.
22. Powell HA, Baldwin DR. Multidisciplinary team management in thoracic oncology: more than just a concept? European Respiratory Journal. 2014;43(6):1776-86.
23. National Institute for Health and Care Excellence. Suspected cancer: recognition and referral. NICE guideline [NG12]. 2015.
24. Neal RD, Tharmanathan P, France B, Din NU, Cotton S, Fallon-Ferguson J, et al. Is increased time to diagnosis and treatment in symptomatic cancer associated with poorer outcomes? Systematic review. British Journal of Cancer. 2015;112:S92-S107.
25. Torring ML, Frydenberg M, Hansen RP, Olesen F, Vedsted P. Evidence of increasing mortality with longer diagnostic intervals for five

common cancers: A cohort study in primary care. European Journal of Cancer. 2013;49(9):2187-98.
26. Department of Health. The NHS Cancer Plan. 2000.
27. Department of Health. Cancer Reform Strategy. 2007.
28. Vansteenkiste J, Dooms C, Mascaux C, Nackaerts K. Screening and early detection of lung cancer. Annals of Oncology. 2012;23:320-7.
29. Canc Genome Atlas Res N. Comprehensive genomic characterization of squamous cell lung cancers The Cancer Genome Atlas Research Network (vol 489, pg 519, 2012). Nature. 2012;491(7423):288-.
30. Collisson EA, Campbell JD, Brooks AN, Berger AH, Lee W, Chmielecki J, et al. Comprehensive molecular profiling of lung adenocarcinoma. Nature. 2014;511(7511):543-50.
31. Hocking WG, Hu P, Oken MM, Winslow SD, Kvale PA, Prorok PC, et al. Lung Cancer Screening in the Randomized Prostate, Lung, Colorectal, and Ovarian (PLCO) Cancer Screening Trial. Journal of the National Cancer Institute. 2010;102(10):722-31.
32. Gohagan JK, Marcus PM, Fagerstrom RM, Pinsky PF, Kramer BS, Prorok PC, et al. Final results of the Lung Screening Study, a randomized feasibility study of spiral CT versus chest X-ray screening for lung cancer. Lung Cancer. 2005;47(1):9-15.
33. Infante M, Lutman FR, Cavuto S, Brambilla G, Chiesa G, Passera E, et al. Lung cancer screening with spiral CT Baseline results of the randomized DANTE trial. Lung Cancer. 2008;59(3):355-63.
34. Aberle DR, Adams AM, Berg CD, Clapp JD, Clingan KL, Gareen IF, et al. Baseline Characteristics of Participants in the Randomized National Lung Screening Trial. Jnci-Journal of the National Cancer Institute. 2010;102(23):1771-9.
35. Van Iersel CA, de Koning HJ, Draisma G, Mali W, Scholten ET, Nackaerts K, et al. Risk-based selection from the general population in a screening trial: Selection criteria, recruitment and power for the Dutch-Belgian randomised lung cancer multi-slice CT screening trial (NELSON). International Journal of Cancer. 2007;120(4):868-74.
36. Pegna AL, Picozzi G, Mascalchi M, Carrozzi FM, Carozzi L, Comin C, et al. Design, recruitment and baseline results of the ITALUNG trial for lung cancer screening with low-dose CT. Lung Cancer. 2009;64(1):34-40.
37. Pedersen JH, Ashraf H, Dirksen A, Bach K, Hansen H, Toennesen P, et al. The Danish Randomized Lung Cancer CT Screening Trial-Overall Design and Results of the Prevalence Round. Journal of Thoracic Oncology. 2009;4(5):608-14.
38. Blanchon T, Brechot JM, Grenier PA, Ferretti GR, Lemarie E, Milleron B, et al. Baseline results of the Depiscan study: A French randomized pilot trial of lung cancer screening comparing dose CT scan (LDCT) and chest X-ray (CXR). Lung Cancer. 2007;58(1):50-8.

39. Pastorino U, Rossi M, Rosato V, Marchiano A, Sverzellati N, Morosi C, et al. Annual or biennial CT screening versus observation in heavy smokers: 5-year results of the MILD trial. European Journal of Cancer Prevention. 2012;21(3):308-15.
40. Becker W, Delorme S, Kauczor HU. LUSI: The German component of the European trial on the efficacy of multislice-CT for the early detection of lung cancer. Onkologie. 2008;31:130-.
41. Field JK, Duffy SW, Baldwin DR, Whynes DK, Devaraj A, Brain KE, et al. UK Lung Cancer RCT Pilot Screening Trial: baseline findings from the screening arm provide evidence for the potential implementation of lung cancer screening. Thorax. 2016;71(2):161-70.
42. Aberle DR, Adams AM, Berg CD, Black WC, Clapp JD, Fagerstrom RM, et al. Reduced Lung-Cancer Mortality with Low-Dose Computed Tomographic Screening. New England Journal of Medicine. 2011;365(5):395-409.
43. Humphrey LL, Deffebach M, Pappas M, Baumann C, Artis K, Mitchell JP, et al. Screening for Lung Cancer With Low-Dose Computed Tomography: A Systematic Review to Update the U. S. Preventive Services Task Force Recommendation. Annals of Internal Medicine. 2013;159(6):411-+.
44. Field JK, Aberle DR, Altorki N, Baldwin DR, Dresler C, Duffy SW, et al. The International Association Study Lung Cancer (IASLC) Strategic Screening Advisory Committee (SSAC) Response to the USPSTF Recommendations. Journal of Thoracic Oncology. 2014;9(2):141-3.
45. De Koning HJ, Meza R, Plevritis SK, ten Haaf K, Munshi VN, Jeon J, et al. Benefits and Harms of Computed Tomography Lung Cancer Screening Strategies: A Comparative Modeling Study for the US Preventive Services Task Force. Annals of Internal Medicine. 2014;160(5):311-+.
46. Patz EF, Jr, Pinsky P, Gatsonis C, et al. Overdiagnosis in low-dose computed tomography screening for lung cancer. JAMA Internal Medicine. 2014;174(2):269-74.
47. Villanti AC, Jiang Y, Abrams DB, Pyenson BS. A Cost-Utility Analysis of Lung Cancer Screening and the Additional Benefits of Incorporating Smoking Cessation Interventions. Plos One. 2013;8(8).
48. Beral V, Cush S, Ellis IO, Emery J, Faulkner K, Given-Wilson R, et al. Screening for breast cancer in England: past and future. Journal of Medical Screening. 2006;13(2):59-61.
49. Pharoah PDP, Sewell B, Fitzsimmons D, Bennett HS, Pashayan N. Cost effectiveness of the NHS breast screening programme: life table model. Bmj-British Medical Journal. 2013;346.
50. De Gelder R, Bulliard J-L, de Wolf C, Fracheboud J, Draisma G, Schopper D, et al. Cost-effectiveness of opportunistic versus organised

mammography screening in Switzerland. European Journal of Cancer. 2009;45(1):127-38.
51. Van der Aalst CM, van den Bergh KAM, Willemsen MC, de Koning HJ, van Klaveren RJ. Lung cancer screening and smoking abstinence: 2 year follow-up data from the Dutch-Belgian randomised controlled lung cancer screening trial. Thorax. 2010;65(7):600-5.
52. Spiro SG. Screening for lung cancer: yet another problem. Thorax. 2007;62(2):105-6.
53. Mcronald FE, Yadegarfar G Fau - Baldwin DR, Baldwin Dr Fau - Devaraj A, Devaraj A Fau - Brain KE, Brain Ke Fau - Eisen T, Eisen T Fau - Holemans JA, et al. The UK Lung Screen (UKLS): demographic profile of first 88,897 approaches provides recommendations for population screening. (1940-6215 (Electronic)).
54. Ladabaum U. When even people at high risk do not take up colorectal cancer screening. Gut. 2007;56(12):1648-50.
55. Hoare T. Breast screening and ethnic minorities. (0306-9443 (Print)).
56. Palmer CK, Thomas MC, von Wagner C, Raine R. Reasons for non-uptake and subsequent participation in the NHS Bowel Cancer Screening Programme: a qualitative study. Br J Cancer. 2014;110(7):1705-11.
57. Jepson RG, Forbes CA, Sowden AJ, Lewis RA. Increasing informed uptake and non-uptake of screening: evidence from a systematic review. Health Expectations. 2001;4(2):116-30.
58. Silvestri GA, Nietert PJ, Zoller J, Carter C, Bradford D. Attitudes towards screening for lung cancer among smokers and their non-smoking counterparts. Thorax. 2007;62(2):126-30.
59. Chen J, Jiang R, Garces YI, Jatoi A, Stoddard SM, Sun Z, et al. Prognostic factors for limited-stage small cell lung cancer: A study of 284 patients. Lung Cancer. 2010;67(2):221-6.
60. Parsons A, Daley A, Begh R, Aveyard P. Influence of smoking cessation after diagnosis of early stage lung cancer on prognosis: systematic review of observational studies with meta-analysis. British Medical Journal. 2010;340.
61. Khakwani A, Rich AL, Powell HA, Tata LJ, Stanley RA, Baldwin DR, et al. The impact of the 'hub and spoke' model of care for lung cancer and equitable access to surgery. LID - thoraxjnl-2014-205841 [pii] LID - 10.1136/thoraxjnl-2014-205841 [doi]. (1468-3296 (Electronic)).
62. Cai YX, Fu XN, Xu QZ, Sun W, Zhang N. Thoracoscopic Lobectomy versus Open Lobectomy in Stage I Non-Small Cell Lung Cancer: A Meta-Analysis. Plos One. 2013;8(12).
63. Agostini P, Lugg S, Adams K, Vartsaba N, Kalkat M, Rajesh P, et al. S63 Postoperative pulmonary complications and physiotherapy requirements after open thoracotomy versus vats lobectomy: a propensity score-matched analysis. Thorax. 2016;71(Suppl 3):A38.

64. National Institute for Health and Care Excellence. Lung cancer: diagnosis and management. 2011.
65. Le Chevalier T, Arriagada R, Le Pechoux C, Grunenwald D, Dunant A, Pignon JP, et al. Cisplatin-based adjuvant chemotherapy in patients with completely resected non-small-cell lung cancer. New England Journal of Medicine. 2004;350(4):351-60.
66. Burdett S, Stephens R, Stewart L, Tierney J, Auperin A, Le Chevalier T, et al. Chemotherapy in addition to supportive care improves survival in advanced non-small-cell lung cancer: A systematic review and meta-analysis of individual patient data from 16 randomized controlled trials - NSCLC meta-analyses collaborative group. Journal of Clinical Oncology. 2008;26(28):4617-25.
67. Burdett S, Non-Small Cell Lung C. Chemotherapy and supportive care versus supportive care alone for advanced non-small cell lung cancer. Cochrane Database of Systematic Reviews. 2010(5).
68. National Institute for Health and Care Excellence. Erlotinib for the first-line treatment of locally advanced or metastatic EGFR-TK mutation-positive non-small-cell lung cancer. Technology appraisal guidance [TA258]. 2012.
69. National Institute for Health and Care Excellence. Gefitinib for the first-line treatment of locally advanced or metastatic non-small-cell lung cancer. 2010.
70. Rosell R, Carcereny E, Gervais R, Vergnenegre A, Massuti B, Felip E, et al. Erlotinib versus standard chemotherapy as first-line treatment for European patients with advanced EGFR mutation-positive non-small-cell lung cancer (EURTAC): a multicentre, open-label, randomised phase 3 trial. Lancet Oncology. 2012;13(3):239-46.
71. Mok TS, Wu YL, Thongprasert S, Yang CH, Chu DT, Saijo N, et al. Gefitinib or Carboplatin-Paclitaxel in Pulmonary Adenocarcinoma. New England Journal of Medicine. 2009;361(10):947-57.
72. National Institute for Health and Care Excellence. Crizotinib for untreated anaplastic lymphoma kinase-positive advanced non-small-cell lung cancer. Technology appraisal guidance [TA406]. 2016.
73. Solomon BJ, Mok T, Kim DW, Wu YL, Nakagawa K, Mekhail T, et al. First-Line Crizotinib versus Chemotherapy in ALK-Positive Lung Cancer. New England Journal of Medicine. 2014;371(23):2167-77.
74. Tassinari D, Scarpi E, Sartori S, Tamburini E, Santelmo C, Tombesi P, et al. Second-Line Treatments in Non-small Cell Lung Cancer A Systematic Review of Literature and Metaanalysis of Randomized Clinical Trials. Chest. 2009;135(6):1596-609.
75. Noble J, Ellis PM, Mackay JA, Evans WK, Lung Dis Site Grp Canc Care O. Second-line or subsequent systemic therapy for recurrent or progressive non-small cell lung cancer: A systematic review and practice guideline. Journal of Thoracic Oncology. 2006;1(9):1042-58.

76. Sause W, Kolesar P, Taylor S, Johnson D, Livingston R, Komaki R, et al. Final results of phase III trial in regionally advanced unresectable non-small cell lung cancer - Radiation Therapy Oncology Group, Eastern Cooperative Oncology Group, and Southwest Oncology Group. Chest. 2000;117(2):358-64.
77. Saunders M, Dische S, Barrett A, Harvey A, Griffiths G, Parmar M, et al. Continuous, hyperfractionated, accelerated radiotherapy (CHART) versus conventional radiotherapy in non-small cell lung cancer: mature data from the randomised multicentre trial. Radiotherapy and Oncology. 1999;52(2):137-48.
78. Chi A, Liao Z, Nguyen NP, Xu J, Stea B, Komaki R. Systemic review of the patterns of failure following stereotactic body radiation therapy in early-stage non-small-cell lung cancer: Clinical implications. Radiotherapy and Oncology. 2010;94(1):1-11.
79. Patchell RA, Tibbs PA, Walsh JW, Dempsey RJ, Maruyama Y, Kryscio RJ, et al. A randomized trial of surgery in the treatment of single metastases to the brain. New England Journal of Medicine. 1990;322(8):494-500.
80. Vecht CJ, Haaxmareiche H, Noordijk EM, Padberg GW, Voormolen JHC, Hoekstra FH, et al. Treatment of single brain metastasis - radiotherapy alone or combined with neurosurgery. Annals of Neurology. 1993;33(6):583-90.
81. Mulvenna P, Nankivell M, Barton R, Faivre-Finn C, Wilson P, mccoll E, et al. Dexamethasone and supportive care with or without whole brain radiotherapy in treating patients with non-small cell lung cancer with brain metastases unsuitable for resection or stereotactic radiotherapy (QUARTZ): results from a phase 3, non-inferiority, randomised trial. The Lancet.388(10055):2004-14.
82. Temel JS, Greer JA, Muzikansky A, Gallagher ER, Admane S, Jackson VA, et al. Early Palliative Care for Patients with Metastatic Non-Small-Cell Lung Cancer. New England Journal of Medicine. 2010;363(8):733-42.
83. Bakitas MA, Tosteson TD, Li ZG, Lyons KD, Hull JG, Li ZZ, et al. Early Versus Delayed Initiation of Concurrent Palliative Oncology Care: Patient Outcomes in the ENABLE III Randomized Controlled Trial. Journal of Clinical Oncology. 2015;33(13):1438-45.
84. Powell HA, Tata LJ, Baldwin DR, Stanley RA, Khakwani A, Hubbard RB. Early mortality after surgical resection for lung cancer: an analysis of the English National Lung cancer audit. Thorax. 2013;68(9):826-34.
85. Dave S, Petersen I. Creating medical and drug code lists to identify cases in primary care databases. Pharmacoepidemiology and Drug Safety. 2009;18(8):704-7.

86. Iyen-Omofoman B. Lung cancer in United Kingdom general practice and the possibility of developing an early-warning score: University of Nottingham; 2012.
87. Townsend P, Phillimore P, Beattie A. Health and Deprivation: Inequality and the North: Croom Helm; 1988.
88. Experian. Mosaic UK interactive guide 2012.
89. Iyen-Omofoman B, Hubbard RB, Smith CJP, Sparks E, Bradley E, Bourke A, et al. The distribution of lung cancer across sectors of society in the United Kingdom: a study using national primary care data. Bmc Public Health. 2011;11.
90. Powell J, Tapp A, Sparks E. Social marketing in action—geodemographics, alcoholic liver disease and heavy episodic drinking in Great Britain. International Journal of Nonprofit and Voluntary Sector Marketing. 2007;12(3):177-87.
91. Sharma A, Lewis S, Szatkowski L. Insights into social disparities in smoking prevalence using Mosaic, a novel measure of socioeconomic status: an analysis using a large primary care dataset. Bmc Public Health. 2010;10.
92. Lo Re V, III, Haynes K, Forde KA, Localio AR, Schinnar R, Lewis JD. Validity of The Health Improvement Network (THIN) for epidemiologic studies of hepatitis C virus infection. Pharmacoepidemiology and Drug Safety. 2009;18(9):807-14.
93. Hall GC. Validation of death and suicide recording on the THIN UK primary care database. Pharmacoepidemiology and Drug Safety. 2009;18(2):120-31.
94. Szatkowski L, Lewis S, mcneill A, Huang Y, Coleman T. Can data from primary care medical records be used to monitor national smoking prevalence? Journal of Epidemiology and Community Health. 2012;66(9):791-5.
95. Ogdie A, Love T, Haynes K, Hennessy S, Choi H, Gelfand J. Validation of the Health Improvement Network for the Study of Psoriatic Arthritis. Pharmacoepidemiology and Drug Safety. 2013;22:62.
96. Lewis JD, Schinnar R, Bilker WB, Wang X, Strom BL. Validation studies of the health improvement network (THIN) database for pharmacoepidemiology research. Pharmacoepidemiology and Drug Safety. 2007;16(4):393-401.
97. Denburg MR, Haynes K, Shults J, Lewis JD, Leonard MB. Validation of The Health Improvement Network (THIN) database for epidemiologic studies of chronic kidney disease. Pharmacoepidemiology and Drug Safety. 2011;20(11):1138-49.
98. Blak BT, Thompson M, Dattani H, Bourke A. Generalisability of The Health Improvement Network (THIN) database: demographics, chronic disease prevalence and mortality rates. Informatics in Primary Care. 2011;19(4):251-5.

99. Dregan A, Moller H, Murray-Thomas T, Gulliford MC. Validity of cancer diagnosis in a primary care database compared with linked cancer registrations in England. Population-based cohort study. Cancer Epidemiology. 2012;36(5):425-9.
100. Bourke A, Dattani H, Robinson M. Feasibility study and methodology to create a quality-evaluated database of primary care data. Informatics in Primary Care. 2004;12(3):171-7.
101. Schlesselman J, Stolley P. Case-control studies: Design, conduct, analysis: Oxford University Press; 1982.
102. Health and Social Care Information Centre. National Lung Cancer Audit Report 2014: Report for the audit period 2013. 2014.
103. Powell HA. Quantifiying important risk factors and survival following treatment in people with lung cancer using routinely collected national data: University of Nottingham; 2014.
104. Oken MM, Creech RH, Tormey DC, Horton J, Davis TE, mcfadden ET, et al. TOXICITY AND RESPONSE CRITERIA OF THE EASTERN-COOPERATIVE-ONCOLOGY-GROUP. American Journal of Clinical Oncology-Cancer Clinical Trials. 1982;5(6):649-55.
105. Rich A. Validation of the National Lung Cancer Audit database and analysis of the information it contains: University of Nottingham; 2011.
106. Goldstraw P, Crowley J, Chansky K, Giroux DJ, Groome PA, Rami-Porta R, et al. The IASLC lung cancer staging project: Proposals for the revision of he TNM stage groupings in the forthcoming (seventh) edition of the TNM classification of malignant tumours. Journal of Thoracic Oncology. 2007;2(8):706-14.
107. Powell HA, Tata LJ, Stanley RA, Baldwin DR, Hubbard RB. IDENTIFYING PATIENTS WHO HAD SURGICAL RESECTION FOR NON-SMALL CELL LUNG CANCER USING LARGE DATASETS. Thorax. 2013;68:A80-A.
108. Rich AL, Tata LJ, Stanley RA, Free CM, Peake MD, Baldwin DR, et al. Lung cancer in England: Information from the National Lung Cancer Audit (LUCADA). Lung Cancer. 2011;72(1):16-22.
109. Andersen TF, Madsen M, Jorgensen J, Mellemkjaer L, Olsen JH. The Danish National Hospital Register - A valuable source of data for modern health sciences. Danish Medical Bulletin. 1999;46(3):263-8.
110. Jakobsen E, Green A, Oesterlind K, Rasmussen TR, Iachina M, Palshof T. Nationwide Quality Improvement in Lung Cancer Care: The Role of the Danish Lung Cancer Group and Registry. Journal of Thoracic Oncology. 2013;8(10):1238-47.
111. Charlson ME, Pompei P, Ales KL, Mackenzie CR. A new method of classifying prognostic co-morbidity in longitudinal-studies - development and validation. Journal of Chronic Diseases. 1987;40(5):373-83.
112. Quan H, Li B, Couris CM, Fushimi K, Graham P, Hider P, et al. Updating and Validating the Charlson Comorbidity Index and Score for

Risk Adjustment in Hospital Discharge Abstracts Using Data From 6 Countries. American Journal of Epidemiology. 2011;173(6):676-82.
113. World Health Organisation. International statistical classification of diseases and related health problems, 10th revision, Vol.2: Instruction manual. Geneva: 2010.
114. Weller DP, Campbell C. Uptake in cancer screening programmes: a priority in cancer control. British Journal of Cancer. 2009;101:S55-S9.
115. Logan RFA, Patnick J, Nickerson C, Coleman L, Rutter MD, von Wagner C, et al. Outcomes of the Bowel Cancer Screening Programme (BCSP) in England after the first 1 million tests. Gut. 2012;61(10):1439-46.
116. Altobelli E, Lattanzi A, Paduano R, Varassi G, di Orio F. Colorectal cancer prevention in Europe: Burden of disease and status of screening programs. Preventive Medicine. 2014;62:132-41.
117. Altobelli E, Lattanzi A. Breast cancer in European Union: An update of screening programmes as of March 2014 (Review). International Journal of Oncology. 2014;45(5):1785-92.
118. Von Wagner C, Baio G, Raine R, Snowball J, Morris S, Atkin W, et al. Inequalities in participation in an organized national colorectal cancer screening programme: results from the first 2.6 million invitations in England. International Journal of Epidemiology. 2011;40(3):712-8.
119. Goddard M, Smith P. Equity of access to health care services: Theory and evidence from the UK. Social Science & Medicine. 2001;53(9):1149-62.
120. Von Wagner C, Semmler C, Good A, Wardle J. Health literacy and self-efficacy for participating in colorectal cancer screening: The role of information processing. Patient Education and Counseling. 2009;75(3):352-7.
121. Giordano L, Webster P, Anthony C, Szarewski A, Davies P, Arbyn M, et al. Improving the quality of communication in organised cervical cancer screening programmes. Patient Education and Counseling. 2008;72(1):130-6.
122. Cuthbertson SA, Goyder EC, Poole J. Inequalities in breast cancer stage at diagnosis in the Trent region, and implications for the NHS Breast Screening Programme. Journal of Public Health. 2009;31(3):398-405.
123. Weller D, Coleman D, Robertson R, Butler P, Melia J, Campbell C, et al. The UK colorectal cancer screening pilot: results of the second round of screening in England. British Journal of Cancer. 2007;97(12):1601-5.
124. Hestbech MS, Siersma V, Dirksen A, Pedersen JH, Brodersen J. Participation bias in a randomised trial of screening for lung cancer. Lung Cancer. 2011;73(3):325-31.
125. Riaz SP, Horton M, Kang J, Mak V, Luchtenborg M, Moller H. Lung Cancer Incidence and Survival in England An Analysis by Socioeconomic

Deprivation and Urbanization. Journal of Thoracic Oncology. 2011;6(12):2005-10.
126. Henwood KL, Pidgeon NF. QUALITATIVE RESEARCH AND PSYCHOLOGICAL THEORIZING. British Journal of Psychology. 1992;83:97-111.
127. Horeweg N, Scholten ET, de Jong PA, van der Aalst CM, Weenink C, Lammers JWJ, et al. Detection of lung cancer through low-dose CT screening (NELSON): a prespecifi ed analysis of screening test performance and interval cancers. Lancet Oncology. 2014;15(12):1342-50.
128. Yardley L, Bishop F. Mixing qualitative and quantitative methods: a pragmatic approach. In: Willig C, Stainton-Rogers W, editors. The SAGE Handbook of Qualitative Research in Psychology: Sage Publications Ltd; 2007. P. 352-70.
129. Ritchie J LJ. Qualitative research practice: A guide for social science students and researchers. London: Sage; 2003.
130. Quaife SL, Marlow LAV, mcewen A, Janes SM, Wardle J. Attitudes towards lung cancer screening in socioeconomically deprived and heavy smoking communities: informing screening communication. Health Expectations. 2016:n/a-n/a.
131. Patel D, Akporobaro A, Chinyanganya N, Hackshaw A, Seale C, Spiro SG, et al. Attitudes to participation in a lung cancer screening trial: a qualitative study. Thorax. 2012;67(5):418-25.
132. Ali N, Lifford KJ, Carter B, mcronald F, Yadegarfar G, Baldwin DR, et al. Barriers to uptake among high-risk individuals declining participation in lung cancer screening: a mixed methods analysis of the UK Lung Cancer Screening (UKLS) trial. Bmj Open. 2015;5(7).
133. Carter-Harris L, Ceppa DP, Hanna N, Rawl SM. Lung cancer screening: what do long-term smokers know and believe? Health Expectations. 2015:n/a-n/a.
134. Marlow LAV, Waller J, Wardle J. Variation in Blame Attributions across Different Cancer Types. Cancer Epidemiology Biomarkers & Prevention. 2010;19(7):1799-805.
135. Polit DF, Beck CT. Generalization in quantitative and qualitative research: Myths and strategies. International Journal of Nursing Studies. 2010;47(11):1451-8.
136. Quaife SL, Ruparel M, Beeken RJ, mcewen A, Isitt J, Nolan G, et al. The Lung Screen Uptake Trial (LSUT): protocol for a randomised controlled demonstration lung cancer screening pilot testing a targeted invitation strategy for high risk and 'hard-to-reach' patients. Bmc Cancer. 2016;16.
137. Cancer Research UK. Cancer Research UK; 2016 [December 2016]; Available from: http://www.cancerresearchuk.org/health-

professional/early-diagnosis-activities/ace-programme/ace-programme-projects-and-outputs#ACE_projects_wave11.
138. Salomaa ER, Sallinen S, Hiekkanen H, Liippo K. Delays in the diagnosis and treatment of lung cancer. Chest. 2005;128(4):2282-8.
139. Iyen-Omofoman B, Tata LJ, Baldwin DR, Smith CJP, Hubbard RB. Using socio-demographic and early clinical features in general practice to identify people with lung cancer earlier. Thorax. 2013;68(5):451-9.
140. Rich AL, Tata LJ, Free CM, Stanley RA, Peake MD, Baldwin DR, et al. Inequalities in outcomes for non-small cell lung cancer: the influence of clinical characteristics and features of the local lung cancer service. Thorax. 2011;66(12):1078-84.
141. Huber PJ. A robust version of the probability ratio test. Annals of Mathematical Statistics. 1965;36(6):1753-8.
142. Dalton SO, Steding-Jessen M, Engholm G, Schuz J, Olsen JH. Social inequality and incidence of and survival from lung cancer in a population-based study in Denmark, 1994-2003. European Journal of Cancer. 2008;44(14):1989-95.
143. Donnelly DW, Gavin A. Socio-economic inequalities in cancer incidence - The choice of deprivation measure matters. Cancer Epidemiology. 2011;35(6):E55-E61.
144. Thomas L, Doyle LA, Edelman MJ. Lung cancer in women - Emerging differences in epidemiology, biology, and therapy. Chest. 2005;128(1):370-81.
145. Tammemagi CM, Neslund-Dudas C, Simoff M, Kvale P. Smoking and lung cancer survival - The role of comorbidity and treatment. Chest. 2004;125(1):27-37.
146. Weinberger M, Greene JY, Mamlin JJ, Jerin MJ. HEALTH BELIEFS AND SMOKING-BEHAVIOR. American Journal of Public Health. 1981;71(11):1253-5.
147. Cheyne L, Milton R, Fear J, Callister MEJ. Variability in gp referral rates for chest x-ray does not appear to affect stage or performance status of patients diagnosed with lung cancer. Thorax. 2012;67:A90-A.
148. Baldwin DR, White B, Schmidt-Hansen M, Champion AR, Melder AM. Diagnosis and treatment of lung cancer: summary of updated NICE guidance. BMJ. 2011;342.
149. Muhm JR, Miller WE, Fontana RS, Sanderson DR, Uhlenhopp MA. Lung-cancer detected during a screening-program using 4-month chest radiographs. Radiology. 1983;148(3):609-15.
150. Hamilton W, Sharp D. Diagnosis of lung cancer in primary care: a structured review. Family Practice. 2004;21(6):605-11.
151. Hamilton W, Peters TJ, Round A, Sharp D. What are the clinical features of lung cancer before the diagnosis is made? - A population based case-control study. Thorax. 2005;60(12):1059-65.

152. Bach PB, Kattan MW, Thornquist MD, Kris MG, Tate RC, Barnett MJ, et al. Variations in lung cancer risk among smokers. Journal of the National Cancer Institute. 2003;95(6):470-8.
153. Spitz MR, Etzel CJ, Dong Q, Amos CI, Wei Q, Wu X, et al. An Expanded Risk Prediction Model for Lung Cancer. Cancer Prevention Research. 2008;1(4):250-4.
154. Cassidy A, Myles JP, van Tongeren M, Page RD, Liloglou T, Duffy SW, et al. The LLP risk model: an individual risk prediction model for lung cancer. British Journal of Cancer. 2008;98(2):270-6.
155. O'Dowd EL, mckeever TM, Baldwin DR, Anwar S, Powell HA, Gibson JE, et al. What characteristics of primary care and patients are associated with early death in patients with lung cancer in the UK? Thorax. 2014.
156. Peake MD. Deprivation, distance and death in lung cancer. Thorax. 2015;70(2):108-9.
157. Burki TK. Late detection of lung cancer. The Lancet Oncology.15(13):e590.
158. Rogers TK, Hamilton W, Tod A, Neal R. Author's response: What characteristics of primary care and patients are associated with early death in patients with lung cancer in the UK? Thorax. 2014.
159. O'Dowd EL, mckeever TM, Baldwin DR, Anwar S, Powell HA, Gibson JE, et al. Author's response: What characteristics of primary care and patients are associated with early death in patients with lung cancer in the UK? Thorax. 2015;70(2):185-.
160. Rich AL, Tata L, Free CM, Stanley R, Peake MD, Baldwin D, et al. The impact of patient and hospital features on surgical resection rates and survival for people with non-small cell lung cancer in england. Journal of Thoracic Oncology. 2011;6(6):S1428-S.
161. Powell HA, Tata LJ, Baldwin DR, Potter VA, Stanley RA, Khakwani A, et al. Treatment decisions and survival for people with small-cell lung cancer. Br J Cancer. 2014;110(4):908-15.
162. Royal College of Physicians. National Lung Cancer Audit annual report 2015 (for the audit period 2014). 2015.
163. Luechtenborg M, Jakobsen E, Krasnik M, Linklater KM, Mellemgaard A, Moller H. The effect of comorbidity on stage-specific survival in resected non-small cell lung cancer patients. European Journal of Cancer. 2012;48(18):3386-95.
164. Well E. Shortage of lung cancer nurse specialists leading to 'sub-optimal care'. Nursing Standard. 2014;29(16):0-.
165. Macmillan Cancer Support. Specialist adult cancer nurses in England: A census of the specialist adult cancer nursing workforce in the UK. 2014.

166. Beckett P, Woolhouse I, Stanley R, Tata LJ, Peake MD, Darlinson l. Nurse specialist input is independently associated with anti-cancer treatment in lung cancer. Thorax. 2011;66:A42-A3.
167. Khakwani A, Hubbard RB, Beckett P, Borthwick D, Tod A, Leary A, et al. Which patients are assessed by lung cancer nurse specialists? A national lung cancer audit study of over 128,000 patients across england. Lung Cancer. 2016;96:33-40.
168. Cusworth K, O'Dowd E, Hubbard R, Beckett P, Peake MD, Woolhouse I. Variation in lung cancer resources and workload: results from the first national lung cancer organisational audit. Thorax. 2015;70(10):1001-3.
169. Mintz BJ, Tuhrim S, Alexander S, Yang WC, Shanzer S. Intracranial metastases in the initial staging of bronchogenic-carcinoma. Chest. 1984;86(6):850-3.
170. Newman SJ, Hansen HH. Frequency, diagnosis, and treatment of brain metastases in 247 consecutive patients with bronchogenic carcinoma. Cancer. 1974;33(2):492-6.
171. Detterbeck FC, Lewis SZ, Diekemper R, Addrizzo-Harris D, Alberts WM. Executive summary: Diagnosis and management of lung cancer, 3rd ed: american college of chest physicians evidence-based clinical practice guidelines. CHEST Journal. 2013;143(5_suppl):7S-37S.
172. Lim E, Baldwin D, Beckles M, Duffy J, Entwisle J, Faivre-Finn C, et al. Guidelines on the radical management of patients with lung cancer. Thorax. 2010;65:1-27.
173. Yoo H, Nam B-H, Yang H-S, Shin SH, Lee JS, Lee SH. Growth rates of metastatic brain tumors in nonsmall cell lung cancer. Cancer. 2008;113(5):1043-7.
174. Escuin jsdc, Menna DM, Gonzalez MAS, Quirantes JZ, Vicente CD, Calvo MCP. Silent brain metastasis in the initial staging of lung cancer: Evaluation by computed tomography and magnetic resonance imaging. Archivos De Bronconeumologia. 2007;43(7):386-91.
175. Cox JD, Yesner RA. Adenocarcinoma of the lung: recent results from the Veterans Administration Lung Group. The American review of respiratory disease. 1979;120(5):1025-9.
176. Mujoomdar A, Austin JHM, Malhotra R, Powell CA, Pearson GDN, Shiau MC, et al. Clinical predictors of metastatic disease to the brain from non small cell lung carcinoma: Primary tumor size, cell type, and lymph node metastases. Radiology. 2007;242(3):882-8.
177. Hubbs JL, Boyd JA, Hollis D, Chino JP, Saynak M, Kelsey CR. Factors Associated With the Development of Brain Metastases Analysis of 975 Patients With Early Stage Nonsmall Cell Lung Cancer. Cancer. 2010;116(21):5038-46.

178. Schouten LJ, Rutten J, Huveneers HAM, Twijnstra A. Incidence of brain metastases in a cohort of patients with carcinoma of the breast, colon, kidney, and lung and melanoma. Cancer. 2002;94(10):2698-705.
179. Bajard A, Westeel V, Dubiez A, Jacoulet P, Pernet D, Dalphin JC, et al. Multivariate analysis of factors predictive of brain metastases in localised non-small cell lung carcinoma. Lung Cancer. 2004;45(3):317-23.
180. Ou S-HI, Ziogas A, Zell JA. Asian ethnicity is a favorable prognostic factor for overall survival in non-small cell lung cancer (NSCLC) and is independent of smoking status. Journal of thoracic oncology : official publication of the International Association for the Study of Lung Cancer. 2009;4(9):1083-93.
181. Kawaguchi T, Matsumura A, Fukai S, Tamura A, Saito R, Zell JA, et al. Japanese Ethnicity Compared with Caucasian Ethnicity and Never-Smoking Status Are Independent Favorable Prognostic Factors for Overall Survival in Non-small Cell Lung Cancer A Collaborative Epidemiologic Study of the National Hospital Organization Study Group for Lung Cancer (NHSGLC) in Japan and a Southern California Regional Cancer Registry Databases. Journal of Thoracic Oncology. 2010;5(7):1001-10.
182. Sekine I, Yamamoto N, Nishio K, Saijo N. Emerging ethnic differences in lung cancer therapy. British Journal of Cancer. 2008;99(11):1757-62.
183. Figlin RA, Piantadosi S, Feld R. Intracranial recurrence of carcinoma after complete surgical resection of stage-i, stage-ii, and stage-iii non-small-cell lung-cancer. New England Journal of Medicine. 1988;318(20):1300-5.
184. Sakamoto J, Sonobe M, Kobayashi M, Ishikawa M, Kikuchi R, Nakajima D, et al. Prognostic factors for patients in postoperative brain metastases from surgically resected non-small cell lung cancer. International Journal of Clinical Oncology. 2014;19(1):50-6.
185. Kanou T, Okami J, Tokunaga T, Ishida D, Kuno H, Higashiyama M. Prognostic factors in patients with postoperative brain recurrence from completely resected non-small cell lung cancer. Thoracic Cancer. 2015;6(1):38-42.
186. Yokoi K, Kamiya N, Matsuguma H, Machida S, Hirose T, Mori K, et al. Detection of brain metastasis in potentially operable non-small cell lung cancer - A comparison of CT and MRI. Chest. 1999;115(3):714-9.
187. Bae MK, Yu WS, Byun GE, Lee CY, Lee JG, Kim DJ, et al. Prognostic factors for cases with no extracranial metastasis in whom brain metastasis is detected after resection of non-small cell lung cancer. Lung Cancer. 2015;88(2):195-200.
188. Lee HY, Lee KS, Kim B-T, Cho Y-S, Lee EJ, Yi CA, et al. Diagnostic Efficacy of PET/CT Plus Brain MR Imaging for Detection of Extrathoracic Metastases in Patients with Lung Adenocarcinoma. Journal of Korean Medical Science. 2009;24(6):1132-8.

189. Demange L, Tack L, Morel M, Dubois de Montreynaud JM, Pauchet P, Froissart D, et al. Single brain metastasis of non-small cell lung carcinoma. Study of survival among 54 patients. British journal of neurosurgery. 1989;3(1):81-7.
190. Kim YS, Kondziolka D Fau - Flickinger JC, Flickinger Jc Fau - Lunsford LD, Lunsford LD. Stereotactic radiosurgery for patients with nonsmall cell lung carcinoma metastatic to the brain. (0008-543X (Print)).
191. O'Dowd EL, Kumaran M, Anwar S, Palomo B, Baldwin DR. Brain metastases following radical surgical treatment of non-small cell lung cancer: Is preoperative brain imaging important? Lung Cancer. 2014;86(2):185-9.
192. Riaz SP, Linklater KM, Page R, Peake MD, Møller H, Lüchtenborg M. Recent trends in resection rates among non-small cell lung cancer patients in England. Thorax. 2012.
193. Brunelli A, Charloux A, Bolliger CT, Rocco G, Sculier JP, Varela G, et al. Ers/ests clinical guidelines on fitness for radical therapy in lung cancer patients (surgery and chemo-radiotherapy) (vol 34, pg 17, 2009). European Respiratory Journal. 2009;34(3):782-.
194. Mcmillan RR, Berger A, Sima CS, Lou F, Dycoco J, Rusch V, et al. Thirty-Day Mortality Underestimates the Risk of Early Death After Major Resections for Thoracic Malignancies. Annals of Thoracic Surgery. 2014;98(5):1769-74.
195. Pezzi CM, Mallin K, Mendez AS, Gay EG, Putnam JB, Jr. Ninety-day mortality after resection for lung cancer is nearly double 30-day mortality. Journal of Thoracic and Cardiovascular Surgery. 2014;148(5):2269-77.
196. Bradley A, Marshall A, Abdelaziz M, Hussain K, Agostini P, Bishay E, et al. Thoracoscore fails to predict complications following elective lung resection. European Respiratory Journal. 2012;40(6):1496-501.
197. Poullis M, mcshane J, Shaw M, Woolley S, Shackcloth M, Page R, et al. Prediction of in-hospital mortality following pulmonary resections: improving on current risk models. European Journal of Cardio-Thoracic Surgery. 2013;44(2):238-43.
198. Barua A, Handagala SD, Socci L, Barua B, Malik M, Johnstone N, et al. Accuracy of two scoring systems for risk stratification in thoracic surgery. Interactive cardiovascular and thoracic surgery. 2012;14(5):556-9.
199. Sharkey A, Ariyaratnam P, Anikin V, Belcher E, Kendall S, Lim E, et al. Thoracoscore and European Society Objective Score Fail to Predict Mortality in the UK. World J Oncol. 2015;6(1):270-5.
200. Qadri SSA, Jarvis M, Ariyaratnam P, Chaudhry MA, Cale ARJ, Griffin S, et al. Could Thoracoscore predict postoperative mortality in patients undergoing pneumonectomy? European Journal of Cardio-Thoracic Surgery. 2014;45(5):864-9.

201. Copeland GP, Jones D, Walters M. POSSUM: a scoring system for surgical audit. The British journal of surgery. 1991;78(3):355-60.
202. Brunelli A, Fianchini A, Gesuita R, Carle F. POSSUM scoring system as an instrument of audit in lung resection surgery. Annals of Thoracic Surgery. 1999;67(2):329-31.
203. Haga Y, Ikei S, Ogawa M. Estimation of Physiologic Ability and Surgical Stress (E-PASS) as a new prediction scoring system for postoperative morbidity and mortality following elective gastrointestinal surgery. Surgery Today-the Japanese Journal of Surgery. 1999;29(3):219-25.
204. Yamashita S, Haga Y, Nemoto E, Nagai S, Ohta M. E-PASS (the Estimation of Physiologic Ability and Surgical Stress) scoring system helps the prediction of postoperative morbidity and mortality in thoracic surgery. European Surgical Research. 2004;36(4):249-55.
205. Berrisford R, Brunelli A, Rocco G, Treasure T, Utley M, Audit Guidelines Comm European S, et al. The European Thoracic Surgery Database project: modelling the risk of in-hospital death following lung resection. European Journal of Cardio-Thoracic Surgery. 2005;28(2):306-11.
206. Brunelli A, Varela G, Van Schil P, Salati M, Novoa N, Hendriks JM, et al. Multicentric analysis of performance after major lung resections by using the European Society Objective Score (ESOS). European Journal of Cardio-Thoracic Surgery. 2008;33(2):284-8.
207. Falcoz PE, Conti M, Brouchet L, Chocron S, Puyraveau M, Mercier M, et al. The Thoracic Surgery Scoring System (Thoracoscore): Risk model for in-hospital death in 15,183 patients requiring thoracic surgery. Journal of Thoracic and Cardiovascular Surgery. 2007;133(2):325-32.
208. Chamogeorgakis T, Toumpoulis I, Tomos P, Ieromonachos C, Angouras D, Georgiannakis E, et al. External validation of the modified Thoracoscore in a new thoracic surgery program: prediction of in-hospital mortality. Interactive cardiovascular and thoracic surgery. 2009;9(3):463-6.
209. Bernard A, Rivera C, Pages PB, Falcoz PE, Vicaut E, Dahan M. Risk model of in-hospital mortality after pulmonary resection for cancer: A national database of the French Society of Thoracic and Cardiovascular Surgery (Epithor). Journal of Thoracic and Cardiovascular Surgery. 2011;141(2):449-58.
210. Kozower BD, Sheng S, O'Brien SM, Liptay MJ, Lau CL, Jones DR, et al. STS Database Risk Models: Predictors of Mortality and Major Morbidity for Lung Cancer Resection. Annals of Thoracic Surgery. 2010;90(3):875-81.
211. Damhuis R, Coonar A, Plaisier P, Dankers M, Bekkers J, Linklater K, et al. A case-mix model for monitoring of postoperative mortality after surgery for lung cancer. Lung Cancer. 2006;51(1):123-9.

212. Safi S, Benner A, Walloschek J, Renner M, op den Winkel J, Muley T, et al. Development and Validation of a Risk Score for Predicting Death after Pneumonectomy. Plos One. 2015;10(4).
213. Yamashita S-i, Haga Y, Nemoto E, Imanishi N, Ohta M, Kawahara K. Comparison of surgical outcome using the prediction scoring system of E-PASS for thoracic surgery. The Japanese journal of thoracic and cardiovascular surgery : official publication of the Japanese Association for Thoracic Surgery = Nihon Kyobu Geka Gakkai zasshi. 2006;54(9):391-5.
214. Chamogeorgakis TP, Connery CP, Bhora F, Nabong A, Toumpoulis IK. Thoracoscore predicts midterm mortality in patients undergoing thoracic surgery. The Journal of thoracic and cardiovascular surgery. 2007;134(4):883-7.
215. Sankar A, Johnson SR, Beattie WS, Tait G, Wijeysundera DN. Reliability of the American Society of Anesthesiologists physical status scale in clinical practice. British Journal of Anaesthesia. 2014.
216. Aronson WL, mcauliffe MS, Miller K. Variability in the American Society of Anesthesiologists Physical Status Classification Scale. AANA journal. 2003;71(4):265-74.
217. Mak PHK, Campbell RCH, Irwin MG. The ASA physical status classification: Inter-observer consistency. Anaesthesia and Intensive Care. 2002;30(5):633-40.
218. O'Dowd EL, mckeever T, Baldwin DR, Anwar S, Hubbard R. 174: Validation of a surgical predictive score for 90 day mortality in lung cancer and comparison with Thoracoscore. Lung Cancer.87:S64.
219. O'Dowd EL, Luchtenborg M, Baldwin DR, mckeever TM, Powell HA, Moller H, et al. Predicting death from surgery for lung cancer: A comparison of two scoring systems in two European countries. Lung Cancer. 2016;95:88-93.
220. Gomes B, Higginson IJ, Calanzani N, Cohen J, Deliens L, Daveson BA, et al. Preferences for place of death if faced with advanced cancer: a population survey in England, Flanders, Germany, Italy, the Netherlands, Portugal and Spain. Annals of Oncology. 2012;23(8):2006-15.
221. Wright AA, Keating NL, Balboni TA, Matulonis UA, Block SD, Prigerson HG. Place of Death: Correlations With Quality of Life of Patients With Cancer and Predictors of Bereaved Caregivers' Mental Health. Journal of Clinical Oncology. 2010;28(29):4457-64.
222. Mitchell AJ, Chan M, Bhatti H, Halton M, Grassi L, Johansen C, et al. Prevalence of depression, anxiety, and adjustment disorder in oncological, haematological, and palliative-care settings: a meta-analysis of 94 interview-based studies. Lancet Oncology. 2011;12(2):160-74.
223. Jordhoy MS, Fayers P, Saltnes T, Ahlner-Elmqvist M, Jannert M, Kaasa S. A palliative-care intervention and death at home: a cluster randomised trial. Lancet. 2000;356(9233):888-93.

224. Marie Curie Cancer Care. Understanding the cost of end of life care in different settings. London: 2012.
225. Gao W, Ho YK, Verne J, Glickman M, Higginson IJ, Project GC. Changing Patterns in Place of Cancer Death in England: A Population-Based Study. Plos Medicine. 2013;10(3).
226. Gomes B, Calanzani N, Higginson IJ. Reversal of the British trends in place of death: Time series analysis 2004-2010. Palliative Medicine. 2012;26(2):102-7.
227. Davies E, Linklater KM, Jack RH, Clark L, Moller H. How is place of death from cancer changing and what affects it? Analysis of cancer registration and service data. British Journal of Cancer. 2006;95(5):593-600.
228. Brumley R, Enguidanos S, Jamison P, Seitz R, Morgenstern N, Saito S, et al. Increased satisfaction with care and lower costs: Results of a randomized trial of in-home palliative care. Journal of the American Geriatrics Society. 2007;55(7):993-1000.
229. Mack JW, Cronin A, Taback N, Huskamp HA, Keating NL, Malin JL, et al. End-of-Life Care Discussions Among Patients With Advanced Cancer A Cohort Study. Annals of Internal Medicine. 2012;156(3):204-U65.
230. Wright AA, Zhang B, Ray A, Mack JW, Trice E, Balboni T, et al. Associations between end-of-life discussions, patient mental health, medical care near death, and caregiver bereavement adjustment. Jama-Journal of the American Medical Association. 2008;300(14):1665-73.
231. Prigerson HG. Determinants of hospice utilization among terminally ill geriatric patients. Home health care services quarterly. 1991;12(4):81-112.
232. Kawaguchi T, Takada M, Kubo A, Matsumura A, Fukai S, Tamura A, et al. Performance Status and Smoking Status Are Independent Favorable Prognostic Factors for Survival in Non-small Cell Lung Cancer A Comprehensive Analysis of 26,957 Patients with NSCLC. Journal of Thoracic Oncology. 2010;5(5):620-30.
233. Coupland VH, Madden P, Jack RH, Moller H, Davies EA. Does place of death from cancer vary between ethnic groups in South East England? Palliative Medicine. 2011;25(4):314-22.
234. Gatrell AC, Wood DJ. Variation in geographic access to specialist inpatient hospices in England and Wales. Health & Place. 2012;18(4):832-40.
235. O'Dowd EL, mckeever T, Baldwin DR, Anwar S, Hubbard R. 121: Place and cause of death in patients with lung cancer in the United Kingdom. Lung Cancer.87:S44.
236. O'Dowd EL, mckeever TM, Baldwin DR, Hubbard RB. Place of Death in Patients with Lung Cancer: A Retrospective Cohort Study from 2004-2013. Plos One. 2016;11(8).

237. Coleman MP, Quaresma M, Berrino F, Lutz J-M, De Angelis R, Capocaccia R, et al. Cancer survival in five continents: a worldwide population-based study (CONCORD). The Lancet Oncology. 2008;9(8):730-56.
238. Allemani C, Weir HK, Carreira H, Harewood R, Spika D, Wang XS, et al. Global surveillance of cancer survival 1995-2009: analysis of individual data for 25 676 887 patients from 279 population-based registries in 67 countries (CONCORD-2). Lancet. 2015;385(9972):977-1010.
239. Burki TK. Late detection of lung cancer. Lancet Oncology. 2014;15(13):E590-E.

APPENDICES

Appendix A: Code lists used for this thesis

THIN dataset

Lung cancer Read codes

Read code	Description
B22..00	Malignant neoplasm of trachea, bronchus and lung
B220.00	Malignant neoplasm of trachea
B220z00	Malignant neoplasm of trachea NOS
B221.00	Malignant neoplasm of main bronchus
B221000	Malignant neoplasm of carina of bronchus
B221100	Malignant neoplasm of hilus of lung
B221z00	Malignant neoplasm of main bronchus NOS
B222.00	Malignant neoplasm of upper lobe, bronchus or lung
B222.11	Pancoast's syndrome
B222000	Malignant neoplasm of upper lobe bronchus
B222100	Malignant neoplasm of upper lobe of lung
B222z00	Malignant neoplasm of upper lobe, bronchus or lung NOS
B223.00	Malignant neoplasm of middle lobe, bronchus or lung
B223000	Malignant neoplasm of middle lobe bronchus
B223100	Malignant neoplasm of middle lobe of lung
B223z00	Malignant neoplasm of middle lobe, bronchus or lung NOS
B224.00	Malignant neoplasm of lower lobe, bronchus or lung
B224000	Malignant neoplasm of lower lobe bronchus
B224100	Malignant neoplasm of lower lobe of lung
B224z00	Malignant neoplasm of lower lobe, bronchus or lung NOS
B225.00	Malignant neoplasm of overlapping lesion of bronchus & lung
B22y.00	Malignant neoplasm of other sites of bronchus or lung
B22z.00	Malignant neoplasm of bronchus or lung NOS

B22z.11	Lung cancer
B26..00	Malignant neoplasm, overlap lesion of resp & intrathor orgs
B2zz.00	Malignant neoplasm of respiratory tract NOS
B551100	Malignant neoplasm of chest wall NOS
B551z00	Malignant neoplasm of thorax NOS
Byu2.00	[X]Malignant neoplasm of respiratory and intrathoracic orga
Byu2000	[X]Malignant neoplasm of bronchus or lung, unspecified
Byu2400	[X]Malignant neoplasm/ill-defined sites within resp system
B812.00	Carcinoma in situ of bronchus and lung
B812000	Carcinoma in situ of carina of bronchus
B812100	Carcinoma in situ of main bronchus
B812200	Carcinoma in situ of upper lobe bronchus and lung
B812300	Carcinoma in situ of middle lobe bronchus and lung
B812400	Carcinoma in situ of lower lobe bronchus and lung
B812z00	Carcinoma in situ of bronchus or lung NOS
ZV10100	[V]Personal history of malig neop of trachea/bronchus/lung
ZV10111	[V]Personal history of malignant neoplasm of bronchus

Smoking status Read codes

Read code	Description	Status
137..00	Tobacco consumption	see AHD
137..11	Smoker - amount smoked	Current
1371.00	Never smoked tobacco	Never
1371.11	Non-smoker	see AHD
1372.00	Trivial smoker - < 1 cig/day	Current
1372.11	Occasional smoker	Current

1373.00	Light smoker - 1-9 cigs/day	Current
1374.00	Moderate smoker - 10-19 cigs/d	Current
1375.00	Heavy smoker - 20-39 cigs/day	Current
1376.00	Very heavy smoker - 40+cigs/d	Current
1377.00	Ex-trivial smoker (<1/day)	Ex
1378.00	Ex-light smoker (1-9/day)	Ex
1379.00	Ex-moderate smoker (10-19/day)	Ex
137A.00	Ex-heavy smoker (20-39/day)	Ex
137B.00	Ex-very heavy smoker (40+/day)	Ex
137C.00	Keeps trying to stop smoking	Current
137D.00	Admitted tobacco cons untrue?	Unknown
137E.00	Tobacco consumption unknown	Unknown
137F.00	Ex-smoker - amount unknown	Ex
137G.00	Trying to give up smoking	Current
137H.00	Pipe smoker	Current
137J.00	Cigar smoker	Current
137K.00	Stopped smoking	Ex
137L.00	Current non-smoker	see AHD
137M.00	Rolls own cigarettes	Current
137N.00	Ex pipe smoker	Ex
137O.00	Ex cigar smoker	Ex
137P.00	Cigarette smoker	Current
137P.11	Smoker	Current
137Q.00	Smoking started	Current
137Q.11	Smoking restarted	Current
137R.00	Current smoker	Current

137S.00	Ex smoker	Ex
137T.00	Date ceased smoking	Ex
137V.00	Smoking reduced	Current
137X.00	Cigarette consumption	see AHD
137Y.00	Cigar consumption	see AHD
137Z.00	Tobacco consumption NOS	see AHD
137a.00	Pipe tobacco consumption	see AHD
137b.00	Ready to stop smoking	Current
137c.00	Thinking about stopping smoking	Current
137d.00	Not interested in stopping smoking	Current
137e.00	Smoking restarted	Current
137f.00	Reason for restarting smoking	Current
137g.00	Cigarette pack-years	Unknown
137h.00	Minutes from waking to first tobacco consumption	Current
13p..00	Smoking cessation milestones	Unknown
13p0.00	Negotiated date for cessation of smoking	Current
13p1.00	Smoking status at 4 weeks	Unknown
13p2.00	Smoking status between 4 and 52 weeks	Unknown
13p3.00	Smoking status at 52 weeks	Unknown
13p4.00	Smoking free weeks	Unknown
13p5.00	Smoking cessation programme start date	Current
13p6.00	Carbon monoxide reading at 4 weeks	Unknown
4I90.00	Expired carbon monoxide concentration	Unknown
6791.00	Health ed. - smoking	Current
67A3.00	Pregnancy smoking advice	Current
67H1.00	Lifestyle advice regarding smoking	Current

6893.00	Tobacco usage screen	see AHD
68T..00	Tobacco usage screen	see AHD
745H.00	Smoking cessation therapy	Unknown
745H000	Nicotine replacement therapy using nicotine patches	Current
745H100	Nicotine replacement therapy using nicotine gum	Current
745H200	Nicotine replacement therapy using nicotine inhalator	Current
745H300	Nicotine replacement therapy using nicotine lozenges	Current
745H400	Smoking cessation drug therapy	Current
745Hy00	Other specified smoking cessation therapy	Current
745Hz00	Smoking cessation therapy NOS	Unknown
8B2B.00	Nicotine replacement therapy	Current
8B3Y.00	Over the counter nicotine replacement therapy	Current
8B3f.00	Nicotine replacement therapy provided free	Current
8BP3.00	Nicotine replacement therapy provided by community pharmacis	Current
8CAL.00	Smoking cessation advice	Current
8CAg.00	Smoking cessation advice provided by community pharmacist	Current
8H7i.00	Referral to smoking cessation advisor	Current
8HTK.00	Referral to stop-smoking clinic	Current
8I2I.00	Nicotine replacement therapy contraindicated	Current
8I39.00	Nicotine replacement therapy refused	Current
9N2k.00	Seen by smoking cessation advisor	Unknown
9N4M.00	DNA - Did not attend smoking cessation clinic	Unknown

9OO..00	Anti-smoking monitoring admin.	Unknown
9OO..11	Stop smoking clinic admin.	Unknown
9OO..12	Stop smoking monitoring admin.	Unknown
9OO1.00	Attends stop smoking monitor.	Unknown
9OO2.00	Refuses stop smoking monitor	Unknown
9OO3.00	Stop smoking monitor default	Unknown
9OO4.00	Stop smoking monitor 1st lettr	Unknown
9OO5.00	Stop smoking monitor 2nd lettr	Unknown
9OO6.00	Stop smoking monitor 3rd lettr	Unknown
9OO7.00	Stop smoking monitor verb.inv.	Current
9OO8.00	Stop smoking monitor phone inv	Current
9OO9.00	Stop smoking monitoring delete	Unknown
9OOA.00	Stop smoking monitor.chck done	Unknown
9OOZ.00	Stop smoking monitor admin.NOS	Unknown
9hG..00	Exception reporting: smoking quality indicators	Exception
9hG0.00	Excepted from smoking quality indicators: Patient unsuitable	Exception
9hG1.00	Excepted from smoking quality indicators: Informed dissent	Exception
E023.00	Nicotine withdrawal	Unknown
E251.00	Tobacco dependence	Current
E251100	Tobacco dependence, continuous	Current
E251300	Tobacco dependence in remission	Ex
E251z00	Tobacco dependence NOS	Current
ZG23300	Advice on smoking	Current
ZRBm200	Fagerstrom test for nicotine dependence	Current

ZRBm211	FTND - Fagerstrom test for nicotine dependence	Current
ZRaM.00	Motives for smoking scale	Current
ZRaM.11	MFS - Motives for smoking scale	Current
ZRao.00	Occasions for smoking scale	Current
ZRh4.00	Reasons for smoking scale	Current
ZRh4.11	RFS - Reasons for smoking scale	Current
ZV11600	[V]Personal history of tobacco abuse	Unknown
ZV4K000	[V]Tobacco use	see AHD
ZV6D800	[V]Tobacco abuse counselling	Current
137j.00	Ex-cigarette smoker	Ex

Read codes used to derive Charlson Score

Acquired Immune Deficiency Syndrome Read codes

Read code	Description
43C3.11	HIV positive
65QA.00	AIDS carrier
65VE.00	Notification of AIDS
A788000	Acute human immunodeficiency virus infection
A788100	Asymptomatic human immunodeficiency virus infection
A788200	HIV infection with persistent generalised lymphadenopathy
A788300	Human immunodeficiency virus with constitutional disease
A788400	Human immunodeficiency virus with neurological disease
A788500	Human immunodeficiency virus with secondary infection
A788600	Human immunodeficiency virus with secondary cancers
A788U00	HIV disease result/haematological+immunologic abnorms,NEC
A788V00	HIV disease resulting in multiple diseases CE

A788W00	HIV disease resulting in unspecified malignant neoplasm
A788X00	HIV disease resulting/unspcf infectious+parasitic disease
A788y00	Human immunodeficiency virus with other clinical findings
A788z00	Acquired human immunodeficiency virus infection syndrome NOS
A789000	HIV disease resulting in mycobacterial infection
A789100	HIV disease resulting in cytomegaloviral disease
A789200	HIV disease resulting in candidiasis
A789300	HIV disease resulting in Pneumocystis carinii pneumonia
A789400	HIV disease resulting in multiple infections
A789500	HIV disease resulting in Kaposi's sarcoma
A789600	HIV disease resulting in Burkitt's lymphoma
A789700	HIV dis resulting oth types of non-Hodgkin's lymphoma
A789800	HIV disease resulting in multiple malignant neoplasms
A789900	HIV disease resulting in lymphoid interstitial pneumonitis
A789A00	HIV disease resulting in wasting syndrome
A789X00	HIV dis reslt/oth mal neopl/lymph,h'matopoetc+reltd tissu
AyuC000	[X]HIV disease resulting in other bacterial infections
AyuC100	[X]HIV disease resulting in other viral infections
AyuC200	[X]HIV disease resulting in other mycoses
AyuC300	[X]HIV disease resulting in multiple infections
AyuC400	[X]HIV disease resulting/other infectious+parasitic diseases
AyuC500	[X]HIV disease resulting/unspcf infectious+parasitic disease
AyuC600	[X]HIV disease resulting in other non-Hodgkin's lymphoma
AyuC700	[X]HIV dis reslt/oth mal neopl/lymph,h'matopoetc+reltd tissu
AyuC800	[X]HIV disease resulting in other malignant neoplasms

AyuC900	[X]HIV disease resulting in unspecified malignant neoplasm
AyuCA00	[X]HIV disease resulting in multiple diseases CE
AyuCB00	[X]HIV disease result/haematological+immunologic abnorms,NEC
AyuCC00	[X]HIV disease resulting in other specified conditions
AyuCD00	[X]Unspecified human immunodeficiency virus [HIV] disease
Eu02400	[X]Dementia in human immunodef virus [HIV] disease
R109.00	[D]Laboratory evidence of human immunodefiency virus [HIV]

Congestive cardiac failure Read codes

Read code	Description
R023200	[D]Dropsy
1J60.00	Suspected heart failure
1O1..00	Heart failure confirmed
23E1.00	O/E - pulmonary oedema
388D.00	New York Heart Assoc classification heart failure symptoms
662f.00	New York Heart Association classification - class I
662g.00	New York Heart Association classification - class II
662h.00	New York Heart Association classification - class III
662i.00	New York Heart Association classification - class IV
G210100	Malignant hypertensive heart disease with CCF
G211100	Benign hypertensive heart disease with CCF
G21z100	Hypertensive heart disease NOS with CCF
G232.00	Hypertensive heart&renal dis wth (congestive) heart failure
G234.00	Hyperten heart&renal dis+both(congestv)heart and renal fail
G554000	Congestive cardiomyopathy

G554011	Congestive obstructive cardiomyopathy
G58..00	Heart failure
G58..11	Cardiac failure
G580.00	Congestive heart failure
G580.11	Congestive cardiac failure
G580.12	Right heart failure
G580.13	Right ventricular failure
G580.14	Biventricular failure
G580000	Acute congestive heart failure
G580100	Chronic congestive heart failure
G581.00	Left ventricular failure
G581.12	Pulmonary oedema - acute
G582.00	Acute heart failure
G58z.00	Heart failure NOS
G58z.12	Cardiac failure NOS
H541z00	Pulmonary oedema NOS
H584.00	Acute pulmonary oedema unspecified
H584.11	Acute oedema of lung, unspecified
H584z00	Acute pulmonary oedema NOS
SP11111	Heart failure as a complication of care
ZRad.00	New York Heart Assoc classification heart failure symptoms

Connective tissue disease Read codes

Read code	Description
AD61.00	Behcet's syndrome
F371.00	Polyneuropathy in collagen vascular disease

F371000	Polyneuropathy in disseminated lupus erythematosus
F371100	Polyneuropathy in polyarteritis nodosa
F371z00	Polyneuropathy in collagen vascular disease NOS
F39..00	Muscular dystrophies and other myopathies
F396.00	Symptomatic inflammatory myopathy in disease EC
F396100	Myopathy due to disseminated lupus erythematosus
F396300	Myopathy due to polyarteritis nodosa
F4D3300	Eyelid discoid lupus erythematosus
G7...00	Arterial, arteriole and capillary disease
G7...11	Capillary disease
G75..00	Polyarteritis nodosa and allied conditions
G750.00	Polyarteritis nodosa
G754.00	Wegener's granulomatosis
G759.00	Juvenile polyarteritis
G75z.00	Polyarteritis nodosa and allied conditions NOS
H57y400	Lung disease with systemic lupus erythematosus
K01x300	Nephrotic syndrome in polyarteritis nodosa
M154.00	Lupus erythematosus
M154000	Lupus erythematosus chronicus
M154100	Discoid lupus erythematosus
M154200	Lupus erythematosus migrans
M154300	Lupus erythematosus nodularis
M154400	Lupus erythematosus profundus
M154500	Lupus erythematosus tumidus
M154600	Lupus erythematosus unguium mutilans
M154700	Subacute cutaneous lupus erythematosus

M154z00	Lupus erythematosus NOS
Myu7800	[X]Other local lupus erythematosus
N....00	Musculoskeletal and connective tissue diseases
N....11	Connective tissue diseases
N0...00	Arthropathies and related disorders
N00..00	Diffuse diseases of connective tissue
N00..11	Collagen diseases
N000.00	Systemic lupus erythematosus
N000000	Disseminated lupus erythematosus
N000200	Drug-induced systemic lupus erythematosus
N000300	Systemic lupus erythematosus with organ or sys involv
N000400	Systemic lupus erythematosus with pericarditis
N000z00	Systemic lupus erythematosus NOS
N00y.00	Other specified diffuse collagen diseases
N00z.00	Collagen disease NOS
N012.00	Arthropathy in Behcet's syndrome
N012000	Arthropathy in Behcet's syndrome of unspecified site
N012011	Behcet's syndrome arthropathy
N012100	Arthropathy in Behcet's syndrome of the shoulder region
N012200	Arthropathy in Behcet's syndrome of the upper arm
N012300	Arthropathy in Behcet's syndrome of the forearm
N012400	Arthropathy in Behcet's syndrome of the hand
N012500	Arthropathy in Behcet's syndrome of the pelvis/thigh
N012600	Arthropathy in Behcet's syndrome of the lower leg
N012700	Arthropathy in Behcet's syndrome of the ankle and foot
N012x00	Arthropathy in Behcet's syndrome of multiple sites

N012y00	Arthropathy in Behcet's syndrome of other specified sites
N012z00	Arthropathy in Behcet's syndrome NOS
N2...00	Rheumatism, excluding the back
N20..00	Polymyalgia rheumatica
N20..11	Polymyalgia
N200.00	Giant cell arteritis with polymyalgia rheumatica
N374D00	Scoliosis in connective tissue anomalies
Ny...00	Musculoskeletal or connective tissue diseases OS
Nyu..00	[X] Addtnl musculskeletal+connectv tissue dis classfctn terms
Nyu4.00	[X]Systemic connective tissue disorders
Nyu4000	[X]Other conditions related to polyarteritis nodosa
Nyu4300	[X]Other forms of systemic lupus erythematosus
Nyu4700	[X]Other systemic diseases of connective tissue
Nyu4C00	[X]Systemic disorders/connective tissue in other diseases CE
NyuE.00	[X]Other disord musculoskeletal system and connective tissue
Nz...00	Musculoskeletal and connective tissue diseases NOS
PGz4.00	Unspecified anomaly of connective tissue

Cerebrovascular disease Read codes

Read code	Description
G64..12	Infarction - cerebral
G60..00	Subarachnoid haemorrhage

G601.00	Subarachnoid haemorrhage from carotid siphon and bifurcation
G602.00	Subarachnoid haemorrhage from middle cerebral artery
G603.00	Subarachnoid haemorrhage from anterior communicating artery
G604.00	Subarachnoid haemorrhage from posterior communicating artery
G605.00	Subarachnoid haemorrhage from basilar artery
G606.00	Subarachnoid haemorrhage from vertebral artery
G60X.00	Subarachnoid haemorrh from intracranial artery, unspecif
G60z.00	Subarachnoid haemorrhage NOS
G680.00	Sequelae of subarachnoid haemorrhage
Gyu6000	[X]Subarachnoid haemorrhage from other intracranial arteries
Gyu6100	[X]Other subarachnoid haemorrhage
Gyu6E00	[X]Subarachnoid haemorrh from intracranial artery, unspecif
Q412.00	Perinatal subarachnoid haemorrhage
Q412000	Subarachnoid haemorrhage due to birth injury
S62..12	Subarachnoid haemorrhage following injury
S620.00	Closed traumatic subarachnoid haemorrhage
S620000	Subarachnoid h'ge inj no open intracran wound + unspec consc
S620100	Subarachnoid h'ge inj no open intracran wnd+no loss consc
S620200	Subarachnoid h'ge inj no open intracran wnd+<1hr loss consc

S620300	Subarachnoid h'ge inj no open intracran wound + 1-24hr LOC
S620400	Subarachnoid h'ge inj no open intracran wnd+>24 LOC+recovery
S621.00	Open traumatic subarachnoid haemorrhage
S621000	Subarachnoid h'ge inj + open intracran wound + unspec consc
S621100	Subarachnoid h'ge inj + open intracranial wound + no LOC
S621200	Subarachnoid h'ge inj + open intracran wound+<1hr loss consc
S621300	Subarachnoid h'ge inj + open intracran wnd+1-24hr loss consc
S621z00	Subarachnoid h'ge inj + open intracran wnd+concussion unspec
S627.00	Traumatic subarachnoid haemorrhage
G6...00	Cerebrovascular disease
G61..11	CVA - cerebrovascular accid due to intracerebral haemorrhage
G66..00	Stroke and cerebrovascular accident unspecified
G66..13	CVA - Cerebrovascular accident unspecified
G67..00	Other cerebrovascular disease
G671.00	Generalised ischaemic cerebrovascular disease NOS
G671000	Acute cerebrovascular insufficiency NOS
G671z00	Generalised ischaemic cerebrovascular disease NOS
G67y.00	Other cerebrovascular disease OS
G67z.00	Other cerebrovascular disease NOS
G68..00	Late effects of cerebrovascular disease
G68W.00	Sequelae/other + unspecified cerebrovascular diseases

G6y..00	Other specified cerebrovascular disease
G6z..00	Cerebrovascular disease NOS
Gyu6.00	[X]Cerebrovascular diseases
Gyu6700	[X]Other specified cerebrovascular diseases
Gyu6A00	[X]Other cerebrovascular disorders in diseases CE
Gyu6D00	[X]Sequelae/other + unspecified cerebrovascular diseases

Dementia Read codes

Read code	Description
1461.00	H/O: dementia
E00..11	Senile dementia
E00..12	Senile/presenile dementia
E000.00	Uncomplicated senile dementia
E001.00	Presenile dementia
E001000	Uncomplicated presenile dementia
E001100	Presenile dementia with delirium
E001200	Presenile dementia with paranoia
E001300	Presenile dementia with depression
E001z00	Presenile dementia NOS
E002.00	Senile dementia with depressive or paranoid features
E002000	Senile dementia with paranoia
E002100	Senile dementia with depression
E002z00	Senile dementia with depressive or paranoid features NOS
E003.00	Senile dementia with delirium
E004.00	Arteriosclerotic dementia

E004.11	Multi infarct dementia
E004000	Uncomplicated arteriosclerotic dementia
E004100	Arteriosclerotic dementia with delirium
E004200	Arteriosclerotic dementia with paranoia
E004300	Arteriosclerotic dementia with depression
E004z00	Arteriosclerotic dementia NOS
E041.00	Dementia in conditions EC
E042.00	Chronic confusional state
Eu00.00	[X]Dementia in Alzheimer's disease
Eu00000	[X]Dementia in Alzheimer's disease with early onset
Eu00011	[X]Presenile dementia,Alzheimer's type
Eu00012	[X]Primary degen dementia, Alzheimer's type, presenile onset
Eu00013	[X]Alzheimer's disease type 2
Eu00100	[X]Dementia in Alzheimer's disease with late onset
Eu00111	[X]Alzheimer's disease type 1
Eu00112	[X]Senile dementia, Alzheimer's type
Eu00113	[X]Primary degen dementia of Alzheimer's type, senile onset
Eu00200	[X]Dementia in Alzheimer's dis, atypical or mixed type
Eu00z00	[X]Dementia in Alzheimer's disease, unspecified
Eu00z11	[X]Alzheimer's dementia unspec
Eu01.00	[X]Vascular dementia
Eu01.11	[X]Arteriosclerotic dementia
Eu01000	[X]Vascular dementia of acute onset
Eu01100	[X]Multi-infarct dementia

Eu01111	[X]Predominantly cortical dementia
Eu01200	[X]Subcortical vascular dementia
Eu01300	[X]Mixed cortical and subcortical vascular dementia
Eu01y00	[X]Other vascular dementia
Eu01z00	[X]Vascular dementia, unspecified
Eu02.00	[X]Dementia in other diseases classified elsewhere
Eu02000	[X]Dementia in Pick's disease
Eu02100	[X]Dementia in Creutzfeldt-Jakob disease
Eu02200	[X]Dementia in Huntington's disease
Eu02300	[X]Dementia in Parkinson's disease
Eu02400	[X]Dementia in human immunodef virus [HIV] disease
Eu02y00	[X]Dementia in other specified diseases classif elsewhere
Eu02z00	[X] Unspecified dementia
Eu02z11	[X] Presenile dementia NOS
Eu02z13	[X] Primary degenerative dementia NOS
Eu02z14	[X] Senile dementia NOS
Eu02z16	[X] Senile dementia, depressed or paranoid type
Eu04100	[X]Delirium superimposed on dementia

Diabetes mellitus with end organ damage

Read codes	Description
2BBF.00	Retinal abnormality - diabetes related
2BBL.00	O/E - diabetic maculopathy present both eyes
2BBM.00	O/E - diabetic maculopathy absent both eyes
2BBP.00	O/E - right eye background diabetic retinopathy
2BBQ.00	O/E - left eye background diabetic retinopathy

2BBR.00	O/E - right eye preproliferative diabetic retinopathy
2BBS.00	O/E - left eye preproliferative diabetic retinopathy
2BBT.00	O/E - right eye proliferative diabetic retinopathy
2BBV.00	O/E - left eye proliferative diabetic retinopathy
2BBW.00	O/E - right eye diabetic maculopathy
2BBX.00	O/E - left eye diabetic maculopathy
2BBo.00	O/E - sight threatening diabetic retinopathy
2G51000	Foot abnormality - diabetes related
2G5A.00	O/E - Right diabetic foot at risk
2G5B.00	O/E - Left diabetic foot at risk
2G5C.00	Foot abnormality - diabetes related
2G5E.00	O/E - Right diabetic foot at low risk
2G5F.00	O/E - Right diabetic foot at moderate risk
2G5G.00	O/E - Right diabetic foot at high risk
2G5H.00	O/E - Right diabetic foot - ulcerated
2G5I.00	O/E - Left diabetic foot at low risk
2G5J.00	O/E - Left diabetic foot at moderate risk
2G5K.00	O/E - Left diabetic foot at high risk
2G5L.00	O/E - Left diabetic foot - ulcerated
2G5V.00	O/E - right chronic diabetic foot ulcer
2G5W.00	O/E - left chronic diabetic foot ulcer
7276.00	Pan retinal photocoagulation for diabetes
C101.00	Diabetes mellitus with ketoacidosis
C101000	Diabetes mellitus, juvenile type, with ketoacidosis
C101100	Diabetes mellitus, adult onset, with ketoacidosis
C101y00	Other specified diabetes mellitus with ketoacidosis

C101z00	Diabetes mellitus NOS with ketoacidosis
C102.00	Diabetes mellitus with hyperosmolar coma
C102000	Diabetes mellitus, juvenile type, with hyperosmolar coma
C102100	Diabetes mellitus, adult onset, with hyperosmolar coma
C102z00	Diabetes mellitus NOS with hyperosmolar coma
C103.00	Diabetes mellitus with ketoacidotic coma
C103000	Diabetes mellitus, juvenile type, with ketoacidotic coma
C103100	Diabetes mellitus, adult onset, with ketoacidotic coma
C103y00	Other specified diabetes mellitus with coma
C103z00	Diabetes mellitus NOS with ketoacidotic coma
C104.00	Diabetes mellitus with renal manifestation
C104.11	Diabetic nephropathy
C104000	Diabetes mellitus, juvenile type, with renal manifestation
C104100	Diabetes mellitus, adult onset, with renal manifestation
C104y00	Other specified diabetes mellitus with renal complications
C104z00	Diabetes mellitis with nephropathy NOS
C105.00	Diabetes mellitus with ophthalmic manifestation
C105000	Diabetes mellitus, juvenile type, + ophthalmic manifestation
C105100	Diabetes mellitus, adult onset, + ophthalmic manifestation
C105y00	Other specified diabetes mellitus with ophthalmic complicatn
C105z00	Diabetes mellitus NOS with ophthalmic manifestation
C106.00	Diabetes mellitus with neurological manifestation
C106.11	Diabetic amyotrophy
C106.12	Diabetes mellitus with neuropathy

C106.13	Diabetes mellitus with polyneuropathy
C106000	Diabetes mellitus, juvenile, + neurological manifestation
C106100	Diabetes mellitus, adult onset, + neurological manifestation
C106y00	Other specified diabetes mellitus with neurological comps
C106z00	Diabetes mellitus NOS with neurological manifestation
C107.00	Diabetes mellitus with peripheral circulatory disorder
C107.11	Diabetes mellitus with gangrene
C107.12	Diabetes with gangrene
C107000	Diabetes mellitus, juvenile +peripheral circulatory disorder
C107100	Diabetes mellitus, adult, + peripheral circulatory disorder
C107200	Diabetes mellitus, adult with gangrene
C107300	IDDM with peripheral circulatory disorder
C107400	NIDDM with peripheral circulatory disorder
C107y00	Other specified diabetes mellitus with periph circ comps
C108000	Insulin-dependent diabetes mellitus with renal complications
C108011	Type I diabetes mellitus with renal complications
C108012	Type 1 diabetes mellitus with renal complications
C108100	Insulin-dependent diabetes mellitus with ophthalmic comps
C108111	Type I diabetes mellitus with ophthalmic complications
C108112	Type 1 diabetes mellitus with ophthalmic complications
C108200	Insulin-dependent diabetes mellitus with neurological comps
C108211	Type I diabetes mellitus with neurological complications
C108212	Type 1 diabetes mellitus with neurological complications

C108300	Insulin dependent diabetes mellitus with multiple complicatn
C108311	Type I diabetes mellitus with multiple complications
C108312	Type 1 diabetes mellitus with multiple complications
C108500	Insulin dependent diabetes mellitus with ulcer
C108511	Type I diabetes mellitus with ulcer
C108512	Type 1 diabetes mellitus with ulcer
C108600	Insulin dependent diabetes mellitus with gangrene
C108611	Type I diabetes mellitus with gangrene
C108612	Type 1 diabetes mellitus with gangrene
C108700	Insulin dependent diabetes mellitus with retinopathy
C108711	Type I diabetes mellitus with retinopathy
C108712	Type 1 diabetes mellitus with retinopathy
C108B00	Insulin dependent diabetes mellitus with mononeuropathy
C108B11	Type I diabetes mellitus with mononeuropathy
C108B12	Type 1 diabetes mellitus with mononeuropathy
C108C00	Insulin dependent diabetes mellitus with polyneuropathy
C108C11	Type I diabetes mellitus with polyneuropathy
C108C12	Type 1 diabetes mellitus with polyneuropathy
C108D00	Insulin dependent diabetes mellitus with nephropathy
C108D11	Type I diabetes mellitus with nephropathy
C108D12	Type 1 diabetes mellitus with nephropathy
C108E00	Insulin dependent diabetes mellitus with hypoglycaemic coma
C108E11	Type I diabetes mellitus with hypoglycaemic coma
C108E12	Type 1 diabetes mellitus with hypoglycaemic coma

C108F00	Insulin dependent diabetes mellitus with diabetic cataract
C108F11	Type I diabetes mellitus with diabetic cataract
C108F12	Type 1 diabetes mellitus with diabetic cataract
C108G00	Insulin dependent diab mell with peripheral angiopathy
C108G11	Type I diabetes mellitus with peripheral angiopathy
C108G12	Type 1 diabetes mellitus with peripheral angiopathy
C108H00	Insulin dependent diabetes mellitus with arthropathy
C108H11	Type I diabetes mellitus with arthropathy
C108H12	Type 1 diabetes mellitus with arthropathy
C108J00	Insulin dependent diab mell with neuropathic arthropathy
C108J11	Type I diabetes mellitus with neuropathic arthropathy
C108J12	Type 1 diabetes mellitus with neuropathic arthropathy
C108y00	Other specified diabetes mellitus with multiple comps
C108z00	Unspecified diabetes mellitus with multiple complications
C109000	Non-insulin-dependent diabetes mellitus with renal comps
C109011	Type II diabetes mellitus with renal complications
C109012	Type 2 diabetes mellitus with renal complications
C109100	Non-insulin-dependent diabetes mellitus with ophthalm comps
C109111	Type II diabetes mellitus with ophthalmic complications
C109112	Type 2 diabetes mellitus with ophthalmic complications
C109200	Non-insulin-dependent diabetes mellitus with neuro comps
C109211	Type II diabetes mellitus with neurological complications
C109212	Type 2 diabetes mellitus with neurological complications
C109300	Non-insulin-dependent diabetes mellitus with multiple comps

C109311	Type II diabetes mellitus with multiple complications
C109312	Type 2 diabetes mellitus with multiple complications
C109400	Non-insulin dependent diabetes mellitus with ulcer
C109411	Type II diabetes mellitus with ulcer
C109412	Type 2 diabetes mellitus with ulcer
C109500	Non-insulin dependent diabetes mellitus with gangrene
C109511	Type II diabetes mellitus with gangrene
C109512	Type 2 diabetes mellitus with gangrene
C109600	Non-insulin-dependent diabetes mellitus with retinopathy
C109611	Type II diabetes mellitus with retinopathy
C109612	Type 2 diabetes mellitus with retinopathy
C109A00	Non-insulin dependent diabetes mellitus with mononeuropathy
C109A11	Type II diabetes mellitus with mononeuropathy
C109A12	Type 2 diabetes mellitus with mononeuropathy
C109B00	Non-insulin dependent diabetes mellitus with polyneuropathy
C109B11	Type II diabetes mellitus with polyneuropathy
C109B12	Type 2 diabetes mellitus with polyneuropathy
C109C00	Non-insulin dependent diabetes mellitus with nephropathy
C109C11	Type II diabetes mellitus with nephropathy
C109C12	Type 2 diabetes mellitus with nephropathy
C109D00	Non-insulin dependent diabetes mellitus with hypoglyca coma
C109D11	Type II diabetes mellitus with hypoglycaemic coma
C109D12	Type 2 diabetes mellitus with hypoglycaemic coma

C109E00	Non-insulin depend diabetes mellitus with diabetic cataract
C109E11	Type II diabetes mellitus with diabetic cataract
C109E12	Type 2 diabetes mellitus with diabetic cataract
C109F00	Non-insulin-dependent d m with peripheral angiopath
C109F11	Type II diabetes mellitus with peripheral angiopathy
C109F12	Type 2 diabetes mellitus with peripheral angiopathy
C109G00	Non-insulin dependent diabetes mellitus with arthropathy
C109G11	Type II diabetes mellitus with arthropathy
C109G12	Type 2 diabetes mellitus with arthropathy
C109H00	Non-insulin dependent d m with neuropathic arthropathy
C109H11	Type II diabetes mellitus with neuropathic arthropathy
C109H12	Type 2 diabetes mellitus with neuropathic arthropathy
C109K00	Hyperosmolar non-ketotic state in type 2 diabetes mellitus
C10A000	Malnutrition-related diabetes mellitus with coma
C10A100	Malnutrition-related diabetes mellitus with ketoacidosis
C10A200	Malnutrition-related diabetes mellitus with renal complicatn
C10A300	Malnutrit-related diabetes mellitus wth ophthalmic complicat
C10A400	Malnutrition-related diabetes mellitus wth neuro complicatns
C10A500	Malnutritn-relat diabetes melitus wth periph circul complctn
C10A600	Malnutrition-related diabetes mellitus with multiple comps
C10A700	Malnutrition-related diabetes mellitus without complications

C10AW00	Malnutrit-related diabetes mellitus with unspec complics
C10AX00	Malnutrit-relat diabetes mellitus with other spec comps
C10E000	Type 1 diabetes mellitus with renal complications
C10E011	Type I diabetes mellitus with renal complications
C10E012	Insulin-dependent diabetes mellitus with renal complications
C10E100	Type 1 diabetes mellitus with ophthalmic complications
C10E111	Type I diabetes mellitus with ophthalmic complications
C10E112	Insulin-dependent diabetes mellitus with ophthalmic comps
C10E200	Type 1 diabetes mellitus with neurological complications
C10E211	Type I diabetes mellitus with neurological complications
C10E212	Insulin-dependent diabetes mellitus with neurological comps
C10E300	Type 1 diabetes mellitus with multiple complications
C10E311	Type I diabetes mellitus with multiple complications
C10E312	Insulin dependent diabetes mellitus with multiple complicat
C10E500	Type 1 diabetes mellitus with ulcer
C10E511	Type I diabetes mellitus with ulcer
C10E512	Insulin dependent diabetes mellitus with ulcer
C10E600	Type 1 diabetes mellitus with gangrene
C10E611	Type I diabetes mellitus with gangrene
C10E612	Insulin dependent diabetes mellitus with gangrene
C10E700	Type 1 diabetes mellitus with retinopathy
C10E711	Type I diabetes mellitus with retinopathy
C10E712	Insulin dependent diabetes mellitus with retinopathy

C10EB00	Type 1 diabetes mellitus with mononeuropathy
C10EB11	Type I diabetes mellitus with mononeuropathy
C10EB12	Insulin dependent diabetes mellitus with mononeuropathy
C10EC00	Type 1 diabetes mellitus with polyneuropathy
C10EC11	Type I diabetes mellitus with polyneuropathy
C10EC12	Insulin dependent diabetes mellitus with polyneuropathy
C10ED00	Type 1 diabetes mellitus with nephropathy
C10ED11	Type I diabetes mellitus with nephropathy
C10ED12	Insulin dependent diabetes mellitus with nephropathy
C10EE00	Type 1 diabetes mellitus with hypoglycaemic coma
C10EE11	Type I diabetes mellitus with hypoglycaemic coma
C10EE12	Insulin dependent diabetes mellitus with hypoglycaemic coma
C10EF00	Type 1 diabetes mellitus with diabetic cataract
C10EF11	Type I diabetes mellitus with diabetic cataract
C10EF12	Insulin dependent diabetes mellitus with diabetic cataract
C10EG00	Type 1 diabetes mellitus with peripheral angiopathy
C10EG11	Type I diabetes mellitus with peripheral angiopathy
C10EG12	Insulin dependent diab mell with peripheral angiopathy
C10EH00	Type 1 diabetes mellitus with arthropathy
C10EH11	Type I diabetes mellitus with arthropathy
C10EH12	Insulin dependent diabetes mellitus with arthropathy
C10EJ00	Type 1 diabetes mellitus with neuropathic arthropathy
C10EJ11	Type I diabetes mellitus with neuropathic arthropathy
C10EJ12	Insulin dependent diab mell with neuropathic arthropathy

C10EK00	Type 1 diabetes mellitus with persistent proteinuria
C10EK11	Type I diabetes mellitus with persistent proteinuria
C10EL00	Type 1 diabetes mellitus with persistent microalbuminuria
C10EL11	Type I diabetes mellitus with persistent microalbuminuria
C10EM00	Type 1 diabetes mellitus with ketoacidosis
C10EM11	Type I diabetes mellitus with ketoacidosis
C10EN00	Type 1 diabetes mellitus with ketoacidotic coma
C10EN11	Type I diabetes mellitus with ketoacidotic coma
C10EP00	Type 1 diabetes mellitus with exudative maculopathy
C10EP11	Type I diabetes mellitus with exudative maculopathy
C10F000	Type 2 diabetes mellitus with renal complications
C10F011	Type II diabetes mellitus with renal complications
C10F100	Type 2 diabetes mellitus with ophthalmic complications
C10F111	Type II diabetes mellitus with ophthalmic complications
C10F200	Type 2 diabetes mellitus with neurological complications
C10F211	Type II diabetes mellitus with neurological complications
C10F300	Type 2 diabetes mellitus with multiple complications
C10F311	Type II diabetes mellitus with multiple complications
C10F400	Type 2 diabetes mellitus with ulcer
C10F411	Type II diabetes mellitus with ulcer
C10F500	Type 2 diabetes mellitus with gangrene
C10F511	Type II diabetes mellitus with gangrene
C10F600	Type 2 diabetes mellitus with retinopathy
C10F611	Type II diabetes mellitus with retinopathy
C10FA00	Type 2 diabetes mellitus with mononeuropathy
C10FA11	Type II diabetes mellitus with mononeuropathy

C10FB00	Type 2 diabetes mellitus with polyneuropathy
C10FB11	Type II diabetes mellitus with polyneuropathy
C10FC00	Type 2 diabetes mellitus with nephropathy
C10FC11	Type II diabetes mellitus with nephropathy
C10FD00	Type 2 diabetes mellitus with hypoglycaemic coma
C10FD11	Type II diabetes mellitus with hypoglycaemic coma
C10FE00	Type 2 diabetes mellitus with diabetic cataract
C10FE11	Type II diabetes mellitus with diabetic cataract
C10FF00	Type 2 diabetes mellitus with peripheral angiopathy
C10FF11	Type II diabetes mellitus with peripheral angiopathy
C10FG00	Type 2 diabetes mellitus with arthropathy
C10FG11	Type II diabetes mellitus with arthropathy
C10FH00	Type 2 diabetes mellitus with neuropathic arthropathy
C10FH11	Type II diabetes mellitus with neuropathic arthropathy
C10FK00	Hyperosmolar non-ketotic state in type 2 diabetes mellitus
C10FL00	Type 2 diabetes mellitus with persistent proteinuria
C10FL11	Type II diabetes mellitus with persistent proteinuria
C10FM00	Type 2 diabetes mellitus with persistent microalbuminuria
C10FM11	Type II diabetes mellitus with persistent microalbuminuria
C10FN00	Type 2 diabetes mellitus with ketoacidosis
C10FN11	Type II diabetes mellitus with ketoacidosis
C10FP00	Type 2 diabetes mellitus with ketoacidotic coma
C10FP11	Type II diabetes mellitus with ketoacidotic coma
C10FQ00	Type 2 diabetes mellitus with exudative maculopathy
C10FQ11	Type II diabetes mellitus with exudative maculopathy
C10yy00	Other specified diabetes mellitus with other spec comps

C10yz00	Diabetes mellitus NOS with other specified manifestation
C10z.00	Diabetes mellitus with unspecified complication
C10z000	Diabetes mellitus, juvenile type, + unspecified complication
C10z100	Diabetes mellitus, adult onset, + unspecified complication
C10zy00	Other specified diabetes mellitus with unspecified comps
C10zz00	Diabetes mellitus NOS with unspecified complication
Cyu2100	[X]Malnutrit-relat diabetes mellitus with other spec comps
Cyu2200	[X]Malnutrit-related diabetes mellitus with unspec complics
Cyu2300	[X]Unspecified diabetes mellitus with renal complications
Kyu0300	[X]Glomerular disorders in diabetes mellitus

Diabetes Read codes

Read code	Description
66A1.00	Initial diabetic assessment
66A2.00	Follow-up diabetic assessment
66A3.00	Diabetic on diet only
66A4.00	Diabetic on oral treatment
66A5.00	Diabetic on insulin
66A8.00	Has seen dietician - diabetes
66AJ.11	Unstable diabetes
66AJz00	Diabetic - poor control NOS
66AP.00	Diabetes: practice programme
66AQ.00	Diabetes: shared care programme
66AU.00	Diabetes care by hospital only

66AV.00	Diabetic on insulin and oral treatment
66AZ.00	Diabetic monitoring NOS
9NN8.00	Under care of diabetologist
9NN9.00	Under care of diabetes specialist nurse
C10..00	Diabetes mellitus
C100.00	Diabetes mellitus with no mention of complication
C100000	Diabetes mellitus, juvenile type, no mention of complication
C100011	Insulin dependent diabetes mellitus
C100100	Diabetes mellitus, adult onset, no mention of complication
C100111	Maturity onset diabetes
C100112	Non-insulin dependent diabetes mellitus
C100z00	Diabetes mellitus NOS with no mention of complication
C108.00	Insulin dependent diabetes mellitus
C108.11	IDDM-Insulin dependent diabetes mellitus
C108.12	Type 1 diabetes mellitus
C108.13	Type I diabetes mellitus
C108400	Unstable insulin dependent diabetes mellitus
C108411	Unstable type I diabetes mellitus
C108412	Unstable type 1 diabetes mellitus
C108800	Insulin dependent diabetes mellitus - poor control
C108811	Type I diabetes mellitus - poor control
C108812	Type 1 diabetes mellitus - poor control
C108900	Insulin dependent diabetes maturity onset
C108911	Type I diabetes mellitus maturity onset

C108912	Type 1 diabetes mellitus maturity onset
C108A00	Insulin-dependent diabetes without complication
C108A11	Type I diabetes mellitus without complication
C108A12	Type 1 diabetes mellitus without complication
C109.00	Non-insulin dependent diabetes mellitus
C109.11	NIDDM - Non-insulin dependent diabetes mellitus
C109.12	Type 2 diabetes mellitus
C109.13	Type II diabetes mellitus
C109700	Non-insulin dependent diabetes mellitus - poor control
C109711	Type II diabetes mellitus - poor control
C109712	Type 2 diabetes mellitus - poor control
C109800	Reaven's syndrome
C109900	Non-insulin-dependent diabetes mellitus without complication
C109911	Type II diabetes mellitus without complication
C109912	Type 2 diabetes mellitus without complication
C109J00	Insulin treated Type 2 diabetes mellitus
C109J11	Insulin treated non-insulin dependent diabetes mellitus
C109J12	Insulin treated Type II diabetes mellitus
C10A.00	Malnutrition-related diabetes mellitus
C10B.00	Diabetes mellitus induced by steroids
C10B000	Steroid induced diabetes mellitus without complication
C10C.00	Diabetes mellitus autosomal dominant
C10C.11	Maturity onset diabetes in youth
C10C.12	Maturity onset diabetes in youth type 1
C10D.00	Diabetes mellitus autosomal dominant type 2

C10D.11	Maturity onset diabetes in youth type 2
C10E.00	Type 1 diabetes mellitus
C10E.11	Type I diabetes mellitus
C10E.12	Insulin dependent diabetes mellitus
C10E400	Unstable type 1 diabetes mellitus
C10E411	Unstable type I diabetes mellitus
C10E412	Unstable insulin dependent diabetes mellitus
C10E800	Type 1 diabetes mellitus - poor control
C10E811	Type I diabetes mellitus - poor control
C10E812	Insulin dependent diabetes mellitus - poor control
C10E900	Type 1 diabetes mellitus maturity onset
C10E911	Type I diabetes mellitus maturity onset
C10E912	Insulin dependent diabetes maturity onset
C10EA00	Type 1 diabetes mellitus without complication
C10EA11	Type I diabetes mellitus without complication
C10EA12	Insulin-dependent diabetes without complication
C10F.00	Type 2 diabetes mellitus
C10F.11	Type II diabetes mellitus
C10F700	Type 2 diabetes mellitus - poor control
C10F711	Type II diabetes mellitus - poor control
C10F800	Reaven's syndrome
C10F811	Metabolic syndrome X
C10F900	Type 2 diabetes mellitus without complication
C10F911	Type II diabetes mellitus without complication
C10G.00	Secondary pancreatic diabetes mellitus

C10G000	Secondary pancreatic diabetes mellitus without complication
C10H.00	Diabetes mellitus induced by non-steroid drugs
C10J.00	Insulin autoimmune syndrome
C10K.00	Type A insulin resistance
C10L.00	Fibrocalculous pancreatopathy
C10M.00	Lipoatrophic diabetes mellitus
C10M000	Lipoatrophic diabetes mellitus without complication
C10N.00	Secondary diabetes mellitus
C10N000	Secondary diabetes mellitus without complication
C10y.00	Diabetes mellitus with other specified manifestation
C10y000	Diabetes mellitus, juvenile, + other specified manifestation
C10y100	Diabetes mellitus, adult, + other specified manifestation
C11y000	Steroid induced diabetes
Cyu2.00	[X]Diabetes mellitus
Cyu2000	[X]Other specified diabetes mellitus
L180.00	Diabetes mellitus during pregnancy/childbirth/puerperium
L180000	Diabetes mellitus - unspec whether in pregnancy/puerperium
L180500	Pre-existing diabetes mellitus, insulin-dependent
L180600	Pre-existing diabetes mellitus, non-insulin-dependent
L180700	Pre-existing malnutrition-related diabetes mellitus
L180X00	Pre-existing diabetes mellitus, unspecified
L180z00	Diabetes mellitus in pregnancy/childbirth/puerperium NOS

Lyu2900	[X]Pre-existing diabetes mellitus, unspecified
R10C.00	[D]Drug induced hyperglycaemia
R10D.00	[D]Elevated blood glucose level
R10E.00	[D]Impaired glucose tolerance
ZC2C900	Dietary advice for type I diabetes
ZC2C911	Diet advice for insulin-dependent diabetes
ZC2CA00	Dietary advice for type II diabetes
ZC2CA11	Dietary advice non-insulin-dependent diabetes
ZL62500	Referral to diabetes nurse
ZL62600	Referral to diabetic liaison nurse
ZV65312	[V]Dietary counselling in diabetes mellitus

Hemiplegia Read codes

Read codes	Description
2833.00	O/E - hemiplegia
F22..00	Hemiplegia
F220.00	Flaccid hemiplegia
F221.00	Spastic hemiplegia
F222.00	Left hemiplegia
F223.00	Right hemiplegia
F22z.00	Hemiplegia NOS
F230.11	Paraplegia - congenital
F231.00	Congenital hemiplegia
F234.00	Infantile hemiplegia NOS

Leukaemia Read codes

Read codes	Description
1429.00	H/O: * leukaemia
1J02.00	Suspected leukaemia
B631.00	Plasma cell leukaemia
B64..00	Lymphoid leukaemia
B64..11	Lymphatic leukaemia
B640.00	Acute lymphoid leukaemia
B641.00	Chronic lymphoid leukaemia
B641.11	Chronic lymphatic leukaemia
B642.00	Subacute lymphoid leukaemia
B64y.00	Other lymphoid leukaemia
B64y000	Aleukaemic lymphoid leukaemia
B64y100	Prolymphocytic leukaemia
B64y200	Adult T-cell leukaemia
B64yz00	Other lymphoid leukaemia NOS
B64z.00	Lymphoid leukaemia NOS
B65..00	Myeloid leukaemia
B650.00	Acute myeloid leukaemia
B651.00	Chronic myeloid leukaemia
B651.11	Chronic granulocytic leukaemia
B651000	Chronic eosinophilic leukaemia
B651200	Chronic neutrophilic leukaemia
B651z00	Chronic myeloid leukaemia NOS
B652.00	Subacute myeloid leukaemia
B65y.00	Other myeloid leukaemia

B65y000	Aleukaemic myeloid leukaemia
B65y100	Acute promyelocytic leukaemia
B65yz00	Other myeloid leukaemia NOS
B65z.00	Myeloid leukaemia NOS
B66..00	Monocytic leukaemia
B66..11	Histiocytic leukaemia
B66..12	Monoblastic leukaemia
B660.00	Acute monocytic leukaemia
B661.00	Chronic monocytic leukaemia
B662.00	Subacute monocytic leukaemia
B66y.00	Other monocytic leukaemia
B66y000	Aleukaemic monocytic leukaemia
B66yz00	Other monocytic leukaemia NOS
B66z.00	Monocytic leukaemia NOS
B67..00	Other specified leukaemia
B670.00	Acute erythraemia and erythroleukaemia
B672.00	Megakaryocytic leukaemia
B672.11	Thrombocytic leukaemia
B673.00	Mast cell leukaemia
B67y.00	Other and unspecified leukaemia
B67y000	Lymphosarcoma cell leukaemia
B67yz00	Other and unspecified leukaemia NOS
B67z.00	Other specified leukaemia NOS
B68..00	Leukaemia of unspecified cell type
B680.00	Acute leukaemia NOS
B681.00	Chronic leukaemia NOS

B682.00	Subacute leukaemia NOS
B68y.00	Other leukaemia of unspecified cell type
B68z.00	Leukaemia NOS
B69..00	Myelomonocytic leukaemia
B690.00	Acute myelomonocytic leukaemia
B691.00	Chronic myelomonocytic leukaemia
B692.00	Subacute myelomonocytic leukaemia
BBr..00	[M] Leukaemias
BBr0.00	[M] Leukaemias unspecified
BBr0000	[M]Leukaemia NOS
BBr0100	[M]Acute leukaemia NOS
BBr0111	[M]Blast cell leukaemia
BBr0112	[M]Blastic leukaemia
BBr0113	[M]Stem cell leukaemia
BBr0200	[M]Subacute leukaemia NOS
BBr0300	[M]Chronic leukaemia NOS
BBr0400	[M]Aleukaemic leukaemia NOS
BBr0z00	[M]Leukaemia unspecified, NOS
BBr1.00	[M] Compound leukaemias
BBr1000	[M]Compound leukaemia
BBr1011	[M]Mixed leukaemia
BBr1z00	[M]Compound leukaemia NOS
BBr2.00	[M] Lymphoid leukaemias
BBr2000	[M]Lymphoid leukaemia NOS
BBr2011	[M]Lymphatic leukaemia
BBr2100	[M]Acute lymphoid leukaemia

BBr2200	[M]Subacute lymphoid leukaemia
BBr2300	[M]Chronic lymphoid leukaemia
BBr2400	[M]Aleukaemic lymphoid leukaemia
BBr2500	[M]Prolymphocytic leukaemia
BBr2600	[M]Burkitt's cell leukaemia
BBr2700	[M]Adult T-cell leukaemia/lymphoma
BBr2z00	[M]Other lymphoid leukaemia NOS
BBr3.00	[M] Plasma cell leukaemias
BBr3000	[M]Plasma cell leukaemia
BBr3z00	[M]Plasma cell leukaemia NOS
BBr4.00	[M] Erythroleukaemias
BBr4000	[M]Erythroleukaemia
BBr4011	[M]Erythraemic myelosis
BBr4111	[M]Di Guglielmo's disease
BBr4200	[M]Chronic erythraemia
BBr4z00	[M]Erythroleukaemia NOS
BBr5.00	[M] Lymphosarcoma cell leukaemias
BBr5000	[M]Lymphosarcoma cell leukaemia
BBr5z00	[M]Lymphosarcoma cell leukaemia NOS
BBr6.00	[M] Myeloid leukaemias
BBr6000	[M]Myeloid leukaemia NOS
BBr6011	[M]Granulocytic leukaemia NOS
BBr6100	[M]Acute myeloid leukaemia
BBr6200	[M]Subacute myeloid leukaemia
BBr6300	[M]Chronic myeloid leukaemia
BBr6311	[M]Naegeli-type monocytic leukaemia

BBr6400	[M]Aleukaemic myeloid leukaemia
BBr6500	[M]Neutrophilic leukaemia
BBr6600	[M]Acute promyelocytic leukaemia
BBr6700	[M]Acute myelomonocytic leukaemia
BBr6800	[M]Chronic myelomonocytic leukaemia
BBr6z00	[M]Other myeloid leukaemia NOS
BBr7.00	[M] Basophilic leukaemias
BBr7000	[M]Basophilic leukaemia
BBr7z00	[M]Basophilic leukaemia NOS
BBr8.00	[M] Eosinophilic leukaemias
BBr8000	[M]Eosinophilic leukaemia
BBr8z00	[M]Eosinophilic leukaemia NOS
BBr9.00	[M] Monocytic leukaemias
BBr9000	[M]Monocytic leukaemia NOS
BBr9011	[M]Histiocytic leukaemia
BBr9012	[M]Schilling-type monocytic leukaemia
BBr9100	[M]Acute monocytic leukaemia
BBr9200	[M]Subacute monocytic leukaemia
BBr9300	[M]Chronic monocytic leukaemia
BBr9400	[M]Aleukaemic monocytic leukaemia
BBr9z00	[M]Other monocytic leukaemia NOS
BBrA.00	[M]Miscellaneous leukaemias
BBrA000	[M]Mast cell leukaemia
BBrA100	[M]Megakaryocytic leukaemia
BBrA111	[M]Thrombocytic leukaemia
BBrA400	[M]Hairy cell leukaemia

BBrA411	[M]Leukaemic reticuloendotheliosis
BBrA500	[M]Acute megakaryoblastic leukaemia
BBrA800	[M]Leukaemic reticuloendotheliosis
BBrAz00	[M]Miscellaneous leukaemia NOS
BBrz.00	[M] Leukaemia NOS
ByuD500	[X]Other lymphoid leukaemia
ByuD600	[X]Other myeloid leukaemia
ByuD700	[X]Other monocytic leukaemia
ByuD800	[X]Other specified leukaemias
ByuD900	[X]Other leukaemia of unspecified cell type
ZV10600	[V]Personal history of leukaemia
ZV10611	[V]Personal history of lymphoid leukaemia
ZV10612	[V]Personal history of monocytic leukaemia
ZV10613	[V]Personal history of myeloid leukaemia

Mild liver disease Read codes

Read code	Description
J615H00	Infectious cirrhosis NOS
A392.00	Abdominal actinomycosis
D100.11	Acholuric familial jaundice
A392200	Actinomycosis of liver
J611.00	Acute alcoholic hepatitis
J661000	Acute cholangitis
A705100	Acute delta-(super)infection of hepatitis B carrier
J600100	Acute hepatitis - noninfective
A705200	Acute hepatitis E

J610.00	Alcoholic fatty liver
J617.00	Alcoholic hepatitis
J661400	Ascending cholangitis
J614111	Autoimmune chronic active hepatitis
J63B.00	Autoimmune hepatitis
J64..11	Bile duct calculus
PB6..12	Biliary anomalies
J616.00	Biliary cirrhosis
J616z00	Biliary cirrhosis NOS
J616200	Biliary cirrhosis of children
Q433200	Breast feeding inhibitors causing neonatal jaundice
J64..12	Calculus - biliary
J646.00	Calculus of bile duct with cholangitis
J661.00	Cholangitis
J661z00	Cholangitis NOS
J661500	Cholangitis lenta
J64..00	Cholelithiasis
J614100	Chronic active hepatitis
J617000	Chronic alcoholic hepatitis
J661100	Chronic cholangitis
J614.00	Chronic hepatitis
J614z00	Chronic hepatitis NOS
J614y00	Chronic hepatitis unspecified
J614400	Chronic lobular hepatitis
J614000	Chronic persistent hepatitis
A707.00	Chronic viral hepatitis

A707000	Chronic viral hepatitis B with delta-agent
A707100	Chronic viral hepatitis B without delta-agent
A707200	Chronic viral hepatitis C
A707X00	Chronic viral hepatitis, unspecified
AB31.11	Coccidiomycosis liver
Q409000	Congenital hepatitis A infection
Q409100	Congenital hepatitis B infection
Q409.00	Congenital viral hepatitis
Q409z00	Congenital viral hepatitis NOS
AB65300	Cryptococcosis liver
Q433100	Delayed conjugation causing neonatal jaundice + disease EC
Q433z00	Delayed conjugation causing neonatal jaundice NOS
Q433y00	Delayed conjugation causing neonatal jaundice OS
Q433000	Delayed conjugation causing neonatal jaundice, unspecified
J615300	Diffuse nodular cirrhosis
J....00	Digestive system diseases
Q436.00	Fetal and neonatal jaundice, unspecified
Q434100	Giant cell hepatitis causing neonatal jaundice
A98yy11	Gonococcal hepatitis
A98yy13	Gonococcal perihepatitis
J63X.00	Granulomatous hepatitis, not elsewhere classified
J631600	Hepatitis + adenovirus
2J23.00	Hepatitis A - current infection
43M2.00	Hepatitis A test positive
A70z000	Hepatitis C
J631000	Hepatitis in coxsackie virus

J631100	Hepatitis in cytomegalic inclusion virus
J632z00	Hepatitis in infectious diseases EC NOS
J631200	Hepatitis in infectious mononucleosis
J632100	Hepatitis in late syphilis
J632000	Hepatitis in malaria
J631300	Hepatitis in mumps
J632.00	Hepatitis in other infectious diseases EC
J631500	Hepatitis in other viral disease
J632200	Hepatitis in secondary syphilis
J632300	Hepatitis in toxoplasmosis
J631.00	Hepatitis in viral diseases EC
J631z00	Hepatitis in viral diseases EC NOS
J631400	Hepatitis in yellow fever
A705400	Hepatitis non A non B
J633.00	Hepatitis unspecified
J633z00	Hepatitis unspecified NOS
J61y200	Hepatosplenomegaly
AB4z600	Histoplasmosis liver
A701.11	Infective hepatitis
1675.11	Jaundice - symptom
J615800	Juvenile portal cirrhosis
J620.00	Liver abscess - excluding amoebic liver abscess
J62..00	Liver abscess and sequelae of chronic liver disease
J620100	Liver abscess due to cholangitis
PB6..00	Liver and biliary system anomalies
PB6..14	Liver anomalies

J6...00	Liver, biliary, pancreas + gastrointestinal diseases NEC
Q430000	Neonatal jaundice + glucose-6-phosphate dehydrogenase defic.
Q433y11	Neonatal jaundice - deficiency enzyme for bilirubin conjug.
Q433A00	Neonatal jaundice from breast milk inhibitor
Q433400	Neonatal jaundice with Crigler-Najjar syndrome
Q433500	Neonatal jaundice with Dubin-Johnson syndrome
Q433600	Neonatal jaundice with Gilbert's syndrome
Q433900	Neonatal jaundice with Rotor's syndrome
Q433700	Neonatal jaundice with congenital hypothyroidism
Q433800	Neonatal jaundice with porphyria
Q436200	Newborn physiological jaundice NOS
J61y100	Non-alcoholic fatty liver
J63y100	Nonspecific reactive hepatitis
65V3.00	Notification of inf. jaundice
2274.11	O/E - jaundiced
J661600	Obliterative cholangitis
J66y600	Obstructive jaundice NOS
J66..00	Other biliary tract disorders
J661y00	Other cholangitis
J63..00	Other liver disorders
Q433.00	Other neonatal jaundice - delayed conjugation other cause
J61y.00	Other non-alcoholic chronic liver disease
Q43..00	Other perinatal jaundice
Q409y00	Other specified congenital viral hepatitis
J63y.00	Other specified liver disorder

Qy...00	Other specified perinatal conditions
A705z00	Other specified viral hepatitis without mention of coma NOS
C350012	Pigmentary cirrhosis of liver
J615900	Pigmentary portal cirrhosis
J615A00	Pipe-stem portal cirrhosis
J616000	Primary biliary cirrhosis
J661200	Recurrent cholangitis
J614300	Recurrent hepatitis
J616100	Secondary biliary cirrhosis
J661800	Secondary sclerosing cholangitis
A916100	Secondary syphilitic hepatitis
AA00.11	Spirochaetal jaundice
J61y700	Steatosis of liver
J601100	Subacute hepatitis - noninfective
J601.00	Subacute necrosis of liver
J661300	Suppurative cholangitis
A953.00	Syphilis of liver
J615F00	Syphilitic portal cirrhosis
J633000	Toxic hepatitis
J635.00	Toxic liver disease
J635200	Toxic liver disease with acute hepatitis
J635000	Toxic liver disease with cholestasis
J635500	Toxic liver disease with chronic active hepatitis
J635400	Toxic liver disease with chronic lobular hepatitis
J635300	Toxic liver disease with chronic persistent hepatitis
J635600	Toxic liver disease with fibrosis and cirrhosis of liver

J615B00	Toxic portal cirrhosis
AD05.00	Toxoplasma hepatitis
A17y400	Tuberculosis of liver
J615000	Unilobular portal cirrhosis
Q436z00	Unspecified fetal or neonatal jaundice NOS
A70z.00	Unspecified viral hepatitis
A701.00	Viral (infectious) hepatitis A
A703.00	Viral (serum) hepatitis B
A70..00	Viral hepatitis
A705000	Viral hepatitis C without mention of hepatic coma
J615C00	Xanthomatous portal cirrhosis
J615G00	Zooparasitic portal cirrhosis
R024111	[D]Jaundice
R024.00	[D]Jaundice (not of newborn)
R024z00	[D]Jaundice (not of newborn) NOS
AyuB200	[X]Chronic viral hepatitis, unspecified
Jyu7.00	[X] Diseases of the liver
AyuG400	[X]Echinococcosis, unspecified, of liver
Jyu7700	[X]Granulomatous hepatitis, not elsewhere classified
Qyu5900	[X]Neonatal jaundice due/other specifd excessive haemolysis
Qyu5B00	[X]Neonatal jaundice from other specified causes
Qyu5A00	[X]Neonatal jaundice from other+unspcf hepatocellular damage
Jyu7100	[X]Other and unspecified cirrhosis of liver
AyuB100	[X]Other chronic viral hepatitis
AyuB000	[X]Other specified acute viral hepatitis

Jyu7300	[X]Other specified diseases of liver
Jyu7000	[X]Toxic liver disease with other disorders of liver
AyuB400	[X]Unspecified viral hepatitis without coma
AyuB.00	[X]Viral hepatitis

Moderate or severe liver disease Read codes

Read code	Description
7800.00	Transplantation of liver
7800000	Orthotopic transplantation of liver
7800100	Heterotopic transplantation of liver
7800y00	Other specified transplantation of liver
J622.11	Encephalopathy - hepatic
7800111	Auxillary liver transplant
7800112	Piggy back liver transplant
7800200	Replacement of previous liver transplant
7805211	Exploration of liver transplant
J60..00	Acute and subacute liver necrosis
J600.00	Acute necrosis of liver
J612.00	Alcoholic cirrhosis of liver
J612000	Alcoholic fibrosis and sclerosis of liver
J615D00	Bacterial portal cirrhosis
AB50300	Blastomycosis liver
J615600	Capsular portal cirrhosis
J615700	Cardiac portal cirrhosis
J615E00	Cardituberculous cirrhosis
J636.00	Central haemorrhagic necrosis of liver

J615811	Childhood function cirrhosis
J614200	Chronic aggressive hepatitis
J615.00	Cirrhosis - non alcoholic
J61..00	Cirrhosis and chronic liver disease
J615z13	Cirrhosis of liver NOS
J615711	Congestive cirrhosis
J615z12	Cryptogenic cirrhosis of liver
J612.11	Florid cirrhosis
C310400	Glycogenosis with hepatic cirrhosis
J615500	Hypertrophic portal cirrhosis
J615812	Indian childhood cirrhosis
J612.12	Laennec's cirrhosis
J615z14	Laennec's cirrhosis, non-alcoholic
J615z11	Macronodular cirrhosis of liver
J615200	Mixed portal cirrhosis
J615100	Multilobular portal cirrhosis
J615z00	Non-alcoholic cirrhosis NOS
G852300	Oesophageal varices in alcoholic cirrhosis of the liver
G852200	Oesophageal varices in cirrhosis of the liver
G852.00	Oesophageal varices in diseases EC
A704.00	Other specified viral hepatitis with coma
A704z00	Other specified viral hepatitis with hepatic coma NOS
J615.11	Portal cirrhosis
J615y00	Portal cirrhosis unspecified
J61y300	Portal fibrosis without cirrhosis
J615111	Postnecrotic cirrhosis of liver

J661700	Primary sclerosing cholangitis
J661900	Sclerosing cholangitis unspecified
A706.00	Unspecified viral hepatitis with coma
A700.00	Viral hepatitis A with coma
A702.00	Viral hepatitis B with coma
A704000	Viral hepatitis C with coma
AyuB300	[X]Unspecified viral hepatitis with coma

Chronic pulmonary disease Read codes

Read code	Description
H30..12	Recurrent wheezy bronchitis
H31..00	Chronic bronchitis
H312000	Chronic asthmatic bronchitis
H312011	Chronic wheezy bronchitis
H312100	Emphysematous bronchitis
H312200	Acute exacerbation of chronic obstructive airways disease
H312300	Bronchiolitis obliterans
H312z00	Obstructive chronic bronchitis NOS
H32..00	Emphysema
H320.00	Chronic bullous emphysema
H320000	Segmental bullous emphysema
H320100	Zonal bullous emphysema
H320200	Giant bullous emphysema
H320300	Bullous emphysema with collapse
H320z00	Chronic bullous emphysema NOS
H321.00	Panlobular emphysema

H322.00	Centrilobular emphysema
H32y.00	Other emphysema
H32y100	Atrophic (senile) emphysema
H32y200	MacLeod's unilateral emphysema
H32yz00	Other emphysema NOS
H32z.00	Emphysema NOS
H33..00	Asthma
H33..11	Bronchial asthma
H34..00	Bronchiectasis
H35..00	Extrinsic allergic alveolitis
H35y.00	Other allergic alveolitis
H35yz00	Other allergic alveolitis NOS
H35z.00	Allergic alveolitis and pneumonitis NOS
H35z000	Allergic extrinsic alveolitis NOS
H35zz00	Allergic alveolitis and pneumonitis NOS
H36..00	Mild chronic obstructive pulmonary disease
H37..00	Moderate chronic obstructive pulmonary disease
H38..00	Severe chronic obstructive pulmonary disease
H3y..00	Other specified chronic obstructive airways disease
H3y..11	Other specified chronic obstructive pulmonary disease
H3z..00	Chronic obstructive airways disease NOS
H3z..11	Chronic obstructive pulmonary disease NOS
H464000	Chronic emphysema due to chemical fumes
H464100	Obliterative bronchiolitis due to chemical fumes
H464200	Chronic pulmonary fibrosis due to chemical fumes
H464z00	Chronic respiratory conditions due to chemical fumes NOS

H563.00	Idiopathic fibrosing alveolitis
H563.12	Cryptogenic fibrosing alveolitis
H563z00	Idiopathic fibrosing alveolitis NOS
H58y.00	Other lung disease NEC
H58z.00	Lung disease NOS
Hyu3000	[X]Other emphysema
Hyu3100	[X]Other specified chronic obstructive pulmonary disease

Lymphoma Read codes

Read code	Description
4M20.00	Lymphoma stage I
4M21.00	Lymphoma stage II
4M22.00	Lymphoma stage III
4M23.00	Lymphoma stage IV
A789600	HIV disease resulting in Burkitt's lymphoma
A789700	HIV dis resulting oth types of non-Hodgkin's lymphoma
AyuC600	[X]HIV disease resulting in other non-Hodgkin's lymphoma
B601.00	Lymphosarcoma
B602.00	Burkitt's lymphoma
B602000	Burkitt's lymphoma of unspecified site
B602100	Burkitt's lymphoma of lymph nodes of head, face and neck
B602200	Burkitt's lymphoma of intrathoracic lymph nodes
B602300	Burkitt's lymphoma of intra-abdominal lymph nodes
B602400	Burkitt's lymphoma of lymph nodes of axilla and upper limb

B602500	Burkitt's lymphoma of lymph nodes of inguinal region and leg
B602600	Burkitt's lymphoma of intrapelvic lymph nodes
B602700	Burkitt's lymphoma of spleen
B602800	Burkitt's lymphoma of lymph nodes of multiple sites
B602z00	Burkitt's lymphoma NOS
B60y.00	Other specified reticulosarcoma or lymphosarcoma
B60z.00	Reticulosarcoma or lymphosarcoma NOS
B620.00	Nodular lymphoma (Brill - Symmers disease)
B620.11	Reticulosarcoma - follicular or nodular
B620000	Nodular lymphoma of unspecified site
B620100	Nodular lymphoma of lymph nodes of head, face and neck
B620200	Nodular lymphoma of intrathoracic lymph nodes
B620300	Nodular lymphoma of intra-abdominal lymph nodes
B620400	Nodular lymphoma of lymph nodes of axilla and upper limb
B620500	Nodular lymphoma of lymph nodes of inguinal region and leg
B620600	Nodular lymphoma of intrapelvic lymph nodes
B620700	Nodular lymphoma of spleen
B620800	Nodular lymphoma of lymph nodes of multiple sites
B620z00	Nodular lymphoma NOS
B621.00	Mycosis fungoides
B622.00	Sezary's disease
B623.00	Malignant histiocytosis
B623000	Malignant histiocytosis of unspecified site

B623100	Malignant histiocytosis of lymph nodes head, face and neck
B623200	Malignant histiocytosis of intrathoracic lymph nodes
B623300	Malignant histiocytosis of intra-abdominal lymph nodes
B623400	Malignant histiocytosis of lymph nodes of axilla and arm
B623500	Malignant histiocytosis of lymph nodes inguinal and leg
B623600	Malignant histiocytosis of intrapelvic lymph nodes
B623700	Malignant histiocytosis of spleen
B623800	Malignant histiocytosis of lymph nodes of multiple sites
B623z00	Malignant histiocytosis NOS
B625.00	Letterer-Siwe disease
B625.11	Histiocytosis X (acute, progressive)
B626.00	Malignant mast cell tumours
B626000	Mast cell malignancy of unspecified site
B626100	Mast cell malignancy of lymph nodes of head, face and neck
B626200	Mast cell malignancy of intrathoracic lymph nodes
B626300	Mast cell malignancy of intra-abdominal lymph nodes
B626400	Mast cell malignancy of lymph nodes of axilla and upper limb
B626500	Mast cell malignancy of lymph nodes inguinal region and leg
B626600	Mast cell malignancy of intrapelvic lymph nodes
B626700	Mast cell malignancy of spleen
B626800	Mast cell malignancy of lymph nodes of multiple sites
B626z00	Malignant mast cell tumour NOS
B627.00	Non - Hodgkin's lymphoma

B627000	Follicular non-Hodgkin's small cleaved cell lymphoma
B627100	Follicular non-Hodg mixed sml cleavd & lge cell lymphoma
B627200	Follicular non-Hodgkin's large cell lymphoma
B627300	Diffuse non-Hodgkin's small cell (diffuse) lymphoma
B627400	Diffuse non-Hodgkin's small cleaved cell (diffuse) lymphoma
B627500	Diffuse non-Hodgkin mixed sml & lge cell (diffuse) lymphoma
B627600	Diffuse non-Hodgkin's immunoblastic (diffuse) lymphoma
B627700	Diffuse non-Hodgkin's lymphoblastic (diffuse) lymphoma
B627800	Diffuse non-Hodgkin's lymphoma undifferentiated (diffuse)
B627B00	Other types of follicular non-Hodgkin's lymphoma
B627C00	Follicular non-Hodgkin's lymphoma
B627C11	Follicular lymphoma NOS
B627D00	Diffuse non-Hodgkin's centroblastic lymphoma
B627W00	Unspecified B-cell non-Hodgkin's lymphoma
B627X00	Diffuse non-Hodgkin's lymphoma, unspecified
B62x.00	Malignant lymphoma otherwise specified
B62x000	T-zone lymphoma
B62x100	Lymphoepithelioid lymphoma
B62x200	Peripheral T-cell lymphoma
B62x300	Malignant reticuloendotheliosis
B62x400	Malignant reticulosis
B62x600	True histiocytic lymphoma
B62xX00	Oth and unspecif peripheral & cutaneous T-cell lymphomas

B62y.00	Malignant lymphoma NOS
B62y000	Malignant lymphoma NOS of unspecified site
B62y100	Malignant lymphoma NOS of lymph nodes of head, face and neck
B62y200	Malignant lymphoma NOS of intrathoracic lymph nodes
B62y300	Malignant lymphoma NOS of intra-abdominal lymph nodes
B62y400	Malignant lymphoma NOS of lymph nodes of axilla and arm
B62y500	Malignant lymphoma NOS of lymph node inguinal region and leg
B62y600	Malignant lymphoma NOS of intrapelvic lymph nodes
B62y700	Malignant lymphoma NOS of spleen
B62y800	Malignant lymphoma NOS of lymph nodes of multiple sites
B62yz00	Malignant lymphoma NOS
B62z.00	Malignant neoplasms of lymphoid and histiocytic tissue NOS
B653000	Chloroma
B935.00	Neoplasm of uncertain behaviour of histiocytic and mast cell
B935.11	Histiocytic tumour NOS
B935.12	Mastocytoma NOS
B936.00	Neoplasm of uncertain behaviour of plasma cells
B937.00	Neop uncertain behaviour other lymphatic/haematopoietic tiss
BBB1.00	[M]Adenolymphoma
BBU..00	[M]Lymphatic vessel tumours
BBU..11	[M]Lymphangiomatous tumours

BBg..00	[M]Lymphomas, NOS or diffuse
BBg0.00	[M]Lymphomatous tumour, benign
BBg1.00	[M]Malignant lymphoma NOS
BBg1.11	[M]Lymphoma NOS
BBg1000	[M]Malignant lymphoma, diffuse NOS
BBg2.00	[M]Malignant lymphoma, non Hodgkin's type
BBg2.11	[M]Non Hodgkins lymphoma
BBg3.00	[M]Malignant lymphoma, undifferentiated cell type NOS
BBg4.00	[M]Malignant lymphoma, stem cell type
BBg5.00	[M]Malignant lymphoma, convoluted cell type NOS
BBg6.00	[M]Lymphosarcoma NOS
BBg7.00	[M]Malignant lymphoma, lymphoplasmacytoid type
BBg8.00	[M]Malignant lymphoma, immunoblastic type
BBg9.00	[M]Malignant lymphoma, mixed lymphocytic-histiocytic NOS
BBgA.00	[M]Malignant lymphoma, centroblastic-centrocytic, diffuse
BBgA.11	[M]Germinoblastoma, diffuse
BBgB.00	[M]Malignant lymphoma, follicular centre cell NOS
BBgC.00	[M]Malignant lymphoma, lymphocytic, well differentiated NOS
BBgC.11	[M]Lymphocytic lymphoma NOS
BBgC.12	[M]Lymphocytic lymphosarcoma NOS
BBgD.00	[M]Malig lymphoma, lymphocytic, intermediate different NOS
BBgE.00	[M]Malignant lymphoma, centrocytic

BBgF.00	[M]Malignant lymphoma, follicular centre cell, cleaved NOS
BBgG.00	[M]Malignant lymphoma, lymphocytic, poorly different NOS
BBgG.11	[M]Lymphoblastic lymphosarcoma NOS
BBgG.12	[M]Lymphoblastic lymphoma NOS
BBgG.13	[M]Lymphoblastoma NOS
BBgH.00	[M]Prolymphocytic lymphosarcoma
BBgJ.00	[M] Malignant lymphoma, centroblastic type NOS
BBgJ.11	[M] Germinoblastic sarcoma NOS
BBgK.00	[M]Malig lymphoma, follicular centre cell, non-cleaved NOS
BBgL.00	[M] Malignant lymphoma, small lymphocytic NOS
BBgM.00	[M]Malignant lymphoma, small cleaved cell, diffuse
BBgN.00	[M]Malign lymphoma,lymphocytic,intermediate differn, diffuse
BBgP.00	[M]Malignant lymphoma, mixed small and large cell, diffuse
BBgQ.00	[M]Malignant lymphomatous polyposis
BBgR.00	[M]Malignant lymphoma, large cell, diffuse NOS
BBgS.00	[M]Malignant lymphoma, large cell, cleaved, diffuse
BBgT.00	[M]Malignant lymphoma, large cell, noncleaved, diffuse
BBgV.00	[M]Malignant lymphoma, small cell, noncleaved, diffuse
BBgz.00	[M]Lymphoma, diffuse or NOS
BBh..00	[M] Reticulosarcomas
BBj..00	[M] Hodgkin's disease
BBk..00	[M] Lymphomas, nodular or follicular

BBk0.00	[M]Malignant lymphoma, nodular NOS
BBk0.11	[M]Brill - Symmers' disease
BBk0.12	[M]Follicular lymphosarcoma NOS
BBk0.13	[M]Giant follicular lymphoma
BBk0.14	[M]Nodular lymphosarcoma NOS
BBk1.00	[M]Malig lymphoma, mixed lymphocytic-histiocytic, nodular
BBk1.11	[M]Reticulolymphosarcoma, follicular
BBk1.12	[M]Reticulolymphosarcoma, nodular
BBk2.00	[M]Malignant lymphoma, centroblastic-centrocytic, follicular
BBk2.11	[M]Germinoblastoma, follicular
BBk3.00	[M]Malig lymphoma, lymphocytic, well differentiated,nodular
BBk4.00	[M]Malig lymp, lymphocytic, intermediate different, nodular
BBk5.00	[M]Malig lymp, follicular centre cell, cleaved, follicular
BBk6.00	[M]Malig lymp, lymphocytic, poorly differentiated, nodular
BBk7.00	[M]Malignant lymphoma, centroblastic type, follicular
BBk7.11	[M]Germinoblastic sarcoma, follicular
BBk8.00	[M]Malig lymp,follicular centre cell,noncleaved,follicular
BBkz.00	[M] Lymphoma, nodular or follicular NOS
BBl..00	[M] Mycosis fungoides
BBm..00	[M]Miscellaneous reticuloendothelial neoplasms
BBm4.00	[M]True histiocytic lymphoma
BBm5.00	[M] Peripheral T-cell lymphoma NOS

BBm9.00	[M] Monocytoid B-cell lymphoma
BBmD.00	[M] Cutaneous lymphoma
BBmH.00	[M] Large cell lymphoma
BBmK.00	[M]Waldenstrom's macroglobulinaemia
BBmz.00	[M]Miscellaneous reticuloendothelial neoplasm NOS
BBq..00	[M] Burkitt's tumours
BBq0.00	[M]Burkitt's tumour
BBqz.00	[M]Burkitt's tumour NOS
BBr..00	[M] Leukaemias
BBr2z00	[M]Other lymphoid leukaemia NOS
BBrA311	[M]Chloroma
BBs..00	[M] Misc myeloproliferative and lymphoproliferative disorders
BBv0.00	[M]Monocytoid B-cell lymphoma
BBv2.00	[M]AngiocentricT-cell lymphoma
ByuD000	[X]Other Hodgkin's disease
ByuD100	[X]Other types of follicular non-Hodgkin's lymphoma
ByuD200	[X]Other types of diffuse non-Hodgkin's lymphoma
ByuD300	[X]Other specified types of non-Hodgkin's lymphoma
ByuD400	[X]Other malignant immunoproliferative diseases
ByuDA00	[X]Oth spcf mal neoplsm/lymphoid,haematopoietic+rltd tissue
ByuDB00	[X]Mal neoplasm/lymphoid,haematopoietic+related tissu,unspcf
ByuDC00	[X]Diffuse non-Hodgkin's lymphoma, unspecified
ByuDD00	[X]Oth and unspecif peripheral & cutaneous T-cell lymphomas

ByuDE00	[X]Unspecified B-cell non-Hodgkin's lymphoma
ByuDF00	[X]Non-Hodgkin's lymphoma, unspecified type
ByuDF11	[X]Non-Hodgkin's lymphoma NOS

Metastatic solid tumour Read codes

Read code	Description
1D18.00	Pain from metastases
B153.00	Secondary malignant neoplasm of liver
B56..00	Secondary and unspecified malignant neoplasm of lymph nodes
B56..11	Lymph node metastases
B560.00	Secondary and unspec malig neop lymph nodes head/face/neck
B560000	Secondary and unspec malig neop of superficial parotid LN
B560100	Secondary and unspec malignant neoplasm mastoid lymph nodes
B560200	Secondary and unspec malig neop superficial cervical LN
B560300	Secondary and unspec malignant neoplasm occipital lymph node
B560400	Secondary and unspec malig neop deep parotid lymph nodes
B560500	Secondary and unspec malig neop submandibular lymph nodes
B560600	Secondary and unspec malig neop of facial lymph nodes
B560700	Secondary and unspec malig neop submental lymph nodes
B560800	Secondary and unspec malig neop anterior cervical LN
B560900	Secondary and unspec malig neop deep cervical LN

B560z00	Secondary unspec malig neop lymph nodes head/face/neck NOS
B561.00	Secondary and unspec malig neop intrathoracic lymph nodes
B561000	Secondary and unspec malig neop internal mammary lymph nodes
B561100	Secondary and unspec malig neop intercostal lymph nodes
B561200	Secondary and unspec malig neop diaphragmatic lymph nodes
B561300	Secondary and unspec malig neop ant mediastinal lymph nodes
B561400	Secondary and unspec malig neop post mediastinal lymph nodes
B561500	Secondary and unspec malig neop paratracheal lymph nodes
B561600	Secondary and unspec malig neop superfic tracheobronchial LN
B561700	Secondary and unspec malig neop inferior tracheobronchial LN
B561800	Secondary and unspec malig neop bronchopulmonary lymph nodes
B561900	Secondary and unspec malig neop pulmonary lymph nodes
B561z00	Secondary and unspec malig neop intrathoracic LN NOS
B562.00	Secondary and unspec malig neop intra-abdominal lymph nodes
B562000	Secondary and unspec malig neop coeliac lymph nodes
B562100	Secondary and unspec malig neop superficial mesenteric LN
B562200	Secondary and unspec malig neop inferior mesenteric LN
B562300	Secondary and unspec malig neop common iliac lymph nodes
B562400	Secondary and unspec malig neop external iliac lymph nodes
B562z00	Secondary and unspec malig neop intra-abdominal LN NOS

B563.00	Secondary and unspec malig neop axilla and upper limb LN
B563000	Secondary and unspec malig neop axillary lymph nodes
B563100	Secondary and unspec malig neop supratrochlear lymph nodes
B563200	Secondary and unspec malig neop infraclavicular lymph nodes
B563300	Secondary and unspec malig neop pectoral lymph nodes
B563z00	Secondary and unspec malig neop axilla and upper limb LN NOS
B564.00	Secondary and unspec malig neop inguinal and lower limb LN
B564000	Secondary and unspec malig neop superficial inguinal LN
B564100	Secondary and unspec malig neop deep inguinal lymph nodes
B564200	Secondary and unspec malig neop popliteal lymph nodes
B564z00	Secondary and unspec malig neop of inguinal and leg LN NOS
B565.00	Secondary and unspec malig neop intrapelvic lymph nodes
B565000	Secondary and unspec malig neop internal iliac lymph nodes
B565100	Secondary and unspec malig neop inferior epigastric LN
B565200	Secondary and unspec malig neop circumflex iliac LN
B565300	Secondary and unspec malig neop sacral lymph nodes
B565400	Secondary and unspec malig neop obturator lymph nodes
B565z00	Secondary and unspec malig neop intrapelvic LN NOS
B56y.00	Secondary and unspec malig neop lymph nodes multiple sites
B56z.00	Secondary and unspec malig neop lymph nodes NOS
B57..00	Secondary malig neop of respiratory and digestive systems
B57..11	Metastases of respiratory and/or digestive systems
B57..12	Secondary carcinoma of respiratory and/or digestive systems
B570.00	Secondary malignant neoplasm of lung

B571.00	Secondary malignant neoplasm of mediastinum
B572.00	Secondary malignant neoplasm of pleura
B573.00	Secondary malignant neoplasm of other respiratory organs
B574.00	Secondary malignant neoplasm of small intestine and duodenum
B574000	Secondary malignant neoplasm of duodenum
B574100	Secondary malignant neoplasm of jejunum
B574200	Secondary malignant neoplasm of ileum
B574z00	Secondary malig neop of small intestine or duodenum NOS
B575.00	Secondary malignant neoplasm of large intestine and rectum
B575000	Secondary malignant neoplasm of colon
B575100	Secondary malignant neoplasm of rectum
B575z00	Secondary malig neop of large intestine or rectum NOS
B576.00	Secondary malig neop of retroperitoneum and peritoneum
B576000	Secondary malignant neoplasm of retroperitoneum
B576100	Secondary malignant neoplasm of peritoneum
B576z00	Secondary malig neop of retroperitoneum or peritoneum NOS
B577.00	Secondary malignant neoplasm of liver
B577.11	Liver metastases
B57y.00	Secondary malignant neoplasm of other digestive organ
B57z.00	Secondary malig neop of respiratory or digestive system NOS
B58..00	Secondary malignant neoplasm of other specified sites
B58..11	Secondary carcinoma of other specified sites
B580.00	Secondary malignant neoplasm of kidney
B581.00	Secondary malignant neoplasm of other urinary organs

B581000	Secondary malignant neoplasm of ureter
B581100	Secondary malignant neoplasm of bladder
B581200	Secondary malignant neoplasm of urethra
B581z00	Secondary malignant neoplasm of other urinary organ NOS
B582.00	Secondary malignant neoplasm of skin
B582000	Secondary malignant neoplasm of skin of head
B582100	Secondary malignant neoplasm of skin of face
B582200	Secondary malignant neoplasm of skin of neck
B582300	Secondary malignant neoplasm of skin of trunk
B582400	Secondary malignant neoplasm of skin of shoulder and arm
B582500	Secondary malignant neoplasm of skin of hip and leg
B582600	Secondary malignant neoplasm of skin of breast
B582z00	Secondary malignant neoplasm of skin NOS
B583.00	Secondary malignant neoplasm of brain and spinal cord
B583000	Secondary malignant neoplasm of brain
B583100	Secondary malignant neoplasm of spinal cord
B583200	Cerebral metastasis
B583z00	Secondary malignant neoplasm of brain or spinal cord NOS
B584.00	Secondary malignant neoplasm of other part of nervous system
B585.00	Secondary malignant neoplasm of bone and bone marrow
B585000	Pathological fracture due to metastatic bone disease
B586.00	Secondary malignant neoplasm of ovary
B587.00	Secondary malignant neoplasm of adrenal gland
B58y.00	Secondary malignant neoplasm of other specified sites
B58y000	Secondary malignant neoplasm of breast

B58y100	Secondary malignant neoplasm of uterus
B58y200	Secondary malignant neoplasm of cervix uteri
B58y211	Secondary cancer of the cervix
B58y300	Secondary malignant neoplasm of vagina
B58y400	Secondary malignant neoplasm of vulva
B58y411	Secondary cancer of the vulva
B58y500	Secondary malignant neoplasm of prostate
B58y600	Secondary malignant neoplasm of testis
B58y700	Secondary malignant neoplasm of penis
B58y800	Secondary malignant neoplasm of epididymis and vas deferens
B58y900	Secondary malignant neoplasm of tongue
B58yz00	Secondary malignant neoplasm of other specified site NOS
B58z.00	Secondary malignant neoplasm of other specified site NOS
B594.00	Secondary malignant neoplasm of unknown site
BB03.00	[M]Neoplasm, metastatic
BB03.11	[M]Secondary neoplasm
BB04.00	[M]Neoplasm, malig, uncertain whether primary or metastatic
BB13.00	[M]Carcinoma, metastatic, NOS
BB13.11	[M]Secondary carcinoma
BB2B.00	[M]Squamous cell carcinoma, metastatic NOS
BB53.00	[M]Adenocarcinoma, metastatic, NOS
BB85100	[M]Metastatic signet ring cell carcinoma
BBy2.00	[M]No microscopic confirmation tumour, clinically metastatic
ByuC.00	[X]Malignant neoplasm of ill-defined, secondary and unspeci

ByuC300	[X]Secondary malignant neoplasm/oth+unspc respiratory organs
ByuC400	[X]Secondary malignant neoplasm/oth+unspcfd digestive organs
ByuC700	[X]Secondary malignant neoplasm of other specified sites

Myocardial infarction Read codes

Read code	Description
14A3.00	H/O: myocardial infarct <60
14A4.00	H/O: myocardial infarct >60
14A5.00	H/O: angina pectoris
14AA.00	H/O: heart disease NOS
14AH.00	H/O: Myocardial infarction in last year
14AJ.00	H/O: Angina in last year
322..00	ECG: myocardial ischaemia
3222.00	ECG:shows myocardial ischaemia
322Z.00	ECG: myocardial ischaemia NOS
323..00	ECG: myocardial infarction
3232.00	ECG: old myocardial infarction
3233.00	ECG: antero-septal infarct.
3234.00	ECG:posterior/inferior infarct
3235.00	ECG: subendocardial infarct
3236.00	ECG: lateral infarction
323Z.00	ECG: myocardial infarct NOS
G30..00	Acute myocardial infarction

G30..11	Attack - heart
G30..12	Coronary thrombosis
G30..13	Cardiac rupture following myocardial infarction (MI)
G30..14	Heart attack
G30..15	MI - acute myocardial infarction
G30..16	Thrombosis - coronary
G30..17	Silent myocardial infarction
G300.00	Acute anterolateral infarction
G301.00	Other specified anterior myocardial infarction
G301000	Acute anteroapical infarction
G301100	Acute anteroseptal infarction
G301z00	Anterior myocardial infarction NOS
G302.00	Acute inferolateral infarction
G303.00	Acute inferoposterior infarction
G304.00	Posterior myocardial infarction NOS
G305.00	Lateral myocardial infarction NOS
G306.00	True posterior myocardial infarction
G307.00	Acute subendocardial infarction
G307000	Acute non-Q wave infarction
G307100	Acute non-ST segment elevation myocardial infarction
G308.00	Inferior myocardial infarction NOS
G309.00	Acute Q-wave infarct
G30A.00	Mural thrombosis
G30B.00	Acute posterolateral myocardial infarction
G30X.00	Acute transmural myocardial infarction of unspecif site
G30X000	Acute ST segment elevation myocardial infarction

G30y.00	Other acute myocardial infarction
G30y000	Acute atrial infarction
G30y100	Acute papillary muscle infarction
G30y200	Acute septal infarction
G30yz00	Other acute myocardial infarction NOS
G30z.00	Acute myocardial infarction NOS
G31..00	Other acute and subacute ischaemic heart disease
G310.00	Postmyocardial infarction syndrome
G310.11	Dressler's syndrome
G311.12	Impending infarction
G311500	Acute coronary syndrome
G311z00	Preinfarction syndrome NOS
G31y.00	Other acute and subacute ischaemic heart disease
G31y000	Acute coronary insufficiency
G31y100	Microinfarction of heart
G31y200	Subendocardial ischaemia
G31y300	Transient myocardial ischaemia
G31yz00	Other acute and subacute ischaemic heart disease NOS
G32..00	Old myocardial infarction
G32..11	Healed myocardial infarction
G32..12	Personal history of myocardial infarction
G33z100	Stenocardia
G33z400	Ischaemic chest pain
G33z500	Post infarct angina
G340.12	Coronary artery disease
G341.00	Aneurysm of heart

G342.00	Atherosclerotic cardiovascular disease
G343.00	Ischaemic cardiomyopathy
G344.00	Silent myocardial ischaemia
G34y.00	Other specified chronic ischaemic heart disease
G34y000	Chronic coronary insufficiency
G34y100	Chronic myocardial ischaemia
G34yz00	Other specified chronic ischaemic heart disease NOS
G34z.00	Other chronic ischaemic heart disease NOS
G35..00	Subsequent myocardial infarction
G350.00	Subsequent myocardial infarction of anterior wall
G351.00	Subsequent myocardial infarction of inferior wall
G353.00	Subsequent myocardial infarction of other sites
G35X.00	Subsequent myocardial infarction of unspecified site
G36..00	Certain current complication follow acute myocardial infarct
G360.00	Haemopericardium/current comp folow acut myocard infarct
G361.00	Atrial septal defect/curr comp folow acut myocardal infarct
G362.00	Ventric septal defect/curr comp fol acut myocardal infarctn
G363.00	Ruptur cardiac wall w'out haemopericard/cur comp fol ac MI
G364.00	Ruptur chordae tendinae/curr comp fol acute myocard infarct
G365.00	Rupture papillary muscle/curr comp fol acute myocard infarct
G366.00	Thrombosis atrium,auric append&vent/curr comp foll acute MI
G38..00	Postoperative myocardial infarction
G380.00	Postoperative transmural myocardial infarction anterior wall
G381.00	Postoperative transmural myocardial infarction inferior wall
G382.00	Postoperative transmural myocardial infarction other sites
G383.00	Postoperative transmural myocardial infarction unspec site

G384.00	Postoperative subendocardial myocardial infarction
G38z.00	Postoperative myocardial infarction, unspecified
G501.00	Post infarction pericarditis
G5y6.00	Rupture of papillary muscle
Gyu3100	[X]Other current complicatns following acute myocard infarct
Gyu3400	[X]Acute transmural myocardial infarction of unspecif site
Gyu3500	[X]Subsequent myocardial infarction of other sites
Gyu3600	[X]Subsequent myocardial infarction of unspecified site

Ulcer disease Read codes

Read code	Description
1956.00	Peptic ulcer symptoms
J1...00	Oesophageal, stomach and duodenal diseases
J1...11	Duodenal diseases
J101600	Ulcerative oesophagitis
J102.00	Ulcer of oesophagus
J102000	Peptic ulcer of oesophagus
J102200	Oesophageal ulcer due to aspirin
J102300	Oesophageal ulcer due to chemicals
J102400	Oesophageal ulcer due to medicines
J102500	Barrett's ulcer of oesophagus
J102z00	Ulcer of oesophagus NOS
J11..00	Gastric ulcer - (GU)
J11..11	Prepyloric ulcer
J11..12	Pyloric ulcer
J110.00	Acute gastric ulcer

J110000	Acute gastric ulcer without mention of complication
J110100	Acute gastric ulcer with haemorrhage
J110111	Bleeding acute gastric ulcer
J110200	Acute gastric ulcer with perforation
J110300	Acute gastric ulcer with haemorrhage and perforation
J110400	Acute gastric ulcer with obstruction
J110y00	Acute gastric ulcer unspecified
J110z00	Acute gastric ulcer NOS
J111.00	Chronic gastric ulcer
J111000	Chronic gastric ulcer without mention of complication
J111100	Chronic gastric ulcer with haemorrhage
J111111	Bleeding chronic gastric ulcer
J111200	Chronic gastric ulcer with perforation
J111211	Perforated chronic gastric ulcer
J111300	Chronic gastric ulcer with haemorrhage and perforation
J111400	Chronic gastric ulcer with obstruction
J111y00	Chronic gastric ulcer unspecified
J111z00	Chronic gastric ulcer NOS
J11y.00	Unspecified gastric ulcer
J11y000	Unspecified gastric ulcer without mention of complication
J11y100	Unspecified gastric ulcer with haemorrhage
J11y200	Unspecified gastric ulcer with perforation
J11y300	Unspecified gastric ulcer with haemorrhage and perforation
J11y400	Unspecified gastric ulcer with obstruction
J11yy00	Unspec gastric ulcer; unspec haemorrhage and/or perforation

J11yz00	Unspecified gastric ulcer NOS
J11z.00	Gastric ulcer NOS
J11z.12	Multiple gastric ulcers
J12..00	Duodenal ulcer - (DU)
J120.00	Acute duodenal ulcer
J120000	Acute duodenal ulcer without mention of complication
J120100	Acute duodenal ulcer with haemorrhage
J120200	Acute duodenal ulcer with perforation
J120300	Acute duodenal ulcer with haemorrhage and perforation
J120400	Acute duodenal ulcer with obstruction
J120y00	Acute duodenal ulcer unspecified
J120z00	Acute duodenal ulcer NOS
J121.00	Chronic duodenal ulcer
J121000	Chronic duodenal ulcer without mention of complication
J121100	Chronic duodenal ulcer with haemorrhage
J121111	Bleeding chronic duodenal ulcer
J121200	Chronic duodenal ulcer with perforation
J121211	Perforated chronic duodenal ulcer
J121300	Chronic duodenal ulcer with haemorrhage and perforation
J121400	Chronic duodenal ulcer with obstruction
J121y00	Chronic duodenal ulcer unspecified
J121z00	Chronic duodenal ulcer NOS
J122.00	Duodenal ulcer disease
J124.00	Recurrent duodenal ulcer
J12y.00	Unspecified duodenal ulcer
J12y000	Unspecified duodenal ulcer without mention of complication

J12y100	Unspecified duodenal ulcer with haemorrhage
J12y200	Unspecified duodenal ulcer with perforation
J12y300	Unspecified duodenal ulcer with haemorrhage and perforation
J12y400	Unspecified duodenal ulcer with obstruction
J12yy00	Unspec duodenal ulcer; unspec haemorrhage and/or perforation
J12yz00	Unspecified duodenal ulcer NOS
J12z.00	Duodenal ulcer NOS
J13..00	Peptic ulcer - (PU) site unspecified
J13..11	Stress ulcer NOS
J130.00	Acute peptic ulcer
J130000	Acute peptic ulcer without mention of complication
J130100	Acute peptic ulcer with haemorrhage
J130200	Acute peptic ulcer with perforation
J130300	Acute peptic ulcer with haemorrhage and perforation
J130400	Acute peptic ulcer with obstruction
J130y00	Acute peptic ulcer unspecified
J130z00	Acute peptic ulcer NOS
J131.00	Chronic peptic ulcer
J131000	Chronic peptic ulcer without mention of complication
J131100	Chronic peptic ulcer with haemorrhage
J131200	Chronic peptic ulcer with perforation
J131300	Chronic peptic ulcer with haemorrhage and perforation
J131400	Chronic peptic ulcer with obstruction
J131y00	Chronic peptic ulcer unspecified

J131z00	Chronic peptic ulcer NOS
J13y.00	Unspecified peptic ulcer
J13y000	Unspecified peptic ulcer without mention of complication
J13y100	Unspecified peptic ulcer with haemorrhage
J13y200	Unspecified peptic ulcer with perforation
J13y300	Unspecified peptic ulcer with haemorrhage and perforation
J13y400	Unspecified peptic ulcer with obstruction
J13yy00	Unspec peptic ulcer; unspec haemorrhage and/or perforation
J13yz00	Unspecified peptic ulcer NOS
J13z.00	Peptic ulcer NOS
J14..00	Gastrojejunal ulcer (GJU)
J14..12	Gastrocolic ulcer
J14..13	Jejunal ulcer
J14..14	Marginal ulcer
J14..15	Stomal ulcer
J140.00	Acute gastrojejunal ulcer
J140000	Acute gastrojejunal ulcer without mention of complication
J140100	Acute gastrojejunal ulcer with haemorrhage
J140200	Acute gastrojejunal ulcer with perforation
J140300	Acute gastrojejunal ulcer with haemorrhage and perforation
J140400	Acute gastrojejunal ulcer with obstruction
J140y00	Acute gastrojejunal ulcer unspecified
J140z00	Acute gastrojejunal ulcer NOS
J141.00	Chronic gastrojejunal ulcer
J141000	Chronic gastrojejunal ulcer without mention of complication
J141100	Chronic gastrojejunal ulcer with haemorrhage

J141200	Chronic gastrojejunal ulcer with perforation
J141300	Chronic gastrojejunal ulcer with haemorrhage and perforation
J141400	Chronic gastrojejunal ulcer with obstruction
J141y00	Chronic gastrojejunal ulcer unspecified
J141z00	Chronic gastrojejunal ulcer NOS
J14y.00	Unspecified gastrojejunal ulcer
J14y000	Unspecified gastrojejunal ulcer without mention complication
J14y100	Unspecified gastrojejunal ulcer with haemorrhage
J14y200	Unspecified gastrojejunal ulcer with perforation
J14y300	Unspec gastrojejunal ulcer with haemorrhage and perforation
J14y400	Unspecified gastrojejunal ulcer with obstruction
J14yy00	Unspec gastrojejunal ulcer; unspec haemorrhage/perforation
J14yz00	Unspecified gastrojejunal ulcer NOS
J14z.00	Gastrojejunal ulcer NOS
J17..00	Other stomach and duodenal disorders
J17y.00	Other stomach and duodenal disorders
J57y800	Primary ulcer of intestine
J57y900	Ulceration of colon
J57yA00	Ulceration of intestine NOS

Peripheral vascular disease Read codes

Read code	Description
C107.00	Diabetes mellitus with peripheral circulatory disorder
C107000	Diabetes mellitus, juvenile +peripheral circulatory disorder

C107100	Diabetes mellitus, adult, + peripheral circulatory disorder
C107300	IDDM with peripheral circulatory disorder
C107400	NIDDM with peripheral circulatory disorder
C107z00	Diabetes mellitus NOS with peripheral circulatory disorder
C108G00	Insulin dependent diab mell with peripheral angiopathy
C108G11	Type I diabetes mellitus with peripheral angiopathy
C108G12	Type 1 diabetes mellitus with peripheral angiopathy
C109F00	Non-insulin-dependent d m with peripheral angiopath
C109F11	Type II diabetes mellitus with peripheral angiopathy
C109F12	Type 2 diabetes mellitus with peripheral angiopathy
C10EG00	Type 1 diabetes mellitus with peripheral angiopathy
C10EG11	Type I diabetes mellitus with peripheral angiopathy
C10EG12	Insulin dependent diab mell with peripheral angiopathy
C10FF00	Type 2 diabetes mellitus with peripheral angiopathy
C10FF11	Type II diabetes mellitus with peripheral angiopathy
G42y000	Pulmonary arteritis
G42y100	Pulmonary vessel rupture
G42y200	Pulmonary vessel stricture
G42yz00	Other specified pulmonary circulation disease NOS
G5y2.00	Cardiovascular arteriosclerosis unspecified
G70..11	Arteriosclerosis
G700.11	Aorto-iliac disease
G701.00	Renal artery atherosclerosis
G702.00	Extremity artery atheroma
G702000	Monckeberg's medial sclerosis
G70y.00	Other specified artery atheroma

G70y000	Carotid artery atherosclerosis
G70z.00	Arteriosclerotic vascular disease NOS
G72..00	Other aneurysm
G73..00	Other peripheral vascular disease
G73..11	Peripheral ischaemic vascular disease
G73..12	Ischaemia of legs
G73..13	Peripheral ischaemia
G731000	Buerger's disease
G732.00	Peripheral gangrene
G73y.00	Other specified peripheral vascular disease
G73y000	Diabetic peripheral angiopathy
G73y700	Erythrocyanosis
G73z100	Spasm of peripheral artery
G74..00	Arterial embolism and thrombosis
G74..11	Arterial embolus and thrombosis
G74..12	Thrombosis - arterial
G74..13	Arterial embolic and thrombotic occlusion
G75..00	Polyarteritis nodosa and allied conditions
G750.00	Polyarteritis nodosa
G750.11	Necrotising angiitis
G754.00	Wegener's granulomatosis
G755.00	Giant cell arteritis
G755000	Cranial arteritis
G755100	Temporal arteritis
G755200	Horton's disease
G755z00	Giant cell arteritis NOS

G756.00	Thrombotic microangiopathy
G757.00	Takayasu's disease
G757.11	Aortic arch arteritis
G757.12	Pulseless disease
G758.00	Churg-Strauss vasculitis
G759.00	Juvenile polyarteritis
G75X.00	Necrotising vasculopathy, unspecified
G75z.00	Polyarteritis nodosa and allied conditions NOS
G76..00	Other disorders of arteries and arterioles
G760.00	Acquired arteriovenous fistula
G761.00	Stricture of artery
G762.00	Rupture of artery
G763.00	Hyperplasia of renal artery
G764.00	Coeliac artery compression syndrome
G764.11	Marable's syndrome
G765.00	Necrosis of artery
G766.00	Arteritis unspecified
G766.11	Aortitis
G767.00	Aortitis - syphilitic
G768.00	Other disorders of arteries and arterioles
G769.00	Anterior spinal and vertebral artery compression syndromes
G76A.00	Arterial insufficiency
G76B.00	Vasculitis
G76z.00	Disorders of arteries and arterioles NOS
G77..00	Diseases of capillaries

G7y..00	Other specified arterial, arteriole or capillary disease
G7z..00	Arterial, arteriole and capillary diseases NOS
G8yy200	Phlebosclerosis
Gyu7000	[X]Atherosclerosis of other arteries
Gyu7400	[X]Other specified peripheral vascular diseases
Gyu7500	[X]Embolism and thrombosis of other arteries
Gyu7600	[X]Other specified disorders of arteries and arterioles
Gyu7700	[X]Other diseases of capillaries
Gyu7A00	[X]Peripheral angiopathy in diseases classified elsewhere
Gyu7B00	[X]Oth disorders/arteries,arterioles+capillaries/diseases CE
J42..00	Vascular insufficiency of the intestine
J420.00	Acute intestinal vascular insufficiency
J420z00	Acute intestinal vascular insufficiency NOS
J421.00	Chronic intestinal vascular insufficiency
J421z00	Chronic intestinal vascular insufficiency NOS
J42z.00	Intestinal vascular insufficiency NOS
J577.00	Vascular disorders of intestine
J577100	Gastric antral vascular ectasia
Jyu5000	[X]Other vascular disorders of intestine
K138.00	Vascular disorders of kidney
K138.11	Renal vascular disorders
K138z00	Renal vascular disorders NOS
K275.00	Vascular disorders of penis
K275z00	Penile vascular disorder NOS
K286.00	Male genital organ vascular diseases
K286z00	Male genital vascular diseases NOS

N200.00	Giant cell arteritis with polymyalgia rheumatica
Nyu4000	[X]Other conditions related to polyarteritis nodosa
Nyu4100	[X]Other giant cell arteritis
Nyu4200	[X]Other specified necrotizing vasculopathies
Nyu4D00	[X]Necrotising vasculopathy, unspecified
P76..00	Other peripheral vascular system anomalies
P766.00	Peripheral arterio-venous aneurysm
P766.11	Peripheral arterio-venous malformation
P767.00	Congenital peripheral aneurysm
P76y.00	Congenital anomaly of peripheral vascular system OS
P76yz00	Other congenital anomaly of peripheral vascular system NOS
P76z.00	Peripheral vascular system anomaly NOS
P7y0z00	Cerebrovascular system anomaly NOS
P7yz.00	Other cardiovascular system anomaly NOS
P7yzz00	Other cardiovascular system anomaly NOS
R055000	[D]Failure of peripheral circulation
R055011	[D]Peripheral circulatory failure
SP12.00	Peripheral vascular complications of care
SP12z00	Peripheral vascular complications of care NOS

Moderate or severe renal disease Read codes

Read code	Description
7L1A.11	Dialysis for renal failure
7L1A000	Renal dialysis
7L1A011	Thomas intravascular shunt for dialysis

7L1A100	Peritoneal dialysis
7L1A200	Haemodialysis NEC
7L1Ay00	Other specified compensation for renal failure
7L1Az00	Compensation for renal failure NOS
7L1B.00	Placement ambulatory apparatus compensation renal failure
7L1B.11	Placement ambulatory dialysis apparatus - compens renal fail
7L1B000	Insertion of ambulatory peritoneal dialysis catheter
7L1By00	Placement ambulatory apparatus- compensate renal failure OS
7L1Bz00	Placement ambulatory apparatus- compensate renal failure NOS
7L1C.00	Placement other apparatus for compensation for renal failure
7L1C000	Insertion of temporary peritoneal dialysis catheter
7L1Cy00	Placement other apparatus- compensate for renal failure OS
7L1Cz00	Placement other apparatus- compensate for renal failure NOS
A160.00	Tuberculosis of kidney
A160.11	Renal tuberculosis
A161.00	Tuberculosis of bladder
A162.00	Tuberculosis of ureter
A163.00	Tuberculosis of other urinary organs
A168.00	Tuberculosis of urinary tract
G22..00	Hypertensive renal disease
G22..11	Nephrosclerosis

G220.00	Malignant hypertensive renal disease
G221.00	Benign hypertensive renal disease
G222.00	Hypertensive renal disease with renal failure
G22z.00	Hypertensive renal disease NOS
G22z.11	Renal hypertension
G23..00	Hypertensive heart and renal disease
G230.00	Malignant hypertensive heart and renal disease
G231.00	Benign hypertensive heart and renal disease
G232.00	Hypertensive heart&renal dis wth (congestive) heart failure
G233.00	Hypertensive heart and renal disease with renal failure
G234.00	Hyperten heart&renal dis+both(congestv)heart and renal fail
G23z.00	Hypertensive heart and renal disease NOS
G721.00	Aneurysm of renal artery
G763.00	Hyperplasia of renal artery
G823.00	Embolism and thrombosis of the renal vein
K00..00	Acute glomerulonephritis
K00..11	Acute nephritis
K00..12	Bright's disease
K01..00	Nephrotic syndrome
K02..00	Chronic glomerulonephritis
K02..11	Nephritis - chronic
K02..12	Nephropathy - chronic
K03..00	Nephritis and nephropathy unspecified
K03..11	Nephritis and nephropathy unspecified

K03..12	Nephropathy, unspecified
K030.00	Proliferative nephritis unspecified
K031.00	Membranous nephritis unspecified
K032.00	Membranoproliferative nephritis unspecified
K033.00	Rapidly progressive nephritis unspecified
K034.00	Renal cortical necrosis unspecified
K035.00	Renal medullary necrosis unspecified
K03T.00	Tubulo-interstit nephritis, not specif as acute or chron
K03U.00	Unspecif nephr synd, diff concentric glomerulonephritis
K03V.00	Unspecified nephritic syndrome, dense deposit disease
K03W.00	Unsp nephrit synd, diff endocap prolif glomerulonephritis
K03X.00	Unsp nephrit synd, diff mesang prolif glomerulonephritis
K03y.00	Other nephritis and nephrosis unspecified
K03z.00	Unspecified glomerulonephritis NOS
K04..00	Acute renal failure
K040.00	Acute renal tubular necrosis
K041.00	Acute renal cortical necrosis
K042.00	Acute renal medullary necrosis
K042.11	Necrotising renal papillitis
K043.00	Acute drug-induced renal failure
K04y.00	Other acute renal failure
K04z.00	Acute renal failure NOS
K05..00	Chronic renal failure
K05..11	Chronic uraemia
K05..12	End stage renal failure
K050.00	End stage renal failure

K06..00	Renal failure unspecified
K06..11	Uraemia NOS
K060.00	Renal impairment
K060.11	Impaired renal function
K07..00	Renal sclerosis unspecified
K070.00	Atrophy of kidney
K071.00	Renal fibrosis
K072.00	Glomerulosclerosis
K07z.00	Renal sclerosis NOS
K08..00	Impaired renal function disorder
K080.00	Renal osteodystrophy
K080000	Phosphate-losing tubular disorders
K080z00	Renal osteodystrophy NOS
K081.00	Nephrogenic diabetes insipidus
K08y.00	Other impaired renal function disorder
K08y000	Hypokalaemic nephropathy
K08y200	Lightwood - Albright syndrome
K08y211	Albright's renal tubular acidosis
K08y300	Renal function impairment with growth failure
K08y400	Renal tubular acidosis
K08y412	Renal tubular acidaemia
K08y500	Acute interstitial nephritis
K08yz00	Other impaired renal function disorder NOS
K08yz11	Renal acidaemia
K08yz12	Renotubular acidaemia
K08z.00	Impaired renal function disorder NOS

K09..00	Small kidney of unknown cause
K0A..00	Glomerular disease
K0B..00	Renal tubulo-interstitial disorders in diseases EC
K0B0.00	Ren tubulo-interstital disord infect and parasitic dis EC
K0B1.00	Renal tubulo-interstitial disorder/ neoplastic diseases
K0B2.00	Ren tub-interst disordr/blood dis+disordr inv immune mech
K0B3.00	Renal tubulo-interstitial disorders in metabolic diseases
K0B4.00	Ren tub-interstitl disordr/systemc connectv tiss disorder
K0B4000	Renal tubulo-interstitial disorder in SLE
K0B5.00	Renal tubulo-interstitial disordrs in transplant rejectn
K0B6.00	Balkan nephropathy
K0C..00	Drug/heavy-metal-induced tubulo-interstitial and tub conditn
K0D..00	End-stage renal disease
K0y..00	Other specified nephritis, nephrosis or nephrotic syndrome
K0z..00	Nephritis, nephrosis and nephrotic syndrome NOS
K100.00	Chronic pyelonephritis
K101.00	Acute pyelonephritis
K102.00	Renal and perinephric abscess
K102000	Renal abscess
K102100	Perinephric abscess
K102200	Renal carbuncle
K102z00	Renal and perinephric abscess NOS
K103.00	Pyeloureteritis cystica
K103.11	Ureteritis cystica

K103.12	Infestation of renal pelvis with ureter
K104.00	Xanthogranulomatous pyelonephritis
K10y.00	Pyelonephritis and pyonephrosis unspecified
K11..00	Hydronephrosis
K110.00	Hydrocalycosis
K111.00	Hydroureteronephrosis
K112.00	Hydronephrosis with renal and ureteral calculous obstruction
K113.00	Hydronephrosis with ureteropelvic junction obstruction
K113.11	Hydronephrosis with pelviureteric junction obstruction
K11X.00	Hydronephrosis with ureteral stricture NEC
K11z.00	Hydronephrosis NOS
K12..00	Calculus of kidney and ureter
K12..11	Kidney calculus
K12..12	Urinary calculus
K120.00	Calculus of kidney
K120.11	Nephrolithiasis NOS
K120.12	Renal calculus
K120.13	Renal stone
K120000	Staghorn calculus
K120z00	Renal calculus NOS
K121.00	Calculus of ureter
K121.11	Ureteric calculus
K121.12	Ureteric stone
K121.13	Ureterolithiasis
K122.00	Calculus of kidney with calculus of ureter

K12z.00	Urinary calculus NOS
K13..00	Other kidney and ureter disorders
K13..11	Other kidney disorders
K13..12	Other ureter disorders
K130.00	Nephroptosis
K130.11	Floating kidney
K130.12	Mobile kidney
K131.00	Hypertrophy of kidney
K132.00	Acquired cyst of kidney
K133.00	Stricture of ureter
K134.00	Other ureteric obstruction
K135.00	Hydroureter
K136.00	Benign postural proteinuria
K136.11	Orthostatic proteinuria
K137.00	Vesicoureteric reflux
K137.11	Ureteric reflux
K138.00	Vascular disorders of kidney
K138.11	Renal vascular disorders
K138000	Renal artery embolism
K138011	Renal artery embolus
K138100	Renal artery haemorrhage
K138200	Renal artery thrombosis
K138300	Intrarenal haematoma
K138z00	Renal vascular disorders NOS
K138z11	Renal infarction
K13y.00	Other kidney and ureteric disorders

K13y000	Ureteric fistula
K13y100	Adhesions of kidney
K13y200	Adhesions of ureter
K13y300	Periureteritis
K13y400	Pyelectasia
K13y500	Polyp of ureter
K13y600	Ureterocele - acquired
K13y611	Idiopathic dilation of ureter
K13y700	Megaloureter - acquired
K13y800	Perirenal haematoma
K13y900	Ureteric neuromuscular incoordination
K13yz00	Other kidney and ureteric disorders NOS
K13yz11	Salt-losing nephritis
K13z.00	Kidney and ureter disease NOS
K17..11	Periurethritis
K18..00	Urethral stricture
K18..11	Pinhole meatus
K19..00	Other urethral and urinary tract disorders
K19..11	Other urethral disorders
K1y..00	Other specified diseases of urinary system
K1z..00	Other urinary system diseases NOS
Kyu0.00	[X]Glomerular diseases
Kyu1.00	X]Renal tubulo-interstitial diseases
Kyu1000	[X]Other chronic tubulo-interstitial nephritis
Kyu1100	[X]Other and unspecified hydronephrosis
Kyu1200	[X]Other obstructive and reflux uropathy

Kyu1300	[X]Obstructive and reflux uropathy, unspecified
Kyu1400	[X]Nephropathy induced by other drugs+biological substances
Kyu1500	[X]Toxic nephropathy, not elsewhere classified
Kyu1600	[X]Other specified renal tubulo-interstitial diseases
Kyu1700	[X]Renal tubulo-interstitial disordr/infect+parasitic dis CE
Kyu1800	[X]Renal tubulo-interstitial disordrs/neoplastic diseases CE
Kyu1900	[X]Renal tub-interstl disord/bld dis+disord invl imm mech CE
Kyu1A00	[X]Renal tubulo-interstitial disorders/metabolic diseases CE
Kyu1B00	[X]Renal tubul-interstitl disordrs/connectv tissu disordr CE
Kyu1C00	[X]Renal tubulo-interstitial disorders/transplant rejection
Kyu1D00	[X]Renal tubulo-interstitial disorders in other diseases CE
Kyu1E00	[X]Tubulo-interstit nephritis, not specif as acute or chron
Kyu1F00	[X]Hydronephrosis with ureteral stricture NEC
Kyu2.00	[X]Renal failure
Kyu2000	[X]Other acute renal failure
Kyu2100	[X]Other chronic renal failure
Kyu3.00	[X]Urolithiasis
Kyu4.00	[X]Other disorders of kidney and ureter
Kyu4000	[X]Other disorders resulting/impaired renal tubular function
Kyu4100	[X]Other specified disorders of kidney and ureter
Kyu4200	[X]Oth disordrs/kidney+ureter/infects+parasitic diseases CE
Kyu4300	[X]Other disorders of kidney+ureter in other diseases CE

PD0..00	Renal agenesis and dysgenesis
PD00.00	Renal agenesis, unspecified
PD00000	Bilateral renal agenesis
PD00100	Unilateral renal agenesis
PD00z00	Renal agenesis, unspecified NOS
PD01.00	Congenital renal atrophy
PD02.00	Congenital absence of kidney
PD03.00	Hypoplasia of kidney
PD03000	Bilateral renal hypoplasia
PD03011	Potter's syndrome
PD03100	Unilateral renal hypoplasia
PD04.00	Dysplasia of kidney
PD04000	Bilateral renal dysplasia
PD04011	Bilateral renal dysgenesis
PD04100	Unilateral renal dysplasia
PD04111	Unilateral renal dysgenesis
PD04z00	Dysplasia of kidney NOS
PD0z.00	Renal agenesis or dysgenesis NOS
PD1..00	Congenital cystic kidney disease
PD1..11	Congenital cystic renal disease
PD1..12	Fibrocystic kidney
PD1..13	Polycystic kidney
PD1..14	Sponge kidney
PD10.00	Congenital renal cyst, single
PD11.00	Polycystic kidney disease
PD12.00	Medullary cystic disease

PD13.00	Multicystic renal dysplasia
PD13.11	Multicystic kidney
PD1y.00	Other specified congenital cystic kidney disease
PD1y000	Fibrocystic kidney disease
PD1y011	Fibrocystic renal degeneration
PD1yz00	Other congenital cystic kidney disease NOS
PD1z.00	Congenital cystic kidney disease NOS
PD2..00	Renal pelvis and ureter obstructive defects
PD20.00	Atresia of ureter
PD21.00	Occlusion of ureter
PD21.11	Congenital ureteric valves
PD22.00	Congenital stricture of ureter
PD22.11	Congenital stenosis of ureter
PD23.00	Congenital hydronephrosis
PD23.11	Congenital dilated renal pelvis
PD24.00	Congenital dilatation of ureter
PD25.00	Hydroureter - congenital
PD26.00	Megaloureter - congenital
PD27.00	Ureterocele - congenital
PD28.00	Impervious ureter
PD2y.00	Other specified obstructive defect of renal pelvis or ureter
PD2z.00	Obstructive defect of renal pelvis or ureter NOS
PD3..00	Other specified renal anomaly
PD30.00	Accessory kidney
PD30.11	Duplication of kidney
PD30.12	Renal duplication NEC

PD30.13	Supernumerary kidney
PD31.00	Congenital calculus of kidney
PD32.00	Congenital displaced kidney
PD33.00	Discoid kidney
PD34.00	Double kidney with double pelvis
PD34.11	Duplex kidneys
PD34.12	Pyelon duplex
PD35.00	Ectopic kidney
PD35.11	Pelvic kidney
PD36.00	Fusion of kidneys
PD37.00	Giant kidney
PD38.00	Horseshoe kidney
PD39.00	Hyperplasia of kidney
PD3A.00	Lobulation of kidney
PD3A.11	Ren arcuatus
PD3A.12	Ren unguliformis
PD3B.00	Malrotation of kidney
PD3C.00	Triple kidney with triple pelvis
PD3C.11	Trifid kidney
PD3C.12	Pyelon triplex
PD3D.00	Enlarged kidney
PD3z.00	Other specified renal anomaly NOS
PD4..00	Other specified ureter anomalies
PD40.00	Absent ureter
PD41.00	Accessory ureter
PD42.00	Deviation of ureter

PD43.00	Displaced ureteric orifice
PD44.00	Double ureter
PD44.11	Duplication of ureter
PD45.00	Ectopic ureter
PD45.11	Congenital displacement of opening of ureter
PD45.12	Ectopic insertion of ureter
PD46.00	Anomalous ureter implantation
PD47.00	Congenital vesico-uretero-renal reflux
PD4z.00	Other specified ureter anomaly NOS
PD5..00	Exstrophy of urinary bladder
PD5..11	Ectopia vesicae
PD5..12	Ectopic bladder
PD6..00	Urethra and bladder neck atresia and stenosis
PDy..00	Other specified bladder and urethral anomalies
PDz..00	Urinary system anomalies NOS
R135300	[D]Renal scarring
R135z00	[D]Genitourinary x-ray or scan abnormality NOS
R144.00	[D]Renal function test abnormal
R144.11	[D]Kidney function test abnormal
S760000	Kidney injury without open wound into cavity, unspecified
S760100	Kidney haematoma without mention of open wound into cavity
S760111	Renal haematoma without mention of open wound into cavity
S760200	Kidney laceration without mention of open wound into cavity

S760300	Kidney parenchyma disruption without open wound to cavity
S760z00	Kidney injury without mention of open wound into cavity NOS
S761000	Kidney injury with open wound into cavity, unspecified
S761100	Kidney haematoma with open wound into cavity
S761111	Renal haematoma with open wound into cavity
S761200	Kidney laceration with open wound into cavity
S761300	Kidney parenchyma disruption with open wound into cavity
S761z00	Kidney injury with open wound into cavity NOS
SK05.00	Renal failure following crush syndrome
SK05.11	Renal failure after crushing
SK05.12	Traumatic anuria - crush syndrome
SP15200	Oliguria as a complication of care
SP15300	Anuria as a complication of care
SP15400	Renal failure as a complication of care
SP15411	Kidney failure as a complication of care
SP15412	Post operative renal failure
SP15413	Uraemia - post operative
TB00100	Kidney transplant with complication, without blame
TB00111	Renal transplant with complication, without blame
TB11.00	Kidney dialysis with complication, without blame
TB11.11	Renal dialysis with complication, without blame

Tumour Read codes

Read code	**Description**

B50..00	Malignant neoplasm of eye
B51..00	Malignant neoplasm of brain
B51..11	Cerebral tumour - malignant
B52..00	Malig neop of other and unspecified parts of nervous system
B53..00	Malignant neoplasm of thyroid gland
B54..00	Malig neop of other endocrine glands and related structures
B55..00	Malignant neoplasm of other and ill-defined sites
B59..00	Malignant neoplasm of unspecified site
B5y..00	Malignant neoplasm of other and unspecified site OS
B5z..00	Malignant neoplasm of other and unspecified site NOS
B62z.00	Malignant neoplasms of lymphoid and histiocytic tissue NOS
B717011	Endocrine tumour of pancreas
B900000	Neoplasm of uncertain behaviour of parotid gland
B900011	Mixed parotid tumour
B900100	Neoplasm of uncertain behaviour of sublingual gland
B900200	Neoplasm of uncertain behaviour of submandibular gland
B900z00	Neoplasm of uncertain behaviour of major salivary gland NOS
B930.00	Neop of uncertain behaviour of bone and articular cartilage
B931.00	Neop of uncertain behaviour connective and other soft tissue
B932.00	Neoplasm of uncertain behaviour of skin
B933.00	Neoplasm of uncertain behaviour of breast

B933.11	Cystosarcoma phyllodes
B935.00	Neoplasm of uncertain behaviour of histiocytic and mast cell
B935.11	Histiocytic tumour NOS
B935.12	Mastocytoma NOS
B936.00	Neoplasm of uncertain behaviour of plasma cells
B936.11	Myeloma - solitary
B936.12	Plasmacytoma NOS
B937.00	Neop uncertain behaviour other lymphatic/haematopoietic tiss
B937.11	Neoplasm of uncertain behaviour of blood
B93X.00	Neo/uncertn+unknwn behav/lymph,h'matopetc+rel tiss,unspcf
B93y.00	Neoplasm of uncertain behaviour of other specified sites
B93z.00	Neop uncertain behaviour other unspec site and tissue NOS
BB...11	[M]Tumour morphology
BB0..00	[M]Neoplasms NOS
BB01.00	[M]Neoplasm, uncertain whether benign or malignant
BB02.00	[M]Neoplasm, malignant
BB03.00	[M]Neoplasm, metastatic
BB03.11	[M]Secondary neoplasm
BB04.00	[M]Neoplasm, malig, uncertain whether primary or metastatic
BB06.00	[M]Tumour cells, uncertain whether benign or malignant
BB07.00	[M]Tumour cells, malignant
BB08.00	[M]Malignant tumour, small cell type

BB09.00	[M]Malignant tumour, giant cell type
BB0A.00	[M]Malignant tumour, fusiform cell type
BB0z.00	[M]Unspecified tumour cell NOS
BB1..00	[M]Epithelial neoplasms NOS
BB10.00	[M]Epithelial tumour, benign
BB11.00	[M]Carcinoma in situ NOS
BB11.11	[M]Intraepithelial carcinoma NOS
BB12.00	[M]Carcinoma NOS
BB13.00	[M]Carcinoma, metastatic, NOS
BB13.11	[M]Secondary carcinoma
BB14.00	[M]Carcinomatosis
BB15.00	[M]Epithelioma, benign
BB16.00	[M]Epithelioma, malignant
BB17.00	[M]Large cell carcinoma NOS
BB18.00	[M]Carcinoma, undifferentiated type, NOS
BB19.00	[M]Carcinoma, anaplastic type, NOS
BB1A.00	[M]Pleomorphic carcinoma
BB1B.00	[M]Giant cell and spindle cell carcinoma
BB1C.00	[M]Giant cell carcinoma
BB1D.00	[M]Spindle cell carcinoma
BB1E.00	[M]Pseudosarcomatous carcinoma
BB1F.00	[M]Polygonal cell carcinoma
BB1G.00	[M]Spheroidal cell carcinoma
BB1J.00	[M]Small cell carcinoma NOS
BB1J.11	[M]Reserve cell carcinoma
BB1J.12	[M]Round cell carcinoma

BB1K.00	[M]Oat cell carcinoma
BB1L.00	[M]Small cell carcinoma, fusiform cell type
BB1M.00	[M]Small cell carcinoma, intermediate cell
BB1N.00	[M]Small cell-large cell carcinoma
BB1z.00	[M]Unspecified epithelial neoplasm
BB2..00	[M]Papillary and squamous cell neoplasms
BB2..11	[M]Papillary neoplasms
BB2..12	[M]Squamous cell neoplasms
BB3..00	[M]Basal cell neoplasms
BB30.00	[M]Basal cell tumour
BB31.00	[M]Basal cell carcinoma NOS
BB32.00	[M]Multicentric basal cell carcinoma
BB33.00	[M]Basal cell carcinoma, morphoea type
BB34.00	[M]Basal cell carcinoma, fibroepithelial type
BB35.00	[M]Basosquamous carcinoma
BB36.00	[M]Metatypical carcinoma
BB37.00	[M]Intraepidermal epithelioma of Jadassohn
BB38.00	[M]Trichoepithelioma
BB38.11	[M]Brooke's tumour
BB38.12	[M]Epithelioma adenoides cyst
BB39.00	[M]Trichofolliculoma
BB3A.00	[M]Tricholemmoma
BB3B.00	[M]Pilomatrixoma
BB3B.11	[M]Malherbe's calcified epithelioma
BB3z.00	[M]Basal cell neoplasm NOS
BB4..00	[M]Transitional cell papillomas and carcinomas

BB5..00	[M]Adenomas and adenocarcinomas
BB5..11	[M]Adenocarcinomas
BB51.00	[M]Adenocarcinoma in situ
BB52.00	[M]Adenocarcinoma NOS
BB53.00	[M]Adenocarcinoma, metastatic, NOS
BB54.00	[M]Scirrhous adenocarcinoma
BB55.00	[M]Linitis plastica
BB56.00	[M]Superficial spreading adenocarcinoma
BB57.00	[M]Adenocarcinoma, intestinal type
BB58.00	[M]Carcinoma, diffuse type
BB59.00	[M]Monomorphic adenoma
BB5A.00	[M]Basal cell adenoma
BB5B.00	[M]Pancreatic adenomas and carcinomas
BB5B000	[M]Islet cell adenoma
BB5B011	[M]Nesidioblastoma
BB5B100	[M]Islet cell carcinoma
BB5B200	[M]Insulinoma NOS
BB5B211	[M]Beta-cell adenoma
BB5B300	[M]Insulinoma, malignant
BB5B311	[M]Beta-cell tumour, malignant
BB5B400	[M]Glucagonoma NOS
BB5B411	[M]Alpha-cell adenoma
BB5B500	[M]Glucagonoma, malignant
BB5B511	[M]Alpha-cell tumour,malignant
BB5B600	[M]Mixed islet cell and exocrine adenocarcinoma
BB5Bz00	[M]Pancreatic adenoma or carcinoma NOS

BB5C.00	[M]Gastrinoma and carcinomas
BB5C000	[M]Gastrinoma NOS
BB5C011	[M]G cell tumour NOS
BB5C100	[M]Gastrinoma, malignant
BB5C111	[M]G cell tumour, malignant
BB5Cz00	[M]Gastrinoma or carcinoma NOS
BB5D.00	[M]Hepatobiliary tract adenomas and carcinomas
BB5D.11	[M]Biliary tract adenomas and adenocarcinomas
BB5E.00	[M]Trabecular adenoma
BB5F.00	[M]Trabecular adenocarcinoma
BB5J.00	[M]Adenoid cystic carcinoma
BB5J.11	[M]Cylindroid adenocarcinoma
BB5J.13	[M]Cylindroma NOS
BB5K.00	[M]Cribriform carcinoma
BB5L.00	[M]Adenomatous and adenocarcinomatous polyps
BB5M.00	[M]Tubular adenomas and adenocarcinomas
BB5N.00	[M]Adenomatous and adenocarcinomatous polyps of colon
BB5N.11	[M]Adenoma or or adenocarcinoma in polyposis coli
BB5P.00	[M]Solid carcinoma NOS
BB5Q.00	[M]Carcinoma simplex
BB5R.00	[M]Carcinoid tumours
BB5R000	[M]Carcinoid tumour NOS
BB5R100	[M]Carcinoid tumour, malignant
BB5R111	[M]Carcinoid bronchial adenoma
BB5R200	[M]Carcinoid tumour, argentaffin, NOS

BB5R211	[M]Argentaffinoma NOS
BB5R300	[M]Carcinoid tumour, argentaffin, malignant
BB5R400	[M]Carcinoid tumour, nonargentaffin, NOS
BB5R500	[M]Carcinoid tumour, nonargentaffin, malignant
BB5R600	[M]Mucocarcinoid tumour, malignant
BB5R611	[M]Goblet cell tumour
BB5R700	[M]Composite carcinoid
BB5R800	[M]Adenocarcinoid tumour
BB5R900	[M]Neuroendocrine carcinoma
BB5RA00	[M]Merkel cell carcinoma
BB5Rz00	[M]Carcinoid tumours NOS
BB5S.00	[M]Respiratory tract adenomas and adenocarcinomas
BB5T.00	[M]Papillary adenomas and adenocarcinomas
BB5U.00	[M]Villous adenomas and adenocarcinomas
BB5V.00	[M]Pituitary adenomas and carcinomas
BB5W.00	[M]Oxyphilic adenomas and adenocarcinomas
BB5X.00	[M]Clear cell adenomas and adenocarcinomas
BB5Y.00	[M]Hypernephroid tumour
BB5Z.00	[M]Clear cell adenofibroma
BB5a.00	[M]Renal adenoma and carcinoma
BB5a000	[M]Renal cell carcinoma
BB5a011	[M]Grawitz tumour
BB5a012	[M]Hypernephroma
BB5a100	[M]Juxtaglomerular tumour
BB5a111	[M]Reninoma
BB5az00	[M]Renal adenoma or carcinoma NOS

BB5b.00	[M]Granular cell carcinoma
BB5c.00	[M]Parathyroid adenomas and adenocarcinomas
BB5d.00	[M]Mixed cell adenoma and adenocarcinoma
BB5e.00	[M]Lipoadenoma
BB5f.00	[M]Thyroid adenoma and adenocarcinoma
BB5g.00	[M]Multiple endocrine adenomas
BB5h.00	[M]Adrenal cortical tumours
BB5h100	[M]Adrenal cortical carcinoma
BB5h200	[M]Adrenal cortical adenoma, compact cell type
BB5h300	[M]Adrenal cortical adenoma, heavily pigmented variant
BB5h311	[M]Black adenoma
BB5h400	[M]Adrenal cortical adenoma, clear cell type
BB5h500	[M]Adrenal cortical adenoma, glomerulosa cell type
BB5h600	[M]Adrenal cortical adenoma, mixed cell type
BB5hz00	[M]Adrenal cortical tumours NOS
BB5j.00	[M]Endometrioid adenomas and carcinomas
BB5y.00	[M]Adenoma and adenocarcinoms OS
BB5y000	[M]Basal cell adenocarcinoma
BB5y100	[M]Vipoma
BB5y200	[M]Klatskin's tumour
BB5y300	[M]Apudoma
BB5y400	[M]Prolactinoma
BB5y500	[M]Lipid-rich carcinoma
BB5y600	[M]Glycogen-rich carcinoma
BB5z.00	[M]Adenoma or adenocarcinoma NOS
BB6..00	[M]Adnexal and skin appendage neoplasms

BB61100	[M]Sweat gland tumour NOS
BB61200	[M]Sweat gland adenocarcinoma
BB61z00	[M]Sweat gland adenoma or adenocarcinoma NOS
BB7..00	[M]Mucoepidermoid neoplasms
BB70.00	[M]Mucoepidermoid tumour
BB71.00	[M]Mucoepidermoid carcinoma
BB7z.00	[M]Mucoepidermoid neoplasm NOS
BB8..00	[M]Cystic, mucinous and serous neoplasms
BB80.00	[M]Cystadenoma and carcinoma
BB81.00	[M]Ovarian cystic, mucinous and serous neoplasms
BB81.11	[M]Ovarian cystadenoma or carcinoma
BB81.12	[M]Ovarian mucinous tumour
BB81.13	[M]Ovarian papillary tumour
BB81.14	[M]Ovarian serous tumour
BB81000	[M]Serous cystadenoma NOS
BB81100	[M]Serous cystadenoma, borderline malignancy
BB81200	[M]Serous cystadenocarcinoma, NOS
BB81300	[M]Papillary cystadenoma NOS
BB81400	[M]Papillary cystadenoma, borderline malignancy
BB81500	[M]Papillary cystadenocarcinoma, NOS
BB81600	[M]Papillary serous cystadenoma NOS
BB81700	[M]Papillary serous cystadenoma, borderline malignancy
BB81800	[M]Papillary serous cystadenocarcinoma
BB81900	[M]Serous surface papilloma NOS
BB81A00	[M]Serous surface papilloma, borderline malignancy
BB81B00	[M]Serous surface papillary carcinoma

BB81C00	[M]Mucinous cystadenoma NOS
BB81C11	[M]Pseudomucinous cystadenoma NOS
BB81D00	[M]Mucinous cystadenoma, borderline malignancy
BB81E00	[M]Mucinous cystadenocarcinoma NOS
BB81E11	[M]Pseudomucinous adenocarcinoma
BB81F00	[M]Papillary mucinous cystadenoma NOS
BB81G00	[M]Papillary mucinous cystadenoma, borderline malignancy
BB81H00	[M]Papillary mucinous cystadenocarcinoma
BB81J00	[M]Serous cystadenoma, borderline malignancy
BB81K00	[M]Papillary cystadenoma, borderline malignancy
BB81L00	[M]Papillary cystic tumour
BB81M00	[M]Papillary serous cystadenoma, borderline malignancy
BB81z00	[M]Ovarian cystic, mucinous or serous neoplasm NOS
BB82.00	[M]Mucinous adenoma and adenocarcinoma
BB83.00	[M]Pseudomyxoma peritonei
BB84.00	[M]Mucin-producing adenocarcinoma
BB85.00	[M]Signet ring carcinoma
BB85000	[M]Signet ring cell carcinoma
BB85100	[M]Metastatic signet ring cell carcinoma
BB85111	[M]Krukenberg tumour
BB85z00	[M]Signet ring carcinoma NOS
BB8z.00	[M]Cystic, mucinous or serous neoplasm NOS
BB9..00	[M]Ductal, lobular and medullary neoplasms
BBA..00	[M]Acinar cell neoplasms
BBA0.00	[M]Acinar cell adenoma

BBA1.00	[M]Acinar cell tumour
BBA2.00	[M]Acinar cell carcinoma
BBAz.00	[M]Acinar cell neoplasm NOS
BBB..00	[M]Complex epithelial neoplasms
BBB0.00	[M]Adenosquamous carcinoma
BBB1.00	[M]Adenolymphoma
BBB1.11	[M]Warthin's tumour
BBB2.00	[M]Adenocarcinoma with squamous metaplasia
BBB2.11	[M]Adenoacanthoma
BBB3.00	[M]Adenocarcinoma with cartilaginous and osseous metaplasia
BBB4.00	[M]Adenocarcinoma with spindle cell metaplasia
BBB5.00	[M]Adenocarcinoma with apocrine metaplasia
BBB6.00	[M]Thymoma
BBB7.00	[M]Epithelial-myoepithelial carcinoma
BBBz.00	[M]Complex epithelial neoplasm NOS
BBC..00	[M]Specialised gonadal neoplasms
BBC0.00	[M]Sex cord-stromal tumour
BBC0.11	[M]Gonadal stromal tumour
BBC0.12	[M]Ovarian stromal tumour
BBC0.13	[M]Testicular stromal tumour
BBC0000	[M]Sex cord tumour with annular tubules
BBC1.00	[M]Thecal cell neoplasms
BBC2.00	[M]Luteoma NOS
BBC2.11	[M]Luteinoma
BBC3.00	[M]Granulosa cell tumour NOS

BBC3000	[M]Juvenile granulosa cell tumour
BBC4.00	[M]Granulosa cell tumour, malignant
BBC5.00	[M]Granulosa cell-theca cell tumour
BBC6.00	[M]Androblastoma
BBC7.00	[M]Sertoli-Leydig cell tumour
BBC8.00	[M]Gynandroblastoma
BBC9.00	[M]Tubular androblastoma NOS
BBC9.11	[M]Pick's tubular adenoma
BBC9.12	[M]Sertoli cell adenoma
BBC9.13	[M]Sertoli cell tumour
BBC9.14	[M]Testicular adenoma
BBCA.00	[M]Sertoli cell carcinoma
BBCB.00	[M]Tubular androblastoma with lipid storage
BBCB.11	[M]Sertoli cell tumour with lipid storage
BBCC.00	[M]Leydig cell tumour
BBCC000	[M]Leydig cell tumour, benign
BBCC011	[M]Interstitial cell tumour, benign
BBCC100	[M]Leydig cell tumour, malignant
BBCC111	[M]Interstitial cell tumour, malignant
BBCCz00	[M]Leydig cell tumour NOS
BBCCz11	[M]Interstitial cell tumour NOS
BBCD.00	[M]Hilar cell tumour
BBCE.00	[M]Lipid cell tumour of ovary
BBCE.11	[M]Masculinovoblastoma
BBCF.00	[M]Adrenal rest tumour
BBCG.00	[M]Sclerosing stromal tumour

BBCz.00	[M]Specialised gonadal neoplasm NOS
BBD..00	[M]Paragangliomas and glomus tumours
BBD0.00	[M]Paraganglioma NOS
BBD1.00	[M]Paraganglioma, malignant
BBD2.00	[M]Sympathetic paraganglioma
BBD3.00	[M]Parasympathetic paraganglioma
BBD4.00	[M]Glomus jugulare tumour
BBD4.11	[M]Jugular paraganglioma
BBD5.00	[M]Aortic body tumour
BBD6.00	[M]Carotid body tumour
BBD7.00	[M]Extra-adrenal paraganglioma, NOS
BBD7.11	[M]Chemodectoma
BBD8.00	[M]Extra-adrenal paraganglioma, malignant
BBD9.00	[M]Phaeochromocytoma NOS
BBD9.11	[M]Chromaffin paraganglioma
BBD9.12	[M]Chromaffin tumour
BBD9.13	[M]Chromaffinoma
BBDA.00	[M]Phaeochromocytoma, malignant
BBDA.11	[M]Phaeochromoblastoma
BBDB.00	[M]Glomangiosarcoma
BBDB.11	[M]Glomoid sarcoma
BBDC.00	[M]Glomus tumour
BBDD.00	[M]Glomangioma
BBDE.00	[M]Gangliocytic paraganglioma
BBDF.00	[M]Glomangiomyoma
BBDz.00	[M]Paraganglioma or glomus tumour NOS

BBE..00	[M]Naevi and melanomas
BBF..00	[M]Soft tissue tumours and sarcomas NOS
BBF0.00	[M]Soft tissue tumour, benign
BBF1.00	[M]Sarcoma NOS
BBF2.00	[M]Sarcomatosis NOS
BBF3.00	[M]Spindle cell sarcoma
BBF4.00	[M]Giant cell sarcoma (except of bone)
BBF4.11	[M]Pleomorphic cell sarcoma
BBF5.00	[M]Small cell sarcoma
BBF5.11	[M]Round cell sarcoma
BBF6.00	[M]Epithelioid cell sarcoma
BBFz.00	[M]Soft tissue tumour or sarcoma NOS
BBG..00	[M]Fibromatous neoplasms
BBH..00	[M]Myxomatous neoplasms
BBJ..00	[M]Lipomatous neoplasms
BBJ1.00	[M]Liposarcoma NOS
BBJ1.11	[M]Fibroliposarcoma
BBJ3.00	[M]Liposarcoma, well differentiated type
BBJ4.00	[M]Fibromyxolipoma
BBJ4.11	[M]Myxolipoma
BBJ5.00	[M]Myxoid liposarcoma
BBJ5.11	[M]Embryonal liposarcoma
BBJ5.12	[M]Myxoliposarcoma
BBJ6.00	[M]Round cell liposarcoma
BBJ7.00	[M]Pleomorphic liposarcoma
BBJ8.00	[M]Mixed type liposarcoma

BBJ9.11	[M]Infiltrating lipoma
BBJA.00	[M]Spindle cell lipoma
BBJB.00	[M]Angiolipomatous neoplasms
BBJC.00	[M]Myelolipoma
BBJD.11	[M]Brown fat tumour
BBJE.00	[M]Lipoblastomatosis
BBJF.00	[M]Pleomorphic lipoma
BBJH.00	[M]Dedifferentiated liposarcoma
BBJz.00	[M]Lipomatous neoplasms NOS
BBK..00	[M]Myomatous neoplasms
BBK3000	[M]Rhabdomyoma NOS
BBK3100	[M]Rhabdomyosarcoma NOS
BBK3200	[M]Pleomorphic rhabdomyosarcoma
BBK3300	[M]Mixed cell rhabdomyosarcoma
BBK3400	[M]Fetal rhabdomyoma
BBK3500	[M]Adult rhabdomyoma
BBK3511	[M]Glycogenic rhabdomyoma
BBK3600	[M]Embryonal rhabdomyosarcoma
BBK3611	[M]Sarcoma botryoides
BBK3700	[M]Alveolar rhabdomyosarcoma
BBK3800	[M]Smooth muscle tumour NOS
BBK3z00	[M]Rhabdomyomatous neoplasm NOS
BBL..00	[M]Complex mixed and stromal neoplasms
BBL0.00	[M]Endometrial stromal sarcoma
BBL1.00	[M]Endolymphatic stromal myosis
BBL2.00	[M]Adenomyoma

BBL3.00	[M]Pleomorphic adenoma
BBL3.11	[M]Chondroid syringoma
BBL3.12	[M]Mixed tumour NOS
BBL4.00	[M]Mixed tumour, malignant, NOS
BBL5.00	[M]Mullerian mixed tumour
BBL6.00	[M]Mesodermal mixed tumour
BBL7.00	[M]Mixed and stromal renal neoplasms
BBL7.11	[M]Nephromas and nephroblastomas
BBL7000	[M]Mesoblastic nephroma
BBL7100	[M]Nephroblastoma NOS
BBL7111	[M]Adenosarcoma
BBL7112	[M]Wilms' tumour
BBL7200	[M]Epithelial nephroblastoma
BBL7300	[M]Mesenchymal nephroblastoma
BBL7z00	[M]Mixed or stromal renal neoplasm NOS
BBL8.00	[M]Hepatoblastoma
BBL8.11	[M]Embryonal hepatoma
BBL9.00	[M]Carcinosarcoma NOS
BBLA.00	[M]Carcinosarcoma, embryonal type
BBLA.11	[M]Pneumoblastoma
BBLB.00	[M]Myoepithelioma
BBLC.00	[M]Mesenchymomas
BBLD.00	[M]Embryonal sarcoma
BBLE.00	[M]Adenosarcoma
BBLF.00	[M]Endometrial stromal nodule
BBLG.00	[M]Carcinoma in pleomorphic adenoma

BBLH.00	[M]Rhabdoid sarcoma
BBLJ.00	[M]Clear cell sarcoma of kidney
BBLK.00	[M]Pancreatoblastoma
BBLM.00	[M]Pulmonary blastoma
BBLz.00	[M]Complex mixed or stromal neoplasm NOS
BBM..00	[M]Fibroepithelial neoplasms
BBM0.00	[M]Brenner tumours
BBM0000	[M]Brenner tumour, borderline malignancy
BBM0100	[M]Brenner tumour, malignant
BBM0z00	[M]Brenner tumour NOS
BBM1.00	[M]Fibroadenoma NOS
BBM2.00	[M]Intracanalicular fibroadenoma NOS
BBM3.00	[M]Pericanalicular fibroadenoma
BBM4.00	[M]Adenofibroma NOS
BBM4.11	[M]Cystadenofibroma NOS
BBM5.00	[M]Serous adenofibroma
BBM6.00	[M]Mucinous adenofibroma
BBM7.00	[M]Cellular intracanalicular fibroadenoma
BBM7.12	[M]Fibroadenoma phyllodes
BBM7.13	[M]Giant fibroadenoma NOS
BBM7.14	[M]Giant intracanalicular fibroadedoma
BBM8.00	[M]Cystosarcoma phyllodes NOS
BBM9.00	[M]Cystosarcoma phyllodes, malignant
BBMA.00	[M]Juvenile fibroadenoma
BBMB.00	[M]Giant fibroadenoma
BBMz.00	[M]Fibroepithelial neoplasm NOS

BBN..00	[M]Synovial neoplasms
BBP..00	[M]Mesothelial neoplasms
BBP1.00	[M]Mesothelioma, malignant
BBP2.00	[M]Fibrous mesothelioma, benign
BBP3.00	[M]Fibrous mesothelioma, malignant
BBP4.00	[M]Epithelioid mesothelioma, benign
BBP5.00	[M]Epithelioid mesothelioma, malignant
BBP6.00	[M]Mesothelioma, biphasic type, benign
BBP7.00	[M]Mesothelioma, biphasic type, malignant
BBP8.00	[M]Adenomatoid tumour NOS
BBP9.00	[M]Cystic mesothelioma
BBPX.00	[M]Mesothelioma, unspecified
BBPz.00	[M]Mesothelial neoplasm NOS
BBQ..00	[M]Germ cell neoplasms
BBQ0.00	[M]Dysgerminoma
BBQ1.00	[M]Seminomas
BBQ2.00	[M]Germinoma
BBQ3.00	[M]Embryonal carcinoma NOS
BBQ4.00	[M]Endodermal sinus tumour
BBQ4.11	[M]Infantile embryonal carcinoma
BBQ4.12	[M]Orchioblastoma
BBQ4.13	[M]Polyvesicular vitelline tumour
BBQ4.14	[M]Yolk sac tumour
BBQ5.00	[M]Polyembryoma
BBQ5.11	[M]Polyembryonal embryonal carcinoma
BBQ6.00	[M]Gonadoblastoma

BBQ6.11	[M]Gonocytoma
BBQ7.00	[M]Teratomas
BBQ9.00	[M]Dermoid cyst with malignant transformation
BBQA.00	[M]Strumal neoplasms
BBQB.00	[M]Mixed germ cell tumour
BBQz.00	[M]Germ cell neoplasm NOS
BBR..00	[M]Trophoblastic neoplasms
BBR0.00	[M]Hydatidiform mole NOS
BBR0.11	[M]Hydatid mole
BBR1.00	[M]Invasive hydatidiform mole
BBR1.11	[M]Chorioadenoma
BBR1.12	[M]Chorioadenoma destruens
BBR1.13	[M]Invasive mole NOS
BBR2.00	[M]Choriocarcinoma
BBR2.11	[M]Chorioepithelioma
BBR3.00	[M]Choriocarcinoma combined with teratoma
BBR4.00	[M]Malignant teratoma, trophoblastic
BBR5.00	[M]Partial hydatidiform mole
BBR6.00	[M]Placental site trophoblastic tumour
BBR7.00	[M]Classical hydatidiform mole
BBR8.00	[M]Complete hydatidiform mole
BBRz.00	[M]Trophoblastic neoplasm NOS
BBS..00	[M]Mesonephromas
BBS0.00	[M]Mesonephroma, benign
BBS0.11	[M]Wolffian duct adenoma
BBS1.00	[M]Mesonephric tumour

BBS2.00	[M]Mesonephroma, malignant
BBS2.11	[M]Wolffian duct carcinoma
BBS3.00	[M]Endosalpingioma
BBSz.00	[M]Mesonephroma NOS
BBT..00	[M]Blood vessel tumours
BBT..11	[M]Haemangiomatous tumours
BBT0.11	[M]Angioma NOS
BBT0.12	[M]Chorioangioma
BBT1.00	[M]Haemangiosarcoma
BBT1.11	[M]Angiosarcoma
BBT2.00	[M]Cavernous haemangioma
BBT3.00	[M]Venous haemangioma
BBT4.00	[M]Racemose haemangioma
BBT4.11	[M]Arteriovenous haemangioma
BBT5.00	[M]Kupffer cell sarcoma
BBT7.00	[M]Haemangioendothelioma
BBTA.00	[M]Kaposi's sarcoma
BBTA.11	[M]Multiple haemorrhagic sarcoma
BBTD.00	[M]Haemangiopericytic neoplasms
BBTE.11	[M]Juvenile angiofibroma
BBTF.00	[M]Haemangioblastoma
BBTF.11	[M]Angioblastoma
BBTJ.00	[M]Epithelioid haemangioendothelioma NOS
BBTK.00	[M]Epithelioid haemangioendothelioma, malignant
BBTL.00	[M]Intravascular bronchial alveolar tumour
BBTz.00	[M]Blood vessel tumour NOS

BBU..00	[M]Lymphatic vessel tumours
BBU..11	[M]Lymphangiomatous tumours
BBU1.00	[M]Lymphangiosarcoma
BBUz.00	[M]Lymphatic vessel tumour NOS
BBV..00	[M]Osteomas and osteosarcomas
BBV..11	[M]Juxtacortical osteogenic sarcoma
BBV..12	[M]Parosteal osteosarcoma
BBV..13	[M]Periosteal osteogenic sarcoma
BBW..00	[M]Chondromatous neoplasms
BBW0.00	[M]Osteochondroma
BBW0.11	[M]Cartilaginous exostosis
BBW0.12	[M]Ecchondroma
BBW0.13	[M]Osteocartilaginous exostosis
BBW1.00	[M]Osteochondromatosis NOS
BBW1.11	[M]Ecchondrosis
BBW2.00	[M]Chondroma NOS
BBW2.11	[M]Enchondroma
BBW3.00	[M]Chondromatosis NOS
BBW4.00	[M]Chondrosarcoma NOS
BBW4.11	[M]Fibrochondrosarcoma
BBW5.00	[M]Juxtacortical chondroma
BBW5.11	[M]Periosteal chondroma
BBW6.00	[M]Juxtacortical chondrosarcoma
BBW7.00	[M]Chondroblastoma NOS
BBW7.11	[M]Chondromatous giant cell tumour
BBW7.12	[M]Codman's tumour

BBW8.00	[M]Chondroblastoma, malignant
BBW9.00	[M]Mesenchymal chondrosarcoma
BBWA.00	[M]Chondromyxoid fibroma
BBWz.00	[M]Chondromatous neoplasm NOS
BBX..00	[M]Giant cell tumours
BBX0.00	[M]Giant cell tumour of bone NOS
BBX0.11	[M]Osteoclastoma
BBX1.00	[M]Giant cell tumour of bone, malignant
BBX1.11	[M]Giant cell bone sarcoma
BBX1.12	[M]Osteoclastoma, malignant
BBX2.00	[M]Giant cell tumour of soft parts NOS
BBX3.00	[M]Malignant giant cell tumour of soft parts
BBXz.00	[M]Giant cell tumour NOS
BBY..00	[M]Miscellaneous bone tumours
BBY0.00	[M]Ewing's sarcoma
BBY0.11	[M]Endothelial bone sarcoma
BBY1.00	[M]Adamantinoma of long bones
BBY1.11	[M]Tibial adamantinoma
BBYz.00	[M]Miscellaneous bone tumour NOS
BBZ..00	[M]Odontogenic tumours
BBZ1.00	[M]Odontogenic tumour NOS
BBZ2.00	[M]Odontogenic tumour, malignant
BBZ2.11	[M]Intraosseous carcinoma
BBZD.00	[M]Adenomatoid odontogenic tumour
BBZD.11	[M]Adenoameloblastoma
BBZE.00	[M]Calcifying odontogenic cyst

BBZF.00	[M]Ameloblastoma NOS
BBZF.11	[M]Adamantinoma NOS
BBZG.00	[M]Ameloblastoma, malignant
BBZG.11	[M]Adamantinoma, malignant
BBZH.00	[M]Odontoameloblastoma
BBZJ.00	[M]Squamous odontogenic tumour
BBZK.00	[M]Odontogenic myxoma
BBZK.11	[M]Odontogenic myxofibroma
BBZL.00	[M]Odontogenic fibroma NOS
BBZM.00	[M]Ameloblastic fibroma
BBZN.00	[M]Ameloblastic fibrosarcoma
BBZN.11	[M]Odontogenic fibrosarcoma
BBZP.00	[M]Calcifying epithelial odontogenic tumour
BBZz.00	[M]Odontogenic tumour NOS
BBa..00	[M]Miscellaneous tumours
BBa0.00	[M]Craniopharyngioma
BBa0.11	[M]Rathke's pouch tumour
BBa1.00	[M]Pinealoma
BBa2.00	[M]Pineocytoma
BBa3.00	[M]Pineoblastoma
BBa4.00	[M]Melanotic neuroectodermal tumour
BBa4.11	[M]Melanoameloblastoma
BBa4.12	[M]Melanotic progonoma
BBa4.13	[M]Retinal angle tumour
BBa5.00	[M]Chordoma
BBaz.00	[M]Miscellaneous tumour NOS

BBb..00	[M]Gliomas
BBb0.00	[M]Glioma, malignant
BBb0.11	[M]Glioma NOS
BBb0.12	[M]Gliosarcoma
BBb1.00	[M]Gliomatosis cerebri
BBb2.00	[M]Mixed glioma
BBb2.11	[M]Mixed glioma
BBb3.00	[M]Subependymal glioma
BBb3.11	[M]Subependymal astrocytoma NOS
BBb3.12	[M]Subependymal astrocytoma NOS
BBb3.13	[M]Subependymoma
BBb4.00	[M]Subependymal giant cell astrocytoma
BBb5.00	[M]Choroid plexus papilloma NOS
BBb6.00	[M]Choroid plexus papilloma, malignant
BBb7.00	[M]Ependymoma NOS
BBb8.00	[M]Ependymoma, anaplastic type
BBb8.11	[M]Ependymoblastoma
BBb9.00	[M]Papillary ependymoma
BBbA.00	[M]Myxopapillary ependymoma
BBbB.00	[M]Astrocytoma NOS
BBbB.11	[M]Astrocytic glioma
BBbB.12	[M]Astroganglioma
BBbC.00	[M]Astrocytoma, anaplastic type
BBbD.00	[M]Protoplasmic astrocytoma
BBbE.00	[M]Gemistocytic astrocytoma
BBbE.11	[M]Gemistocytoma

BBbF.00	[M]Fibrillary astrocytoma
BBbG.00	[M]Pilocytic astrocytoma
BBbG.11	[M]Juvenile astrocytoma
BBbG.12	[M]Piloid astrocytoma
BBbH.00	[M]Spongioblastoma NOS
BBbJ.00	[M]Spongioblastoma polare
BBbK.00	[M]Astroblastoma
BBbL.00	[M]Glioblastoma NOS
BBbL.11	[M]Glioblastoma multiforme
BBbL.12	[M]Spongioblastoma multiforme
BBbM.00	[M]Giant cell glioblastoma
BBbN.00	[M]Glioblastoma with sarcomatous component
BBbP.00	[M]Primitive polar spongioblastoma
BBbQ.00	[M]Oligodendroglioma NOS
BBbR.00	[M]Oligodendroglioma, anaplastic type
BBbS.00	[M]Oligodendroblastoma
BBbT.00	[M]Medulloblastoma NOS
BBbU.00	[M]Desmoplastic medulloblastoma
BBbV.00	[M]Medullomyoblastoma
BBbW.00	[M]Cerebellar sarcoma NOS
BBbX.00	[M]Monstrocellular sarcoma
BBbZ.00	[M]Pleomorphic xanthoastrocytoma
BBba.00	[M]Primitive neuroectodermal tumour
BBbz.00	[M]Glioma NOS
BBc..00	[M]Neuroepitheliomatous neoplasms
BBc0.00	[M]Ganglioneuromatous neoplasms

BBc1.00	[M]Neuroblastoma NOS
BBc1.11	[M]Sympathicoblastoma
BBc1.12	[M]Sympathicogonioma
BBc1.13	[M]Sympathogonioma
BBc2.00	[M]Medulloepithelioma NOS
BBc2.11	[M]Diktyoma
BBc3.00	[M]Teratoid medulloepithelioma
BBc4.00	[M]Neuroepithelioma NOS
BBc5.00	[M]Spongioneuroblastoma
BBc6.00	[M]Ganglioglioma
BBc6.11	[M]Glioneuroma
BBc7.00	[M]Neurocytoma
BBc7.11	[M]Neuroastrocytoma
BBc8.00	[M]Pacinian tumour
BBc9.00	[M]Retinoblastomas
BBcA.00	[M]Olfactory neurogenic tumour
BBcB.00	[M]Aesthesioneurocytoma
BBcC.00	[M]Aesthesioneuroblastoma
BBcC.11	[M]Olfactory neuroblastoma
BBcD.00	[M]Aesthesioneuroepithelioma
BBcD.11	[M]Olfactory neuroepithelioma
BBcz.00	[M]Neuroepitheliomatous neoplasm NOS
BBe..00	[M]Nerve sheath tumour
BBe1.00	[M]Neurofibromatosis NOS
BBe1.11	[M]Multiple neurofibromatosis
BBe2.00	[M]Neurofibrosarcoma

BBe5.11	[M]Acoustic neuroma
BBe5.13	[M]Schwannoma NOS
BBe6.00	[M]Neurinomatosis
BBe7.00	[M]Neurilemmoma, malignant
BBe7.11	[M]Schwannoma, malignant
BBe9.00	[M]Triton tumour, malignant
BBez.00	[M]Nerve sheath tumour NOS
BBf..00	[M]Granular cell tumours and alveolar soft part sarcoma
BBf0.00	[M]Granular cell tumour NOS
BBf1.00	[M]Granular cell tumour, malignant
BBf2.00	[M]Alveolar soft part sarcoma
BBfz.00	[M]Granular cell tumour or alveolar soft part sarcoma NOS
L241.00	Tumour of uterine body in pregnancy/childbirth/puerperium
L241000	Tumour of uterine body affecting obstetric care
L241100	Tumour of uterine body - baby delivered
L241200	Tumour of uterine body - baby delivered + p/n complication
L241300	Tumour of uterine body complicating a/n care, baby not deliv
L241400	Tumour of uterine body complic p/n care, baby prev delivered
L241z00	Uterine body tumour in pregnancy/childbirth/puerperium NOS

Consultation codes

Location code	Description

A	Clinic (often by nurse)
B	Night visit
C	Follow-up/ routine visit
D	Night visit
F	Night visit
G	Out of hours visit
H	Out of hours visit
I	Surgery Consultation
J	Telephone call from patient
K	Home visit
R	Emergency consultation
X	Home visit
Z	Walk in centre
9	Post-discharge review
a	Minor injury service
b	Community clinic
c	Night visit
d	Out of hours surgery visit
f	Telephone advice
g	Telephone consultation
i	Hotel visit
j	Nursing home visit
k	Residential home visit
l	Twilight visit
m	Out of hours visit

NLCA-HES linked dataset codes

OPCS-4 codes for potentially curative surgery

OPCS-4 code	Description
E391	Open excision of lesion of trachea
E398	Other specified partial excision of trachea
E399	Unspecified partial excision of trachea
E438	Other specified other open operations on trachea
E439	Unspecified other open operations on trachea
E461	Sleeve resection of bronchus and anastomosis HFQ
E463	Excision of lesion of bronchus NEC
E468	Other specified partial extirpation of bronchus
E478	Other specified other open operations on bronchus
E528	Other specified other operations on bronchus
E529	Unspecified other operations on bronchus
E541	Total pneumonectomy
E542	Bilobectomy of lung
E543	Lobectomy of lung
E544	Excision of segment of lung
E545	Partial lobectomy of lung NEC
E548	Other specified excision of lung
E549	Unspecified excision of lung
E552	Open excision of lesion of lung
E558	Other specified open extirpation of lesion of lung
E559	Unspecified open extirpation of lesion of lung
E578	Other specified other open operations on lung
E598	Other specified other operations on lung

E599	Unspecified other operations on lung
T013	Excision of lesion of chest wall
T038	Other specified opening of chest
T039	Unspecified opening of chest
T058	Other specified other operations on chest wall
T059	Unspecified other operations on chest wall

NLCA coding for potentially curative surgery

Code	Description
E54.4A	Wedge resection of lesion of lung (segment)
E54.8A	Multiple wedges resected
E54.4B	Segmental resection
E54.8B	Sleeve resection
E54.8 + T01	Lung resection with resection of chest wall
E44.1	Carinal resection
E54.3	Lobectomy
E54.1	Pneumonectomy
E54.2	Bi-lobectomy
E57.4	Open operation on lung (Incision of lung NEC)
E57.8	Other open operation on lung

ICD-10 codes used to generate Charlson score

Myocardial infarction

I210 I211 I212 I213 I214 I219 I220 I221 I228 I229 I252

Congestive cardiac failure

I110 I130 I132 I500 I501 I509 I420 I425 I426 I427 I428 I429 I430 I431 I432 I438 I099

Peripheral vascular disease

I700 I701 I702 I708 I709 I710 I711 I712 I713 I714 I715 I716 I718 I719 I731 I738 I739 I771 I790 I792 K558 K559 K551 Z958 Z959

Cerebrovascular disease

I600 I601 I602 I603 I604 I605 I606 I607 I608 I609 I610 I611 I612 I613 I614 I615 I616 I618 I619 I620 I621 I629 I630 I631 I632 I633 I634 I635 I636 I638 I639 I640 I650 I651 I652 I653 I658 I659 I660 I661 I662 I663 I664 I668 I669 I670 I671 I672 I673 I674 I675 I676 I677 I678 I679 I680 I681 I682 I688 I690 I691 I692 I693 I694 I698 G450 G451 G452 G453 G454 G458 G459 G460 G461 G462 G463 G464 G465 G466 G467 G468 H340

Dementia

F000 F001 F002 F009 F010 F011 F012 F013 F018 F019 F020 F021 F022 F023 F024 F028 F030 F051 G300 G301 G308 G309 G311

Chronic pulmonary disease

I278 I279 J400 J410 J411 J418 J420 J430 J431 J432 J438 J439 J440 J441 J448 J449 J450 J451 J458 J459 J460 J470 J600 J610 J620 J628 J630 J631 J632 J633 J634 J635 J638 J640 J650 J660 J661 J662 J668 J670 J671 J672 J673 J674 J675 J676 J677 J678 J679 J684J701 J703

Connective tissue disease

M050 M051 M052 M053 M058 M059 M060 M061 M062 M063 M064 M068 M069 M315 M320 M321 M328 M329 M330 M331 M332 M339 M340 M341 M342 M348 M349 M351 M353 M360

Peptic ulcer disease

K250 K251 K252 K253 K254 K255 K256 K257 K258 K259K260 K261 K262 K263 K264 K265 K266 K267 K268 K269K270 K271 K272 K273 K274 K275 K276 K277 K278 K279K280 K281 K282 K283 K284 K285 K286 K287 K288 K289

Diabetes mellitus

E100 E101 E109 E110 E111 E119 E120 E121 E129 E130 E131 E139 E140 E141 E149

Diabetes mellitus with end organ damage

E102 E103 E104 E105 E106 E107 E108 E112 E113 E114 E115 E116 E117 E118 E122 E123 E124 E125 E126 E127 E128 E132 E133 E134 E135 E136 E137 E138 E142 E143 E144 E145 E146 E147 E148

Hemiplegia

G041 G114 G801 G802 G830 G831 G832 G833 G839 G834 G810 G811 G819G820 G821 G822 G823 G824 G825

Moderate/severe renal failure

I120 N032 N033 N034 N035 N036 N037 N052 N053 N054 N055 N056 N057 N181 N182 N183 N184 N185 N189 N190 N250 Z490 Z491 Z492 Z940 Z992

Mild liver disease

B180 B181 B182 B188 B189 K702 K703 K709 K713 K714 K715 K717 K730 K731 K732 K738 K739 K743 K744 K745 K746 Z944 K760 K700 K701 K740 K741 K742

Moderate/severe liver disease

K766 I850 I859 I864 I982 K711 K704 K721 K729 K765 K767

AIDS

B200 B201 B202 B203 B204 B205 B206 B207 B208 B209 B210 B211 B212 B213 B217 B218 B219 B220 B221 B222 B227 B240

Any tumour

Excluded: C340 C341 C342 C343 C348 C349 (lung cancer)

C000 C001 C002 C003 C004 C005 C006 C008 C009 C010 C020 C021 C022 C023 C024 C028 C029 C030 C031 C039 C040 C041 C048 C049 C050 C051 C052 C058 C059 C060 C061 C062 C068 C069 C070 C080 C081 C088 C089 C090 C091 C098 C099 C100 C101 C102 C103 C104 C108 C109 C110 C111 C112 C113 C118 C119 C120 C131 C132 C138 C139 C140 C142 C148 C150 C151 C152 C153 C154 C155 C158 C159 C160 C161 C162 C163 C164 C165 C166 C168 C169 C170 C171 C172 C173 C178 C179 C180 C181 C182 C183 C184 C185 C186 C187 C188 C189 C190 C200 C210 C211 C212 C218 C220 C221 C222 C223 C224 C227 C229 C230 C240 C241 C248 C249 C250 C251 C252 C253 C254 C257 C258 C259 C260 C261 C268 C269 C300 C301 C310 C311 C312 C313 C318 C319 C320 C321 C322 C323 C328 C329 C330 C370 C380 C381 C382 C383 C384 C388 C390 C398 C399 C400 C401 C402 C403 C408 C409 C410 C411 C412 C413 C414 C418 C419 C431 C432 C433 C434 C435 C436 C437 C438 C439 C450 C451 C452 C457 C459 C460 C461 C462

C463 C467 C468 C469 C470 C471 C472 C473 C474 C475 C476 C478 C479 C480 C481 C482 C488 C490 C491 C492 C493 C494 C495 C496 C498 C499 C500 C501 C502 C503 C504 C505 C506 C508 C509 C510 C511 C512 C518 C519 C520 C530 C531 C538 C539 C540 C541 C542 C543 C548 C549 C550 C560 C570 C571 C572 C573 C574 C577 C578 C579 C580 C600 C601 C602 C608 C609 C610 C620 C621 C629 C630 C631 C632 C637 C638 C639 C640 C650 C660 C670 C671 C672 C673 C674 C675 C676 C677 C678 C679 C680 C681 C688 C689 C690 C691 C692 C693 C694 C695 C696 C698 C699 C700 C701 C709 C710 C711 C712 C713 C714 C715 C716 C717 C718 C719 C720 C721 C722 C723 C724 C725 C728 C729 C730 C740 C741 C749 C750 C751 C752 C753 C754 C755 C758 C759 C760 C761 C762 C763 C764 C765 C767 C768

Metastatic solid tumour

C770 C771 C772 C773 C774 C775 C778 C779 C780 C781 C782 C783 C784 C785 C786 C787 C788 C790 C791 C792 C793 C794 C795 C796 C797 C798 C799 C800 C809

Leukaemia

C910 C911 C913 C914 C915 C916 C917 C918 C919 C920 C921 C922 C923 C924 C925 C926 C927 C928 C929 C930 C931 C933 C937 C939 C940 C942 C943 C944 C946 C947 C950 C951 C957 C959 D450

Lymphoma

C810 C811 C812 C813 C814 C817 C819 C820 C821 C822 C823 C824 C825 C826 C827 C829 C830 C831 C833 C835 C837 C838 C839 C840 C841 C844 C845 C846 C847 C848 C849 C851 C852 C857 C859 C880 C900 C901 C902 C903 C960 C962 C964 C965 C966 C967 C968 C969

Appendix B: Supporting documentation related to Chapter 3 mixed-methods study

Direct line/e-mail

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25th August 2014

Dr Emma O'Dowd

Clinical Research Fellow

Epidemiology and Public Health

School of Medicine

Clinical Sciences Building

City Hospital Campus

Nottingham University



Faculty of Medicine and Health Sciences

Research Ethics Committee

School of Medicine Education Centre

B Floor Medical School

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Nottingham University Hospitals

Nottingham

NG7 2UH

Ethics Reference No: I14082014 SoM EPH – please always quote

Study Title: An exploration of attitudes to risk of lung cancer and uptake of lung cancer screening in at risk adults.

Short Title: Lung cancer risk

Chief Academic/Supervisor: Dr Manpreet Bains, Lecturer in qualitative research, Epidemiology & Public Health (EPH), School of Medicine, University of Nottingham (UoN).

Other key researchers/collaborators: Dr Josie Solomon, Joint Head of Postgraduate Pharmacy and CPD; Health and Life Sciences; De Montfort University, Leicester; Dr Richard Hubbard, Professor of Respiratory Epidemiology, Respiratory Medicine, School of Medicine UoN, Dr David Baldwin, Honorary Professor and Consultant Respiratory Physician, Dr Sadia Anwar, Consultant Respiratory Physician, City Hospital Campus Nottingham University Hospitals Trust, Dr Tricia McKeever, Associate Professor in epidemiology and Medical Statistics, EPH, School of Medicine UoN, Dr Emma O'Dowd, Clinical Research Fellow, School of Medicine, UoN. **Duration of Study:** 09/2014-08/2015 12mths **No of Subjects:** 36 (40+ yrs)

Thank you for submitting the above application which was considered by the Committee on 14th August 2014 and the following documents were received:

Lung cancer risk:

- FHMS Research Ethics Committee Application Form, version 1, Date 23/07/2014
- Protocol Final Version 1.0 23/07/2014
- Recruitment Poster version 1.0 23/07/2014
- Participant Information Sheet Final Version 1.0, 23/07/2014
- Consent Form Final version 1.0: date 23/07/2014
- Demographic Information Final Version 1.0 23/07/2014
- Focus Group Guide Final Version 1.0 23/07/2014
- "My health, my life" Scenarios for Focus Group Final version 1.0 23/07/2014

These have been reviewed and are satisfactory and the study is approved.

Approval is given on the understanding that the Conditions of Approval set out over the page are followed:

1. Please submit copies of letters of permission/support from the Community leaders when these are available for our records.
2. You must follow the protocol agreed and inform the Committee of any changes using a notification of amendment form (please request a form).
3. You must notify the Chair of any serious or unexpected event.
4. This study is approved for the period of active recruitment requested. The Committee also provides a further 5 year approval for any necessary work to be performed on the study which may arise in the process of publication and peer review.
5. An End of Project Progress Report is completed and returned when the study has finished (Please request a form).

Yours sincerely



Dr Clodagh Dugdale

Chair, Faculty of Medicine & Health Sciences Research Ethics Committee

Example of focus group advert





LET'S TALK ABOUT LUNG HEALTH

Researchers from the University of Nottingham would like to talk with local smokers and ex-smokers

WE NEED YOUR HELP

We want to hear your views on why you would or wouldn't go to see your doctor and what you know and think about screening for cancer

The setting is very informal and non-judgmental- **we want to hear your views not lecture you!**

The meeting will take place in your local area and you will receive a **£20** high street shopping voucher in recognition of giving up your free time to attend and refreshments will be provided

Applicants should be:
Smokers or ex-smokers aged 40 years and upwards

The next informal group discussion will take place from: **To be confirmed**

Interested in coming along?
Please phone or email Emma O'Dowd for more details.
Phone: 01158231717 Email: emma.o'dowd@nottingham.ac.uk

Title of the project: Attitudes to risk of lung cancer and uptake of lung cancer screening in at risk adults

Focus group facilitators: Emma O'Dowd, Manpreet Bains, Josie Solomon

Focus Group Guide

Introduction

- Introduce the interviewers.
- Briefly reiterate the purpose of the focus group.
- Whilst we would like you to be honest, at the same time we would like you to be comfortable, so please do not feel that you have to say anything if you don't want to.
- We will be voice recording the group so that we remember what you say later on.
- Statement on confidentiality:

We will keep your thoughts and opinions confidential. The voice recording of this focus group and any quotes which we might use in project reports will not identify you in any way. It is alright for you to stop taking part at any time without giving a reason.

- Ask if the participants have any questions before starting the focus group.
- Check that they are still happy to proceed and that the consent form has been signed.
- Ground rules:
    - Listen carefully to the questions.
    - Only one person talking at a time.
    - Listen to what each other says.

General discussion about health and life where they live

1. What is life like where you live?
2. What do you think about smoking in your area?

eg. Above average or about normal

3. Does this affect your health?

Barriers to diagnosis

4. How often do you go and see your GP?
5. Have you experienced any problems when you have tried to go and see your GP?
6. If you wouldn't go to the GP would you seek other health advice and if so from where (ED, 111 etc)?
7. If there is lots of resistance to seeking medical advice:
    a. Why would you not go and seek health advice?
    b. Is there anything that could be done to change this view?

Understanding and experience of lung cancer

8. What do you know about lung cancer?
    c. What causes do you know?
    d. What symptoms could be due to lung cancer?
    e. What symptoms would worry you?
    f. What about the prognosis if diagnosed?
9. Have you or anyone you know been affected by lung cancer?
    g. What happened?
    h. Did this change your knowledge of the condition and if so how?

Cancer screening programmes

10. Have you heard of any cancer screening programmes?
    a. Explore understanding of the programme(s) e.g. what's involved
11. How useful are screening programmes for cancer?
    a. Value for money
12. Have you taken part in screening? If yes, unpick thoughts about the experience.
13. If no:

a. How likely are you to attend a screening appointment, if you were invited?

b. What would make you take up a screening offer?

c. Can you think of anything that might prevent you from attending?

d. Would the distance you had to travel play a part?

Lung cancer screening

14. Have you heard anything about screening for lung cancer?

15. What do you think a screening programme for lung cancer would involve?

a. Briefly explain what it is likely to entail.

16. How useful would it be for you?

17. How would you feel if it was offered to you?

a. How likely is it that you would attend an appointment?

18. If no:

a. Why not?

b. Is there anything that could be done to change your mind?

19. What would be the best way to engage people and get them to take up the offer of lung cancer screening?

Summing up and conclusions

20. Has this group raised issues that you hadn't considered before?

21. Is there anything that you want to add based on what we have discussed?

22. Any questions?

23. Thank participants for their time.

Scenarios

If necessary to help prompt discussion of the themes listed above it may be necessary to use scenarios at the correct points during the above discussion format (see attached sheet for example scenarios). If discussion is flowing then the scenarios would not necessarily be utilised.

24. Example questions based on the scenarios:

a. What do you think each of these people would think and feel about their longer term health?

b. Do you think any of them are at risk of getting ill?

c. Do you think any of them are realistically at risk of getting lung cancer?

d. Do you think they would be interested in screening for lung cancer?

e. Thinking about yourself now, what's important to you in terms of your life and your health?

f. How would you feel if you were offered lung cancer screening?

Title of the project: Attitudes to risk of lung cancer and uptake of lung cancer screening

Name of investigators: Dr Emma O'Dowd, Dr Manpreet Bains, Dr Josie Solomon, Professor Richard Hubbard, Professor David Baldwin, Dr Tricia McKeever, Dr Sadia Anwar

PARTICIPANT INFORMATION SHEET

Final version 1.0; 23/07/2014

We would like to invite you to take part in our research project. Before you decide if you would like to join in it is important to understand why this project is being done and what it will involve for you. Please take the time to read the participant information sheet carefully. We are happy to answer any questions that you may have.

Why are we doing the project?

Recent studies have suggested that people in the UK have worse outcomes from lung cancer than in other countries and we are not sure why this is. We want to know what people understand about lung cancer, what signs or symptoms people find worrying and why they would or wouldn't go to see the doctor. It is possible that a screening test for lung cancer will be introduced in the UK and we are keen to find out whether people would be interested in this and whether they would participate in screening.

Why have I been invited to take part?

You are being asked because you currently smoke or have smoked in the past and lung cancer screening is likely to be offered to people who are current or ex-smokers.

Do I have to take part?

Participation is entirely voluntary. Once you have read this information sheet, and asked any questions that you might have, if you decide to take part, you will be asked to sign a consent form. You may withdraw from the study at any time and without giving a reason.

What do I have to do?

If you agree to take part we will contact you with the date and time of the group discussion in your local area. Each group will have between 8 and 12 people in it. Before you start, the researcher will explain what will happen and if you are still happy to take part you will need to sign a consent form. Your

group will be asked to talk about your understanding and (if relevant) any previous experiences of lung cancer, any barriers that you see to obtaining medical advice for worrying symptoms and to talk about lung cancer screening and any reasons why you would or wouldn't participate. The group discussion should take between 60 and 90 minutes. A voice recorder will be used to record what the group says so that the researcher asking the questions does not have to take notes.

Expenses and payments

You will be offered light refreshments during the focus group (tea, coffee, juice and biscuits) and you will receive a £20 shopping voucher in recognition of giving up your free time to attend.

What are the possible advantages/ disadvantages of taking part?

Your views about lung cancer, access to healthcare and cancer screening will help us to understand how a screening programme might be put in place in the future and what changes, if any, need to be made to the healthcare system. There are no foreseeable disadvantages of taking part.

What if there is a problem or something goes wrong?

If you have any problems about the project you should ask to speak to one of the researchers who will do their best to answer your questions. In case you have a complaint on your treatment by a member of staff or anything to do with the study, you can initially approach the lead investigator, contact details at the end of this sheet. If this achieves no satisfactory outcome, you should then contact the Faculty of Medicine & Health Sciences Research Ethics Committee Administrator, c/o The University of Nottingham, School of Medicine Education Centre, B Floor, Medical School, Queen's Medical Centre Campus, Nottingham University Hospitals, Nottingham, NG7 2UH. E-mail: louise.sabir@nottingham.ac.uk.

What will happen to the results of the study?

The voice recordings from the small group discussions will be analysed by the research team to see what opinions the group had about the issues and topics discussed. All information collected is strictly confidential and any personal information will be deleted from transcripts of the group discussions. Quotes used in any reports or publications will not identify you in any way. The voice recordings will be kept securely by Emma O'Dowd, who is one of the researchers conducting this project, at the University of Nottingham in a locked filing cabinet and on a password-protected computer.

The results may be presented in scientific journals and at conferences. If you would like to receive a summary of the results please let us know, however please bear in mind that this may be some time after your participation as the results have to be analysed.

All research data will be kept securely for 7 years. After this time your data will be disposed of securely. During this time all precautions will be taken by all those involved to maintain your confidentiality, only members of the research team will have access to your personal data.

Who is funding and who has reviewed this project?

This study is funded by the Roy Castle Lung Cancer Foundation and will be conducted by researchers from the University of Nottingham. This project has been approved by the University of Nottingham Medical School Ethics Committee.

Who can I contact for more information?

Emma O'Dowd	**Manpreet Bains**
University of Nottingham	University of Nottingham
Division of Epidemiology and Public Health	Division of Epidemiology and Public Health
Clinical Sciences Building	Clinical Sciences Building
Nottingham City Hospital	Nottingham City Hospital
Nottingham	Nottingham
NG5 1PB	NG5 1PB
Tel: 0115 8231717	Tel: 0115 8231360
Email: emma.o'dowd@nottingham.ac.uk	Email: manpreet.bains@nottingham.ac.uk

Thank you for reading this information sheet and considering taking part in this project.

Please keep a copy of the information sheet

CONSENT FORM

Final version 1.0: date 23/07/2014

Title of Study: An exploration of attitudes to risk of lung cancer and uptake of lung cancer screening in at risk adults

REC ref: I14082014 SoM EPH

Name of Researchers: Dr Emma O'Dowd, Dr Manpreet Bains, Dr Josie Solomon, Professor Richard Hubbard, Professor David Baldwin, Dr Tricia McKeever, Dr Sadia Anwar

Name of Participant: **Please initial box**

1. I confirm that I have read and understand the information sheet version number 1.0 dated 23/07/2014 for the above study and have had the opportunity to ask questions. ☐

2. I understand that my participation is voluntary and that I am free to withdraw at any time, without giving any reason. I understand that should I withdraw then the information collected so far cannot be erased and that this information may still be used in the project analysis. ☐

3. I understand that relevant sections of my data collected in the study may be looked at by the research group and by other responsible individuals for monitoring and audit purposes. I give permission for these individuals to have access to these records and to collect, store, analyse and publish information obtained from my participation in this study. I understand that my personal details will be kept confidential. ☐

4. I understand that the focus group will be audio recorded and that anonymous direct quotes from the focus group may be used in the study reports. ☐

5. I understand that all data will be anonymous and confidential with the exception of information being revealed which may need reporting (i.e. potential risks to another person or to myself, criminal behaviour). ☐

6. I agree to maintain the confidentiality of focus group discussions. ☐

7. I understand that confidentiality cannot be guaranteed during the focus group ☐

8. I understand that information about me recorded during the study will be kept in a secure database. If the data is transferred is will be made anonymous. Data will be kept for 7 years after the study has ended and then securely destroyed. ☐

9. I agree to take part in the above study. ☐

_____ _____ _____

Name of Participant Date Signature

_____ _____ _____

Name of Person taking consent Date Signature

2 copies: 1 for participant, 1 for the project notes.

Copy of questionnaire used

Lung Health Questionnaire

Thank you for taking the time to fill in this questionnaire. We are very interested in hearing your views and all information is strictly confidential and will be anonymised. Please tick the box or boxes that best describe your answer for each of questions 1-6. Please feel free to add additional comments if you feel that they are needed.

1. In the healthcare system, do you feel that smokers are blamed for their illnesses?

Never ☐ Rarely ☐ Some of the time ☐
Always ☐

Other comments

2. Based on your response to question 1, do you feel that this affects how likely you are to seek medical attention if you are worried about your health?

Would never put me off ☐ Would rarely put me off ☐ Would sometimes put me off ☐

Would always put me off ☐

Other comments

3. Have you attended for screening for any of the following conditions? Please tick whichever are relevant.

Men and women Bowel ☐

Women only Breast (mammogram) ☐
Cervical (smear) ☐

Other comments

4. The government are thinking of introducing screening for lung cancer which would involve a detailed scan of the chest. They are not sure yet where this test would take place or how you would be invited to take part.

    a. Would you ever take part in lung cancer screening?

Yes definitely ☐ Possibly ☐ Unsure ☐ Probably not ☐ Never ☐

Please explain why or why not

    b. What would be your preferred way for screening to take place (Please tick as many as are relevant)?

Drop in session in the community ☐ Drop in session at the hospital ☐

Appointment for scan in community ☐ Appointment for scan at hospital ☐

Other comments

5. We have asked lots of people for their opinions on screening for lung cancer. Below are some of their comments. Please could you tick which, if any, comments you agree with?

“I don’t want to know” ☐

“Unless it's life threatening I'll just wait” ☐

“I think it's really frightening” ☐

“I feel that I'm being targeted and picked on….” because I’m a smoker ☐

“They're going to try and make me stop smoking and I don't want to” ☐

“I think you need to have an amnesty that you can come and be seen and you won't be judged” ☐

“I don't see the benefit” ☐

“I wouldn't mind being screened, but not if I've got to stand in front of somebody who's not smoked or is judgemental” ☐

“If I was going to get lung cancer I'd have it by now” ☐

“If I'm going to get lung cancer I would start to get symptoms, I don't have symptoms” ☐

“I don't want to have unnecessary x-rays” ☐

“I think it should be done now” ☐

6. Have you or has anyone close to you suffered from lung cancer?

Yes ☐ No ☐

Other comments

Finally some questions about you. Again please tick the box that best fits.

7. How old are you?

40-45 ☐ 46-50 ☐ 51-55 ☐ 56-60 ☐ 61-65 ☐ 66-70 ☐ >70 ☐

8. What sex are you?

Male ☐ Female ☐

9. Are you a smoker or ex-smoker?

Smoker ☐ Ex-smoker ☐

10. How many do/ did you smoke in a normal day?

<5 ☐ 5-10 ☐ 11-15 ☐ 16-20 ☐ 21-30 ☐ >30 ☐

Thank you for taking the time to fill in the questionnaire.

Prize draw

We are holding a prize draw for all who fill in and return this questionnaire (3 prizes of high street shopping vouchers- £80, £40 and £20). If you would like to be entered into this draw please give your name and contact number/ email below (this part will be removed so that your answers remain anonymous).

Name ……

Phone number/ email address

……

If you require any additional information or have any concerns please contact:

Emma O'Dowd

Tel: 0115 8231717

Email: emma.o'dowd@nottingham.ac.uk

Appendix C: Media arising from work published in Chapter 4

Radio, TV and newspaper/online publications arising from Thorax paper (October 2014)

Television interview

Sky News (broadcast 14/10/2014)

Radio interviews (All 14/10/2014)

Radio WM

Today Programme Radio 4

Scotland Today

BBC Radio Gloucester

BBC Radio Berkshire

BBC Tees

BBC Radio Nottingham

BBC Radio Derby

Radio 5Live

Siren FM, Lincolnshire

Newspaper/ online (National publications)

BBC News online (http://www.bbc.co.uk/news/health-29596645) 14/10/2014

The Mirror (http://www.mirror.co.uk/lifestyle/health/lung-cancer-deaths-high-because-4433357) 14/10/2014

Daily Mail (http://www.dailymail.co.uk/health/article-2791764/lung-cancer-diagnoses-far-late-patients-condition-diagnosed-just-90-days-die.html (14/10/2014)

Express (http://www.express.co.uk/life-style/health/522288/GPs-fail-to-spot-lung-cancer) 14/10/2014

Pulse (http://www.pulsetoday.co.uk/clinical/therapy-areas/cancer/frequent-gp-visits-linked-to-late-lung-cancer-diagnosis/20008179.article#.VEYkEBZ5HK0) 14/10/2014

Medscape (http://www.medscape.com/viewarticle/833348) 16/10/2014

Journal News summary

The Lancet Oncology News- Late detection of lung cancer

(239)(http://dx.doi.org/10.1016/S1470-2045(14)70371-7)

Appendix D: Poster and oral presentations at conferences and prizes awarded during research time

Poster presentations

Place and cause of death in patients with lung cancer in the United Kingdom

O'Dowd E, McKeever T, Baldwin D, Hubbard R.

IASLC 16th World Conference on Lung Cancer. Denver (Sept 2015)

Validation of a surgical predictive score for lung cancer.

O'Dowd E, McKeever T, Baldwin D, Powell H, Hubbard R.

British Thoracic Oncology Group Meeting (January 2015)

Predictors of early death from lung cancer in Primary Care in the United Kingdom

O'Dowd EL, McKeever TM, Baldwin DR, Anwar S, Powell HA, Gibson JE, Iyen-Omofoman B, Hubbard RB.

American Thoracic Society Conference (May 2014)

Predictors of early death from lung cancer in Primary Care in the United Kingdom

O'Dowd EL, McKeever TM, Baldwin DR, Anwar S, Powell HA, Gibson JE, Iyen-Omofoman B, Hubbard RB.

British Thoracic Oncology Group Meeting (January 2014)

Is PET-CT sufficient to exclude asymptomatic brain metastases prior to radical surgical treatment for lung cancer?

O'Dowd E, Hutchinson J, George L, Baldwin D, Anwar S

British Thoracic Oncology Group Meeting (Jan 2013)

Oral presentations

Validation of a Surgical Predictive Score for 90 Day Mortality in Lung Cancer and Comparison with Thoracoscore

O'Dowd E, McKeever T, Baldwin D, Powell H, Hubbard R. IASLC 16th World Conference on Lung Cancer. Denver (Sept 2015)

Place and cause of death in patients with lung cancer in the United Kingdom

O'Dowd E, McKeever T, Baldwin D, Anwar S, Hubbard R. British Thoracic Oncology Group Meeting (Jan 2015)

Prizes

- President's Prize- East Midlands Thoracic Society Meeting (Sept 2015)
- School of Medicine Post Graduate Research Oral Presentation Event Second Prize (Feb 2015)
- Runner up poster prize – 13th Annual British Thoracic Oncology Group conference (January 2015)