# Validation of the National Lung Cancer Audit database and analysis of the information it contains.

Dr Anna Rich MA, MRCP

MEDICAL LIBRARY
QUEENS MEDICAL CENTRE

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**Abstract**

**Introduction**

Lung cancer is the commonest cause of cancer related death in men and women in England. In 2004 the National Lung Cancer Audit (NLCA) was created, as a national non-mandatory contemporary dataset of clinical features of individuals with lung cancer in part to identify variations in clinical practice and outcomes. The main aims of this dissertation are to determine the validity and representativeness of this dataset and then to investigate what factors influence access to surgery and chemotherapy and subsequent survival. In addition I have taken the opportunity afforded by this large dataset to describe the natural history of lung cancer in young adults (20-40 years).

**Methods**

In order to establish if the dataset was representative, I created a measure of case ascertainment at the level of an NHS Trust, and examined the distribution of patient features and outcomes for varying levels of case ascertainment.

I have then quantified the impact of patient and NHS Trust level features on access to surgery in people with non-small cell lung cancer and access to chemotherapy in people with small cell lung cancer using multivariate logistic regression. I have also conducted a series of survival analyses using Cox regression.

**Results**

I have found no evidence that patient features vary systematically according to levels of case ascertainment in the NLCA.

Age, sex, performance status, stage and co-morbidity all influenced the likelihood of having surgery for people with non-small cell lung cancer. Those patients first seen in a thoracic surgical centre where more likely to receive surgery than patients seen at peripheral centres (adjusted OR 1.51, 95% CI 1.16, 1.97), and surgery had a significant benefit on mortality (adjusted HR 0.41, 95% CI 0.39, 0.44). Although the resection rate was higher for patients first seen at a surgical centre (17% v 12%) these patients did equally well after surgery suggesting they were not a higher risk group.

Individuals with small cell lung cancer first seen in a hospital with a high participation in clinical trials, (>5% of expected lung cancer patients being

entered into clinical trials), were more likely to receive chemotherapy (adjusted OR 1.42, 95% CI 1.06, 1.90). Chemotherapy was associated with an improvement in survival (adjusted HR 0.51, 95% CI 0.46, 0.56), and amongst those patients receiving chemotherapy, mortality was not affected by the trial status of the hospital where they were first seen. In limited stage small cell disease, those patients who had chemo-radiotherapy had an improved survival compared with those patients who received chemotherapy alone (adjusted HR 0.72, 95% CI 0.62, 0.84).

This dataset of English patients with lung cancer contains one of the largest cohorts of young adults (20-40 years) with lung cancer (N=583). I have been able to demonstrate that the majority present with a good performance status (0 or 1 in 80% of those with PS recorded), but advanced (stage IV) disease at diagnosis (55% of those with stage recorded). Those who have surgery have a survival profile similar to their older counterparts.

**Conclusion**

The National Lung Cancer Audit is a representative, contemporary cohort of people with lung cancer, which can provide valuable information for health service research in lung cancer. I have found evidence that there is variation in access to treatment based on the facilities or the performance of individual NHS Trusts. My results suggest that by improving access to thoracic surgery for those individuals with non-small cell lung cancer we may be able to raise the resection rate and improve five year survival. The pattern is similar for people with small cell lung cancer and access to chemotherapy.

What this research cannot explain is the aetiology for this variation, and where in the diagnostic pathway changes need to be made to improve the active management and access to potentially curative regimes. As the audit matures with more detailed information on NHS Trust level care, further analyses will be possible to try and determine more clearly what explains these variations, and how we might intervene to reduce them.

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**Publications arising**

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**Table of contents**

Abstract ..... i

Acknowledgements ..... iii

Publications arising ..... iv

Conference contributions ..... iv

Table of contents ..... v

Abbreviations ..... xiii

List of Tables ..... xv

List of Figures ..... xix

Chapter one: Introduction ..... 1

Introduction ..... 2

Lung cancer in England and Wales ..... 2

1.1 Epidemiology ..... 2

1.1.1 Histology ..... 3

1.1.2 Survival ..... 3

1.1.3 Race and Ethnicity ..... 4

1.1.4 Socioeconomic status ..... 5

1.1.5 Worldwide ..... 5

1.1.6 Historical information relating to lung cancer and smoking ..... 6

1.2 Comparison with international data; European and North American ..... 8

1.3 Department of Health initiatives to address lung cancer care ..... 9

1.3.1 Lung Cancer Audit (1999) (23) ..... 10

1.3.2 The NHS Cancer Plan (2000) (24) ..... 11

1.3.3 Cancer Reform Strategy (2007) (27) ..... 12

1.4 National audit changing practice ..... 15

1.4.1 Stroke ..... 15

1.5 Thesis plan ..... 16

1.6 Chapter outline (dataset used) ..... 18

Chapter Two: Needs Assessment of the NICE Lung Cancer Update 2011 ..... 20

2.1 Introduction ..... 21

2.2 Needs Assessment ..... 22

2.2.1 Incidence ..... 24

2.2.2 Sex variation ..... 25

2.2.3 Histological subtypes ..... 26

2.2.4 Socio-econom ic status (SES) ..... 29

2.2.5 Ethnic variation ..... 31

2.2.6 Stage and Performance status ..... 32

2.2.7 Treatment received ..... 35

2.2.7.1 Surgery ..... 35

2.2.7.2 Chemotherapy ..... 39

2.2.7.3 Radiotherapy ..... 41

2.2.8 Survival ..... 42

2.2.8.1 One year survival ..... 46

2.2.8.2 Five year survival ..... 47

2.3 Facilities available at NHS Trusts in England and Wales ..... 48

2.3.1 Lung Cancer Specialist Nurses ..... 50

2.3.2 Access to diagnostic and endobronchial therapeutic facilities ..... 52

2.3.3 PET scanning ..... 54

2.3.4 Pathological services ..... 55

2.3.5 Pulmonary rehabilitation services ..... 55

2.3.6 Access to treatment facilities ..... 56

Chapter Three: Description and initial validation of the NLCA dataset ..... 59

3.1 Introduction ..... 60

3.2 Methods ..... 61

3.2.1 The NLCA dataset ..... 61

3.2.1.1 Data collection and the NLCA population ..... 61

3.2.1.2 Data cleaning ..... 62

3.2.2 Examining the data based on NHS Trust size using funnel plots ..... 65

3.2.3 Creating a measure of case ascertainment for each NHS Trust ..... 66

3.2.3.1 Using data from the Office of National Statistics ..... 66

3.2.3.2 Using data from Hospital Episode Statistics (HES) ..... 68

3.2.3.3 Comparing the level of agreement between NHS Stratification derived using data from ONS and HES ..... 70

3.2.4 Assessing the accuracy of NLCA to provide observed cases ..... 70

3.3 Results ..... 71

3.3.1 Results of Funnel plots ..... 71

3.3.2 Results of case ascertainment ..... 75

3.3.2.1 Observed:expected ratios at the level of PCT using ONS data ..... 75

3.3.2.2 Observed:expected ratios at the level of NHS Trusts ..... 76

3.3.2.3 Observed:expected ratios for NHS Trusts using HES data ..... 77

3.3.3 Comparing the NHS Trust strata created via these two methods ..... 78

3.3.4 Result of the observed cases of lung cancer (postal request) ..... 80

3.4 Discussion ..... 81

Chapter Four: Validating the NLCA using Cancer Registry data ..... 82

4.1 Introduction ..... 83

4.2 Methods ..... 84

4.2.1 Description of data entry into NLCA ..... 84

4.2.2 Observed:Expected ratios: Case ascertainment ..... 84

4.2.3 Access to curative or active palliative treatment ..... 85

4.2.4 Socio-economic status and the receipt of specific treatments ..... 85

4.2.5 Evaluating patient survival ..... 86

4.2.6 Comparison of NHS Trust strata with previous estimations using data from ONS and HES ..... 86

4.3 Results ..... 87

4.3.1 Overall cohort analysis ..... 87

4.3.2 Observed:expected ratios: results of case ascertainment ..... 87

4.3.3 Access to curative and active palliative treatment ..... 90

4.3.4 Socio-economic status and receipt of specific treatments ..... 93

4.3.5 Patient Survival ..... 97

4.3.6 Results of NHS Trust stratification using different data sources ..... 99

4.4 Discussion ..... 100

4.4.1 Overall summary ..... 100

4.4.2 Strengths and weaknesses ..... 100

4.4.3 Comparison with other studies ..... 101

4.4.4 Implications of this study ..... 103

Chapter five: Linking the National Lung Cancer Audit with Hospital Episode Statistics (HES) ..... 104

5.1 Introduction ..... 105

5.2 Methods ..... 107

5.2.1 Patient features within National Lung Cancer Audit (NLCA) ..... 107

5.2.2 Patient features within Hospital Episode Statistics (HES) ..... 107

5.2.3 NHS Trust features ..... 112

5.2.3.1 Cardio-thoracic surgical centres ..... 112

5.2.3.2 Radiotherapy centres ..... 112

5.2.3.3 Clinical trial entry data ..... 112

5.2.3.4 Peer Review ..... 113

5.2.4 Outcome measures ..... 114

5.2.4.1 Treatment received ..... 114

5.2.4.2 Overall survival ..... 115

5.2.5 Analysis plan ..... 116

5.3 Results ..... 118

5.3.1 Patient features within NLCA ..... 118

5.3.2 Patient features within Hospital Episode Statistics (HES) ..... 124

5.3.3 NHS Trust features ..... 140

5.3.4 Outcome measures ..... 143

5.3.4.1 Treatment ..... 143

5.3.4.2 Survival ..... 143

5.3.5 Summary of results ..... 145

5.4 Discussion ..... 146

5.4.1 Treatment received ..... 146

5.4.2 Survival ..... 149

Chapter six: Inequalities in outcomes for non-small cell lung cancer: the influence of clinical characteristics and features of the local lung cancer service ..... 150

6.1 Introduction ..... 151

6.2 Methods ..... 152

6.2.1 Surgery ..... 153

6.2.2 Survival ..... 153

6.3 Results ..... 154

6.3.1 Surgery ..... 154

6.3.2 Survival ..... 158

6.4 Discussion ..... 163

6.4.1 Principle findings ..... 163

6.4.2 Strengths and weaknesses ..... 164

6.4.3 Comparison with other studies ..... 165

6.4.4 Implications of this study ..... 166

Chapter seven: How do patient and hospital features influence outcomes in small cell lung cancer in England? ..... 168

7.1 Introduction ..... 169

7.2 Methods ..... 170

7.2.1 Chemotherapy ..... 170

7.2.2 Survival ..... 171

7.3 Results ..... 173

7.3.1 Chemotherapy ..... 173

7.3.2 Survival ..... 176

7.4 Discussion ..... 181

7.4.1 Principle findings ..... 181

7.4.2 Strengths and weaknesses ..... 181

7.4.3 Comparison with other studies ..... 182

7.4.4 Implications of this study ..... 184

Chapter eight: Lung cancer in young adults: a different disease entity? ..... 185

8.1 Introduction ..... 186

8.2 Methods ..... 187

8.2.1 Non-small cell lung cancer ..... 188

8.3 Results ..... 189

8.3.1 Treatment received ..... 196

8.3.2 Survival ..... 198

8.3.3 Non-small cell lung cancer ..... 201

8.4 Discussion ..... 205

8.4.1 Principle findings ..... 205

8.4.2 Strengths and weaknesses ..... 206

8.4.3 Comparison with other studies ..... 207

8.4.4 Implications of this study ..... 208

Chapter 9: Summary and future research ..... 210

9.1 Summary ..... 211

9.2 Future research ..... 212

Appendices ..... 215

Appendix 1: Tutorials ..... 216

Appendix 2: Scoping document for the NICE lung cancer update ..... 217

Appendix 3: NICE Lung cancer update 2010: ..... 222

Appendix 4: Letter sent to Lung cancer lead physicians ..... 225

Appendix 5: ICD-10 codes for diagnoses pertinent to the Charlson Index .. 226

Appendix 6: The key standards used in the Peer Review process 2003-07 . 235

Appendix 7: Postgraduate training courses ..... 236

References ..... 237

**Abbreviations**

| | |
|---|---|
| AIDS | Acquired Immuno-Deficiency Syndrome |
| BME | Black and Minority Ethnic groups |
| CANISC | Cancer Network Information System Cymru |
| CEEU | Clinical Effectiveness and Evaluation Unit |
| CHART | Continuous Hyperfractionated Accelerated RadioTherapy |
| CHI | Commission for Health Improvement |
| CI | Confidence Interval |
| COPD | Chronic obstructive pulmonary disease |
| CRS | Cancer Reform Strategy |
| CT | Computerised tomography |
| CT RTx | Chemo-radiotherapy |
| EBUS | EndoBronchial Ultra-Sound |
| ECOG | Eastern Cooperative Oncology Group |
| EUS | Endoscopic Ultra-Sound |
| FEV1 | Forced Expiratory Volume in 1 second (L/min) |
| FTE | Full Time Equivalent |
| GDG | Guideline Development Group |
| GP | General Practitioner |
| HES | Hospital Episode Statistics |
| HQuIP | Healthcare Quality Improvement Programme |
| IASLC | International Association for the Study of Lung Cancer |
| IC | Information Centre for Health and Social Care |
| ICD-10 | International Classification of Diseases version 10 |
| IHD | Ischaemic heart disease |
| IQR | Inter quartile range |
| LSOA | Lower Super Output Area |
| MDT | Multi-Disciplinary Team |
| MRC | Medical Research Council |

| | |
|---|---|
| NCAT | National Cancer Action Team |
| NCC-C | National Collaborating Centre for Cancer |
| NCIN | National Cancer Intelligence Network |
| NCRI | National Cancer Research Institute |
| NHS | National Health Service |
| NICE | National Institute for Health and Clinical Excellence |
| NLCA | National Lung Cancer Audit |
| NRT | Nicotine replacement therapy |
| NSCLC | Non-small cell lung cancer |
| NSCLC NOS | Non-small cell lung cancer not-otherwise specified |
| NSSG | Network Site-Specific Group |
| O:E | Observed:expected |
| ONS | Office of National Statistics |
| OPCS4 | Surgical Classification of Operations and Procedures version 4 |
| PCT | Primary Care Trust |
| PET-CT | Positron Emitting Tomography-Computerised Tomography |
| PS | Performance Status |
| RCP | Royal College of Physicians, London |
| SEER | Surveillance Epidemiology and End Results programme |
| SES | Socio-economic status |
| SHA | Strategic Health Authority |
| TBNA | Trans-Bronchial Needle Aspiration (ultra-sound guided) |
| UICC | Union Internationale Contre le Cancer |
| UK | United Kingdom |

## List of Tables

### Chapter 2


Table 2.1 Frequency of stage IV disease based on age groups in England and Wales (2006-08).

Table 2.2 Duties of a Specialist Lung Cancer nurse.


### Chapter 3


Table 3.1 Regional variation in lung cancer incidence (ONS 2005)

Table 3.2 Extract from HES detailing acute admissions within one SHA.

Table 3.3 Number of lung cancer patients in each SHA/Government region.

Table 3.4 Extract of table describing process of combining HES and ONS data.

Table 3.5 Comparison of NHS Trust strata created using ONS and HES data


### Chapter 4


Table 4.1 Distribution of key patient features for the overall cohort, and NHS Trust strata based case ascertainment

Table 4.2 Chi squared analyses for missing data and key patient variables by quartile of data completeness at NHS Trusts

Table 4.3 Logistic regression analyses of curative treatment; NHS Trust strata and key patient features.

Table 4.4 Logistic regression analyses of active palliative treatment; NHS Trust strata and key patient features.

Table 4.5 Logistic regression analyses for surgery in NSCLC only.

Table 4.6 Logistic regression analyses for chemotherapy.

Table 4.7 Logistic regression analyses for radiotherapy.

Table 4.8 Cox regression analyses for socio-economic status

Table 4.9 Results of uni and multivariate Cox regression analyses; using NHS Trust strata and key patient features.

Table 4.10 Concordance between ONS and Registry derived NHS Trust strata

Table 4.11 Concordance between HES and Registry derived NHS Trust strata

**Chapter 5**


Table 5.1 Illustrates the diseases used within the Charlson Index and the score assigned to each disease group.

Table 5.2 Final set of patient and NHS Trust features.

Table 5.3 Histological subtypes at diagnosis (N=80,966)

Table 5.4 Stage at diagnosis (N=80,966)

Table 5.5 Division of cohort into Charlson Index quintiles

Table 5.6 Logistic regression for Charlson Index and access to treatment.

Table 5.7 Results of Cox regression illustrating the influence of the Charlson Index on overall mortality (N=80,264)

Table 5.8 Number of patients with each disease group.

Table 5.9 Logistic regression for surgery in patients with NSCLC.

Table 5.10 Logistic regression for chemotherapy in patients with small cell lung cancer.

Table 5.11 Cox regression evaluating the influence of individual disease groups within the Charlson Index on overall survival (N=80,264).

Table 5.12 Admission time

Table 5.13 Results of multivariate logistic regression illustrating the influence of time in hospital pre-diagnosis with lung cancer on access to treatment.

Table 5.14 Cox regression evaluating the influence of admission time pre diagnosis on overall survival.

Table 5.15 Illustrates the detailed breakdown of ethnic group amongst this cohort of English lung cancer patients.

Table 5.16 Results of logistic regression assessing the influence of an overall Peer Review score on the likelihood of receiving treatment for lung cancer.

Table 5.17 Cox regression for overall score at Peer Review and overall mortality.

**Chapter 6**

Table 6.1 Results of logistic regression regarding the influence of patient features on likelihood of having surgery (clustered by NHS Trust).

Table 6.2 Results of Cox regression analyses using all patient features, all NHS Trusts level features, surgical intervention or not, and clustering by NHS Trust.

Table 6.3 Demographic features of patients with NSCLC based on where they are first seen.

Table 6.4 Cox regression for patients with proven NSCLC who received surgery, based on where they were first seen.

**Chapter 7**

Table 7.1 Distribution of Charlson Indices for the overall cohort of patients with lung cancer, and those with proven small cell lung cancer.

Table 7.2 Results of logistic regression analyses evaluating the influence of patient features on the likelihood of receiving chemotherapy.

Table 7.3 Results of Cox regression analyses evaluating the influence of patient and NHS Trust features on overall survival for patients with small cell lung cancer.

Table 7.4 Results of Cox regression analyses assessing the influence of chemo-radiotherapy versus other treatment regimes.

Table 7.5 Demographic features of patients with small cell lung cancer based on where they were first seen.

**Chapter 8**

Table 8.1 Histological subtypes based on age

Table 8.2 Distribution of stage at presentation across age groups.

Table 8.3 Distribution of disease groups in young adult subgroup.

Table 8.4 Logistic regression analyses examining the influence of age on access to treatment.

Table 8.5 Cox regression analyses assessing the influence of age on overall survival.

Table 8.6 Cox regression for all individuals excluding those with carcinoid disease.

Table 8.7 Cox regression for those individuals with proven non-small cell lung cancer.

Table 8.8 Cox regression for those individuals with proven small cell lung cancer

Table 8.9 Cox regression for those individuals with "missing" data for histology.

Table 8.10 Distribution of stage in proven NSCLC patients across age groups.

Table 8.11 Cox regression analyses of the subgroup of patients with proven NSCLC who underwent surgical resection.

## List of Figures

### Chapter 2


Figure 2.1 Age-standardised incidence rates in the European Union (2000); Reproduced with the permission of Cancer Research UK.

Figure 2.2 Rates of smoking and incidence of lung cancer in England and Wales 1975-2005. Reproduced with the permission of Cancer Research UK

Figure 2.3 Histological subtypes in proven primary lung cancer; NLCA (England and Wales) 2010.

Figure 2.4 Subgroups of non-small cell lung cancer in England and Wales (N=32,432; NLCA 2006-08).

Figure 2.5 Age-standardised incidence rates (per 100,000) across quintiles of socio-economic status (Reproduced by kind permission of NCIN).

Figure 2.6 Variation in age-standardised relative male survival at 1 and 3 years by major ethnic groups in England and Wales (Reproduced by kind permission of NCIN).

Figure 2.7 Stage at presentation in those patients with stage recorded (N=40,492). NLCA (England and Wales) 2006-08.

Figure 2.8 Variation in performance status at diagnosis based on patient age group (N=46,897). NLCA (England and Wales) 2006-08.

Figure 2.9 Proportion of patients with proven NSCLC receiving surgery in England and Wales based on age (N=3998).

Figure 2.10 Number of resections for primary lung cancer at surgical centres in Great Britain and Northern Ireland (Reproduced by kind permission of Society of Cardiothoracic Surgery - Data 2005-08).

Figure 2.11 Types of resection for primary lung cancer at surgical centres in Great Britain and Northern Ireland (Reproduced by kind permission of Society of Cardiothoracic Surgery - Data 2005-08).

Figure 2.12 Proportion of patients with proven small cell lung cancer receiving chemotherapy in England and Wales based on age (N=4,530). Data from NLCA and CANISC (2006-08).

Figure 2.13 Proportion of patients with small cell lung cancer receiving chemotherapy at level of Cancer Network (England and Wales). Data provided by NLCA.

Figure 2.14 Proportion of overall cohort receiving radiotherapy in England and Wales based on age (N=73,730). Data from NLCA and CANISC (2006-08)

Figure 2.15 Kaplan-Meier curve demonstrating overall survival of English patients with lung cancer (N=67,730). NLCA (2006-08).

Figure 2.16 Kaplan-Meier curve demonstrating the variation in survival based on whether data is entered on histology in NLCA (N=67,730).

Figure 2.17 Kaplan-Meier curve demonstrating the observed outcome of a subgroup of patients with proven NSCLC, stage IA-IIB, and performance status 0-1. (England only).

Figure 2.18 One year survival data for England and Wales (2006-08).

Figure 2.19 Five year survival data over time. Reproduced with kind permission of Cancer Research UK.

Figure 2.20 Number of (FTE) specialist nurses at NHS Trusts in England.

Figure 2.21 The variation in workload of new patients per (FTE) specialist nurse. (England only data).

Figure 2.22 Endobronchial diagnostic facilities available at an NHS Trust (Survey data)

Figure 2.23 Endobronchial diagnostic facilities available within a Cancer Network (England only data).

Figure 2.24 Distance required to access certain diagnostic and therapeutic services.

Figure 2.25 Interval between referral and access for certain diagnostic and therapeutic services.

Figure 2.26 Proportion of NHS Trusts and Cancer Networks with PET scanners (England only data).

Figure 2.27 Distance travelled to access a PET scanner (England only data).

Figure 2.28 Interval between referral and access to PET scanning (England only data).

Figure 2.29 Proportion of NHS Trusts and Cancer Networks with pulmonary rehabilitation services (England only data).

Figure 2.30 Treatment facilities available at an NHS Trust (England only data).

Figure 2.31 Treatment facilities available within a Cancer Network (England only data).

Figure 2.32 Distance required to access specific treatment modalities (England only data).

Figure 2.33 Interval between referral and access to specific treatment modalities (England only data).

**Chapter 3**


Figure 3.1 Flow diagram depicting the method used to calculate the start date.

Figure 3.2 Diagram illustrating the median intervals between key dates in the patient pathway.

Figure 3.3 Scatter plot illustrating the distribution of sex depending on "size" of NHS Trust.

Figure 3.4 Scatter plot illustrating the distribution of mean age depending on "size" of NHS Trust.

Figure 3.5 Scatter plot illustrating the proportion of patients over the age of 80 years depending on "size" of NHS Trust.

Figure 3.6 Scatter plot illustrating the proportion of patients with a histological diagnosis depending on "size" of NHS Trust.

Figure 3.7 Scatter plot illustrating the proportion of patients with early stage disease (Ia-IIIa) depending on "size" of NHS Trust.

Figure 3.8 Scatter plot illustrating the proportion of patients with curative treatment intent depending on "size" of NHS Trust.

Figure 3.9 Histogram depicting the range of O:E ratios across primary care trusts (PCTs) using data from ONS

Figure 3.10 Histogram depicting the range of O:E ratios across NHS Trusts created via mapping technique from PCT O:E ratios.

Figure 3.11 Histogram depicting the range of O:E ratios across NHS Trusts created using data from HES

Figure 3.12 Bland-Altman plot depicting the comparison between ONS and HES methods for calculating O:E ratios for NHS Trusts

Figure 3.13 Scatter plot depicting the relationship between observed cases of lung cancer in 2007, reported directly from NHS Trusts, or in NLCA

**Chapter 5**


Figure 5.1 Histogram showing range in proportion of patients entered into clinical trials.

Figure 5.2 Relationship between Audit variables pertaining to surgery.

Figure 5.3 Illustrates performance status at diagnosis if recorded (N=49,076)

Figure 5.4 Histogram illustrating the variation in basic spirometry.

Figure 5.5 Distribution of socio-economic status using Townsend quintiles in the English cohort of patients with lung cancer.

Figure 5.6 Distribution of performance status across each Townsend quintile.

Figure 5.7 Distribution of stage across each Townsend quintile.

Figure 5.8 Histogram showing the distribution of Charlson Indices at diagnosis.

Figure 5.9 Distribution of Charlson Indices across Townsend quintiles.

Figure 5.10 Histogram illustrating the ethnic composition of this cohort.

Figure 5.11 Histogram illustrating the variation in success at Peer Review.

Figure 5.12 Kaplan-Meier survival curve based on histology

Figure 5.13 Kaplan-Meier survival curve based on stage at diagnosis

Figure 5.14 Kaplan-Meier survival curve based on Charlson Index at diagnosis.


**Chapter 7**


Figure 7.1 Kaplan-Meier survival curve comparing the observed survival in those who did, compared with those who did not, have chemotherapy.


**Chapter 8**


Figure 8.1 Flow diagram depicting the method used to calculate "start" dates.

Figure 8.2 Median intervals between dates along the patient pathway.

Figure 8.3 Histogram of age range in this young adult subgroup.

Figure 8.4 Distribution of performance status across age groups.

Figure 8.5 Distribution of Townsend quintiles across age groups (N=91,088).

Figure 8.6 Kaplan-Meier survival curve for individuals with NSCLC who have undergone surgical resection (N=5,013).

# Chapter one: Introduction

## Introduction

### Lung cancer in England and Wales

The aim of this MD is to examine a national dataset, evaluate its validity and then analyse the data within it, to assess how patient and hospital features influence treatment and survival for individuals with lung cancer in England. The aim of this chapter is to set the scene by describing the epidemiology of lung cancer nationally and internationally, and commenting on important Government initiatives that have been designed to improve the standard of care for individuals with lung cancer in England and Wales. The development of the National Lung Cancer Audit was driven by concerns that widespread inequality in lung cancer outcome existed in England. Data generated by the National Lung Cancer Audit have formed the basis for the analysis throughout this thesis.

### 1.1 Epidemiology

Lung cancer remains one of the leading causes of preventable death in the 21st century despite the knowledge of its aetiology, and the dramatic fall in smoking rates over the past three decades. More than 40,500 individuals are diagnosed with lung cancer each year in the United Kingdom (1). The incidence rate for lung cancer increased in men until the late 1980's and has gradually fallen since. In women the incidence overall has remained stable over the past two decades, but in women aged over 75 years the incidence has continued to rise (2). This trend in lung cancer incidence mirrors the pattern of smoking in the United Kingdom, with a 20 year lag phase (3). The prevalence of smoking in young middle aged men has halved between 1950 and 1990 (4), and the death rate from lung cancer (between the ages 35-54 years) has fallen even more sharply, suggesting a reduction in the risk for those who continued smoking too. The incidence of lung cancer in women has not begun to fall yet, and it remains the leading cause of cancer related mortality in women.

### 1.1.1 Histology

Lung cancer has four main groups of histology: squamous cell, adenocarcinoma, large cell and small cell carcinoma. These account for >90% of all lung cancers. Changes in the relative frequency of these different tumours have occurred over time, and world-wide adenocarcinoma has become the commonest type of lung cancer, above squamous cell carcinoma (3). The dose-response relationship between smoking and lung cancer is steepest for small cell carcinoma closely followed by squamous cell carcinoma, and there appears to be a link between adenocarcinoma and peripheral lesions, in contrast to squamous cell carcinoma and central lesions (3).

### 1.1.2 Survival

Survival from lung cancer remains poor, which is primarily related to late presentation of this aggressive disease, and the advanced stage of the disease at diagnosis which limits the treatment options. It is generally accepted that only a third of patients are potentially curable at diagnosis, in other words have localised disease and are fit enough to receive radical treatment. In these patients with Stage Ia or Ib disease, the five year survival figures are 54-80% and 38-65% respectively.

Survival figures in England and Wales from 2000-2001, suggest that 25% of men and 26% of women were alive a year after diagnosis. This is a dramatic improvement compared with the one year survival in 1971-76 of 15% and 13% respectively. However, five year survival has improved very little over the same timeframe. In 1971-76 the five year survival for men and women was 4%, and in 2000-01 it was 7% (5). This apparent discrepancy between one and five year survival may reflect a combination of improved diagnostic practice and better chemotherapy, so that whilst the majority of individuals have incurable disease

at diagnosis (and fail to survive five years), they may show partial response to chemotherapy and survive between one and two years from diagnosis.

Doll published evidence in 2005 which showed that the mortality rate of lung cancer in men in the UK is comparable with other economically equivalent European countries, whilst for women the UK has one of the highest mortality rates (6). However, Coleman et al have published data from several national cancer Registries which show higher mortality in England, Northern Ireland and Wales compared with Australia, Canada and several Scandinavian countries, regardless of sex. This was particularly relevant for the first year after diagnosis and for those individuals aged >65 years at diagnosis (7). Deaths within the first year of diagnosis suggest late presentation of lung cancer patients in the UK.

### 1.1.3 Race and Ethnicity

There is evidence from the Cancer Reform Strategy (CRS) Equality Impact Assessment (8) document that smoking levels are higher in Black and Minority Ethnic (BME) communities compared with the national average, and that the uptake of 'Stop smoking' services is low in these communities. There appears to be lower cancer mortality in these groups. This can be partially explained by the younger age profile, and the fact that some older patients will return to their country of birth to die. There is also evidence that individuals from these ethnic groups are underrepresented in cancer research. The reason for this is not clear. In England and Wales, individuals from the White-British race group are more likely than individuals from BME groups to attend screening programmes and to be referred under the two week wait system (8).

### 1.1.4 Socioeconomic status

In developed countries it has been noted that lung cancer is more common amongst individuals from lower socioeconomic classes (9, 10) and those who are less educated (11). In Canada, the risk of lung cancer in both sexes is inversely related to income, education, and social class even after adjustment for cigarette smoking (12). It has also been observed that those from lower socioeconomic classes present later and hence will have a worse prognosis. A difference of 1.4% in 5 year survival has been reported between individuals in the most affluent sections of society in England and Wales compared with those in the most deprived sections of society (5).

The CRS Equality Impact Assessment (8) reported several features relating to lung cancer, smoking and socioeconomic status. Lung cancer incidence in England and Wales is significantly higher in deprived groups compared with more affluent groups; and the prevalence of smoking is 29% in manual groups compared with 19% in non-manual groups. An encouraging finding was that the 'Stop smoking' services have been most successful in the most deprived areas of England and Wales.

### 1.1.5 Worldwide

Lung cancer is the most commonly diagnosed cancer worldwide, but there is marked regional variation in incidence. The areas with the highest incidence rate are the developed countries of North America, Europe, Australia and for men the former Soviet Union, whilst for women China is a country with a high incidence rate (13). Although diagnostic techniques and coding of cancer registrations will affect the reliability of this information, it is widely accepted that lung cancer remains a disease of developed countries. It is interesting to note that African-Americans have one of the highest incidence rates in the world

(3) despite Africa itself being a low incidence area. This suggests environmental factors play a much larger role than genetics, in the aetiology of lung cancer. In the past ten years much more has been understood about the molecular biology of lung cancers, and this has led to the production of novel targeted therapies including several epidermal growth factor receptor (EGFR) tyrosine kinase inhibitors (14), and vascular endothelial growth factor (VEGF) inhibitors (15).

### 1.1.6 Historical information relating to lung cancer and smoking

The increase in the incidence of lung cancer in England and Wales began in the first half of the 20th century. Doll reported a fifteen-fold increase in the annual number of deaths attributed to lung carcinoma between 1922 and 1947 (612 to 9,287 respectively) (16). Although some of this increase could be accounted for by the population increase, standardised death rates showed that this could not be the main cause for the increase. In 1901-20 the death rate for lung cancer in men was 1.1 per 100,000 and 0.7 per 100,000 in women. By 1936-39 this had increased to 10.6 and 2.5 per 100,000 respectively (17). This increase in deaths attributed to lung cancer was also reported in other European countries, North America, Australia and parts of south east Asia (16). Two main theories were offered for this increase in the incidence of lung cancer, namely atmospheric pollution (car exhaust fumes, coal fires and industrial plants), and smoking of tobacco. Although tobacco had been used for centuries, it was thought that the introduction of manufactured cigarettes in the 20th century, with addictive properties, led to a more sustained pattern of exposure which was the cause of the rise in lung cancer incidence.

In 1950, approximately 80% of men and 40% of women were smoking, and that same year Doll and Hill published the results of a case-control study, which included 709 patients with lung cancer and an equal number of age and sex

matched controls (16). In those patients with lung cancer, few were non-smokers and the majority of smokers fell into the 'heavier smoking' categories. In 1951 Doll and Hill began a longitudinal cohort study amongst doctors on the medical register in the United Kingdom. Questionnaires were completed which reported current smoking status, age of initial smoking, method of smoking and amount of tobacco consumed (18). A total of almost 35,000 male doctors were recruited, and their smoking habits as well as cause specific mortality have been monitored periodically until 2001, a total of fifty years. Excess mortality was associated with neoplastic, vascular and respiratory disease (19). The results showed that men born between 1900-30, who smoked cigarettes, died on average about ten years younger than lifelong non-smokers. The study also showed that the age at which smokers stopped affected the years of life expectancy that an individual could expect to gain: 3, 6, 9 and 10 years, if men stopped smoking at age 60, 50, 40 and 30 years respectively. The cohort has also revealed a progressive increase in the smoker *v* non-smoker death rate ratio at the end of the 20$^{th}$ century, with a three-fold death rate ratio in men surviving between the ages of 70-90 years.

The cause of death amongst this cohort of male doctors can be divided into three main groups: vascular (including ischaemic heart disease and cerebrovascular disease), neoplastic, and respiratory disease which accounted for 55%, 21% and 9% of the deaths respectively. Within the subgroup who died of a neoplastic process, lung cancer accounted for 20% of deaths. Doll reports that a quarter of the excess mortality amongst smokers is accounted for by lung cancer or chronic obstructive pulmonary disease (COPD), and a further quarter by ischaemic heart disease (IHD).

Since 1950 the prevalence of smoking has fallen steadily for men, reported as 36% in 2000, whilst the peak level of smoking in women did not occur until

1970, when 50% of women smoked, and by 2000 this level had fallen to 28% (4). Worldwide, approximately 30% of young adults become smokers, but in the U.K this figure is lower at 23%. A report from Peto et al in 2000, reported that mortality from smoking in the first half of the 21st century will be affected predominantly by the number of smokers who quit rather than by the number of young adults who start (4).

It is known that the risk of lung cancer is related to the duration of smoking and the number of cigarettes smoked per day. Whilst cigar and pipe smoking are linked to lung cancer, their influence is less than cigarettes; and this is thought to be due to differences in frequency and in the depth of inhalation. Smokers of any age can reduce their risk of lung cancer by quitting, and if this is achieved by middle-age, then almost 90% of the risk attributable to lung cancer can be avoided (4).

There have been a number of initiatives to reduce the public health impact of smoking. These include: filtered and low tar cigarettes, stronger advice warnings on packets, smoking cessation workshops, quit-lines, a ban on cigarette advertising at all sporting events, and in July 2007 the ban on smoking in all public places including workplaces, restaurants and pubs in England. Nicotine replacement therapy has also been a major advance in helping those individuals who are trying to quit smoking achieve long term cessation. A Cochrane review article in 2008 states that nicotine replacement therapy increases the chance of quitting by 50 to 70%, and this is true regardless of the type of replacement therapy used (20).

### 1.2 Comparison with International data; European and North American

There have been a number of European collaborations regarding cancer survival since 1999, EUROCARE 1-4. These studies incorporate data from 47 cancer

registries in 21 countries, and include 4 regional registries from England. The latest paper, EUROCARE-4 (21), was published in 2007, and used period analysis to report survival data. The relative 5 year survival for lung cancer across the U.K was reported as 8.4% in England, 10.4% in Wales, 8.2% in Scotland, 10.7% Northern Ireland, and 10.9% in the Republic of Ireland. The highest rate of 5 year survival for lung cancer was in central Europe, with a rate of 13.4%. There are also noted differences in lung cancer resection rates, which for the U.K. are quoted as 11%, compared with 17% for the rest of Europe and 21% for North America (5).

The Surveillance, Epidemiology and End Results (SEER) programme (22) in America is a registry linked dataset recording information on all cancers, including stage at diagnosis, and covers approximately 26% of the population of the United States. It produces statistical reports covering all cancers and includes data from 1973 onwards, with links to the National Longitudinal Mortality Study which provides socioeconomic and demographic information. The latest figures for 5 year survival for lung cancer in America are 13% for men and 17% for women (22).

An international benchmarking project is underway, using Registry data from six countries including the United Kingdom, Australia, Canada, Denmark, Sweden and Norway. The first results have been published and they confirm that the UK has the lowest lung cancer survival data of these countries, with a 5 year survival rate of 9% (7).

### 1.3 Department of Health initiatives to address lung cancer care

Despite a National Health Service that is free at point of access, medical professionals with a good reputation both clinically and for research, England and Wales have appeared to lag behind other European countries and North America

in terms of outcome measures for lung cancer. There have therefore been a number of government policy changes over the past 15 years which have tried to address inequalities in the system and to improve clinical standards across England and Wales. These policy documents and the establishment of the National Lung Cancer Audit are outlined below.

### 1.3.1 Lung Cancer Audit (1999) (23)

The Clinical Effectiveness and Evaluation Unit (CEEU) of the Royal College of Physicians of London produced an Internal Report funded by the Department of Health in August 1999. This document included the findings on 1600 patients from 48 National Health Service (NHS) Trusts in England, Wales and Northern Ireland. The patients were those on whom a bronchoscopy had been performed for suspected lung cancer, and the follow-up period was 6 months. Although the cohort is not adequate for definitive evaluations on treatment offered and survival, there were several observations of interest. The first was that more than a third of patients with suspected lung cancer were not referred directly by their General Practitioner (GP), but entered the lung cancer pathway via an alternative route. Another observation, linked with the 'process' of managing individuals with suspected lung cancer, was the variation and length of time between points along their pathway, for example bronchoscopy and the initiation of treatment. Both these points were addressed in "commitment 2" of the NHS Cancer Plan (24) (see below). It was also noted that for this specific cohort, those without a histological diagnosis at four weeks, two thirds failed to have any proven histology at six months. The results in this document were not published in a peer reviewed journal; but, as the first national audit addressing lung cancer care in the United Kingdom, it was a useful exercise which did produce evidence of inequality around the country and which has informed the Clinical Effectiveness and Evaluation Unit (CEEU) of the Royal College of Physicians who, in partnership with The Information Centre, established the

National Lung Cancer Audit in 2004. The first full year of data collection of the National Lung Cancer Audit (NLCA) was 2005, and initially recruitment was slow. However, over the past 5 years there has been a steady improvement with every NHS Trust in England having participated at some point, and the vast majority now upload data on people with lung cancer as part of routine clinical practice. In the Annual report of 2010 (based on data from 2009), the level of case ascertainment was reported to be 95%, and the data completeness has also increased, with data on histology, performance status and stage reported as being 78%, 79% and 82% complete (25). It is now mandated that all NHS Trusts should participate in the NLCA, and the NLCA has been endorsed by the National Institute of Health and Clinical Excellence (NICE) Lung cancer guideline in 2005 (26).

### 1.3.2 The NHS Cancer Plan (2000) (24)

Published in September 2000 'The NHS Cancer Plan' was designed to lay out the strategies by which the Department of Health intended to improve cancer services across England and Wales, and, in so doing, address the inequalities that exist in incidence, survival and provision of cancer care around the country and in comparison with other European countries. It had four main aims;

- To save more lives.
- To ensure people with cancer get the right professional support and care as well as the best treatments.
- To tackle the inequalities in health that mean unskilled workers are twice as likely to die from cancer as professionals.
- To build for the future through investment in the cancer workforce, through strong research, and through preparation for the genetics revolution, so that the NHS never falls behind in cancer care again.

It also had 3 specific new commitments, namely: to reduce smoking rates, to create targeted waiting times for new referrals with suspected cancer, and to invest an extra £50 million by 2004 in hospices and specialist palliative care. There were a number of areas in which the proposals would affect lung cancer care specifically. Addressing the burden of cancer which results from smoking was one of the key areas discussed. Methods to control smoking related cancer burden included: a ban on tobacco advertising, the introduction of smoking cessation services and nicotine replacement therapy (NRT) on prescription, which have subsequently become available 'over-the-counter', and enforcing the law on the sale of tobacco products to under 16 year olds. Screening services for lung cancer were also mentioned, and a national pilot feasibility study is underway with funding from the Health Technology Assessment Scheme. A number of new national bodies were created such as the National Institute for Health and Clinical Excellence (NICE) which have produced recommendations on the structure of lung cancer services and the drugs that should be available, regardless of one's place of residence in an attempt to eradicate the 'postcode lottery'. The Commission for Health Improvement (CHI) was also created. This has been involved with the Peer Review process to evaluate if recommendations made by the Department of Health are actually being translated to the public. The National Cancer Research Institute (NCRI) was established to ensure high level research, and a specific recommendation was made to support audit database development for all cancer sites.

### 1.3.3 Cancer Reform Strategy (2007) (27)

Published in 2007 the Cancer Reform Strategy was designed to build on the progress made since the NHS Cancer Plan in 2000, and, with a strict timeframe, to implement improvements within the next five years. Cancer mortality had fallen by 17% between 1996 and 2005, and survival rates were improving for a

number of cancers (for example, breast and bowel), although not for lung cancer. The creation of multi-disciplinary teams (Cancer Plan 2000) made a huge difference to the patient pathway (28), from suspicion of cancer to the instigation of a management plan (29); and the generation of specialist cancer nurses has improved the patients' experience (30, 31). Almost all patients are seen within two weeks of referral from their GP, and more than 99% receive their first treatment within a month of diagnosis, compared with 31% in 2000 (29). But there remain areas of need, in particular the rise in the incidence rate of cancer as people live longer, and the increase in people living beyond the disease, which leads to an increase in disease prevalence. The Cancer Reform Strategy set out to address these challenges and is divided into ten key areas of change. Six areas of change are designed to improve cancer outcomes:

- Preventing cancer

Over half of all cancers could be prevented through changes to lifestyle; these include smoking cessation, avoiding obesity and excess alcohol consumption.

- Diagnosing cancer earlier

The CRS aims to achieve this by using a combination of increased public awareness and cancer screening, whilst ensuring cancer wait targets are met.

- Ensuring better treatment

There is a shortage of radiotherapy facilities which needs to be addressed, alongside concerns regarding the delay in uptake of new cancer drugs, and encouraging new surgical techniques.

- Living with and beyond cancer

Communication is the main priority here, both directly with health professionals and also by using other media formats.

- Reducing cancer inequalities

There are persisting inequalities in cancer incidence and survival on many levels, including sex, age, ethnicity, religion, and socioeconomic class. To tackle this, the CRS recommends better data collection, research, and sharing best practice.

- Delivering care in the most appropriate setting

This involves the creation of service models that can be adapted for individual Trust situations whilst ensuring the key components remain.

Four areas of change are designed to ensure improved delivery of this care:

- Using information to improve quality and choice

Improving the collection and publication of information should lead to service improvement and strengthen the commissioning from Primary Care Trusts.

- Stronger commissioning

The needs of every population will differ, and so there needs to be more focussed planning at a local level on the services that should be commissioned from the NHS Trusts serving that population.

- Funding world class cancer care

The government has made various pledges regarding funding, but has stressed the need for primary care trusts (PCTs) to ensure that money is spent wisely, and NHS Trusts are cost effective.

- Building for the future

This aim is over-arching, but it makes special mention of national data collection, and the creation of the National Cancer Intelligence Network (NCIN). The funding for research on data collated by the NCIN will come from the National Cancer Research Institute (established by the Cancer Plan 2000).

### 1.4 National audit changing practice

The Royal College of Physicians, London, is committed to clinical audit as a means of improving provision of healthcare and is involved in several national audits. These include the Inflammatory Bowel disease Audit; Multiple Sclerosis Audit; the COPD Audit; the Myocardial Ischaemia National Audit Project and the National Sentinel Stroke Audit. The latter is a good example of a large national audit being used to evaluate current medical practice, create standards to which NHS Trusts can be measured and then re-evaluating NHS Trust performance. Over time, changes in the structure of health care can be evaluated, and national health policy informed.

#### 1.4.1 Stroke

The National Sentinel Audit of Stroke was established in 1998, and has been completed every two years since then. In 1998 all NHS Trusts in England, Wales and Northern Ireland completed the survey. The results of the audit, which look at consecutive patients seen over a two month period every other year, have been used to inform national policy in terms of the National Clinical Guidelines for Stroke (2004) and the NICE guidelines of 2008. In 2005 Irwin et al, published some of the results of the first 3 rounds of the Audit (1998, 1999 and 2001/02) and demonstrated that the standard of care achieved on a specialist Stroke Unit exceeded that on a general ward, but that there had been a reduction in the likelihood of a patient being managed on a Stroke Unit (32). There have now been seven rounds of the audit process and over the last 10 years several changes have occurred: specialist Stroke Units are now universal, and the importance of Specialist Stroke Nurses has been highlighted; and several centres now offer thrombolytic therapy. The Audit report describes the shortcomings as well as the improvements in the system (33). Two related Audits have now been established, the UK Carotid Interventions Audit, and the Stroke Improvement National Audit Programme.

## 1.5 Thesis plan

This MD thesis is based on the research I performed as part of a Royal College of Physicians (RCP) research fellowship, the aim of which was to evaluate the data within the National Lung Cancer Audit (NLCA). The initial application for the research fellowship was designed by Dr David Baldwin and Prof. Richard Hubbard in collaboration with Dr Laila Tata, Dr Catherine Free and myself. The main aim of the research was to assess the validity of the NLCA dataset, and then to use the data within it to try and investigate the potential causes of inequality in lung cancer care across England. In order to achieve this, a period of training in research methods, both epidemiology and statistics was required. There were two other elements to the fellowship, extended training in the clinical aspects of lung cancer care, and training in clinical effectiveness. In terms of extended clinical training I had a number of tutorials with Dr Baldwin discussing a range of topics within the field of lung cancer care (appendix 1). I also attended clinics with the allied specialities, thoracic surgeons, oncologists and specialist nurses. I also attended theatre to observe surgical procedures and have been trained to perform EndoBronchial UltraSound guided lymph node biopsies (EBUS). Clinical Effectiveness is a measure of how well an intervention works not just for the individual but for the wider population, and my training in this included:

Attending Network level Lung cancer meetings, and presenting my research at local Lung Cancer meetings.

Spending a day at the RCP Clinical Effectiveness and Evaluation Unit (CEEU); meeting with members of all the different audit teams.

Spending a day with Dr Peter Lachman and the Change Management team at Great Ormond Street Hospital to hear about their work.

Finally I was invited to join the Guideline Development Group (GDG) of the NICE Lung cancer guideline update, with the specific role of writing the Needs Assessment chapter, and in so doing describing the current state of lung cancer epidemiology in England and Wales.

The main aims of the research were to using existing datasets to assess the validity of the NLCA dataset, and then to go on to interrogate the dataset to try and answer specific clinical questions regarding the geographical variation in lung cancer outcomes that have been reported in the past (23). In order to answer whether geographical inequality is primarily due to patient features, a robust marker of co-morbidity was required. I have been able to link the NLCA with Hospital Episode Statistics (HES) and calculate a composite score of co-morbidity, the Charlson Index (34) for this cohort of English patients with lung cancer, and incorporate this into regression models to assess its independent influence on outcome measures. I have also tried to quantify the features of NHS Trusts across England, for example whether or not they are surgical or radiotherapy centres; and I have tried to establish which features of both patients and the hospitals where they are first seen have the greatest influence on clinical outcomes of lung cancer. To ensure clinical relevance I have analysed the use of surgery in patients with non-small cell lung cancer only, and the use of chemotherapy in patients with small cell lung cancer only. The National Lung Cancer Audit contains a large number of young adults with the disease, and this provided a unique opportunity to describe the pattern of disease and outcomes observed in this young and economically viable population.

During the course of the research period, three separate datasets were downloaded from the Information Centre for Health and Social Care, and I have used these at different points within this thesis.

**Dataset 1:** Downloaded on 17th November 2008.

Includes all patients first seen between 1st January 2004 & 31st December 2007.

**Dataset 2:** Linked with HES. Downloaded on 30th September 2009.

Includes all patients first seen between 1st January 2004 & 31st December 2008.

**Dataset 3:** Downloaded on 30th January 2010.

Includes all patients first seen between 1st January 2004 & 31st December 2008.

### 1.6 Chapter outline (dataset used)

**Chapter 2:** Needs Assessment of the NICE Lung Cancer Update 2011 (3)

This is an independent piece of work using the NLCA dataset to describe the current patterns of lung cancer demography in England and Wales.

**Chapter 3:** Description and validation of the NLCA dataset (1)

This was the first step in the research project, and describes the use of existing national datasets (ONS, HES) to try and establish if the NLCA is a representative and unbiased cohort of patients.

**Chapter 4:** Validating the NLCA using cancer Registry data (1)

This chapter describes the use of cancer Registry data to repeat the validation process of chapter 3, and to assess the influence of socio-economic status on clinical outcomes.

**Chapter 5:** Linking the NLCA to Hospital Episode Statistics (2)

This chapter will describe the process of cleaning the linked data and generating a composite score for co-morbidity. There is also a description of how features of NHS Trusts were generated.

**Chapter 6:** Inequalities in outcomes for non-small cell lung cancer: the influence of clinical characteristics and features of the local lung cancer service (2)

**Chapter 7:** How do patient and hospital features influence outcomes in small cell lung cancer in England (2)

**Chapter 8:** Young adults with lung cancer: a different disease entity? (3)

This is a descriptive report of the features of young adults who are diagnosed with lung cancer. I have also looked specifically at survival post-surgery for those with NSCLC, to allow comparison with published literature.

**Chapter 9:** Future research

This chapter describes proposals for future research in order to build on the research carried out so far, and to try and answer some of the questions raised during the course of this research fellowship.

Throughout my formal period of research I was supported by a steering group which was chaired by Prof Anne Tattersfield, who offered an impartial opinion on the direction of the project and advice regarding publications. The members of the steering group included my MD supervisors; Prof Richard Hubbard, Dr Laila Tata, and Dr David Baldwin. Dr Catherine Free who had been a co-applicant on the initial fellowship application was also on the group. Other members of the group were: Dr Mick Peake, as the director of the National Lung Cancer Audit; Dr Roz Stanley, Project Manager of the NLCA; and Dr Paul Beckett, Associate Director, Clinical Effectiveness and Evaluation Unit, Royal College of Physicians, London. I was also supported by a lay member Mr Ken Pursiow, who ensured the project direction was pertinent to patients and their carers.

The ideas regarding the validation and analysis of the NLCA dataset were primarily generated by Prof Hubbard, Dr Baldwin, Dr Tata and myself. I performed all the data management, cleaning and statistical analysis of the data. I have written this document and been lead author on three papers which have arisen from this work, which have been accepted for publication in peer reviewed journals. The co-authors on the papers were: LJ Tata, CM Free, RA Stanley, MD Peake, DR Baldwin and RB Hubbard.

## Chapter Two: Needs Assessment of the NICE Lung Cancer Update 2011

## 2.1 Introduction

During my research period I was invited by the Guideline Development Group of the National Collaborating Centre for Cancer (NCC-C) to produce the Needs Assessment for the NICE Lung Cancer Update 2011. This was an excellent opportunity to participate in the creation of a NICE guideline and fitted nicely within the aims of my RCP fellowship. The scope of the guideline had already been agreed (appendix 2). The remit of the Needs Assessment was to provide the context for this guideline update, to describe the burden of disease and to assess whether variation exists in the treatment and outcome for individuals with lung cancer in England and Wales. Given my knowledge of the National Lung Cancer Audit dataset, I was in an ideal position to describe the results of this unselected and contemporary cohort. However, the NLCA only contains individuals diagnosed with lung cancer in England, and so I had to obtain permission to receive the corresponding years (2006-2008 inclusive) of data from Cancer Network Information System Cymru (CANISC) in Wales.

Data from within the NLCA were used not only for the Needs Assessment but also for the Health Economic component, and I was able to work closely with Dr Sarah Willis (health economist commissioned by NICE) to provide the numbers and proportions from within the dataset to furnish her economic models. Finally, in order to assess the facilities available at NHS Trusts across England and Wales, I created and distributed, via an on-line survey programme, a questionnaire for all Lung Cancer Lead Physicians. This primarily looked at the diagnostic and therapeutic facilities available, as well as the role of the lung cancer specialist nurse. It describes the on-going variation in access to diagnostic and therapeutic facilities, which may well influence clinical outcomes.

What follows is the Needs Assessment chapter as it appears in the NICE Lung Cancer Update 2011.

## 2.2 Needs Assessment

The following chapter provides a summary of the full Needs Assessment that was carried out as part of the evidence review for this guideline. It includes information regarding the epidemiology of lung cancer regionally, nationally and internationally. This guideline update is not a comprehensive review of all aspects of lung cancer management but is limited to priority areas that were identified before and during the scoping exercise that were thought to be key topics that might help improve the overall standard and equity of care provided geographically. The purpose of this chapter therefore is to provide the context for the guideline, to describe the burden of disease and to assess whether variation exists in the treatment and outcome for individuals with lung cancer in England and Wales. We shall illustrate the need for improved diagnostic and staging procedures, and the link to selecting patients for their optimal therapy for improving survival and quality of life; whilst addressing the important issues of informed patient choice.

Since the 2005 NICE Guideline on Diagnosis and Treatment of lung cancer was published, the National Lung Cancer Audit has been established, and accrual has increased steadily over the past five years. It is estimated that the Audit gathered information on 85% of the incident cases of lung cancer in England and Wales in 2008 (35). It is the largest contemporary, non-registry, clinical database of lung cancer patients in Europe, with over 100,000 patients in total. It is a non-mandatory dataset of clinical and socio-demographic features, and also records details of the treatment received. The dataset has been shown to be unbiased and representative of lung cancer patients in England (36). These data have been used within this NICE Lung Cancer Update along with contemporary data from Cancer Network Information System Cymru (CANISC) in Wales to describe the current demographics of individuals with lung cancer in England and Wales; the patterns of treatment they receive and their survival.

Other information sources include the National Cancer Intelligence Network (NCIN), the National Cancer Registry, and the British Society of Cardiothoracic Surgery.

This NICE Lung Cancer Update has included a revision of several sections from the original guideline in 2005 (26), and provided the opportunity to assess the progress that has been made over the last five years, and identify areas that have shown no improvement. In 2002 there were 29,000 deaths from lung cancer, and it was the second most common cause of cancer related death in women. In 2008, there were more than 35,000 deaths (5), and it is now the leading cause of cancer related death in men *and* women. There has been an encouraging improvement in 1 year survival compared with the data quoted in the 2005 guideline; although regional variation in this outcome measure persists (37). Regional variation was also described in 5 year survival, but contemporary data from the NLCA will not be available until 2011. The proportion of the overall patient cohort with small cell lung cancer was estimated as 20% in 2005. Current data reports the proportion having fallen to around 11% of all reported lung cancers (18% of *histologically confirmed* lung cancers). Data from 1986-1994 (North Yorkshire Cancer Registry Information Services) demonstrated that 34% of patients had no histological confirmation of their lung cancer (38), and this figure has fallen very little over the last 15 years.

### 2.2.1 Incidence

The incidence of lung cancer in England and Wales is believed to be 47.4 per 100,000 population (5). Data from ONS showed a total of 34,897 incident cases in England and Wales in 2008. It is the second commonest cancer in men, after prostate and, in women, after breast cancer. The prognosis is very poor with a mortality rate of 40.1/100,000 population. The prevalence reflects this poor prognosis with an estimate of 65,000 individuals living with lung cancer in 2008. In the 2005 NICE Lung Cancer Guideline (26), deaths from lung cancer were believed to be the commonest cause of cancer related deaths in men, and the second most common cause in women. However, lung cancer has since become the commonest cause of cancer related death in both sexes.

Comparison within the European Union reveals that the incidence in men is similar to most of western Europe and lower than most of eastern Europe. The incidence in women is amongst the highest in the European Union (figure 2.1).

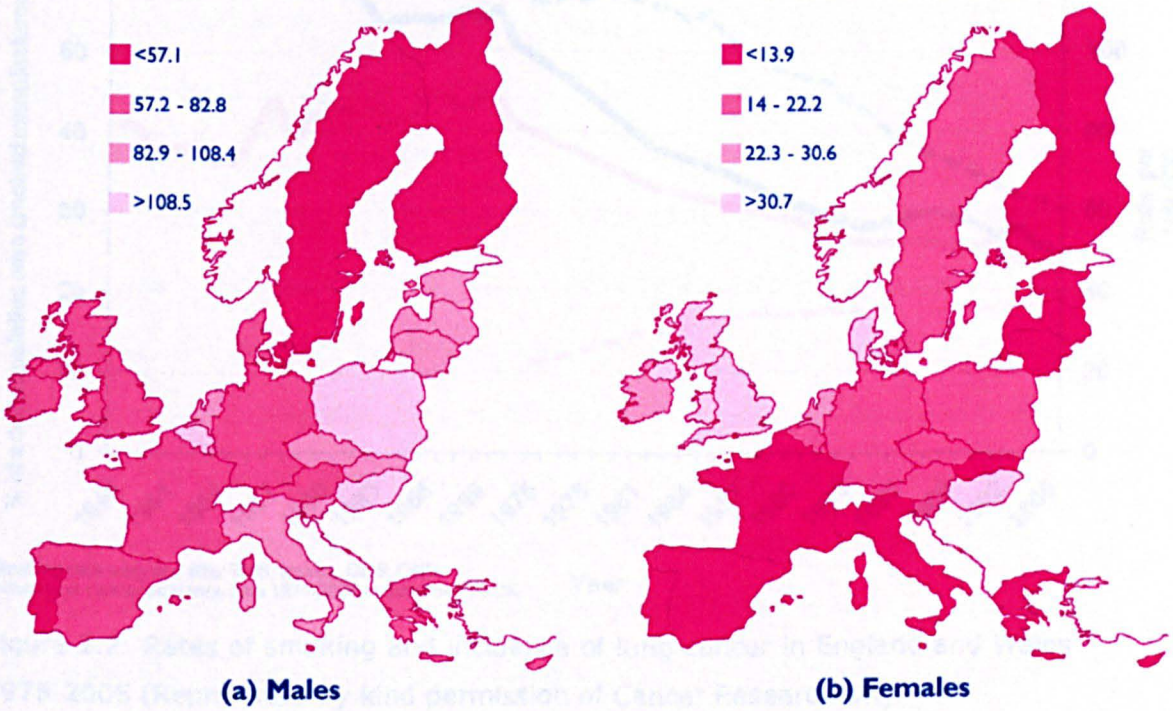



Figure 2.1: Age-standardised incidence rates in the European Union (2000); Reproduced with the permission of Cancer Research UK.

### 2.2.2 Sex variation

The majority of individuals with lung cancer are male, and this is almost certainly a direct reflection of the proportion of smokers that are male. However, the proportion of men who smoke has fallen by 26% since the mid 1970's (39) and there has been a similar decline in the proportion of women who smoke over the same timeframe (figure 2.2). There is known to be a twenty year lag phase between smoking and the onset of lung cancer and so changes in the pattern of smoking between the sexes is a precursor of changes in the sex ratio amongst individuals with lung cancer (figure 2.2). The peak prevalence of smoking in *young* women was only reached in the 1990's, and so the incidence of lung cancer amongst older women has only recently stabilised. The male:female ratio was >6:1 in 1973 compared with 1.5:1 in 2008 (35).

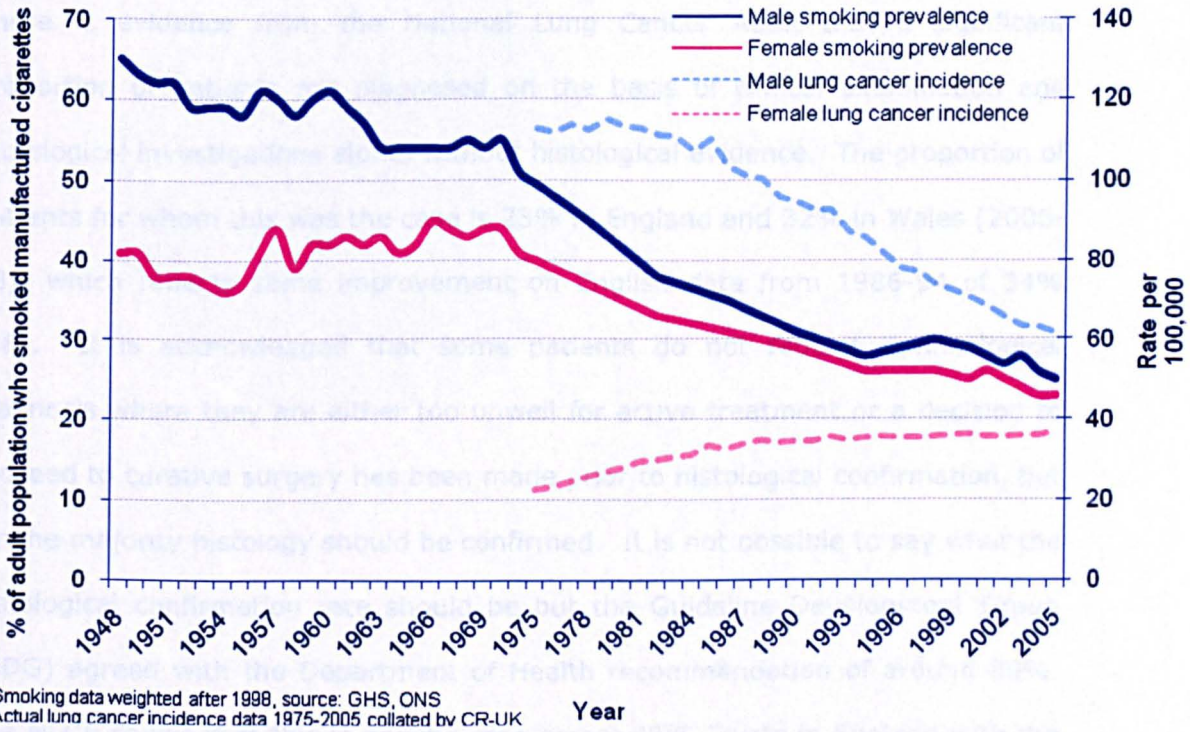



Figure 2.2: Rates of smoking and incidence of lung cancer in England and Wales 1975-2005 (Reproduced by kind permission of Cancer Research UK).

There is also evidence from the National Lung Cancer Audit that females have better overall survival than males, with an adjusted hazard ratio of 0.89, $p<0.001$ (95% confidence intervals, 0.88, 0.91) (36). This result indicates that women with lung cancer are 11% less likely to die than men, and this observation has been identified in a number of other populations (40, 41).

### 2.2.3 Histological subtypes

Obtaining a histological diagnosis for a lung tumour is usually necessary to ensure the most appropriate treatment regime is considered. If targeted treatment is an option, it is vital that samples and their analysis are adequate to allow identification of histological subtypes and specific mutations that directly determine suitability for specific treatments.

There is evidence from the National Lung Cancer Audit that a significant proportion of patients are diagnosed on the basis of clinical examination and radiological investigations alone, without histological evidence. The proportion of patients for whom this was the case is 23% in England and 32% in Wales (2006-08); which reflects some improvement on English data from 1986-94 of 34% (38). It is acknowledged that some patients do not require a histological diagnosis where they are either too unwell for active treatment or a decision to proceed to curative surgery has been made prior to histological confirmation, but for the majority histology should be confirmed. It is not possible to say what the histological confirmation rate should be but the Guideline Development Group (GDG) agreed with the Department of Health recommendation of around 80%. The NLCA shows that this is not the case across NHS Trusts in England with the median Histological Confirmation Rate being only 63% (interquartile range 47 to 72%) (36).

The prevalence of the different subtypes has changed with time, which is believed to be due to the temporal change in smoking prevalence, and also the use of filters and low tar cigarettes. Small cell lung cancer is believed to be most closely linked to smoking pack history, and the proportion of all lung cancers due to small cell has decreased from 20 to 10% (42). In 1950 the ratio of adencarcinoma:squamous cell carcinoma was 1:18; but in 1994 was reported as 1:1.3 (43). This increase in adenocarcinoma was seen in both sexes and all ethnic groups.

Data from the National Lung Cancer Audit demonstrate contemporary results for the variation in histological types, although these data are missing in 40% of the English and 32% of the Welsh cohorts.

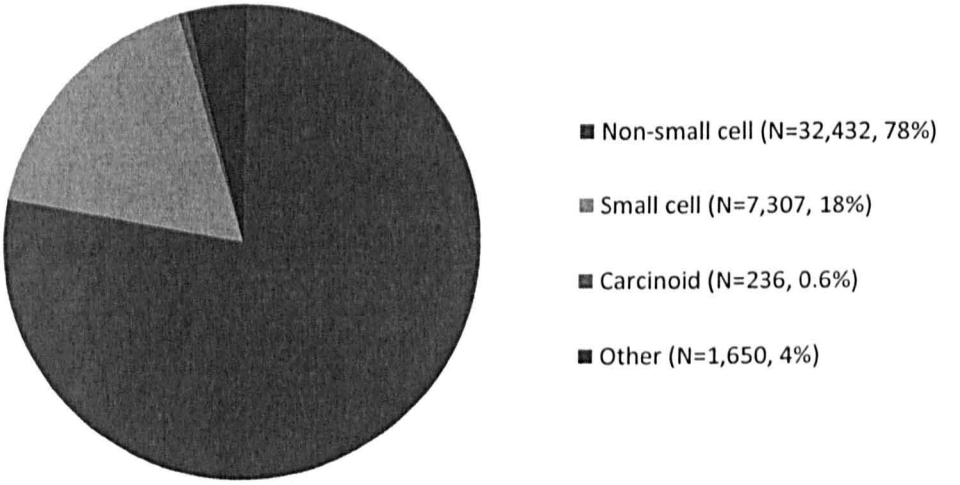



Figure 2.3: Histological subtypes in proven primary lung cancer; NLCA (England and Wales) 2010.

The NLCA holds data for the breakdown of subgroups of Non-small cell lung cancer, which highlights the increase in prevalence of adenocarcinoma, and also the large proportion of patients in whom an exact histological subtype is missing, Non-small cell "Not otherwise specified" (NOS).

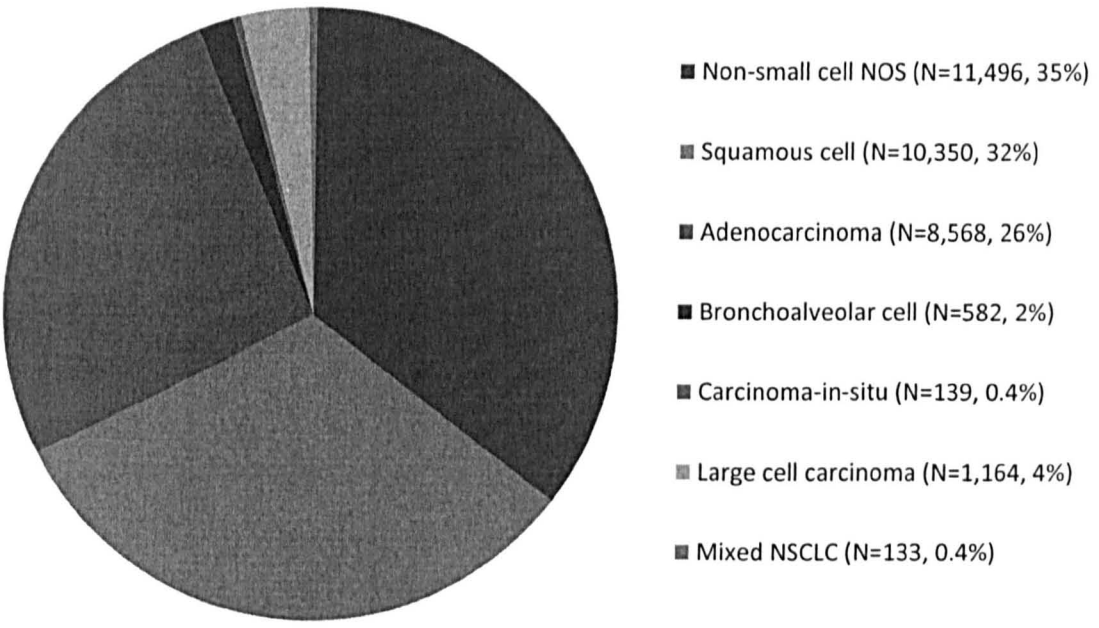



Figure 2.4: Subgroups of non-small cell lung cancer in England and Wales (N=32,432; NLCA 2006-08).

### 2.2.4 Socio-economic status (SES)

A number of papers have been published which indicate that there is an increased incidence of lung cancer in individuals from the lowest level of socio-economic strata, the least affluent group (9-11). Historically this difference has been attributed to the increased rate of smoking in the least affluent group (9), and there is evidence that histological subtypes vary with SES reflecting the variable influence of smoking on specific histological subtypes (44). However, other factors will be involved including diet, nature of employment (manual vs professional), and educational attainment (11, 12, 45). Differences also exist between individuals from different SES in terms of access to health services and health seeking behaviour (46). Crawford et al found individuals from the most deprived group were less likely to receive a histological diagnosis (47). Shack et al (48) noted that the gradient in incidence of lung cancer across socio-economic groups in England was more marked in the North East, the North West and Yorkshire and Humber regions. Data from the National Cancer Intelligence Network illustrates a more than two fold variation in age standardised incidence rate in both men and women between the most and least affluent strata (figure 2.5).

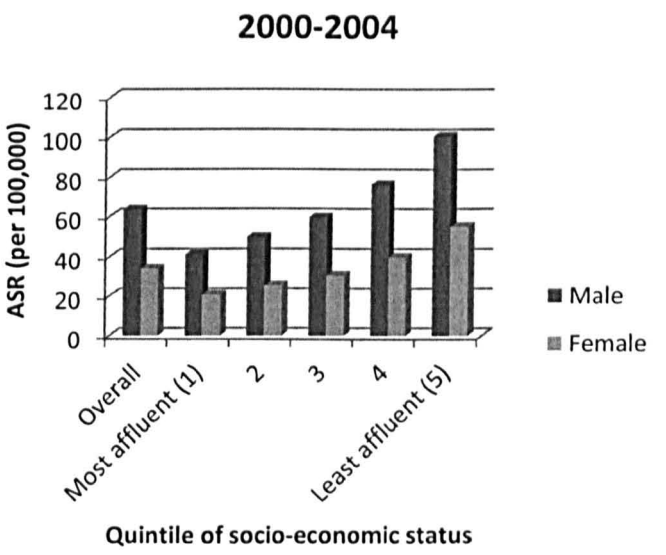



Figure 2.5: Age standardised incidence rate (per 100,000) across quintiles of socio-economic status (Reproduced by kind permission of NCIN).

As well as the increase in incidence of lung cancer in the least affluent social group, there is evidence that these individuals present with more advanced disease (45, 49) and demonstrate a reduced uptake of resection for lung cancer (46, 47, 50). Data using Hospital Episode Statistics (HES) between 1992-95 demonstrated a 40% reduction in the use of surgery between the least compared with the most affluent group of patients with lung cancer (unadjusted OR 0.58, 95% confidence interval 0.48, 0.70) (50). However this figure may be misleading as it is not adjusted for age, sex, performance status, or stage. Contemporary data (2005-2008) from the NLCA demonstrated no variation in the use of surgery in proven NSCLC, based on socio-economic status, with an adjusted OR of 1.11 (95% confidence interval 0.96, 1.27) (36). Jack et al (2006) reported a lower rate of chemotherapy use in patients within the South East region from the least affluent group (51), which has been reproduced using contemporary data from the NLCA (36). However, in neither study was social deprivation linked to poorer survival (36, 51). Data from the NLCA demonstrated no variation in the use of radiotherapy for the overall cohort of patients with lung cancer, based on socio-economic status (36).

### 2.2.5 Ethnic variation

There is evidence of variation in the incidence of lung cancer amongst ethnic groups in England and Wales, which is related to demographic features, socio-economic deprivation and smoking prevalence. Black and minority ethnic groups (BME), have higher than average smoking rates, and are more likely to be from deprived areas with increased unemployment and lower levels of educational attainment (8, 52). Evidence from America demonstrated that African-Americans were more likely to present with advanced stage of lung cancer than Caucasians, which was related to socio-economic status rather than directly to ethnicity (45). In contrast race was an independent risk factor for advanced stage at presentation in breast and prostate cancer (45). In England and Wales, an increase in relative mortality was found in migrant individuals with lung cancer from Jamaica (52). Differences also exist in terms of accessing health services such as smoking cessation and screening between ethnic groups, with White-British individuals more likely to present via a two-week wait appointment than individuals from BME groups (8). There is also evidence that individuals from BME groups are underrepresented in cancer research (8).

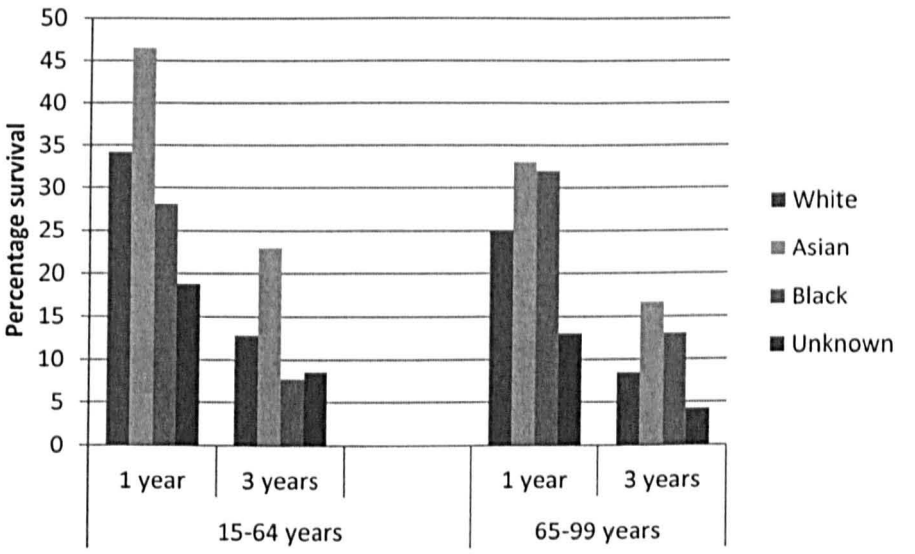



Figure 2.6: Variation in age standardised relative male survival at 1 and 3 years by major ethnic groups in England and Wales (Reproduced with kind permission of NCIN).

Asian individuals with lung cancer have a significantly higher percentage survival at 1 and 3 years compared with white patients, regardless of age. There was no significant difference in relative survival between BME groups at 1 or 3 years. Similar results were seen for women as for men.

Given potential cultural and language barriers for individuals from BME groups accessing lung cancer services within the NHS, it is very important that every effort is made to ensure that each component of the patient pathway is clear and user-friendly.

### 2.2.6 Stage and Performance status

The stage of lung cancer at diagnosis is crucially important in terms of determining which patients have potentially curable disease, and which do not. Stage is also an important determinant of prognosis. The routine use of CT scans of the thorax and upper abdomen along with PET-CT has improved the accuracy of staging. Recently the International Association for the Study of Lung Cancer group (IASLC) has produced a revised TNM staging system that has been adopted by the Union Internationale Contre le Cancer (UICC). Plans are already underway to collect more accurate staging data and relate this to prognosis to produce a yet more accurate staging system. Information regarding stage of disease at presentation is not collected by the Cancer Registries but is collected within the NLCA and CANISC, although these data are incomplete. Stage data were missing in 46% English and 30% Welsh patients overall, and in 27% and 17% of English and Welsh patients with proven NSCLC respectively.

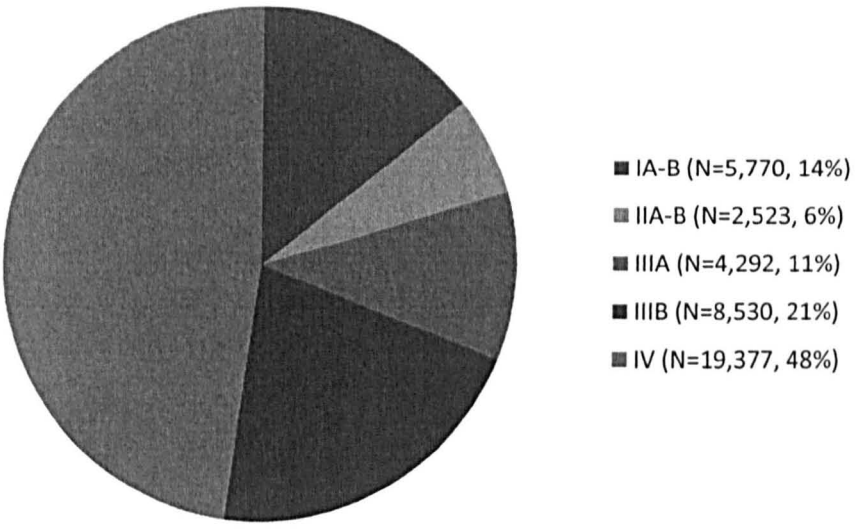



Figure 2.7: Stage at presentation in those patients with stage recorded (N=40,492). NLCA (England and Wales) 2006-08.

Table 2.1 demonstrates that across England and Wales a significant proportion of each age group presents with late stage metastatic disease. As a proportion of those patients with stage recorded, the youngest age groups have a similar burden of advanced disease to other groups, with the most elderly (>80 years) having significantly less. A significant proportion of people who are economically active and more likely to have dependent children will present with advanced disease. Late presentation in the younger age group will be multi-factorial but may reflect fear or ignorance on the part of young adults, and a lack of clinical suspicion in healthcare professionals.

Table 2.1: Frequency of Stage IV disease based on age groups in England and Wales (2006-08). Data provided by NLCA and CANISC

| Age groups (years) | N | %* | %* if stage recorded |
|---|---|---|---|
| 20-40 | 95 | 27 | 58 |
| 41-50 | 615 | 27 | 51 |
| 51-60 | 2807 | 29 | 52 |
| 61-70 | 5682 | 27 | 48 |
| 71-80 | 6711 | 26 | 47 |
| >80 years | 3397 | 24 | 45 |

%* percentage of each age group with Stage IV disease

Data are also collected by the NLCA and CANISC on performance status at diagnosis, although these data were missing in 38% of the English and 23% of the Welsh cohorts. Figure 2.8 demonstrates that as age increases so does the proportion of patients with performance status 3 or 4 at diagnosis. This will have implications on the treatment options available to elderly patients.

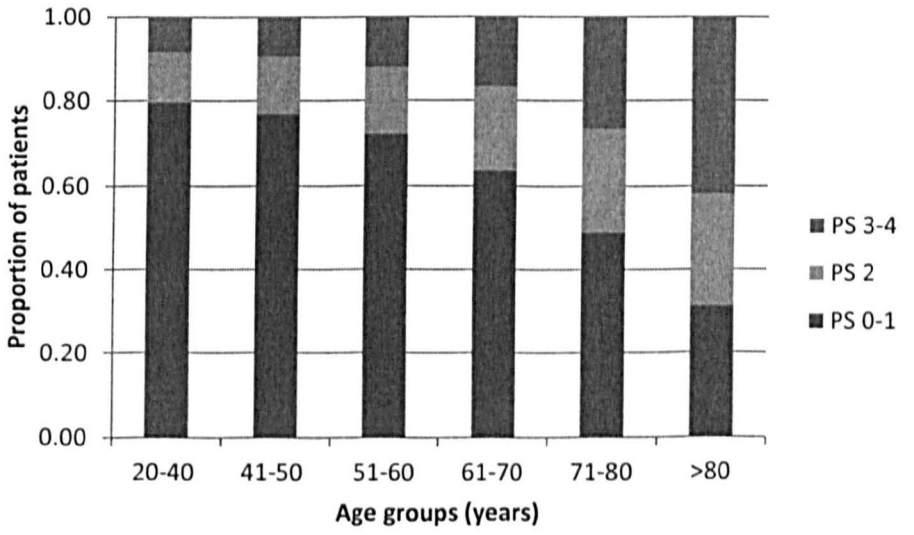



Figure 2.8: Variation in performance status at diagnosis based on patient age group (N=46,897). NLCA (England and Wales) 2006-08.

Information on co-morbidities is not reliable within the NLCA, and so work is on-going to link the NLCA dataset to other datasets, such as Hospital Episode

Statistics (HES), in order to evaluate the potential influence of patient co-morbidity and outcome measures for lung cancer. This work is described in Chapter 5 and incorporated into the analyses in Chapters 6-8.

### 2.2.7 Treatment received

Data from the NLCA (total for this analysis 67,730 records) show that overall 13.5% of patients are recorded as receiving treatment with curative intent, 52.5% treatment with palliative intent and 17.7% supportive care only. In 16.3% no treatment was specified or data were missing.

**2.2.7.1 Surgery** remains the mainstay of treatment with curative intent for NSCLC. Data from the NLCA for England reports an overall resection rate of 11%, which for the subgroup of patients with proven NSCLC rises to 14%. The data for Wales, indicates a resection rate of 6% overall, rising to 9% in proven NSCLC patients. Within this subgroup, the use of surgery varies according to age group of the patient as illustrated in figure 2.9.

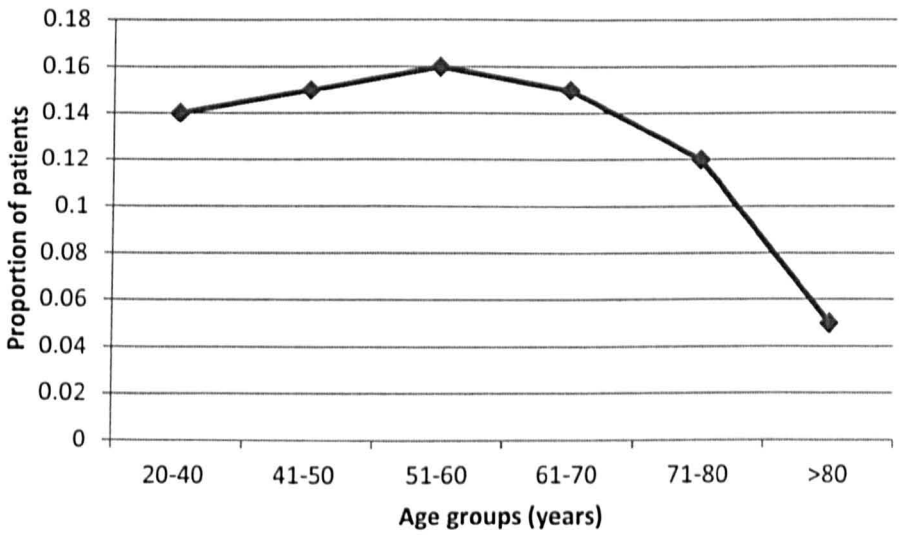



Figure 2.9: Proportion of patients with proven NSCLC receiving surgery in England and Wales based on age (N=3,998). Data from NLCA and CANISC (2006-2008).

The resection rate in proven NSCLC patients appears to drop above the age of 70 years, and there is evidence that even adjusting for stage and performance status, those over 75 years are significantly less likely to be treated surgically, than those less than 65 years (36, 53, 54). It is known that as age increases so does the level of co-morbid illness (55), however it is important to ensure that patient's treatment is planned on the basis of their clinical state, including co-morbidities and performance status etc, not simply their chronological age.

Recent published evidence based on operation codes recorded in Hospital Episode Statistics (HES) shows no increase in the rate of resection for lung cancer in England and Wales between 1999 and 2006 (46). In view of the fact surgical resection is the main component of potentially curative treatment, this is disappointing, and does illustrate apparent differences in practice between other parts of Europe and North America (17% and 21% resection rates respectively) (56).

There are data on the number and type of resections being performed in surgical centres throughout Great Britain and Ireland, and these are shown below as figures 2.10 and 2.11. These data demonstrate that there is significant variability in the number of resections being performed in different surgical centres, although it is not known how much this reflects differences in patient population, or surgical practice.

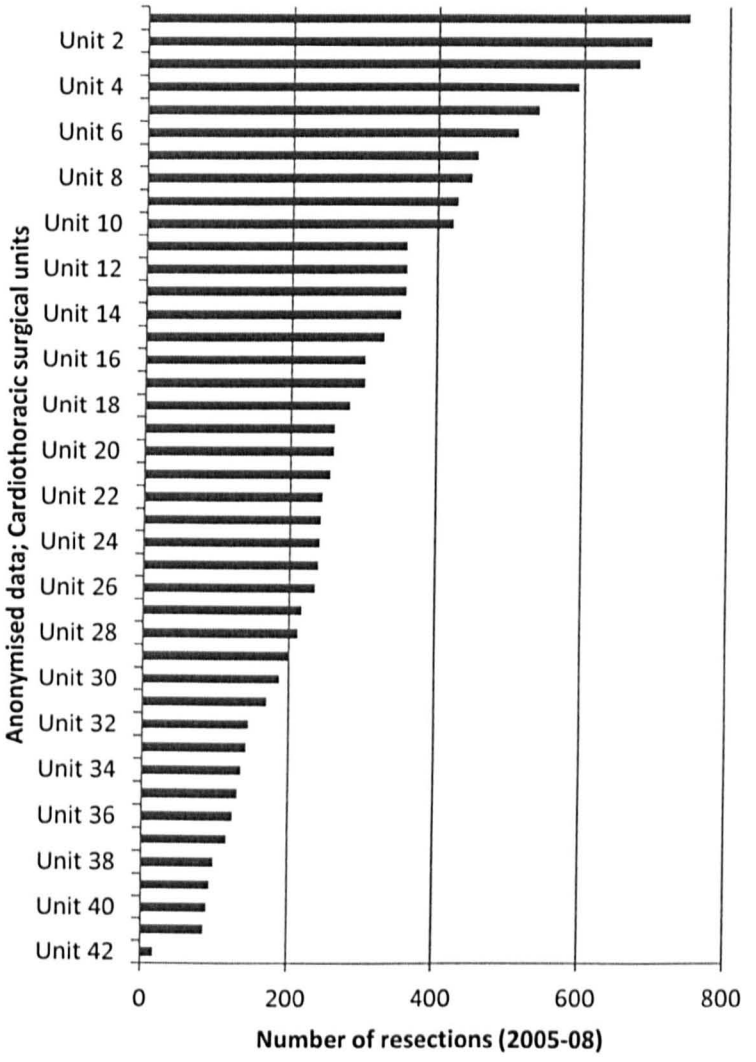



Figure 2.10: Number of resections for primary lung cancer at surgical centres in Great Britain and Ireland (Reproduced by kind permission of Society of Cardiothoracic Surgery–Data 2005-2008).

There is no clear evidence as to what the 'optimal' number of resections per surgical centre should be. Anecdotally the theory is that fewer centres performing more resections would reduce the post-operative mortality and improve the long-term survival. There is evidence from America which describes a difference of >5% adjusted mortality rate between low volume and high volume institutions for pneumonectomies (57), whilst the effect on lobectomy

adjusted mortality was <2%. However, research from Britain in 2003 found no such link between the number of lobectomies performed by an individual surgeon and in-hospital mortality (58). Of note, 40% of the 102 surgeons performed <24 lobectomies per year, which is a reflection of the fact that the majority of lobectomies were performed by cardiothoracic, not pure thoracic, surgeons at the time of this study.

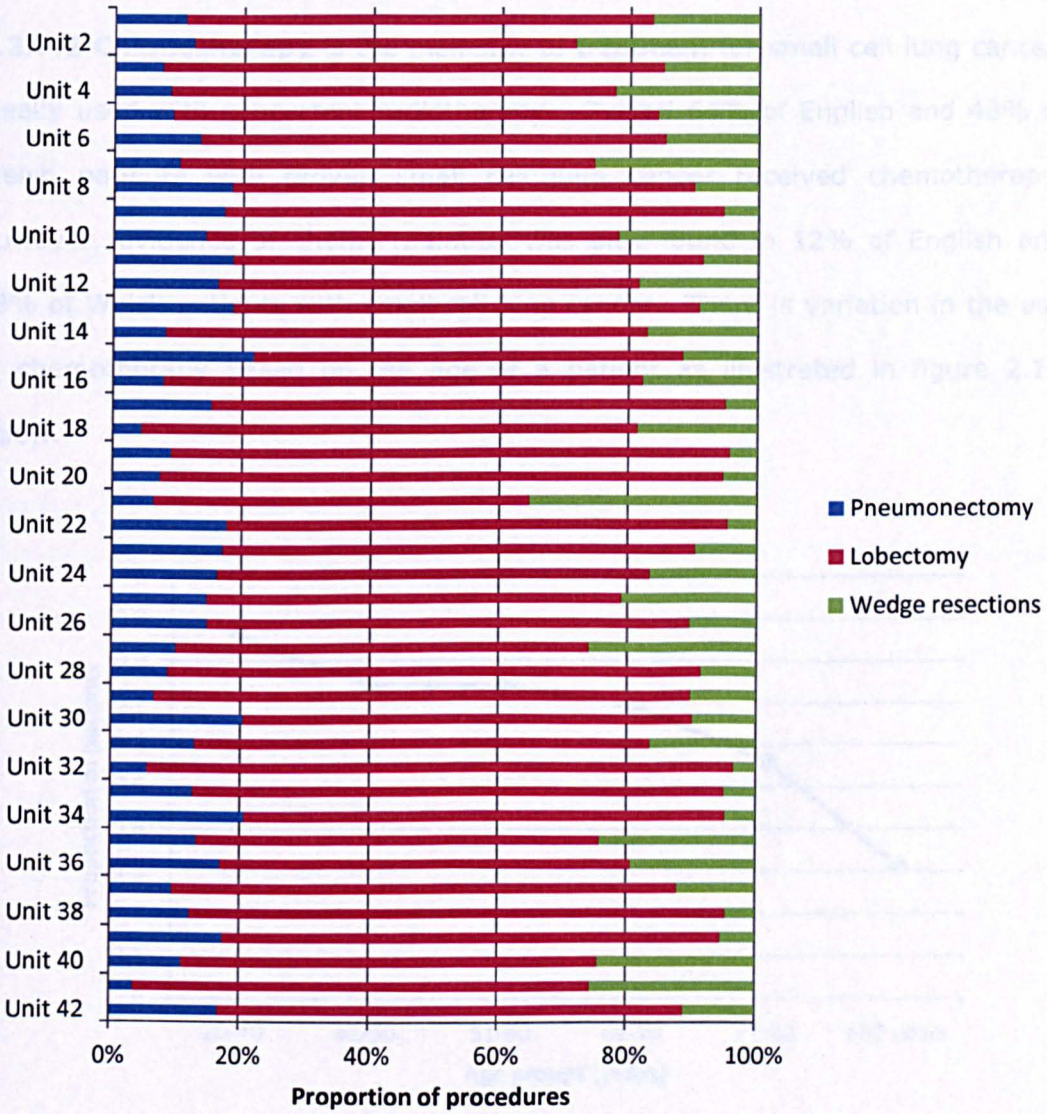



Figure 2.11: Types of resection for primary lung cancer at surgical centres in Great Britain and Ireland (Reproduced by kind permission of Society of Cardiothoracic Surgery–Data 2005-08).

There is also evidence that the type of procedure performed for lung cancer resection varies at different surgical centres (figure 2.11). The 2005 NICE guideline (26) states that the procedure of choice in stage I or II NSCLC should be lobectomy, rather than pneumonectomy, and figure 2.11 confirms the low proportion of patients that underwent pneumonectomy. Only three surgical centres had >20% of resections recorded as pneumonectomies.

**2.2.7.2 Chemotherapy** is the mainstay of treatment for small cell lung cancer, ideally used with concurrent radiotherapy. Overall 64% of English and 48% of Welsh patients with proven small cell lung cancer received chemotherapy. However, evidence of chemo-radiation was only found in 12% of English and 28% of Welsh patients with small cell lung cancer. There is variation in the use of chemotherapy based on the age of a patient as illustrated in figure 2.12 below.

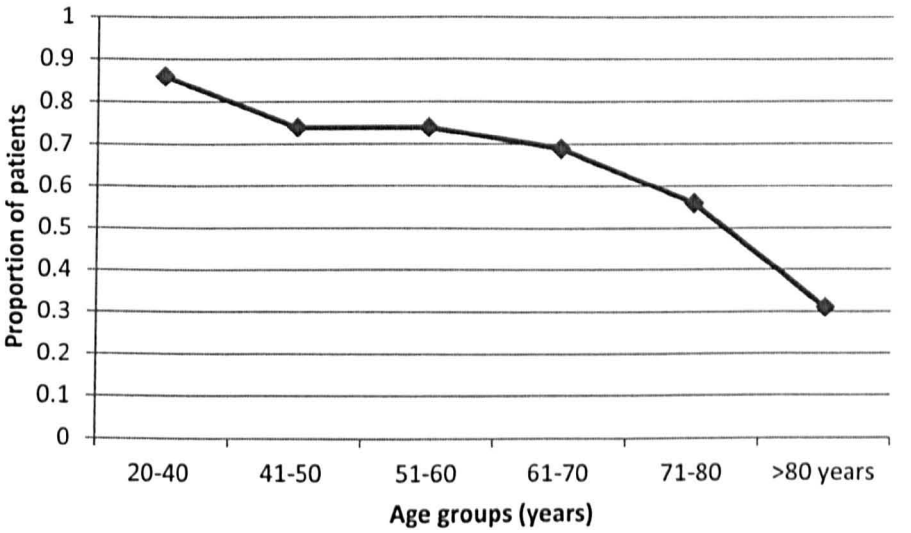



Figure 2.12: Proportion of patients with proven small cell lung cancer receiving chemotherapy in England and Wales based on age (N=4,530). Data from NLCA and CANISC (2006-2008).

The NLCA 2009 Annual report published evidence that demonstrated variation in the proportion of patients with small cell lung cancer receiving chemotherapy across the Cancer Networks in England and Wales (35) (figure 2.13).

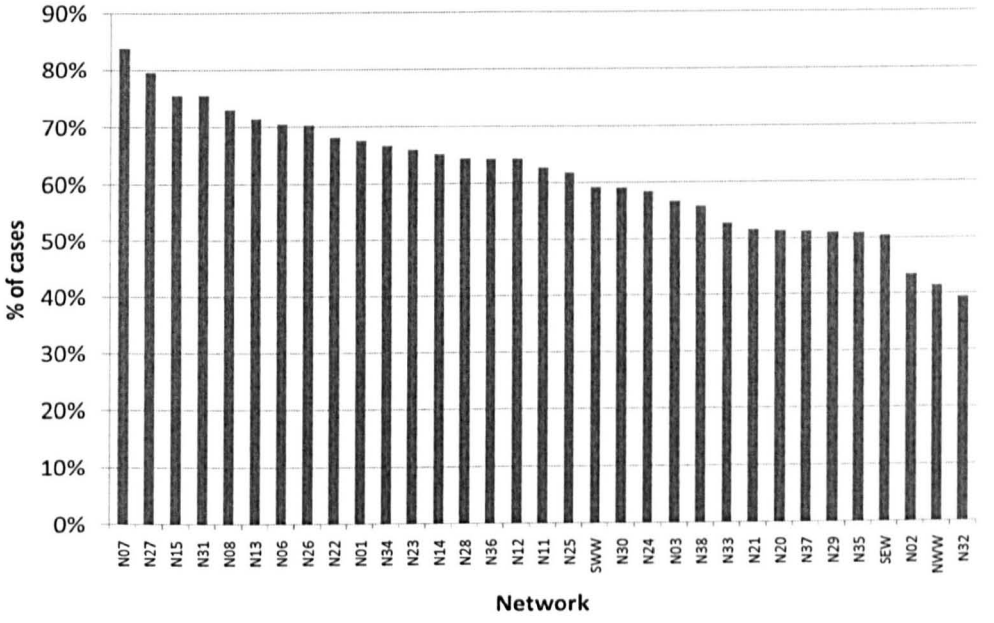



Figure 2.13: Proportion of patients with small cell lung cancer receiving chemotherapy at level of Cancer Network (England and Wales). Data provided by NLCA.

**2.2.7.3 Radiotherapy** can be used in all histological subtypes and with both curative and palliative intent. It is not possible to differentiate accurately the treatment intent from data held within the NLCA, and so figure 2.14 illustrates the variation in use of radiotherapy with age for the whole cohort, regardless of histology.

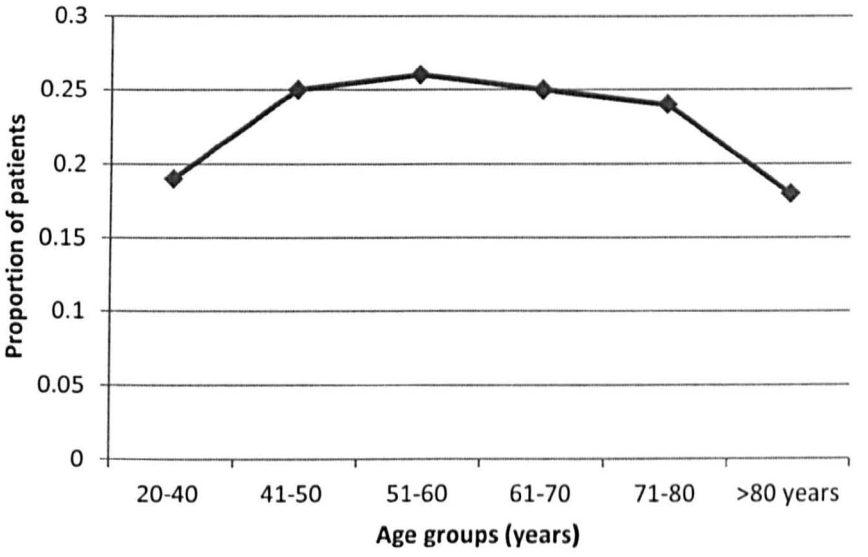



Figure 2.14: Proportion of overall cohort receiving radiotherapy in England and Wales based on age (N=73,730). Data from NLCA and CANISC (2006-2008).

### 2.2.8 Survival

The prognosis from lung cancer is poor, and it is the commonest cause of cancer related death in England and Wales, as well as worldwide. The median survival for individuals with lung cancer in England, is 203 days (interquartile range 62 to 545 days), and this is illustrated in figure 2.15 below.

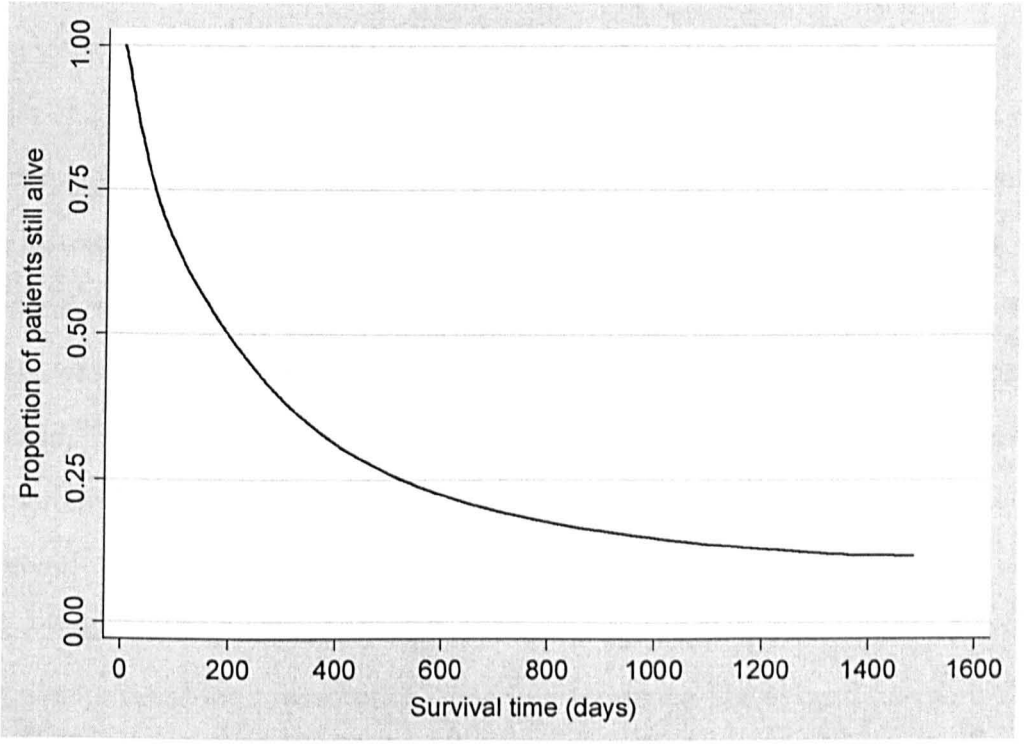



Figure 2.15: Kaplan-Meier curve demonstrating overall survival of English patients with lung cancer (N=67,730). Data from NCLA (2006-08).

Evidence from the EUROCARE-4 (21) report suggests there is significant variation in the 5 year survival rate across European countries, with a relative 5 year survival in England and Wales of 8.4% and 10.4% respectively. The mean 5 year survival rate for all countries within EUROCARE-4 was 10.9%, and for 13 registries within the American Surveillance Epidemiology and End Result (SEER) dataset was 15.7%. Survival rates were highest in Scandinavia, Belgium and Switzerland. It was noted, that for all areas, except central Europe, but including England and Wales, 5 year survival rates in lung cancer increased

between 1991 and 2002. No adjustment can be made for stage of disease at presentation within EUROCARE-4, and this may be an important limitation of the study.

There is evidence from a recent paper comparing national lung cancer survival between England, Sweden and Norway that the excess mortality observed in England is primarily caused by excess deaths within the first three months after diagnosis (59). The comparisons of excess mortality between the countries for years 1-2, and 2-5 years post diagnosis showed very little variation. There was evidence that English patients were older than their Scandinavian counterparts. No histological data were used in this study, but previous research has not demonstrated any significant variation between European countries (44). This study was based on registry data, and it was not possible to compare stage of disease, nor patient co-morbidity, and both these features will influence the proportion of patients receiving treatment with curative intent and their overall survival. Therefore the high rate of early death in individuals diagnosed with lung cancer in England could be the result of a number of features: advanced stage of disease at presentation; poor performance status and co-morbidity; access to healthcare being via a primary care physician rather than direct to secondary care; or different attitudes towards and rates of anti-cancer treatment.

The lack of histological data for a large proportion of patients has already been mentioned, and may well be due in part to poor data entry to the NLCA. However, it may reflect ambivalence amongst clinicians to ensure a histological diagnosis is made in patients who are not candidates for radical treatment. Therefore it is interesting to note that the survival curves for these two subgroups of patients, those with and those without a histological diagnosis, show early divergence with confluence latterly (figure 2.16). The median

survival for those with a histological diagnosis is 217 days (interquartile range 71 to 527 days), compared to a median survival of 158 days (interquartile range 43 to 513 days) for those without histology recorded. Cox regression analysis reveals a small but significant benefit for those patients with, compared to those without, a histological diagnosis (unadjusted hazard ratio 0.93, 95% confidence interval 0.91, 0.94, $p<0.001$). This is despite it being likely that obtaining a histological diagnosis lengthens the time to diagnosis and hence shortens survival time in the histology confirmed group. The most likely explanation for this observation is that fitter patients are more likely to be offered chemotherapy with a resultant short term survival benefit. Ensuring that all NHS Trusts offer the same proportion of their patients active treatment, might confer a meaningful improvement in median survival; via a modest reduction in early deaths.

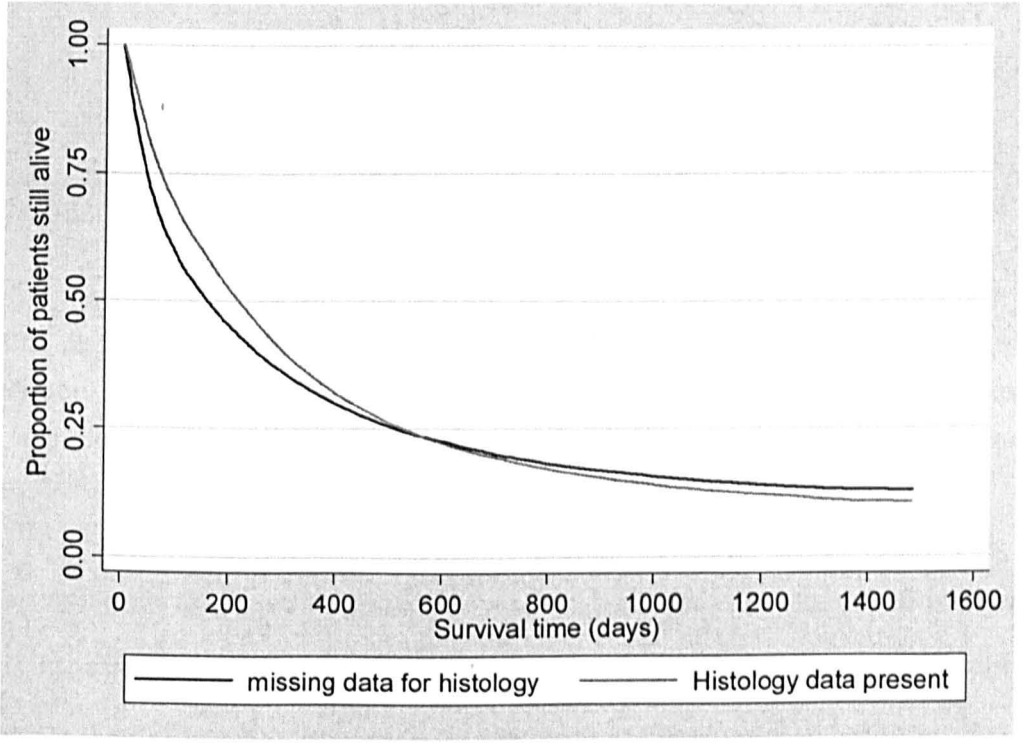



Figure 2.16: Kaplan-Meier curve demonstrating the variation in survival based on whether data is entered on histology in NLCA (England only data, N=67,730).

It is possible to illustrate the effect of surgery on those patients with proven NSCLC who were performance status 0 or 1, and who had a stage recorded of IA-IIB. Although the numbers are relatively small, N=2,753, the Kaplan-Meier survival curve demonstrates a stark variation in their observed outcome (figure 2.17).

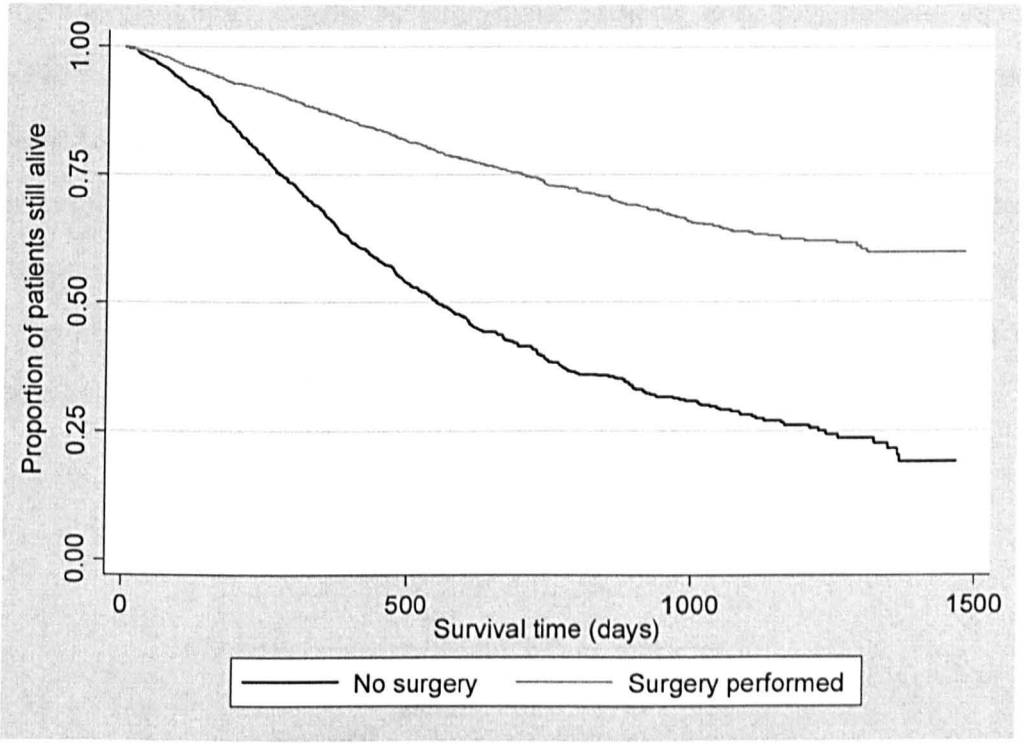



Figure 2.17: Kaplan-Meier curve demonstrating the observed outcome of a subgroup of patients with proven NSCLC, stage IA-IIB, and performance status 0-1 (England only; N=2,753, of whom 1,698 had surgery, and 1,055 did not). Data from NLCA.

This highlights the need to proactively stage patients accurately and to assess their fitness for surgery, and if required optimise their co-morbidities prior to surgery, given the improved outcome observed in these patients after surgery.

### 2.2.8.1 One year survival

There has been a dramatic improvement in one year survival for individuals with lung cancer over the last 10 years. This may reflect improved cancer services within the National Health Service secondary to recommendations within the National Cancer Plan (24), and the Cancer Reform Strategy (27) in England and the Designed to Tackle Cancer in Wales Strategic Framework (60). Contemporary data reveals 32% of male patients and 35% female patients survive to one year in England, and 33% male and 37% female Welsh patients survive to one year (figure 2.18). These contemporary data suggest that one year survival in England and Wales is now approaching the figure of 37% quoted as 'good practice' in the EUROCARE-4 publication (21). 'Good practice' is based on the highest one year survival rates of countries with 100% registration in EUROCARE-4.

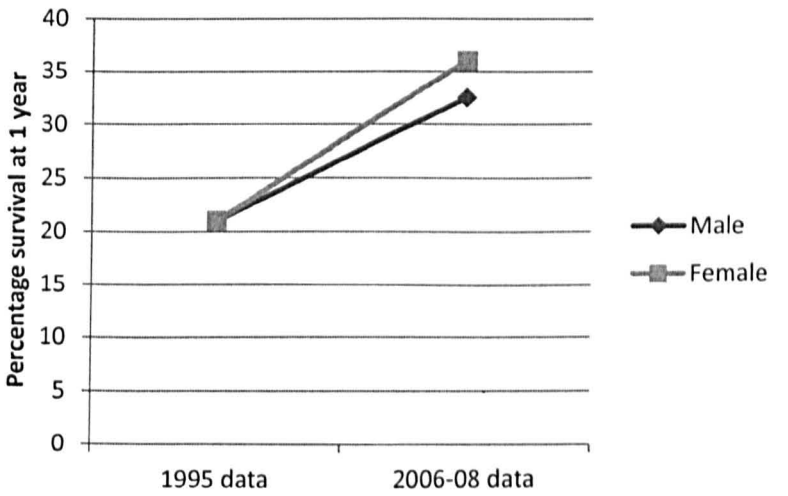


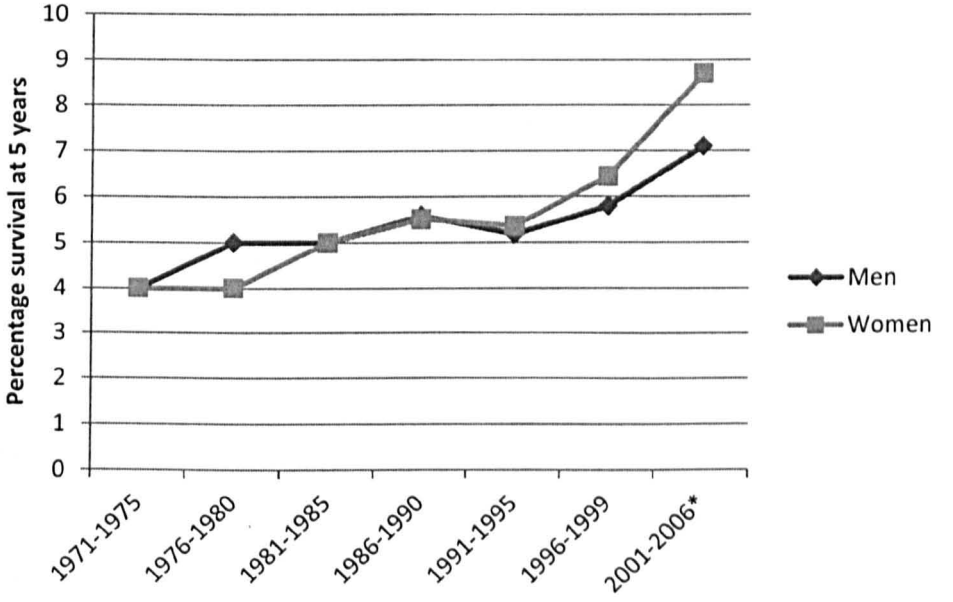

Figure 2.18: One year survival data for England and Wales (2006-2008); Data from NLCA and CANISC.

However, the improvement in overall percentage of patients alive one year after diagnosis conceals the geographical variation that has been described between Primary Care Trusts (PCT) in England ranging from 15.4% to 43.7% (37). This apparent discrepancy in survival will be influenced by the total number of

patients, patient features, the infrastructure of the health service (specifically the availability of diagnostic and treatment facilities in individual PCTs) but importantly, may be influenced by the approach the local MDT takes to selection of patients for active treatment.

### 2.2.8.2 Five year survival

The percentage of patients surviving to 5 years, by definition cured, remains low, 7% for males and 9% for females. Although this has improved over the last 40 years, it remains lower than comparable European and North American countries (21).




Legend: * 5 year survival data incomplete for patients diagnosed in 2006

Figure 2.19: Five year survival data over time (Reproduced with kind permission of Cancer Research UK).

### 2.3 Facilities available at NHS Trusts in England and Wales

As part of the Needs Assessment exercise an online survey was distributed to all lung cancer MDT leads at NHS Trusts in England, and all Local Health Boards in Wales (appendix 3). The lung cancer leads were invited to complete the survey which primarily focussed on the composition of the multi-disciplinary team (MDT), and the diagnostic and therapeutic facilities available within their Trust or their cancer Network. The response rate was 101 (66%) in England and 6 (43%) in Wales. The NHS in Wales underwent a major reorganisation in October 2009, with the formation of seven Local Health Boards from the previous configuration of Local Health Boards and Trusts. Each new Local Health Board therefore encompasses several MDTs.

Cancer MDTs, which were recommended in the NHS Cancer Plan in England (24), and in the Cameron Report in Wales (61) have been adopted across all cancer sites. The aim was to provide a body of experience and breadth of knowledge such that patients under investigation for cancer could be rapidly assessed and the appropriate treatment started at the earliest opportunity. There are no fixed criteria on which medical disciplines should comprise the MDT, and the National Cancer Peer Review Programme in England (which is led by the National Cancer Action Team, NCAT) have recommended that all personnel deemed relevant to the decision making process should be involved either in person or via video/teleconferencing. The majority of lung cancer MDTs would include a chest physician, radiologist, pathologist, and specialist nurse; as well as oncologists, surgeons and members of the palliative care team if available. The Peer Review Programme provides important information on the number, structure, function and quality of all cancer MDTs across England. Between 2004 and 2008, peer reviews of cancer services were carried out in each cancer network, for each cancer site. The process has been modified over the last 6 years, and now occurs on an annual basis, involves a degree of self assessment, and there are

32 measures to which a Lung Cancer MDT is assessed for compliance. There are currently 161 lung cancer MDTs across 157 English NHS Trusts, and 14 MDTs in Wales.

In Wales the Welsh Assembly Government launched the National Cancer Standards in 2005, including lung cancer (62), with the objective that compliance should be achieved by March 2009. The National Cancer Standards have provided NHS Wales with a clear set of quality requirements that have been central to the Welsh Assembly Governments Cancer Policy since 2005 (60). Compliance to these standards has been determined by using information provided by self assessment by NHS Trusts in Wales and the most recent data were published in 2009.

The survey distributed by the NICE GDG revealed that between 90-100% of MDTs in England and Wales had a respiratory physician, chest radiologist, pathologist, specialist nurse and clinical oncologist on the MDT. However, only 80% of MDTs had a medical oncologist, and 85% had a thoracic surgeon on the MDT.

Of those English and Welsh MDTs responding to the survey, all now have an MDT co-ordinator, 95% have an electronic database, and 65% have a data administrator. These figures suggest that the lung cancer MDT is now an established component of every NHS Trust and the majority have adequate support staff.

The analyses described in the remainder of the Needs Assessment use only the on-line results from lung cancer leads at English NHS Trusts, because the number of Welsh responses would not allow appropriate statistical analysis nor could they be merged with the English responses.

### 2.3.1 Lung Cancer Specialist Nurses

The workload of the Specialist nurse was also evaluated in the survey, and revealed significant variation in the number of new cases allocated to each full time equivalent (FTE) nurse, and the number of additional tasks they are expected to perform.

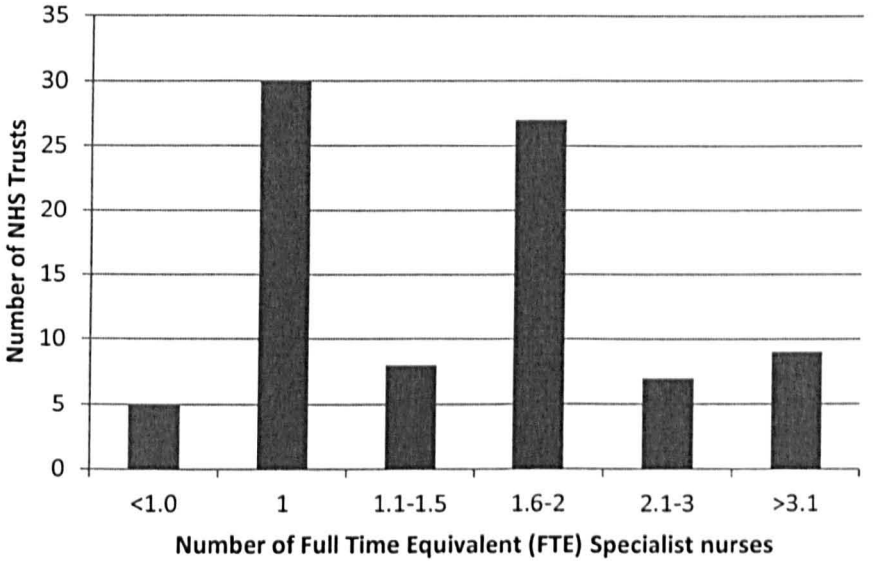



Figure 2.20: Number of (FTE) specialist nurses at NHS Trusts in England.

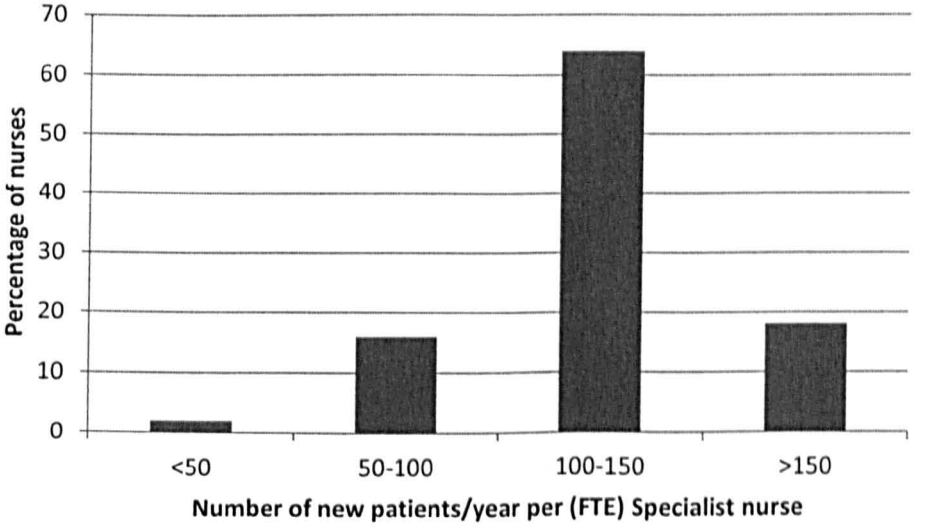



Figure 2.21: The variation in workload of new patients per (FTE) specialist nurse (England only data).

The responsibilities of the specialist nurse can vary, and often involve inappropriate tasks that reduce the time they can spend with patients, their families and carers. The table below lists some of the tasks performed by Specialist nurses in England.

Table 2.2: Duties of a Specialist Lung Cancer Nurse

| **Duties of the Specialist nurse** | **% of nurses** |
|---|---|
| Telephone support | 100 |
| Nurse-led clinics | 44 |
| Support groups | 52 |

Only 44% of Specialist nurses have secretarial support, and 57% have formal cover arrangements for sick leave.

### 2.3.2 Access to diagnostic and endobronchial therapeutic facilities

The results of this NICE lung cancer GDG survey reveal wide variation in the availability of diagnostic facilities at NHS Trusts in England (figure 2.22) and at the level of Cancer Networks (figure 2.23). Consequently some patients will be expected to travel considerable distances to undergo diagnostic procedures and for which there may be a moderate delay of more than 2 weeks (figures 2.24 and 2.25, England only data).

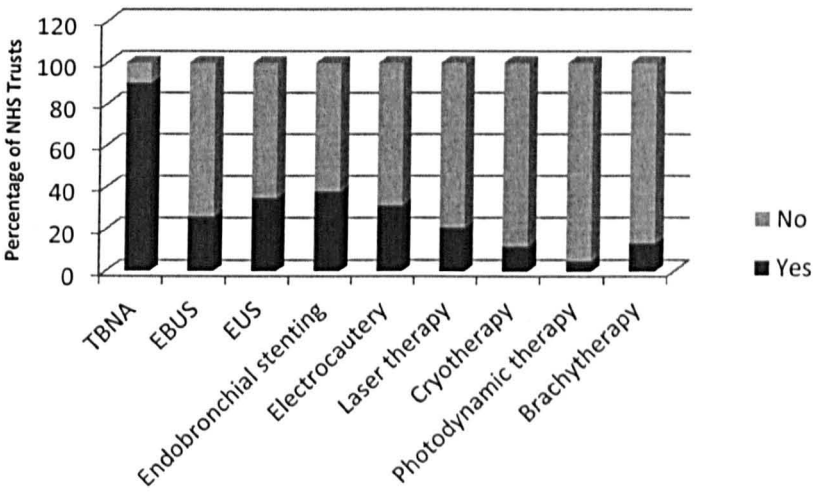



Figure 2.22: Endobronchial diagnostic facilities available at an NHS Trust.

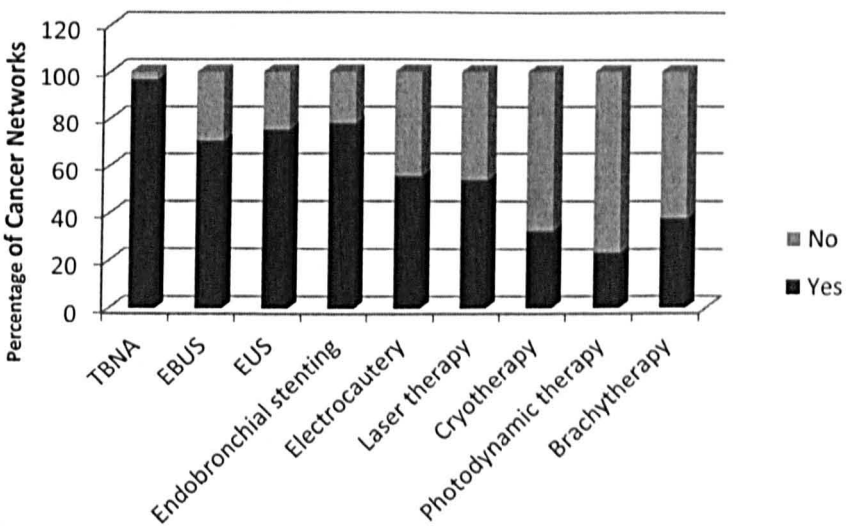



Figure 2.23: Endobronchial diagnostic facilities available within a Cancer Network.

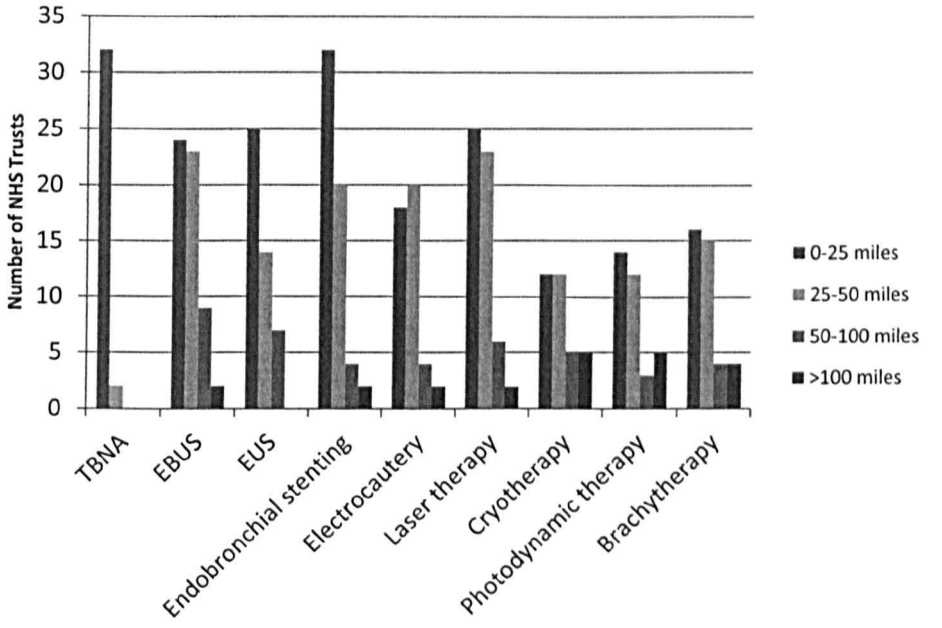



Figure 2.24: Distance required to access certain diagnostic and therapeutic services.

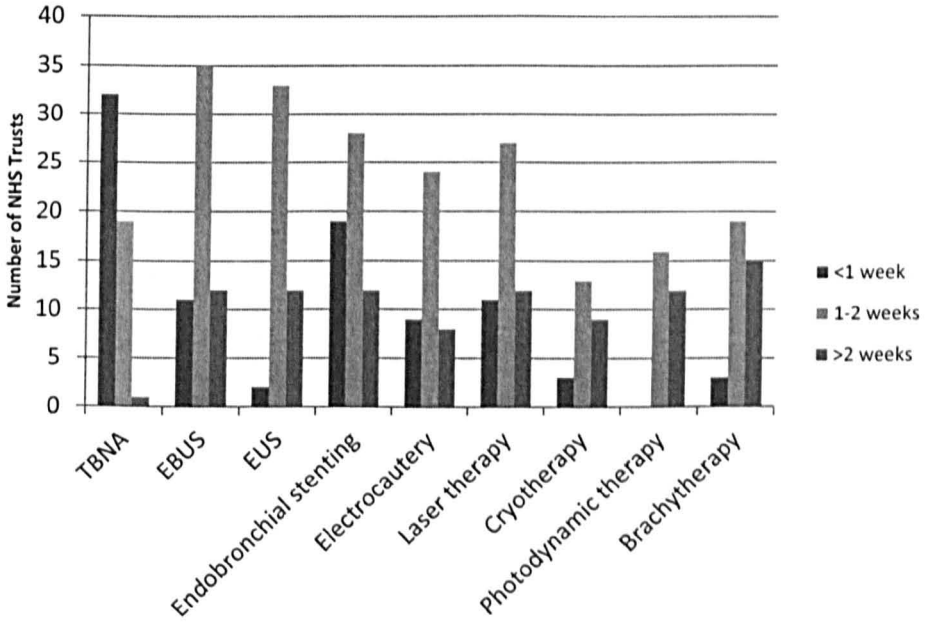



Figure 2.25: Interval between referral and access for certain diagnostic and therapeutic services

### 2.3.3 PET scanning

Over the past 15 years a number of publications have supported the use of FDG-PET scanning to assist the staging process of lung cancer. The 2005 NICE Guidelines for Diagnosis and Treatment of Lung Cancer (26) recommended the use of this imaging modality, and the availability of PET-CT scanners has become almost universal. However, this availability may be at the level of the Cancer Network, rather than at individual NHS Trusts (see figure 2.26-2.28, England only data).

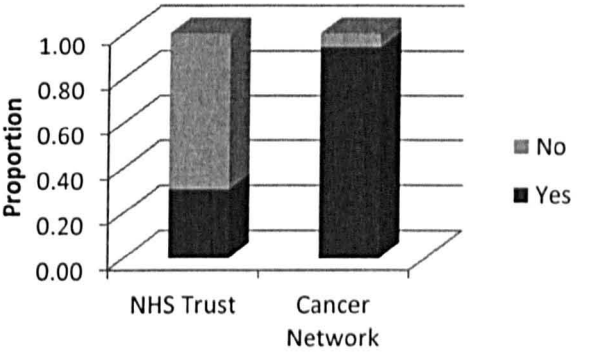



Figure 2.26: Proportion of NHS Trusts and Cancer Networks with PET scanners.

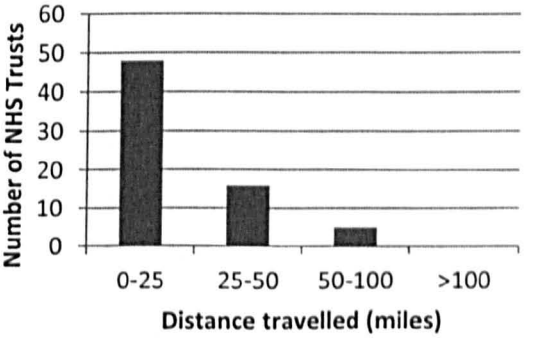



Figure 2.27: Distance travelled to access a PET scanner.

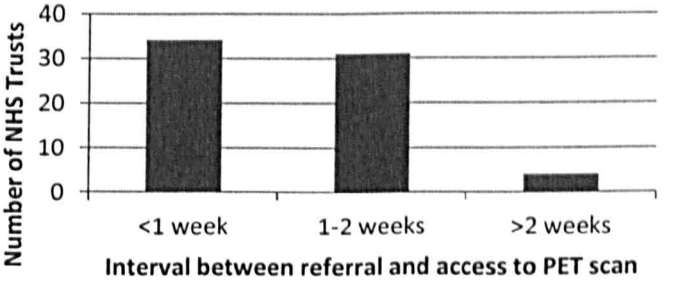



Figure 2.28: Interval between referral and access to PET scanning.

### 2.3.4 Pathological services

The importance of increasing the histological confirmation rate has already been emphasised, but it is also important that there is not an unnecessary delay in obtaining the histological report as this will delay the final diagnostic and therapeutic decision of the MDT. Results from the survey of lung cancer leads revealed 80% of diagnostic samples are returned within 5 days, i.e. within a working week, ensuring the result is available for the next MDT meeting.

### 2.3.5 Pulmonary rehabilitation services

There was good availability of pulmonary rehabilitation services across English lung cancer MDTs who completed the survey, with 78% NHS Trusts having access to this service, and 79% of Cancer Networks (figure 2.29). 92% of NHS Trusts reported a patient would not have to travel more than 25 miles to receive this service, although 86% stated that there would be a delay of more than 2 weeks to access this service.

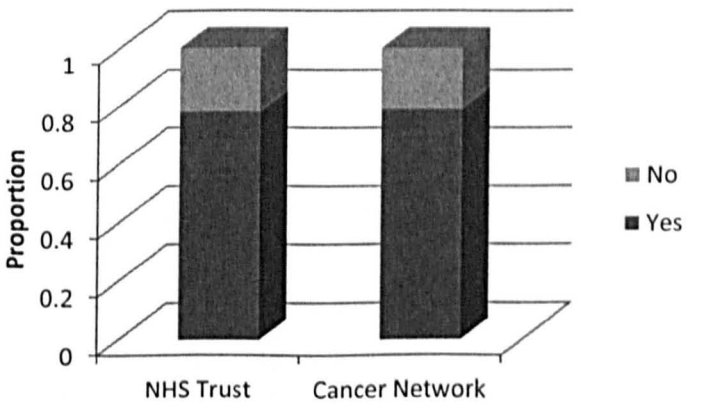



Figure 2.29: Proportion of NHS Trusts and Cancer Networks with pulmonary rehabilitation services (England only data).

### 2.3.6 Access to treatment facilities

There is significant variation in the treatment facilities available at individual NHS Trusts. Amongst the 157 NHS Trusts in England there are only 31 Cardiothoracic surgical centres and 49 Radiotherapy centres. Figure 2.30 illustrates the variation in treatment facilities available at the level of an individual NHS Trust; although the majority of treatments are available within a Cancer Network (figure 2.31). There may well be a significant distance to travel and delay to receive the recommended treatment modality (figure 2.32 and 2.33 below, England only data).

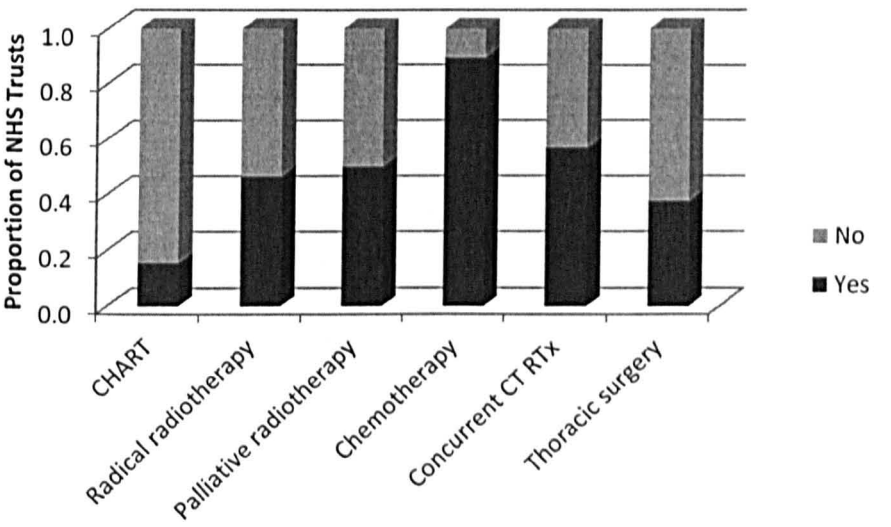



Figure 2.30: Treatment facilities available at an NHS Trust.

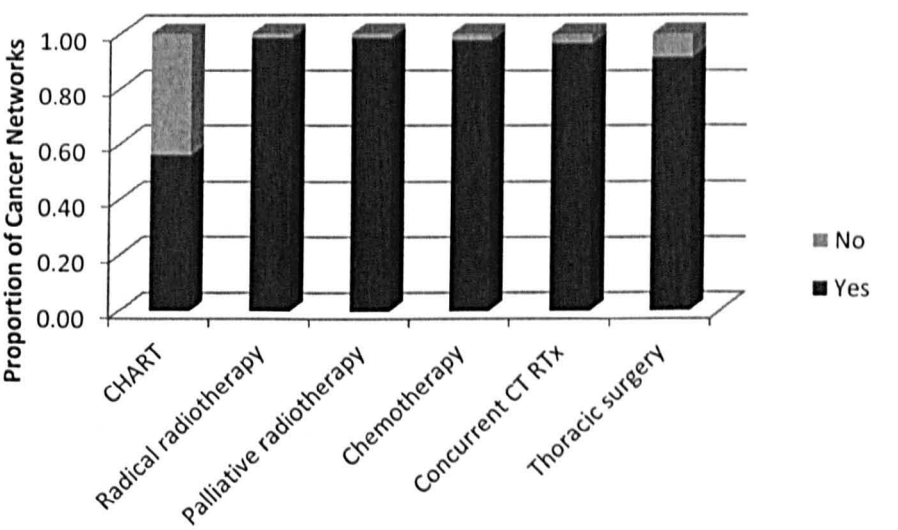



Figure 2.31: Treatment facilities available within a Cancer Network.

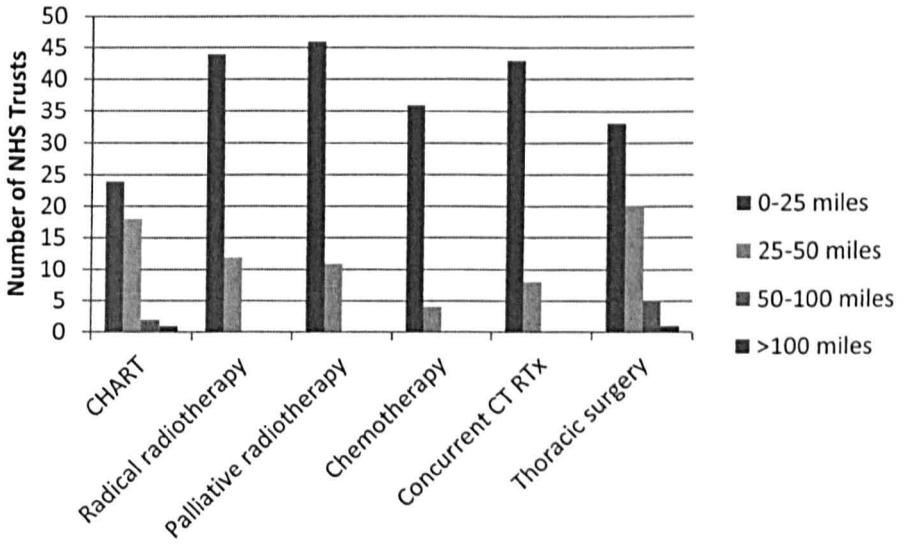



Figure 2.32: Distance required to access specific treatment modalities.

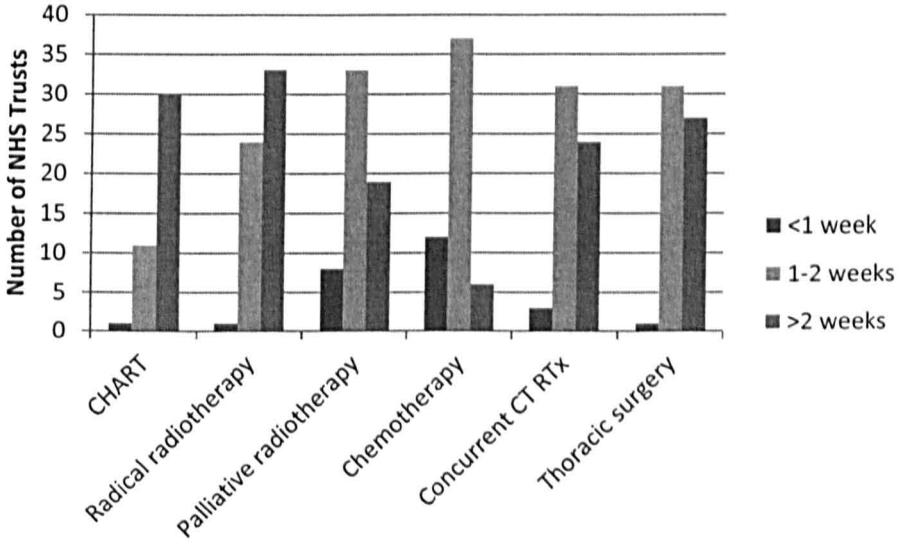



Figure 2.33: Interval between referral and access to specific treatment modalities.

There have been a number of publications which suggest that the further a patient with cancer must travel to a treatment centre the less likely they are to undergo treatment (47, 54). Amongst patients with lung cancer in Northern England; the adjusted odds ratio for receiving surgery, chemotherapy and radiotherapy, was 0.76 (95% CI 0.68, 0.85), 0.70 (95% CI 0.63, 0.79), and 0.86 (95% CI 0.80, 0.91) respectively, for those living furthest, compared with those living closest, to the treatment centre (54).

Therefore, whilst specialised treatment centres may have increased expertise as the high throughput of patients will increase experience, this benefit must be balanced with the potential impact that fewer, centralised, specialised centres may result in reduced uptake of treatment by individuals in remote areas.

# Chapter Three: Description and initial validation of the NLCA dataset

### 3.1 Introduction

Before any conclusions can be drawn from analysis of data within the National Lung Cancer Audit, the validity of the dataset needs to be tested, proven, and accepted by the medical profession. Anecdotally, the main concern levied at the dataset arises from the fact that data entry is non-mandatory and hence incomplete. This may result in data that are not truly representative of the spectrum of disease. There is marked variation between NHS Trusts in the amount of data entered into the dataset (63). For those NHS Trusts with incomplete data entry, it is important to ensure that data are not biased in terms of the type of patients selected for inclusion in the audit.

The aim of this chapter is to describe the basic properties of the data within the NLCA dataset and to look for evidence of variation depending on the level of NHS Trust reporting. In order to do this, I used funnel plots to examine the variation in patient demographics based on the actual number of patients entered into the NLCA by each NHS Trust. I will then describe the creation of an observed:expected ratio of individuals with lung cancer for every NHS Trust. This allows me to divide all NHS Trusts into strata based on this measure of case ascertainment. The actual dataset used during this validation process (chapters 3 and 4) was downloaded on 17th November 2008, and includes all patients first seen up to the 31st December 2007. Other sources of data for comparison included the Office of National Statistics (ONS) and Hospital Episode Statistics (HES). In May 2009, I was given access to the most recent data from Thames cancer Registry, the national Registry for Lung, and this allowed me to perform additional analyses (including survival analyses) which are reported in Chapter 4.

## 3.2 Methods

### 3.2.1 The NLCA dataset

The National Lung Cancer Audit database, commissioned by the Healthcare Commission and then HQIP (Healthcare Quality Improvement Partnership), was established in July 2004, in a partnership between the NHS Information Centre and the Royal College of Physicians. It has been formally acknowledged and supported by the National Institute for Clinical Excellence (NICE) guidelines on "The Diagnosis and Treatment of Lung Cancer" (2005) (26).

#### 3.2.1.1 Data collection and the NLCA population

Data are entered into NLCA from individual NHS Trusts in England, usually via the lung cancer multi-disciplinary team, and are collected via the Open Exeter portal. The individuals collecting and uploading the information include respiratory physicians, lung cancer specialist nurses, lung cancer co-ordinators and specialist audit data managers. Data entry follows a pro-forma which can be accessed on line at:

http://www.ic.nhs.uk/webfiles/Services/NCASP/Cancer/New%20web%20documents%20(Lung)/LUCADA%20proforma%20v3%20+%20Key%20Fields.doc. Data can be entered periodically, and the closing date for inclusion in the annual report is the 30th June the following year. However, data entry is never closed, and so an NHS Trust could upload information on patients covering a number of years in one go, although not all would be included in the relevant annual report. It is possible for a patient to have their first hospital attendance at one NHS Trust and then to receive their treatment at another NHS Trust, and so information about the diagnostic and treatment pathway of one patient can be entered by two or more NHS Trusts. The latest entry chronologically overwrites all preceding entries regarding that one particular patient.

The patient population in the NLCA database consists of all individuals receiving a diagnosis of lung cancer; be that with proven histology or by clinical means alone. It also includes individuals who have lung cancer reported on a death certificate, for which no formal diagnosis was made ante-mortem.

#### 3.2.1.2 Data cleaning

The initial dataset downloaded and delivered to Nottingham University for the purposes of this research fellowship included all patients within the dataset who had had their first hospital appointment before 31st December 2007. It included 67,824 patients. An important first step in data cleaning was the creation of start and end dates for survival analyses which will be performed in all subsequent chapters. The date of diagnosis, where present, was used as the start date. In the absence of this a surrogate date of diagnosis was calculated using an alternative available date in the following sequential order: date of first NHS Trust appointment, date of referral from general practitioner, and, finally, the date of the multi-disciplinary team meeting where a decision on patient treatment was made (figure 3.1). Using the median number of days for the whole cohort between the date of diagnosis (where available) and each of the alternative dates, a surrogate date of diagnosis was interpolated and hence a surrogate start date for people without an actual start date (figure 3.2). It was not possible to calculate a start date in 3,962 individuals (6%) and they were excluded from the cohort, leaving 63,862 patients. An end date was generated using either the date of death (obtained from the Personal Demographics Service), or the date the dataset was downloaded, which was the 17th November 2008. Data were incorporated into the statistical programme Stata SE version 10 (Stata corp. TX USA) and this was used for all subsequent analyses.

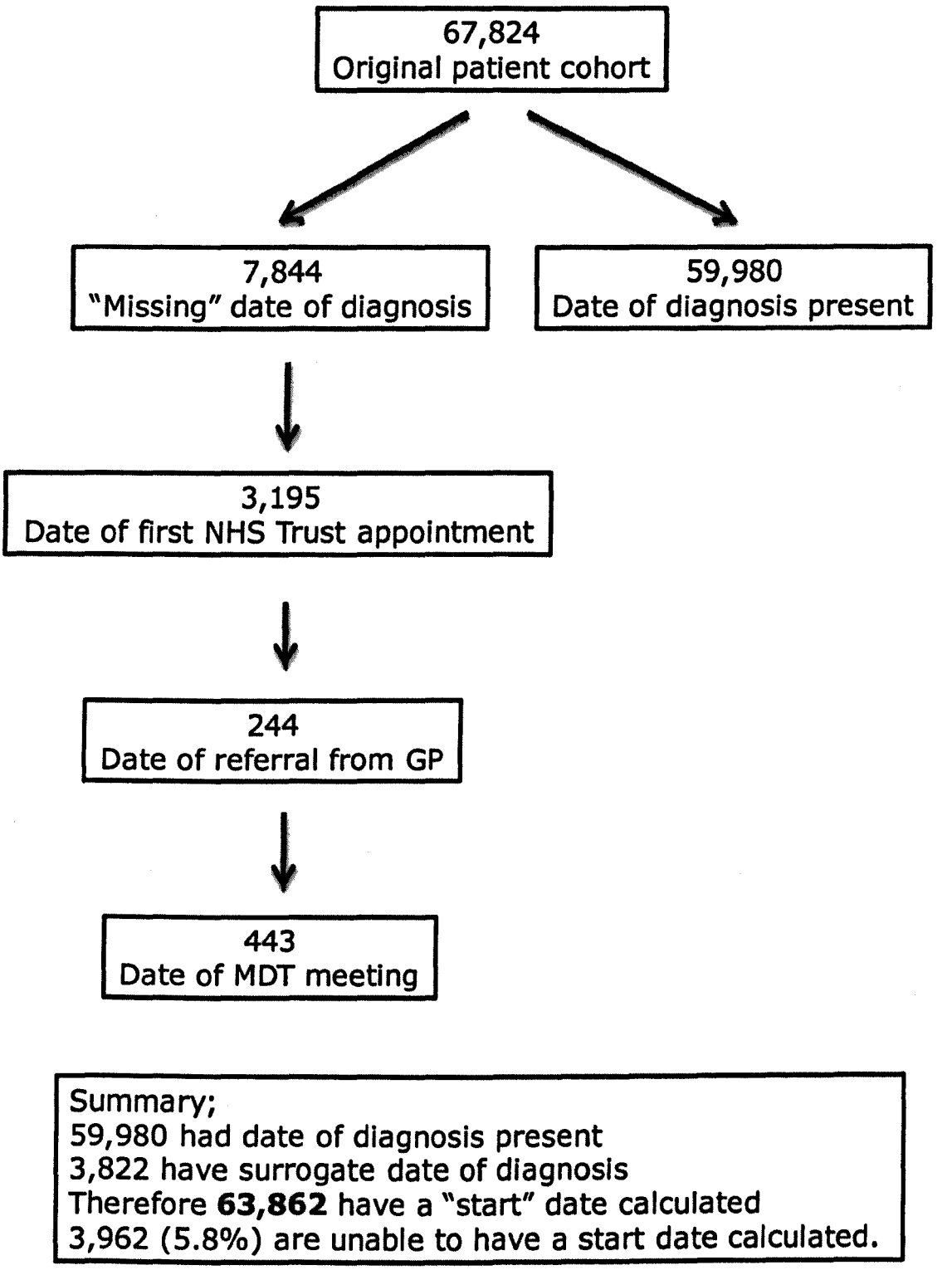



Figure 3.1: Flow diagram depicting the method used to calculate start date.

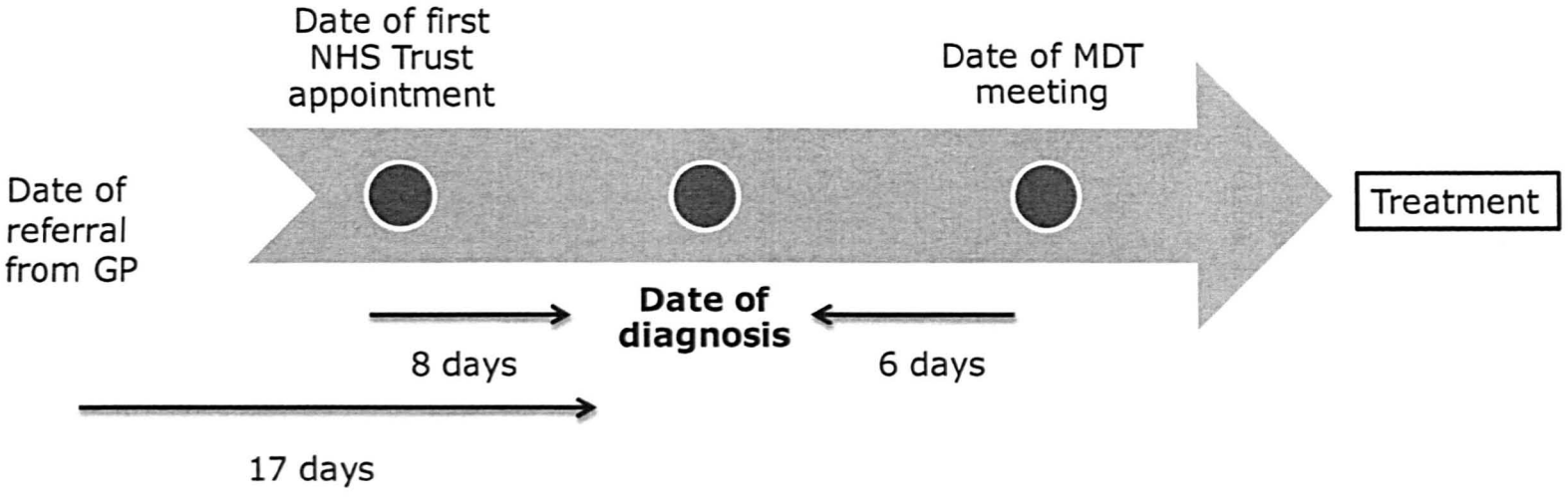



Figure 3.2: Diagram illustrating the median intervals between key dates in the patient pathway which were used to interpolate a "start" date if the date of diagnosis was missing.

In the remaining cohort there were two individuals without a sex ascribed, and a further 74 who had an age at diagnosis of less than 30 years and in whom it was felt that either the data may be unreliable or that their disease was not representative of the overall cohort, and these two groups of individuals were also excluded. This left a total of 63,786 patients with a start date calculated, a sex assigned, and over the age of 30 years at diagnosis.

Patients may receive their diagnosis and treatment in more than one NHS Trust. For this evaluation a patient was assigned to the NHS Trust at which they had their first appointment. This would allow subsequent analysis of possible inequalities in treatment offered and survival based on the NHS Trust at which a patient is first seen. A total of 3,039 (5%) patients had "unknown" as the NHS Trust at which they were first seen and so they were excluded from this analysis, leaving a total of 60,747 patients.

### 3.2.2 Examining the data based on NHS Trust size using funnel plots

Conventionally used to evaluate publication bias of studies included in meta-analyses, a funnel plot is a scatter plot of treatment effect against a measure of study size. A symmetrical inverted funnel shape, with most studies lying evenly to both sides of a central estimate of treatment effect, and larger studies lying closest to the peak of the funnel, suggests no evidence of publication or reporting bias.

In this setting a funnel plot was created to examine the effect of NHS Trust size, i.e. the number of patients who had their first appointment at each NHS Trust, on six key patient features. These features were selected on the basis that they might reveal evidence of bias in the patients being selected for inclusion in the NLCA dataset. The features chosen were: sex, mean age at diagnosis, proportion of patients over 80 years, proportion of patients with a histological

diagnosis, proportion of patients with early stage disease (Ia-IIIa, according to the Union Internationale Contre Cancer version 6) and the proportion of patients with curative treatment intent.

### 3.2.3 Creating a measure of case ascertainment for each NHS Trust

To quantify the level of data completeness, in other words case ascertainment, at the level of an NHS Trust, an observed:expected ratio was calculated. The level of an NHS Trust was chosen as this is the level of interest for clinicians. However there are no published data on the expected number of lung cancer patients at this level, instead the level of a Primary Care Trust (PCT) is often used. The NLCA dataset contains information on the number of patients within each Primary Care Trust, based on a patient's postcode and so this formed the "observed" number of patients within each PCT. Data from the Office of National Statistics (ONS) and then Hospital Episode Statistics (HES) were used to estimate an "expected" number of patients for each PCT. This allowed a two stage process to be undertaken, firstly to create an observed:expected ratio at the level of a Primary Care Trust (PCT), and then to extrapolate this to the level of an NHS Trust.

#### 3.2.3.1 Using data from the Office of National Statistics

In the absence of definitive data from Cancer Registry, unavailable initially, data from The Office of National Statistics (ONS) were used. Data from the 2005 annual report of Cancer Incidence were used, as the most up-to-date at the time of study (64). These data of lung cancer incidence (per 100,000 population) are recorded in age/sex strata nationally. The ONS also has data for the population of each of the 152 primary care trusts (PCTs) for the same age/sex strata. It is therefore possible to use direct standardisation to calculate the expected number of individuals with lung cancer for each of these PCTs, for each age/sex stratum. This information was then reduced to create an expected number of patients of each sex for each PCT.

However, lung cancer incidence is not distributed equally across England, and so it was necessary to account for this geographical variation. The Office of National Statistics documents the variation in lung cancer incidence across the nine Government Office regions, and states the national rate for each sex. Table 3.1 illustrates these data, and the regional:national ratio for each Government office. Government offices were linked to primary care trusts and the regional:national ratio was used to correct the expected number of patients at each PCT, accounting for geographical variation in lung cancer incidence. The expected number of men and women were then totalled to generate an overall expected number of lung cancer patients for each PCT. Using the NLCA data ("observed" numbers) an observed:expected ratio at the level of a PCT could now be created.

Table 3.1: Regional variation in lung cancer incidence (ONS 2005)(64)

| Government Office Region | Male* | Female* | Male R:N | Female R:N |
|---|---|---|---|---|
| North East | 102.5 | 78.5 | 1.41 | 1.55 |
| North West | 90.3 | 67.9 | 1.24 | 1.34 |
| Yorkshire and the Humber | 80.2 | 60.7 | 1.1 | 1.2 |
| East Midlands | 76.6 | 49.4 | 1.05 | 0.98 |
| West Midlands | 75.8 | 45.1 | 1.04 | 0.89 |
| East | 67.2 | 44.4 | 0.92 | 0.88 |
| London | 54.8 | 39.6 | 0.75 | 0.78 |
| South East | 62.4 | 41.9 | 0.86 | 0.83 |
| South West | 70.7 | 46.0 | 0.97 | 0.91 |
| **England** | **72.9** | **50.6** | | |

* Directly age-standardised incidence rate using European standard population (per 100,000). R:N regional:national ratio

To translate our primary care trust results to the level of an NHS Trust, websites of both primary care trusts and NHS Trusts were researched, and primary care trusts were mapped to the NHS Trusts from which they commission services. Whilst 93 (61%) of the 152 primary care trusts commissioned services from a

single NHS Trust, 25 primary care trusts used two NHS Trusts, a further 27 used three, five used four, and two primary care trusts had a total of five NHS Trusts from whom they commissioned services. Where an NHS Trust was associated with multiple primary care trusts, the mean primary care trust observed:expected ratio was calculated. NHS Trusts were then stratified by generating quartiles of the observed:expected ratios.

#### 3.2.3.2 Using data from Hospital Episode Statistics (HES)

In order to try and strengthen the stratification of NHS Trusts, a second method was used to generate an observed:expected ratio at this level. Hospital Episode Statistics (HES) are mandatorily collected nationally and include data on admissions and out-patient appointments at NHS Trusts (65). Data are available on the annual number of admissions to NHS Trusts and the total number of admissions for all the Trusts within a Strategic Health Authority (SHA). It is therefore possible to create a proportion of admissions for each NHS Trust within a Strategic Health Authority.

Table 3.2: Extract from HES detailing acute admissions within one SHA (2006/7)

| | Number | Proportion* |
|---|---|---|
| **East Midlands Strategic Health Authority** | **958,315** | |
| Chesterfield Royal Hospital NHS Foundation Trust | 64,995 | 0.07 |
| Sherwood Forest Hospitals NHS Foundation Trust | 71,251 | 0.07 |
| Kettering General Hospital NHS Trust | 67,538 | 0.07 |
| Northampton General Hospital NHS Trust | 82,362 | 0.09 |
| Derby Hospitals NHS Foundation Trust | 126,325 | 0.13 |
| United Lincolnshire Hospitals NHS Trust | 134,515 | 0.14 |
| University Hospitals of Leicester NHS Trust | 217,524 | 0.23 |
| Nottingham University Hospitals NHS Trust | 193,805 | 0.20 |

Legend: * proportion of all acute admissions in the SHA seen in each NHS Trust

The Office of National Statistics publishes the actual number of lung cancer patients for each Government Office region, and these map almost directly to Strategic Health Authorities. The only exception is the Government Office for the South East, which includes the South Central and South East coast SHAs.

Therefore the total number of admissions for these two SHAs were combined and the proportion for each individual NHS Trust recalculated.

Table 3.3: Number of lung cancer patients in each SHA/Government region

| Strategic Health Authorities/Government Offices | Number |
|---|---|
| East Midlands | 2718 |
| East of England | 3092 |
| London | 3515 |
| North East | 2300 |
| North West | 5396 |
| South Central and South East | 4251 |
| South West | 2953 |
| West Midlands | 3223 |
| Yorkshire and Humber | 3589 |

Assuming that the proportion of admissions and the proportion of lung cancer patients at each NHS Trust, within each SHA, were virtually equal, it was possible to calculate an expected number of lung cancer patients for each NHS Trust.

Table 3.4: Extract of table describing process of combining HES and ONS data

| | Number of acute admissions | Proportion* | Expected number lung cancer patients |
|---|---|---|---|
| **East Midlands Strategic Health Authority** | **958,315** | | **2718** |
| Chesterfield Royal Hospital NHS Foundation Trust | 64,995 | 0.07 | 184 |
| Sherwood Forest Hospitals NHS Foundation Trust | 71,251 | 0.07 | 202 |
| Kettering General Hospital NHS Trust | 67,538 | 0.07 | 192 |
| Northampton General Hospital NHS Trust | 82,362 | 0.09 | 234 |
| Derby Hospitals NHS Foundation Trust | 126,325 | 0.13 | 358 |
| United Lincolnshire Hospitals NHS Trust | 134,515 | 0.14 | 382 |
| University Hospitals of Leicester NHS Trust | 217,524 | 0.23 | 617 |
| Nottingham University Hospitals NHS Trust | 193,805 | 0.20 | 550 |

The data from NLCA again provided the "observed" number of patients for each NHS Trust based on the Trust at which they had been first seen. Therefore it was possible to create a second observed:expected ratio for each NHS Trust

using HES data, and then to stratify these by creating quartiles of the observed:expected ratios.

#### 3.2.3.3 Comparing the level of agreement between NHS Stratification derived using data from ONS and HES

NHS Trusts were divided into four equal groups by creating quartiles of the observed:expected ratios which had been created using ONS data (mapped from PCTs to NHS Trusts) and using HES data. The level of agreement between these two methods was evaluated by creating a table of concordance, calculating a weighted Kappa value, and generating a Bland-Altman plot.

### 3.2.4 Assessing the accuracy of NLCA to provide observed cases

A written request was sent to the lead lung cancer physician and the lung cancer audit manager at 40 NHS Trusts, ten from each of the four strata generated using data from ONS and HES. These were randomly selected by the data manager at the Information Centre in Leeds. A copy of the letter is included in Appendix 4. They were asked to report the number of patients with lung cancer who had been first seen at their NHS Trust between 1st January and 31st December 2007. This figure was then compared with the number of patients within the NLCA dataset for the same time period.

### 3.3 Results

There were 67,824 patients in the first dataset downloaded from the NLCA. After cleaning the dataset to ensure all patients had a start date, a sex assigned, were aged over 30 years and had an NHS Trust where they were first seen, the total number of individuals remaining was 60,747. There are 157 NHS Trusts in England, and all except 2 had entered patients at some point into the NLCA. There were 13 NHS Trusts who had entered more than 1000 patients (the largest having entered 2054), and 23 that had entered less than 100 patients.

#### 3.3.1 Results of Funnel plots

Figures 3.3 to 3.8 depict the funnel plots created for this cohort. The inverted symmetrical funnel shape is depicted in Figures 3.3, 3.4, and 3.5, with the largest NHS Trusts tending towards the mean value, which illustrates no suggestion of bias for these features on the basis of NHS Trust "size" alone. Figures 3.6 to 3.8 do not depict the traditional inverted 'funnel' shape. There are a few small NHS Trusts (with less than 10 patients) who appear to have all their patients with either a histological diagnosis, early disease, or being offered curative treatment. But if this were a more widespread deliberate technique to skew the data, for example recording only their patients with early disease and curative intent, there would have been a more pronounced pattern on these graphs with a high frequency of dots in the bottom right hand corner (figures 3.6 to 3.8), which is not the case.

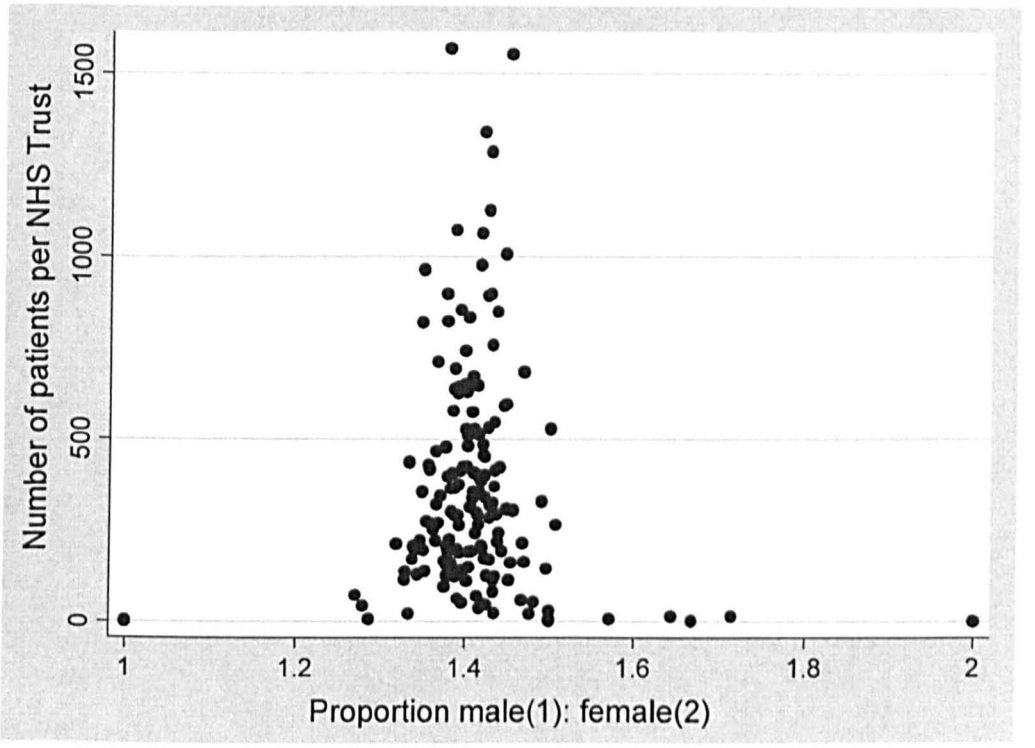



Figure 3.3: Scatter plot illustrating the distribution of sex depending on size of NHS Trust.

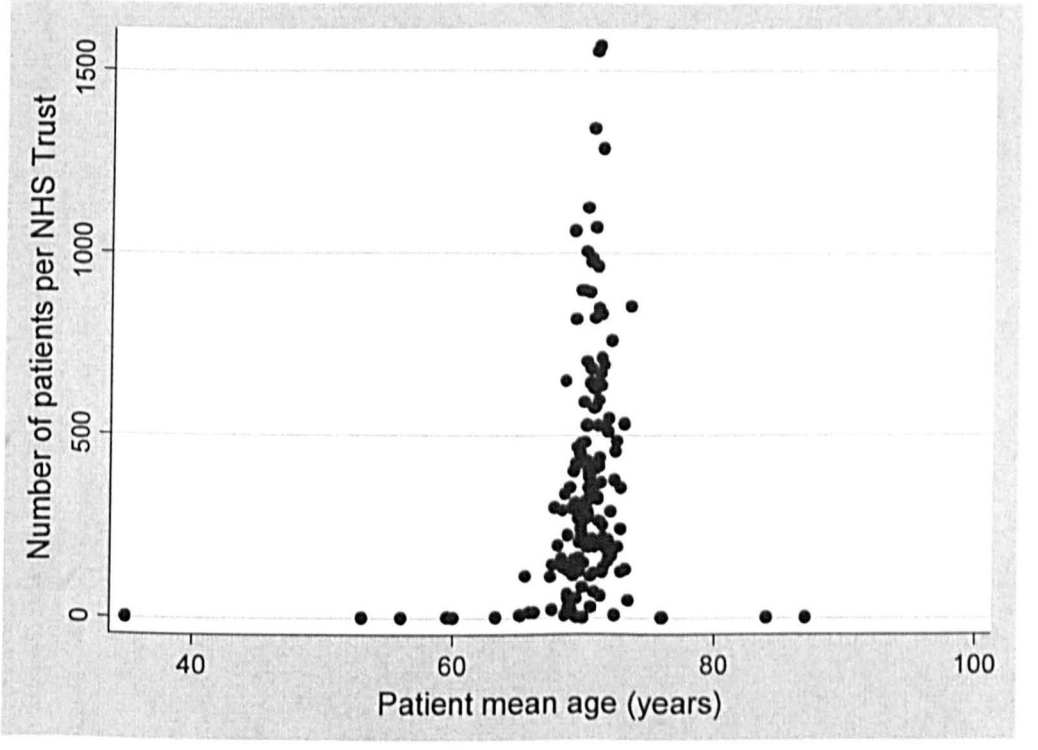



Figure 3.4: Scatter plot illustrating the distribution of mean age at diagnosis depending on size of NHS Trust.

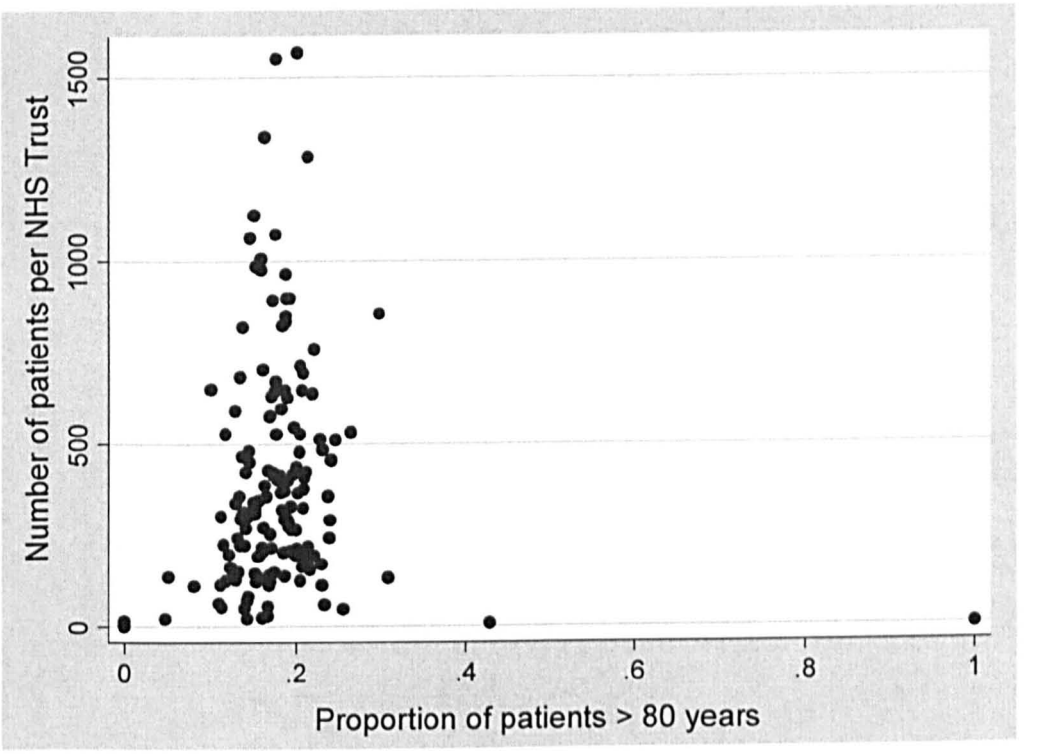



Figure 3.5: Scatter plot illustrating the proportion of patients over the age of 80 years depending on size of NHS Trust.

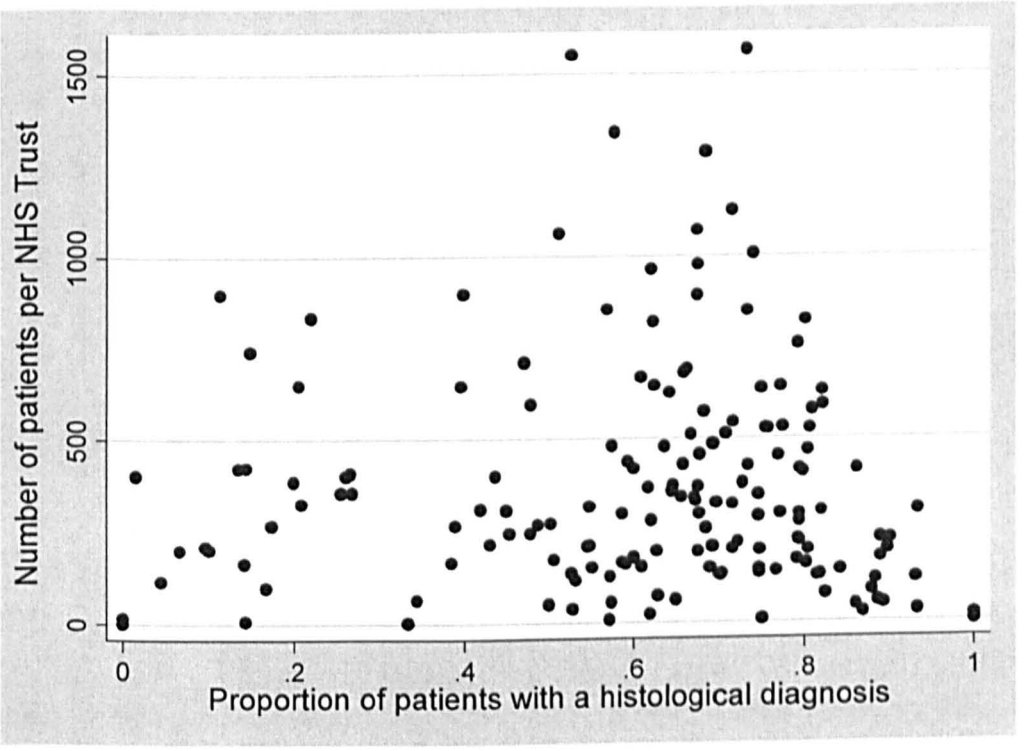



Figure 3.6: Scatter plot illustrating the proportion of patients with a histological diagnosis depending on size of NHS Trust.

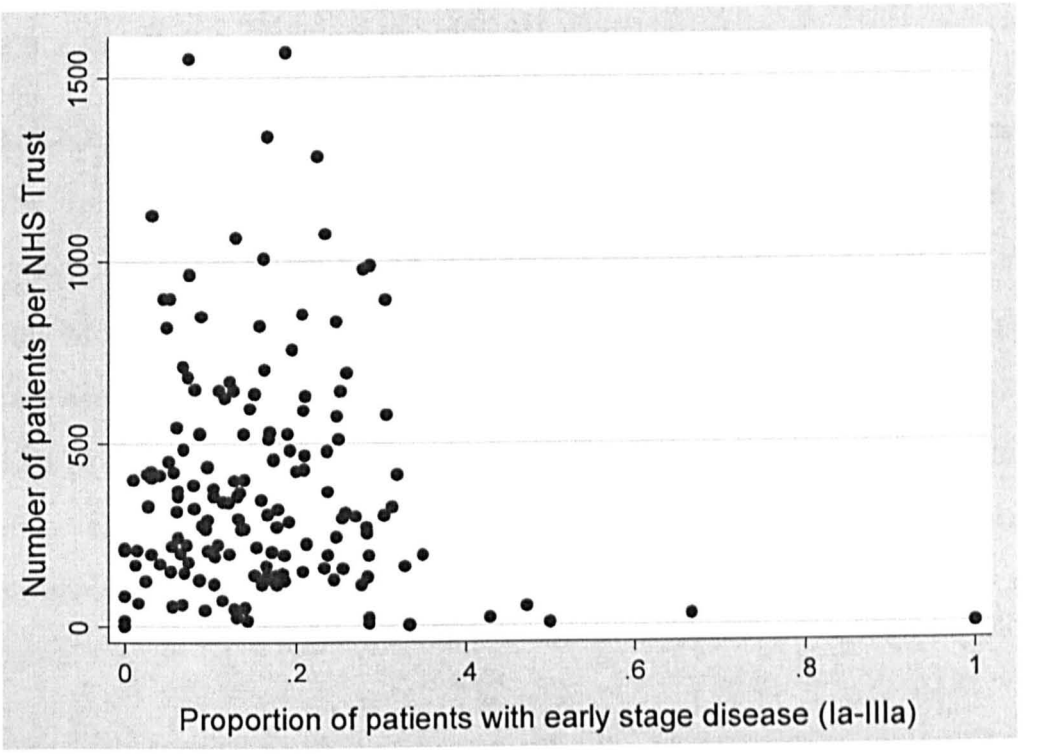



Figure 3.7: Scatter plot illustrating the proportion of patients with early stage disease (Ia-IIIa) depending on size of NHS Trust.

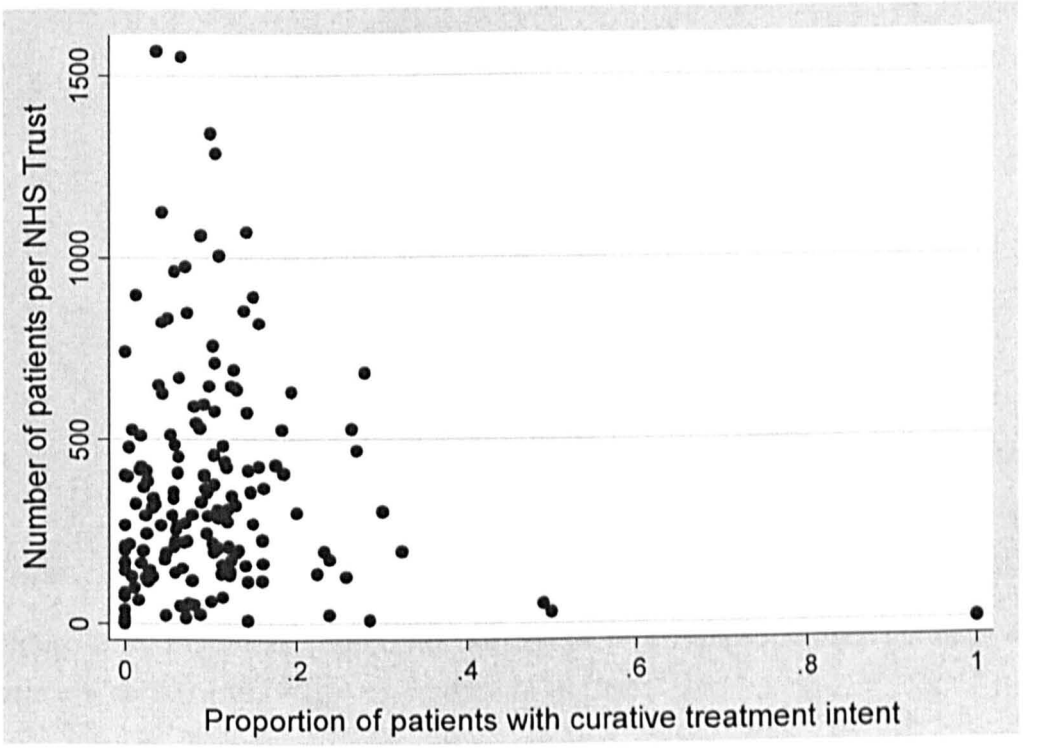



Figure 3.8: Scatter plot illustrating the proportion of patients with curative treatment intent depending on size of NHS Trust.

### 3.3.2 Results of case ascertainment

#### 3.3.2.1 Observed:expected ratios at the level of PCT using ONS data

The median observed:expected ratio for a primary care trust was 0.56 (interquartile range (IQR) 0.37 to 0.77). It was possible to calculate an annual figure for the three years 2005 to 2007, which showed a steady improvement in case ascertainment. In 2005 the median observed:expected ratio was 0.43 (IQR 0.14 to 0.67), in 2006 it was 0.64 (IQR 0.36 to 0.85), and in 2007 the median observed:expected ratio was 0.71 (IQR 0.49 to 0.94). The distribution of observed:expected ratios across primary care trusts are depicted graphically in figure 3.9.

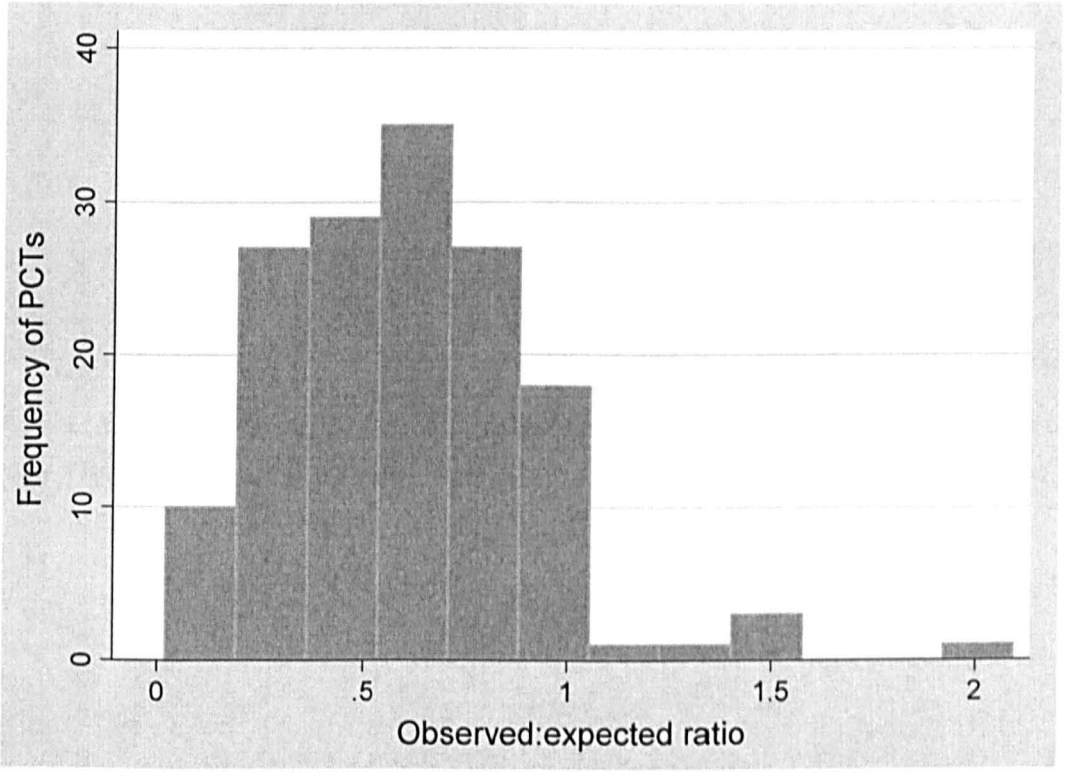



Figure 3.9: Histogram depicting the range of observed:expected ratios across primary care trusts (PCTs) using data from ONS.

### 3.3.2.2 Observed:expected ratios at the level of NHS Trusts

The median observed:expected ratio at the level of an NHS Trust, via the mapping method described in 3.2.3.1, was 0.56 (interquartile range 0.37 to 0.72), and the distribution is depicted graphically in figure 3.10.

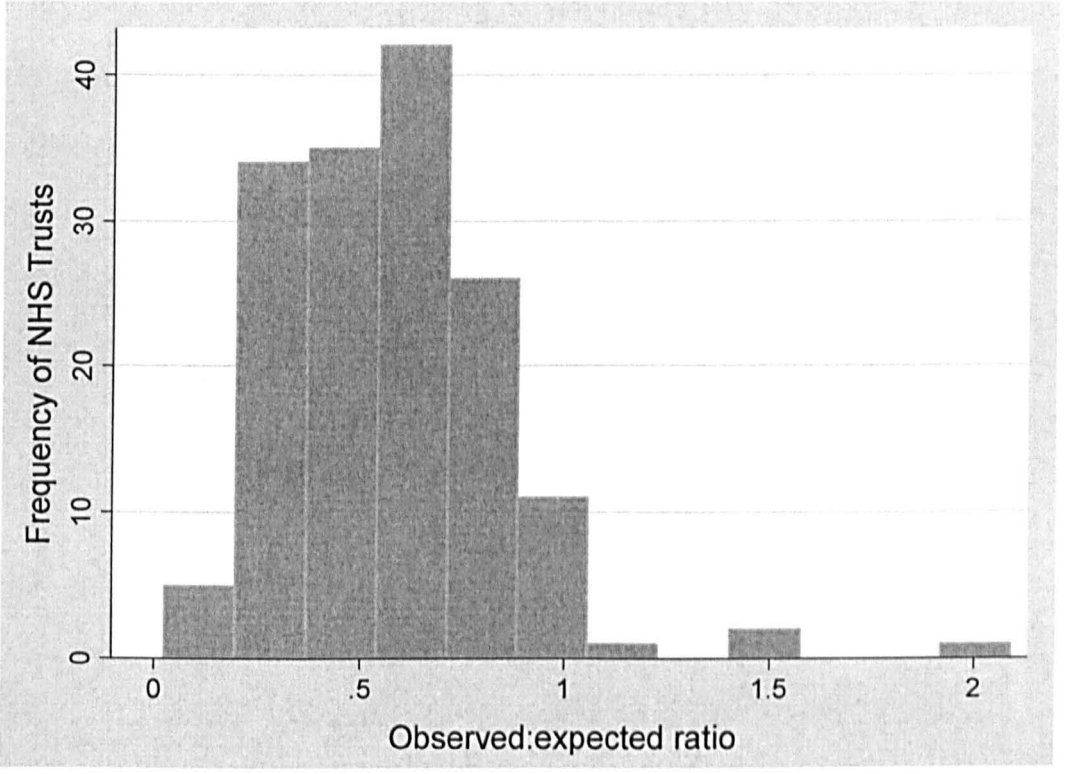



Figure 3.10: Histogram depicting the range of observed:expected ratios across NHS Trusts created via mapping technique from PCT observed:expected ratios.

### 3.3.2.3 Observed:expected ratios for NHS Trusts using HES data

The median observed:expected ratio at the level of an NHS Trust was 0.53 (IQR 0.30 to 0.87). Again there was evidence of improved data completeness year on year, with a median observed:expected ratio in 2005 of 0.32 (IQR 0.05 to 0.75), and a median value of 0.75 (IQR 0.38 to 0.96) in 2007.

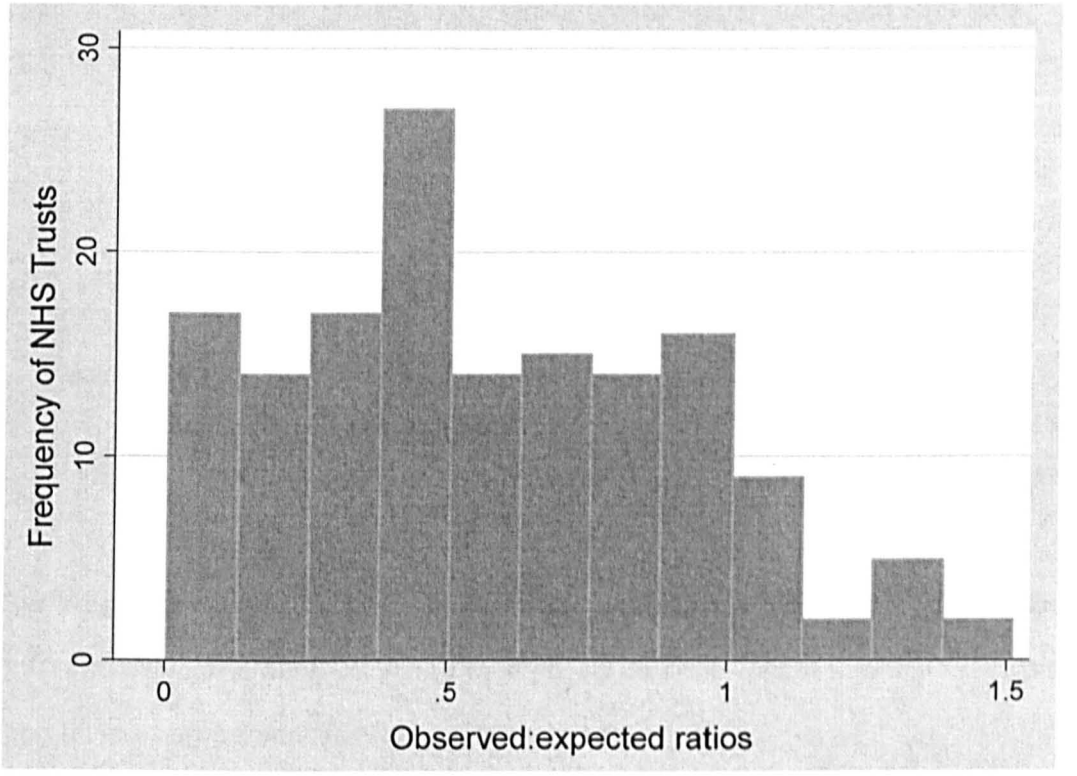



Figure 3.11: Histogram depicting the range of observed:expected ratios across NHS Trusts created using data from HES.

### 3.3.3 Comparing the NHS Trust strata created via these two methods

In order to compare NHS Trust stratification using ONS and HES data, a table of concordance was created, see Table 3.5. Further comparisons of similarity were performed using weighted Kappa values and by generating a Bland-Altman plot (figure 3.12).

Table 3.5: Comparison of NHS Trust strata created using ONS and HES data

| | | **NHS Trust strata calculated using HES data** | | | | | |
|---|---|---|---|---|---|---|---|
| **NHS Trust strata calculated using ONS data** | | 1 | 2 | 3 | 4 | 'Missing' | Total |
| | 1 | **23** | 12 | 3 | 1 | 0 | 39 |
| | 2 | 10 | **16** | 6 | 4 | 0 | 36 |
| | 3 | 4 | 10 | **19** | 7 | 1 | 41 |
| | 4 | 1 | 1 | 10 | **27** | 2 | 41 |
| | 'Missing' | 0 | 0 | 0 | 0 | 11 | 11 |
| | Total | 38 | 39 | 38 | 39 | 14 | 168 |

NHS Trust stratum; 1=quartile with highest observed:expected ratio, 4=quartile with lowest observed:expected ratio.

The weighted Kappa value for NHS Trust strata using these two methods was 0.70 (actual agreement 93.9%, expected agreement 79.5%), which confirms a high level of agreement for these two methods.

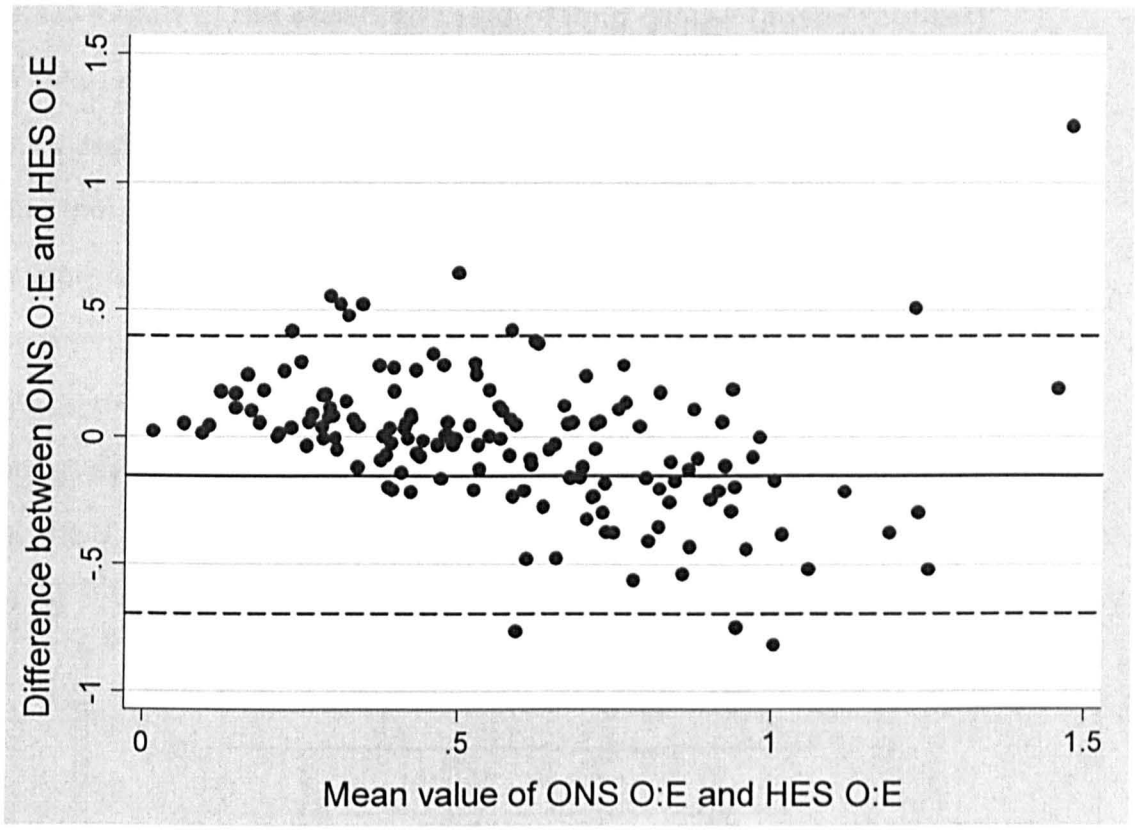



Figure 3.12: Bland-Altman plot depicting the comparison between ONS and HES methods for calculating observed:expected (O:E) ratios for NHS Trusts.

Note: Mean=-0.15 and Standard Deviation=0.27

### 3.3.4 Result of the observed cases of lung cancer (postal request)

A total of 26 responses were received, 65% of the number requested. Figure 3.13 depicts the relationship between observed cases as per the postal request, and those reported in the NLCA. The correlation coefficient was 0.828, showing a high level of agreement. Of note, the NHS Trusts with greatest disparity between both sources of observed cases were those in the 4th stratum, in other words the NHS Trusts from the lowest stratum of case ascertainment, as per observed:expected ratios. The NLCA contained fewer cases than were reported by the NHS Trusts themselves.

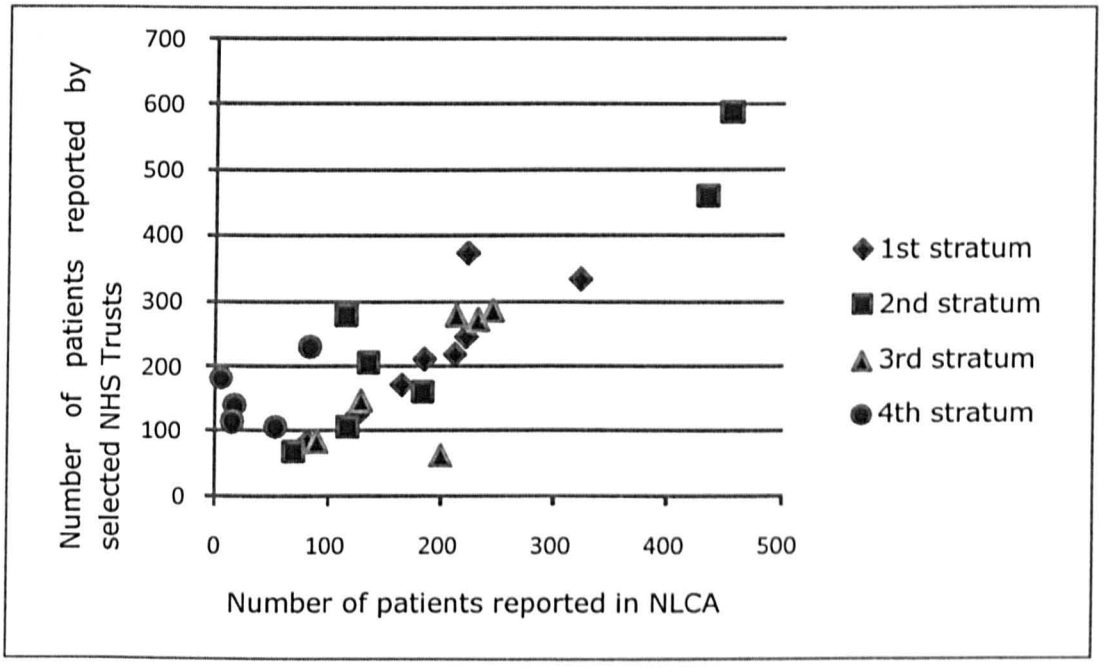



Figure 3.13: Scatter plot depicting the relationship between observed cases of lung cancer in 2007, reported directly from the NHS Trusts, or in the NLCA.

### 3.4 Discussion

There was no strong evidence that key demographic features varied based on the number of cases reported at each NHS Trust (i.e. the size of the NHS Trust). There was no evidence that centres reporting a small number of cases were reporting only those with specific features, such as early stage and good performance status in whom surgery was possible.

In order to quantify data completeness, an observed:expected ratio was calculated, and NHS Trusts stratified on this basis. In the absence of cancer Registry data and published data with an expected number of lung cancer cases at the level of an NHS Trust, it was necessary to use published data from ONS, (and perform a mapping process from primary care trusts to NHS Trusts), and HES data (based on acute admissions to an NHS Trust) as comparators. There was a high level of agreement on the stratification of NHS Trusts by these two methods.

The next step would be to evaluate the differences between patients within these NHS Trust strata to establish if there was any evidence of bias, on the basis of an observed:expected ratio acting as a marker of case ascertainment.

In May 2009, data from the Thames cancer Registry was provided. This is the gold standard record of lung cancer incidence in England. These data are held at the level of a PCT and so the mapping process performed in Chapter 3 was repeated. Chapter 4 describes the variation observed in patient features, access to treatment and survival across strata of NHS Trusts based on case ascertainment.

## Chapter Four: Validating the NLCA using Cancer Registry data

## 4.1 Introduction

Outcome measures for lung cancer in the UK are worse than those in comparable European and North American countries (21), but the reasons for this are unclear. The National Lung Cancer Audit (NLCA) was established in 2004 to identify possible inequalities within the National Health Service (NHS) and highlight the potential for service improvements.

The NLCA database is a record of detailed clinical information of individuals diagnosed with lung cancer in England and Wales. As such it is a unique dataset, offering more detailed information on lung cancer patients than the large registry linked datasets of both Europe (EUROCARE-4) and America (SEER, Surveillance Epidemiology and End Results programme) (66). NHS Trusts are requested to upload information on all lung cancer patients, but data entry is non-mandatory and this has raised concerns about the validity of the database because of the potential bias which could arise if patients were 'selected' for inclusion in the audit.

The aims of this chapter were two-fold; firstly to determine whether demographic and outcome data from individual NHS Trusts held in the NLCA are influenced by the level of data completeness; and secondly to describe the features of people with lung cancer currently in England and to determine whether the socio-economic status of an individual with lung cancer contributes to either the treatment they receive or their overall survival.

## 4.2 Methods

### 4.2.1 Description of data entry into NLCA

Data used in this chapter were entered into the NLCA dataset as per section 3.2.1, and the same data cleaning process was used as described in 3.2.1.2.

### 4.2.2 Observed:Expected ratios: Case ascertainment

An observed:expected ratio was calculated as described in section 3.2.3, except that to generate an expected number of patients, data from the Thames Cancer Registry (Dr H Møller) were used. These are mandatory records of lung cancer incidence and were reported at the level of a primary care trust. So after creation of an observed:expected ratio for each primary care trust, the mapping technique employed in section 3.2.3.1 was repeated.

NHS Trusts were divided into four equal groups on the basis of their ascertainment of lung cancer cases by creating quartiles of the observed:expected ratios. In order to assess the validity of the dataset, I examined the distribution across these NHS Trust quartiles of the following key patient features: sex, age at diagnosis, performance status at diagnosis (as classified by the Eastern Cooperative Oncology Group), basis of diagnosis (e.g. histology of the primary tumour, cytology), histology of the tumour, pre-treatment stage of the tumour (as classified by the American Joint Committee on Cancer and Union Internationale Contre le Cancer version 6), treatment modality used, and median number of days survived from diagnosis. I used a chi square test for trend to determine whether the proportion of missing data for each variable increased as data completeness decreased. A similar approach was used for the other non missing data by recoding each variable into a binary variable as follows: performance status 0/1 versus performance status 2/3/4, diagnosis made by histology versus diagnosis made by another approach, non-

small cell histology versus small cell histology, stage I and II versus stage III and IV.

I used logistic regression to assess the variation in MDT treatment intent across the NHS Trust quartiles of data completeness, and constructed a model which was adjusted for all patient features.

### 4.2.3 Access to curative or active palliative treatment

The NLCA contains information on the treatment decision of the multi-disciplinary team in terms of curative (surgery or radical radiotherapy), or active palliative treatment (chemo or radiotherapy). It also records the option of best supportive care for individuals in whom symptom relief was the most appropriate management. An option of no specific anti-cancer treatment could be recorded and for some patients this data field was missing. Logistic regression was used to assess the variation in treatment being offered to patients across the NHS Trust strata, and on the basis of the key patient features. Curative treatment was compared to all other treatment options. A similar analysis was conducted for active palliative treatment, although patients referred for curative treatment were excluded from the baseline comparator group. Multivariate logistic regression was used to construct a model which was fully adjusted for all patient and NHS Trust strata.

### 4.2.4 Socio-economic status and the receipt of specific treatments

The NLCA dataset also contains the details of each individual patient's Lower Super Output Area (LSOA), which is a geographical unit (encompassing approximately 1500 homes) derived from their postcode. Every LSOA can be linked with the Townsend score for deprivation, and this is usually divided into quintiles to simplify analyses; 1 is most affluent and quintile 5 represents the least affluent quintile of society. The Townsend quintile was the marker of socio-economic status used throughout the remainder of this research. In order to

evaluate the potential influence of socio-economic status on treatment received, the dates of either: surgery, chemotherapy, or radiotherapy were used, and binary variables created to allow logistic regression to be performed. Cox regression was used to assess the influence of socio-economic status on overall survival. For both these regression analyses a similar modelling strategy, adjusting for patient features, was used to that outlined above, and in addition the final model was clustered by NHS Trust to ensure data entry at individual NHS Trusts did not influence the results.

### 4.2.5 Evaluating patient survival

For survival analyses the start and end dates described in section 3.2.1.2 were used. Cox regression analyses were performed to calculate hazard ratios (HR) across the NHS Trust strata and for each of the key patient features individually. A multivariate model was then constructed to adjust mutually for all key patient features and NHS Trust strata. The proportional hazards assumptions for this model were checked by inspecting Nelson-Aaleen plots.

### 4.2.6 Comparison of NHS Trust strata with previous estimations using data from ONS and HES

The strata of NHS Trusts created using data from the Cancer Registry were compared to those previously created (see Chapter 3) using data from Office of National Statistics and Hospital Episode Statistics. Weighted Kappa values were calculated to evaluate the level of agreement between these different methods of creating NHS Trust strata.

## 4.3 Results

### 4.3.1 Overall cohort analysis

The NLCA subset initially contained 67,824 patients at English NHS Trusts with their first hospital attendance before 1st January 2008. As described in section 3.2.1.2, a total of 60,747 patients remained after the data cleaning process. A further 688 were dropped as they were first seen at an NHS Trust that could not be linked to Registry data, primarily because of changes in infrastructure over time. This left 60,059 patients for analysis: 21,976 from 2007, 18,229 from 2006, 12,910 from 2005, and 6944 from 2004. The median age at diagnosis was 71 years (interquartile range 64 to 78 years) and the majority were male (59%) (table 4.1). The commonest histological subgroup was non-small cell lung cancer, contributing 39% of the cohort; 10% were proven small cell cancer, a further 3% had mesothelioma. A total of 44% of the cohort had no histology data recorded, of whom 50% had a clinical diagnosis of lung cancer, whilst the other half appear to have had histology or cytology sought, but the specific result is missing from the NLCA record. The majority of patients (36%) received active palliative treatment, with 9% of the overall cohort receiving treatment with a curative intent.

### 4.3.2 Observed:expected ratios: results of case ascertainment

The median observed:expected ratio for NHS Trusts was 0.52 (interquartile range 0.37 to 0.71). There was evidence that this figure had improved over the four years that the NLCA had been established. NHS Trusts in the top stratum reported a median of 0.85 of expected cases (interquartile range 0.80 to 0.91), representing 40% of the overall patient cohort. The corresponding values for the second, third and fourth quartiles which comprised 30%, 21% and 9% of the overall patient cohort, respectively, are listed in table 4.1.

Table 4.1: Distribution of key patient features for the overall cohort, and NHS Trust strata based on case ascertainment.

| Trust strata | Highest O:E | | 2 | | 3 | | Lowest O:E | | Total | |
|---|---|---|---|---|---|---|---|---|---|---|
| Number of Trusts | 39 | | 39 | | 39 | | 40 | | 157 | |
| Median O:E ratio (IQR) | 0.85 (0.8, 0.91) | | 0.63 (0.56, 0.68) | | 0.46 (0.43, 0.48) | | 0.31 (0.23, 0.35) | | 0.52 (0.37, 0.71) | |
| Number of patients | 24261 | | 17980 | | 12498 | | 5320 | | 60059 | |
| ***Sex*** | | | | | | | | | | |
| Male | 14449 | (60) | 10583 | (59) | 7417 | (59) | 3244 | (61) | 35693 | (59) |
| Female | 9812 | (40) | 7397 | (41) | 5081 | (41) | 2076 | (39) | 24366 | (41) |
| ***Age at diagnosis*** | | | | | | | | | | |
| Median (IQR) years | 72 (64 to 79) | | 71 (63 to 78) | | 71 (63 to 78) | | 71 (63 to 78) | | 71 (64 to 78) | |
| ***Performance status (PS)*** | | | | | | | | | | |
| PS 0 | 3596 | (15) | 1921 | (11) | 1284 | (10) | 633 | (12) | 7434 | (12) |
| PS 1 | 6023 | (25) | 3135 | (17) | 1757 | (14) | 893 | (17) | 11808 | (20) |
| PS 2 | 3595 | (15) | 2307 | (13) | 1171 | (9) | 538 | (10) | 7611 | (13) |
| PS 3 | 2751 | (11) | 1964 | (11) | 956 | (8) | 355 | (7) | 6026 | (10) |
| PS 4 | 986 | (4) | 648 | (4) | 339 | (3) | 95 | (2) | 2068 | (3) |
| Don't know | 2874 | (12) | 3272 | (18) | 3458 | (28) | 997 | (19) | 10601 | (18) |
| "Missing" | 4436 | (18) | 4733 | (26) | 3533 | (28) | 1809 | (34) | 14511 | (24) |
| ***Basis of diagnosis*** | | | | | | | | | | |
| Histology | 13522 | (56) | 9103 | (51) | 4861 | (39) | 2824 | (53) | 30310 | (51) |
| Cytology | 2365 | (10) | 1571 | (9) | 1775 | (14) | 428 | (8) | 6139 | (10) |
| Clinical | 5691 | (23) | 3741 | (21) | 3115 | (25) | 644 | (12) | 13191 | (22) |
| Tumour markers | 2 | (0) | 6 | (0) | 27 | (0) | 2 | (0) | 37 | (0) |
| Death Certificate | 56 | (0) | 9 | (0) | 18 | (0) | 0 | (0) | 83 | (0) |
| Don't know | 351 | (1) | 1598 | (9) | 959 | (8) | 326 | (6) | 3234 | (5) |
| "Missing" | 2274 | (9) | 1952 | (11) | 1743 | (14) | 1096 | (21) | 7065 | (12) |
| ***Histology of primary tumour*** | | | | | | | | | | |
| Non Small cell | 10168 | (42) | 6603 | (37) | 4267 | (34) | 2095 | (39) | 23133 | (39) |
| Small cell | 2636 | (11) | 1585 | (9) | 1064 | (9) | 491 | (9) | 5776 | (10) |
| Carcinoid | 67 | (0) | 39 | (0) | 31 | (0) | 15 | (0) | 152 | (0) |
| Mesothelioma | 918 | (4) | 535 | (3) | 343 | (3) | 179 | (3) | 1975 | (3) |
| Other | 948 | (4) | 559 | (3) | 634 | (5) | 241 | (5) | 2382 | (4) |
| "Missing" | 9525 | (39) | 8659 | (48) | 6159 | (49) | 2301 | (43) | 26641 | (44) |
| ***Stage of tumour*** | | | | | | | | | | |
| IA | 707 | (3) | 520 | (3) | 289 | (2) | 173 | (3) | 1689 | (3) |
| IB | 1173 | (5) | 711 | (4) | 348 | (3) | 249 | (5) | 2481 | (4) |
| IIA | 127 | (1) | 73 | (0) | 40 | (0) | 33 | (1) | 273 | (0) |
| IIB | 702 | (3) | 439 | (2) | 252 | (2) | 177 | (3) | 1590 | (3) |
| IIIA | 1476 | (6) | 844 | (5) | 448 | (4) | 291 | (5) | 3059 | (5) |
| IIIB | 2914 | (12) | 1592 | (9) | 898 | (7) | 576 | (11) | 5980 | (10) |
| IV | 6595 | (27) | 3661 | (2) | 1962 | (16) | 1060 | (20) | 13278 | (22) |
| Occult | 22 | (0) | 34 | (0) | 8 | (0) | 1 | (0) | 65 | (0) |
| Uncertain | 1124 | (5) | 1628 | (9) | 965 | (8) | 531 | (10) | 4248 | (7) |
| "Missing" | 9421 | (39) | 8478 | (47) | 7288 | (58) | 2229 | (42) | 27416 | (46) |
| ***MDT treatment intent*** | | | | | | | | | | |
| No specific anti-cancer | 1256 | (5) | 885 | (5) | 568 | (5) | 223 | (4) | 2932 | (5) |
| Curative intent | 2421 | (10) | 1475 | (8) | 1044 | (8) | 527 | (10) | 5467 | (9) |
| Palliative intent | 9936 | (41) | 5914 | (33) | 4041 | (32) | 1510 | (28) | 21401 | (36) |
| Best supportive Care | 3854 | (16) | 1943 | (11) | 1224 | (10) | 376 | (7) | 7397 | (12) |
| Don't know | 651 | (3) | 3026 | (17) | 1018 | (8) | 334 | (6) | 5029 | (8) |
| "Missing" | 6143 | (25) | 4737 | (26) | 4603 | (37) | 2350 | (44) | 17833 | (30) |
| ***Survival*** | | | | | | | | | | |
| Median (days) | 193 | | 201 | | 200 | | 223 | | 203 | |
| IQR (days) | 58-522 | | 61-527 | | 60-566 | | 70-547 | | 62-545 | |
| One year survival (%) | 31.3 | | 31.5 | | 32.3 | | 31.9 | | 31.6 | |

Legend: IQR interquartile range; ( ) percentage

There was a proportion of missing data present for each of the key patient variables and in general this proportion tended to increase as the level of data completeness decreased (table 4.2). There was also some evidence of variation in the non-missing data between these quartiles. For example, people in NHS Trusts with the lowest quartile of data completeness tended to have a more favourable disease stage and to be more likely to have their diagnosis made on the basis of histology. However, although the p values for these analyses were small, reflecting the large size of the dataset, the absolute differences in the proportions were small. In contrast distribution of good versus poor performance status and non-small cell versus small cell lung cancer was very similar across all four quartiles.

Table 4.2: Chi square analyses for missing data and key patient variables (having excluded missing data) by quartile of data completeness at NHS Trusts.

| **Trust quartiles** | **Highest O:E** | **2** | **3** | **Lowest O:E** | **$Chi^2$ for trend (p)** |
|---|---|---|---|---|---|
| **Performance status** | | | | | |
| Missing/don't know | 30% | 45% | 56% | 53% | <0.001 |
| 0/1 | 57% | 51% | 55% | 61% | 0.94 |
| 2/3/4 | 43% | 49% | 45% | 39% | |
| **Basis of diagnosis** | | | | | |
| Missing/don't know | 11% | 20% | 22% | 27% | <0.001 |
| Histology | 63% | 63% | 50% | 72% | <0.001 |
| Other | 37% | 37% | 50% | 28% | |
| **Histology** | | | | | |
| Missing | 39% | 48% | 49% | 43% | <0.001 |
| Non-small cell | 79% | 81% | 80% | 81% | 0.06 |
| Small cell | 21% | 19% | 20% | 19% | |
| **Stage** | | | | | |
| Missing/uncertain | 43% | 56% | 66% | 52% | <0.001 |
| I/II | 20% | 23% | 22% | 25% | <0.001 |
| III/IV | 80% | 77% | 78% | 75% | |

### 4.3.3 Access to curative and active palliative treatment

The results of logistic regression analyses assessing access to curative and active palliative treatment across NHS Trust strata are depicted in Tables 4.3 and 4.4 respectively. There was little variation in referral for curative treatment across all four NHS Trust strata of ascertainment, which became even smaller after key patient features were included in the model. There was a progressive decline in the likelihood of curative treatment being offered as age increased, with an adjusted odds ratio (OR) of 0.30 (95% CI 0.26, 0.34) for the quintile of oldest age (>81 years) compared with the youngest age group (<61 years). There was a marked reduction in the likelihood of being offered curative treatment once an individual was classed as performance status 2 (adjusted odds ratio 0.28, 95% CI 0.25, 0.32), and once their tumour was staged as IIIa or above (adjusted odds ratio 0.18, 95% CI 0.15, 0.21). Table 4.4 shows the results of logistic regression for referral for active palliative treatment once those patients referred for curative treatment (n=5467) had been removed. It shows there was an apparent reduction in the likelihood of active palliative treatment being used in the stratum with lowest observed:expected ratios (adjusted OR 0.72, 95% CI 0.66, 0.77). There was a progressive decline in the likelihood of active palliative treatment being used as age at diagnosis increased (adjusted OR in oldest quintile (>81 years) 0.63, 95% CI 0.59, 0.67). There was no variation in the likelihood of active palliative treatment being used in patients with performance status 0-2, but there was a reduction for those patients with performance status 3 and 4 (adjusted OR 0.41, 95% CI 0.36, 0.46 for performance status 4). In contrast, odds ratios increased for patients staged IIa or greater, with patients staged as IIIb having a four-fold increased likelihood of receiving active palliative treatment compared with those with stage Ia disease (adjusted OR 3.95, 95% CI 3.29, 4.74). Patients with metastatic spread (stage IV), had a slightly lower adjusted odds ratio of 3.68 (95% CI 3.0, 4.39).

Table 4.3: Logistic Regression analyses of curative treatment; NHS Trust strata and key patient features

| | Absolute no. of patients (%) * | | Unadjusted OR (95% CI) | | Adjusted OR** (95% CI) | |
|---|---|---|---|---|---|---|
| ***Trust strata based on O:E ratio*** | | | | | | |
| Highest O:E | 2421 | (10) | | | | |
| 2 | 1475 | (8) | 0.81 | (0.75-0.86) | 0.83 | (0.77-0.90) |
| 3 | 1044 | (8) | 0.82 | (0.76-0.89) | 1.03 | (0.94-1.12) |
| Lowest O:E | 527 | (10) | 0.99 | (0.90-1.10) | 0.97 | (0.86-1.09) |
| ***Sex*** | | | | | | |
| Male | 3233 | (9) | | | | |
| Female | 2234 | (9) | 1.01 | (0.96-1.07) | 1.03 | (0.96-1.10) |
| ***Age quintile*** | | | | | | |
| 1 (30-61 years) | 1408 | (12) | | | | |
| 2 (62-69 years) | 1603 | (12) | 0.97 | (0.90-1.05) | 0.92 | (0.84-1.01) |
| 3 (70-74 years) | 1026 | (10) | 0.82 | (0.75-0.89) | 0.77 | (0.69-0.85) |
| 4 (75-80 years) | 1046 | (8) | 0.65 | (0.60-0.70) | 0.63 | (0.57-0.70) |
| 5 (81-101 years) | 384 | (4) | 0.27 | (0.24-0.31) | 0.30 | (0.26-0.34) |
| ***Performance status (PS)*** | | | | | | |
| PS 0 | 1687 | (23) | | | | |
| PS 1 | 1738 | (15) | 0.59 | (0.55-0.63) | 0.73 | (0.67-0.79) |
| PS 2 | 392 | (5) | 0.18 | (0.16-0.21) | 0.28 | (0.25-0.32) |
| PS 3 | 75 | (1) | 0.04 | (0.03-0.05) | 0.08 | (0.07-0.11) |
| PS 4 | 6 | (0) | 0.01 | (0.00-0.02) | 0.03 | (0.01-0.06) |
| PS not known | 890 | (8) | 0.31 | (0.29-0.34) | 0.48 | (0.43-0.53) |
| "Missing" | 679 | (5) | 0.17 | (0.15-0.18) | 0.32 | (0.29-0.36) |
| ***Basis of diagnosis*** | | | | | | |
| Histology of tumour | 3743 | (13) | | | | |
| Histology of metastases | 58 | (3) | 0.17 | (0.12-0.22) | 0.33 | (0.25-0.43) |
| Cytology | 507 | (8) | 0.58 | (0.53-0.64) | 0.73 | (0.65-0.81) |
| Clinical (investigations) | 727 | (8) | 0.53 | (0.48-0.57) | 0.76 | (0.67-0.86) |
| Clinical (no investigations) | 114 | (3) | 0.22 | (0.18-0.26) | 0.34 | (0.27-0.43) |
| Tumour markers | 5 | (14) | 1.01 | (0.39-2.60) | 1.35 | (0.48-3.79) |
| Death certificate only | 0 | (0) | | | | |
| Don't know | 136 | (4) | 0.28 | (0.24-0.34) | 0.28 | (0.23-0.34) |
| "Missing" | 177 | (3) | 0.17 | (0.14-0.19) | 0.21 | (0.18-0.25) |
| ***Histology of tumour*** | | | | | | |
| Non Small Cell | 3175 | (14) | | | | |
| Small Cell | 290 | (5) | 0.33 | (0.29-0.38) | 0.45 | (0.39-0.52) |
| Carcinoid | 71 | (47) | 5.51 | (4.00-7.59) | 3.32 | (2.25-4.90) |
| Mesothelioma | 70 | (4) | 0.23 | (0.18-0.29) | 0.21 | (0.17-0.28) |
| "Other" histology | 272 | (11) | 0.81 | (0.71-0.92) | 0.85 | (0.73-0.98) |
| "Missing" | 1589 | (6) | 0.40 | (0.37-0.42) | 0.78 | (0.70-0.86) |
| ***Stage of tumour*** | | | | | | |
| Stage Ia | 749 | (44) | | | | |
| Stage Ib | 1006 | (41) | 0.86 | (0.76-0.97) | 0.84 | (0.73-0.97) |
| Stage IIa | 117 | (43) | 0.94 | (0.73-1.21) | 0.83 | (0.62-1.10) |
| Stage IIb | 510 | (32) | 0.60 | (0.52-0.70) | 0.52 | (0.45-0.61) |
| Stage IIIa | 466 | (15) | 0.23 | (0.20-0.26) | 0.18 | (0.15-0.21) |
| Stage IIIb | 395 | (7) | 0.09 | (0.08-0.10) | 0.07 | (0.06-0.08) |
| Stage IV | 250 | (2) | 0.02 | (0.02-0.03) | 0.02 | (0.02-0.03) |
| Occult | 12 | (18) | 0.28 | (0.15-0.54) | 0.34 | (0.17-0.67) |
| Uncertain | 522 | (12) | 0.18 | (0.15-0.20) | 0.20 | (0.17-0.23) |
| "Missing" | 1440 | (5) | 0.07 | (0.06-0.08) | 0.11 | (0.10-0.12) |

Legend: The comparator variables are the first subgroup of each patient feature.
* percentage of patients from each subgroup referred for curative treatment.
** Odds Ratio adjusted for all other features listed in the table.

Table 4.4: Logistic regression for active palliative treatment; NHS Trust strata and key patient features

| | Absolute no. of patients (%) * | | Unadjusted OR (95% CI) | | Adjusted OR** (95% CI) | |
|---|---|---|---|---|---|---|
| ***Trust strata based on O:E ratio*** | | | | | | |
| Highest O:E | 9936 | (41) | | | | |
| 2 | 5914 | (33) | 0.67 | (0.64-0.70) | 0.84 | (0.81-0.88) |
| 3 | 4041 | (32) | 0.65 | (0.62-0.68) | 0.94 | (0.89-0.99) |
| Lowest O:E | 1510 | (28) | 0.55 | (0.52-0.59) | 0.72 | (0.66-0.77) |
| ***Sex*** | | | | | | |
| Male | 12954 | (36) | | | | |
| Female | 8447 | (35) | 0.93 | (0.90-0.96) | 0.98 | (0.94-1.02) |
| ***Age quintile*** | | | | | | |
| 1 (30-61 years) | 4697 | (39) | | | | |
| 2 (62-69 years) | 5369 | (39) | 0.96 | (0.91-1.01) | 0.95 | (0.89-1.00) |
| 3 (70-74 years) | 3815 | (27) | 0.85 | (0.80-0.90) | 0.87 | (0.81-0.92) |
| 4 (75-80 years) | 4463 | (34) | 0.73 | (0.69-0.77) | 0.80 | (0.75-0.85) |
| 5 (81-101 years) | 3057 | (28) | 0.51 | (0.48-0.54) | 0.63 | (0.59-0.67) |
| ***Performance status (PS)*** | | | | | | |
| PS 0 | 2872 | (39) | | | | |
| PS 1 | 5816 | (49) | 1.37 | (1.28-1.46) | 1.33 | (1.24-1.43) |
| PS 2 | 3689 | (48) | 1.05 | (0.97-1.12) | 1.13 | (1.04-1.22) |
| PS 3 | 2211 | (37) | 0.59 | (0.55-0.64) | 0.70 | (0.64-0.76) |
| PS 4 | 498 | (24) | 0.32 | (0.28-0.36) | 0.41 | (0.36-0.46) |
| PS not known | 3374 | (32) | 0.53 | (0.50-0.57) | 0.70 | (0.65-0.76) |
| "Missing" | 2941 | (20) | 0.27 | (0.25-0.29) | 0.43 | (0.40-0.46) |
| ***Basis of diagnosis*** | | | | | | |
| Histology of tumour | 12576 | (45) | | | | |
| Histology of metastases | 1373 | (59) | 1.45 | (1.33-1.58) | 1.34 | (1.22-1.47) |
| Cytology | 2805 | (46) | 0.92 | (0.87-0.98) | 0.98 | (0.92-1.04) |
| Clinical (investigations) | 2686 | (28) | 0.39 | (0.37-0.41) | 0.77 | (0.71-0.83) |
| Clinical (no investigations) | 839 | (24) | 0.30 | (0.28-0.33) | 0.60 | (0.55-0.67) |
| Tumour markers | 15 | (41) | 0.82 | (0.41-1.64) | 1.51 | (0.74-3.09) |
| Death certificate only | 6 | (7) | 0.07 | (0.03-0.17) | 0.12 | (0.05-0.29) |
| Don't know | 461 | (14) | 0.16 | (0.15-0.18) | 0.21 | (0.19-0.24) |
| "Missing" | 700 | (10) | 0.11 | (0.10-0.11) | 0.21 | (0.19-0.23) |
| ***Histology of tumour*** | | | | | | |
| Non Small Cell | 10259 | (44) | | | | |
| Small Cell | 3225 | (56) | 1.35 | (1.27-1.43) | 1.46 | (1.36-1.56) |
| Carcinoid | 18 | (12) | 0.27 | (0.16-0.46) | 0.31 | (0.18-0.54) |
| Mesothelioma | 1037 | (53) | 1.13 | (1.03-1.24) | 1.30 | (1.18-1.44) |
| "Other" histology | 867 | (36) | 0.66 | (0.60-0.72) | 0.84 | (0.76-0.93) |
| "Missing" | 5995 | (23) | 0.30 | (0.29-0.31) | 0.62 | (0.59-0.67) |
| ***Stage of tumour*** | | | | | | |
| Stage Ia | 70 | (4) | | | | |
| Stage Ib | 414 | (17) | 1.77 | (1.45-2.16) | 1.63 | (1.32-2.01) |
| Stage IIa | 42 | (15) | 1.67 | (1.12-2.47) | 1.32 | (0.88-2.00) |
| Stage IIb | 415 | (26) | 2.91 | (2.37-3.58) | 2.48 | (2.00-3.09) |
| Stage IIIa | 1203 | (39) | 3.92 | (3.26-4.71) | 3.08 | (2.54-3.73) |
| Stage IIIb | 2971 | (50) | 5.15 | (4.32-6.13) | 3.95 | (3.29-4.74) |
| Stage IV | 6495 | (49) | 4.50 | (3.80-5.34) | 3.68 | (3.08-4.39) |
| Occult | 11 | (17) | 1.19 | (0.60-2.35) | 0.99 | (0.49-2.02) |
| Uncertain | 1455 | (34) | 2.90 | (2.43-3.47) | 2.91 | (2.41-3.51) |
| "Missing" | 8225 | (30) | 2.10 | (1.77-2.48) | 2.71 | (2.27-3.23) |

Legend: Patients receiving curative treatment (N=5467) were excluded from this analysis.
The comparator variable is the first subgroup of each of the key patient features.
* percentage of patients from each subgroup referred for palliative treatment.
** Odds Ratio adjusted for all other variables listed in this table.

### 4.3.4 Socio-economic status and receipt of specific treatments

Overall, the percentage of patients receiving surgery was 9%, but for the subgroup of patients with proven non-small cell lung cancer, the rate of surgical resection was 14%. Within this subgroup, logistic regression confirmed that increasing age, a performance status of ≥2, and a stage at diagnosis of IIb or worse were all linked with a reduced likelihood of receiving surgical treatment (table 4.5). However the socio-economic status of a patient did not affect the likelihood of receiving surgery (table 4.5). For the cohort overall, the percentage of patients receiving chemotherapy was 24%, but for the subgroup of patients with proven small cell lung cancer the figure was 61%. Logistic regression for the cohort overall revealed a stage at diagnosis of IIIa and over, was linked to a significant increase in the likelihood of chemotherapy being used; whilst a performance status of 3 or worse was associated with a reduced likelihood of chemotherapy being used (table 4.6). Table 4.6 demonstrates that patients within the least affluent Townsend quintile were found to have a reduced likelihood of receiving chemotherapy despite adjusting for stage and performance status (adjusted OR 0.85, 95% CI 0.79, 0.91, p for trend <0.01). The results for radiotherapy show that 20% of the cohort overall received this treatment modality. Logistic regression revealed that there was no effect of increasing age, or socio-economic status on the likelihood of receiving radiotherapy (table 4.7). There was a progressive increase in the likelihood of radiotherapy being used as stage of the disease increased supporting the role radiotherapy plays in active palliative care; and only at performance status 4 was there a reduction in the likelihood of it being used (table 4.7).

Table 4.5: Logistic regression for access to surgery in proven NSCLC (N=25,667)

| | N | N who had surgery | (%)* | OR (95% CI) | Adj OR** (95% CI) | P for trend |
|---|---|---|---|---|---|---|
| ***Sex*** | | | | | | |
| Male | 15671 | 2170 | 14 | | | |
| Female | 9996 | 1507 | 15 | 1.10 (1.03, 1.19) | 1.05 (0.96, 1.14) | 0.29^ |
| ***Age quintile*** | | | | | | |
| 1 (30-61 years) | 5620 | 941 | 17 | | | <0.001 |
| 2 (52-69 years) | 6438 | 1114 | 17 | 1.04 (0.95, 1.14) | 0.93 (0.83, 1.04) | |
| 3 (70-74 years) | 4723 | 722 | 15 | 0.90 (0.81, 1.00) | 0.79 (0.69, 0.89) | |
| 4 (75-80 years) | 5503 | 702 | 13 | 0.73 (0.65, 0.81) | 0.65 (0.57, 0.74) | |
| 5 (81-101 years) | 3383 | 198 | 6 | 0.31 (0.26, 0.36) | 0.27 (0.23, 0.33) | |
| ***Performance status*** | | | | | | |
| PS 0 | 4454 | 1312 | 29 | | | 0.001 |
| PS 1 | 6862 | 1078 | 16 | 0.45 (0.41, 0.49) | 0.51 (0.46, 0.57) | |
| PS 2 | 3702 | 202 | 5 | 0.14 (0.12, 0.16) | 0.19 (0.16, 0.22) | |
| PS 3 | 2220 | 53 | 2 | 0.06 (0.04, 0.08) | 0.10 (0.08, 0.14) | |
| PS 4 | 540 | 8 | 1 | 0.04 (0.02, 0.07) | 0.08 (0.04, 0.16) | |
| "missing" | 7889 | 1024 | 13 | 0.36 (0.33,0.39) | 0.42 (0.37, 0.47) | |
| ***Stage*** | | | | | | |
| Stage Ia | 931 | 599 | 64 | | | <0.001 |
| Stage Ib | 1582 | 795 | 50 | 0.56 (0.47, 0.66) | 0.58 (0.48, 0.69) | |
| Stage IIa | 162 | 105 | 65 | 1.02 (0.72, 1.45) | 0.96 (0.65, 1.42) | |
| Stage IIb | 1061 | 415 | 39 | 0.36 (0.30, 0.43) | 0.35 (0.29, 0.43) | |
| Stage IIIa | 1987 | 262 | 13 | 0.08 (0.07, 0.10) | 0.07 (0.06, 0.09) | |
| Stage IIIb | 3807 | 190 | 5 | 0.03 (0.01, 0.04) | 0.03 (0.02, 0.03) | |
| Stage IV | 7554 | 197 | 3 | 0.01 (0.01, 0.02) | 0.02 (0.01, 0.02) | |
| Occult | 35 | 12 | 34 | 0.32 (0.14, 0.59) | 0.36 (0.17, 0.77) | |
| "Missing" | 8548 | 1102 | 13 | 0.08 (0.07, 0.10) | 0.09 (0.08, 0.11) | |
| ***Townsend quintile*** | | | | | | |
| 1 (most affluent) | 3838 | 539 | 14 | | | 0.235 |
| 2 | 4772 | 710 | 15 | 1.07 (0.95, 1.21) | 1.13 (0.98, 1.32) | |
| 3 | 4960 | 719 | 14 | 1.04 (0.92, 1.17) | 1.18 (1.02, 1.37) | |
| 4 | 5348 | 744 | 14 | 0.99 (0.88, 1.11) | 1.01 (0.87, 1.16) | |
| 5 (least affluent) | 6698 | 955 | 14 | 1.02 (0.91, 1.14) | 1.11 (0.96, 1.27) | |
| "missing" | 51 | 10 | 20 | 1.49 (0.74, 3.00) | 1.76 (0.78, 3.99) | |

Legend: N who had surgery, Number who had surgery from each subgroup.
(%)* percentage of each subgroup who had surgery.
Adj OR** Odds ratio adjusted for all features in the table.
^ p value

Table 4.6: Logistic regression for chemotherapy for whole cohort (N=60,059)

| | N | N who had CTx | (%)* | OR (95% CI) | Adj OR** (95% CI) | P for trend |
|---|---|---|---|---|---|---|
| ***Sex*** | | | | | | |
| Male | 35693 | 8367 | 23 | | | |
| Female | 24366 | 5820 | 24 | 1.02 (0.99, 1.06) | 1.02 (0.97, 1.06) | 0.43^ |
| ***Age quintile*** | | | | | | |
| 1 (30-61 years) | 11895 | 4807 | 40 | | | <0.001 |
| 2 (52-69 years) | 13866 | 4471 | 32 | 0.70 (0.67, 0.74) | 0.73 (0.69, 0.77) | |
| 3 (70-74 years) | 10378 | 2543 | 25 | 0.48 (0.45, 0.51) | 0.52 (0.49, 0.55) | |
| 4 (75-80 years) | 13077 | 1865 | 14 | 0.25 (0.23, 0.26) | 0.28 (0.26, 0.30) | |
| 5 (81-101 years) | 10843 | 501 | 5 | 0.07 (0.06, 0.08) | 0.10 (0.09, 0.11) | |
| ***Performance status (PS)*** | | | | | | |
| PS 0 | 7434 | 2951 | 40 | | | <0.001 |
| PS 1 | 11808 | 4389 | 37 | 0.90 (0.85, 0.95) | 0.93 (0.87, 1.00) | |
| PS 2 | 7611 | 1644 | 22 | 0.42 (0.39, 0.45) | 0.43 (0.39, 0.46) | |
| PS 3 | 6026 | 416 | 7 | 0.11 (0.10, 0.13) | 0.13 (0.11, 0.14) | |
| PS 4 | 2068 | 44 | 2 | 0.03 (0.02, 0.04) | 0.03 (0.03, 0.05) | |
| "Missing" | 25122 | 4743 | 19 | 0.35 (0.33, 0.37) | 0.46 (0.43, 0.49) | |
| ***Histology*** | | | | | | |
| NSCLC | 25667 | 7122 | 28 | | | |
| Small cell | 5921 | 3589 | 61 | 4.01 (3.78, 4.25) | 5.31 (4.94, 5.70) | |
| Carcinoid | 197 | 11 | 6 | 0.15 (0.08, 0.28) | 0.12 (0.06, 0.21) | |
| Mesothelioma | 2071 | 302 | 15 | 0.44 (0.39, 0.50) | 0.41 (0.36, 0.47) | |
| Other | 958 | 179 | 19 | 0.60 (0.51, 0.71) | 0.80 (0.73, 0.89) | |
| "Missing" | 25245 | 2984 | 12 | 0.35 (0.33, 0.37) | 0.50 (0.47, 0.52) | |
| ***Stage*** | | | | | | |
| Stage Ia | 1689 | 116 | 7 | | | 0.095 |
| Stage Ib | 2481 | 247 | 10 | 1.50 (1.19, 1.89) | 1.58 (1.25, 2.01) | |
| Stage IIa | 273 | 38 | 14 | 2.19 (0.48, 3.24) | 1.79 (1.18, 2.72) | |
| Stage IIb | 1570 | 275 | 18 | 2.88 (2.29, 3.62) | 2.83 (2.23, 3.60) | |
| Stage IIIa | 3059 | 986 | 32 | 6.45 (5.26, 7.90) | 7.44 (6.01, 9.20) | |
| Stage IIIb | 5980 | 2042 | 34 | 7.03 (5.78, 8.55) | 8.49 (6.92, 10.42) | |
| Stage IV | 13278 | 3544 | 27 | 4.94 (4.07, 5.98) | 6.35 (5.19, 7.76) | |
| Occult | 65 | 8 | 12 | 1.90 (0.89, 4.08) | 2.23 (1.01, 4.94) | |
| "Missing" | 31664 | 6931 | 22 | 3.80 (3.14, 4.60) | 5.19 (4.25, 6.34) | |
| ***Townsend quintile*** | | | | | | |
| 1 (most affluent) | 8946 | 2222 | 25 | | | 0.005 |
| 2 | 11009 | 2702 | 25 | 0.98 (0.92, 1.05) | 0.97 (0.90, 1.04) | |
| 3 | 11911 | 2715 | 23 | 0.89 (0.84, 0.95) | 0.89 (0.83, 0.96) | |
| 4 | 12867 | 2880 | 22 | 0.87 (0.82, 0.93) | 0.83 (0.77, 0.89) | |
| 5 (least affluent) | 15219 | 3649 | 24 | 0.95 (0.90, 1.01) | 0.85 (0.79, 0.91) | |
| "missing" | 107 | 19 | 18 | 0.65 (0.40, 1.08) | 0.67 (0.39, 1.17) | |

Legend: N who had CTx, Number who had chemotherapy from each subgroup.
(%)* percentage of each subgroup who had chemotherapy
Adj OR** Odds ratio adjusted for all features in the table.
^ p value.

Table 4.7: Logistic regression for radiotherapy for the whole cohort (N=60,059)

| | N | N who had RTx | (%)* | OR (95% CI) | Adj OR* (95% CI) | P for trend |
|---|---|---|---|---|---|---|
| ***Sex*** | | | | | | |
| Male | 35693 | 7454 | 21 | | | |
| Female | 24366 | 4642 | 19 | 0.89 (0.86, 0.93) | 0.94 (0.90, 0.98) | 0.001^ |
| ***Age quintile*** | | | | | | |
| 1 (30-61 years) | 11895 | 2378 | 20 | | | 0.521 |
| 2 (52-69 years) | 13866 | 2826 | 20 | 1.02 (0.96, 1.09) | 1.00 (0.94, 1.06) | |
| 3 (70-74 years) | 10378 | 2199 | 21 | 1.08 (1.01, 1.15) | 1.06 (0.99, 1.13) | |
| 4 (75-80 years) | 13077 | 2827 | 22 | 1.10 (1.04, 1.17) | 1.11 (1.04, 1.18) | |
| 5 (81-101 years) | 10843 | 1866 | 17 | 0.83 (0.78, 0.89) | 0.90 (0.83, 0.96) | |
| ***Performance status (PS)*** | | | | | | |
| PS 0 | 7434 | 1417 | 19 | | | <0.001 |
| PS 1 | 11808 | 3098 | 26 | 1.51 (1.41, 1.62) | 1.48 (1.38, 1.60) | |
| PS 2 | 7611 | 2196 | 29 | 1.72 (1.60, 1.86) | 1.79 (1.66, 1.94) | |
| PS 3 | 6026 | 1043 | 17 | 0.89 (0.81, 0.97) | 0.96 (0.88, 1.06) | |
| PS 4 | 2068 | 148 | 7 | 0.33 (0.27, 0.39) | 0.38 (0.32, 0.45) | |
| "Missing" | 25122 | 4194 | 17 | 0.85 (0.80, 0.91) | 1.02 (0.95, 1.10) | |
| ***Histology*** | | | | | | |
| NSCLC | 25667 | 6438 | 25 | | | |
| Small cell | 5921 | 883 | 15 | 0.52 (0.48, 0.57) | 0.56 (0.52, 0.61) | |
| Carcinoid | 197 | 8 | 4 | 0.13 (0.06, 0.26) | 0.15 (0.08, 0.31) | |
| Mesothelioma | 2071 | 556 | 27 | 1.10 (0.99, 1.21) | 1.24 (1.12, 1.38) | |
| Other | 958 | 191 | 20 | 0.74 (0.63, 0.87) | 0.82 (0.74, 0.91) | |
| "Missing" | 25245 | 4020 | 16 | 0.57 (0.54, 0.59) | 0.69 (0.65, 0.72) | |
| ***Stage of tumour*** | | | | | | |
| Stage Ia | 1689 | 222 | 13 | | | <0.001 |
| Stage Ib | 2481 | 514 | 21 | 1.73 (1.45, 2.05) | 1.63 (1.37, 1.94) | |
| Stage IIa | 273 | 53 | 19 | 1.59 (1.15, 2.22) | 1.60 (1.15, 2.24) | |
| Stage IIb | 1570 | 379 | 24 | 2.10 (1.75, 2.52) | 1.95 (1.63, 2.35) | |
| Stage IIIa | 3059 | 865 | 28 | 2.61 (2.21, 3.06) | 2.44 (2.08, 2.88) | |
| Stage IIIb | 5980 | 1624 | 27 | 2.46 (2.11, 2.87) | 2.34 (2.01, 2.73) | |
| Stage IV | 13278 | 3100 | 23 | 2.01 (1.74, 2.33) | 2.03 (1.75, 2.36) | |
| Occult | 65 | 11 | 17 | 1.35 (0.69, 2.61) | 1.15 (0.59, 2.25) | |
| "Missing" | 31664 | 5328 | 17 | 1.34 (1.16, 1.54) | 1.57 (1.36, 1.82) | |
| ***Townsend quintile*** | | | | | | |
| 1 (most affluent) | 8946 | 1728 | 19 | | | 0.359 |
| 2 | 11009 | 2259 | 21 | 1.08 (1.00, 1.16) | 1.08 (1.01, 1.16) | |
| 3 | 11911 | 2470 | 21 | 1.09 (1.02, 1.17) | 1.12 (1.04, 1.20) | |
| 4 | 12867 | 2655 | 21 | 1.09 (1.01, 1.16) | 1.12 (1.04, 1.20) | |
| 5 (least affluent) | 15219 | 2967 | 19 | 1.01 (0.95, 1.08) | 1.02 (0.95, 1.09) | |
| "missing" | 107 | 17 | 16 | 0.79 (0.47, 1.33) | 0.80 (0.47, 1.36) | |

Legend: N who had RTx, Number who had radiotherapy from each subgroup.
(%)* percentage of each subgroup who had radiotherapy
Adj OR** Odds ratio adjusted for all features in the table.
^ p value

### 4.3.5 Patient Survival

The median survival from diagnosis for the whole cohort was 203 days (interquartile range 62 to 545 days), with 32% of patients surviving one year from diagnosis. Table 4.8 illustrates that socio-economic status had no independent influence on survival, once adjusted for all patient features. Table 4.9 illustrates the hazard ratios of specific patient features as well as the strata of NHS Trust case ascertainment, and the year of diagnosis. It shows that females had a slightly lower relative mortality compared with men, (adjusted HR 0.89, 95% CI 0.88, 0.91, $p<0.01$); and the mortality of patients with a performance status of 3 was more than three times that of patients with performance status 0, (adjusted HR 3.32, 95% CI 3.13, 3.53, $p<0.01$). Patients with stage IV disease had a more than five-fold increase in mortality compared with patients who were stage Ia (adjusted HR 5.57, 95% CI 4.73, 6.56, $p<0.01$). There was no variation in hazard ratio based on the level of case ascertainment at NHS Trusts, nor based on the year of diagnosis. There was no evidence that the proportional hazards assumption was incorrect.

Table 4.8: Results of Cox regression based on socio-economic status

| | **Absolute no. deaths (%)*** | | **Univariate HR (95% CI)** | | **Adjusted HR** (95% CI)** | |
|---|---|---|---|---|---|---|
| ***Townsend quintile*** | | | | | | |
| 1 (most affluent) | 7139 | (80) | | | | |
| 2 | 8896 | (81) | 1.03 | (1.00, 1.07) | 1.03 | (1.00, 1.06) |
| 3 | 9668 | (81) | 1.05 | (1.02, 1.08 | 1.02 | (0.99, 1.05) |
| 4 | 10420 | (81) | 1.06 | (1.02, 1.09) | 1.03 | (0.99, 1.06) |
| 5 (least affluent) | 12250 | (80) | 1.03 | (0.97, 1.09) | 1.00 | (0.95, 1.06) |

Legend: (%)* percentage of deaths for each variable subgroup.
Adj HR** Hazard ratio adjusted for sex, age quintile, performance status, histology, and stage at diagnosis.

Table 4.9: Results of uni and multivariate Cox regression analyses; using NHS Trust strata and key patient features.

| | Absolute number deaths (%)* | | Univariate HR (95% CI) | | Adjusted HR** (95% CI) | |
|---|---|---|---|---|---|---|
| ***Trust strata based on O/E ratio*** | | | | | | |
| Highest O:E | 19825 | (82) | | | | |
| 2 | 14553 | (81) | 0.99 | (0.96-1.01) | 1.01 | (0.99-1.03) |
| 3 | 9983 | (80) | 0.95 | (0.93-0.98) | 0.99 | (0.97-1.02) |
| Lowest O:E | 4092 | (77) | 0.94 | (0.90-0.97) | 1.07 | (1.03-1.11) |
| ***Sex*** | | | | | | |
| Male | 29218 | (82) | | | | |
| Female | 19235 | (79) | 0.92 | (0.90-0.94) | 0.89 | (0.87-0.90) |
| ***Age quintile*** | | | | | | |
| 1 (30-61 years) | 8800 | (74) | | | | |
| 2 (62-69 years) | 10731 | (77) | 1.13 | (1.10-1.17) | 1.11 | (1.08-1.15) |
| 3 (70-74 years) | 8337 | (80) | 1.26 | (1.22-1.30) | 1.18 | (1.15-1.22) |
| 4 (75-80 years) | 10982 | (84) | 1.45 | (1.41-1.50) | 1.31 | (1.27-1.35) |
| 5 (81-101 years) | 9603 | (89) | 1.78 | (1.73-1.83) | 1.41 | (1.37-1.46) |
| ***Performance status (PS)*** | | | | | | |
| PS 0 | 4660 | (63) | | | | |
| PS 1 | 9022 | (76) | 1.50 | (1.45-1.55) | 1.31 | (1.26-1.35) |
| PS 2 | 6776 | (89) | 2.44 | (2.35-2.53) | 1.88 | (1.81-1.95) |
| PS 3 | 5736 | (95) | 4.06 | (3.90-4.22) | 2.88 | (2.76-3.00) |
| PS 4 | 2032 | (98) | 7.35 | (6.97-7.76) | 4.91 | (4.64-5.19) |
| PS not known | 8578 | (81) | 1.95 | (1.88-2.02) | 1.73 | (1.67-1.80) |
| "Missing" | 11629 | (80) | 1.74 | (1.68-1.80) | 1.66 | (1.60-1.73) |
| ***Histology of tumour*** | | | | | | |
| Non Small Cell | 18538 | (80) | | | | |
| Small cell | 5175 | (90) | 1.34 | (1.30-1.38) | 1.24 | (1.20-1.28) |
| Carcinoid | 25 | (16) | 0.11 | (0.08-0.17) | 0.17 | (0.12-0.26) |
| Mesothelioma | 1626 | (82) | 0.98 | (0.93-1.03) | 0.90 | (0.85-0.95) |
| "Other" histology | 1785 | (75) | 0.91 | (0.87-0.96) | 0.97 | (0.92-1.02) |
| "Missing" | 21304 | (80) | 1.06 | (1.04-1.08) | 0.95 | (0.92-0.98) |
| ***Stage of tumour*** | | | | | | |
| Stage IA | 661 | (39) | | | | |
| Stage IB | 1319 | (53) | 1.46 | (1.33-1.60) | 1.44 | (1.31-1.58) |
| Stage IIA | 114 | (42) | 1.10 | (0.91-1.35) | 1.10 | (0.90-1.34) |
| Stage IIB | 985 | (62) | 1.98 | (1.80-2.19) | 1.90 | (1.72-2.09) |
| Stage IIIA | 2280 | (75) | 2.63 | (2.41-2.87) | 2.25 | (2.06-2.46) |
| Stage IIIB | 5074 | (85) | 3.74 | (3.45-4.06) | 2.96 | (2.72-3.21) |
| Stage IV | 12348 | (93) | 5.98 | (5.52-6.47) | 4.37 | (4.04-4.73) |
| Occult | 45 | (69) | 2.15 | (1.58-2.92) | 1.98 | (1.46-2.69) |
| Uncertain | 3183 | (75) | 3.21 | (2.95-3.49) | 2.55 | (2.34-2.78) |
| "Missing" | 22444 | (82) | 3.55 | (3.28-3.83) | 2.90 | (2.67-3.13) |
| ***MDT treatment intent*** | | | | | | |
| No specific anti-cancer Rx | 2626 | (90) | | | | |
| Curative intent | 2548 | (47) | 0.23 | (0.22-0.25) | 0.47 | (0.44-0.50) |
| Palliative intent | 18879 | (88) | 0.83 | (0.80-0.86) | 1.01 | (0.97-1.05) |
| Best Supportive Care | 6792 | (92) | 1.22 | (1.16-1.27) | 1.26 | (1.20-1.32) |
| Don't know | 4046 | (80) | 0.65 | (0.62-0.68) | 0.85 | (0.81-0.90) |
| "Missing" | 13562 | (76) | 0.59 | (0.57-0.62) | 0.87 | (0.84-0.92) |
| ***Year of diagnosis*** | | | | | | |
| 2007 | 15774 | (72) | | | | |
| 2006 | 15199 | (83) | 1.03 | (1.00-1.05) | 1.03 | (1.00-1.05) |
| 2005 | 11248 | (87) | 1.01 | (0.98-1.03) | 1.01 | (0.99-1.04) |
| 2004 or earlier | 6232 | (90) | 1.02 | (0.99-1.05) | 1.02 | (0.99-1.05) |

Legend: (%)* percentage of the total number of patients within each subgroup of each variable who have died.

** Hazard ratios are mutually adjusted for all variables in the table.

### 4.3.6 Results of NHS Trust stratification using different data sources

NHS Trust stratification using these three sources of data showed a high level of agreement. The level of concordance between Registry derived strata and ONS and HES derived strata are depicted in tables 4.10 and 4.11 respectively. The weighted kappa value for agreement between Registry and ONS derived stratification was 0.85, and between Registry and HES derived NHS Trust stratification was 0.75.

Table 4.10: Concordance between ONS and Registry derived NHS Trust strata.

| | | **NHS Trust strata calculated using ONS data** | | | | | |
|---|---|---|---|---|---|---|---|
| **NHS Trust strata using calculated Registry data** | | 1 | 2 | 3 | 4 | 'Missing' | Total |
| | 1 | **25** | 11 | 3 | 0 | 0 | 39 |
| | 2 | 11 | **17** | 11 | 0 | 0 | 39 |
| | 3 | 3 | 8 | **21** | 7 | 0 | 39 |
| | 4 | 0 | 0 | 6 | **34** | 0 | 40 |
| | 'Missing' | 0 | 0 | 0 | 0 | **11** | 11 |
| | Total | 39 | 36 | 41 | 41 | 11 | 168 |

Table 4.11: Concordance between HES and Registry derived NHS Trust strata.

| | | **NHS Trust strata calculated using HES data** | | | | | |
|---|---|---|---|---|---|---|---|
| **NHS Trust Strata using calculated Registry data** | | 1 | 2 | 3 | 4 | 'Missing' | Total |
| | 1 | **24** | 13 | 0 | 1 | 1 | 39 |
| | 2 | 10 | **18** | 7 | 4 | 0 | 39 |
| | 3 | 3 | 8 | **20** | 8 | 0 | 39 |
| | 4 | 1 | 0 | 11 | **26** | 2 | 40 |
| | 'Missing' | 0 | 0 | 0 | 0 | 11 | 11 |
| | Total | 38 | 39 | 38 | 39 | 14 | 168 |

NHS Trust stratum; 1=quartile with highest observed:expected ratio,

4=quartile with lowest observed:expected ratio.

## 4.4 Discussion

### 4.4.1 Overall summary

I have found that despite variation in the NHS Trust level of case ascertainment within the NLCA dataset, there was little variation related to this in patient demographics, access to treatment and survival. This suggests that overall the data within the NLCA are unbiased and are representative of people with lung cancer in England, which implies the NLCA is a useful dataset for health service research.

I have found that although only a minority of patients undergo surgery, for the subgroup of patients with proven non-small cell lung cancer this figure is 14%, which is approaching the figure of 17% amongst comparable European countries (5). Less than a third (32%) of all patients are surviving for one year after their diagnosis, which is below the standard of 'good practice' stated as 37%, in the Cancer Reform Strategy - second annual report (37). This figure is based on the highest rate of one year survival amongst countries with 100% registration in EUROCARE-4 (21). Overall survival is affected by several patient features; namely increasing age, poor performance status and advanced stage of the disease at diagnosis. Of note socio-economic deprivation does not affect overall survival, or the likelihood of receiving surgery or radiotherapy; but it did have a small effect on reducing the likelihood of receiving chemotherapy, even after allowing for variation in stage and performance status.

### 4.4.2 Strengths and weaknesses

The strength of the NLCA dataset lies in the fact it is the largest (non Registry), contemporary, and unselected cohort of individuals with lung cancer in Europe, including both surgical and non-surgical patients. Data collection is on-going and the production of an annual report (35) allows policy changes to be evaluated and the audit cycle to be completed. The weaknesses of the NLCA

dataset are that it does not contain detailed information on patient co-morbidity, nor information regarding the treatment facilities available at individual NHS Trusts, and that a number of the data fields have missing data. These results have shown that in general NHS Trusts that submitted a lower proportion of cases also tended to have higher levels of missing data for individual variables. There is evidence that the proportion of missing data is decreasing progressively and that the quality of the dataset is therefore improving each year (35). Furthermore my aim is to link the NLCA dataset with other healthcare datasets and thereby to evaluate the influence of overall and individual co-morbidities on treatment received and overall survival. Despite these limitations the NLCA is the largest available dataset for lung cancer health services research and my results suggest it is a valid resource tool which should now be used to answer important service provision questions.

Finally it is reassuring to note that there was a good level of correlation between the strata of NHS Trusts based on case ascertainment calculated using cancer Registry data, and those created using ONS and HES data.

### 4.4.3 Comparison with other studies

Whilst there are few published national studies of health service research involving lung cancer in England, there have been smaller audits at a regional level which have described geographical variation in treatment and survival for people with lung cancer (51, 67). Jack et al (2003) (51) found that a deprived socio-economic status was linked to a reduced likelihood of receiving chemotherapy, but that it had no impact on 1 or 3 year survival, findings consistent with my results. In 1998 an audit (23) was carried out by the Clinical Effectiveness and Evaluation Unit of the Royal College of Physicians (London) which comprised 1600 patients across 48 hospitals in England, Wales and Northern Ireland. Information was collected retrospectively and prospectively

about clinical presentation, treatment received and survival at six months post procedure on patients who had undergone a bronchoscopy. There was geographical variation in the timing of and intervals between several points along the diagnostic pathway. Variation was also reported between hospitals in terms of the treatments used; rates of surgical resection (excluding known small cell cancers) ranged from 3-33%, of chemotherapy (small cell cancers only) ranged from 14-100%, and for radiotherapy ranged from 20-77%. However, within a small cohort like this, small changes in patient numbers will dramatically alter the percentages reported. Within this small cohort, 46% of patients had died within six months of bronchoscopy, which is in keeping with our finding that median survival from diagnosis is only 203 days (interquartile range 62 to 545 days). Some of these inequalities in the patient lung cancer pathway may be mitigated by implementation of the NHS Cancer Plan (2000) (24), and the Cancer Reform Strategy (2007) (27). Standards for the treatment of individuals diagnosed with lung cancer in England and Wales have also been set by the National Institute for Clinical Excellence (NICE) in 2005 (26).

The second annual report since the Cancer Reform Strategy (37) described regional variation in lung cancer one year survival at the level of primary care trusts. Given these results confirm that individual level socio-economic status does not affect the likelihood of receiving surgery nor overall survival, it seems unlikely that individual socio-economic status explains the regional variation in treatment received by individuals with lung cancer (23, 35) nor their survival (37). This in turn suggests that the factors underpinning these Trust level variations are more likely to be related to primary or secondary care practice, and not individual patient features.

There are two international comparators, namely the EUROCARE-4 study (21), and the ongoing SEER (22) (Surveillance, Epidemiology and End Results)

programme in America. Both of these are registry linked datasets; the former is a European collaboration involving 47 cancer registries from 21 countries (and includes 4 regional registries for England), whilst the latter represents 26% of the overall American population. Neither of these large datasets are specific for lung cancer, but they do contain information on incidence, treatment and survival for all major cancers including lung. The NLCA dataset contains more patient specific details, including stage of disease at diagnosis (not present in EUROCARE-4) but the survival data within the NLCA are currently inadequate to calculate 5 year survival, although this will be possible by the end of 2011. Comparison between this cohort and results from SEER show good agreement on age and stage at diagnosis. As the NLCA database increases over time, more comprehensive comparisons will be possible with these international datasets.

### 4.4.4 Implications of this study

The implications of this study are two-fold; firstly the validation of the NLCA dataset on the basis of data completeness suggests that these data reflect the current state of lung cancer in England. As such, it is a unique dataset which has enormous potential to inform and influence policy change and to improve the standard of care for lung cancer patients.

Secondly these analyses provide contemporary estimates of treatment received and overall survival in people with lung cancer in England, and they provide reassurance that an individual's socio-economic status has little influence on either of these outcome markers. Future studies of geographical variation in lung cancer care should focus mainly on potential variation in NHS Trust level features.

# Chapter five: Linking the National Lung Cancer Audit with Hospital Episode Statistics (HES)

## 5.1 Introduction

The analyses so far have established there is no evidence of bias in the demographic features of patients entered into the dataset, nor their outcome, based on case ascertainment at NHS Trusts. Therefore the National Lung Cancer Audit is a contemporary dataset, which can be used to investigate the geographical inequalities in lung cancer care in England. However, the Audit does not contain robust data on co-morbidity, and so this chapter will describe the process of cleaning a dataset from the NLCA linked to Hospital Episode Statistics; and the creation of a composite score of co-morbidity, the Charlson Index.

My aim was to study the influence of both patient level and NHS Trust level features on the management and clinical outcome of people with lung cancer. In order to try and quantify the influence of the NHS Trust where a patient was first seen on outcome measures, details relating to facilities at every NHS Trust were obtained. These include whether or not it is a cardio-thoracic surgical centre, and/or a radiotherapy centre, the level of participation in clinical trials and the individual NHS Trust results from Peer Review (2003-2007).

This chapter will describe the results of basic patient features for the whole cohort, including the relationship between socio-economic status and performance status, stage of disease and co-morbidity at diagnosis. I have used logistic regression to investigate whether the composite score of co-morbidity, the Charlson Index, or the individual component disease groups, influenced the likelihood of receiving certain treatment modalities. I have also looked at the time spent in hospital prior to the diagnosis of lung cancer, to assess if this is an independent predictor of the likelihood of having certain treatments. From the perspective of an NHS Trust I will discuss the results of the Peer Review data (2003-2007) and the incorporation of these data, which theoretically reflect the

performance of a lung cancer multi-disciplinary team, into logistic regression analyses investigating treatment use. The same four variables will be analysed using multivariate Cox regression to assess their influence on overall survival in this cohort of patients with lung cancer.

The influence of patient and NHS Trust features on the likelihood of receiving surgery in patients with non-small cell lung cancer, and chemotherapy for those with small cell lung cancer have been investigated in detail and will be described in chapters 6 and 7 respectively.

## 5.2 Methods

### 5.2.1 Patient features within National Lung Cancer Audit (NLCA)

The dataset used for this section of research was the second download received from the Information Centre (downloaded 17th November 2009), and linked to Hospital Episode Statistics. The NLCA component of the linked dataset required cleaning to ensure that the statistical package Stata 11 could process the data, and this was described in chapter 3.

The National Lung Cancer Audit dataset contains the following patient features: sex, age at diagnosis, performance status (ECOG), histological subtype, and stage of the disease at diagnosis. The NLCA dataset also contains the details of each individual patient's Lower Super Output Area (LSOA), which can be converted to a Townsend score for deprivation, generating a marker of socio-economic status (see section 4.2.4). The Townsend quintile was the marker of socio-economic status used throughout the remainder of this research.

### 5.2.2 Patient features within Hospital Episode Statistics (HES)

Co-morbidity

Hospital Episode Statistics is a national database that all NHS Trusts use which records the ICD-10 diagnostic codes assigned to every patient who attends an NHS institution, and also the operation codes (OPCS4) for any procedures performed. This coding practice is one element of the administration process by which an NHS Trust can invoice Primary Care Trusts. In-patient data were available from 1997 to 2007 (inclusive), so all patients within the NLCA dataset as of the 17th September 2009, with a date first seen before 31st December 2008, were linked to HES. This provided 11 files (following the financial years between 1997 and 2007) with in-patient details including all diagnoses assigned, the frequency and duration of admissions, the operations performed and also

ethnicity of each individual. Within an admission, every patient can have multiple 'episodes' which should represent any change in the management of the patient, for example if a consultant from a different discipline takes over the patient's care. For each episode, a patient can have up to 20 diagnoses recorded. This level of detail can allow the influence of specific co-morbidities to be examined, and also allows the creation of a composite score of co-morbidity.

The composite score of co-morbidity chosen for this research, and used throughout the remainder of this project was the Charlson Index. It was first described by Dr ME Charlson in 1987 (34) as a method of creating a composite score of co-morbid severity in hospital within a cohort of breast cancer patients, which was then used to predict ten year survival. It has since been validated in other groups of patients, often with a malignant disease (68, 69), and has been found to be strongly predictive of survival, independent of age. For this reason it is an appropriate composite score to use in a cohort of individuals with lung cancer. The Charlson Index is composed of 16 disease groups each with an individual 'score' which are weighted according to the influence this disease group is deemed to have on survival, see table 5.1. However, the Charlson Index does not score on the severity of a condition, therefore two patients with COPD would contribute 1 to their overall score, and yet one patient could be on reliever inhalers only, and the other on full medical therapy including long-term oxygen. It is worth noting that when the Charlson Index was created, a diagnosis of AIDS was essentially a terminal illness and hence it carries the same 'weight' as metastatic disease. However, over the past 20 years, the development of Highly Active Anti-Retroviral Treatment (HAART) has meant that a diagnosis of AIDS is no longer a terminal event. Within this cohort of individuals with lung cancer, AIDS is unlikely to be a common co-morbidity, and so the Charlson Index remains an appropriate composite score of co-morbidity.

Table 5.1: Illustrates the diseases used within the Charlson Index and the score assigned to each disease group.

| Disease | Individual score |
|---|---|
| Myocardial infarction/heart failure | 1 |
| Cerebrovascular disease | 1 |
| Chronic pulmonary disease | 1 |
| Dementia | 1 |
| Peptic ulcer disease | 1 |
| Diabetes (without complications) | 1 |
| Peripheral vascular disease | 1 |
| Connective Tissue disorder | 1 |
| Mild liver disease | 1 |
| Cancer (solid organ) | 2 |
| Haematological Malignancy | 2 |
| Diabetes with complications | 2 |
| Hemiplegia and paraplegia | 2 |
| Renal disease | 2 |
| Moderate or severe liver disease | 3 |
| Metastatic cancer | 6 |
| AIDS | 6 |

In order to create a composite co-morbidity score, the first challenge was to merge the 11 files with details of in-patient admissions, and create a master file. This dataset contained all patients held within the National Lung Cancer Audit, between January 2004 and the end of December 2008, and details of all diagnoses recorded for those who had been admitted to hospital since 1997. There were more than 1.5 million lines of data.

In order to assess the influence of co-morbidity on the treatment decision of the multi-disciplinary team, a Charlson Index was created for each patient within this NLCA/HES linked dataset at the time of diagnosis. The date of diagnosis is held

within the NLCA dataset. Where the date of diagnosis was missing the date of first clinic appointment was interpolated, adjusting for the median interval between clinic appointment and diagnosis within the whole cohort, which was 10 days. Only admissions before the date of diagnosis were considered.

Not all patients within this linked dataset had an in-patient record reflecting their diagnosis of lung cancer. Therefore in order to remove this discrepancy all seven ICD-10 codes for lung cancer were deleted from the dataset. Consequently, only patients who had a 'non-lung' malignancy prior to their diagnosis of lung cancer would contribute two points to their overall Charlson Index. However, it could be that patients with metastatic lung cancer contributed six points to their composite score on the basis of metastatic disease, rather than a specific diagnosis of lung cancer.

It was important to ensure that every diagnosis pertinent to a Charlson Index should contribute only once to the overall score (appendix 5). Therefore, duplicate ICD-10 codes were dropped after their first appearance in the NLCA/HES linked dataset. For example an individual with renal failure generated a Charlson Index of more than 700, when every time she attended for haemodialysis she added two points to her overall score. Furthermore, should an individual have more than one diagnosis (ICD-10 code) within the same Charlson disease group, only the first diagnosis should contribute to their overall score.

'Bed days'

Hospital Episode Statistics contains details of in-patient duration, 'bed days', and this has been studied previously in relation to survival from cancer (70, 71). Therefore a variable 'bed days' was created which was the sum of all the time spent in hospital over a twelve month period prior to the diagnosis of lung

cancer. However, so as to exclude the possibility of reverse causation, i.e. that in the immediate period of time leading up to the diagnosis of lung cancer (say three months) an individual may attend hospital for seemingly unrelated problems, which may in fact relate to the underlying malignancy, the period of time chosen for analysis should not include this 'lead time' period. Therefore it was decided to examine the time spent in hospital by patients between 15 and 3 months (i.e. a 12 month period) prior to the diagnosis of lung cancer. The number of days spent in hospital was then converted to a categorical variable, by creating quartiles.

Ethnicity

Finally, HES contains information regarding the ethnic origin of in-patients, and this information was coded and grouped into the following categories; White, Black (African and Caribbean), Asian, Mixed race, other ethnicity, and missing.

### 5.2.3 NHS Trust features

In order to investigate the role of the hospital where a patient is first seen in determining the clinical outcomes of individuals with lung cancer, I have quantified the services pertinent to lung cancer care available at every NHS Trust, and the performance of the lung cancer MDT within every Trust.

#### 5.2.3.1 Cardio-thoracic surgical centres

The National Society of Cardiothoracic Surgeons has shared information regarding which NHS Trusts are also Cardio-thoracic surgical centres. This was used to create a binary variable for each NHS Trust, based on whether the Trust is a surgical centre or not.

#### 5.2.3.2 Radiotherapy centres

Based on a report from the National Cancer Action Team (NCAT) (2007/2008) it has been possible to identify which NHS Trusts within England have radiotherapy facilities. This information was used to create a binary variable for each NHS Trust, based on whether the Trust is a radiotherapy centre or not.

#### 5.2.3.3 Clinical trial entry data

All NHS Trusts can provide chemotherapy, and all multi-disciplinary teams are encouraged to consider patients for clinical trials. Clinical trials will predominantly involve chemotherapy, but not exclusively; some are related to surgery, radiotherapy, and palliative care. The National Cancer Research Network (NCRN) kindly supplied trial entry figures, specific to lung cancer, for 2008-09. In order to allow comparison between NHS Trusts with different caseloads, the proportion of patients being entered into clinical trials was calculated by dividing the number of patients entered into trials by the expected number of patients at each NHS Trust according to Cancer Registry data (2007). There was a wide range of values for the proportion of expected patients entered into trials at individual NHS Trusts. Having evaluated the results (figure 5.1) a

cut-off of 5% (0.05) was made, as this accounted for an above average proportion of patients being entered into clinical trials; but yet an achievable target, as approximately a third of all patients were first seen in NHS Trusts who entered 5% or more of their expected lung cancer patients into clinical trials. Hence, a binary variable reflecting trial entry at the level of an NHS Trust was created, a high trial centre entered 5% or more of its expected lung cancer patients into clinical trials, and a low trial centre did not achieve this.

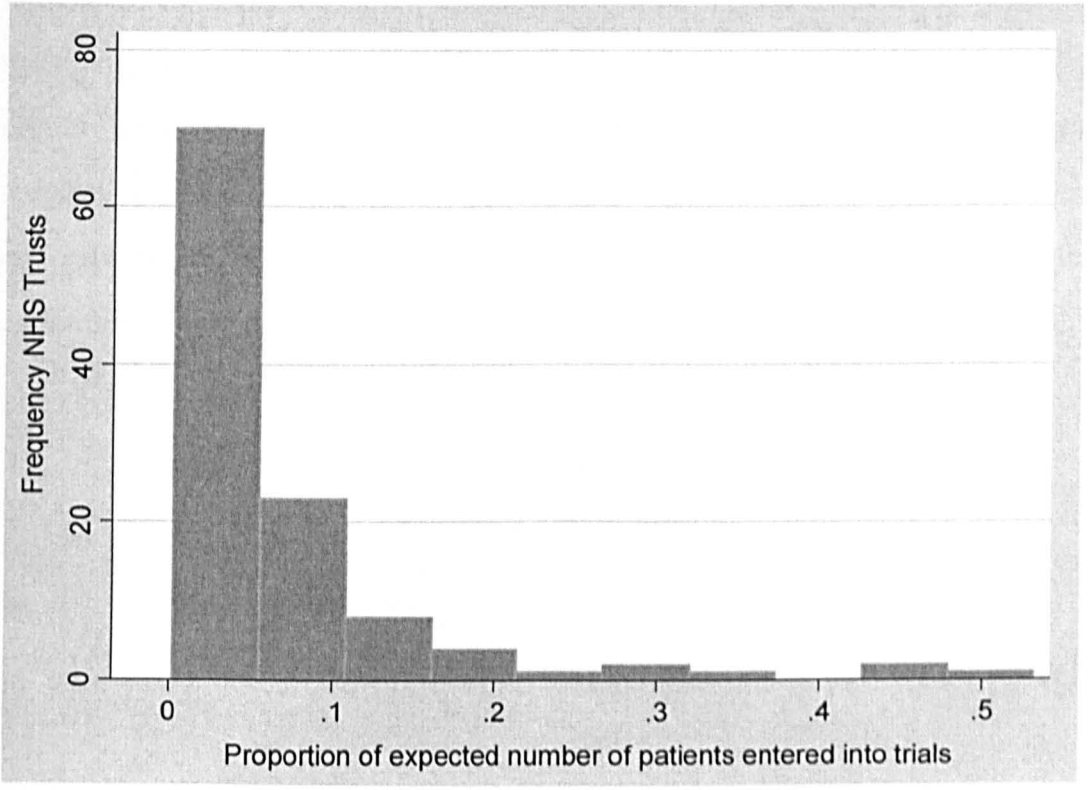



Figure 5.1: Histogram showing range in proportion of patients entered into clinical trials

#### 5.2.3.4 Peer Review

The National Cancer Action Team, Department of Health, performs a Peer review evaluation process of all cancer services at NHS Trusts in England and Wales. Originally this was every 4 years, but it has now become an annual process. Therefore all lung cancer multidisciplinary teams (MDTs) are inspected and required to demonstrate evidence of how they performed when measured against 32 key standards (appendix 6). The results of the Peer review process

2004-2007 were made available for this research project. The overall score achieved by each NHS Trust was included as a marker of NHS Trust performance, and to establish if this influenced lung cancer outcomes.

### 5.2.4 Outcome measures

#### 5.2.4.1 Treatment received

Of the three treatment modalities used for lung cancer, surgery has the greatest number of variables within the National Lung Cancer Audit dataset, namely: the NHS Trust where the surgery took place, the date of the operation and the primary procedure (OPCS4) code. The degree of overlap between these three surgical variables was explored (figure 5.2). I decided to use the date of surgery as a reliable marker that surgery had taken place, which captured almost 80% of patients with any reference to surgery.

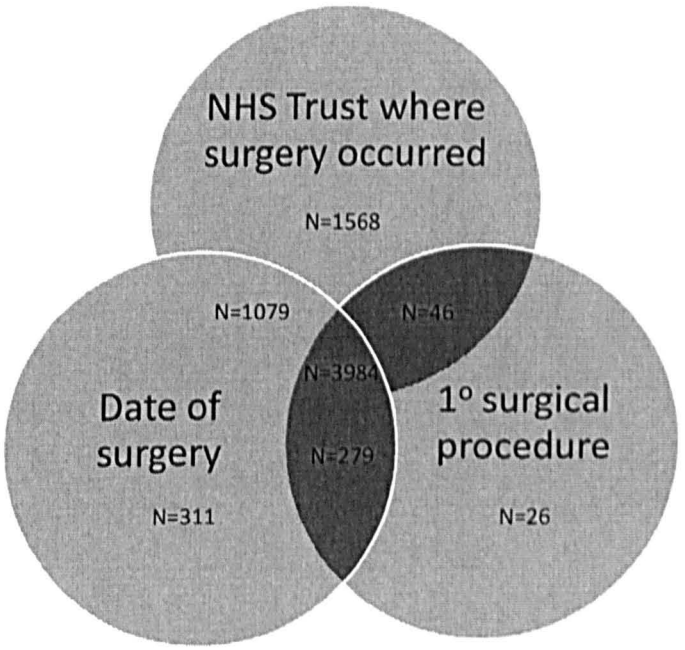



Figure 5.2: Relationship between Audit variables pertaining to surgery.

Radiotherapy and Chemotherapy have variables recording the NHS Trust where these took place and the date the therapy started. There is discrepancy in the

completeness of these data fields, but again it was felt the date of treatment was the most reliable piece of data. Therefore the presence of a 'date of treatment' was used to create a binary variable for whether treatment had actually taken place.

#### 5.2.4.2 Overall survival

The start date was taken as the date of diagnosis as per the National Lung Cancer Audit, and, if missing, the date of the first clinic appointment was interpolated, adjusting for the median interval between these two dates on the patient pathway for the whole cohort (10 days). The end date was taken as the date of death as per NLCA (obtained from the Patient Demographics Service), or the date the dataset was downloaded, which was the 30th September 2009. Patients with a date of diagnosis on or after the date of death were excluded from survival analyses, and represent patients diagnosed by death certificate only.

### 5.2.5 Analysis plan

One aspect of this stage of the research has simply been the creation of key variables based on important patient features and pertinent features of an NHS Trust. These are outlined in Table 5.2 below. Each patient feature was analysed for the cohort as a whole and the results are shown in section 5.3

Table 5.2: Final set of patient and NHS Trust features

| Patient feature | Source | Comment |
|---|---|---|
| Sex | NLCA | |
| Age at diagnosis | NLCA | |
| Histology | NLCA | |
| Performance status | NLCA | Based on ECOG |
| Spirometry | NLCA | Absolute value (L/min) |
| Stage | NLCA | UICC version 6 |
| Townsend quintile | NLCA derived | Mapped via LSOA |
| Ethnicity | HES | |
| Charlson Index | HES derived | Generated using ICD-10 codes for in-patient admissions between 1997 and 2007. |
| Bed days | HES derived | Total days spent in hospital in 12 month period prior to diagnosis of lung cancer. |
| Date of surgery | NLCA | |
| Date of radiotherapy | NLCA | |
| Date of chemotherapy | NLCA | |
| Date of diagnosis | NLCA | |
| Start date | NLCA derived | Date of diagnosis or interpolated from date of clinic appointment. |
| Date of death | NLCA | Patient Demographics Service |
| | | |
| Surgical centre | CT Society | Binary variable |
| Radiotherapy centre | NCAT | Binary variable |
| Trial entry data | NCRN | Binary variable created with 5% of expected lung cancer patients entered into trials as the threshold for a high trial centre. |
| Peer Review | NCAT | Overall score |

Legend:

| | |
|---|---|
| NLCA | National Lung Cancer Audit dataset (LUCADA) |
| HES | Hospital Episode Statistics |
| CT Society | Cardio-Thoracic Society |
| NCRN | National Cancer Research Network |
| NCAT | National Cancer Action Team |
| ECOG | Eastern Cooperative Oncology Group |
| UICC | Union International Contre le Cancer (version 6) |
| LSOA | Lower Super Output Area |

In order to evaluate the influence on treatment received for the following variables: Charlson Index, the individual component disease groups of the Charlson Index, 'bed days' and the overall score from Peer Review, multivariate logistic regression analyses were performed. The models were adjusted mutually for all patient features.

Multivariate Cox regression analyses were performed to assess the influence on overall survival of the same variables, namely: Charlson Index, the individual component disease groups of the Charlson Index, 'bed days' and the overall score from Peer Review. The proportional Hazards assumption was checked using Nelson-Aaleen plots.

## 5.3 Results

The NLCA/HES linked dataset (2nd dataset made available for this research) contained 87,254 patients who were first seen at an English NHS Trust between January 2004 and 31st December 2008. Two patients had no database identifier and were excluded, and 6,286 (7%) were excluded on the basis there was no record of the NHS Trust at which they were first seen. This left 80,966 unselected English patients with lung cancer, all of whom had either a date of diagnosis or date of first appointment.

### 5.3.1 Patient features within NLCA

The basic demographic features of this second cohort of English lung cancer patients were very similar to those of the original dataset. The sex ratio, male:female was 60:40, and the median age at diagnosis was 72 years (interquartile range 62 to 79 years). The histological subtypes at diagnosis are depicted in Table 5.3 and were broadly grouped into non-small cell lung cancer (NSCLC) 40%, small cell 10%, and mesothelioma 3%. Within the subset of patients with NSCLC, 33% had proven squamous cell carcinoma, 27% had adenocarcinoma, and 34% had non-small cell lung cancer not-otherwise-specified (NOS).

Table 5.3; Histological subtypes at diagnosis (N=80,966)

| Histology | N | % |
|---|---|---|
| Squamous | 11,487 | 14.2 |
| Adenocarcinoma | 9,257 | 11.5 |
| NSCLC, NOS | 11,531 | 14.2 |
| Mixed NSCLC | 138 | 0.2 |
| Small cell | 7,845 | 9.7 |
| Carcinoid | 240 | 0.3 |
| Neuroendocrine | 244 | 0.3 |
| CarcinoSarcoma | 39 | 0.1 |
| Large cell/other | 3,001 | 3.7 |
| Bronchoalveolar cell | 525 | 0.7 |
| Carcinoma-in-situ | 167 | 0.2 |
| Mesothelioma | 2,772 | 3.4 |
| Missing | 33,964 | 42.0 |
| **Total** | **80,966** | |

Stage is recorded in the NLCA dataset as per the sixth version of the Union International Contre le Cancer (UICC). Table 5.4 illustrates the variation in stage of disease at diagnosis, and demonstrates the large subgroup of patients who present with metastatic disease (Stage IV), for whom a cure is not possible.

Table 5.4: Stage at diagnosis (N=80,966)

| Stage | N | % | %* |
|---|---|---|---|
| IA | 2,439 | 3.0 | 5.9 |
| IB | 3,591 | 4.4 | 8.7 |
| IIA | 376 | 0.5 | 0.9 |
| IIB | 2,217 | 2.7 | 5.4 |
| IIIA | 4,351 | 5.4 | 10.6 |
| IIIB | 8,627 | 10.7 | 20.9 |
| IV | 19,547 | 24.1 | 47.3 |
| Occult | 92 | 0.1 | 0.2 |
| Missing | 39,726 | 49.1 | NA |
| **Total** | **80,966** | | |

Legend: * percentage of patients with each stage of disease excluding those with 'missing' data

Performance status

Data on Performance Status (PS) at diagnosis were missing in 31,890 (40%) patients, but the variation in PS at diagnosis in those with these data is illustrated in the figure 5.3 below. It demonstrates the large group of patients (26,357) who have a good performance status (PS 0-1) at diagnosis. This suggests their co-morbidities, if they have any, should not preclude potentially curative treatment.

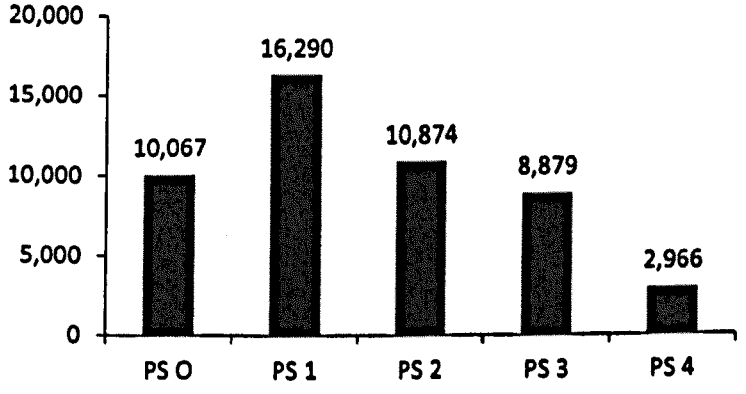



Figure 5.3; Illustrates performance status at diagnosis if recorded (N=49,076).

Lung function

Results of basic spirometry were available on 22,233 patients, and these data demonstrate a wide range of values of pre-operative $FEV_1$ (see figure 5.4). However, this is unlikely to be a representative sample, as those patients with significant co-morbidities or a poor performance status may not be sent for basic spirometry. For this reason, $FEV_1$ was not included in multivariate logistic and Cox regression analyses in the remainder of this research.

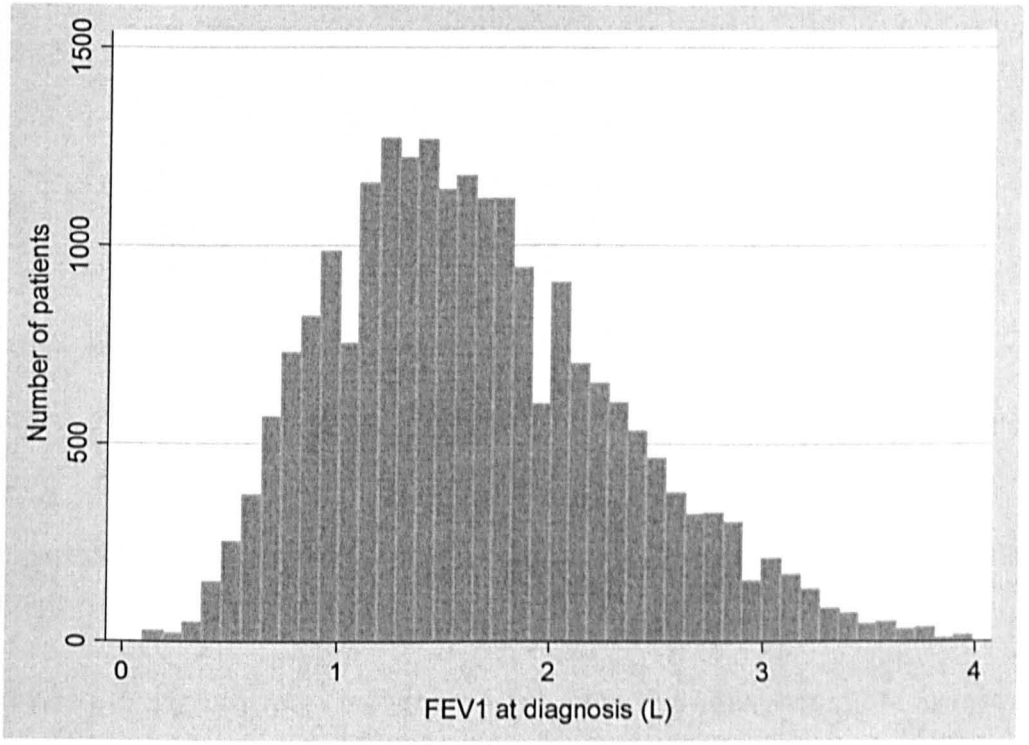



Figure 5.4: Histogram illustrating the variation in basic spirometry.

Socio-economic status

Almost all patients within the National Lung Cancer Audit dataset have a lower super output area (LSOA) code based on their residential postcode. The LSOA was missing in 170 patients within this cohort, therefore it was not possible to derive a Townsend score for these individuals. The distribution of Townsend quintile scores (N=80,796) for the remaining cohort are illustrated in figure 5.5.

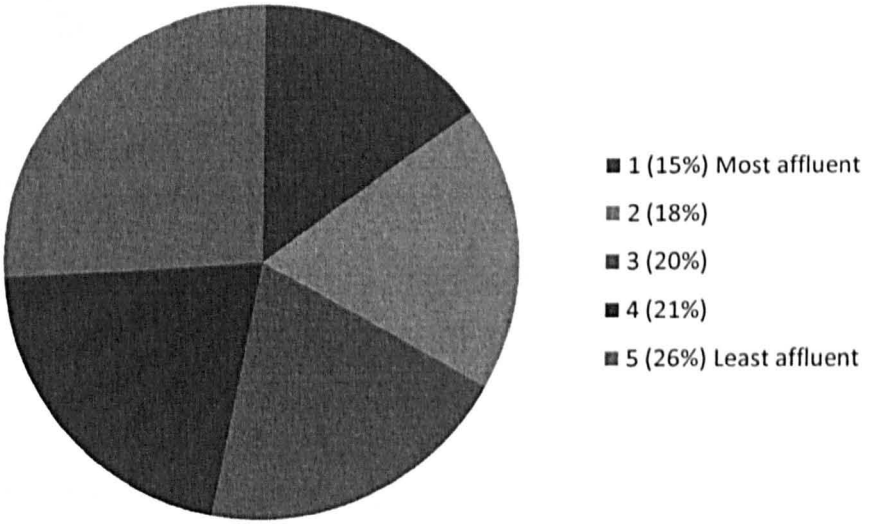



Figure 5.5: Distribution of socio-economic status using Townsend quintiles in this English cohort of patients with lung cancer.

Figure 5.5 demonstrates that there were more individuals from the lowest socio-economic stratum within this cohort of patients with lung cancer, and fewest from the most affluent subgroup. Whether the socio-economic stratum of an individual was linked to any other differences in terms of clinical features has also been investigated.

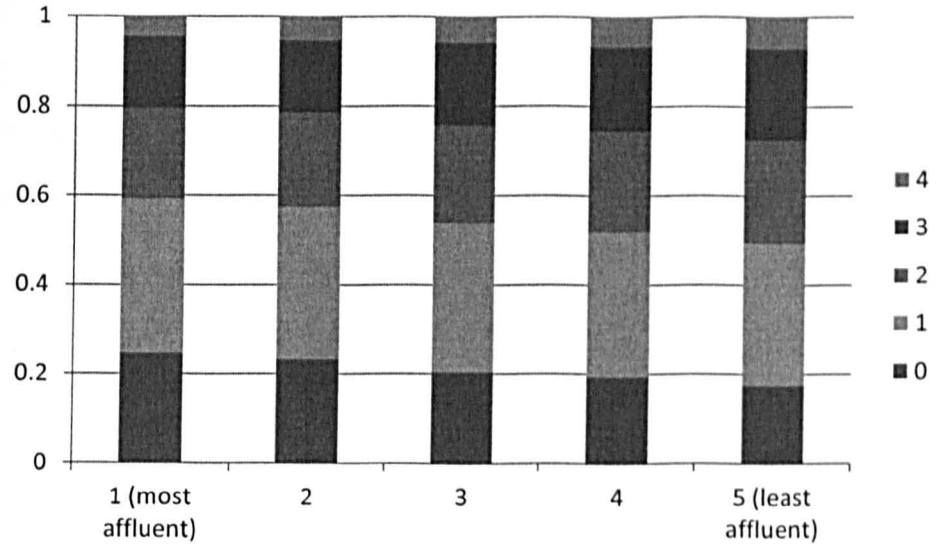



Figure 5.6: Distribution of performance status across each Townsend quintile.

There was a small reduction in the proportion of patients with performance status 0, normal physical function, in the least affluent compared to the most affluent quintile of socio-economic status.

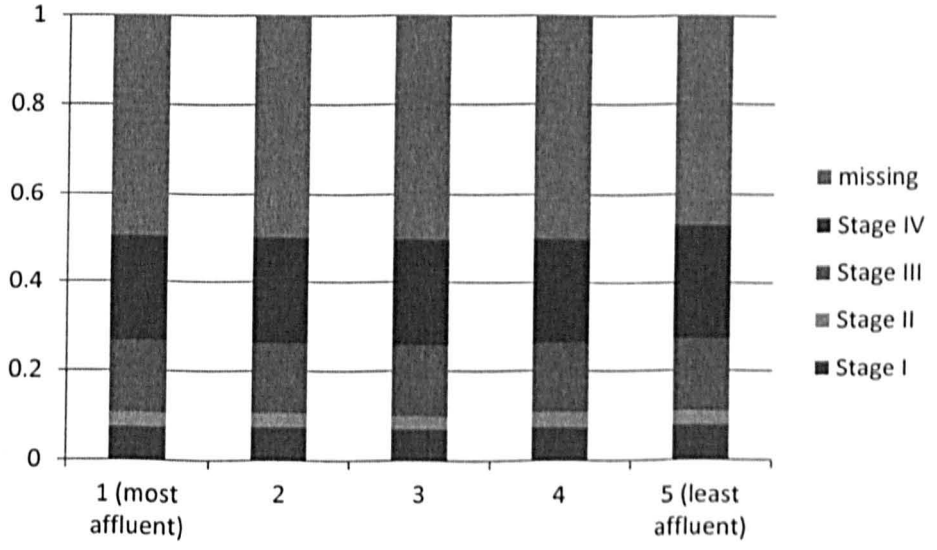



Figure 5.7: Distribution of stage across each Townsend quintile.

There was very little variation in the data on stage at diagnosis of these patients based on their socio-economic status. Data within the National Lung Cancer Audit have been analysed previously (chapter 4), to assess the influence of socioeconomic status on access to treatment, and the results are depicted in tables 4.5, 4.6 and 4.7. Socioeconomic status had no influence on the likelihood

of receiving surgery in patients with non-small cell lung cancer, nor radiotherapy for the cohort overall, but there was evidence that those patients in the least affluent stratum were less likely to receive chemotherapy compared with those patients in the most affluent stratum.

### 5.3.2 Patient features within Hospital Episode Statistics (HES)

Charlson Index

For the cohort of 80,966 patients, there were >1.5 million episodes over the 11 years of in-patient data supplied. The median Charlson Index at diagnosis for this cohort was 1, with an interquartile range of 0 to 4. This reflects the fact that whilst 39,537 (45%) patients had been in-patients prior to their diagnosis of lung cancer being made, the diagnostic ICD-10 codes assigned were not pertinent for the Charlson Index composite co-morbidity score. Hence they had a Charlson Index at diagnosis of zero. Figure 5.8 shows the distribution of Charlson Indices at diagnosis. Note that 979 patients had a Charlson Index at diagnosis of greater than or equal to 10 (n=576); the number of patients with a Charlson Index at diagnosis of 11 was 222, of 12 was 112, of 13 was 38, of 14 was 18, of 15 was 9, of 16 was 3 and one patient had a Charlson Index at diagnosis of 17. The maximum score possible is 34.

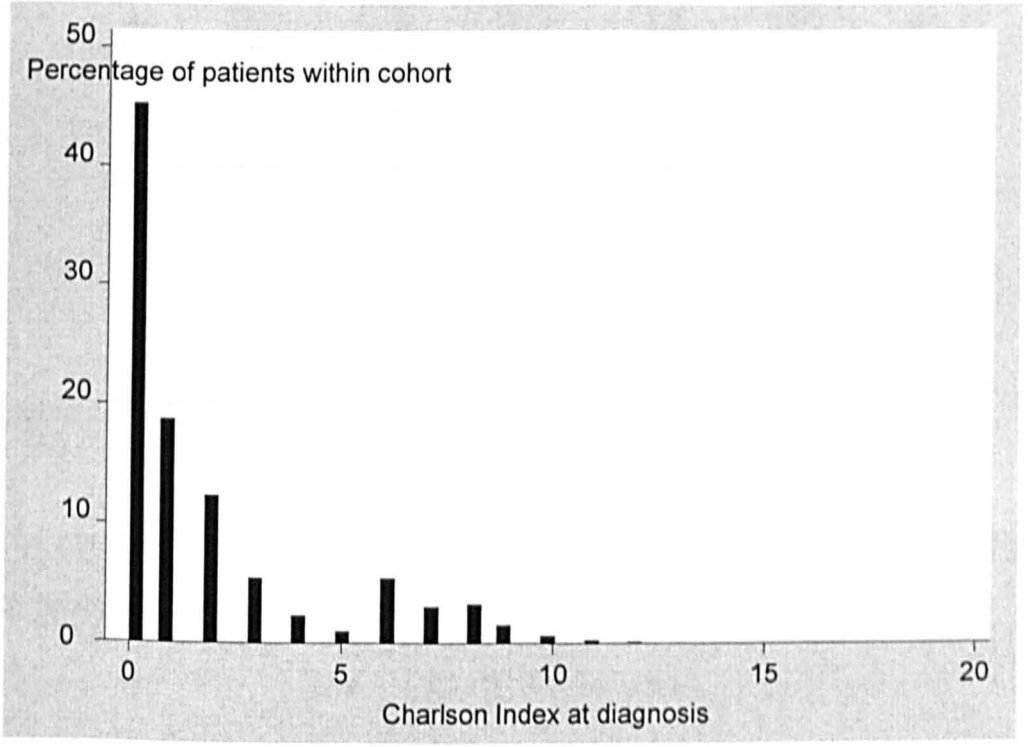



Figure 5.8: Histogram showing the distribution of Charlson Indices at diagnosis.

The Charlson Index was divided into quintiles to allow regression analyses of this continuous variable, but in view of the large number of patients with a Charlson Index at diagnosis of zero, this group actually comprised two quintiles. The division of the cohort on the basis of co-morbidity is shown in the Table 5.5 below.

Table 5.5: Division of cohort into Charlson Index quintiles

| Charlson quintile | N (%) | Charlson Index at diagnosis |
|---|---|---|
| 1 (+2) | 34,711 (43) | 0 |
| 3 | 15,915 (20) | 1 |
| 4 | 15,085 (19) | 2 or 3 |
| 5 | 15,255 (19) | 4+ |

Figure 5.9 illustrates that in this cohort of patients with lung cancer there was no evidence that the level of co-morbidity increased as affluence declined.

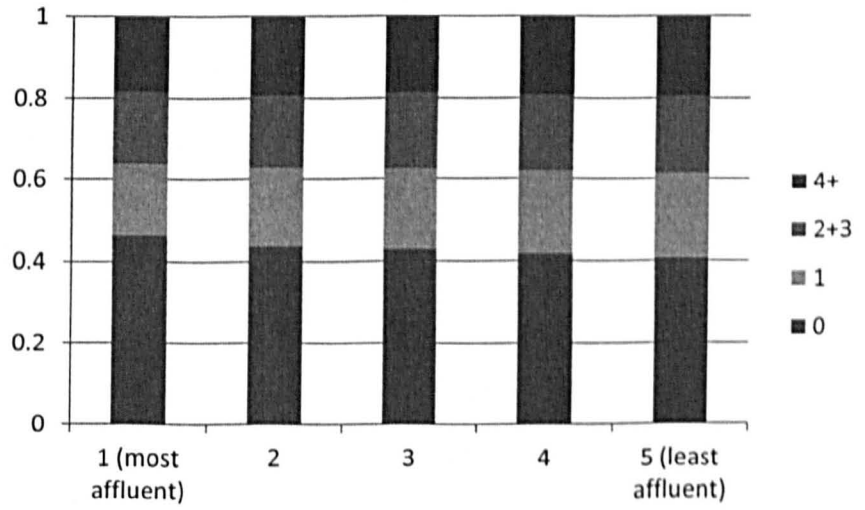



Figure 5.9: Distribution of Charlson Indices across Townsend quintiles.

The results of logistic regression analyses assessing the influence of the Charlson Index on access to treatment are illustrated in table 5.6.

Table 5.6: Logistic regression for Charlson Index and access to treatment

| | N | N* | %** | Unadj OR (95% CI) | Adj OR*** (95% CI) | p for trend |
|---|---|---|---|---|---|---|
| **Surgery (NSCLC only: N=34,315)** | | | | | | |
| **Charlson Index** | | | | | | |
| 0 | 15573 | 2341 | 15 | | | <0.001 |
| 1 | 6951 | 985 | 14 | 0.93 (0.86, 1.01) | 0.95 (0.86, 1.04) | |
| 2 or 3 | 5828 | 752 | 13 | 0.84 (0.77, 0.91) | 0.89 (0.80, 0.99) | |
| 4+ | 6161 | 407 | 7 | 0.40 (0.36, 0.45) | 0.69 (0.60, 0.78) | |
| **Radiotherapy (N=80,966)** | | | | | | |
| **Charlson Index** | | | | | | |
| 0 | 34711 | 7668 | 22 | | | 0.748 |
| 1 | 15915 | 3376 | 21 | 0.95 (0.91, 0.99) | 0.97 (0.92, 1.01) | |
| 2 or 3 | 15085 | 3242 | 21 | 0.97 (0.92, 1.01) | 1.00 (0.95, 1.04) | |
| 4+ | 15255 | 3143 | 21 | 0.92 (0.87, 0.96) | 1.00 (0.95, 1.05) | |
| **Chemotherapy (small cell only; N=7845)** | | | | | | |
| **Charlson Index** | | | | | | |
| 0 | 3482 | 2441 | 70 | | | <0.001 |
| 1 | 1492 | 904 | 61 | 0.66 (0.58, 0.74) | 0.79 (0.69, 0.91) | |
| 2 or 3 | 1090 | 625 | 57 | 0.57 (0.50, 0.66) | 0.77 (0.66, 0.90) | |
| 4+ | 1781 | 850 | 48 | 0.39 (0.35, 0.44) | 0.50 (0.44, 0.57) | |

Legend: N* Number of patients within each subgroup who have had treatment.
%** percentage of patients within each subgroup who have had treatment.
Adj OR***; adjusted Odds Ratio, mutually adjusted for sex, age quintile, histology (radiotherapy only), stage, performance status, ethnic group and socio-economic status.
NSCLC; non-small cell lung cancer

Table 5.6 shows that the Charlson Index has a strong influence on the likelihood of receiving surgery and chemotherapy. If the composite co-morbidity score is 4 or more, then the patient is 31% less likely to receive surgery and 50% less likely to receive chemotherapy compared with patients with a Charlson Index of zero. There did not appear to be any evidence that increasing co-morbidity was associated with a reduced likelihood of receiving radiotherapy. This is a treatment used in both radical (potentially curative) and palliative settings, and this may be why individuals with increasing co-morbidity do not appear to be at a disadvantage in accessing radiotherapy.

Table 5.7: Results of Cox regression illustrating the influence of the Charlson Index on overall mortality (N=80,264)

| | N | N died | %* | Unadj HR (95% CI) | Adj HR** (95% CI) | p for trend |
|---|---|---|---|---|---|---|
| **Charlson Index** | | | | | | |
| 0 | 34,556 | 27,125 | 78 | | | <0.001 |
| 1 | 15,806 | 12,655 | 80 | 1.15 (1.13, 1.18) | 1.08 (1.06, 1.11) | |
| 2 or 3 | 14,937 | 12,393 | 83 | 1.26 (1.23, 1.28) | 1.14 (1.12, 1.17) | |
| 4+ | 14,965 | 14,218 | 95 | 2.19 (2.14, 2.23) | 1.76 (1.72, 1.80) | |

Legend: %* percentage of patients within each subgroup who have died.
Adj HR**; adjusted Hazard Ratio, mutually adjusted for sex, age quintile, histology, stage, performance status, ethnic group and socio-economic status.

Table 5.7 demonstrates that as the Charlson Index rises, so the patient is more likely to die. The adjusted Hazard Ratio for individuals with a Charlson Index of 4 or more was 1.76 (95% CI 1.72, 1.80), suggesting that these individuals are almost 80% more likely to die than those with a Charlson Index of zero. Even patients with a single co-morbid illness, scoring one point, had a statistically significant increased likelihood of death compared with those patients with a Charlson Index of zero.

Individual diseases

The frequency of each component disease of the Charlson Index within this cohort of lung cancer patients is illustrated in table 5.8 below.

Table 5.8: Number of patients within each disease group.

| Component disease group | Number | % cohort |
|---|---|---|
| Myocardial infarction/heart failure | 8,552 | 11 |
| Cerebrovascular disease | 4,628 | 6 |
| Chronic pulmonary disease | 18,087 | 22 |
| Dementia | 839 | 1 |
| Peptic ulcer disease | 2,745 | 3 |
| Diabetes (without complications) | 7,497 | 9 |
| Peripheral vascular disease | 7,020 | 9 |
| Connective tissue disease | 1,558 | 2 |
| Cancer (solid organ) | 11,588 | 14 |
| Haematological malignancy | 631 | 1 |
| Diabetes with complications | 642 | 1 |
| Hemiplegia/paraplegia | 1,002 | 1 |
| Renal disease | 1,972 | 2 |
| Severe liver failure | 112 | 1 |
| Metastases | 11,762 | 14 |
| AIDS | 31 | 0.04 |

The commonest co-morbidity is respiratory disease (22% of cohort) which includes primarily chronic obstructive pulmonary disease (COPD), and interstitial lung fibrosis. Given the link between smoking and lung cancer, and smoking with both ischaemic heart disease and other malignancies, it is expected that a significant proportion of this cohort of patients with lung cancer will have both these co-morbidities. It is also worth noting that 14% of this cohort of patients with lung cancer had metastatic disease at diagnosis as per Hospital Episode

Statistics which is not dissimilar to the percentage of patients recorded as having Stage IV disease in the National Lung Cancer Audit (24%).

Treatment received and survival

The results of logistic regression analyses regarding surgery and chemotherapy if the patient had known non-small cell, and small cell lung cancer respectively, are illustrated in Tables 5.9 and 5.10. Table 5.9 shows that individuals with certain conditions were less likely to have surgery than those without. Dementia was a strong negative predictor, with an adjusted Odds ratio of 0.26 (95% CI 0.08, 0.88) compared with those without the illness. A total of 4 patients out of a total of 150 with non-small cell lung cancer and dementia had surgery. The presence of cardiac and renal disease also played a strong negative predictive role. Individuals with cardiac disease were 21% less likely to have surgery compared with those without (adjusted Odds ratio 0.79, 95% CI 0.96, 0.91). Individuals with renal disease were 31% less likely to have surgery than those without this disease (adjusted Odds ration 0.69, 95% CI 0.50, 0.96). Cardiac and renal impairment would be important from an anaesthetic perspective, as well as recovery in the post-operative period. Diabetes with complications also had a negative influence on the likelihood of having surgery. Individuals with this condition were almost half as likely to have surgery as those without this disease (adjusted Odds ratio 0.51, 95% CI 0.30, 0.87).

Table 5.10 shows the results of logistic regression on access to chemotherapy for those patients with proven small cell lung cancer. It shows that several diseases had a negative influence including: chronic respiratory disease (adjusted Odds Ratio 0.84, 95% CI 0.75, 0.95), cerebrovascular disease (adjusted Odds Ratio 0.77, 95% CI 0.61, 0.97), peptic ulcer disease (adjusted Odds Ratio 0.65, 95% CI 0.50, 0.84) and renal failure (adjusted Odds Ratio 0.60, 95% CI 0.42, 0.88).

Table 5.9: Logistic regression for surgery in patients with NSCLC (N=34,513).

| Disease group | N | N* | %** | Unadj OR (95% CI) | Adj OR*** (95% CI) | P |
|---|---|---|---|---|---|---|
| **Cardiac** | | | | | | |
| No | 31223 | 4173 | 13 | | | |
| Yes | 3290 | 312 | 9 | 0.68 (0.6, 0.77) | 0.79 (0.68, 0.91) | <0.01 |
| **Stroke** | | | | | | |
| No | 32843 | 4311 | 13 | | | |
| Yes | 1670 | 174 | 10 | 0.74 (0.63, 0.88) | 0.85 (0.70, 1.03) | 0.10 |
| **Peripheral vascular disease** | | | | | | |
| No | 31547 | 4161 | 13 | | | |
| Yes | 2966 | 324 | 11 | 0.82 (0.73, 0.93) | 0.88 (0.77, 1.02) | 0.09 |
| **Dementia** | | | | | | |
| No | 34363 | 4481 | 13 | | | |
| Yes | 150 | 4 | 3 | 0.14 (0.04, 0.44) | 0.26 (0.08, 0.88) | 0.03 |
| **Respiratory** | | | | | | |
| No | 27178 | 3623 | 13 | | | |
| Yes | 7335 | 862 | 12 | 0.88 (0.81, 0.95) | 0.83 (0.76, 0.92) | <0.01 |
| **Connective tissue diseases** | | | | | | |
| No | 33832 | 4371 | 13 | | | |
| Yes | 681 | 114 | 17 | 1.34 (1.08, 1.65) | 1.11 (0.87, 1.43) | 0.40 |
| **Ulcer** | | | | | | |
| No | 33409 | 4335 | 13 | | | |
| Yes | 1104 | 150 | 14 | 1.06 (0.89, 1.27) | 1.06 (0.86, 1.31) | 0.58 |
| **Diabetes** | | | | | | |
| No | 31403 | 4131 | 13 | | | |
| Yes | 3110 | 354 | 11 | 0.83 (0.74, 0.94) | 0.90 (0.78, 1.03) | 0.12 |
| **Hemiplegia** | | | | | | |
| **No** | 34163 | 4459 | 13 | | | |
| Yes | 350 | 26 | 7 | 0.55 (0.37, 0.83) | 0.64 (0.40, 1.02) | 0.06 |
| **Diabetes with complications** | | | | | | |
| No | 34251 | 4465 | 13 | | | |
| Yes | 262 | 20 | 8 | 0.54 (0.34, 0.87) | 0.51 (0.30, 0.87) | 0.01 |
| **Renal failure** | | | | | | |
| No | 33817 | 4425 | 13 | | | |
| Yes | 696 | 60 | 9 | 0.63 (0.48, 0.82) | 0.69 (0.50, 0.96) | 0.03 |
| **Haematological malignancy** | | | | | | |
| No | 34210 | 4445 | 13 | | | |
| Yes | 303 | 40 | 13 | 1.05 (0.75, 1.47) | 1.03 (0.69, 1.52) | 0.90 |
| **Cancer (not lung)** | | | | | | |
| No | 30053 | 3963 | 13 | | | |
| Yes | 4460 | 522 | 12 | 0.88 (0.79, 0.97) | 1.01 (0.90, 1.13) | 0.93 |
| **Severe liver failure** | | | | | | |
| No | 34472 | 4480 | 13 | | | |
| Yes | 41 | 5 | 12 | 1.18 (0.49, 2.81) | 0.82 (0.29, 2.33) | 0.71 |
| **Metastases** | | | | | | |
| No | 29633 | 4201 | 14 | | | |
| Yes | 4880 | 284 | 6 | 0.38 (0.33, 0.43) | 0.73 (0.63, 0.84) | <0.01 |
| **AIDS** | | | | | | |
| No | 34494 | 4481 | 13 | | | |
| Yes | 19 | 4 | 21 | 1.48 (0.5, 4.39) | 1.08 (0.21, 5.46) | 0.92 |

Legend: N* number of patients within each disease group who had surgery.
%** percentage of patients within each disease group who had surgery.
Adj OR*** adjusted Odds Ratio adjusted for sex, age quintile, stage, performance status, Townsend quintile and ethnic group.

Table 5.10; Logistic regression for chemotherapy in patients with small cell lung cancer (N=7845).

| Disease group | N | N* | %** | Unadj OR (95% CI) | Adj OR*** (95% CI) | P |
|---|---|---|---|---|---|---|
| **Cardiac** | | | | | | |
| No | 7127 | 4437 | 62 | | | |
| Yes | 718 | 388 | 53 | 0.71 (0.61, 0.82) | 0.97 (0.82, 1.15) | 0.74 |
| **Stroke** | | | | | | |
| No | 7472 | 4644 | 62 | | | |
| Yes | 373 | 176 | 47 | 0.55 (0.45, 0.68) | 0.77 (0.61, 0.97) | 0.03 |
| **Peripheral vascular disease** | | | | | | |
| No | 7229 | 4498 | 62 | | | |
| Yes | 616 | 322 | 52 | 0.68 (0.58, 0.8) | 0.86 (0.71, 1.03) | 0.10 |
| **Dementia** | | | | | | |
| No | 7816 | 4813 | 62 | | | |
| Yes | 29 | 7 | 24 | 0.2 (0.9, 0.48) | 0.47 (0.18, 1.23) | 0.13 |
| **Respiratory** | | | | | | |
| No | 6225 | 3941 | 63 | | | |
| Yes | 1620 | 879 | 54 | 0.71 (0.63, 0.79) | 0.84 (0.75, 0.95) | 0.01 |
| **Connective Tissue Disease** | | | | | | |
| No | 7722 | 4756 | 62 | | | |
| Yes | 123 | 64 | 52 | 0.7 (0.49, 1.00) | 0.69 (0.47, 1.02) | 0.06 |
| **Peptic Ulcer disease** | | | | | | |
| No | 7567 | 4680 | 62 | | | |
| Yes | 278 | 140 | 50 | 0.63 (0.49, 0.80) | 0.65 (0.50, 0.84) | <0.01 |
| **Diabetes** | | | | | | |
| No | 7131 | 4442 | 62 | | | |
| Yes | 714 | 378 | 53 | 0.7 (0.60, 0.81) | 0.82 (0.70, 0.98) | 0.03 |
| **Hemiplegia** | | | | | | |
| No | 7772 | 4788 | 62 | | | |
| Yes | 73 | 32 | 44 | 0.51 (0.32, 0.81) | 0.76 (0.45, 1.28) | 0.31 |
| **Diabetes with complications** | | | | | | |
| No | 7789 | 4795 | 62 | | | |
| Yes | 56 | 25 | 45 | 0.52 (0.30, 0.88) | 0.61 (0.34, 1.09) | 0.10 |
| **Renal failure** | | | | | | |
| No | 7708 | 4768 | 62 | | | |
| Yes | 137 | 52 | 38 | 0.38 (0.27, 0.54) | 0.60 (0.42, 0.88) | 0.01 |
| **Haematological malignancy** | | | | | | |
| No | 7787 | 4787 | 61 | | | |
| Yes | 58 | 33 | 57 | 0.85 (0.50, 1.42) | 0.98 (0.56, 1.71) | 0.93 |
| **Cancer (not lung)** | | | | | | |
| No | 7020 | 4370 | 62 | | | |
| Yes | 825 | 450 | 55 | 0.74 (0.64, 0.85) | 0.85 (0.72, 1.00) | 0.05 |
| **Severe liver failure** | | | | | | |
| No | 7835 | 4815 | 61 | | | |
| Yes | 10 | 5 | 50 | 0.64 (0.19, 2.22) | 0.57 (0.15, 2.17) | 0.41 |
| **Metastases** | | | | | | |
| No | 6283 | 4060 | 65 | | | |
| Yes | 1562 | 760 | 49 | 0.53 (0.48, 0.59) | 0.58 (0.51, 0.66) | <0.01 |
| **AIDS** | | | | | | |
| No | 7842 | 4820 | 61 | | | |
| Yes | 3 | 0 | 0 | **** | | |

Legend: N* number of patients within each disease group who had chemotherapy.
%** percentage of patients within each disease group who had chemotherapy.
Adj OR*** adjusted Odds Ratio adjusted for sex, age quintile, stage (limited or extensive), performance status, Townsend quintile and ethnic group.
**** Unable to calculate Odds Ratio as number of patients with AIDS too small.

Table 5.11 shows the results of Cox regression analyses for the individual disease groups. These results demonstrate that for every disease the socio-economic status and ethnicity of a patient had little effect on the Hazard Ratio. Instead it was the adjustment for sex, age quintile, histology, stage and performance status which had the greatest effect on the Hazard Ratio. The adjusted Hazard Ratio for the majority of diseases was approximately 1.20, indicating that should an individual with lung cancer also have this disease they are 20% more likely to die compared with those patients with lung cancer who do not have this disease. These diseases include: cardiac disease, stroke, peripheral vascular disease, respiratory disease, gastric ulcers, and hemiplegia. Certain diseases had an adjusted Hazard Ratio of less than 1.20, and these were: connective tissue disease, diabetes with and without complications, and haematological malignancy. Individuals with metastatic disease at diagnosis were at the greatest risk of death, with an adjusted Hazard Ratio of 2.10. Very few patients had AIDS but those that did had an increased likelihood of death (adjusted HR 1.87, 95% CI 1.34, 2.62). Severe liver failure and renal failure also led to an increased likelihood of death (adjusted HR 1.59, 95% CI 1.30, 1.94 and adjusted HR 1.36, 95% CI 1.29, 1.42 respectively). Therefore, with the exception of metastatic disease, which is incorporated into the stage of disease at diagnosis, no single component disease within the Charlson Index was the predominant influence on overall survival.

Table 5.11: Cox regression evaluating the influence of individual disease groups within the Charlson Index on overall survival (N=80,264).

| Individual disease groups | N | N* | %** | HR (95% CI) | | |
|---|---|---|---|---|---|---|
| **Cardiac disease** | 8552 | 7349 | 86 | | | |
| Unadjusted | | | | 1.41 | 1.38 | 1.45 |
| Adjusted for age and sex | | | | 1.31 | 1.28 | 1.34 |
| Adj for age, sex, histo, stage, PS | | | | 1.24 | 1.21 | 1.27 |
| Adjusted for SES and ethnic | | | | 1.41 | 1.38 | 1.45 |
| Fully adjusted for all the above | | | | 1.24 | 1.21 | 1.27 |
| | | | | | | |
| **Stroke** | 4628 | 4010 | 87 | | | |
| Unadjusted | | | | 1.48 | 1.43 | 1.53 |
| Adjusted for age and sex | | | | 1.37 | 1.33 | 1.42 |
| Adj for age, sex, histo, stage, PS | | | | 1.22 | 1.18 | 1.26 |
| Adjusted for SES and ethnic | | | | 1.48 | 1.43 | 1.53 |
| Fully adjusted for all the above | | | | 1.21 | 1.17 | 1.25 |
| | | | | | | |
| **Peripheral Vascular disease** | 7020 | 5917 | 84 | | | |
| Unadjusted | | | | 1.33 | 1.30 | 1.37 |
| Adjusted for age and sex | | | | 1.27 | 1.24 | 1.30 |
| Adj for age, sex, histo, stage, PS | | | | 1.21 | 1.18 | 1.25 |
| Adjusted for SES and ethnic | | | | 1.33 | 1.30 | 1.37 |
| Fully adjusted for all the above | | | | 1.21 | 1.18 | 1.25 |
| | | | | | | |
| **Dementia** | 839 | 785 | 94 | | | |
| Unadjusted | | | | 2.12 | 1.98 | 2.28 |
| Adjusted for age and sex | | | | 1.78 | 1.65 | 1.91 |
| Adj for age, sex, histo, stage, PS | | | | 1.38 | 1.28 | 1.48 |
| Adjusted for SES and ethnic | | | | 2.12 | 1.97 | 2.27 |
| Fully adjusted for all the above | | | | 1.38 | 1.28 | 1.48 |
| | | | | | | |
| **Respiratory disease** | 18,087 | 15,068 | 83 | | | |
| Unadjusted | | | | 1.31 | 1.28 | 1.33 |
| Adjusted for age and sex | | | | 1.28 | 1.26 | 1.30 |
| Adj for age, sex, histo, stage, PS | | | | 1.23 | 1.21 | 1.25 |
| Adjusted for SES and ethnic | | | | 1.31 | 1.28 | 1.33 |
| Fully adjusted for all the above | | | | 1.23 | 1.21 | 1.26 |

Legend: N* Number of patients with each individual disease who have died
%** percentage of individuals with each disease who have died.

Table 5.11: continued

| Individual disease groups | N | N* | %** | HR | 95% CI | |
|---|---|---|---|---|---|---|
| **Connective Tissue Disorders** | 1558 | 1269 | 81 | | | |
| Unadjusted | | | | 1.16 | 1.25 | 1.35 |
| Adjusted for age and sex | | | | 1.18 | 1.11 | 1.24 |
| Adj for age, sex, histo, stage, PS | | | | 1.17 | 1.11 | 1.24 |
| Adjusted for SES and ethnic | | | | 1.15 | 1.09 | 1.22 |
| Fully adjusted for all the above | | | | 1.17 | 1.11 | 1.24 |
| | | | | | | |
| **Ulcer disease** | 2745 | 2297 | 84 | | | |
| Unadjusted | | | | 1.30 | 1.25 | 1.35 |
| Adjusted for age and sex | | | | 1.25 | 1.20 | 1.30 |
| Adj for age, sex, histo, stage, PS | | | | 1.22 | 1.17 | 1.27 |
| Adjusted for SES and ethnic | | | | 1.30 | 1.25 | 1.35 |
| Fully adjusted for all the above | | | | 1.22 | 1.17 | 1.27 |
| | | | | | | |
| **Diabetes (no complications)** | 7497 | 6295 | 84 | | | |
| Unadjusted | | | | 1.31 | 1.27 | 1.34 |
| Adjusted for age and sex | | | | 1.26 | 1.22 | 1.29 |
| Adj for age, sex, histo, stage, PS | | | | 1.17 | 1.14 | 1.20 |
| Adjusted for SES and ethnic | | | | 1.31 | 1.27 | 1.34 |
| Fully adjusted for all the above | | | | 1.18 | 1.15 | 1.21 |
| | | | | | | |
| **Hemiplegia** | 1002 | 899 | 89 | | | |
| Unadjusted | | | | 1.57 | 1.47 | 1.67 |
| Adjusted for age and sex | | | | 1.50 | 1.41 | 1.60 |
| Adj for age, sex, histo, stage, PS | | | | 1.19 | 1.12 | 1.27 |
| Adjusted for SES and ethnic | | | | 1.57 | 1.47 | 1.68 |
| Fully adjusted for all the above | | | | 1.19 | 1.12 | 1.27 |
| | | | | | | |
| **Diabetes with complications** | 642 | 555 | 86 | | | |
| Unadjusted | | | | 1.36 | 1.25 | 1.48 |
| Adjusted for age and sex | | | | 1.29 | 1.19 | 1.41 |
| Adj for age, sex, histo, stage, PS | | | | 1.16 | 1.07 | 1.26 |
| Adjusted for SES and ethnic | | | | 1.36 | 1.25 | 1.48 |
| Fully adjusted for all the above | | | | 1.16 | 1.07 | 1.26 |

Legend: N* Number of patients with each individual disease who have died
%** percentage of individuals with each disease who have died.

Table 5.11: continued

| Individual disease groups | N | N* | %** | HR | 95% CI | |
|---|---|---|---|---|---|---|
| **Renal failure** | 1972 | 1762 | 89 | | | |
| Unadjusted | | | | 1.61 | 1.54 | 1.69 |
| Adjusted for age and sex | | | | 1.41 | 1.38 | 1.51 |
| Adj for age, sex, histo, stage, PS | | | | 1.36 | 1.30 | 1.43 |
| Adjusted for SES and ethnic | | | | 1.61 | 1.54 | 1.69 |
| Fully adjusted for all the above | | | | 1.36 | 1.29 | 1.42 |
| **Haematological malignancy** | 631 | 514 | 81 | | | |
| Unadjusted | | | | 1.13 | 1.04 | 1.23 |
| Adjusted for age and sex | | | | 1.12 | 1.03 | 1.23 |
| Adj for age, sex, histo, stage, PS | | | | 1.16 | 1.06 | 1.26 |
| Adjusted for SES and ethnic | | | | 1.13 | 1.04 | 1.23 |
| Fully adjusted for all the above | | | | 1.15 | 1.05 | 1.25 |
| **Cancer (non Lung)** | 11588 | 9864 | 85 | | | |
| Unadjusted | | | | 1.31 | 1.28 | 1.34 |
| Adjusted for age and sex | | | | 1.27 | 1.25 | 1.30 |
| Adj for age, sex, histo, stage, PS | | | | 1.28 | 1.25 | 1.31 |
| Adjusted for SES and ethnic | | | | 1.31 | 1.28 | 1.34 |
| Fully adjusted for all the above | | | | 1.28 | 1.25 | 1.31 |
| **Severe Liver failure** | 112 | 96 | 86 | | | |
| Unadjusted | | | | 1.49 | 1.22 | 1.83 |
| Adjusted for age and sex | | | | 1.59 | 1.30 | 1.94 |
| Adj for age, sex, histo, stage, PS | | | | 1.59 | 1.30 | 1.95 |
| Adjusted for SES and ethnic | | | | 1.48 | 1.21 | 1.81 |
| Fully adjusted for all the above | | | | 1.59 | 1.30 | 1.94 |
| **Metastases** | 11762 | 11207 | 95 | | | |
| Unadjusted | | | | 2.45 | 2.40 | 2.50 |
| Adjusted for age and sex | | | | 2.58 | 2.53 | 2.64 |
| Adj for age, sex, histo, stage, PS | | | | 2.10 | 2.06 | 2.14 |
| Adjusted for SES and ethnic | | | | 2.45 | 2.40 | 2.50 |
| Fully adjusted for all the above | | | | 2.10 | 2.06 | 2.15 |
| **AIDS** | 31 | 27 | 87 | | | |
| Unadjusted | | | | 1.81 | 1.29 | 2.53 |
| Adjusted for age and sex | | | | 2.15 | 1.54 | 3.01 |
| Adj for age, sex, histo, stage, PS | | | | 1.84 | 1.32 | 2.58 |
| Adjusted for SES and ethnic | | | | 1.81 | 1.29 | 2.53 |
| Fully adjusted for all the above | | | | 1.87 | 1.34 | 2.62 |

Legend: N* Number of patients with each individual disease who have died
%** percentage of individuals with each disease who have died.

Bed days

The majority of patients within this cohort, 66,952 (83%), were not admitted to hospital within the 12 month period leading up to their diagnosis of lung cancer. A small group (914, 1%) were admitted for more than 30 days. A categorical variable for admission time was created and is illustrated in table 5.12.

Table 5.12: Admission time

| Admission time | Number | (%) |
|---|---|---|
| Zero | 66,952 | (83) |
| 1-5 days | 7,910 | (10) |
| 6-10 days | 2,521 | (3) |
| 11-30 days | 2,699 | (3) |
| >30 days | 914 | (1) |

In order to assess the influence of 'admission time' pre-diagnosis on the likelihood of receiving treatment, logistic regression (uni and multivariate) was used. Only patients with histologically proven non-small cell lung cancer were used for analysis of access to surgery, and only those with small cell lung cancer were used for analysis of access to chemotherapy. The whole cohort was used to assess the likelihood of receiving radiotherapy based on admission time pre-diagnosis. The results are illustrated in table 5.13. There is evidence that those patients with a prolonged admission time (more than 30 days) were 26% less likely to receive radiotherapy than those without an admission, even after adjusting for all other patient features. Although there appeared to be a similar trend in the access to chemotherapy for those patients with small cell lung cancer, it did not achieve statistical significance. There was no evidence that admission time pre-diagnosis influenced the likelihood of having surgery for those patients with non-small cell lung cancer.

Table 5.13: Results of multivariate logistic regression illustrating the influence of time in hospital pre-diagnosis with lung cancer on access to treatment.

| **Time** (days) | **N** | **N Rx** | **(%)*** | **Unadj OR (95% CI)** | **Adj OR** (95% CI)** | **P for trend** |
|---|---|---|---|---|---|---|
| **Surgery (NSCLC only; N=34,315)** | | | | | | |
| Zero | 29,178 | 3705 | 13 | | | 0.162 |
| 1-5 | 3,198 | 490 | 15 | 1.24 (1.12, 1.38) | 1.17 (1.03, 1.32) | |
| 6-10 | 964 | 153 | 16 | 1.30 (1.08, 1.55) | 1.20 (0.97, 1.49) | |
| 11-30 | 898 | 102 | 11 | 0.88 (0.71, 1.09) | 0.99 (0.77, 1.26) | |
| >30 | 275 | 35 | 13 | 1.00 (0.70, 1.43) | 0.94 (0.61, 1.45) | |
| **Radiotherapy (N=80,966)** | | | | | | |
| Zero | 66,952 | 14684 | 22 | | | <0.001 |
| 1-5 | 7,910 | 1645 | 21 | 0.93 (0.88, 0.99) | 0.97 (0.91, 1.02) | |
| 6-10 | 2,521 | 500 | 20 | 0.88 (0.80, 0.97) | 0.94 (0.85, 1.04) | |
| 11-30 | 2,669 | 468 | 18 | 0.76 (0.68, 0.84) | 0.83 (0.75, 0.92) | |
| >30 | 914 | 132 | 14 | 0.6 (0.50, 0.72) | 0.74 (0.61, 0.90) | |
| **Chemotherapy (small cell only; N=7,845)** | | | | | | |
| Zero | 6,691 | 4170 | 62 | | | 0.138 |
| 1-5 | 689 | 405 | 59 | 0.86 (0.73, 1.01) | 1.02 (0.86, 1.22) | |
| 6-10 | 208 | 116 | 56 | 0.76 (0.58, 1.01) | 0.97 (0.72, 1.32) | |
| 11-30 | 203 | 110 | 54 | 0.72 (0.54, 0.95) | 0.91 (0.67, 1.23) | |
| >30 | 54 | 19 | 35 | 0.33 (0.19, 0.57) | 0.45 (0.24, 0.85) | |

Legend: Rx; treatment
(%)* percentage of patients who received treatment from each subgroup of admission time.
Adj OR** adjusted Odds Ratio for sex, age quintile, performance status, histology (radiotherapy only), stage (limited or extensive in chemotherapy), Townsend quintile and ethnic group.
NSCLC; non-small cell lung cancer.

If an individual has been in hospital for a total of less than a month in the year prior to diagnosis with lung cancer, there appears to be very little effect on the likelihood of receiving treatment for their cancer.

Cox regression analyses showed that time spent in hospital prior to the diagnosis of lung cancer had no impact on overall survival once the diagnosis had been made (Table 5.14). This is almost certainly related to the poor prognosis from the condition, with a median survival of just 203 days.

Table 5.14: Cox regression evaluating the influence of admission time pre-diagnosis on overall survival (N=80,264).

| | N | N died | %* | Unadj HR (95% CI) | Adj HR** (95% CI) | p for trend |
|---|---|---|---|---|---|---|
| **Bed days' (days)** | | | | | | |
| zero | 66474 | 54309 | 82 | | | 0.738 |
| 1-5 | 7817 | 6348 | 81 | 1.01 (0.98, 1.03) | 0.97 (0.95, 1.00) | |
| 6-10 | 2474 | 2023 | 82 | 1.02 (0.97, 1.06) | 0.96 (0.92, 1.01) | |
| 11-30 | 2611 | 2229 | 85 | 1.17 (1.12, 1.22) | 1.05 (1.01, 1.09) | |
| >30 | 888 | 780 | 88 | 1.28 (1.19, 1.37) | 1.01 (0.94, 1.09) | |

Legend: %* percentage of patients within each subgroup who have died.
Adj HR**; adjusted Hazard Ratio, mutually adjusted for sex, age quintile, histology, stage, performance status, ethnic group and socio-economic status.

Ethnicity

Data on ethnicity revealed the vast majority of patients were White, with Asians comprising the second largest group with 4,627 patients (6%). Within this ethnic subgroup Pakistani patients were the most common representing 87%. Ethnicity data were missing in 18% of the cohort. Figure 5.10 illustrates the distribution of ethnic groups.

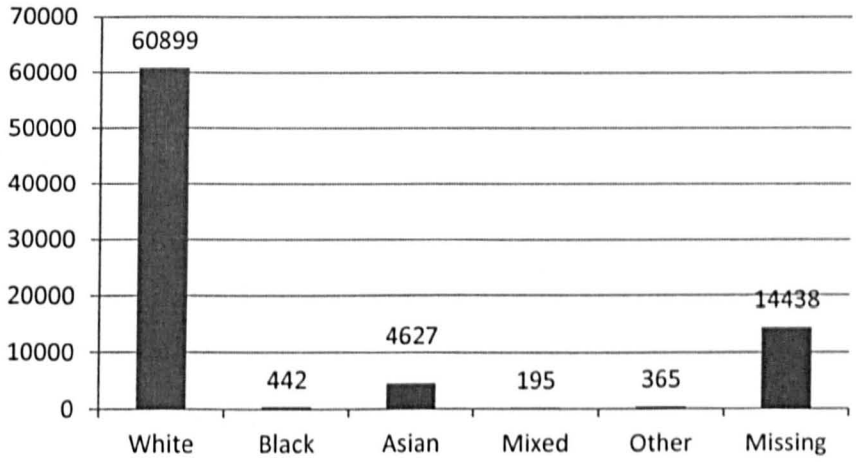



Figure 5.10: Histogram illustrating the ethnic composition of this cohort.

Table 5.15: Illustrates the detailed breakdown of ethnic group amongst this cohort of English lung cancer patients.

| Ethnic group | N | % |
|---|---|---|
| White | 57,986 | 72 |
| Irish/white | 786 | 1 |
| Other white | 2,127 | 3 |
| African | 87 | 0.1 |
| Caribbean | 272 | 0.3 |
| Other Black | 83 | 0.1 |
| Pakistani | 4,051 | 5 |
| Indian | 317 | 0.4 |
| Bangledeshi | 102 | 0.1 |
| Chinese | 73 | 0.1 |
| Other Asian | 84 | 0.1 |
| White/Black Caribbean | 50 | 0.1 |
| White/Black African | 48 | 0.1 |
| White/Asian | 41 | 0.1 |
| Other mixed race | 56 | 0.1 |
| Other Ethnicity | 365 | 0.5 |
| Not stated | 14,438 | 18 |
| **Total** | **80,966** | |

### 5.3.3 NHS Trust features

There were 31 cardiothoracic surgical centres, and 49 Radiotherapy centres at the time of this research. There were 44 NHS Trusts who fulfilled the criteria for high trial centre status.

Peer Review results

The process of Peer review incorporates an element of self evaluation and independent external assessment of every cancer multidisciplinary team. There are 32 standards to which each MDT is measured (appendix 6). For each target an NHS Trust will score 0 or 1, however if there is more than one lung cancer multidisciplinary team within an NHS Trust, it is possible for a Trust to score between 0 and 1. In other words, if an NHS Trust has three lung cancer MDTs then it could score either: 0, 0.33, 0.67 or 1 for each target. Every NHS Trust will have a total score between 0 and 1 for their overall attainment of Peer Review targets. Figure 5.11 illustrates the variation in success at Peer Review across all NHS Trusts for the period 2003-2007.

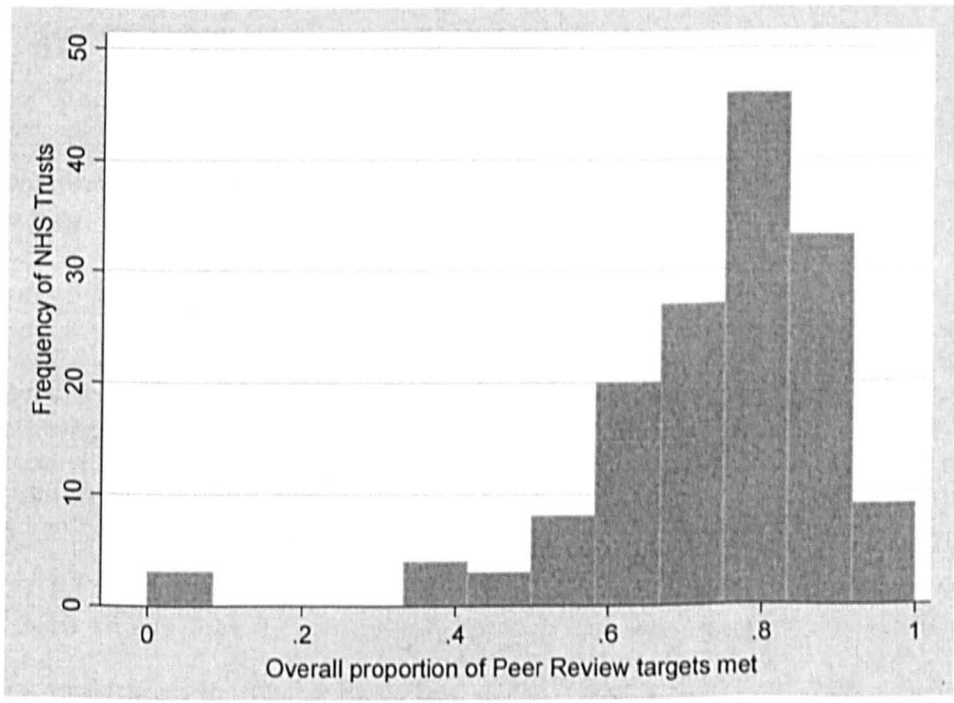



Figure 5.11: Histogram illustrating the variation in success at Peer Review.

The median overall Peer Review score was 0.80, with an interquartile range of 0.71 to 0.84. In order to allow inclusion in regression analyses, a binary variable for the overall score was created with 0.84 as the cut-off. This represented the top quarter of NHS Trusts, who had entered 25,672 (32%) patients into the cohort. The remaining NHS Trusts who scored <0.84 in their Peer Review overall score, accounted for 75% of Trusts, and had entered 55,294 (68%) patients. The results of uni and multivariate logistic regression analyses assessing the influence of the overall Peer Review score on the likelihood of receiving treatment for lung cancer are depicted in table 5.16.

Table 5.16: Results of logistic regression assessing the influence of an overall Peer Review score on the likelihood of receiving treatment for lung cancer.

| | N | N* | (%)** | Unadj OR 95% CI | | Adj OR*** 95% CI | | p for trend |
|---|---|---|---|---|---|---|---|---|
| **Surgery (NSCLC only: N=34,513)** | | | | | | | | |
| **Peer Review score** | | | | | | | | |
| <0.84 | 23461 | 3114 | 13 | | | | | 0.204 |
| >0.84 | 11052 | 1371 | 12 | 0.93 | (0.86, 0.99) | 0.95 | (0.88, 1.03) | |
| **Chemotherapy (small cell only: N=7845)** | | | | | | | | |
| **Peer Review score** | | | | | | | | |
| <0.84 | 5275 | 3221 | 61 | | | | | 0.949 |
| >0.84 | 2570 | 1599 | 62 | 1.05 | (0.95, 1.16) | 1.00 | (0.90, 1.12) | |
| **Radiotherapy (whole cohort: N=80,966)** | | | | | | | | |
| **Peer Review score** | | | | | | | | |
| <0.84 | 55294 | 11377 | 21 | | | | | <0.001 |
| >0.84 | 25672 | 6052 | 24 | 1.19 | (1.15, 1.23) | 1.19 | (1.15, 1.24) | |

Legend: N* number of patients within each subgroup who received treatment
(%)** percentage of patients within each subgroup who received treatment
Adj OR*** adjusted for sex, age quintile, performance status, histology (radiotherapy only), stage (UICC version 6 if NSCLC, and limited vs extensive for small cell lung cancer), Townsend quintile, ethnic group, Charlson Index and admission time pre diagnosis.
NSCLC: non-small cell lung cancer

Table 5.16 shows that a high overall score in the Peer Review process was not associated with an increased likelihood of receiving surgery or chemotherapy in those patients with non-small cell and small cell lung cancer respectively. But there is evidence that patients first seen in those NHS Trusts which scored >0.84

In the Peer Review process, were almost 20% more likely to receive radiotherapy than patients first seen in those NHS Trusts scoring less than 0.84 (adjusted Odds Ratio 1.19, 95% CI 1.15, 1.24).

Cox regression analyses found that the overall score at Peer Review had no influence on survival. The adjusted Hazard Ratio for death for those patients first seen in an NHS Trust which scored >0.84 at Peer Review was 1.01 (95% CI 0.99, 1.03) compared with those patients first seen in an NHS Trust scoring <0.84 (table 5.17). This will be related to the poor prognosis of lung cancer, but it could also highlight the inadequacies of the current Peer Review process. It could be that the indicators measured are inappropriate or inadequate to detect a difference in patient survival based on the NHS Trust where that individual was first seen.

Table 5.17: Cox regression for overall score at Peer review and overall mortality

| | N | N died | %* | Unadj HR (95% CI) | Adj HR ** (95% CI) | p for trend |
|---|---|---|---|---|---|---|
| **Peer Review score** | | | | | | |
| <0.84 | 55294 | 44981 | 81 | | | 0.179 |
| >0.84 | 25672 | 21410 | 83 | 1.01 (0.99, 1.02) | 1.01 (0.99, 1.03) | |

Legend: %* percentage of patients within each subgroup who have died.
Adj HR**; adjusted Hazard Ratio, mutually adjusted for sex, age quintile, histology, stage, performance status, ethnic group and socio-economic status.

Individual patient survival is determined by several key clinical features, as well as pre-existing co-morbidities and the treatment given. Figure 5.12 shows the good prognosis of carcinoid disease, in contrast to the poor outlook for individuals with small cell lung cancer and mesothelioma. Figure 5.13 shows the variation in observed survival based on stage at presentation.

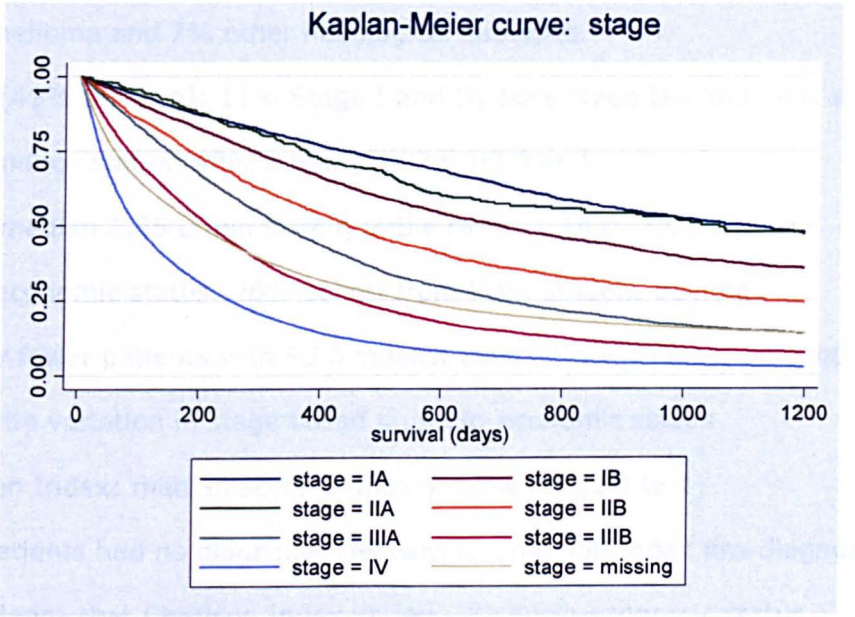



Figure 5.13: Kaplan-Meier (KM) survival curve based on stage at diagnosis.

Figure 5.14 shows the survival curves for those patients with no evidence of co-morbid illness in HES, compared with those with a Charlson Index of 4 or more.

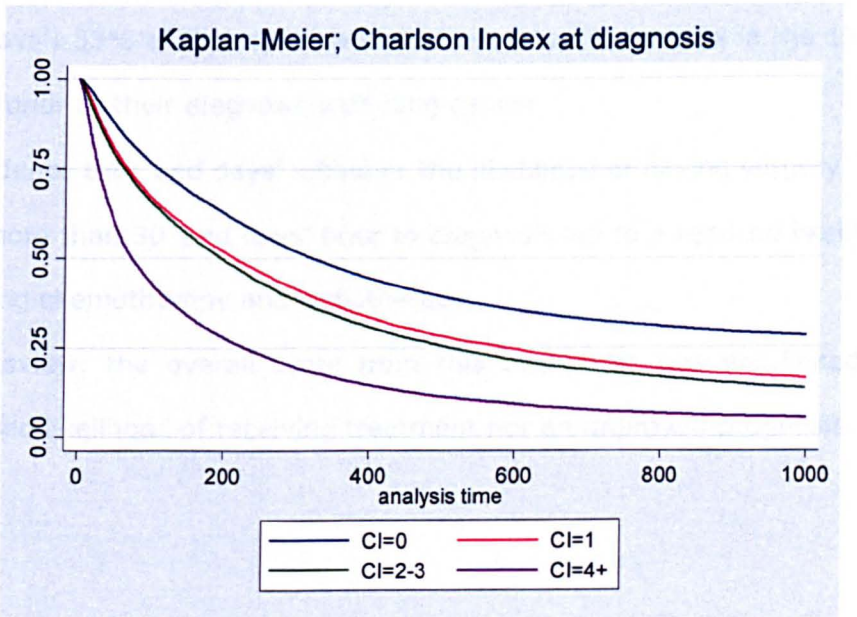



Figure 5.14: KM survival curve based on Charlson Index (CI) at diagnosis.

Individual patient survival is determined by several key clinical features, as well as pre-existing co-morbidities and the treatment given. Figure 5.12 shows the good prognosis of carcinoid disease, in contrast to the poor outlook for individuals with small cell lung cancer and mesothelioma. Figure 5.13 shows the variation in observed survival based on stage at presentation.

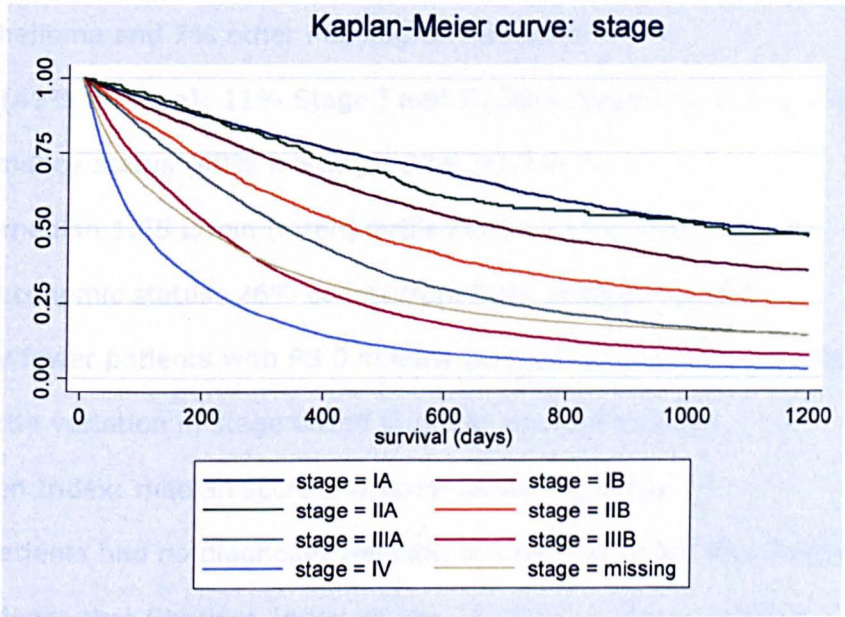



Figure 5.13: Kaplan-Meier (KM) survival curve based on stage at diagnosis.

Figure 5.14 shows the survival curves for those patients with no evidence of co-morbid illness in HES, compared with those with a Charlson Index of 4 or more.

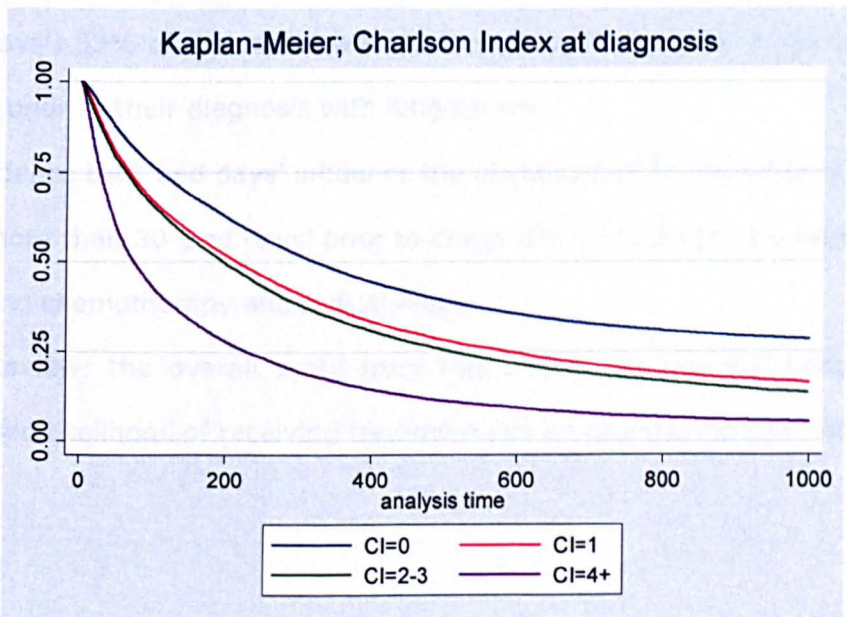



Figure 5.14: KM survival curve based on Charlson Index (CI) at diagnosis.

### 5.3.5 Summary of results

Basic demographic features for the cohort as a whole:

- 60% of the cohort were male
- Median age 72 years (interquartile range 62 to 79 years)
- Histology (40% missing): 40% non-small cell lung cancer, 10% small cell,3% mesothelioma and 7% other histological subtypes.
- Stage (49% missing): 11% Stage I and II, 16% stage III, and 24% stage IV
- Performance status (40% missing): 32% PS 0 or 1
- FEV1: median 1.55 L/min (interquartile range 1.14 to 2.06 L/min)
- Socio-economic status: 26% cohort from least affluent quintile

  Slightly fewer patients with PS 0 in least compared with most affluent quintile

  Very little variation in stage based on socio-economic status
- Charlson Index: median score 1 (interquartile range 0 to 4)

  45% patients had no diagnoses relevant to Charlson Index pre-diagnosis.

  No evidence that Charlson Index varied with socio-economic status.
- Individual disease groups: high prevalence of smoking related pathologies

  22% respiratory disease, 14% non-lung malignancy and metastatic disease, and 11% cardiac disease.
- 'Bed days': 83% of the cohort were not admitted to hospital in the 12 month period prior to their diagnosis with lung cancer.

  No evidence that 'bed days' influence the likelihood of having surgery

  Only more than 30 'bed days' prior to diagnosis led to a reduced likelihood of receiving chemotherapy and radiotherapy.
- Peer Review: the overall score from this evaluation was not linked to an increased likelihood of receiving treatment nor an improved prognosis.

## 5.4 Discussion

### 5.4.1 Treatment received

The proportion of individuals within this cohort who underwent surgery for their lung cancer was 10%, which improved to 13% in those with proven NSCLC. For those patients with small cell lung cancer the chemotherapy rate was 61%. And the overall rate of radiotherapy, regardless of underlying histology, was 22%. One of the main aims of this research has been to investigate co-morbidity in a cohort of patients with lung cancer. The linked NLCA/HES dataset provided the opportunity to investigate three markers of co-morbid illness. The time spent in hospital in the 12 month period prior to diagnosis was provided by HES already, but the Charlson Index was calculated from the record of ICD-10 disease codes. As well as the overall composite score, the individual component diseases were investigated to see if any one disease group played the dominant role in influencing disease outcome. The results show that the Charlson Index had a strong influence on access to treatment and overall survival, independent of other clinical features such as stage and performance status. As the level of co-morbid illness increased, the likelihood of having surgery or chemotherapy fell. There was no affect on the likelihood of receiving radiotherapy as co-morbid illness increased, but this could be because radiotherapy is used with both potentially curative and palliative intent, for example individuals with significant co-morbid illness may receive single fraction palliative radiotherapy to a bone metastasis when they would not be suitable for chemotherapy or surgery. The NLCA does not currently have the capability to differentiate between the treatment intent of the radiotherapy given, and for this reason, access to radiotherapy was not evaluated for individual histological subtypes. The NLCA will soon be linked to the national radiotherapy database, and so it will be possible to analyse details regarding the number of fractions etc that a patient with lung cancer has received, and the influence on survival too.

In terms of socioeconomic status, this cohort had an increased proportion of individuals from the lowest Townsend quintile, but there was no evidence of wide variation in stage or co-morbidity between strata of socioeconomic status. In contrast to published literature, there was no evidence that as socioeconomic status declined the stage at presentation was more advanced (45, 49). Previous publication using the NLCA dataset (36) has not shown any evidence that resection rate falls as socio-economic status declines, in contrast to the paper from Pollack et al (50).

Analysis of the individual component diseases found that certain diseases were important in determining the likelihood of patients receiving surgery and chemotherapy. With regard to surgery, the presence of dementia was the strongest negative predictor but it was only present in 150 of the 34,513 patients with non-small cell lung cancer. Cardiac disease, renal failure and diabetes with complications were all linked with a reduced likelihood of receiving surgery. These conditions would all pose an increased anaesthetic and operative risk, and this result makes clinical sense. With regard to chemotherapy, dementia again appeared to have a strong influence but because only 29 of the 7845 patients with small cell lung cancer also had dementia, it did not achieve statistical significance. Renal failure was a strong negative predictor for receiving chemotherapy, and given the need for renal clearance of chemotherapy agents, this result again makes good clinical sense. No individual disease group, with the exception of dementia which was uncommon in this cohort, had a stronger independent influence on the likelihood of receiving surgery or chemotherapy than the Charlson Index. Therefore I did not include individual disease groups amongst the patient features used in chapters 6 and 7, when looking at the influence of patient and NHS Trust features on surgery and chemotherapy for non-small cell and small cell lung cancer respectively.

The evaluation of the influence of 'bed days' on access to treatment revealed heterogeneity amongst the treatment types. No effect was demonstrated for surgery. In those patients with more than 30 days in hospital, there was a reduced likelihood of both chemotherapy and radiotherapy. However, only for radiotherapy was the p for trend significant. It appears that the observation of time spent in hospital, 'bed days', as a marker of co-morbid illness has too much error within it. For example, an individual may have a heart attack but only be in hospital five days, whilst another may have a total hip replacement and be an in-patient for two weeks. Only, once a high threshold was reached, i.e. 30 days, was an influence on outcome observed for both chemotherapy and radiotherapy. Variables which are prone to error are unlikely to demonstrate significant results from regression analyses, as the Odds Ratio will converge with the comparator. Therefore, 'bed days' was not used in the remainder of this thesis as a marker of co-morbid illness. This variable has been used as a marker of co-morbidity in Scottish studies before but with inconsistent results. Brewster et al found that as 'bed days' increased there was no increased likelihood of dying within 30 days of diagnosis for individuals with either breast or colorectal cancer (70). In contrast Parks et al found that the Hazard Ratio for death in individuals with pancreatic cancer increased if the number of 'bed days' in the six months prior to diagnosis was more than five days (71).

The overall score from Peer Review for each NHS Trust was only found to influence the likelihood of receiving radiotherapy. No effect was demonstrated for surgery or chemotherapy. I had anticipated that as a marker of Trust performance rather than facilities per se, this would prove a potentially useful indicator of outcome from lung cancer. However, given the lack of influence demonstrated during regression analyses, the overall Peer Review score was not used in the remainder of my thesis.

### 5.4.2 Survival

Lung cancer continues to have a very poor prognosis, and the median survival for the entire cohort (dataset 2) was 198 days (interquartile range 59 to 532). In spite of the disappointing survival from the disease as a whole, the Charlson index was found to be an independent marker of prognosis. As the composite score of co-morbidity increased so the likelihood of death increased too. Amongst individual disease groups, the presence of metastases had the greatest influence on overall survival. Other individual diseases which were shown to affect survival were, AIDS (n=31 only), liver failure, renal failure and dementia. Only metastatic disease had an adjusted Hazard Ratio above that of the Charlson Index of 4 or more. Time spent in hospital prior to diagnosis was not found to influence overall survival, even amongst those patients who had been in hospital for more than a month in the year before their lung cancer was diagnosed.

Finally the overall score from Peer Review for each NHS Trust did not influence overall survival. This result along with the fact that Peer Review did not influence access to treatment, suggests that it is not a good discriminator of MDT performance.

In order to look more closely at the influence of patient and NHS Trust features, I decided to look at the access to treatment and survival for two distinct histological subgroups, namely non-small cell lung cancer (surgery) and small cell lung cancer (chemotherapy). The indicator of co-morbidity used for the remainder of this research was the Charlson Index, rather than individual diseases or 'bed days'. In terms of NHS Trust features, the binary variables of cardio-thoracic surgical centres, radiotherapy centres, and high vs low trial participation, have been used. The overall scores from Peer Review have not.

# Chapter six: Inequalities in outcomes for non-small cell lung cancer: the influence of clinical characteristics and features of the local lung cancer service

## 6.1 Introduction

In this chapter I have looked specifically at non-small cell lung cancer. Non-small cell lung cancer accounts for more than 80% of all lung cancers (72, 73), and for these people surgical resection represents the best chance of cure (74). The National Institute for Health and Clinical Excellence (NICE) recommended surgical resection for all patients with stage I and II disease who had no medical contra-indications and adequate lung function (26). At present only a small minority of people with non-small cell lung cancer will have disease which is suitable for surgical resection (75). There is evidence that surgical resection rates for lung cancer and survival from the disease vary between and within countries (37, 73, 76, 77). This variation is anecdotally attributed to geographical differences in patient features, for example individuals from one area being older, presenting with late stage disease, or having significant co-morbidities which preclude an anaesthetic. My intention was to adjust for all patient features and investigate whether the variation in outcomes at a hospital level were still evident.

In this chapter I have used the National Lung Cancer Audit (NLCA) dataset linked to Hospital Episode Statistics (dataset 2) to quantify the influence of patient and National Health Service (NHS) Trust level features on access to surgery and survival for people with non-small cell lung cancer in England. There are 157 NHS Trusts in England and only 31 have thoracic surgery available on-site. There are 28 cancer Networks in England. Within each one there is a 'hub and spoke' system whereby specialist cancer centres, with thoracic surgeons available on-site, act as the 'hub' and provide specialist cancer services, such as surgery and radiotherapy, for the hospitals that compose the 'spokes'. Some thoracic centres are purely thoracic, others are cardio-thoracic, but I have used the term thoracic surgical centre as a means of describing the service they provide regardless of the sub-speciality of the surgeons.

## 6.2 Methods

The NLCA-HES linked dataset (dataset 2) was used for this piece of research and included all English patients first seen between January 2004 and 31st December 2008. For this chapter I restricted my analyses to people with a proven histological diagnosis of non-small cell lung cancer. The NLCA dataset includes the following information on all patients:

sex,

age at diagnosis,

histological sub-type,

Lower Super Output Area (census derived),

performance status (as classified by ECOG),

stage at presentation (as classified by UICC version 6),

details of the NHS Trust where a patient was first seen

and whether surgical resection had occurred (date of surgery).

Although the National Lung Cancer Audit records information on co-morbid illness, these data are incomplete, and are limited to only six disease groups. The audit records only whether or not the presence of this co-morbid illness influenced the treatment decision. I created a composite score of co-morbidity, the Charlson Index (34), as described in section 5.2.2. I also used data from the Hospital Episode Statistics dataset to provide information on ethnicity.

In order to describe variation in the facilities available at NHS Trusts I created three binary variables, as described in section 5.2.3. These were, whether or not a Trust is a thoracic surgical centre, whether or not it is a radiotherapy centre, and whether or not the centre was actively entering patients into clinical trials for lung cancer. A fourth binary variable thought to quantify lung cancer MDT performance was also created based on the results of the Peer Review process 2004-2007, as described in section 5.2.3.4. However, I dropped this

from multivariate regression analyses, given the lack of evidence to support the assumption that it was influential (table 5.16).

### 6.2.1 Surgery

I performed logistic regression analyses to estimate the odds ratios for receiving surgery, adjusting these analyses for all patient and NHS Trust level features and clustering on NHS Trusts. In order to look more specifically at variation in access to surgery in patients in whom I would have expected a high chance of undergoing surgery, I repeated the analyses in a subgroup of patients with stage I or II disease.

### 6.2.2 Survival

For the survival analyses I used a start and end date as described in section 5.2.4.2. Because some patients with lung cancer are diagnosed at post-mortem I excluded people from the survival analysis when the date of death was the same as, or earlier than, the date of diagnosis. I performed Cox regression analyses to calculate Hazard ratios and then constructed a multivariate model to adjust mutually for all patient and NHS Trust features. The final Cox regression model included clustering by NHS Trusts. I then repeated the survival analysis for the subgroup of patients with stage I and II disease as outlined above. I checked the proportional hazards assumption for the model by inspecting Nelson-Aaleen plots.

Finally, to determine whether people first seen at a thoracic surgical centre were different to those seen at a non-surgical centre, I compared the demographic features of the two patient groups and, for the subgroup of people who had an operation, I estimated survival according to where the person was first seen.

## 6.3 Results

The NLCA-HES linked dataset contained a total of 87,252 patients who were first seen at an English NHS Trust between January 2004 and 31st December 2008. Histological diagnosis was based on a pre-treatment histology as this would be the information available to multidisciplinary teams. Data in the early years of the NLCA were poorly completed, and so 33,964 (42%) of this dataset have no pre-treatment histology recorded. Small cell lung cancer accounts for 7845 (10%) of patients, 2772 (3%) have mesothelioma and 1872 (2%) had other diagnoses. There were 34,513 (43%) patients with a histological diagnosis of non-small cell lung cancer. 33% of patients had squamous cell carcinoma, 27% adenocarcinoma, 33% non-small cell lung cancer not-otherwise specified and the remaining 7% had large cell tumours, bronchoalveolar cell carcinoma and carcinoma-in-situ. The median age at diagnosis was 71 years (interquartile range 63 to 77 years) and 60% were male. A total of 4,485 patients (13%) underwent a surgical procedure. The median Charlson Index at diagnosis was 1 (interquartile range 0 to 2), with a minimum score of 0, and maximum of 17. There are 31 cardiothoracic surgical centres in England, 49 radiotherapy centres, and 44 NHS Trusts which were defined as high trial participation, which was equivalent to putting 5% or more of their expected lung cancer patients into clinical trials. Amongst the thoracic surgical centres, 19 were radiotherapy centres too, and 15 were trial active. Twelve NHS Trusts possessed all three features. Of the 34,513 patients 9,168 (27%) were first seen in thoracic surgical centres.

### 6.3.1 Surgery

Table 6.1 shows the results of univariate and multivariate logistic regression analyses for the associations between having surgery and both patient and NHS Trust features. As the Charlson Index increased, indicating a higher level of co-morbid illness, the likelihood of having surgery decreased. The odds ratio for

having surgery, mutually adjusted for all patient and NHS Trust features, for patients with a Charlson Index of 4 or more compared with patients with a Charlson index of 0, was 0.67 (95% confidence interval 0.56, 0.80). Patients in the 4th age quintile (76-80 years) were almost half as likely to undergo surgery as those in the youngest quintile (adjusted Odds Ratio 0.56, 95% confidence interval 0.49, 0.56). People with more advanced disease stage and poorer performance status were also less likely to have an operation. There was no evidence that ethnic group or socio-economic status influenced the likelihood of receiving surgery.

If a patient was first seen in a thoracic surgical centre, they were 51% more likely to have surgery, even after adjusting for all of the patient level features (adjusted Odds Ratio 1.51, 95% confidence interval 1.16, 1.97). There was some evidence that this difference between surgical and non-surgical centres varied year on year (test for interaction p=0.003) - but there was no obvious trend over time as the odds ratios for 2004, 2005, 2006, 2007 and 2008 were 1.58 (95% confidence interval 0.82 to 3.05), 2.50 (1.57 to 3.88), 1.80 (1.18 to 2.72), 1.11 (0.76 to 1.64) and 1.47 (1.09 to 1.99) respectively. In the multivariate analyses, whether the NHS Trust was a radiotherapy centre or a high trial centre did not influence the likelihood of having surgery.

I identified 4,966 patients who had stage I or II disease and in this subgroup 2,387 (48%) had surgery. In these patients the likelihood of having surgery was 53% higher in patients first seen at NHS Trusts that were thoracic surgical centres compared with those seen in non-surgical centres (adjusted Odds Ratio 1.53, 95% confidence interval 1.09, 2.13).

Table 6.1: Results of logistic regression regarding the influence of patient features on likelihood of having surgery (clustered by NHS Trust)

| | N | N who had surgery | (%)* | Unadj OR | Adj OR** | P value |
|---|---|---|---|---|---|---|
| **Sex** | | | | | | |
| Male | 20,945 | 2637 | 13 | | | |
| Female | 13,568 | 1848 | 14 | 1.09 (1.02, 1.17) | 1.06 (0.99, 1.15) | 0.086 |
| **Age quintile** | | | | | | |
| 1 (30-62 years) | 8221 | 1290 | 16 | | | <0.001*** |
| 2 (63-69 years) | 7635 | 1232 | 16 | 1.03 (0.95, 1.13) | 0.95 (0.85, 1.05) | |
| 3 (70-75 years) | 7693 | 1050 | 14 | 0.85 (0.78, 0.93) | 0.79 (0.71, 0.89) | |
| 4 (76-80 years) | 6115 | 652 | 11 | 0.64 (0.58, 0.71) | 0.56 (0.49, 0.65) | |
| 5 (81-100 years) | 4849 | 261 | 5 | 0.31 (0.27, 0.35) | 0.26 (0.22, 0.32) | |
| **Stage** | | | | | | |
| IA | 1178 | 722 | 61 | | | 0.001*** |
| IB | 2138 | 1029 | 48 | 0.59 (0.51, 0.68) | 0.63 (0.52, 0.76) | |
| IIA | 202 | 121 | 60 | 0.94 (0.70, 1.28) | 0.96 (0.72, 1.28) | |
| IIB | 1448 | 515 | 35 | 0.35 (0.30, 0.41) | 0.35 (0.28, 0.43) | |
| IIIA | 2777 | 380 | 14 | 0.10 (0.09, 0.12) | 0.09 (0.07, 0.11) | |
| IIIB | 5427 | 297 | 5 | 0.04 (0.03, 0.04) | 0.03 (0.03, 0.04) | |
| IV | 10,968 | 271 | 2 | 0.02 (0.01, 0.02) | 0.02 (0.01, 0.02) | |
| Occult | 50 | 15 | 30 | 0.27 (0.15, 0.50) | 0.26 (0.13, 0.52) | |
| missing | 10,325 | 1135 | 11 | 0.08 (0.07, 0.09) | 0.09 (0.07, 0.12) | |
| **Performance status** | | | | | | |
| 0 | 5847 | 1651 | 28 | | | <0.001*** |
| 1 | 9282 | 1372 | 15 | 0.44 (0.41, 0.48) | 0.52 (0.46, 0.59) | |
| 2 | 5317 | 264 | 5 | 0.13 (0.12, 0.15) | 0.19 (0.15, 0.24) | |
| 3 | 3251 | 67 | 2 | 0.05 (0.04, 0.08) | 0.10 (0.08, 0.14) | |
| 4 | 760 | 13 | 2 | 0.04 (0.03, 0.88) | 0.11 (0.06, 0.18) | |
| missing | 10,056 | 1118 | 11 | 0.32 (0.29, 0.35) | 0.40 (0.32, 0.49) | |
| **Ethnic group** | | | | | | |
| White | 26,511 | 3443 | 13 | | | 0.39^ |
| Black | 234 | 27 | 12 | 0.87 (0.58, 1.31) | 0.84 (0.47, 1.49) | |
| Asian | 1905 | 262 | 14 | 1.07 (0.93, 1.22) | 1.13 (0.96, 1.33) | |
| Mixed race | 103 | 10 | 10 | 0.72 (0.37, 1.38) | 0.77 (0.33, 1.78) | |
| Other | 161 | 29 | 18 | 1.47 (0.98, 2.20) | 1.41 (0.88, 2.27) | |
| missing | 5599 | 714 | 13 | 0.98 (0.90, 1.07) | 1.04 (0.92, 1.17) | |
| **Townsend quintile** | | | | | | |
| 1 (most affluent) | 5184 | 701 | 14 | | | 0.132*** |
| 2 | 6393 | 856 | 13 | 0.99 (0.89, 1.10) | 0.99 (0.88, 1.11) | |
| 3 | 6660 | 872 | 13 | 0.96 (0.87, 1.07) | 1.04 (0.92, 1.19) | |
| 4 | 7148 | 942 | 13 | 0.97, 0.87, 1.08) | 0.98 (0.84, 1.13) | |
| 5 (least affluent) | 9051 | 1110 | 12 | 0.89 (0.81, 0.99) | 0.86 (0.71, 1.04) | |
| missing | 77 | 4 | 5 | 0.35 (0.13, 0.96) | 0.43 (0.15, 1.23) | |

Table 6.1 continued.

| | N | N who had surgery | (%)* | Unadj OR | Adj OR** | P |
|---|---|---|---|---|---|---|
| **Charlson Index** | | | | | | |
| 0 | 15,573 | 2341 | 15 | | | <0.001*** |
| 1 | 6951 | 985 | 14 | 0.93 (0.86, 1.01) | 0.95 (0.86, 1.04) | |
| 2 or 3 | 5828 | 752 | 13 | 0.83 (0.77, 0.91) | 0.89 (0.80, 0.99) | |
| 4 + | 6161 | 407 | 7 | 0.40 (0.36, 0.45) | 0.67 (0.56, 0.80) | |
| **Surgical centre** | | | | | | |
| No | 25,248 | 2947 | 12 | | | |
| Yes | 9265 | 1538 | 17 | 1.51 (1.41, 1.61) | 1.51 (1.16, 1.97) | <0.001 |
| **Radiotherapy centre** | | | | | | |
| No | 21,646 | 2614 | 12 | | | |
| Yes | 12,867 | 1871 | 15 | 1.24 (1.16, 1.32) | 1.02 (0.83, 1.27) | 0.854 |
| **Trial entry** | | | | | | |
| Low | 23,136 | 2817 | 12 | | | |
| High | 11,377 | 1668 | 15 | 1.24 (1.16, .32) | 1.15 (0.88, 1.50) | 0.34 |

Legend: N=total number of patients in each variable.
(%)* percentage of each variable who had surgery.
Adj OR** Odds ratio for surgery adjusted for all other variables in the table.
*** p for trend
^ this is the result of a log likelihood ratio test

### 6.3.2 Survival

A small number of patients (148) had a date of death on or before the date of diagnosis and so were excluded from the survival analyses. In my survival analyses females had a better prognosis than males but as age, stage and performance status increased prognosis worsened (table 6.2). Patients with a Charlson Index of 4 or more had an adjusted Hazard Ratio of death of 1.59 (95% confidence interval 1.52, 1.66) compared with those with a Charlson Index of zero. There was no evidence that social deprivation was linked to worse survival. Whether the NHS Trust where a patient was first seen was a thoracic surgical centre or not had no significant effect on overall mortality. The results of Peer Review had no effect on overall mortality (adjusted Hazard Ratio 1.01, 95% confidence interval 0.98, 1.04). There was no evidence that my proportional hazards assumption was incorrect.

Patients who had surgery had an almost 60% lower overall mortality, (adjusted Hazard Ratio 0.41, 95% confidence interval 0.39, 0.44), compared with those who did not have surgery, even after adjusting for all patient features. In the subgroup of people with stage I or II disease where 48% had surgery, the fully adjusted Hazard Ratio was very similar at 0.41 (95% confidence interval 0.37 to 0.46). The median survival for patients stage I or II disease who had surgery was 774 days (interquartile range 305 days to 2150 days), compared with a median survival of just 174 days (interquartile range 63 to 394 days) for those who did not have surgery.

Table 6.2: Results of Cox regression analyses using all patient features, all NHS Trust level features, surgical intervention or not, and clustering by NHS Trust.

| | N | N who died | (%)* | Unadj HR | Adj HR** | P |
|---|---|---|---|---|---|---|
| **Sex** | | | | | | |
| Male | 20,848 | 17,144 | 82 | | | |
| Female | 13,517 | 10,616 | 79 | 0.90 (0.88, 0.92) | 0.90 (0.88, 0.92) | <0.001 |
| **Age quintile** | | | | | | |
| 1 (30-62 years) | 8183 | 6372 | 78 | | | <0.001*** |
| 2 (63-69 years) | 7616 | 5897 | 77 | 1.02 (0.98, 1.06) | 1.04 (1.00, 1.07) | |
| 3 (70-75 years) | 7660 | 6210 | 81 | 1.15 (1.11, 1.19) | 1.10 (1.06, 1.14) | |
| 4 (76-80 years) | 6084 | 5068 | 83 | 1.28 (1.24, 1.33) | 1.17 (1.13, 1.22) | |
| 5 (81-100 years) | 4822 | 4213 | 87 | 1.57 (1.51, 1.64) | 1.32 (1.26, 1.39) | |
| **Stage** | | | | | | |
| IA | 1177 | 448 | 38 | | | <0.001*** |
| IB | 2137 | 1062 | 50 | 1.43 (1.28, 1.60) | 1.27 (1.11, 1.46) | |
| IIA | 202 | 79 | 39 | 1.03 (0.81, 1.31) | 1.00 (0.79, 1.28) | |
| IIB | 1446 | 905 | 63 | 2.08 (1.85, 2.32) | 1.71 (1.48, 1.99) | |
| IIIA | 2772 | 2083 | 75 | 2.82 (2.55, 3.13) | 1.98 (1.73, 2.27) | |
| IIIB | 5410 | 4564 | 84 | 4.09 (3.71, 4.50) | 2.67 (2.33, 3.05) | |
| IV | 10,913 | 10,106 | 93 | 6.37 (5.80, 7.01) | 3.85 (3.35, 4.42) | |
| Occult | 50 | 26 | 52 | 1.56 (1.05, 2.31) | 1.24 (0.83, 1.86) | |
| missing | 10,258 | 8487 | 83 | 3.93 (3.57, 4.32) | 2.53 (2.19, 2.91) | |
| **Performance status** | | | | | | |
| 0 | 5839 | 3804 | 65 | | | <0.001*** |
| 1 | 9267 | 7226 | 78 | 1.49 (1.43, 1.55) | 1.28 (1.22, 1.33) | |
| 2 | 5300 | 4737 | 89 | 2.50 (2.40, 2.61) | 1.87 (1.76, 1.99) | |
| 3 | 3230 | 3103 | 96 | 4.51 (4.30, 4.74) | 3.12 (2.91, 3.35) | |
| 4 | 737 | 722 | 98 | 7.62 (7.03, 8.25) | 5.21 (4.39, 6.17) | |
| missing | 9992 | 8168 | 82 | 1.82 (1.75, 1.89) | 1.54 (1.45, 1.62) | |
| **Ethnic group** | | | | | | |
| White | 26,408 | 21,488 | 81 | | | 0.0004^ |
| Black | 231 | 177 | 77 | 0.84 (0.72, 0.97) | 0.81 (0.70, 0.93) | |
| Asian | 1897 | 1433 | 76 | 0.98 (0.93, 1.03) | 0.95 (0.89, 1.02) | |
| Mixed race | 103 | 84 | 82 | 0.86 (0.77, 1.18) | 0.96 (0.79, 1.18) | |
| Other | 160 | 115 | 72 | 0.83 (0.69, 1.00) | 0.86 (0.73, 1.02) | |
| missing | 5566 | 4463 | 80 | 1.03 (1.00, 1.06) | 1.05 (1.01, 1.09) | |
| **Townsend quintile** | | | | | | |
| 1 (most affluent) | 5172 | 4161 | 80 | | | 0.661*** |
| 2 | 6363 | 5128 | 81 | 1.01 (0.97, 1.05) | 1.00 (0.96, 1.05) | |
| 3 | 6627 | 5345 | 81 | 1.03 (0.99, 1.06) | 1.00 (0.96, 1.05) | |
| 4 | 7115 | 5671 | 80 | 1.01 (0.97, 1.05) | 0.99 (0.94, 1.03) | |
| 5 (least affluent) | 9011 | 7390 | 82 | 1.04 (1.00, 1.08) | 0.99 (0.94, 1.05) | |
| missing | 77 | 65 | 84 | 1.12 (0.87, 1.42) | 0.87 (0.67, 1.14) | |

Table 6.2 continued.

| | N | N who died | (%)* | Unadj HR | Adj HR** | P |
|---|---|---|---|---|---|---|
| **Charlson Index** | | | | | | |
| 0 | 15,536 | 12,105 | 78 | | | <0.001*** |
| 1 | 6931 | 5431 | 78 | 1.10 (1.06, 1.13) | 1.06 (1.02, 1.09) | |
| 2 or 3 | 5795 | 4592 | 79 | 1.16 (1.12, 1.20) | 1.07 (1.03, 1.11) | |
| 4 + | 6103 | 5632 | 92 | 2.00 (1.93, 2.06) | 1.59 (1.52, 1.66) | |
| **Surgery** | | | | | | |
| No | 29,887 | 25,940 | 87 | | | |
| Yes | 4478 | 1820 | 41 | 0.24 (0.23, 0.25) | 0.41 (0.39, 0.44) | <0.001 |
| **Surgical centre** | | | | | | |
| No | 25,131 | 20,517 | 82 | | | |
| Yes | 9234 | 7243 | 79 | 0.91 (0.89, 0.94) | 0.95 (0.89, 1.01) | 0.09 |
| **Radiotherapy centre** | | | | | | |
| No | 21,536 | 17,550 | 81 | | | |
| Yes | 12,829 | 10,210 | 80 | 0.97 (0.95, 0.99) | 1.02 (0.96, 1.09) | 0.539 |
| **Trial centre** | | | | | | |
| Low | 23,043 | 18,642 | 81 | | | |
| High | 11,322 | 9118 | 81 | 0.98 (0.95, 1.00) | 1.01 (0.96, 1.06) | 0.734 |

Legend
N=total number of patients in each variable.
(%)* percentage of patients in each variable who have died.
Adj OR** Odds ratio for surgery adjusted for all other variables in the table.
*** p for trend
^ this is the result of a likelihood ratio test.

The demographic features of patients first seen at thoracic surgical and non-surgical centres were similar (table 6.3) although the proportion of patients from the least affluent quintile of society was higher for the thoracic surgical centres than the non-surgical centres ($p<0.001$). Of the 4,485 (13%) patients who had surgery 34% were first seen in a thoracic surgical centre.

Table 6.3: Demographic features of patients with NSCLC based on where they are first seen. Total number with NSCLC is 34,513.

| | Thoracic surgical centre | | Non-surgical centre | | P value |
|---|---|---|---|---|---|
| | **Number** | **%** | **Number** | **%** | |
| **Total** | 9,265 | 27 | 25,248 | 73 | |
| **Sex** | | | | | 0.529 |
| male | 5,648 | 61 | 15,297 | 61 | |
| female | 3,617 | 39 | 9951 | 39 | |
| **Median age** | 70 years (IQR 63, 77) | | 71 years (IQR 63, 77) | | |
| **Performance status** | | | | | <0.001 |
| 0 | 1804 | 19 | 4043 | 16 | |
| 1 | 2487 | 27 | 6795 | 27 | |
| 2 | 1388 | 15 | 3929 | 16 | |
| 3 | 824 | 9 | 2427 | 10 | |
| 4 | 169 | 2 | 591 | 2 | |
| Missing | 2593 | 28 | 7463 | 30 | |
| **Stage** | | | | | 0.003 |
| IA | 372 | 4 | 806 | 3 | |
| IB | 582 | 6 | 1556 | 6 | |
| IIA | 62 | 0.7 | 140 | 0.5 | |
| IIB | 381 | 4 | 1067 | 4 | |
| IIIA | 746 | 8 | 2031 | 8 | |
| IIIB | 1388 | 15 | 4039 | 16 | |
| IV | 3003 | 32 | 7965 | 32 | |
| Occult | 16 | | 34 | | |
| missing | 2715 | 29 | 7610 | 30 | |
| **Charlson Index** | | | | | 0.074 |
| 0 | 4221 | 46 | 11,352 | 45 | |
| 1 | 1784 | 19 | 5167 | 20 | |
| 2 or 3 | 1564 | 17 | 4262 | 17 | |
| 4 + | 1696 | 18 | 4465 | 18 | |
| **Townsend quintile** | | | | | <0.001 |
| 1 (most affluent) | 1116 | 12 | 4068 | 16 | |
| 2 | 1602 | 17 | 4791 | 19 | |
| 3 | 1470 | 16 | 5190 | 21 | |
| 4 | 1724 | 19 | 5424 | 21 | |
| 5 (least affluent) | 3339 | 36 | 5712 | 23 | |
| **Surgery** | | | | | <0.001 |
| No | 7727 | 83 | 22,301 | 88 | |
| Yes | 1538 | 17 | 2947 | 12 | |

Survival after surgery did not appear to be related to where the patient was first seen. Those patients with NSCLC who were first seen in a thoracic surgical centre and had surgery performed, had an adjusted Hazard Ratio of 1.01 (95% confidence interval 0.87, 1.19). This demonstrates no increased mortality after surgery in those patients first seen in a thoracic surgical centre (table 6.4).

Table 6.4: Cox regression for patients with proven NSCLC who received surgery, based on where they were first seen.

| | N who had surgery | N who died | (%)* | Unadj HR (95% CI) | Adj HR** (95% CI) | P |
|---|---|---|---|---|---|---|
| **Surgical centre** | | | | | | |
| No | 2947 | 1188 | 40 | | | |
| Yes | 1538 | 639 | 42 | 1.06 (0.97, 1.17) | 1.01 (0.87, 1.19) | 0.859 |

Legend: (%)* percentage of patients who have died.
** Hazard ratio adjusted for sex, age quintile, performance status, stage, ethnic group, Townsend quintile, and Charlson Index. Analysis clustered by NHS Trust.

## 6.4 Discussion

### 6.4.1 Principle findings

My results demonstrate that the likelihood of having surgery for people with a histological diagnosis of non-small cell lung cancer is independently influenced not only by patient level features, including age, stage, performance status and co-morbidity, but also whether or not the patient is first seen at a thoracic surgical centre. Even after allowing for patient level features people first seen at a surgical centre were 51% more likely to have an operation. This difference persisted amongst the subgroup of people with early stage disease, where surgery would be the preferred treatment modality and one might expect little variation in practice.

These results also show that female sex, younger age, good performance status at diagnosis, and early stage disease were all associated with better survival. By linking in information from Hospital Episode Statistics I was able to quantify co-morbid illness relating to hospital admissions by calculating a Charlson score, and show that as this score increased, survival became poorer. Whether or not an individual had surgery as part of their treatment plan was also an important determinant of survival for that individual, with those that did have surgery having a 60% reduction in their likelihood of death. This difference was identical in the subgroup of patients with early stage disease. In order to determine whether the higher surgical resection rates for people first seen at thoracic surgical centres reflected these centres operating on people with more advanced disease and/or a worse prognosis I compared the patient features between people seen first at a thoracic surgical centre and those seen elsewhere and found no difference in either survival or patient level features with the exception that the thoracic surgical centres had a higher proportion of people from more deprived backgrounds. This suggests that if the clinical pathway was altered to

ensure that the 73% of people first seen at a non-surgical centre had the same chance of having surgery as those first seen at a thoracic surgical centre then this would increase the overall resection rate in this patient group from 13% to 17% with no detrimental impact on survival after surgery. The fact that there was no observed improvement in survival in those patients who had surgery, if they were first seen in a surgical centre, reflects the difference between the survival advantage of surgery itself conferred to the individual; rather than an observed survival advantage of being first seen in a surgical centre, above and beyond the increased likelihood of receiving surgery.

### 6.4.2 Strengths and weaknesses

Although the National Lung Cancer Audit is not mandatory, there is evidence within their annual reports that case ascertainment has increased steadily and is now in excess of 90% (35, 63, 78). In chapter 4 I studied the validity of this dataset, and found no evidence of bias dependent on the levels of reporting by individual NHS Trusts (36) providing reassurance that the dataset reflects the full spectrum of lung cancer in England. Although a large proportion of this cohort had missing data for histology, I was still able to analyse a subgroup of more than 30,000 patients with histologically proven non-small cell lung cancer. Alongside case ascertainment, data completeness has improved year on year (35, 63). The marker of co-morbid illness that I used was derived from codes relating only to hospital admissions and so will not have captured details of conditions managed independently by general practitioners. This means that, despite being a strong predictor of both survival and having surgery, the Charlson Indices I calculated may be too low and this raises the possibility of residual confounding by co-morbidity. However, when I adjusted the model for surgical resection and site first seen, the odds ratio for Charlson score did not change at all, suggesting that co-morbidity is not a confounder for this association. The distribution of Charlson Indices in this cohort is very similar to

those in both general practitioner datasets (55) and cohorts of patients with non-small cell lung cancer (79, 80). One potential weakness is that there is no information on whether some people who were offered surgery declined this intervention. My research does not represent a randomised control trial looking at the impact of surgery in patients with non-small cell lung cancer, and there has never been such a trial. The National Lung Cancer Screening Trial (U.S.A) was recently stopped because the primary outcome of a significant reduction in mortality from lung cancer was reached (more than 20%). This study compared chest X-ray with CT and patients found to have lung cancer at an early enough stage were treated surgically. This is the first time that screening has been shown to reduce mortality (81). What I am able to report is observational data from a large unselected cohort, which illustrates the survival advantage of surgery in spite of adjusting for many patient features. It is possible that my results are still subject to some residual confounding or selection bias and this may mean that the marked benefit of surgery I have observed may be an over estimate of the true benefit.

The main strengths of this study are the large size and the quality of the National Lung Cancer Audit dataset and the addition of an independent co-morbidity score in the form of the Charlson Index. The Charlson Index was originally developed and used prospectively in a cohort of people with breast cancer (34), and it has subsequently been validated in patient cohorts encompassing both malignant (68, 69) and non-malignant disease processes (82). Previous research has shown that the Charlson co-morbidity Index is associated with lung cancer incidence (83) and also survival (84).

### 6.4.3 Comparison with other studies

This study found that people with non-small cell lung cancer who are first seen in a thoracic surgical centre have an advantage over people with similar disease

seen at non-surgical centres with regards to access to surgery. I also found that having surgery had a large beneficial impact on survival and this highlights the importance of access to this intervention. Previous research in this area in Scotland has shown that as distance from a cancer centre increases survival decreases (85), suggesting that accessibility of services is a key factor in lung cancer outcome. Other research has shown that being first seen in a radiotherapy centre is associated with an increased likelihood of receiving 'active treatment' (51); and that being first seen in a specialist 'cancer centre' is associated with a small improvement in overall survival (86, 87). There have been several large-scale reviews and policy documents in the UK designed to address inequality in cancer outcome including the Calman-Hine report (88), the NHS Cancer Plan (24) and the Cancer Reform Strategy (27). Creating specialist cancer centres has been pivotal to this programme of change, and whilst centralising services will create greater experience and expertise in one centre, it may potentially disadvantage individuals in remote settings, and increase geographical inequalities. The results I have described suggest that more reforms are needed to ensure that all people with lung cancer have equal access to surgical intervention where this is appropriate.

### 6.4.4 Implications of this study

The Department of Health has published guidance that as many as 20% of patients with non-small cell lung cancer may be suitable for surgical resection (89). My findings suggest that if all people with non-small cell lung cancer had the same access to this intervention as people first seen at a thoracic surgical centre then the English resection rates would increase from 13% to 17% with no detrimental impact on survival after surgery. However, what my research does not show is what aspects of "being a surgical centre" are crucial to increasing resection rates. It is possible that this may simply be the presence of a surgeon 'on-site', but other aspects of the lung cancer service within these specialist

centres may also be important, such as the composition of the multidisciplinary team, improved access to specialist radiological and cardiovascular investigations and the geographical location of these thoracic surgical centres. Given the terrible prognosis of lung cancer in the UK, understanding the care pathways in more detail, and, in particular, the barriers to surgical intervention that currently exist for people seen in non-surgical centres, is a pressing priority. The Peer Review data available at the time of this research did not influence clinical outcome measures in lung cancer, and it is an area for further research in terms of what performance measures should be collected in order to accurately describe variation in practice. As the National Lung Cancer Audit matures the addition of more specific information on the composition of local cancer centres and Networks is essential to allow these questions to be answered.

## Chapter seven: How do patient and hospital features influence outcomes in small cell lung cancer in England?

## 7.1 Introduction

Chemotherapy is recommended by the National Institute for Health and Clinical Excellence (NICE) for the treatment of individuals with small cell lung cancer (26), but there is evidence that geographical variation exists in its use across England (35). The extent to which this variation is due to patient features, including co-morbidity and performance status, or features of the hospital where the patient is first seen, is not known; and establishing this is a priority given the poor survival for people with lung cancer seen in the U.K (7, 21).

The aim of this chapter was to use the NLCA together with co-morbidity data from Hospital Episode Statistics to study the impact of patient features and features of the NHS Trust on the use of chemotherapy in people with small cell lung cancer. In addition I have also studied survival in this cohort. Since data on radiotherapy are also available in the National Lung Cancer Audit I have evaluated the impact on survival of radiotherapy use in addition to chemotherapy in patients with small cell lung cancer.

## 7.2 Methods

The data used in this chapter were downloaded from the National Lung Cancer Audit (NLCA) and included all patients first seen between January 2004 and 31st December 2008 (dataset 2). The analyses were restricted to those patients with histologically-proven small cell lung cancer. As has been discussed in chapters 5 and 6 the NLCA dataset contains the following details:

sex,

age at diagnosis,

Lower Super Output Area (census derived),

performance status (as classified by ECOG),

stage at presentation (limited or extensive disease),

details of the NHS Trust where a patient was first seen,

and whether chemotherapy was given (date of chemotherapy).

The data held by the National Lung Cancer Audit on co-morbidity were incomplete and are limited to only six disease groups. Therefore I created a composite co-morbidity score, Charlson Index (34), as described in section 5.2.2. I also used data from Hospital Episode Statistics to provide information on ethnicity.

### 7.2.1 Chemotherapy

All NHS Trusts can provide chemotherapy, and so to assess whether there was a range in the provision of chemotherapy across NHS Trusts during the study period, I calculated the proportion receiving chemotherapy in each Trust and then used logistic regression to assess the likelihood of receiving chemotherapy after adjusting for all patient features. I used the largest NHS Trust as the comparator in the regression model and I included only NHS Trusts that had at least 30 patients with histologically-proven small cell lung cancer to ensure robust estimates.

To identify the most important factors associated with an individual's treatment with chemotherapy, I performed logistic regression analyses to assess the likelihood of patients with histologically-proven small cell lung cancer receiving chemotherapy, adjusting for all patient features and clustering on NHS Trust. In this analysis I also adjusted for a marker of an NHS Trust's participation in clinical trials by estimating whether NHS Trusts were entering a certain proportion of their expected lung cancer patients into clinical trials (described in section 5.2.3.3). I also tried to quantify lung cancer MDT performance by using the results of the Peer Review process 2004-2007 (described in section 5.2.3.4) This was subsequently dropped from multivariate regression analyses due to the lack of evidence to support the assumption that it influenced the likelihood of a patient having chemotherapy (table 5.16) or survival (table 5.17).

### 7.2.2 Survival

For the survival analyses, I created a start and end date as detailed in section 5.2.4.2. Because the objective was to assess the effect of chemotherapy on survival, patients with a date of death the same as, or earlier than, the date of diagnosis were excluded from the survival analyses. I performed Cox regression analyses to calculate hazard ratios for overall mortality in patients receiving chemotherapy compared with those receiving no chemotherapy and then constructed a multivariate model mutually to adjust for all patient features and NHS Trust trial involvement. The final Cox regression model included clustering by NHS Trusts. I then restricted this multivariate Cox regression model to include only patients who had received chemotherapy, to assess whether chemo-radiotherapy conferred any survival advantage over chemotherapy alone. The proportional hazards assumption for our models was checked by inspecting Nelson-Aalen plots.

Finally, to determine whether patients first seen at a centre with high trial participation were different from those first seen in a centre with low trial participation, I compared the demographic features of patients between these two groups of NHS Trusts. For the subgroup of patients who had received chemotherapy, I used a Cox regression model to assess survival according to whether a patient had been first seen in a centre with high compared with low trial participation, adjusting for all patient features and clustering by NHS Trust.

### 7.3 Results

This second dataset (NLCA-HES linked) contained a total of 87,252 patients who were first seen at an English NHS Trust between January 2004 and 31st December 2008. I excluded 6,286 patients (7%) because there were missing data for the NHS Trust where the patient had first been seen. There were 7,845 (10%) patients with histologically-proven small cell lung cancer of whom 54% were male, and the median age of these patients was 69 years (interquartile range 62 to 76 years), two years younger than for the cohort overall. In total 1781 patients (23%) had evidence of co-morbid disease with a Charlson score of 4 or more, compared with 19% of the cohort overall (table 7.1).

Table 7.1: Distribution of Charlson Indices for the overall cohort of patients with lung cancer, and those with proven small cell lung cancer.

| | Complete cohort | | Small cell only | |
|---|---|---|---|---|
| **Charlson Index** | **N** | **(%)** | **N** | **(%)** |
| 0 | 34,711 | 43 | 3482 | 44 |
| 1 | 15,915 | 21 | 1492 | 19 |
| 2 or 3 | 15,085 | 19 | 1090 | 14 |
| 4+ | 15,255 | 19 | 1781 | 23 |

There were 44 NHS Trusts with >5% of expected lung cancer patients being entered into clinical trials, called centres with high trial participation. Of the 7,845 patients with histologically-proven small cell lung cancer, 2,524 (32%) were first seen in centres with high trial participation which was a similar proportion to the cohort overall (31%).

#### 7.3.1 Chemotherapy

The analysis of the use of chemotherapy at each NHS Trust in England showed wide variation. In the NHS Trusts with more than 30 patients the overall proportion receiving chemotherapy was 0.61, the same as for the whole group with small cell lung cancer. The actual proportion ranged from 0.14 to 0.86 at individual NHS Trusts (interquartile range 0.53 to 0.71). Adjusting for all patient features, there was significant variation ($p<0.001$) in the odds ratios for

receiving chemotherapy in the same group of NHS Trusts, with the largest Trust as comparator. The individual NHS Trust level odds ratios ranged from 0.03 (95% confidence interval 0.014, 0.07) to 4.47 (95% confidence interval 1.46, 13.72), with an interquartile range of 0.42 to 1.02.

A total of 4,820 (61%) patients with histologically-proven small cell lung cancer received chemotherapy, of whom 861 (18%) also received radiotherapy. Table 7.2 shows the results of logistic regression analyses of likelihood of receiving chemotherapy. Age at diagnosis, performance status, stage and co-morbidity all showed important independent associations with the likelihood of receiving chemotherapy. As age increased, the likelihood of receiving chemotherapy decreased, with an odds ratio of 0.74 (95% CI 0.64, 0.86) in the second quintile (63-69 years), and an odds ratio of 0.59 (95% CI 0.50, 0.69) in the 3rd quintile (70-75 years) compared with the youngest group. Patients with a performance status of 2 were less likely to receive chemotherapy compared with patients with a performance status of zero (adjusted odds ratio 0.58, 95% confidence interval 0.45, 0.74). Extensive stage disease at diagnosis was associated with a reduction in the likelihood of receiving chemotherapy compared with those patients with limited disease (adjusted odds ratio 0.61, 95% confidence interval 0.47, 0.78). A Charlson Index of 4 or more was associated with a reduced likelihood of receiving chemotherapy compared a Charlson Index of zero (adjusted odds ratio 0.50, 95% confidence interval 0.42, 0.58). Sex, ethnicity and socio-economic status were not associated with access to chemotherapy.

If a patient was first seen in an NHS Trust defined as a centre with high trial participation, they were more likely to receive chemotherapy than those at a centre with low trial participation, even after adjusting for all patient features (adjusted odds ratio 1.42, 95% confidence interval 1.06, 1.90). When I performed a restricted analysis with only those patients without missing data (N=3059), the results were very similar (adjusted odds ratio for centres with high v low trial participation 1.50, 95% confidence interval 1.03, 2.16).

Table 7.2: Results of logistic regression analyses evaluating the influence of patient features on the likelihood of receiving chemotherapy (CTx).

| | Total N | N having CTx | (%)* | Unadj OR (95% CI) | Adj OR** (95% CI) | P value |
|---|---|---|---|---|---|---|
| **Sex** | | | | | | |
| Male | 4245 | 2560 | 60 | | | 0.106 |
| Female | 3600 | 2260 | 63 | 1.11 (1.01, 1.22) | 1.08 (0.98, 1.19) | |
| **Age quintile** | | | | | | |
| 1 (30-62 years) | 2174 | 1616 | 74 | | | <0.001 |
| 2 (63-69 years) | 1928 | 1292 | 67 | 0.70 (0.61, 0.80) | 0.74 (0.64, 0.86) | |
| 3 (70-75 years) | 1771 | 1079 | 61 | 0.54 (0.47, 0.62) | 0.59 (0.50, 0.69) | |
| 4 (76-80 years) | 1170 | 580 | 50 | 0.34 (0.29, 0.39) | 0.39 (0.32, 0.47) | |
| 5 (81-101 years) | 802 | 253 | 32 | 0.16 (0.13, 0.19) | 0.19 (0.15, 0.24) | |
| **PS** | | | | | | |
| PS 0 | 977 | 779 | 80 | | | <0.001 |
| PS 1 | 1925 | 1504 | 78 | 0.91 (0.75, 1.10) | 1.08 (0.87, 1.35) | |
| PS 2 | 1444 | 901 | 62 | 0.42 (0.35, 0.51) | 0.58 (0.45, 0.74) | |
| PS 3 | 876 | 341 | 39 | 0.16 (0.13, 0.20) | 0.25 (0.19, 0.33) | |
| PS 4 | 284 | 30 | 11 | 0.03 (0.02, 0.05) | 0.05 (0.03, 0.07) | |
| Missing | 2339 | 1265 | 54 | 0.30 (0.25, 0.36) | 0.42 (0.32, 0.55) | |
| **Stage** | | | | | | |
| Limited | 1323 | 1025 | 77 | | | <0.001 |
| Extensive | 3078 | 1873 | 61 | 0.45 (0.39, 0.52) | 0.61 (0.47, 0.78) | |
| Missing | 3444 | 1922 | 56 | 0.37 (0.32, 0.42) | 0.45 (0.34, 0.59) | |
| **Townsend quintile** | | | | | | |
| 1 (most affluent) | 1087 | 675 | 62 | | | 0.075 |
| 2 | 1385 | 876 | 63 | 1.05 (0.89, 1.24) | 1.02 (0.85, 1.24) | |
| 3 | 1530 | 922 | 60 | 0.93 (0.79, 1.09) | 0.92 (0.77, 1.11) | |
| 4 | 1669 | 1008 | 60 | 0.93 (0.80, 1.09) | 0.87 (0.72, 1.09) | |
| 5 (least affluent) | 2154 | 1327 | 62 | 0.98 (0.84, 1.14) | 0.85 (0.67, 1.08) | |
| Missing | 20 | 12 | 60 | 0.92 (0.37, 2.26) | 0.65 (0.25, 1.87) | |
| **Ethnic group** | | | | | | |
| White | 6061 | 3739 | 62 | | | 0.107^ |
| Black | 31 | 16 | 52 | 0.66 (0.33, 1.34) | 0.38 (0.11, 1.29) | |
| Asian | 399 | 240 | 60 | 0.94 (0.76, 1.15) | 1.02 (0.80, 1.27) | |
| Mixed | 14 | 10 | 71 | 1.55 (0.49, 4.96) | 1.75 (0.58, 5.32) | |
| Other | 38 | 20 | 53 | 0.69 (0.36, 1.31) | 0.60 (0.34, 1.10) | |
| Missing | 1302 | 795 | 61 | 0.97 (0.86, 1.10) | 0.94 (0.81, 1.09) | |
| **Charlson Index** | | | | | | |
| 0 | 3482 | 2441 | 70 | | | <0.001 |
| 1 | 1492 | 904 | 61 | 0.66 (0.58, 0.74) | 0.79 (0.69, 0.91) | |
| 2 or 3 | 1090 | 625 | 57 | 0.57 (0.50, 0.66) | 0.76 (0.65, 0.90) | |
| 4 + | 1781 | 850 | 48 | 0.39 (0.35, 0.44) | 0.50 (0.42, 0.58) | |
| **Trial entry** | | | | | | |
| <5% | 5321 | 3162 | 59 | | | 0.017 |
| >5% | 2524 | 1658 | 66 | 1.31 (1.18, 1.44) | 1.42 (1.06, 1.90) | |

Legend: (%)* percentage of patients who received chemotherapy.
** Odds ratio adjusted for all other variables in the table.
Analysis clustered by NHS Trust.
^ this is the result of a likelihood ratio test

### 7.3.2 Survival

A small number of patients (63) had a date of death on or before the date of diagnosis and so were excluded from the survival analyses. The median survival for the remaining cohort of 7,782 patients with histologically-proven small cell lung cancer was 182 days (inter-quartile range 44 to 368 days). Table 7.3 shows the results of univariate and multivariate Cox regression analyses, and demonstrates that females had a better prognosis than males. As age, stage, performance status and co-morbidity increased, prognosis worsened. The adjusted Hazard ratio for patients with a Charlson Index of 4 or more was 1.62 (95% confidence interval 1.49, 1.77) compared with those patients with a Charlson Index of zero. Socio-economic status and ethnicity had no effect on overall survival. Whether the NHS Trust where a patient was first seen was a centre with high trial participation or not did not affect overall survival (adjusted Hazard ratio 0.99, 95% confidence interval 0.88, 1.10). There was no evidence that our proportional hazards assumption was not met.

Table 7.3 also shows that patients who received chemotherapy had a lower mortality compared with those who did not, in spite of adjusting for all patient features (adjusted Hazard ratio 0.51, 95% confidence interval 0.46, 0.56). When I performed a restricted analysis with only those patients without missing data (N=3059), the results were very similar (adjusted Hazard ratio for yes v no chemotherapy 0.49, 95% confidence interval 0.41, 0.58). The survival of patients over time who did and did not receive chemotherapy is shown in figure 7.1. In the subgroup of patients with limited disease (1,319 patients) where 78% received chemotherapy there was a lower overall mortality rate compared with those who did not receive chemotherapy (adjusted Hazard ratio 0.62, 95% confidence interval 0.50, 0.76). The median survival for patients with limited stage disease who received chemotherapy was 399 days (inter-quartile range 241 to 686 days), compared with a median survival of just 139 days (inter-quartile range 37 to 381 days) in those who did not receive chemotherapy.

Table 7.3: Cox regression analysis of patient features, NHS Trust trial-entry and the patient's receipt of chemotherapy on overall survival. 63 patients were death certificate only (N=7782). Total number that had died, 6,981.

| | Total patients | N died | (%)* | Unadj HR (95% CI) | Adj HR** (95% CI) | P value |
|---|---|---|---|---|---|---|
| **Sex** | | | | | | |
| Male | 4206 | 3838 | 91 | | | <0.001 |
| Female | 3576 | 3143 | 88 | 0.84 (0.80, 0.88) | 0.86 (0.82, 0.90) | |
| **Age quintile** | | | | | | |
| 1 (30-62 years) | 2161 | 1859 | 86 | | | <0.001 |
| 2 (63-69 years) | 1917 | 1731 | 90 | 1.22 (1.14, 1.30) | 1.12 (1.04, 1.21) | |
| 3 (70-75 years) | 1757 | 1561 | 89 | 1.31 (1.23, 1.40) | 1.20 (1.11, 1.30) | |
| 4 (76-80 years) | 1159 | 1079 | 93 | 1.62 (1.51, 1.75) | 1.31 (1.19, 1.44) | |
| 5 (81-101 years) | 788 | 751 | 95 | 2.07 (1.90, 2.25) | 1.47 (1.32, 1.64) | |
| **PS** | | | | | | |
| PS 0 | 975 | 772 | 79 | | | <0.001 |
| PS 1 | 1919 | 1653 | 86 | 1.39 (1.28, 1.52) | 1.34 (1.24, 1.45) | |
| PS 2 | 1437 | 1344 | 94 | 2.19 (2.01, 2.40) | 1.83 (1.67, 2.00) | |
| PS 3 | 868 | 847 | 98 | 3.82 (3.46, 4.21) | 2.65 (2.36, 2.99) | |
| PS 4 | 269 | 265 | 99 | 8.63 (7.40, 9.95) | 5.01 (4.05, 6.19) | |
| Missing | 2314 | 2100 | 91 | 1.86 (1.71, 2.02) | 1.63 (1.50, 1.77) | |
| **Stage** | | | | | | |
| Limited | 1319 | 1043 | 79 | | | 0.001 |
| Extensive | 3053 | 2894 | 95 | 2.45 (2.28, 2.63) | 2.07 (1.92, 2.25) | |
| missing | 3410 | 3044 | 89 | 1.74 (1.62, 1.87) | 1.43 (1.31, 1.57) | |
| **Townsend quintile** | | | | | | |
| 1 (most affluent) | 1075 | 947 | 88 | | | 0.341 |
| 2 | 1378 | 1234 | 90 | 1.04 (0.96, 1.13) | 1.07 (0.98, 1.17) | |
| 3 | 1523 | 1365 | 90 | 1.08 (0.99, 1.17) | 1.07 (0.97, 1.17) | |
| 4 | 1650 | 1490 | 90 | 1.05 (0.97, 1.14) | 1.07 (0.98, 1.18) | |
| 5 (least affluent) | 2138 | 1929 | 90 | 1.05 (0.97, 1.13) | 1.07 (0.96, 1.19) | |
| Missing | 18 | 16 | 89 | 1.13 (0.69, 1.85) | 1.52 (1.15, 2.02) | |
| **Ethnic group** | | | | | | |
| White | 6015 | 5439 | 90 | | | 0.422^ |
| Black | 31 | 26 | 84 | 0.71 (0.49, 1.05) | 0.79 (0.56, 1.11) | |
| Asian | 396 | 344 | 87 | 1.06 (0.95, 1.19) | 1.01 (0.88, 1.15) | |
| Mixed | 14 | 11 | 79 | 0.69 (0.38, 1.24) | 0.78 (0.47, 1.31) | |
| Other | 37 | 32 | 87 | 1.00 (0.71, 1.42) | 0.84 (0.46, 1.52) | |
| Missing | 1289 | 1129 | 88 | 1.00 (0.93, 1.06) | 1.04 (0.94, 1.14) | |
| **Charlson Index** | | | | | | |
| 0 | 3466 | 3015 | 87 | | | <0.001 |
| 1 | 1483 | 1301 | 88 | 1.23 (1.15, 1.32) | 1.07 (1.01, 1.14) | |
| 2 or 3 | 1080 | 967 | 90 | 1.35 (1.25, 1.45) | 1.11 (1.02, 1.22) | |
| 4 + | 1753 | 1698 | 97 | 2.09 (1.97, 2.22) | 1.62 (1.49, 1.77) | |
| **Chemotherapy** | | | | | | |
| No | 2967 | 2825 | 95 | | | <0.001 |
| Yes | 4815 | 4156 | 86 | 0.43 (0.41, 0.45) | 0.51 (0.46, 0.56) | |
| **Trial entry** | | | | | | |
| <5% | 5282 | 4739 | 90 | | | 0.83 |
| >5% | 2500 | 2242 | 90 | 0.96 (0.91, 1.01) | 0.99 (0.88, 1.10) | |

Legend: (%)* percentage of patients from each subgroup who have died
** Hazard ratio adjusted for all other variables in the table.
Analysis clustered by NHS Trust.
^ this is the result of a likelihood ratio test.

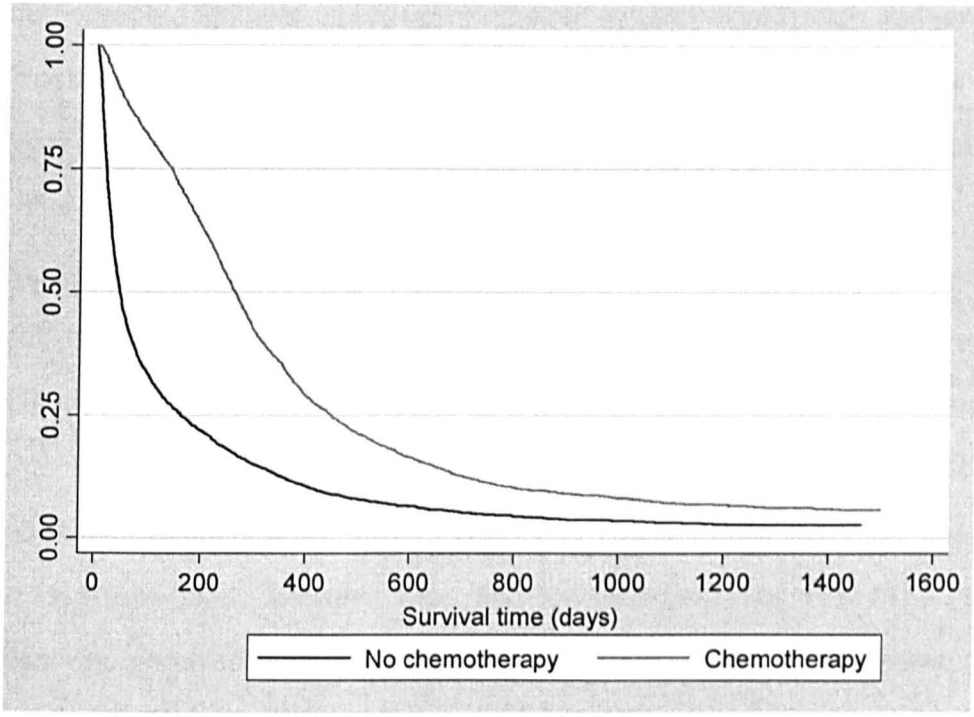



Figure 7.1; Kaplan-Meier survival curve comparing the observed survival in those who did, compared with those who did not, have chemotherapy.

Table 7.4 demonstrates that those patients with limited stage disease who received chemo-radiotherapy had a better overall survival than those who received chemotherapy alone (adjusted Hazard ratio 0.72, 95% confidence interval 0.62, 0.84).

Table 7.4: Results of Cox regression analyses assessing the influence of chemo-radiotherapy versus other treatment regimes. Clustered by NHS Trust.

| | N | N who died | %* | Unadj. HR (95% CI) | Adj. HR** (95% CI) | P value |
|---|---|---|---|---|---|---|
| **Whole cohort** | **7782** | | | | | |
| CTx alone | 3914 | 3463 | 88 | | | <0.001 |
| CTx and RTx | 861 | 670 | 78 | 0.66 (0.61, 0.72) | 0.70 (0.65, 0.76) | |
| **Limited stage** | **1319** | | | | | |
| CTx alone | 737 | 594 | 81 | | | <0.001 |
| CTx and RTx | 280 | 184 | 66 | 0.69 (0.58, 0.81) | 0.72 (0.62, 0.84) | |

Legend: N= Number of patients
(%)* percentage of patients from each subgroup who have died
** Hazard ratio adjusted for sex, age quintile, performance status, stage (whole cohort only), ethnic group, Townsend quintile, Charlson Index.
**Footnote;** some patients had no record of any treatment received, and some received surgery, whilst others received radiotherapy only.
Whole cohort; no treatment N=2360; surgery N=148; radiotherapy only N=499.
Limited stage: no treatment N=218; surgery N=20; radiotherapy only N=64.

The demographic features of patients first seen in centres with high and low trial participation were similar (table 7.5), although the proportion of patients from the least affluent quintile of society was higher in centres with high compared with low trial participation. Although there were differences in stage and performance status between the two types of centres this will in part reflect the size of the cohort. The main difference between the high and low trial participation centres were in the missing data. Most importantly in the group of patients likely to receive chemotherapy, good performance status (0-1) and limited stage disease the proportions were very similar (36% and 37% and 16% and 17% respectively between high and low centres). Of the 4820 (61%) patients who received chemotherapy, 34% were first seen in centres with high trial participation. Survival after chemotherapy was not affected by whether or not a patient had been first seen in a centre with high compared with low trial participation, adjusted Hazard ratio 1.05 (95% confidence interval 0.97, 1.13).

Table 7.5: Demographic features of patients with small cell lung cancer based on the where they were first seen. Total number of patients with small cell lung cancer is 7,845.

| | Centre with high trial participation | | Centre with low trial participation | | P value |
|---|---|---|---|---|---|
| | (N=2,524) | (%)* | (N=5,321) | (%)* | |
| **Sex** | | | | | 0.446 |
| Male | 1401 | 56 | 2844 | 53 | |
| Female | 1123 | 44 | 2477 | 47 | |
| **Median age** | 69 years (IQR 61 to 75) | | 69 years (IQR 62 to 76) | | |
| **Performance status** | | | | | 0.001 |
| 0 | 331 | 13 | 646 | 12 | |
| 1 | 579 | 23 | 1346 | 25 | |
| 2 | 420 | 17 | 1024 | 19 | |
| 3 | 254 | 10 | 622 | 12 | |
| 4 | 74 | 3 | 210 | 4 | |
| Missing | 866 | 34 | 1473 | 28 | |
| **Stage** | | | | | 0.001 |
| Limited | 393 | 16 | 930 | 17 | |
| Extensive | 844 | 33 | 2234 | 42 | |
| Missing | 1287 | 51 | 2157 | 41 | |
| **Charlson Index** | | | | | 0.175 |
| 0 | 1124 | 46 | 2358 | 44 | |
| 1 | 460 | 18 | 1032 | 19 | |
| 2 or 3 | 350 | 14 | 740 | 14 | |
| 4+ | 590 | 23 | 1191 | 22 | |
| **Townsend quintile** | | | | | <0.001 |
| 1 (most affluent) | 351 | 14 | 736 | 14 | |
| 2 | 406 | 16 | 979 | 18 | |
| 3 | 460 | 18 | 1070 | 20 | |
| 4 | 483 | 19 | 1186 | 22 | |
| 5 (least affluent) | 821 | 33 | 1333 | 25 | |
| **Chemotherapy** | | | | | <0.001 |
| No | 866 | 34 | 2159 | 41 | |
| Yes | 1658 | 66 | 3162 | 59 | |

Legend: (%)* percentage

## 7.4 Discussion

### 7.4.1 Principle findings

These results demonstrate that there is considerable variation in the use of chemotherapy in people with small cell lung cancer. Older age and the presence of co-morbidity were both associated with a decrease in the use of chemotherapy, but even after allowing for these there was wide variations in use between NHS Trusts in England. Trusts with an interest in recruiting people into lung cancer clinical trials in general were more likely to give chemotherapy to people with small cell lung cancer, and this difference was not explained by individual patient features.

My results show that male sex, increasing age, co-morbidity, worsening performance status, and extensive stage disease were all independently associated with a worse survival. Whether or not a patient received chemotherapy was also independently associated with survival (adjusted Hazard ratio of 0.51, 95% confidence interval 0.46, 0.56). The beneficial effects of chemotherapy on survival amongst the patients who were treated with chemotherapy were the same whether a patient was first seen in a high or low trial centre, suggesting that the increased use of chemotherapy in centres with high trial participation was not associated with an increase in chemotherapy related deaths. This in turn suggests that the high trial centres are not tending to over treat people and that there is scope to increase the use of chemotherapy in the centres with low trial participation.

### 7.4.2 Strengths and weaknesses

Although the National Lung Cancer Audit (NLCA) is non-mandatory, I have previously shown that this is a valid and representative dataset (36). There is also evidence that the case ascertainment rate in the NLCA is now in excess of 90% (35, 63), and so this chapter is based on one of the largest, contemporary

clinical lung cancer datasets in the world. One potential weakness of this research is that my data on co-morbidity relate only to diagnoses associated with hospital admissions. As a result I may not have captured details of every condition managed independently by general practitioners, and so my derived Charlson Indices may be too low, and there may be some residual confounding by co-morbidity. However, I think that this is unlikely to be the case, as the range of Charlson Indices observed in this cohort is similar to those in cohorts of patients from a general practitioner dataset (55) and patients with lung cancer (79, 80). Furthermore my analyses showed that although co-morbidity was an important predictor of survival it did not confound the association between the use of chemotherapy and survival.

I acknowledge that using entry into clinical trials as a surrogate for chemotherapy practice may in itself explain the variation in access to chemotherapy described. However, the cut-off for the centres with high trial participation was only 5% entry of expected patients into clinical trials, and so the majority of individuals with small cell lung cancer would have received chemotherapy outside a clinical trial. Furthermore, this study analyses the extent of variation amongst NHS Trusts having accounted for all patient features.

It is not possible to elicit from the dataset the number of patients who were offered chemotherapy but declined, nor the frequency of side-effects and toxicity from the chemotherapy.

### 7.4.3 Comparison with other studies

The annual reports from the National Lung Cancer Audit have described variation in chemotherapy use amongst individuals with small cell lung cancer across England although they have not adjusted for co-morbidity. In the 2009 report (which assessed data from patients first seen in 2008) this proportion ranged from 0.00 to 1.00, which shows that the variation over the years 2004-2008 that

I have described in this chapter, still holds at the end of the study period. In a separate study Jack et al described variation in treatment rates and overall survival in lung cancer patients in South East England, but again no adjustment was made for performance status or co-morbidity (51). Patients first seen at a radiotherapy centre were more likely to receive 'active treatment', chemotherapy and radiotherapy (51). Several major policy documents have been published by the Department of Health over the past fifteen years (24, 27, 88). One of the major themes has been the creation of specialist cancer centres, and there is evidence that patients first seen by a lung cancer specialist are more likely to receive 'active treatment', including chemotherapy, than those who are not (67), and centralised referral for lung cancer has been associated with improved survival rates (87). However, the creation of specialist cancer centres will potentially generate greater inequality in access to treatment as the distance and time spent travelling increases. Jones and Crawford have both described a reduction in the likelihood of receiving chemotherapy in lung cancer patients as distance to hospital increased (47, 86), and Campbell reported a poorer survival after diagnosis for individuals with lung cancer as distance from a cancer centre increased (85). Given chemotherapy is available in all NHS Trusts, and recommended for the treatment of all patients with small cell lung cancer (26, 89), it should be possible to make access to this treatment more equitable. My results have shown that the increased use of chemotherapy in centres with high trial participation is not at the detriment of overall patient survival. Therefore there is reason to expect that increasing the rate of chemotherapy use in small cell lung cancer would result in patient benefit.

I have also been able to demonstrate in a large cohort, that chemo-radiotherapy has a survival advantage over chemotherapy alone. This supports the previously reported long-term survival gain of this multimodality treatment (90, 91), and would suggest that chemo-radiotherapy becomes the treatment of choice in

individuals with good performance status and limited stage small cell lung cancer.

My research also showed that as age increased the use of chemotherapy decreased even after adjusting for stage, performance status and co-morbidity. This is in keeping with several publications (92-94), despite evidence that overall response to chemotherapy is not diminished in people with small cell lung cancer aged over 70 years (95). Janssen-Heijnen et al (1998) found that, in patients over the age of 70 years the presence of even a single co-morbid illness reduced the use of chemotherapy (96), suggesting a reluctance to use these treatments in older patients. This supports my evidence that it is not the associated co-morbidity rise with age that is wholly responsible for the observed decline in chemotherapy use as patients get older. The apparent reluctance to provide chemotherapy in elderly patients with small cell lung cancer is not supported by evidence of a poor safety record (94, 97, 98).

### 7.4.4 Implications of this study

My results have shown evidence of the beneficial effects of chemotherapy for people with small cell lung cancer in England, but also the evidence of variations in access to this treatment dependent upon age and hospital attended. The main determinants of Trust level variation are not known and this is an important research question that needs addressing in the future development of the NLCA. The standards set in the 2004-2007 Peer Review process do not appear to have captured sufficient detail to distinguish between the performance of multi-disciplinary teams in different NHS Trusts. With regard to age it is clear that further debate is needed in the lung cancer community about the decision to withhold treatment from older people with lung cancer.

# Chapter eight: Lung cancer in young adults: a different disease entity?

## 8.1 Introduction

Lung cancer is primarily a disease of older age, but approximately 1-2% of patients are less than 40 years of age at diagnosis (99). Some studies have reported a poorer prognosis in this young adult subgroup (100, 101), although it is not known if this reflects late presentation on behalf of the patient, or a more aggressive disease. Other studies have reported an equivalent prognosis following surgery for young adults with lung cancer and their older counterparts (102-104). However, these studies tend to be small case series in single centres evaluating one treatment modality, where the number of patients is inadequate to allow robust conclusions to be drawn.

Young adults often have dependent children and are in paid employment and so a condition with such a poor prognosis will generate a significant socio-economic burden. Any research which can influence the prompt diagnosis of lung cancer and optimise its management, will improve clinical effectiveness.

The aim of this chapter was to use the National Lung Cancer Audit dataset to examine the clinical and socio-demographic features of a large cohort of young adults (aged 20-40 years) with lung cancer, and to compare these findings with their older counterparts and with published literature on lung cancer in young adults. In particular I was keen to quantify the variation in access to treatment and post-operative survival in this young adult cohort.

## 8.2 Methods

I used the third dataset downloaded from the National Lung Cancer Audit, which included all patients first seen before 31st December 2008. Individuals without a sex recorded were excluded, as were those aged less than 20 years at diagnosis, and those patients in whom it was not possible to generate a start date. In order to assess the effect of age at diagnosis on clinical features and outcome measures, all patients aged between twenty and forty years (inclusive) at diagnosis were grouped together. The remainder of the cohort were divided into decades up to those aged 81 years and above.

The dataset was examined for any variation in key clinical features, namely: sex, histology, performance status (as classified by the Eastern Cooperative Oncology Group), and stage at presentation (as classified by the American Joint Committee on Cancer and Union Internationale Contre le Cancer version 6). In order to evaluate socio-economic status, the Townsend quintile for each patient was derived from the Lower Super Output Area (LSOA) based on their residential postcode. In order to create a binary variable for treatment received, I used the date of surgery, chemotherapy and radiotherapy as recorded in the NLCA. Multivariate logistic regression was performed to assess the likelihood of receiving each treatment modality across the age groups, adjusting for all the patient features mentioned above.

Although the third dataset was the most up-to-date and contained the largest number of young adults, it did not contain information regarding co-morbidities which had been derived from the HES linked dataset (dataset 2). Therefore I decided to perform a sensitivity analysis using a subset of this cohort of young adults. This subset included all individuals aged between 20 and 40 years (inclusive) present in the HES linked dataset (dataset 2). This allowed me to record the distribution of disease groups pertinent to the Charlson Index as well

as calculating a composite score for co-morbidity, the Charlson Index, to determine the relevance of co-morbid illness in this young adult subgroup.

For the survival analyses a start date was created as described in section 5.2.4.2. An end date was generated using either the date of death (obtained from the Personal Demographics Service), or the date the dataset was downloaded, 25th January 2010. Those patients who were diagnosed on death certificate only, and had a date of death on or before their date of diagnosis were excluded from survival analyses. Cox regression analyses were performed to calculate Hazard ratios for mortality across the age groups, and then a multivariate model was constructed to adjust for all patient features. Nelson Aalen plots were inspected.

### 8.2.1 Non-small cell lung cancer

In addition, within this cohort of young adult patients, I focussed on the subgroup with pre-treatment proven non-small cell lung cancer (NSCLC), and examined their clinical features (including histological subtype), their likelihood of receiving surgery, and their post-operative survival. These features have been reported in the literature before and I was keen to see if our unselected, national Audit dataset would produce similar results.

## 8.3 Results

The NLCA dataset included a total of 95,932 patients seen at English NHS Trusts with their first hospital appointment before 31st December 2008. Figure 8.1 describes the exclusion of certain individuals on the basis that they had no sex recorded (2), were less than 20 years old at diagnosis (17), or that it was not possible to assign a start date (4,603, 5%). Therefore the overall cohort contained 91,310 individuals with lung cancer of whom 583 patients (0.6%) were aged between 20-40 years, and this was the subgroup used for all subsequent analyses. Figure 8.2 illustrates the median interval between several points along the patient pathway, and figure 8.3 shows the distribution of the young adult subgroup based on age at diagnosis.

The sex ratio in the young adult group was 1.3:1, male:female. This was similar to that for the whole cohort, 1.4:1, male:female. Table 8.1 shows the variation in histological subtypes across the different age groups. The young adult group demonstrated a higher proportion of adenocarcinomas, and carcinoid tumours. Despite the long latency period from exposure to disease, there were 5 patients with proven mesothelioma in this young adult subgroup.

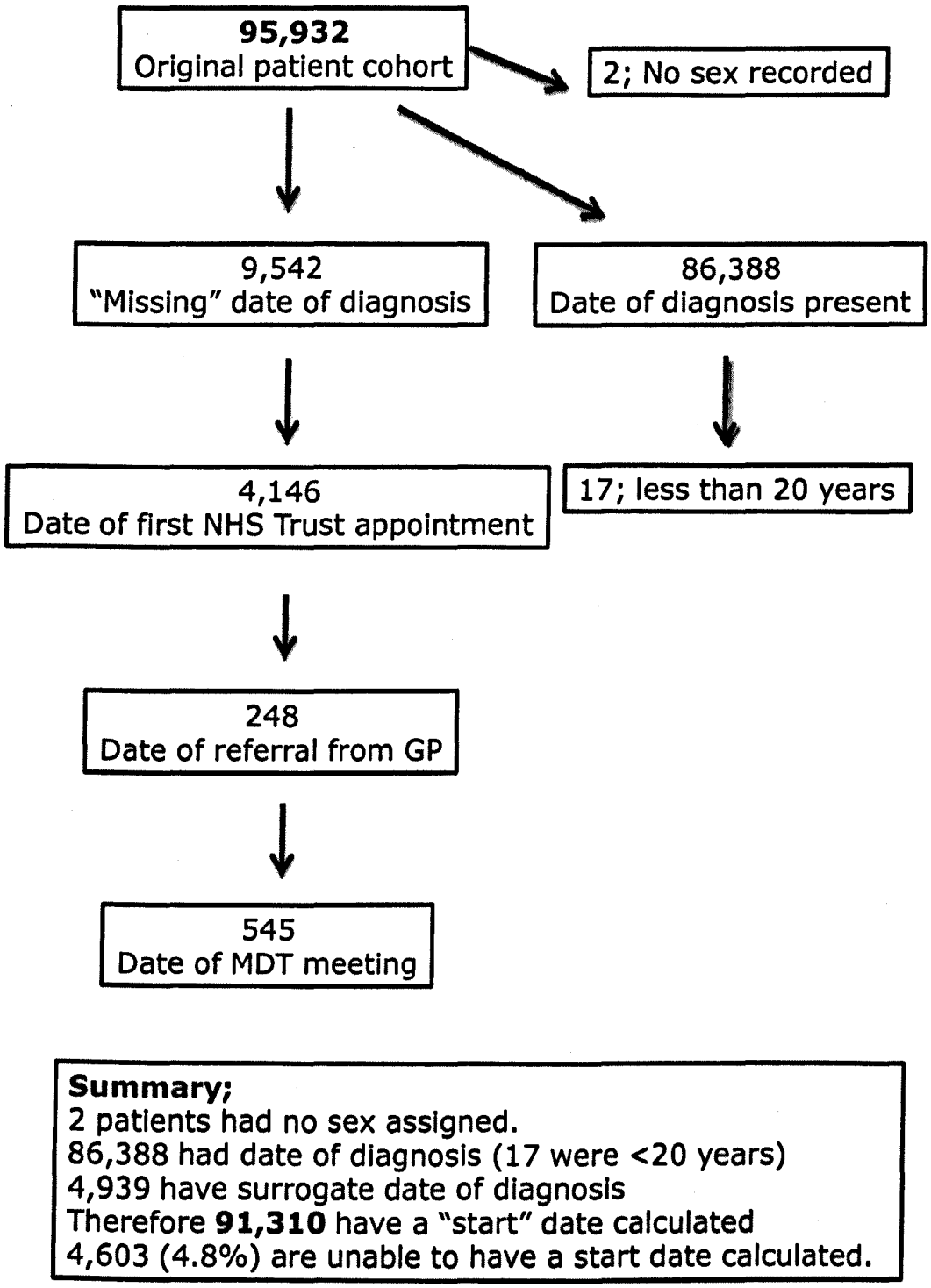



Figure 8.1: Flow diagram depicting the method used to calculate start dates.

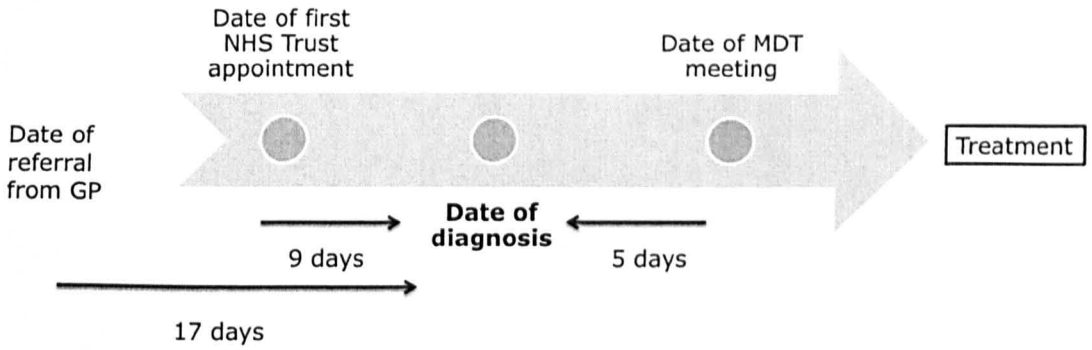



Figure 8.2: Median interval between dates along the patient pathway.

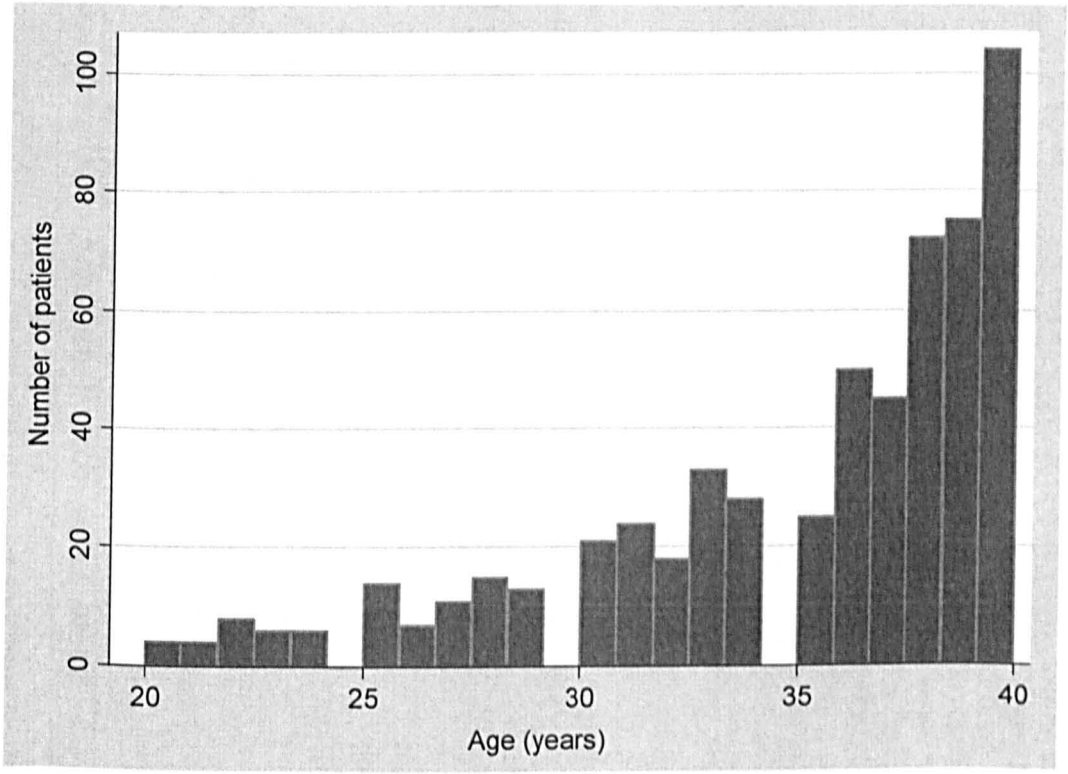



Fig 8.3: Histogram of age range for this young adult subgroup

Table 8.1: Histological subtypes based on age.

| Histology | 20-40 | (%) | 40's | (%) | 50's | (%) | 60's | (%) | 70's | (%) | >80 | (%) | Total |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Non Small Cell** | 227 | | 1345 | | 5746 | | 12,009 | | 13,812 | | 5260 | | (38,399) |
| NOS | 72 | (12) | 474 | (16) | 1979 | (16) | 3943 | (15) | 4594 | (14) | 1761 | (10) | 12824 |
| Squamous | 36 | (6) | 303 | (10) | 1593 | (13) | 4037 | (15) | 4884 | (15) | 1832 | (11) | 12685 |
| Adenocarcinoma | 102 | (17) | 468 | (16) | 1772 | (14) | 3237 | (12) | 3479 | (11) | 1325 | (8) | 10385 |
| Large cell | 11 | (2) | 72 | (2) | 268 | (2) | 484 | (2) | 519 | (2) | 194 | (1) | 1548 |
| Mixed | 0 | | 4 | (0) | 29 | (0) | 45 | (0) | 49 | (0) | 21 | (0) | 148 |
| Bronchoalveolar cell | 5 | (1) | 20 | (1) | 85 | (1) | 210 | (1) | 223 | (1) | 88 | (1) | 631 |
| Carcinoma-in-situ | 1 | (0) | 4 | (0) | 20 | (0) | 53 | (0) | 64 | (0) | 39 | (0) | 181 |
| **Small cell** | 29 | (5) | 327 | (11) | 1556 | (13) | 3005 | (11) | 2882 | (9) | 854 | (5) | 8653 |
| **Carcinoid** | 34 | (6) | 29 | (1) | 52 | (0) | 82 | (0) | 64 | (0) | 23 | (0) | 284 |
| Other | 40 | (7) | 100 | (3) | 297 | (2) | 571 | (2) | 668 | (2) | 363 | (2) | 2039 |
| Mesothelioma | 5 | (1) | 48 | (2) | 398 | (3) | 1076 | (4) | 1133 | (3) | 462 | (3) | 3122 |
| Missing | 248 | (43) | 1079 | (37) | 4201 | (34) | 9553 | (36) | 13881 | (43) | 9851 | (59) | 38,813 |
| **Total** | **583** | | **2928** | | **12,250** | | **26,296** | | **32,440** | | **16,813** | | **91,310** |

Legend: (SNOMed codes for histology; SNOMed III (1992)/ICD-O-2)
NOS: Not otherwise specified (M8046/3)
Squamous cell carcinoma (M8070/3)
Adenocarcinoma (M8140/3)
Mixed: Mixed non-small cell lung cancer (M8940/3)
Broncho-alveolar cell carcinoma (M8250/3)
Carcinoma-in-situ (M8010/2)
Other (including Carcino-sarcoma): (M8980/3, M9999/9)
Mesothelioma: (M9050/3, M9052/3, M9051/3)

The performance status at diagnosis was missing in 51% of this young adult subgroup. However, it was 0 or 1 in 80% of those individuals who had a performance status recorded. Only 4 patients were recorded with a performance status of 4 (1%), compared with 1,093 (7%) of the patients aged over 80 years (figure 8.4).

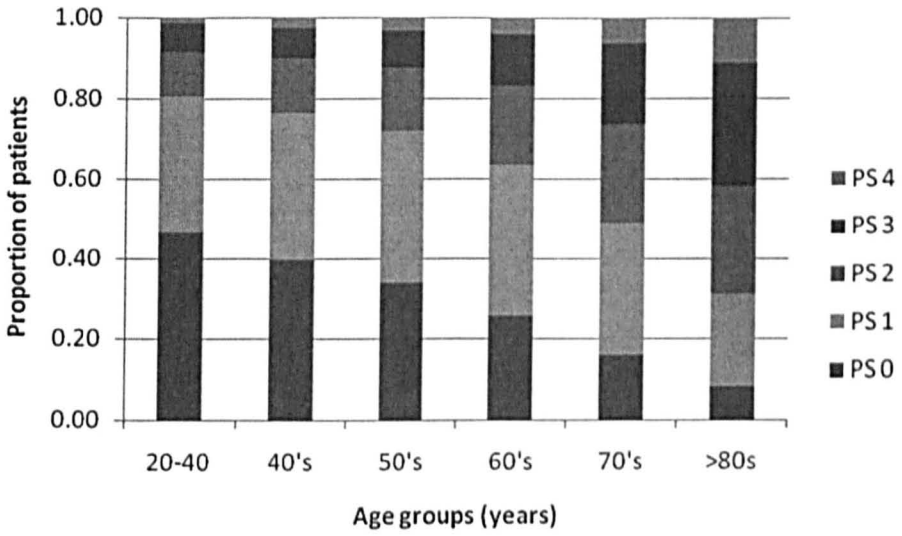



Figure 8.4: Distribution of performance status across age groups (if recorded).

Unfortunately 372 (64%) young adult patients did not have stage at diagnosis recorded. Of the remaining 211 patients, 116 (55%) had stage IV disease, and only 35 (17%) had stage I or II disease. The results for stage at diagnosis across the age groups are illustrated in Table 8.2.

Table 8.2: Distribution of stage (UICC version 6) at presentation across age groups

| Stage | 20-40 | (%) | 40's | (%) | 50's | (%) | 60's | (%) | 70's | (%) | >81 | (%) | Total |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| IA | 11 | (2) | 77 | (3) | 321 | (3) | 793 | (3) | 1016 | (3) | 449 | (3) | 2667 |
| IB | 16 | (3) | 81 | (3) | 389 | (3) | 1048 | (4) | 1587 | (5) | 816 | (5) | 3937 |
| IIA | 0 | (0) | 9 | (0) | 58 | (0) | 133 | (1) | 144 | (0) | 62 | (0) | 406 |
| IIB | 8 | (1) | 58 | (2) | 297 | (2) | 766 | (3) | 916 | (3) | 426 | (3) | 2471 |
| IIIA | 24 | (4) | 143 | (5) | 574 | (5) | 1418 | (5) | 1793 | (6) | 825 | (5) | 4777 |
| IIIB | 36 | (6) | 303 | (10) | 1350 | (11) | 2813 | (11) | 3268 | (10) | 1809 | (11) | 9579 |
| IV | 116 | (20) | 731 | (25) | 3228 | (26) | 6417 | (24) | 7666 | (24) | 3780 | (22) | 21938 |
| Occult | 0 | 0 | 3 | 0 | 9 | 0 | 33 | 0 | 37 | 0 | 12 | 0 | 94 |
| Missing | 372 | (64) | 1523 | (52) | 6024 | (49) | 12875 | (49) | 16013 | (49) | 8634 | (51) | 45441 |
| **Total** | **583** | | **2928** | | **12,250** | | **26,296** | | **32,440** | | **16,813** | | **91,310** |

With respect to socio-economic status the data revealed a third of patients within this young adult subgroup were from the least affluent quintile, whilst only 9% were from the most affluent. In contrast, 21% of patients aged >80 years at diagnosis were from the least affluent, and 16% were from the most affluent quintile. This variation does reach statistical significance when tested using a $chi^2$ test ($p<0.001$). Figure 8.5 illustrates the variation in socio-economic status across the age groups. It was not possible to calculate a Townsend quintile in 222 patients as they did not have data on their LSOA (N=91,088).

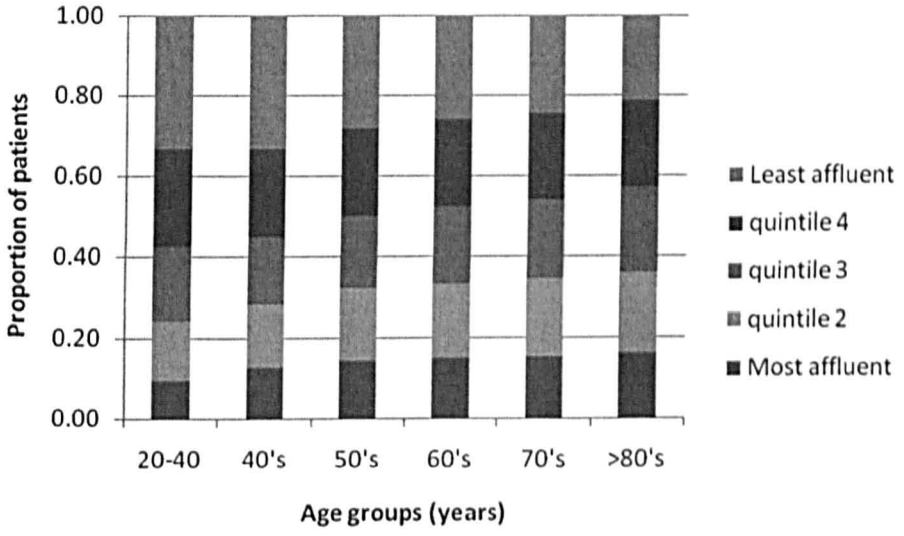



Figure 8.5: Distribution of Townsend quintiles across age groups (N=91,088)

Co-morbidity

The earlier download from the NLCA which was linked to HES (dataset 2) had 461 individuals with lung cancer aged between 20 and 40 years inclusive. In this subgroup the median Charlson Index was zero, with an interquartile range of 0 to 1. Therefore only 25% of this cohort had a Charlson Index of 1 and above. The maximum Charlson Index was 12, and this was in a patient with AIDS who had metastatic disease at diagnosis. The distribution of disease groups is shown in table 8.3.

Table 8.3: Distribution of disease groups in young adult subgroup (N=461).

| Component disease group | Number | % cohort |
|---|---|---|
| Myocardial infarction/heart failure | 3 | 0.7 |
| Cerebrovascular disease | 4 | 0.8 |
| Chronic pulmonary disease | 43 | 9 |
| Dementia | 0 | |
| Peptic ulcer disease | 1 | |
| Diabetes (without complications) | 9 | 2 |
| Peripheral vascular disease | 9 | 2 |
| Connective tissue disease | 3 | 0.7 |
| Cancer (solid organ) | 36 | 8 |
| Haematological malignancy | 7 | 1.5 |
| Diabetes with complications | 3 | 0.7 |
| Hemiplegia/paraplegia | 1 | |
| Renal disease | 1 | |
| Severe liver failure | 0 | |
| Metastases | 66 | 14 |
| AIDS | 2 | 0.4 |

Table 8.3 demonstrates the low level of co-morbid illness in this young adult subgroup, supporting the high proportion of individuals with a good performance status. However, 8% of these young adults had had another malignant disease before being diagnosed with lung cancer, although this is less than the cohort as a whole, described in chapter 5, when the proportion was 14%. The proportion of young adults with metastatic disease at diagnosis (14%) is the same as for the whole cohort described in chapter 5.

### 8.3.1 Treatment received

Within the cohort of young adult patients, 100 (17%) underwent surgical resection, of whom 3 received adjuvant chemotherapy and 10 adjuvant radiotherapy, and 3 adjuvant chemo-radiotherapy. Chemotherapy alone was

given to 158 (27%), and radiotherapy alone to 40 (7%) of the young adult cohort. A further 41 (7%) received combination chemo-radiotherapy. A total of 247 (42%) individuals within the young adult subgroup had no record of a 'date of treatment' within the NLCA dataset. Table 8.4 demonstrates the relationship between the age group of a patient and the influence this may have on the likelihood of receiving treatment. For those patients with proven non-small cell lung cancer there was no significant variation in the likelihood of receiving surgery between the young adult group and patients over 40 years of age, until the subgroup of patients aged 71-80 years. This older age group were 40% less likely to receive surgery for their NSCLC than the young adult subgroup (adjusted OR 0.62, 95% CI 0.40, 0.96, p=0.03). Older patients with small cell lung cancer were less likely to receive chemotherapy compared with the young adults, although this only achieved statistical significance over the age of 60 years (adjusted OR 0.29, 95% CI 0.09, 1.00, p=0.05). However the results for radiotherapy were quite different. This analysis included all patients within the cohort, regardless of underlying histology or treatment intent (palliative vs radical). Table 8.4 shows that as patients get older, up to the age of 80 years, they are more likely to receive radiotherapy compared with the young adult subgroup. Over the age of 80 years the adjusted Odds Ratio falls a little, although it remains significantly higher than in the young adult subgroup (adj OR 1.39, 95% CI 1.09, 1,77). This may reflect the use of radiotherapy in both active palliative and potentially curative regimes, which suggests individuals in the older age groups were perhaps receiving radiotherapy with palliative intent. Although the treatment intent is recorded within the NLCA, it is not clear whether this can reliably differentiate between palliative and radical radiotherapy. These results suggest that, with the exception of radiotherapy, patients in the young adult subgroup are no less likely to receive active treatment than older adults.

Table 8.4: Logistic regression analyses examining the influence of age on access to treatment.

| | N | Number who received treatment | (%)* | Unadjusted OR (95% CI) | Adjusted** OR (95% CI) |
|---|---|---|---|---|---|
| **Surgery (NSCLC only; N=38,399)** | | | | | |
| 20-40 | 227 | 30 | 13 | | |
| 41-50 | 1345 | 209 | 16 | 1.21 (0.80, 1.82) | 0.94 (0.59, 1.49) |
| 51-60 | 5746 | 896 | 16 | 1.21 (0.82, 1.79) | 0.93 (0.60, 1.43) |
| 61-70 | 12009 | 1897 | 16 | 1.23 (0.84, 1.81) | 0.86 (0.56, 1.32) |
| 71-80 | 13812 | 1703 | 12 | 0.92 (0.63, 1.36) | 0.62 (0.40, 0.96) |
| >80's | 5260 | 278 | 5 | 0.37 (0.24, 0.55) | 0.24 (0.15, 0.37) |
| **Chemotherapy (Small cell only; N=8653)** | | | | | |
| 20-40 | 29 | 26 | 90 | | |
| 41-50 | 327 | 243 | 74 | 0.33 (0.10, 1.13) | 0.33 (0.10, 1.15) |
| 51-60 | 1556 | 1163 | 75 | 0.34 (0.10, 1.13) | 0.38 (0.11, 1.30) |
| 61-70 | 3005 | 2030 | 68 | 0.24 (0.07, 0.80) | 0.29 (0.09, 1.00) |
| 71-80 | 2882 | 1590 | 55 | 0.14 (0.04, 0.47) | 0.18 (0.05, 0.61) |
| >80's | 854 | 271 | 32 | 0.05 (0.02, 0.18) | 0.07 (0.02, 0.25) |
| **Radiotherapy (whole cohort; N=91,310)** | | | | | |
| 20-40 | 583 | 81 | 14 | | |
| 41-50 | 2928 | 630 | 22 | 1.70 (1.32, 2.18) | 1.59 (1.23, 2.05) |
| 51-60 | 12250 | 2828 | 23 | 1.86 (1.47, 2.36) | 1.68 (1.32, 2.15) |
| 61-70 | 26296 | 6001 | 23 | 1.83 (1.45, 2.32) | 1.65 (1.30, 2.10) |
| 71-80 | 32440 | 7315 | 23 | 1.80 (1.42, 2.28) | 1.67 (1.31, 2.13) |
| >80's | 16813 | 3052 | 18 | 1.37 (1.08, 1.74) | 1.39 (1.09, 1.77) |

Legend: (%)* percentage of each age group receiving specific treatment.
** Odds Ratio (OR) adjusted for sex, performance status, histology (unless otherwise specified), stage and Townsend quintile.

### 8.3.2 Survival

Cox regression analysis for the whole cohort, revealed young adult patients were less likely to die than patients from all other age groups (table 8.5). Specifically, even patients in their forties were 57% more likely to die than those between 20-40 years of age at diagnosis (adjusted HR 1.57, $p<0.01$, 95% CI 1.40, 1.77).

Table 8.5: Cox regression analyses assessing the influence of age on overall survival.

| Age groups | N | N who died | (%)* | HR (95% CI) | Adj HR** (95% CI) |
|---|---|---|---|---|---|
| 20-40 years | 583 | 317 | 54 | | |
| 40's | 2928 | 2121 | 72 | 1.66 (1.47, 1.87) | 1.57 (1.40, 1.77) |
| 50's | 12250 | 9611 | 78 | 1.96 (1.75, 2.20) | 1.79 (1.60, 2.01) |
| 60's | 26296 | 21192 | 81 | 2.16 (1.93, 2.41) | 1.97 (1.76, 2.21) |
| 70's | 32440 | 27719 | 85 | 2.63 (2.35, 2.94) | 2.30 (2.05, 2.57) |
| >80's | 16813 | 15250 | 91 | 3.38 (3.02, 3.78) | 2.70 (2.41, 3.02) |

Legend: (%)* percentage of each age group who have died.
** Hazard Ratio (HR) adjusted for sex, performance status, histology, stage and Townsend quintile.

However, given carcinoid disease does not have the typical prognostic profile of lung cancer per se, and given there was a high proportion of individuals with carcinoid disease amongst the subgroup of young adults, I repeated the overall Cox regression analysis excluding all patients with carcinoid disease. The results are depicted in table 8.6.

Table 8.6: Cox regression for all individuals excluding those with carcinoid disease (N=91,026)

| Age groups | N | N who died | (%)* | HR (95% CI) | Adj HR** (95% CI) |
|---|---|---|---|---|---|
| 20-40 years | 549 | 316 | 58 | | |
| 40's | 2899 | 2118 | 73 | 1.55 (1.38, 1.74) | 1.61 (1.43, 1.81) |
| 50's | 12198 | 9606 | 79 | 1.96 (1.63, 2.04) | 1.85 (1.66, 2.08) |
| 60's | 26214 | 21174 | 81 | 2.00 (1.79, 2.24) | 2.03 (1.82, 2.27) |
| 70's | 32376 | 27701 | 86 | 2.43 (2.17, 2.72) | 2.34 (2.09, 2.62) |
| >80's | 16790 | 15239 | 91 | 3.38 (2.79, 3.49) | 2.79 (2.41, 3.02) |

Legend: (%)* percentage of each age group who have died.
** Hazard Ratio adjusted for sex, performance status, histology, stage and Townsend quintile.

Table 8.6 shows that, even after all those individuals with proven carcinoid disease were excluded, the likelihood of death continued to rise considerably with age. Those individuals who are in their forties were 60% more likely to die compared with those between the age of 20 and 40 years (adjusted Hazard Ratio 1.61, 95% confidence interval 1.43, 1.81). I repeated the analyses in those

individuals with proven non-small cell lung cancer and small cell lung cancer, tables 8.7 and 8.8 respectively. These results show that once the histological subgroup is defined, it is only really those individuals in their seventies and over who have an increased likelihood of death compared to those between 20 and 40 years of age at diagnosis.

Table 8.7: Cox regression for those individuals with proven non-small cell lung cancer (N=38,399)

| Age groups | N | N who died | (%)* | HR (95% CI) | Adj HR** (95% CI) |
|---|---|---|---|---|---|
| 20-40 years | 227 | 181 | 80 | | |
| 40's | 1345 | 1065 | 79 | 1.01 (0.86, 1.18) | 1.13 (0.97, 1.33) |
| 50's | 5746 | 4601 | 80 | 1.03 (0.89, 1.19) | 1.13 (0.97, 1.31) |
| 60's | 12009 | 9560 | 80 | 1.04 (0.90, 1.21) | 1.17 (1.01, 1.35) |
| 70's | 13812 | 11636 | 84 | 1.24 (1.07, 1.44) | 1.31 (1.13, 1.52) |
| >80's | 5260 | 4703 | 89 | 1.60 (1.38, 1.86) | 1.55 (1.34, 1.81) |

Legend: (%)* percentage of each age group who have died.
** Hazard Ratio adjusted for sex, performance status, stage and Townsend quintile.

Table 8.8: Cox regression for those individuals with proven small cell lung cancer (N=8653)

| Age groups | N | N who died | (%)* | HR (95% CI) | Adj HR** (95% CI) |
|---|---|---|---|---|---|
| 20-40 years | 29 | 27 | 93 | | |
| 40's | 327 | 282 | 86 | 0.84 (0.57, 1.25) | 1.01 (0.64, 1.60) |
| 50's | 1556 | 1355 | 87 | 0.92 (0.63, 1.34) | 0.95 (0.61, 1.48) |
| 60's | 3005 | 2735 | 91 | 1.10 (0.76, 1.61) | 1.07 (0.69, 1.67) |
| 70's | 2882 | 2663 | 92 | 1.34 (0.92, 1.95) | 1.26 (0.81, 1.96) |
| >80's | 854 | 827 | 97 | 1.91 (1.30, 2.80) | 1.73 (1.11, 2.71) |

Legend: (%)* percentage of each age group who have died.
** Hazard Ratio adjusted for sex, performance status, stage (limited or extensive) and Townsend quintile.

Finally, I decided to perform survival analyses for those individuals without histology prior to treatment. In contrast to the analyses where histology is known, non-small cell and small cell lung cancer (table 8.7 and 8.8 respectively), in the absence of known histology there is a significant increase in likelihood of death as age increases. An individual over the age of 80 years, with 'missing'

data for histology, is more than 4 times as likely to die compared with someone between the ages of 20 and 40 years with 'missing' histology (adjusted HR 4.26, 95% CI 3.48, 5.21) (table 8.9).

Table 8.9: Cox regression for those individuals with 'missing' data for histology (N=38,277)

| Age groups | N | N who died | (%)* | HR (95% CI) | Adj HR** (95% CI) |
|---|---|---|---|---|---|
| 20-40 years | 248 | 100 | 40 | | |
| 40's | 1079 | 681 | 63 | 1.97 (1.60, 1.97) | 2.01 (1.63, 2.50) |
| 50's | 4201 | 3144 | 75 | 2.71 (2.21, 3.32) | 2.72 (2.22, 3.34) |
| 60's | 9553 | 7603 | 80 | 3.20 (2.62, 3.91) | 3.17 (2.59, 3.87) |
| 70's | 13881 | 11898 | 86 | 4.03 (3.30, 4.93) | 3.77 (3.09, 4.61) |
| >80's | 9851 | 8982 | 91 | 5.07 (4.15, 6.20) | 4.26 (3.48, 5.21) |

Legend: (%)* percentage of each age group who have died.
** Hazard Ratio adjusted for sex, performance status, stage and Townsend quintile.

### 8.3.3 Non-small cell lung cancer

There were 227 patients with proven non-small cell lung cancer (NSCLC) in the young adult subgroup, of whom 45% were adenocarcinoma, 30% Non-small cell not-otherwise-specified (NOS), and only 16% were squamous cell carcinoma. Within this young adult subgroup with proven NSCLC only 25 (11%) were staged IA to IIIA, and 94 (41%) had stage IV disease at diagnosis (table 8.10). Despite this advanced stage the performance status at diagnosis was good, with 118 recorded as PS 0 or 1 (52%). The number of young adult patients with NSCLC having surgery was 30 (13%), of whom 13 had stage I to IIIA disease, 3 had stage IIIB and a further 3 had stage IV disease. The remaining 11 surgical patients had missing data for stage.

Table 8.10: Distribution of stage in proven NSCLC patients across age groups (N=38,399).

| Stage | 20-40 | (%) | 40's | (%) | 50's | (%) | 60's | (%) | 70's | (%) | >80's | (%) | Total |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| IA | 2 | (1) | 38 | (3) | 187 | (3) | 443 | (4) | 473 | (3) | 146 | (3) | 1289 |
| IB | 4 | (2) | 55 | (4) | 246 | (4) | 679 | (6) | 985 | (7) | 366 | (7) | 2335 |
| IIA | 0 | (0) | 6 | (0) | 38 | (1) | 72 | (1) | 72 | (1) | 30 | (1) | 218 |
| IIB | 4 | (2) | 39 | (3) | 204 | (4) | 546 | (5) | 585 | (4) | 230 | (4) | 1608 |
| IIIA | 15 | (7) | 103 | (8) | 403 | (7) | 987 | (8) | 1148 | (8) | 394 | (7) | 3050 |
| IIIB | 28 | (12) | 208 | (15) | 922 | (16) | 1934 | (16) | 2103 | (15) | 860 | (16) | 6055 |
| IV | 94 | (41) | 504 | (37) | 2139 | (37) | 3941 | (33) | 4210 | (30) | 1475 | (28) | 12363 |
| Occult | 0 | (0) | 1 | (0) | 6 | (0) | 23 | (0) | 17 | (0) | 3 | (0) | 50 |
| Missing | 80 | (35) | 391 | (29) | 1601 | (28) | 3384 | (28) | 4219 | (31) | 1756 | (33) | 11431 |
| **Total** | **227** | | **1345** | | **5746** | | **12,009** | | **13,812** | | **5260** | | **38,399** |

As previously mentioned, there was no evidence that young adults with proven NSCLC were less likely to receive surgery than any other age group. Cox regression for this specific subgroup of patients, with proven NSCLC who underwent surgery, revealed no variation in overall mortality across the age groups (table 8.11). There was no evidence that young adults had a worse prognosis after surgical resection than any other age group.

Table 8.11: Cox regression analysis on the subgroup of patients with proven NSCLC who underwent surgical resection (N=5,013).

| Age (years) | N | N who died | (%)* | Unadj HR (95% CI) | Adj HR** (95% CI) |
|---|---|---|---|---|---|
| 20-40 | 30 | 13 | 43 | | |
| 40's | 209 | 81 | 39 | 0.85 (0.47, 1.53) | 1.10 (0.61, 1.97) |
| 50's | 896 | 361 | 40 | 0.95 (0.55, 1.65) | 1.08 (0.62, 1.89) |
| 60's | 1897 | 757 | 40 | 0.94 (0.54, 1.63) | 1.12 (0.64, 1.93) |
| 70's | 1703 | 799 | 47 | 1.21 (0.70, 2.10) | 1.42 (0.82, 2.46) |
| >80's | 278 | 152 | 55 | 1.57 (0.89, 2.77) | 1.74 (0.98, 3.07) |

Legend: (%)* percentage of each age group who have died.
** Hazard Ratio (HR) adjusted for sex, performance status, stage and Townsend quintile.

These results can also be illustrated in a Kaplan-Meier survival curve. Figure 8.6 shows that for those patients with NSCLC who had an operation, the order in which half an age subgroup had died, was as follows: >80 years, seventies, young subgroup, sixties, fifties and then those in their forties.

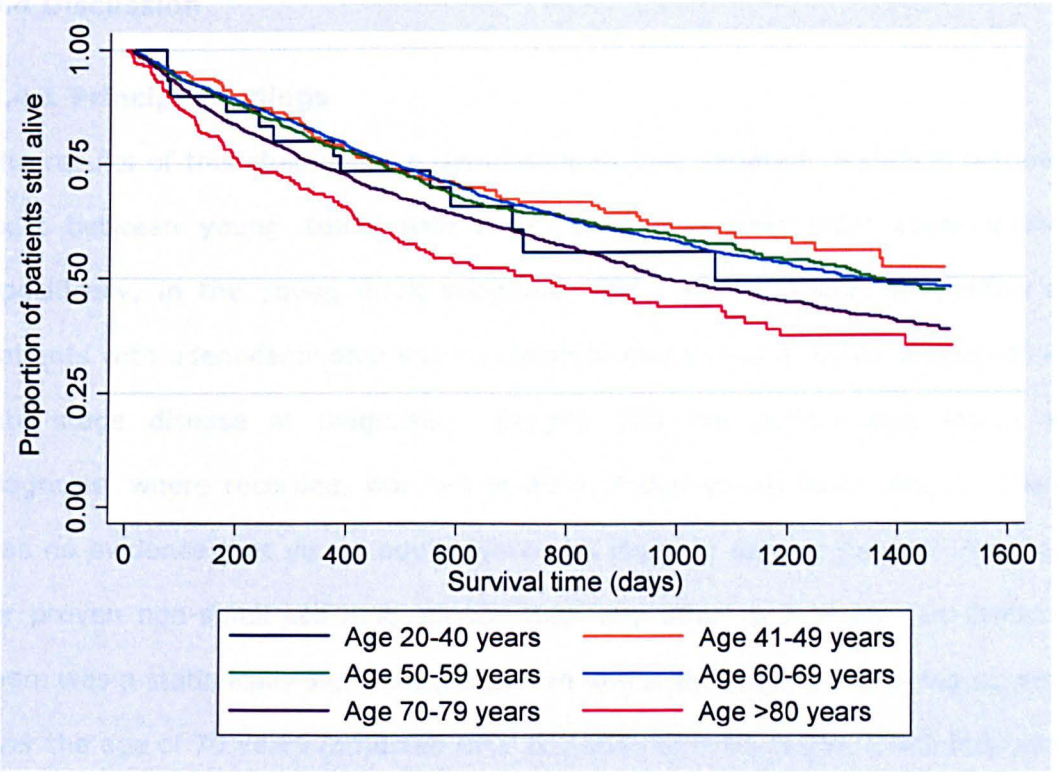



Figure 8.6: Kaplan-Meier survival curve for individuals with NSCLC who have undergone surgical resection (N=5,013).

## 8.4 Discussion

### 8.4.1 Principle findings

The results of this chapter have demonstrated that variation in clinical features exist between young adults with lung cancer and their older counterparts. Specifically, in the young adult subgroup, there was a greater proportion of patients with adenocarcinoma and carcinoid tumours, and a higher proportion of late stage disease at diagnosis. Despite this the performance status at diagnosis, where recorded, was 0-1 in 80% of this young adult cohort. There was no evidence that young adults were less likely to receive surgical resection for proven non-small cell lung cancer, than any other age group. In contrast there was a statistically significant reduction in the likelihood of receiving surgery over the age of 70 years (adjusted OR 0.62, 95% CI 0.40, 0.96), which has been described elsewhere (53, 92).

The likelihood of receiving chemotherapy for proven small cell lung cancer was reduced in all decades above the age of 40 years, although this did not reach statistical significance until the subgroup of patients in their sixties. This has also been reported by me in Chapter 7 and elsewhere (92-94), and may reflect the poorer performance status of patients as they got older (92), which can preclude the use of chemotherapy.

The likelihood of receiving radiotherapy, regardless of histological subtype, was approximately equal amongst all patients aged between 40-80 years, and was significantly higher than in the young adult subgroup. This may reflect the use of radiotherapy in palliative as well as potentially curative treatment regimes. The data recorded in the National Lung Cancer Audit at the time of my research were inadequate to differentiate the treatment intent.

Cox regression analyses revealed an increased likelihood of death as age increased, regardless of histological subtype, despite adjusting for sex, performance status, stage, and socio-economic status. Subgroup analysis revealed that this effect persisted when all individuals with carcinoid disease were excluded. However, when individual histological subgroup analyses were performed (non-small cell and small cell), the effect was less marked. In those individuals with 'missing' data for histology, the age related increase in likelihood of death was greatest. It is worth noting that in none of these subgroup analyses did the young adult subgroup have a poorer prognosis than their older counterparts.

In the subgroup of patients with proven non-small cell lung cancer who underwent surgical resection, there was no evidence of a reduction in overall survival amongst the young adult subgroup.

### 8.4.2 Strengths and weaknesses

The strength of this research lies in the large cohort of patients aged between 20 and 40 years, which have been drawn from an unbiased, unselected, contemporary national cohort of patients with lung cancer (36). The size of the cohort provides robust clinical and demographic data, which can be used to assess potential inequalities in patient care and survival based on age. The weaknesses of the NLCA dataset are that it does not contain detailed information on patient co-morbidity, and that a number of the data fields have missing data. There is evidence that the proportion of missing data is decreasing year on year and that the quality of the dataset is therefore improving (35, 63). Furthermore when I used a slightly earlier download from the NLCA which had been linked to HES, I found that very few of these young adults had any co-morbid illness, except 14% who presented with metastatic disease, although it is not known whether or not this is directly attributable to their underlying lung cancer.

Despite these limitations, this cohort of 583 young adult patients remains the largest cohort of young adults with lung cancer described in published literature.

### 8.4.3 Comparison with other studies

There is very little published literature on lung cancer in a young adult population, and these studies are usually small, retrospective case series in the one medical institution. This study is not restricted to one histological subtype, one treatment modality, or one medical institution. These data corroborate previously published evidence that adenocarcinoma and carcinoid tumours are more common in this young adult subgroup (99, 105-108). Retrospective studies have also demonstrated the low rate of early stage disease in the young adult subgroup observed here (100-102, 108). Of note, a study from Mexico in 1987, found 46 of 48 young adult patients had stage IV disease at diagnosis (100). This may reflect the duration of symptoms prior to diagnosis, which has been reported as longer in young adults compared to older counterparts (108), but these data are not held in the NLCA dataset.

The proportion of patients without evidence of treatment appears high (42%), but it may reflect poor data entry into the NLCA dataset, in addition to late stage at presentation. Green et al described a population with a similar high proportion of late stage disease, and the rate of "no treatment" was also 42% (100).

There was no evidence that survival was worse in the young adult subgroup overall, in contrast to some published data (100, 101), but in keeping with others (99, 102). Bourke et al published a multicentre retrospective study looking at variation in clinical features, treatment received and survival in young adult patients in Chicago, Israel and northern Italy (108). This paper allows comparison of young adult patients in three distinct geographical areas, and

found variation in survival of the young adult subgroup between countries. This inequality is not a result of histological subtype, differences in sex ratio, smoking history nor treatment received; but is almost certainly a reflection of stage of disease at diagnosis. Within the Chicago cohort (n=83), only 7% were stage I, compared with 16% of the cohort in Israel (N=43), and five year survival in Chicago was 8% compared to 25% in the Israeli young adult subgroup. Within my cohort of 583 young adults, although there was a large amount of missing data for stage, only 5% of patients had stage I disease. Five year survival data for this cohort is not yet available, but the results of Cox regression demonstrated no increased rate of mortality in the young compared to older patient groups.

Amongst published surgical case series, with between 22 and 110 young adult patients (103, 104), there does not appear to be any adverse survival affect of young age, which is in keeping with these findings (n=30 with resected non-small cell lung cancer).

### 8.4.4 Implications of this study

This research has demonstrated that amongst a large cohort of young adult patients with lung cancer in England, very few patients have early stage disease at diagnosis. This could suggest denial or ignorance on the part of patients, and highlights the need for a public health response in terms of educating society, regarding the symptoms and signs of lung cancer and the importance of early detection. There also needs to be a greater level of clinical suspicion amongst general practitioners, and hospital doctors to ensure lung cancer is on the differential diagnosis of adults less than 40 years who present with relevant symptoms and signs.

Despite this, there was no evidence that survival overall, nor in the subgroup with proven NSCLC treated surgically, was adversely affected in the young adult subgroup. Given their good performance status, and the likelihood their co-morbidities are few, it would seem reasonable to recommend a proactive, even aggressive approach in managing these young adults with lung cancer.

# Chapter 9: Summary and future research

## 9.1 Summary

During my period of research and demonstrated by this thesis I have been able to establish that the National Lung Cancer Audit dataset is an unbiased and representative, unselected cohort of individuals with lung cancer in England. I have also created, for the first time, a composite score of co-morbidity for every individual with lung cancer, and to accurately assess the influence this has on access to treatment and survival. This work has culminated in the publication of three papers in peer review journals, as well as several abstracts at national and international conferences. This has led to the acceptance of the National Lung Cancer Audit within the lung cancer clinical field, and reinforced the importance of prospective audit in health service research.

The main findings are:

- that socio-economic status does not affect the likelihood of an individual going on to have either surgery or radiotherapy, but that as deprivation increased the likelihood of having chemotherapy declined.
- an individual with NSCLC is more likely to have surgery if they are first seen in an NHS Trust that is a thoracic surgical centre, and surgery has a positive independent influence on overall survival.
- an individual with small cell lung cancer is more likely to have chemotherapy if they are first seen in an NHS Trust that has a higher level of participation in clinical trials, and chemotherapy has a positive independent influence on overall survival.
- a large proportion of young adults with lung cancer have advanced disease at diagnosis which makes curative treatment impossible, despite a good performance status. There was no evidence that young adults with NSCLC who underwent surgery had a poorer survival than their older counterparts.

In order to address the geographical variation previously reported for outcomes from lung cancer, I have tried to quantify the facilities and performance of MDTs in NHS Trusts across England. There is wide variation in the practice observed which appears to be based on the facilities available. However, there needs to be a more detailed analysis of what it is within a thoracic surgical centre which leads to the increased likelihood of a patient undergoing surgery if first seen there. This will need to be a piece of qualitative research, evaluating the MDTs, the access to investigations, the number of lung cancer nurse specialists, and/or perhaps the personalities of the members of the MDT themselves.

### 9.2 Future research

The NLCA contains good data on patient features, but there is a need to collect more information regarding the NHS Trusts, and the multi-disciplinary teams involved in lung cancer care. Although the overall score from Peer Review appeared to be a poor marker of clinical outcomes for lung cancer it may be that individual standards within the overall score are more discriminating. Further research needs to focus on specific aspects of the lung cancer MDT, and the attendance of specific team members. It may also be important to evaluate more recent results from the, now annual, Peer Review process, which will allow a more contemporaneous comparison with up-to-date data from within the NLCA.

The following list contains features which may well contribute to the patient pathway and encourage both efficiency and a proactive approach to lung cancer management.

- the number of clinical and medical oncologists,
- the number of thoracic surgeons,
- a dedicated lung cancer lead physician,
- formal administrative support to the lung multi-disciplinary team,

- a dedicated radiologist, and on-site PET scanners,
- a dedicated histopathologist,
- ITU facilities on site,
- the surgical capacity of the Trust,
- the number of lung cancer specialist nurses
- on-site cardiology/respiratory physiology assessment.

The influence of these features warrants further research and is an area I am particularly interested in.

The National Lung Cancer Audit has huge research potential, and will allow detailed investigation into several key clinical questions. I am grateful to the RCP Clinical Effectiveness and Evaluation Unit for allowing me to use the remaining research grant to continue my research. This will allow me to dedicate 4 hours a week (1PA of my consultant job plan) to pursue my interest in health service research. Specifically I intend to:

1: use the NLCA dataset and other data sources to evaluate in more detail the results of Peer Review and whether they reflect clinical outcomes for individuals with lung cancer. I would also like to use the NLCA/HES linked dataset to investigate clinical outcomes based on route of entry to hospital (emergency, out-patient or planned admission).

2: assist Dr Helen Powell (a respiratory SpR), who starts a PhD continuing the research I started in lung cancer health service research in August 2011. Within her PhD plan we intend to investigate:

-What is the current rate of death within 30 days of surgery or chemotherapy?

-Which patient features help to predict survival post-operatively, or post-chemotherapy?

-What level of risk is an individual with lung cancer willing to accept?

-Who sets the bar for an acceptable level of risk?

-What reasons are given for refusing the treatment recommended by the MDT?

3: pursue my role as co-chair of the ERS taskforce in Quality Management of Lung Cancer Care. Within this role I have already produced, distributed and begun to collate the results of, a national questionnaire of lung cancer physicians from 42 European countries. I have also co-ordinated the production of an on-line survey of local lung cancer services in every European country, and we have had more than 400 responses so far.

## Appendices

**Appendix 1: Tutorials**

The National Agenda for Lung Cancer and Mesothelioma

Essential Documents in Lung Cancer and Mesothelioma

The Cancer Reform Strategy

Recent developments in lung cancer

Running an MDT meeting

Professional relationships and the MDT

An effective lung cancer service

Clinical Trials in Lung Cancer and Mesothelioma

Clinical aspects 1 – selection for radical treatment

Clinical aspects 2 – palliative chemotherapy

Clinical aspects 3 – palliative radiotherapy

Clinical aspects 4 – endobronchial therapy

Clinical aspects 5 – Specialist Palliative Care

Clinical aspects 6 – keeping patients informed

Clinical aspects 7 – The lung cancer clinical nurse specialist

Clinical aspects 8 – approach to diagnosis

Change management

Managing Conflict

## Appendix 2: Scoping document for the NICE lung cancer update

### 1 Guideline title

The diagnosis and treatment of lung cancer (update of NICE clinical guideline 24)

### *1.1 Short title*

Lung cancer update

### 2 Background

a) The National Institute for Health and Clinical Excellence ('NICE' or 'the Institute') has commissioned the National Collaborating Centre for Cancer to review recent evidence on the management of lung cancer and to update the existing guideline 'The diagnosis and treatment of lung cancer' (NICE clinical guideline 24, 2005) for use in the NHS in England and Wales. The update will provide recommendations for good practice that are based on the best available evidence of clinical and cost effectiveness.

b) NICE clinical guidelines support the implementation of National Service Frameworks (NSFs) in those aspects of care for which a Framework has been published. The statements in each NSF reflect the evidence that was used at the time the Framework was prepared. The clinical guidelines and technology appraisals published by NICE after an NSF has been issued have the effect of updating the Framework.

c) NICE clinical guidelines support the role of healthcare professionals in providing care in partnership with patients, taking account of their individual needs and preferences, and ensuring that patients (and their carers and families, if appropriate) can make informed decisions about their care and treatment.

### 3 Clinical need for the guideline

a) There are more than 38,000 new cases of lung cancer in the UK each year and more than 35,000 people die from the condition; more than for breast cancer and colorectal cancer combined.

b) Lung cancer is now the leading cause of cancer death in women.

c) About 90% of lung cancers are caused by smoking. Now that fewer men smoke, lung cancer deaths in men have decreased by more than a quarter in the UK (a 27% reduction between 1971 and 2006). However, the number of women who smoke has risen and deaths from lung cancer in women have increased.

d) Only about 5.5% lung cancers can be cured. Although the cure rate is rising slowly, the rate of improvement has been slower than that for other common cancers.

e) Outcomes in the UK are worse than those in some European countries and North America.

f) There is evidence that outcomes vary within the UK, which – among other factors – may be explained by variations in the standard of care.

g) NICE clinical guidelines are regularly reviewed, and updated as necessary. As part of its review of NICE clinical guideline 24, the National Collaborating Centre for Cancer convened a Lung Cancer Expert Advisory Group in June 2007 to discuss whether any part (or all) of the existing guideline needed updating. The advisory group comprised members of the original Guideline Development Group and other invited specialists involved in the delivery of lung cancer services.

h) The Advisory Group identified significant progression and expansion of the evidence base since the publication of NICE clinical guideline 24, indicating that a large number of recommendations would need to be updated. It also identified new topics not included in the original guideline.

i) In September 2007 the NICE Guidance Executive agreed to a partial update of the guideline (including new topics where appropriate) with an 18 month development time. In order to produce a high quality update within the allotted time, in line with the methods set out in 'The guidelines manual' (2009), it will not be possible to update the entire lung cancer guideline. Therefore we intend to focus on topics:

- for which there is important new published evidence
- that are still controversial or uncertain
- in which there continues to be identifiable variation in practice, and
- that will have the most significant impact on the clinical service and management of patients with lung cancer.

j) A draft list of the prioritised clinical topics to be included in the updated guideline were then developed using advice from the Advisory Group, the GDG chair, the GDG clinical lead and attendees at the stakeholder scoping workshop. These topics were included as an Appendix in the draft scope that was issued to stakeholders for consultation in November 2008.

## 4 The guideline

a) The guideline development process is described in detail in two publications that are available from the NICE website (see 'Further information'). 'The guideline development process: an overview for stakeholders, the public and the NHS' describes how organisations can become involved in the development of a guideline. 'The guidelines manual' provides advice on the technical aspects of guideline development.

b) This scope defines exactly what this guideline will (and will not) examine, and what the guideline developers will consider.

c) The guideline update will include:

- updated topics and recommendations, and supporting evidence
- new topics and recommendations, and supporting evidence
- 'old' topics and recommendations that do not need updating and are therefore still valid. The evidence that supported these recommendations will not be updated.

d) There will be some important topics that need updating but are not part of the final prioritised list. These will be added to a holding list for future consideration and the final guideline will make this clear to the reader.

e) The areas that will be addressed by the guideline are described in the following sections.

### *4.1 Population*

#### 4.1.1 Groups that will be covered

a) Adults (18 years and older) with newly diagnosed non-small-cell lung cancer (NSCLC).

b) Adults with newly diagnosed small cell lung cancer (SCLC).

c) Adults with relapsed NSCLC.

d) Adults with relapsed SCLC.

#### 4.1.2 Groups that will not be covered

a) Adults with mesothelioma.

b) Adults with lung metastases arising from primary cancers originating outside the lung.

c) Children (younger than 18) with lung cancer.

d) Adults with rare lung tumours (for example, pulmonary blastoma).

e) Adults with benign lung tumours (for example, bronchial adenoma).

### *4.2 Healthcare setting*

a) Primary care – excluding population-based and opportunistic screening and prevention.

b) Secondary care.

c) Tertiary care by services offering specialist care (for example, thoracic surgery, radiotherapy and interventional bronchoscopy).

### *4.3 Clinical management (including service delivery where appropriate)*

a) Diagnosis and staging.

b) Information for patient and carers.

c) Radical treatment of patients with NSCLC.

d) Palliative endobronchial therapies.

e) Management of patients with SCLC.

f) Follow up.

g) Service organisation and inequality of management at key decision points to be addressed by the needs assessment Status

#### 4.3.1 Scope

This is the final scope.

#### 4.3.2 Guideline

The development of the guideline recommendations will begin in February 2009.

## 5 Related NICE guidance

### Published guidance

The following guidance will be cross referred to as appropriate:

- Bevacizumab for the treatment of non-small-cell lung cancer (terminated appraisal). NICE technology appraisal 148 (2008). See www.nice.org.uk/TA148
- Erlotinib for the treatment of non-small cell lung cancer. NICE technology appraisal guidance 162 (2008). Available from www.nice.org.uk/TA162
- Endobronchial ultrasound-guided transbronchial needle aspiration (EBUS-TBNA) for mediastinal masses. NICE interventional procedure guidance 254 (2008). Available from www.nice.org.uk/IPG254
- Pemetrexed for the treatment of non-small-cell lung cancer. NICE technology appraisal guidance 124 (2007). Available from www.nice.org.uk/TA124
- Percutaneous radiofrequency ablation for primary and secondary lung cancers. NICE interventional procedure guidance 185 (2006). Available from www.nice.org.uk/IPG185

• Referral guidelines for suspected cancer. NICE clinical guideline 27 (2005). Available from www.nice.org.uk/CG027

• Photodynamic therapy for localised inoperable endobronchial carcinoma. NICE interventional procedure guidance 137 (2005). Available from www.nice.org.uk/IPG137

• Photodynamic therapy for advanced bronchial carcinoma. NICE Interventional procedure guidance 87 (2004). Available from www.nice.org.uk/IPG087

• Cryosurgery for malignant endobronchial obstruction. NICE interventional procedure guidance 142 (2005). Available from www.nice.org.uk/IPG142

• Improving supportive and palliative care for adults with cancer. Guidance on cancer services (2004). Available from www.nice.org.uk/csgsp

• Docetaxel, paclitaxel, gemcitabine and vinorelbine for the treatment of non-small cell lung cancer. NICE technology appraisal guidance 26 (2001). (updated by and incorporated into NICE clinical guideline 24).

**Appendix 3: NICE Lung cancer update 2010:**

**Needs Assessment questionnaire**

**1. MDT composition and attendance:**

a) What specialty is the current named Lung cancer lead? *(please circle)*

Resp physician Oncologist (Clinical/Medical) Radiologist Surgeon Pathologist

b) Do you have a designated member of the MDT from the following disciplines?
Do they form part of your MDT quorum?
And approximately what percentage of MDTs did each member attend last year?

| | Designated member? | How many? | Part of MDT quorum? | % meetings attended? |
|---|---|---|---|---|
| Thoracic Surgeon | Yes/no | | Yes/no | |
| Medical Oncologist | Yes/no | | Yes/no | |
| Clinical Oncologist | Yes/no | | Yes/no | |
| Histopathologist | Yes/no | | Yes/no | |
| Radiologist | Yes/no | | Yes/no | |
| Respiratory physicians | Yes/no | | Yes/no | |
| Member of Palliative Care team | Yes/no | | Yes/no | |
| Cancer Nurse specialist | Yes/no | | Yes/no | |
| Cardiothoracic Nurse | Yes/no | | Yes/no | |

c) Does this MDT discuss cases from outside the immediate NHS Trust?
Yes/no *(please circle)*

**2. Lung cancer nurses:**

a) How many Full-Time Equivalent (FTE) Lung cancer nurses are there in your NHS Trust? _____

b) Approximately how many ***new*** patients would each nurse be allocated per year? _____

c) Are there any formal cover arrangements made for sick leave and annual leave? Yes/no

d) Is there any secretarial support provided for the nurses? Yes/no

e) Is there a designated lung cancer palliative care/Macmillan nurse? Yes/no

f) Do the lung cancer nurses provide 'support groups' Yes/no
To allow patients and carers to discuss the diagnosis and treatment etc

g) Are there any nurse-led follow-up clinics? Yes/no

h) Do the nurses provide telephone support for patients and carers? Yes/no

**3. Cardiothoracic (surgical) Nurse Specialist:**

a) Do you have access to a Thoracic Nurse specialist? Yes/no

b) If so, do they see patients pre-operatively? Yes/no

c) Does the patient get a telephone number to contact with post-operative concerns? Yes/no

d) Are there nurse-led post-op clinics? Yes/no

**4. MDT decision making:**

a) How many patients were discussed at your MDT in 2009? _____

b) How many/what percentage of these patients had a PET scan? _____

c) How many/what percentage of the total number actually received radical treatment? _____

d) Of those patients receiving radical treatment,

What percentage received surgery? _____

What percentage received radical radiotherapy? _____

e) What percentage of patients enter clinical trials?

<5% 5-10% >10%

**5. Administrative support:**

a) Does your Trust have an MDT co-ordinator? Yes/no

b) Does your Trust have an electronic database? Yes/no

c) Does your Trust have a data administrator? Yes/no

d) Does your Trust routinely upload information to LUCADA? Yes/no

## 6. Availability of specialist services:

a) Please confirm which of the following services are available either within your hospital, your NHS Trust, your lung cancer network, or at a higher regional level.

***(please tick appropriate column)***

If services are ***not available*** at your hospital; please indicate the distance from your hospital to the treatment site and the approximate waiting time to utilise the specialist service (**1**, < 1 week; **2**, 1-2 weeks; **3**, >2 weeks)

| | ***Available?*** | | | | | |
|---|---|---|---|---|---|---|
| | Hospital | NHS Trust | Network | Region | Distance (miles) | Waiting time? |
| PET scanning | | | | | | |
| ***Interventional bronchoscopy*** | | | | | | |
| TBNA | | | | | | |
| EBUS | | | | | | |
| EUS | | | | | | |
| Endobronchial stenting | | | | | | |
| Electrocautery | | | | | | |
| Laser therapy | | | | | | |
| Cryotherapy | | | | | | |
| Photodynamic therapy (PDT) | | | | | | |
| Brachytherapy | | | | | | |
| ***Thoracoscopy*** | | | | | | |
| Medical (LA) | | | | | | |
| Surgical (VATS) | | | | | | |
| ***Other services*** | | | | | | |
| Mediastinoscopy | | | | | | |
| Pulmonary rehabilitation | | | | | | |
| Specialist SOB clinics | | | | | | |
| ***Treatment options*** | | | | | | |
| CHART | | | | | | |
| Radical RTx | | | | | | |
| Palliative RTX | | | | | | |
| Chemotherapy | | | | | | |
| Thoracic surgery | | | | | | |

Legend: TBNA; TransBronchial Needle Aspiration;
EBUS; EndoBronchial UltraSound (needle biopsy)
EUS; Endoscopic UltraSound (needle biopsy)
SOB; Shortness of breath
RTx; Radiotherapy

b) Please indicate the pathology 'turn around' time;
Diagnostic samples _____ (days)
Surgical samples _____ (days)

**Appendix 4: Letter sent to Lung cancer lead physicians**

Division of Epidemiology and Public Health

University of Nottingham

NG5 1PB

anna.rich@nottingham.ac.uk

5th March 2009

Dear Lung Cancer lead,

We are a research team funded by the Royal College of Physicians to host a Fellow in Lung Cancer (Dr Anna Rich) with the remit to examine the LUCADA dataset and look at ways in which it can be used to influence a change in service. As part of the initial validation process, we are investigating the completeness of LUCADA to ensure that lack of completeness does not bias future analyses. We have already completed some work in this area but need your help.

We need to know the total number of lung cancer and mesothelioma patients 'first seen' at your trust for the period 01/01/2007 to 31/12/2007. Your trust has been randomly selected, and this correspondence comes via Dr Roz Stanley at the Information Centre in Leeds. She has kindly agreed to distribute these letters, and forward the responses to us.

We are very grateful for your attention to this as the information you provide will greatly assist in correlating LUCADA figures with your own.

Yours faithfully,

Dr Anna Rich, RCP Fellow.

Dr David Baldwin, Consultant Physician, Lung Cancer Lead, Hon Lecturer.

Prof Richard Hubbard, BLF Professor of Respiratory Epidemiology.

**Appendix 5: ICD-10 codes for diagnoses pertinent to the Charlson Index**

| | | | | | |
|---|---|---|---|---|---|
| **ICD-10** | **disease** | **score** | C048 | cancer | 2 |
| B200 | aids | 6 | C049 | cancer | 2 |
| B201 | aids | 6 | C050 | cancer | 2 |
| B202 | aids | 6 | C051 | cancer | 2 |
| B203 | aids | 6 | C052 | cancer | 2 |
| B204 | aids | 6 | C058 | cancer | 2 |
| B205 | aids | 6 | C059 | cancer | 2 |
| B206 | aids | 6 | C060 | cancer | 2 |
| B207 | aids | 6 | C061 | cancer | 2 |
| B208 | aids | 6 | C062 | cancer | 2 |
| B209 | aids | 6 | C068 | cancer | 2 |
| B210 | aids | 6 | C069 | cancer | 2 |
| B211 | aids | 6 | C07X | cancer | 2 |
| B212 | aids | 6 | C080 | cancer | 2 |
| B213 | aids | 6 | C081 | cancer | 2 |
| B217 | aids | 6 | C088 | cancer | 2 |
| B218 | aids | 6 | C089 | cancer | 2 |
| B219 | aids | 6 | C090 | cancer | 2 |
| B220 | aids | 6 | C091 | cancer | 2 |
| B221 | aids | 6 | C098 | cancer | 2 |
| B222 | aids | 6 | C099 | cancer | 2 |
| B227 | aids | 6 | C100 | cancer | 2 |
| B230 | aids | 6 | C101 | cancer | 2 |
| B231 | aids | 6 | C102 | cancer | 2 |
| B232 | aids | 6 | C103 | cancer | 2 |
| B238 | aids | 6 | C104 | cancer | 2 |
| B24X | aids | 6 | C108 | cancer | 2 |
| C000 | cancer | 2 | C109 | cancer | 2 |
| C001 | cancer | 2 | C110 | cancer | 2 |
| C002 | cancer | 2 | C111 | cancer | 2 |
| C003 | cancer | 2 | C112 | cancer | 2 |
| C004 | cancer | 2 | C113 | cancer | 2 |
| C005 | cancer | 2 | C118 | cancer | 2 |
| C006 | cancer | 2 | C119 | cancer | 2 |
| C008 | cancer | 2 | C12X | cancer | 2 |
| C009 | cancer | 2 | C130 | cancer | 2 |
| C01X | cancer | 2 | C131 | cancer | 2 |
| C020 | cancer | 2 | C132 | cancer | 2 |
| C021 | cancer | 2 | C138 | cancer | 2 |
| C022 | cancer | 2 | C139 | cancer | 2 |
| C023 | cancer | 2 | C140 | cancer | 2 |
| C024 | cancer | 2 | C148 | cancer | 2 |
| C028 | cancer | 2 | C150 | cancer | 2 |
| C029 | cancer | 2 | C151 | cancer | 2 |
| | | | C152 | cancer | 2 |

| C030 | cancer | 2 | C153 | cancer | 2 |
|---|---|---|---|---|---|
| C031 | cancer | 2 | C154 | cancer | 2 |
| C039 | cancer | 2 | C155 | cancer | 2 |
| C040 | cancer | 2 | C158 | cancer | 2 |
| C041 | cancer | 2 | C159 | cancer | 2 |
| C160 | cancer | 2 | C259 | cancer | 2 |
| C161 | cancer | 2 | C260 | cancer | 2 |
| C162 | cancer | 2 | C261 | cancer | 2 |
| C163 | cancer | 2 | C268 | cancer | 2 |
| C164 | cancer | 2 | C269 | cancer | 2 |
| C165 | cancer | 2 | C300 | cancer | 2 |
| C166 | cancer | 2 | C301 | cancer | 2 |
| C168 | cancer | 2 | C310 | cancer | 2 |
| C169 | cancer | 2 | C311 | cancer | 2 |
| C170 | cancer | 2 | C312 | cancer | 2 |
| C171 | cancer | 2 | C313 | cancer | 2 |
| C172 | cancer | 2 | C318 | cancer | 2 |
| C173 | cancer | 2 | C319 | cancer | 2 |
| C178 | cancer | 2 | C320 | cancer | 2 |
| C179 | cancer | 2 | C321 | cancer | 2 |
| C180 | cancer | 2 | C322 | cancer | 2 |
| C181 | cancer | 2 | C323 | cancer | 2 |
| C182 | cancer | 2 | C328 | cancer | 2 |
| C183 | cancer | 2 | C329 | cancer | 2 |
| C184 | cancer | 2 | C33X | cancer | 2 |
| C185 | cancer | 2 | C340 | cancer | 2 |
| C186 | cancer | 2 | C341 | cancer | 2 |
| C187 | cancer | 2 | C342 | cancer | 2 |
| C188 | cancer | 2 | C343 | cancer | 2 |
| C189 | cancer | 2 | C348 | cancer | 2 |
| C19X | cancer | 2 | C349 | cancer | 2 |
| C20X | cancer | 2 | C37X | cancer | 2 |
| C210 | cancer | 2 | C380 | cancer | 2 |
| C211 | cancer | 2 | C381 | cancer | 2 |
| C212 | cancer | 2 | C382 | cancer | 2 |
| C218 | cancer | 2 | C383 | cancer | 2 |
| C220 | cancer | 2 | C384 | cancer | 2 |
| C221 | cancer | 2 | C388 | cancer | 2 |
| C222 | cancer | 2 | C390 | cancer | 2 |
| C223 | cancer | 2 | C398 | cancer | 2 |
| C224 | cancer | 2 | C399 | cancer | 2 |
| C227 | cancer | 2 | C400 | cancer | 2 |
| C229 | cancer | 2 | C401 | cancer | 2 |
| C23X | cancer | 2 | C402 | cancer | 2 |
| C240 | cancer | 2 | C403 | cancer | 2 |
| C241 | cancer | 2 | C408 | cancer | 2 |

| C248 | cancer | 2 | C409 | cancer | 2 |
|---|---|---|---|---|---|
| C249 | cancer | 2 | C410 | cancer | 2 |
| C250 | cancer | 2 | C411 | cancer | 2 |
| C251 | cancer | 2 | C412 | cancer | 2 |
| C252 | cancer | 2 | C413 | cancer | 2 |
| C253 | cancer | 2 | C414 | cancer | 2 |
| C254 | cancer | 2 | C418 | cancer | 2 |
| C257 | cancer | 2 | C419 | cancer | 2 |
| C258 | cancer | 2 | C430 | cancer | 2 |
| C431 | cancer | 2 | C498 | cancer | 2 |
| C432 | cancer | 2 | C499 | cancer | 2 |
| C433 | cancer | 2 | C500 | cancer | 2 |
| C434 | cancer | 2 | C501 | cancer | 2 |
| C435 | cancer | 2 | C502 | cancer | 2 |
| C436 | cancer | 2 | C503 | cancer | 2 |
| C437 | cancer | 2 | C504 | cancer | 2 |
| C438 | cancer | 2 | C505 | cancer | 2 |
| C439 | cancer | 2 | C506 | cancer | 2 |
| C440 | cancer | 2 | C508 | cancer | 2 |
| C441 | cancer | 2 | C509 | cancer | 2 |
| C442 | cancer | 2 | C510 | cancer | 2 |
| C443 | cancer | 2 | C511 | cancer | 2 |
| C444 | cancer | 2 | C512 | cancer | 2 |
| C445 | cancer | 2 | C518 | cancer | 2 |
| C446 | cancer | 2 | C519 | cancer | 2 |
| C447 | cancer | 2 | C52X | cancer | 2 |
| C448 | cancer | 2 | C530 | cancer | 2 |
| C449 | cancer | 2 | C531 | cancer | 2 |
| C450 | cancer | 2 | C538 | cancer | 2 |
| C451 | cancer | 2 | C540 | cancer | 2 |
| C452 | cancer | 2 | C541 | cancer | 2 |
| C457 | cancer | 2 | C542 | cancer | 2 |
| C459 | cancer | 2 | C543 | cancer | 2 |
| C460 | cancer | 2 | C548 | cancer | 2 |
| C461 | cancer | 2 | C549 | cancer | 2 |
| C462 | cancer | 2 | C55X | cancer | 2 |
| C463 | cancer | 2 | C570 | cancer | 2 |
| C467 | cancer | 2 | C571 | cancer | 2 |
| C469 | cancer | 2 | C572 | cancer | 2 |
| C470 | cancer | 2 | C573 | cancer | 2 |
| C471 | cancer | 2 | C574 | cancer | 2 |
| C472 | cancer | 2 | C577 | cancer | 2 |
| C473 | cancer | 2 | C578 | cancer | 2 |
| C474 | cancer | 2 | C58X | cancer | 2 |
| C475 | cancer | 2 | C600 | cancer | 2 |
| C476 | cancer | 2 | C601 | cancer | 2 |

| C478 | cancer | 2 | C602 | cancer | 2 |
|---|---|---|---|---|---|
| C479 | cancer | 2 | C608 | cancer | 2 |
| C480 | cancer | 2 | C620 | cancer | 2 |
| C481 | cancer | 2 | C621 | cancer | 2 |
| C482 | cancer | 2 | C629 | cancer | 2 |
| C488 | cancer | 2 | C630 | cancer | 2 |
| C490 | cancer | 2 | C631 | cancer | 2 |
| C491 | cancer | 2 | C632 | cancer | 2 |
| C492 | cancer | 2 | C637 | cancer | 2 |
| C493 | cancer | 2 | C638 | cancer | 2 |
| C494 | cancer | 2 | C639 | cancer | 2 |
| C495 | cancer | 2 | C64X | cancer | 2 |
| C496 | cancer | 2 | C65X | cancer | 2 |
| C66X | cancer | 2 | C752 | cancer | 2 |
| C670 | cancer | 2 | C753 | cancer | 2 |
| C671 | cancer | 2 | C754 | cancer | 2 |
| C672 | cancer | 2 | C755 | cancer | 2 |
| C673 | cancer | 2 | C758 | cancer | 2 |
| C674 | cancer | 2 | C759 | cancer | 2 |
| C675 | cancer | 2 | C760 | cancer | 2 |
| C676 | cancer | 2 | C761 | cancer | 2 |
| C677 | cancer | 2 | C762 | cancer | 2 |
| C678 | cancer | 2 | C763 | cancer | 2 |
| C679 | cancer | 2 | C764 | cancer | 2 |
| C680 | cancer | 2 | C765 | cancer | 2 |
| C688 | cancer | 2 | C770 | mets | 6 |
| C689 | cancer | 2 | C771 | mets | 6 |
| C690 | cancer | 2 | C772 | mets | 6 |
| C691 | cancer | 2 | C773 | mets | 6 |
| C692 | cancer | 2 | C774 | mets | 6 |
| C693 | cancer | 2 | C775 | mets | 6 |
| C694 | cancer | 2 | C778 | mets | 6 |
| C695 | cancer | 2 | C779 | mets | 6 |
| C696 | cancer | 2 | C780 | mets | 6 |
| C698 | cancer | 2 | C781 | mets | 6 |
| C699 | cancer | 2 | C782 | mets | 6 |
| C700 | cancer | 2 | C783 | mets | 6 |
| C701 | cancer | 2 | C784 | mets | 6 |
| C709 | cancer | 2 | C785 | mets | 6 |
| C710 | cancer | 2 | C786 | mets | 6 |
| C711 | cancer | 2 | C787 | mets | 6 |
| C712 | cancer | 2 | C788 | mets | 6 |
| C713 | cancer | 2 | C790 | mets | 6 |
| C714 | cancer | 2 | C791 | mets | 6 |
| C715 | cancer | 2 | C792 | mets | 6 |
| C716 | cancer | 2 | C793 | mets | 6 |

| C717 | cancer | 2 | C794 | mets | 6 |
|---|---|---|---|---|---|
| C718 | cancer | 2 | C795 | mets | 6 |
| C719 | cancer | 2 | C796 | mets | 6 |
| C720 | cancer | 2 | C797 | mets | 6 |
| C721 | cancer | 2 | C798 | mets | 6 |
| C722 | cancer | 2 | C80X | cancer | 2 |
| C723 | cancer | 2 | C810 | haem | 2 |
| C724 | cancer | 2 | C811 | haem | 2 |
| C725 | cancer | 2 | C812 | haem | 2 |
| C728 | cancer | 2 | C813 | haem | 2 |
| C729 | cancer | 2 | C817 | haem | 2 |
| C73X | cancer | 2 | C819 | haem | 2 |
| C740 | cancer | 2 | C820 | haem | 2 |
| C741 | cancer | 2 | C821 | haem | 2 |
| C749 | cancer | 2 | C822 | haem | 2 |
| C750 | cancer | 2 | C827 | haem | 2 |
| C751 | cancer | 2 | C829 | haem | 2 |
| C830 | haem | 2 | C945 | haem | 2 |
| C831 | haem | 2 | C947 | haem | 2 |
| C832 | haem | 2 | C950 | haem | 2 |
| C833 | haem | 2 | C951 | haem | 2 |
| C834 | haem | 2 | C952 | haem | 2 |
| C835 | haem | 2 | C957 | haem | 2 |
| C836 | haem | 2 | C959 | haem | 2 |
| C837 | haem | 2 | C960 | haem | 2 |
| C838 | haem | 2 | C961 | haem | 2 |
| C839 | haem | 2 | C962 | haem | 2 |
| C840 | haem | 2 | C963 | haem | 2 |
| C841 | haem | 2 | C967 | haem | 2 |
| C842 | haem | 2 | C969 | haem | 2 |
| C843 | haem | 2 | C97X | cancer | 2 |
| C844 | haem | 2 | E101 | dm | 1 |
| C845 | haem | 2 | E102 | dmcomp | 2 |
| C850 | haem | 2 | E103 | dmcomp | 2 |
| C851 | haem | 2 | E104 | dmcomp | 2 |
| C857 | haem | 2 | E105 | dm | 1 |
| C859 | haem | 2 | E106 | dmcomp | 2 |
| C880 | haem | 2 | E107 | dmcomp | 2 |
| C883 | cancer | 2 | E108 | dmcomp | 2 |
| C887 | cancer | 2 | E109 | dm | 1 |
| C889 | cancer | 2 | E111 | dm | 1 |
| C900 | cancer | 2 | E112 | dmcomp | 2 |
| C901 | haem | 2 | E113 | dmcomp | 2 |
| C901 | haem | 2 | E114 | dmcomp | 2 |
| C902 | haem | 2 | E115 | dm | 1 |
| C910 | haem | 2 | E116 | dmcomp | 2 |

| C911 | haem | 2 | E117 | dmcomp | 2 |
|---|---|---|---|---|---|
| C912 | haem | 2 | E118 | dmcomp | 2 |
| C913 | haem | 2 | E119 | dm | 1 |
| C914 | haem | 2 | E121 | dm | 1 |
| C915 | haem | 2 | E122 | dmcomp | 2 |
| C917 | haem | 2 | E127 | dmcomp | 2 |
| C919 | haem | 2 | E129 | dm | 1 |
| C920 | haem | 2 | E131 | dm | 1 |
| C921 | haem | 2 | E132 | dmcomp | 2 |
| C922 | haem | 2 | E133 | dmcomp | 2 |
| C923 | haem | 2 | E134 | dmcomp | 2 |
| C924 | haem | 2 | E135 | dm | 1 |
| C925 | haem | 2 | E136 | dmcomp | 2 |
| C927 | haem | 2 | E138 | dmcomp | 2 |
| C929 | haem | 2 | E139 | dm | 1 |
| C930 | haem | 2 | E141 | dm | 1 |
| C931 | haem | 2 | E142 | dmcomp | 2 |
| C939 | haem | 2 | E143 | dmcomp | 2 |
| C940 | haem | 2 | E144 | dmcomp | 2 |
| C942 | haem | 2 | E145 | dm | 1 |
| C943 | haem | 2 | E146 | dmcomp | 2 |
| E147 | dmcomp | 2 | I252 | cardiac | 1 |
| E148 | dmcomp | 2 | I500 | cardiac | 1 |
| E149 | dm | 1 | I501 | cardiac | 1 |
| F000 | dementia | 1 | I509 | cardiac | 1 |
| F001 | dementia | 1 | I600 | stroke | 1 |
| F002 | dementia | 1 | I601 | stroke | 1 |
| F009 | dementia | 1 | I602 | stroke | 1 |
| F010 | dementia | 1 | I603 | stroke | 1 |
| F011 | dementia | 1 | I604 | stroke | 1 |
| F012 | dementia | 1 | I605 | stroke | 1 |
| F013 | dementia | 1 | I606 | stroke | 1 |
| F018 | dementia | 1 | I607 | stroke | 1 |
| F019 | dementia | 1 | I608 | stroke | 1 |
| F020 | dementia | 1 | I609 | stroke | 1 |
| F021 | dementia | 1 | I610 | stroke | 1 |
| F022 | dementia | 1 | I611 | stroke | 1 |
| F023 | dementia | 1 | I612 | stroke | 1 |
| F024 | dementia | 1 | I613 | stroke | 1 |
| F028 | dementia | 1 | I614 | stroke | 1 |
| F03X | dementia | 1 | I615 | stroke | 1 |
| F051 | dementia | 1 | I616 | stroke | 1 |
| G450 | stroke | 1 | I618 | stroke | 1 |
| G451 | stroke | 1 | I619 | stroke | 1 |
| G452 | stroke | 1 | I620 | stroke | 1 |
| G458 | stroke | 1 | I621 | stroke | 1 |

| G459 | stroke | 1 | I629 | stroke | 1 |
|---|---|---|---|---|---|
| G460 | stroke | 1 | I630 | stroke | 1 |
| G464 | stroke | 1 | I631 | stroke | 1 |
| G468 | stroke | 1 | I632 | stroke | 1 |
| G810 | hemi | 2 | I633 | stroke | 1 |
| G811 | hemi | 2 | I634 | stroke | 1 |
| G819 | hemi | 2 | I635 | stroke | 1 |
| I210 | cardiac | 1 | I636 | stroke | 1 |
| I211 | cardiac | 1 | I638 | stroke | 1 |
| I212 | cardiac | 1 | I639 | stroke | 1 |
| I213 | cardiac | 1 | I64X | stroke | 1 |
| I214 | cardiac | 1 | I650 | stroke | 1 |
| I219 | cardiac | 1 | I651 | stroke | 1 |
| I220 | cardiac | 1 | I652 | stroke | 1 |
| I221 | cardiac | 1 | I653 | stroke | 1 |
| I228 | cardiac | 1 | I658 | stroke | 1 |
| I229 | cardiac | 1 | I659 | stroke | 1 |
| I230 | cardiac | 1 | I660 | stroke | 1 |
| I231 | cardiac | 1 | I661 | stroke | 1 |
| I232 | cardiac | 1 | I662 | stroke | 1 |
| I233 | cardiac | 1 | I663 | stroke | 1 |
| I234 | cardiac | 1 | I664 | stroke | 1 |
| I235 | cardiac | 1 | I668 | stroke | 1 |
| I236 | cardiac | 1 | I669 | stroke | 1 |
| I238 | cardiac | 1 | I670 | stroke | 1 |
| I671 | stroke | 1 | J449 | resp | 1 |
| I672 | stroke | 1 | J450 | resp | 1 |
| I674 | stroke | 1 | J451 | resp | 1 |
| I675 | stroke | 1 | J458 | resp | 1 |
| I676 | stroke | 1 | J459 | resp | 1 |
| I677 | stroke | 1 | J46X | resp | 1 |
| I678 | stroke | 1 | J47X | resp | 1 |
| I679 | stroke | 1 | J60X | resp | 1 |
| I682 | stroke | 1 | J61X | resp | 1 |
| I690 | stroke | 1 | J628 | resp | 1 |
| I691 | stroke | 1 | J630 | resp | 1 |
| I692 | stroke | 1 | J632 | resp | 1 |
| I693 | stroke | 1 | J634 | resp | 1 |
| I694 | stroke | 1 | J64X | resp | 1 |
| I698 | stroke | 1 | J65X | resp | 1 |
| I710 | pvd | 1 | J668 | resp | 1 |
| I711 | pvd | 1 | J670 | resp | 1 |
| I712 | pvd | 1 | J672 | resp | 1 |
| I713 | pvd | 1 | J677 | resp | 1 |
| I714 | pvd | 1 | J841 | resp | 1 |
| I715 | pvd | 1 | J848 | resp | 1 |

| I716 | pvd | 1 | J849 | resp | 1 |
|---|---|---|---|---|---|
| I718 | pvd | 1 | J961 | resp | 1 |
| I719 | pvd | 1 | J982 | resp | 1 |
| I738 | pvd | 1 | J983 | resp | 1 |
| I739 | pvd | 1 | K250 | ulcer | 1 |
| I790 | pvd | 1 | K251 | ulcer | 1 |
| I800 | pvd | 1 | K252 | ulcer | 1 |
| I801 | pvd | 1 | K253 | ulcer | 1 |
| I802 | pvd | 1 | K254 | ulcer | 1 |
| I803 | pvd | 1 | K255 | ulcer | 1 |
| I808 | pvd | 1 | K256 | ulcer | 1 |
| I809 | pvd | 1 | K257 | ulcer | 1 |
| I830 | pvd | 1 | K259 | ulcer | 1 |
| I831 | pvd | 1 | K260 | ulcer | 1 |
| I832 | pvd | 1 | K261 | ulcer | 1 |
| I839 | pvd | 1 | K262 | ulcer | 1 |
| J40X | resp | 1 | K263 | ulcer | 1 |
| J410 | resp | 1 | K264 | ulcer | 1 |
| J411 | resp | 1 | K265 | ulcer | 1 |
| J418 | resp | 1 | K266 | ulcer | 1 |
| J42X | resp | 1 | K267 | ulcer | 1 |
| J430 | resp | 1 | K269 | ulcer | 1 |
| J431 | resp | 1 | K270 | ulcer | 1 |
| J432 | resp | 1 | K271 | ulcer | 1 |
| J438 | resp | 1 | K272 | ulcer | 1 |
| J439 | resp | 1 | K273 | ulcer | 1 |
| J440 | resp | 1 | K274 | ulcer | 1 |
| J441 | resp | 1 | K275 | ulcer | 1 |
| J448 | resp | 1 | K276 | ulcer | 1 |
| K277 | ulcer | 1 | M349 | ctd | 1 |
| K279 | ulcer | 1 | M368 | ctd | 1 |
| K280 | ulcer | 1 | N011 | renal | 2 |
| K281 | ulcer | 1 | N014 | renal | 2 |
| K282 | ulcer | 1 | N017 | renal | 2 |
| K283 | ulcer | 1 | N018 | renal | 2 |
| K284 | ulcer | 1 | N019 | renal | 2 |
| K285 | ulcer | 1 | N030 | renal | 2 |
| K286 | ulcer | 1 | N031 | renal | 2 |
| K287 | ulcer | 1 | N032 | renal | 2 |
| K289 | ulcer | 1 | N033 | renal | 2 |
| K702 | liver | 1 | N034 | renal | 2 |
| K703 | liver | 1 | N035 | renal | 2 |
| K717 | liver | 1 | N037 | renal | 2 |
| K721 | badliver | 3 | N038 | renal | 2 |
| K729 | badliver | 3 | N039 | renal | 2 |
| K730 | liver | 1 | N052 | renal | 2 |

| K731 | liver | 1 | N053 | renal | 2 |
|---|---|---|---|---|---|
| K732 | liver | 1 | N054 | renal | 2 |
| K738 | liver | 1 | N055 | renal | 2 |
| K739 | liver | 1 | N056 | renal | 2 |
| K740 | liver | 1 | N057 | renal | 2 |
| K742 | liver | 1 | N072 | renal | 2 |
| K743 | liver | 1 | N074 | renal | 2 |
| K744 | liver | 1 | N180 | renal | 2 |
| K745 | liver | 1 | N188 | renal | 2 |
| K746 | liver | 1 | N189 | renal | 2 |
| K766 | badliver | 3 | N19X | renal | 2 |
| K767 | badliver | 3 | N250 | renal | 2 |
| M050 | ctd | 1 | N251 | renal | 2 |
| M051 | ctd | 1 | N258 | renal | 2 |
| M052 | ctd | 1 | N259 | renal | 2 |
| M053 | ctd | 1 | R02X | pvd | 1 |
| M058 | ctd | 1 | Z958 | pvd | 1 |
| M059 | ctd | 1 | Z959 | pvd | 1 |
| M060 | ctd | 1 | ‡C5. | cancer | 2 |
| M063 | ctd | 1 | ‡C5. | cancer | 2 |
| M069 | ctd | 1 | ‡C5. | cancer | 2 |
| M320 | ctd | 1 | ‡C6. | cancer | 2 |
| M321 | ctd | 1 | ‡C6. | cancer | 2 |
| M328 | ctd | 1 | **Legend;** haem; haematological malignancy | | |
| M329 | ctd | 1 | mets; metastatic disease | | |
| M330 | ctd | 1 | ctd; connective tissues disease | | |
| M331 | ctd | 1 | ulcer; gastric ulcer disease | | |
| M332 | ctd | 1 | pvd; peripheral vascular disease | | |
| M339 | ctd | 1 | resp; chronic respiratory disease | | |
| M340 | ctd | 1 | dm; diabetes mellitus | | |
| M341 | ctd | 1 | dmcomp; diabetes with complications | | |
| M342 | ctd | 1 | badliver; liver failure | | |
| M348 | ctd | 1 | hemi; hemiplegia | | |

## Appendix 6: The key standards used in the Peer Review process 2003-07

### 08-2C-1-Lung Multidisciplinary Team (MDT)

| Measure number | Measure |
|---|---|
| 08-2C-101 | Single named lead clinician |
| 08-2C-102 | Named core team members |
| 08-2C-103 | Team attendance at NSSG meetings |
| 08-2C-104 | If separate pre-diagnostic MDT membership named |
| 08-2C-105 | Meet fortnightly and record core attendance and protocols for referral to next scheduled meeting |
| 08-2C-106 | MDT agreed cover arrangements for core members |
| 08-2C-107 | Core member (or cover) present 2/3 of meetings |
| 08-2C-108 | Annual meeting to discuss operational policy |
| 08-2C-109 | Policy for all new patients to be reviewed by MDT |
| 08-2C-110 | Policy for communication of diagnosis to GP |
| 08-2C-111 | Operational policy for named key worker |
| 08-2C-112 | Core histopathology member taking part in histopathology EQA |
| 08-2C-113 | Core nurse member completed specialist study |
| 08-2C-114 | Agreed responsibility for core nurse members |
| 08-2C-115 | Agreed list of additional responsibilities for one core nurse member |
| 08-2C-116 | Attendance at national advanced communication skills training programme |
| 08-2C-117 | Extended membership of MDT |
| 08-2C-118 | Patient permanent consultation record |
| 08-2C-119 | Patient experience exercise |
| 08-2C-120 | Presentation and discussion of patient experience exercise |
| 08-2C-121 | Provision of written patient information |
| 08-2C-122 | Agree and record individual patient treatment plans |
| 08-2C-123 | NSSG agreed clinical guidelines |
| 08-2C-124 | NSSG agreed referral guidelines |
| 08-2C-125 | NSSG agreed diagnosis assessment imaging guidelines |
| 08-2C-126 | NSSG agreed diagnosis assessment pathology guidelines |
| 08-2C-127 | MDT/Network agreed collection of minimum dataset |
| 08-2C-128 | MDT/NSSG agreed policy for the electronic collection of specific portions of MDS |
| 08-2C-129 | MDT/NSSG agreed participation in network audit |
| 08-2C-130 | MDT present results from participation in network audit |
| 08-2C-131 | MDT/NSSG agreed list of approved trials |
| 08-2C-132 | MDT/NSSG remedial action from MDT's recruitment results |

Legend: NSSG Network Site Specific Group (i.e. Lung)

## Appendix 7: Postgraduate training courses

| Date | Course | Credits |
|---|---|---|
| August 2008 | Basic Epidemiology and Statistics | |
| September 2008 | Advanced Epidemiology and Statistics | 5 |
| Nov 26th 2008 | Word 2007 | 1 |
| June 3rd 2009 | Long documents in Word 2007 | 2 |
| June 17th 2009 | Postgraduate Forum (poster presentation) | 4 |
| | Myers-Briggs | 1 |
| | Advanced Presentations skills (on-line) | 2 |
| | Getting into thesis writing | 1 |
| | CV writing and interview skills | 1 |
| March 15-17th 2010 | Clinical management and Leadership | 6 |

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