



# Risk factors and survival outcome for non-elective referral in non-small cell lung cancer patients – Analysis based on the National Lung Cancer Audit



P. Beckett<sup>a,\*</sup>, L.J. Tata<sup>b</sup>, R.B. Hubbard<sup>b</sup>

<sup>a</sup> Burton Hospitals NHS Foundation Trust, UK

<sup>b</sup> Nottingham Respiratory Research Unit, University of Nottingham, City Hospital, Nottingham, UK

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## ABSTRACT

**Introduction:** Survival after diagnosis of lung cancer is poor and seemingly lower in the UK than other Western countries, due in large part to late presentation with advanced disease precluding curative treatment. Recent research suggests that around one-third of lung cancer patients reach specialist care after emergency presentation and have a worse survival outcome. Confirmation of these data and understanding which patients are affected may allow a targeted approach to improving outcomes.

**Methods:** We used data from the UK National Lung Cancer Audit in a multivariate logistic regression model to quantify the association of non-elective referral in non-small cell lung cancer patients with covariates including age, sex, stage, performance status, co-morbidity and socioeconomic status and used the Kaplan–Meier method and Cox proportional hazards model to quantify survival by source of referral.

**Results:** In an analysis of 133,530 cases of NSCLC who presented 2006–2011, 19% of patients were referred non-electively (following an emergency admission to hospital or following an emergency presentation to A&E). This route of referral was strongly associated with more advanced disease stage (e.g. in Stage IV – OR: 2.34, 95% CI: 2.14–2.57,  $p < 0.001$ ) and worse performance status (e.g. in PS 4 – OR: 7.28, 95% CI: 6.75–7.86,  $p < 0.001$ ), but was also independently associated with worse socioeconomic status, and extremes of age. These patients were more likely to have died within 1 year of diagnosis (hazard ratio of 1.51 (95% CI: 1.49–1.54) after adjustment for key clinical variables.

**Conclusion:** Our data confirm and quantify poorer survival in lung cancer patients who are referred non-electively to specialist care, which is more common in patients with poorer performance status, higher disease stage and less advantaged socioeconomic status. Work to tackle this late presentation should be urgently accelerated, since its realisation holds the promise of improved outcomes and better healthcare resource utilisation.

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## 1. Introduction

Survival after a diagnosis of cancer appears to be lower in the UK compared to similar healthcare systems [1] with late presentation to specialist care providing the major explanation for the differences [2]. The National Cancer Intelligence Network recently published an analysis of 739,667 cases of cancer diagnosed between 2006 and 2008 from the National Cancer Data Repository, where Administrative Hospital Episode Statistics data are linked with Cancer Waiting Times data, data from the cancer screening programmes and cancer registration data and showed that 24% of all cancers had an emergency presentation to secondary care as their

“route to diagnosis” [3]. This figure was higher for lung cancer at 39% with early indications that 1 year survival is particularly poor for these patients. Understanding the demographics and clinical features of patients who present as an emergency is important as it potentially facilitates targeted earlier intervention. Such interventions might be expected to improve survival outcomes, patient experience and utilisation of healthcare resources.

The National Lung Cancer Audit is an audit of lung cancer and mesothelioma commissioned by the Healthcare Quality Improvement Partnership (HQIP) and has collected data on people with lung cancer of progressively improving completeness since 2005 [4]. The audit records the route of referral of the patient to the lung cancer team as well as other key clinical information such as stage and performance status that is not available in other datasets. We have used these data to quantify the extent to which a non-elective mode of referral occurs in people with lung cancer, to identify the

\* Corresponding author. Tel.: +44 1283 511511; fax: +44 1283 593129.  
E-mail address: [paul.beckett1@nhs.net](mailto:paul.beckett1@nhs.net) (P. Beckett).

demographics of the people most affected, and to determine the impact upon survival.

## 2. Methods

We obtained data on all cases of non-small cell lung cancer (NSCLC) submitted to the National Lung Cancer Audit in England between 2006 and 2011. This cohort includes those with histologically confirmed NSCLC and those with presumed NSCLC (i.e. not histologically confirmed small cell lung cancer, and not clinically or histologically diagnosed mesothelioma). We excluded patients with small cell lung cancer since their staging has until recently been recorded as limited/extensive which cannot be accurately transposed into the TNM system used to stage the much more common non-small cell tumours.

After an initial descriptive analysis comparing proportions, we used multivariate logistic regression to calculate odds ratios to quantify the association of non-elective referral to specialist care with a number of covariates including age at diagnosis (grouped into ten year age bands), sex, stage (as classified by the American Joint Committee on Cancer and Union Internationale Contre le Cancer version 6), performance status (as classified by the Eastern Cooperative Oncology Group), recording of a significant diagnosed co-morbidity and socioeconomic status (as classified by the Index of Multiple deprivations based on postcode, separated into quintiles). Initially, all variables were assessed in a series of univariate analyses, but then a multivariate model was fitted which included all of the variables. Non-elective referral was defined as patients with a source of referral recorded as “following an emergency admission” or “following an A&E attendance”. We also utilised a social segmentation classification based on postcode (Experian MOSAIC Pubic Sector) to examine whether particular social groups were disproportionately represented in the non-elective referrals by completing a simple quantitative analysis and did not adjust this analysis as this classification already takes account of age, sex and socioeconomic status. Finally, survival by type of referral was assessed using the Kaplan–Meier method and Cox proportional hazards model. In these analyses, the start date was the date of diagnosis and the end date was the date of death or last data

collection. To assess the proportional hazards assumption for these survival models we assessed the Kaplan–Meier plots.

All statistical analyses were carried out using Stata SE11.

## 3. Results

There were 133,546 cases of non-small cell lung cancer submitted to the National Lung Cancer Audit in England between 2006 and 2011, of which we excluded 16 patients with a calculated survival of less than zero (diagnosed post-mortem), leaving 133,530 cases of histologically confirmed or presumed NSCLC which we used as our study population. The median age was 72 years and 57% of patients were male. Approximately 50% of patients were diagnosed with metastatic or locally advanced (Stage IIIB/IV) disease.

### 3.1. Referral pathways

In patients with NSCLC, just under half of our patients (47%) were referred to the specialist lung cancer team by their General Practitioner, 20% were referred by another secondary care consultant (not A&E), 13% were referred following an emergency admission to hospital, 7% were referred following an emergency presentation to A&E, 7% were referred by other elective routes and in 6% the route of referral was unknown.

For the remaining analyses we created three groups of patients, namely those referred non-electively following an emergency admission to hospital or referred following an emergency presentation to A&E (‘Non-Elective’), those where the route of referral was unknown (‘Unknown’) and all remaining cases (‘Elective’). Using this grouping, the proportion of patients having a non-elective source of referral has remained relatively constant across time (17% in 2006, 18% in 2007, 18% in 2008, 21% in 2009, 20% in 2010 and 20% in 2011).

### 3.2. Characteristics of patients

Table 1 shows the demographics and clinical features of the patients in the dataset. Patients with unknown route of referral had less complete data and were not analysed further. Those patients

**Table 1**  
Demographics and clinical features by referral route.

	Non-elective	Elective	Unknown	Total
Number of patients	25,675 (19.2%)	99,522 (74.5%)	8333 (6.2%)	133,530 (100%)
Males (% male)	14,372 (56.0%)	56,866 (57.1%)	4828 (57.9%)	71,238 (57.0%)
Median Age (IQR)	74 (66–81)	72 (64–79)	72 (64–79)	72 (64–79)
FEV <sub>1</sub> recorded	15.7%	37.9%	14.6%	32.2%
Median FEV <sub>1</sub> litres (IQR)	1.4L (1.0–1.9)	1.6L (1.2–2.1)	1.6L (1.2–2.1)	1.6 (1.2–2.1)
Mean FEV <sub>1</sub> % predicted	61.4%	68.5%	67.0%	67.8%
Stage IA	614 (2.4%)	5574 (5.6%)	410 (4.9%)	6598 (4.9%)
Stage IB	816 (3.2%)	7106 (7.1%)	450 (5.4%)	8372 (6.3%)
Stage IIA	266 (1.0%)	1847 (1.9%)	89 (1.1%)	2202 (1.7%)
Stage IIB	646 (2.5%)	4560 (4.6%)	279 (3.4%)	5485 (4.1%)
Stage IIIA	1532 (6.0%)	9612 (9.7%)	505 (6.1%)	11,649 (8.7%)
Stage IIIB	2769 (10.8%)	12,211 (12.3%)	802 (9.6%)	15,782 (11.8%)
Stage IV	12,516 (48.8%)	34,418 (34.6%)	2340 (28.1%)	49,274 (36.9%)
Stage unknown	6516 (25.4%)	24,194 (24.3%)	3458 (41.5%)	34,168 (25.6%)
PS 0	1594 (7.1%)	17,546 (20.1%)	1071 (12.9%)	20,211 (15.1%)
PS 1	4072 (18.1%)	26,792 (30.7%)	1573 (18.9%)	32,437 (24.3%)
PS 2	4437 (19.7%)	15,530 (17.8%)	1044 (12.5%)	21,011 (15.7%)
PS 3	6341 (28.1%)	12,114 (13.9%)	918 (11.0%)	19,373 (14.5%)
PS 4	2807 (12.5%)	3380 (3.9%)	373 (4.5%)	6560 (4.9%)
PS unknown	6424 (25.0%)	24,160 (24.3%)	3354 (40.3%)	33,938 (25.4%)
Co-morbidity recorded	4411 (17.2%)	15,201 (15.3%)	569 (6.8%)	20,181 (15.1%)
IMD quintile 1 (most deprived)	5340 (21.3%)	19,324 (19.7%)	1657 (20.1%)	26,321 (20%)
IMD quintile 2	5351 (21.4%)	19,296 (19.6%)	1643 (20.0%)	26,290 (20%)
IMD quintile 3	4952 (19.8%)	19,781 (20.1%)	1569 (19.1%)	26,302 (20%)
IMD quintile 4	4700 (18.8%)	19,956 (20.3%)	1646 (20.0%)	26,302 (20%)
IMD quintile 5 (least deprived)	4686 (18.7%)	19,908 (20.3%)	1709 (20.8%)	26,303 (20%)

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