# The effect of emergency presentation on surgery and survival in lung cancer patients in England, 2006-2008

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## **Abstract**

**Background:** A large proportion of lung cancer patients in England are diagnosed through an emergency route. We investigated the association between emergency presentation and the odds of undergoing surgical resection and subsequent survival as well as all other lung cancer patients.

**Methods:** Details of 93,783 lung cancers were extracted from the National Cancer Data Repository. For non-small cell lung cancer (NSCLC) patients we calculated odds ratios for undergoing surgical resection. Survival was assessed for resected NSCLC and for all other lung cancer patients in three different time intervals: short-term, intermediate and long-term.

**Results:** Compared with those who did not, NSCLC patients presenting through an emergency route were less likely to undergo surgical resection (adjusted OR=0.22, 95% CI: 0.20-0.24). Patients who underwent surgical resection after an emergency presentation had lower survival in the intermediate period (adjusted HR=1.27, 95% CI: 1.06-1.54) and long term (adjusted HR=1.20, 95% CI: 0.99-1.45). Among all other lung cancer patients, those diagnosed through an emergency route had lower survival, particularly in the short-term (adjusted HR=3.54, 95% CI: 3.42-3.67), but the association remained in the intermediate (adjusted HR=1.66, 95% CI: 1.63-1.69) and long term (adjusted HR=1.10, 95% CI: 1.05-1.15).

**Conclusion:** The reduced access to surgical resection and lower survival among lung cancer patients who present through an emergency admission, highlights the importance of ensuring symptoms are recognised early so that presentation as an emergency can be reduced.

**Keywords:** Emergency presentation; routes to diagnosis; surgical resection; survival; lung cancer; England.

# Introduction

Lung cancer is the second most common cancer among women and men in England and the leading cause of cancer related mortality  ([Office for National Statistics, 2012](#_ENREF_11)). Survival of patients with lung cancer is lower in the UK compared with other countries with similar health care expenditure and lower than the European average, with less than 30% surviving one year after diagnosis in the UK  ([Coleman *et al*, 2011](#_ENREF_3); [Holmberg *et al*, 2010](#_ENREF_6); [Walters *et al*, 2013](#_ENREF_16)). These survival differences are greater during the first year after diagnosis and greatest in the first 3 months of follow-up. English patients surviving more than a year after their diagnosis have a lower survival than patients from other countries. One of the explanations for this may lie in how lung cancer patients present to the health care system prior to diagnosis. It has been shown that in England the most common route to diagnosis of lung cancer patients is as an emergency presentation (39%) and that lung cancer patients presenting via emergency route have a significantly lower one year survival (12%) than those presenting through a non-emergency route (34%-44%)  ([Elliss-Brookes *et al*, 2012](#_ENREF_5)).

The National Institute for Health and Clinical Excellence (NICE) recommends that patients diagnosed with non-small cell lung cancer who present with early stage disease and are medically fit should be offered surgical resection to improve their survival  ([National Institute for Health and Clinical Excellence, 2011](#_ENREF_10)). However, fewer lung cancer patients in England undergo surgical treatment than in other countries, with around 10% of patients in England offered surgery during the study period 2006-2008  ([Strand *et al*, 2006](#_ENREF_14); [The Health and Social Care Information Centre, 2009](#_ENREF_15)).

The aim of the present analysis was to investigate the association between the route to diagnosis and the odds of non-small cell lung cancer patients undergoing surgical resection and their survival thereafter. The survival of lung cancer patients presenting through an emergency route was examined separately for all non-resected lung cancer patients. Moreover, since previous studies have shown the largest differences in survival between groups of lung cancer patients in the first months after diagnosis  ([Holmberg *et al*, 2010](#_ENREF_6); [McPhail *et al*, 2013](#_ENREF_7)), the association between emergency presentation and survival was investigated overall and for three time periods of follow-up.

# Methods

**Data**

Cancer registration records for 98,530 lung cancers (ICD10 C33-34) diagnosed between 2006 and 2008 in residents of England were extracted from the National Cancer Data Repository (NCDR)  ([National Cancer Intelligence Network, 2008](#_ENREF_8)). We excluded records with missing National Health Service (NHS) number and death certificate only (DCO) registrations (4409, 4.5%). For patients with multiple lung cancer diagnoses (n=338), we retained only the first primary lung cancer for the analysis. The lung cancers were categorised according to their histological type into small cell lung cancers (SCLC) (ICD-O-2 8041, 8042, 8043, 8044, 8045) and all other cancers, including unknown, were classified as non-small cell lung cancers (NSCLC).

Socioeconomic deprivation was measured by lower super output area of residence (each comprising a population of around 1500 people) based on the income domain of the Indices of Deprivation 2007 ([Department for Communities and Local Government, 2008](#_ENREF_4)) and grouped into quintiles. Each patient was assigned to a socioeconomic quintile based on their postcode of residence at the time of the cancer diagnosis.

The study dataset was linked to three datasets. In order to obtain comorbidity information and surgical treatment details, the records were matched to the day case and inpatient Hospital Episode Statistics (HES) dataset. For each patient, comorbidity information was obtained using diagnosis codes recorded in HES. All diagnoses from two years to three months before the patient’s date of diagnosis were classified according to the scores from the weighted Charlson comorbidity index  ([Charlson et al, 1987](#_ENREF_2)), and modified to exclude cancer as a comorbid condition. The resulting scores were aggregated into four categories of increasing severity of comorbidity (0, 1, 2, and 3+). For NSCLC patients we extracted details of surgical treatment from the linked HES data. Operations recorded within HES are coded using OPCS4 codes, a coding classification system for surgical procedures and operations. Surgical resections for lung cancer included: lobectomy, total pneumonectomy, partial lobectomy, excision of lung segment, bilobectomy and other, less common procedures  ([Riaz et al, 2012](#_ENREF_13)).

In addition, records were linked to the National Lung Cancer Audit  ([The Health and Social Care Information Centre, 2009](#_ENREF_15)) to retrieve stage and performance status information.

Finally, we linked the study dataset to the Routes to Diagnosis dataset to extract details of diagnosis route for each patient. The Routes to Diagnosis dataset defined the routes to the point of diagnosis for cancer patients in England diagnosed between 2006 and 2008  ([Elliss-Brookes *et al*, 2012](#_ENREF_5)). The algorithm defining the routes to diagnosis used HES data to identify an inpatient or outpatient episode taking place within six months prior to the diagnosis date that most likely led to the cancer diagnosis. A patient was assigned to an emergency presentation route if the method of admission for the inpatient episode was emergency in nature (Accident and Emergency (A&E) admission, emergency transfer or admission) or if the referral to the outpatient episode was an emergency referral (emergency GP referral, emergency consultant outpatient referral). In addition, emergency presentation patients with a record of a two-week wait urgent referral for suspected cancer were assigned to the two-week wait route unless they had an emergency admission within 28 days before the decision to treat date. Lung cancer patients were thus assigned to one of six routes: emergency presentation, two-week wait, GP referral, inpatient elective, other outpatient and unknown. For the present analysis, we grouped two-week wait, GP referral, inpatient elective and other outpatient routes into one ‘non-emergency’ route.

**Statistical analysis**

The number and proportions of patients presenting through each diagnosis route were calculated by sex, age, socioeconomic deprivation, performance status, comorbidity score and clinical stage.

We used logistic regression models and χ² tests to determine the association between diagnosis route and having surgical treatment for NSCLC patients. We performed two multivariable analyses, adjusting first for age and sex only, and then adjusting for age, sex, socioeconomic deprivation, histological type, performance status, clinical stage and comorbidity score in the multivariable logistic regression model.

We assessed the survival of lung cancer patients by diagnosis route separately for resected NSCLC patients and for all other lung cancer patients. For the resected NSCLC patients the survival time was calculated from the date of surgery until the date of death from any cause or the censor date on 31st December 2009. For all other lung cancer patients survival was calculated from the date of diagnosis. Survival curves were plotted using the Kaplan-Meier method. Cox proportional hazard regression analyses were used to assess survival according to emergency presentation, both adjusted for age and sex only, and adjusted for age, sex, socioeconomic deprivation, histological type, performance status, clinical stage and comorbidity score. Stage at diagnosis is a strong prognostic factor for survival of lung cancer patients but this information is frequently missing. We considered multivariable models with and without stage as a covariate, and found the model that included stage was a better fit. The analysis was performed for three different time intervals: short‑term (the first month following surgery or diagnosis), intermediate (one month to one year) and long‑term (after one year).

# Results

A total of 93,783 lung cancer patients were included in the analysis. Overall, 35,042 (37.4%) patients presented through an emergency route, 51,957 (55.4%) were non-emergency presentations and 6,784 (7.2%) had an unknown route (Table 1). The proportion of patients diagnosed through an emergency route increased with age, with nearly half of patients aged 80 years and over presenting as an emergency. The proportion of emergency presentations was higher for females than for males, and increased with deprivation, as well as with increasing performance status and comorbidity. Lung cancer patients diagnosed following an emergency presentation, were more often of more advanced stage than those who presented through a non-emergency route.

Overall, of the 82,384 NSCLC patients, 8,214 (10.0%) underwent surgical resection. However, only 2.3% of patients presenting through an emergency route received surgery compared with 15.8% of those presenting through a non‑emergency route. The odds ratio of undergoing surgical resection for NSCLC patients diagnosed through the emergency route compared to non-emergency route was 0.15, 95% CI: 0.12‑0.14 when adjusted for age and sex. Further adjustment for socioeconomic deprivation, histological type, performance status, clinical stage and comorbidity score attenuated this association, but remained statistically significant (adjusted OR=0.22, 95% CI: 0.20‑0.24).

Figure 1: Kaplan-Meier survival by route to diagnosis for resected non-small cell lung cancer patients diagnosed in England, 2006-2008



Overall, resected NSCLC patients presenting via an emergency route had lower survival than those presenting through a non‑emergency route (Figure 1). For resected NSCLC patients, the Kaplan-Meier survival estimates for emergency and non-emergency routes were 96% and 97% at one month, 78% and 83% at one year, and 50% and 54% at four years after surgical treatment. By contrast, all lung cancer (excluding resected NSCLC) Kaplan-Meier survival estimates for emergency and non-emergency routes were 61% and 90% at one month, 10% and 31% at one year, and 1% and 5% at four years after diagnosis.

Table 1: Patient characteristics by route to diagnosis for lung cancer patients diagnosed in England, 2006-2008

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
|  | Total | Emergency | | Non-emergency | | Unknown | |
|  |  | n | % | N | % | n | % |
|  | 93,783 | 35,042 | 37.4 | 51,957 | 55.4 | 6,784 | 7.2 |
| Age | | | | | | | |
| <50 years | 2,789 | 892 | 32.0 | 1,648 | 59.1 | 249 | 8.9 |
| 50-59 years | 10,431 | 3,197 | 30.7 | 6,484 | 62.2 | 750 | 7.2 |
| 60-69 years | 24,427 | 7,598 | 31.1 | 15,244 | 62.4 | 1,585 | 6.5 |
| 70-79 years | 32,645 | 11,892 | 36.4 | 18,583 | 56.9 | 2,170 | 6.7 |
| 80+ years | 23,491 | 11,463 | 48.8 | 9,998 | 42.6 | 2,030 | 8.6 |
| Sex | | | | | | | |
| Male | 53,535 | 19,546 | 36.5 | 30,213 | 56.4 | 3,776 | 7.1 |
| Female | 40,248 | 15,496 | 38.5 | 21,744 | 54.0 | 3,008 | 7.5 |
| Socioeconomic deprivation quintile | | | | | | | |
| 1 (most affluent) | 13,081 | 4,489 | 34.3 | 7,583 | 58.0 | 1,009 | 7.7 |
| 2 | 16,571 | 5,901 | 35.6 | 9,498 | 57.3 | 1,172 | 7.1 |
| 3 | 19,050 | 7,052 | 37.0 | 10,743 | 56.4 | 1,255 | 6.6 |
| 4 | 21,405 | 8,304 | 38.8 | 11,709 | 54.7 | 1,392 | 6.5 |
| 5 (most deprived) | 23,676 | 9,296 | 39.3 | 12,424 | 52.5 | 1,956 | 8.3 |
| Performance status score | | | | | | | |
| 0 | 7,511 | 1,025 | 13.7 | 6,133 | 81.7 | 353 | 4.7 |
| 1 | 12,291 | 2,647 | 21.5 | 9,007 | 73.3 | 637 | 5.2 |
| 2 | 8,049 | 2,782 | 34.6 | 4,854 | 60.3 | 413 | 5.1 |
| 3 | 6,513 | 3,435 | 52.7 | 2,700 | 41.5 | 378 | 5.8 |
| 4 | 2,003 | 1,403 | 70.0 | 470 | 23.5 | 130 | 6.5 |
| Not known | 57,416 | 23,750 | 41.4 | 28,793 | 50.2 | 4,873 | 8.5 |
| Clinical stage | | | | | | | |
| IA | 1,727 | 264 | 15.3 | 1,355 | 78.5 | 108 | 6.3 |
| IB | 2,709 | 432 | 16.0 | 2,130 | 78.6 | 147 | 5.4 |
| IIA | 287 | 49 | 17.1 | 221 | 77.0 | 17 | 5.9 |
| IIB | 1,783 | 307 | 17.2 | 1,377 | 77.2 | 99 | 5.6 |
| IIIA | 3,523 | 705 | 20.0 | 2,659 | 75.5 | 159 | 4.5 |
| IIIB | 7,046 | 1,949 | 27.7 | 4,766 | 67.6 | 331 | 4.7 |
| IV | 16,135 | 6,235 | 38.6 | 9,006 | 55.8 | 894 | 5.5 |
| Not known | 60,573 | 25,101 | 41.4 | 30,443 | 50.3 | 5,029 | 8.3 |
| Comorbidity score | | | | | | | |
| 0 | 43,323 | 13,234 | 30.6 | 27,275 | 63.0 | 2,814 | 6.5 |
| 1 | 26,608 | 10,978 | 41.3 | 14,473 | 54.4 | 1,157 | 4.4 |
| 2 | 9,760 | 4,836 | 49.6 | 4,587 | 47.0 | 337 | 3.5 |
| 3+ | 6,723 | 3,773 | 56.1 | 2,716 | 40.4 | 234 | 3.5 |
| Not known | 7,369 | 2,221 | 30.1 | 2,906 | 39.4 | 2,242 | 30.4 |

Table 2 shows the hazard ratios for resected NSCLC patients in the different time periods after surgery. We found that in the short‑term, there was no significant difference in survival between the different routes to diagnosis (emergency route adjusted HR=1.12, 95% CI: 0.76-1.65; unknown route adjusted HR=1.26, 95% CI: 0.70-2.27). However, patients presenting via an emergency route had a higher death rate in the intermediate period following surgery (adjusted HR=1.27, 95% CI: 1.06‑1.54). Among patients who had survived a year after their surgery, there was a borderline significant association with emergency presentation (adjusted HR=1.20, 95% CI: 0.99-1.45).

Table 2: Hazard ratios (HR) and 95% confidence intervals for resected non-small cell lung cancer patients and all lung cancer patients (excluding resected non-small cell patients) diagnosed in England, 2006-2008, by time period: < one month, one month to one year, and >one year.

\*Adjusted for age, sex, socioeconomic deprivation, histological type, performance status, clinical stage and comorbidity score.

Figure 2: Kaplan-Meier survival by route to diagnosis for all lung cancer patients (excluding resected non-small cell patients) diagnosed in England, 2006-2008.



All lung cancer (excluding resected NSCLC) patients who presented through an emergency route had lower survival than those presenting through other routes (Figure 2). The effect of being diagnosed through an emergency route decreased over the periods following diagnosis in all lung cancer (excluding resected NSCLC) patients (Table 2). In the short‑term, up to a month following diagnosis, emergency route patients had an almost five‑fold risk of dying (HR=4.65, 95% CI: 4.49‑4.81). Adjustment for all other factors attenuated the association (HR=3.54, 95% CI: 3.42‑3.67). The adjusted hazard ratios were lower but remained statistically significant in the intermediate (HR=1.66, 95% CI: 1.63‑1.69) and long‑term (HR=1.10, 95% CI: 1.05‑1.15) periods.

# Discussion

An association between lower one-year relative survival and lung cancer patients presenting through an emergency route compared to other presentation routes in England has previously been identified in a study by Elliss-Brookes et al.  ([Elliss-Brookes *et al*, 2012](#_ENREF_5)). In a subsequent study by McPhail et al.  ([McPhail *et al*, 2013](#_ENREF_7)), it was shown that the excess mortality rate was higher the first month after diagnosis compared to later time periods among patients who were diagnosed through an emergency route compared to other presentation routes. However, these studies did not take into account whether patients underwent a surgical resection. By distinguishing between resected NSCLC patients and the other lung cancer patients, we have shown that there are important differences in the associations between emergency presentation and short term and long term survival for these two groups.

A major strength of our study is the use of a large national population-based cancer registration dataset, the English National Cancer Data Repository. We were able to link this dataset to the NLCA dataset to extract clinical stage and performance status details, which was available for 80% and 70% of patients included in the audit, respectively. Linkage could only be established for 63% of lung cancer patients identified in the cancer registration, which gave rise to low stage completeness (46%) and low performance status completeness (34%) for patients undergoing surgical resection. Another limitation of this study is the potential underestimation of comorbidity as the comorbidity score used in this study is based on inpatient and day case hospital records. There may therefore be residual confounding of stage, performance status and comorbidity on the association between emergency presentation and survival.

We found that NSCLC patients presenting via an emergency route were 78% less likely to undergo surgery. Patients with lung cancer tumours with mild but persistent respiratory symptoms may first present to primary care, and then follow a non-emergency referral pathway, whereas patients with very aggressive or rapidly growing lung cancers and/or with sudden symptoms are more likely to present through an emergency route. These patients may present with more aggressive types of tumours than those who present through a non-emergency route, have more advanced stage disease and poor prognosis, and they may be in poorer overall health condition, all of which could limit treatment options. Although socioeconomic deprivation, histological type, performance status, clinical stage and comorbidity explained the association to a large extent, a significant and strong association remained, of which potential residual confounding is unlikely to explain all. It needs to be borne in mind all patients presenting through an emergency route are analysed as one group in this study, whereas this constitutes a heterogeneous group. The majority of patients diagnosed as an emergency present to an A&E department (64%)  ([National Cancer Intelligence Network, 2013](#_ENREF_9)) (correct reference?) and may experience a different work up than those seen in a respiratory clinic, and as a result their diagnosis may be delayed or the surgical treatment not offered.

There was a weak association between emergency presentation and survival among the NSCLC patients undergoing surgical resection. Socioeconomic deprivation, histological type, performance status, clinical stage and comorbidity explained most of the association between emergency presentation and poorer survival in the first month following diagnosis, but less so in the longer term, where the association with emergency presentation diminished but persisted. It seems unlikely that residual confounding would explain all of the remaining survival difference observed for emergency presentation. This may indicate that other factors related to emergency presentation that are not captured may be important. For a small proportion of patients, the inpatient or outpatient activity that led to them being assigned an emergency route to diagnosis may not necessarily be in connection to the cancer itself. This group will include patients with urgent but limited health problems, their lung cancer being diagnosed at an early stage, as well as patients with serious or life-threatening comorbidities that are not captured in the Charlson index, all of which may affect their medium term survival.

*In contrast, among the lung cancer patients not undergoing surgical resection those presenting through an emergency route had a lower survival than other patients, which was most pronounced in the first month following diagnosis. The different reasons why lung cancer patients diagnosed through an emergency route have poor outcomes beyond those included in our modelling, are not immediately obvious. There is some evidence that within the group of lung cancer patients diagnosed through one of the emergency routes there is variation in survival  (*[*National Cancer Intelligence Network, 2013*](#_ENREF_9)*). Most emergency presentations occur via A&E, and these lung cancer patients together with those diagnosed following an emergency GP referral have the lowest relative survival at one month and one year, whereas patients diagnosed following an emergency referrals to outpatients has survival approaching that of the non-emergency routes  (*[*National Cancer Intelligence Network, 2013*](#_ENREF_9)*). These patients may present with advanced stage, severe comorbidities or lower performance score affecting their immediate outcome. Although we controlled for these factors in our model, the observed differences may be explained at least in part by possible residual confounding by these variables. These patients, who are more often elderly and with worse performance status, are other than less likely to undergo surgical resection of their tumour, also probably less likely to receive chemotherapy or radiotherapy treatment, which may help explain their poor outcomes  (*[*Patel et al, 2007*](#_ENREF_12)*). The patients presenting through A&E may include patients with serious or life-threatening comorbidities that are not captured in the Charlson index, and that may affect their short term survival.*

*The findings of this study support the notion that ensuring lung cancer symptoms are recognised early enough so that patients are not diagnosed as an emergency will be an important part of improving survival of lung cancer patients in the future. However, this may change the stage distribution to become more favourable, thus increase the eligibility for surgical resection. However, since this only explains a small part of the observed differences, and part of the factors playing into this may not be modifiable (e.g., lung cancer related complications other than stage, limiting operability as well as chemotherapy or radiotherapy options, plus and concomitant life threatening conditions other than lung cancer). It could be of interest to direct further investigations to explore what factors in the emergency pathway that may potentially delay diagnosis and/or limit treatment options being offered, but I doubt that that would make a big enough contribution to warrant investigation?!*

**Competing interests**

All authors declare that they have no conflict of interest.

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