Treatment and survival of non-small cell lung cancer patients in the Netherlands

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MicroAbstract

Non-small cell lung cancer (NSCLC) survival is compared between patients treated in academic (n=1,289) versus non-academic (n=12,698) hospitals, using Kaplan Meier estimates and a Cox proportional hazards model. For 1,009 patients, treatment patterns are described. Diagnosis in an academic hospital is associated with a decreased hazard ratio of mortality. Possibilities for improvement of NSCLC care are suggested.

Abstract

Background

The aims of this study are to analyse differences in survival between academic and non-academic hospitals and to provide insight into treatment patterns for non-small cell lung cancer (NSCLC). Results show the state of NSCLC survival and care in the Netherlands and serve as foundation for future cost and cost-effectiveness studies of treatment alternatives.

Methods

The Netherlands Cancer Registry provided data on NSCLC survival for all Dutch hospitals. We used the Kaplan Meier estimate to calculate median survival time by hospital type and a Cox proportional hazards model to estimate the relative risk of mortality (expressed as hazard ratios, HRs) for patients diagnosed in academic versus non-academic hospitals, with adjustment for age, gender and tumour histology and stratifying for disease stage.
Data on treatment patterns in Dutch hospitals was obtained from four hospitals (two academic, two non-academic). A random sample of patients diagnosed with NSCLC from January 2009 until January 2011 was identified through hospital databases. Data was obtained on patient characteristics, tumour characteristics and treatments.

Results

The Cox proportional hazards model shows a significantly decreased hazard ratio of mortality for patients diagnosed in academic hospitals, as opposed to patients diagnosed in non-academic hospitals. This is specifically true for primary radiotherapy patients and patients who receive systemic treatment for non-metastasised NSCLC.

Conclusion

Patients treated in academic hospitals have better median overall survival than patients treated in non-academic hospitals, for patients treated with radiotherapy, systemic treatment or combinations. A wide variety of surgical, radiotherapeutic and systemic treatments is prescribed.

Keywords

Non-Small-Cell Lung Carcinoma, academic medical centers, general hospitals, mortality, therapy.

Clinical Practice Points

Treatment of non-small cell lung cancer patients differs between hospitals and may result in differences in survival. In the Netherlands, differences in treatment between hospitals have been shown for surgery for stage I and II disease, combination treatment for stage III and chemotherapy for stage IV disease. Standards and guidelines, including minimum treatment volumes, aim to minimize these differences.

This study shows a significantly decreased hazard ratio of mortality for patients diagnosed in academic hospitals, as opposed to patients diagnosed in non-academic hospitals. Furthermore, detailed treatment patterns are prescribed for a selection of hospitals (2 academic, 2 non-academic). The study provides an overview of current NSCLC care in the Netherlands. It raises questions about the cause of the differences in survival between hospital types and suggests possibilities for improvement in NSCLC care.

Introduction

Incidence as well as mortality from lung cancer is relatively high in the Netherlands. In 2012, lung cancer incidence was 66.1 males and 44.5 females per 100.000 person years (European Standardised Rates). Lung cancer mortality was 59.6 males and 35.6 females per 100.000 person years.[1]

More than 85% of lung cancers are from the non-small cell type.[2] Patients in early stage of disease (stage I-II) that are eligible for surgery have a relatively good prognosis. Even so, the estimated 5-year survival for early stage patients is only between 45% and 50%. Unfortunately, only 20% of the patients are eligible for a tumour resection. For patients that are ineligible for resection, stereotactic radiotherapy is the best alternative for surgery, that is, if no locoregional metastases are present and the tumour is located centrally.[3]

Alternatively, concurrent chemoradiotherapy is the standard treatment option for inoperable non-metastatic patients. There is evidence from a meta-analysis that radiotherapy with concurrent chemotherapy reduces locally recurrent disease and mortality compared to sequential chemoradiotherapy.[4] In the absence of distant metastases these patients have a 5-year survival of 5%-30%. Patients in advanced stage of disease (stage IV) are treated with combinations of chemotherapeutic agents or targeted therapy. The 5-year survival is 1%.[5]

Within the Netherlands, differences exist between hospitals with respect to treatment and survival of patients with NSCLC. For patients diagnosed with stage I and II NSCLC in 2001-2006, the probability of tumour resection increased with the surgical experience (lung resection volume) of the hospital as well as the available expertise.[6] Therefore, various conditions have been agreed upon in order to concentrate lung resections in specialised centres.[7]

For stage III NSCLC, probability of receiving combination treatment in the Netherlands was highly dependent on hospital as well, but no correlation was demonstrated with defined structural hospital characteristics such as teaching status or the availability of radiotherapy facilities.[6] The same was true for the probability of receiving chemotherapy for stage IV NSCLC.[8] Unfortunately, it was not reported if and how treatment variability between hospitals affected overall survival.

Apart from the minimum surgical volumes, broader standards exist for Dutch hospitals treating patients with lung carcinoma. They include requirements regarding (multidisciplinary) staff composition and available facilities.[9] Furthermore, a Dutch evidence-based guideline for the diagnosis and treatment of NSCLC exists and (modular) revisions are performed regularly to ensure actuality.[3]

Despite efforts to standardise NSCLC treatments across the Netherlands, differences may exist in diagnostic and treatment patterns between hospitals and may result in differences in survival. The aims of this study are to analyse differences in survival between academic and non-academic hospitals and to provide the reader with more information regarding NSCLC treatment patterns in the Netherlands. Current results will show the state of NSCLC survival and care in the Netherlands and will serve as foundation for future cost and cost-effectiveness studies of treatment alternatives.

FEV1 = forced expiratory volume in 1 second, HR = hazard ratio, ICD-O = International Classification of Diseases for Oncology, NCR = Netherlands Cancer Registry, NSCLC = non-small cell lung cancer.

Materials and methods

Patients and data

Population-based NCR data was used to analyse survival differences between academic and non-academic hospitals. The NCR provided data on all patients diagnosed with NSCLC between January 2009 until January 2011, as identified through the automated pathological archive (PALGA) and The National Registry of Hospital Discharge Diagnoses. Clinical information was manually abstracted from medical records and coded by trained NCR (Netherlands Cancer Registry) data managers, using a national manual and case report form. Data was obtained on patient characteristics, tumour characteristics, primary treatment and overall survival. Hospital type (academic versus non-academic) represents the type of hospital of diagnosis as registered in the NCR.

Detailed data on treatment patterns in Dutch hospitals was not available from the NCR and was therefore obtained from four, not randomly selected hospitals (two academic, two non-academic). A random sample of unselected patients diagnosed with NSCLC between 31 January 2009 and 31 January 2011 was identified through the four hospital databases. This sample included patients who were referred to one of the four selected hospitals from elsewhere. The random selection was performed by listing all NSCLC patients in Microsoft Excel, randomising their order and including them from the top. Clinical data was manually abstracted from medical records and coded by trained data assistants, using a web-based case report form. Data was obtained on patient characteristics, tumour characteristics and treatments. Data from the NCR was used to validate tumour histology and disease stage collected from the four hospital databases.

Selected tumour histologies included ICD-O (International Classification of Diseases for Oncology) codes 8010 to 8035, 8046 to 8230, 8244 to 8246 and 8250 to 8576 (all NSCLC). Presence of distant metastasis was recorded following the NSCLC stage classification system in use at diagnosis of the tumour, being either the sixth (2009) or the seventh (2010, 2011) TNM edition. However, TNM stage can change during the diagnostic period, can differ between clinicians, and cannot always reliably be obtained from patient charts. This was a limitation of both the data we collected and the NCR data, which we used to validate our stage information. We therefore decided not to separate stages I-III, in order to minimise potential misclassification.

As our study design is not subject to the Medical Research Involving Human Subjects Act, the Medical Research Ethics Committee of VU University Medical Centre exempted the study from ethical appraisal. Informed consent was not required for chart review.

Statistical analyses

All analyses were performed in IBM SPSS Statistics 21. We compared overall survival for patients diagnosed in academic hospitals and patients diagnosed in non-academic hospitals, for the following groups: (1) patients with non-metastatic NSCLC, (2) patients with metastatic NSCLC, (3) patients treated with primary surgery for non-metastatic NSCLC, (4) patients treated with primary surgery for metastatic NSCLC, (5) patients treated with primary radiotherapy for non-metastatic NSCLC, (6) patients treated with primary radiotherapy for metastatic NSCLC, (7) patients treated with primary systemic treatment for non-metastatic NSCLC, (8) patients treated with primary systemic treatment for metastatic NSCLC, and (9) NSCLC patients who did not receive anti-tumour treatment.

We used Kaplan Meier methods to estimate overall survival rates by hospital type and Cox proportional hazards models to estimate the relative risk of mortality (expressed as hazard ratios, HRs) and their 95% confidence intervals (95% CI) per hospital type, with all non-

academic hospitals as the reference group, with and without adjustment for age, gender and tumour histology and stratifying for disease stage at diagnosis (M0 or M+).

We used descriptive analyses to report treatment patterns. Treatments were allocated to the categories “aimed at non-metastasised disease” or “aimed at metastasised disease” dependent on disease stage (M0 or M+) at treatment start. Treatments were classified to be either surgery, radiotherapy, systemic treatment (including chemotherapy and targeted therapies) or combinations of the above. Chemoradiation was defined as definitive radiotherapy combined with concurrent or sequential systemic treatment.

Results

Baseline characteristics

The NCR included 13,992 patients fulfilling the selection criteria, 1,289 (9%) of whom were diagnosed in academic hospitals. In the four selected hospitals, data was collected on 1,067 patients. 58 patients (5.4%) were excluded because they came for a second opinion only. Only limited information was available about these patients, since they were treated in other hospitals than the four study hospitals. The distribution of the remaining 1,009 patients over the study hospitals was 556 patients in academic versus 453 patients in non-academic hospitals.

Table 1 shows baseline characteristics of both study populations. Within the total Dutch population, 9% of patients were diagnosed in academic hospitals as opposed to non-academic hospitals. In these academic hospitals, there were less elderly patients (over 75 years of age, n=239, 19% versus n=3,275, 26% in non-academic hospitals), less squamous cell carcinomas (n=327, 25% versus n=3,734, 29%) and less large cell carcinomas (n=125, 10% versus 1,757, 14%) as opposed to adenocarcinomas (n=649, 51% versus 5,572, 44%). In the academic hospitals, relatively many patients (n=644, 50%) were diagnosed with stage <IV NSCLC, though not as many as in the four selected hospitals (n=616, 61%).

Distributions of age, gender and tumour histology in the four selected hospitals are similar to these distributions in the total Dutch population. The total Dutch population also includes the patients from the four selected hospitals. In the four selected hospitals, a relatively high proportion of tumours was classified as clinical stage <IV (n=616, 61% versus 6,552, 47%), mainly due to referrals from other hospitals for specialised treatments. In addition to the 363 patients diagnosed with stage IV NSCLC at baseline in the four study hospitals, 113 patients initially had other stage disease that metastasised during our study period.
Unfortunately, WHO performance status and forced expiratory volume in 1 second (FEV1) were often not reported in the medical charts (WHO performance status 80.8% and FEV1 76% not reported).

[Table 1]

Total Dutch population, survival

Table 2 shows median overall survival of NSCLC patients per hospital and treatment type, not adjusted for case mix. Patients with non-metastasised disease treated in academic hospitals had superior overall survival as compared to patients with non-metastasised disease treated in non-academic hospitals. Survival for patients with metastasised disease was similar in both hospital types.

For non-metastasised as well as metastasised disease, no significant differences were found in overall survival of operated patients between the different hospital types. Patients treated with radiotherapy and/or systemic treatment for non-metastasised disease survived significantly longer when diagnosed in an academic hospital as opposed to a non-academic hospital. For patients treated with palliative radiotherapy for metastasised disease, and for patients who did not receive any antitumor treatment, median overall survival was similar between academic and non-academic hospitals.

[Table 2]

Cox proportional hazard models show a significantly decreased hazard ratio of mortality for patients diagnosed in academic hospitals, as opposed to patients diagnosed in non-academic hospitals. This is specifically true for primary radiotherapy patients and patients who receive systemic treatment for non-metastasised NSCLC. For primary surgery patients and patients who receive systemic treatment for metastasised NSCLC, no significant differences in mortality existed between hospital types. For patients receiving radiotherapy for metastasised disease, the improved survival in academic hospitals was non-significant when corrected for age, gender and tumour histology (Table 3).

[Table 3]

Treatment patterns in four selected hospitals

Surgery patients

Out of 616 patients with non-metastasised disease, 268 patients (43.5%) were operated in the study hospitals. Including reoperations, a total of 292 surgeries for non-metastasised disease were performed during the 2-year study period. Majority of surgeries were lobectomies (66.1%, n=193), followed by wedge resections (10.3%, n=30) and pneumonectomies (7.2%, n=21). For 148 operated patients (55.2%), surgery was the only antitumour treatment received in the study hospital.

Adjuvant radiotherapy is common in case of R1 or R2 (tumor positive) resections. In the study hospitals, 7.5% of operated patients (n=20) received adjuvant radiotherapy within two months of attempted surgery. Adjuvant systemic therapy is recommended for stage II-IIIA patients with a good performance score. Unfortunately it was not known for which proportion of patients adjuvant chemotherapy was indicated in the study hospitals, but it was prescribed within two months of the surgery to 48 patients (17.9%). Chemoradiation preceded surgery in 6.0% of cases (n=16).

Including patients who developed metastasis during the course of their disease (n=113), 41 patients with metastasised disease were operated (8.6%), receiving a total of 45 operations. Most of these surgeries (n=24) were non-locoregional (53.3%), mostly targeting the brain (n=9). 46.7% of surgeries (n=21) were locoregional, most often lobectomy (n=8) or wedge resection (n=7).

Radiotherapy patients

In addition to the 268 patients operated for non-metastasised disease, 142 patients received stereotactic radiotherapy (SBRT). In total, 353 out of 616 patients with non-metastasised disease (57.3%) received any type of radiotherapy, including combined modality treatments. 25 patients received locoregional radiotherapy that was classified as being of palliative intent (n=25, 7.1%).

Including patients who developed metastasis during the course of their disease (n=113), 273 patients with metastasised disease were treated with (any) radiotherapy (57.4%, including combined modality treatments), 198 of whom received at least one fraction on a distant metastasis (72.5%).

Patients treated with systemic therapy

242 patients with non-metastasised NSCLC (39.3%) received systemic treatment in the study hospital (including combined modality treatments). The most commonly prescribed drug regimen for non-metastasised disease was gemcitabine+cisplatin (n=70, see Table 4). Hundred thirty-seven patients were registered to receive chemoradiation, defined as systemic treatment with concurrent or sequential definitive, locoregional radiotherapy.

[Table 4]

Including patients who developed metastasis during the course of their disease (n=113), 234 patients with metastasised NSCLC (49.2%) received systemic treatment in the study hospital (including combined modality treatments), see Table 5. For 50.8% of the patients with metastasised disease, no systemic treatment was prescribed in the study hospital. Most commonly prescribed drug regimen was pemetrexed with platinum (n=105). For patients who did not receive antitumour treatment, reasons are provided below.

[Table 5]

Patients who did not receive primary antitumour treatment (selected hospitals)

In the selected hospitals, 114 patients (11.3%) did not receive any antitumour treatment. 14 out of 114 patients were registered to have received previous treatment in another hospital (n=5) or to be referred for treatment to another hospital during the study period (n=9). Fifty-six (56.0%) of the remaining patients without antitumour treatment received supportive care only. An additional 18 patients did not receive antitumour treatment following their own specific wishes (18.0%). Fifteen patients died before treatment was started (15.0%), 4 patients had limited/no treatment options due to comorbidities (4.0%), in 4 cases a wait and see policy was followed (4.0%) and for one patient, treatment for another type of cancer had priority over the symptom-free lung cancer (1.0%). For 2 patients, reason for not receiving antitumour treatment was not registered.

Discussion

Patients with NSCLC in academic hospitals have better median overall survival than patients with NSCLC in non-academic hospitals. These differences mainly reflect differences in overall survival for patients treated with radiotherapy, systemic treatment or combinations. No significant differences in overall survival between hospital types were found for the subgroup of patients treated with surgery.

The generally improved survival of patients from academic hospitals might be explained by unmeasured confounders. In Cox proportional hazards analyses, hazard rates were adjusted for age, gender and tumour histology and stratified for disease stage at diagnosis. However, we did not have the necessary information to correct for other relevant prognostic factors, such as WHO performance status and FEV1. Although performance status is one of the most important prognostic factors, unfortunately it was not recorded for the majority of our

study population. Possibly the WHO performance status for patients diagnosed in academic hospitals was relatively high.

Another reason for improved survival in academic hospitals may be a different use of treatments, such as the proportion of patients receiving chemotherapy for metastasised disease. From the current study it is unknown to what extent this may explain differences in survival. Another explanation may be the higher level of experience available in (generally large) academic centres as well as their pioneer role in adopting innovations. New or improved treatment regimens are usually not uniformly implemented in all hospitals from the start. This can be a matter of (un)awareness or (lack of) available information on the new treatment and outcomes.

If survival differences exist due to differences in experience or expertise, possibilities for improvement exist. Data collection, sharing, self-reflection and communication between doctors are crucial feedback and improvement tools.[10] Also, further centralisation of NSCLC treatments may improve treatment outcomes and reduce variability between hospitals. While literature about differences in treatments and/or survival between hospital types is mostly about surgery, recent innovation in cancer care has been mainly about combining treatment modalities.[8] Therefore, patients may benefit from additional critical assessment of the minimum skills and experience in hospitals prescribing and applying these treatments for NSCLC.[9]

Obviously, “treatment in an academic hospital” does not automatically mean good quality of care, or the other way around. Academic or non-academic hospital type is probably not the main predictor of treatment or survival differences. Other important factors might be hospital and treatment volume, infrastructure, dedication of multidisciplinary teams and adoption of innovative treatments.[8]

Next to survival of the Dutch NSCLC population, this article describes treatment patterns for patients treated and/or followed for NSCLC in four selected hospitals. Our study as well as other studies[11] show a multitude of treatments to be prescribed to these patients. Choice of treatment is very much patient and tumour dependent. This heterogeneity poses a challenge for cost-effectiveness studies, amongst others in selecting appropriate comparator treatment groups.

It would be interesting to study if differences in treatment patterns between academic and non-academic hospitals may explain differences in survival. Unfortunately, this was not possible with our data since we did not include a representative sample of academic and non-academic hospitals. The four participating hospitals are teaching hospitals, are relatively large, and they employ some of the key opinion leaders in the Dutch field of lung oncology. Therefore treatment patterns and survival in the two non-academic hospitals are probably not representative for non-academic hospitals in the rest of the Netherlands.

A challenge in this study was the registration of disease stages. The TNM staging system has changed to the 7th edition halfway the study period, so for each patient we used the TNM edition in use at the time the clinician recorded the disease stage in the patient chart. However, TNM stage can change during the diagnostic period, can differ between clinicians, and cannot always reliably be obtained from patient charts. This was a limitation of both the data we collected and the NCR data, which we used to validate our stage information. We therefore decided not to separate stages I-III, in order to minimise potential misclassification.

In the treatment pattern part of this study, selection bias may have occurred since patients referred to the study hospitals from other hospitals were included. Treatment patterns were presented as such, so they include patients who were referred for specialised treatment. This reduces the generalisability of treatment patterns to other, non-specialised hospitals.

Furthermore, in the treatment pattern part of this study, the follow-up time of this study was relatively short. Since patients were included in the study as they were diagnosed within a two-year time frame, we collected relatively more data on the early phases of disease. Patients with a relatively good prognosis become censored cases as they survive end of the study follow-up. Therefore, information about later treatment lines for these patients was lacking.

Since the data was collected retrospectively and was subtracted from medical charts, the resulting data was dependent on the patient information obtained by the hospital and on the registration in medical charts. Moreover, some patients were treated in multiple hospitals. Permission to collect and use patient chart data could only be obtained for the four study hospitals. Therefore, patients were “lost” and considered “censored” from the moment they were referred to a different hospital than the study hospitals. It would be more insightful to follow patients during their entire disease course, even when multiple hospitals are visited for diagnosis and treatment.

The demand for real-world evidence has increased recently, as policy makers recognise its value in providing information on treatment patterns, treatment effectiveness and cost-effectiveness. This type of data is important to evaluate the large number of new, mainly targeted, therapies that are expected to be launched in the coming years. This study is first to provide a broad overview of current NSCLC care in the Netherlands.

Conclusions

A wide variety of treatments was prescribed for NSCLC patients. Differences in survival between hospital types suggest possibilities for improvement in NSCLC care in the Netherlands. However, due to limitations of the data from the current study, confirmation by other studies is advised.

Acknowledgements

Funding for this study was provided by GlaxoSmithKline BV. GlaxoSmithKline was not involved with the data collection, data analysis or reporting.

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Table 1 Baseline characteristics

	Total Dutch population 2009-2011 n (%)	**Dutch population, patients diagnosed in academic hospitals 2009-2011 n (%)**	**Dutch population, patients diagnosed in non-academic hospitals 2009-2011 n (%)**	**Population in four selected hospitals (two academic, two non-academic) 2009-2011 n (%)**
Total patients	13,992 (100)*	1,289 (100)	12,698 (100)	1,009 (100)
Age (years)				
<60	3,566 (26)	391 (30)	3,175 (25)	272 (27)
60-74	6,910 (49)	659 (51)	6,248 (49)	501 (50)
≥75	3,516 (25)	239 (19)	3,275 (26)	236 (23)
Gender				
Male	8,841 (63)	780 (61)	8,059 (64)	660 (65)**
Histology				
Adenocarcinoma	6,222 (45)	649 (51)	5,572 (44)	490 (49)
Squamous cell carcinoma	4,062 (29)	327 (25)	3,734 (29)	256 (25)
Large cell carcinoma	1,884 (14)	125 (10)	1,757 (14)	101 (10)
Other histology	407 (3)	48 (4)	358 (3)	33 (3)
Unknown	1,417 (10)	140 (11)	1,277 (10)	129 (13)
Clinical stage				
Stage <IV	6,552 (47)	644 (50)	5,904 (47)	616 (61)
Stage =IV	6,887 (49)	588 (46)	6,298 (50)	363 (36)
Unknown	553 (4)	57 (4)	496 (4)	30 (3)

*For five patients, hospital type was not registered.
**For one patient, gender was not registered.

Table 2 Median overall survival per hospital type per treatment, unadjusted (total Dutch population)

	Dutch population, diagnosed in academic hospitals, 2009-2011 Median overall survival in years (95%CI), n	
	Academic hospitals	Non-academic hospitals
Total		
Non-metastasised	2.66 (2.14-3.18), 644	1.83 (1.73-1.93), 5,904
Metastasised	0.41 (0.35-0.48), 588	0.39 (0.38-0.41), 6,298
Primary surgery		
Non-metastasised	3.16 (3.02-3.30)*, 321	3.05 (3.00-3.10)*, 2,485
Metastasised	1.48 (0.12-2.85), 29	1.55 (0.92-2.18), 128
Primary radiotherapy		
Non-metastasised	2.11 (1.72-2.50), 278	1.64 (1.55-1.72), 2,474
Metastasised	0.45 (0.36-0.54), 308	0.43 (0.40-0.46), 2,372
Primary systemic treatment		
Non-metastasised	2.22 (1.95-2.49), 261	1.66 (1.57-1.76), 2,582
Metastasised	0.81 (0.74-0.89), 306	0.69 (0.66-0.71), 3,087
No antitumor treatment	0.10 (0.07-0.14), 211	0.15 (0.14-0.16), 2,861

*These numbers represent mean instead of median overall survival, since >50% of patients were still alive at end of follow-up.

Table 3 Crude and adjusted hazard ratios of mortality for patients diagnosed in academic hospitals versus patients diagnosed in non-academic hospitals by treatment type.

	Dutch population, diagnosed in academic hospitals 2009-2011			
	Crude HR*		Adjusted** HR*	
	95% CI	Sig	95% CI	Sig
Total Non-metastasised Metastasised	 0.755 (0.674-0.845) 0.876 (0.802-0.956)	 0.000 0.003	 0.775 (0.685-0.876) 0.892 (0.812-0.980)	 0.000 0.018
Primary surgery Non-metastasised Metastasised	 0.875 (0.711-1.078) 0.997 (0.591-1.682)	 0.210 0.992	 0.907 (0.733-1.121) 0.979 (0.564-1.698)	 0.364 0.940
Primary radiotherapy Non-metastasised Metastasised	 0.789 (0.673-0.926) 0.883 (0.780-0.998)	 0.004 0.047	 0.767 (0.640-0.920) 0.890 (0.778-1.018)	 0.004 0.089
Primary systemic treatment Non-metastasised Metastasised	 0.808 (0.686-0.952) 0.887 (0.785-1.003)	 0.011 0.057	 0.787 (0.656-0.942) 0.894 (0.784-1.019)	 0.009 0.092
No antitumor treatment	1.046 (0.907-1.206)	0.537	0.980 (0.840-1.144)	0.800
*Reference category: Dutch population, patients diagnosed in non-academic hospitals 2009-2011. **Models directly adjusted for age, gender and tumor histology.				

Table 4 Frequency of prescription of systemic treatment regimens for non-metastasised disease (including combined modality treatments) in the four selected hospitals

Treatment	**Number of patients receiving at least one administration of treatment (%)**
Gemcitabine / cisplatin	70 (28.9)
Pemetrexed / cisplatin	59 (24.4)
Vinorelbine / cisplatin	24 (9.9)
Etoposide / cisplatin	22 (9.1)
Gemcitabine / carboplatin	15 (6.2)
Gemcitabine	13 (5.4)
Pemetrexed / carboplatin	10 (4.1)
Docetaxel / carboplatin	7 (2.9)
Docetaxel	6 (2.5)
Vinorelbine / carboplatin	6 (2.5)
Other	14 (5.8)
Unknown	15 (6.2)

Table 5 Frequency of prescription of systemic treatment regimens for metastasised disease in the four selected hospitals

Treatment	**Number of patients receiving at least one administration of treatment (%)**
Pemetrexed / cisplatin	57 (24.4)
Pemetrexed / carboplatin	48 (20.5)
Erlotinib	44 (18.8)
Gemcitabine / cisplatin	23 (9.8)
Docetaxel / carboplatin	22 (9.4)
Docetaxel	19 (8.1)
Gemcitabine / carboplatin	18 (7.7)
Pemetrexed	18 (7.7)
Paclitaxel / carboplatin	15 (6.4)
Sorafenib	10 (4.3)
Paclitaxel / carboplatin / bevacizumab	10 (4.3)
Gefitinib	7 (3.0)
Etoposide / cisplatin	6 (2.6)
Gemcitabine	5 (2.1)
GDC0941 (PI3K inhibitor, clinical trial)	5 (2.1)
Paclitaxel	5 (2.1)
Other	30 (12.8)
Unknown	11 (4.7)