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Temporal Patterns of Care and Outcomes of Non-Small Cell Lung Cancer Patients in the United States Diagnosed in 1996, 2005, and 2010

Filip Kaniski[a], **Lindsey Enewold**[a], **Anish Thomas**[b], **Shakuntala Malik**[c], **Jennifer L. Stevens**[d], and **Linda C. Harlan**[a]

[a]National Cancer Institute, Division of Cancer Control and Population Sciences, Healthcare Delivery Research Program

[b]National Cancer Institute, Center for Cancer Research, Thoracic and Gastrointestinal Oncology Branch

[c]National Cancer Institute, Division of Cancer Treatment and Diagnosis, Cancer Therapy Evaluation Program

[d]Information Management Services, Inc

Abstract

Introduction—Lung cancer remains a common and deadly cancer in the United States. This study evaluated factors associated with stage-specific cancer therapy and survival focusing on temporal trends and sociodemographic disparities.

Methods—A random sample (n=3,318) of non-small cell lung cancer (NSCLC) patients diagnosed in 1996, 2005 and 2010, and reported to the National Cancer Institute's Surveillance Epidemiology and End Results (SEER) program was analyzed. Logistic regression was utilized to identify factors associated with receipt of surgery among stage I/II patients and chemotherapy among stage IIIB/IV patients. Cox proportional hazard regression was utilized to assess factors associated with all-cause mortality, stratified by stage.

Results—Surgery among stage I/II patients decreased non-significantly overtime (1996: 78.8%; 2010: 68.5%; p=0.18), whereas receipt of chemotherapy among stage IIIB/IV patients increased significantly overtime (1996: 36.1%; 2010: 51.2%; p<0.01). Receipt of surgery (70–79 and ≥80 vs. <70: Odds Ratio(OR):0.31; 95% Confidence Interval (CI): 0.16–0.63 and OR:0.04; 95% CI: 0.02–

Corresponding author: Lindsey Enewold, PhD MPH, Healthcare Delivery Research Program, National Cancer Institute, 9609 Medical Center Drive, Room 3E506, Bethesda, MD 20892-9762, Telephone: 240-276-6856, Fax: 240-276-7906, lindsey.enewold@nih.gov.

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0.10, respectively) and chemotherapy (≥80 vs. <70: OR: 0.26; 95% CI:0.15–0.45) was less likely among older patients. Median survival improved non-significantly among stage I/II patients 51 to 64 months (p=0.75) and significantly among IIIB/IV patients from 4 to 5 months (p<0.01).

Conclusion—Treatment disparities were observed in both stage groups, notably among older patients. Among stage I/II patients, survival did not change significantly possibly due to stable surgery utilization. Among stage IIIB/IV patients, although the use of chemotherapy increased and survival improved, the one-month increase in median survival highlights the need for addition research.

Keywords

lung cancer; treatment; surgery; radiation; chemotherapy; targeted therapy survival

Introduction

Lung cancer, the vast majority (85%) of which is non-small cell lung cancer (NSCLC), is the leading cause of cancer mortality in the United States. It is estimated that 158,040 people died from lung cancer in 2015, accounting for 27% of all cancer deaths.[1] Although recent trends show significant decreases in lung cancer incidence and mortality, in large part due to the decline in national smoking rates, more effective treatment and improved delivery of care (e.g., cancer-directed and supportive), the 5- year survival rate remains low at 18%.[1]

For the past two decades, the recommended treatment for early stage disease, particularly for patients with good performance status, has been surgery and for late stage has been systemic therapy.[2–4] However, improvements in treatment efficacy have been made, especially for late stage disease due to the introduction of platinum-based chemotherapies in the mid-1990s and systemic targeted therapies (e.g., antibodies and tyrosine kinase inhibitors) over the following decade.[5–7]

Though there is a strong base of evidence for the efficacy of recently developed systemic therapies in the treatment of late stage NSCLC,[7] the implementation of these therapies into general practice, regardless of tumor stage, as well as variations in administration of traditional modalities (e.g., surgery, radiotherapy and older chemotherapy agents) over time, have not been comprehensively studied.

A growing base of evidence has demonstrated disparities by race,[8–10] age[10–12] and insurance status[13, 14] with respect to receipt of appropriate care. However, many of these studies have had narrow scopes in terms of study period, patient population, and the number of sociodemographic factors examined.

A better understanding of the temporal treatment patterns and outcomes among NSCLC patients could lead to more equitable evidence-based care, particularly if the influence of sociodemographic characteristics can be better understood. In this analysis we use a population-based sample of NSCLC patients, stratified by stage adjusting for factors such as age, race/ethnicity, insurance, and comorbidities, to investigate how treatment practices and survival have changed between 1996–2010.

Methods

Data Sources

The data used in this analysis was obtained from the National Cancer Institute (NCI) Patterns of Care (POC) studies, which are conducted annually and include a stratified random sample of cancer patients ascertained through the Surveillance, Epidemiology, and End Results (SEER) program. The aim of the POC studies is to describe the dissemination of state-of-the-art cancer therapies into community practice.

Each year, a random sample of patients who have been reported to SEER as having been diagnosed with the selected cancer are included in the POC study. Patient demographics (e.g., sex, race/ethnicity) and clinical information (e.g., date of diagnosis, and tumor characteristics) are obtained via hospital medical records. To ensure complete treatment information, treating physicians are also contacted to verify the administration of systemic therapy, which is not routinely documented in hospital records. Prior to initiating the POC study, each SEER registry obtained institutional review board approval as required.

Study Population

Patients who were reported to SEER as having been diagnosed in 1996, 2005, or 2010 with histologically-confirmed first primary NSCLC and were at least 20 years old were eligible for inclusion. Patients diagnosed at autopsy or by death certificate only were not eligible. For each year, all eligible patients were stratified by registry, race/ethnicity, and sex; a random sample was then drawn from each stratum. Patients with in situ NSCLC (n = 1), unstaged NSCLC (n = 245), or unknown race/ethnicity (n = 3) were excluded from these analyses.

Variables of Interest

Race/ethnicity was categorized as non-Hispanic white (NHW), non-Hispanic black (NHB), non-Hispanic other and Hispanic. Non-Hispanic other patients were not included in the 1996 sample. The median age at lung cancer diagnosis is 70 years[15] and treatment patterns/recommendations have been shown to vary according to patient age;[16] therefore, age at diagnosis was assessed as <70, 70–79, and ≥80 years. Patients were classified as ever or never smokers based on information abstracted from their medical records. All coexisting conditions listed in the medical records were abstracted and centrally coded. Chronic obstructive pulmonary disease (COPD) can be a severe, debilitating condition and is a common comorbidity among NSCLC patients that may independently influence treatment decisions; it was, therefore, assessed separately. Other comorbidities were assessed using a combined Charlson score that did not take into account NSCLC or COPD.[17] Marital status was classified as married (married, living as married) and not married (never married, separated, divorced, or widowed). Patients were grouped into four categories according to insurance status: any Medicaid coverage, Medicare only, uninsured or unknown insurance status and “other” insurance (e.g., private, including HMO, or Veteran Affairs/Tri-care). Morphology codes for histology were categorized as squamous cell carcinoma (8050–8078, 8083–8084), adenocarcinoma (8140, 8211, 8230–8231,8250–8260, 8323, 8480–8490, 8550–8551, 8570–8574, 8576), large cell carcinoma (8010–8012, 8014–8031,8035, 8310),

or carcinoma not otherwise specified.[18] Cancer stage was determined according to the SEER modified American Joint Committee on Cancer (AJCC) Staging Manual, 3rd Edition (1996)[19] and 6th edition (2005, 2010)[20] and grouped as I/II, IIIA, IIIB/IV to assess stage specific treatment and survival.

Statistical Analysis

In order to provide more stable estimates, Hispanic and NHB patients were oversampled in all years and women were oversampled in 2005 and 2010. Sample weights were calculated as the inverse sampling proportion for each stratum in order to obtain estimates that reflected all NSCLC patients diagnosed in the SEER areas during the study years.

Differences in patient demographics, clinical characteristics, and treatments received over time were evaluated using the Chi Square test. Factors associated with receipt of surgery among stage I/II patients and chemotherapy among stage III/IV patients were assessed using bivariate chi-square tests and multivariate logistic regression. Kaplan Meier methods were utilized to estimate median survival time. Cox proportional hazards models were created to examine factors associated with all-cause mortality. Follow-up was considered from the first day month of diagnosis (exact day was not available) until death or study end (12/2013). Variables that were found to be significantly associated ($p \leq 0.05$) with the outcome of interest during bivariate analyses were included in multivariate regression models. To account for the complex sampling, all analyses were conducted using SAS (version 9.3; SAS Institute Inc., Cary, NC) and SAS-callable SUDAAN (version 11.0.0; Research Triangle Institute, Research Triangle Park, NC).

Results

Overall, there were 3,318 patients included: 906 diagnosed in 1996; 1,061 diagnosed in 2005; and 1,351 diagnosed in 2010 (Table 1). Patient sex, race/ethnicity, and COPD status did not differ by year of diagnosis. However, age at diagnosis, insurance status, marital status, Charlson score, smoking status, stage and histology were significantly associated with year of diagnosis.

Stage I/II

There were 836 stage I/II patients included. Due to the small number of patients in this group who received targeted therapy, a systemic therapy variable that included both chemotherapy and targeted therapy was assessed. Administration of systemic therapy to these patients increased significantly from 9% in 1996 to 29% in 2010 ($p < 0.01$, data not shown) while radiation therapy administration did not change significantly (1996: 25%, 2010: 29%; data not shown). The proportion of stage I/II patients receiving surgery, the generally recommended modality of treatment for this group, decreased from 79% to 69% between 1996 and 2010; however, this temporal variation was not statistically significant ($p=0.18$; Table 2). In bivariate analyses receipt of surgery was found to be significantly associated age, race/ethnicity, insurance status, marital status, COPD status, smoking history, histology, radiation and systemic therapy. When included in a multivariate model, surgery was significantly less likely among patients diagnosed at age 70 or older [70–79 and >80 vs.

<70: odds ratio (OR): 0.31, 95% confidence interval (CI): 0.16 – 0.63 and OR: 0.04; 95% CI: 0.02–0.10, respectively]; and patients with any Medicaid or Medicare only (OR range: 0.14–0.34); Table 2). Receipt of surgery was significantly more common among patients with adenocarcinomas and large cell tumors compared to those with squamous cell tumors (OR range: 2.92–6.11) and less common among patients who received radiation (OR: 0.03, 95% CI: 0.01 – 0.06).

Stage IIIA

Due to less definitive treatment guidelines and small sample size (n=313), multivariate assessments of factors associated with treatment were not conducted among stage IIIA patients. For these patients, only basic temporal trends in treatment were examined: receipt of systemic therapy was found to increase significantly between 1996 and 2010 (1996 = 45%, 2010 = 73%, $p = 0.01$), while radiation therapy (1996 = 57%, 2010 = 55%, $p = 0.86$) and surgery (1996 = 39%, 2010 = 33%, $p = 0.68$) did not vary significantly with time (data not shown).

Stage IIIB/IV

There were 2,169 stage IIIB/IV patients included. Among this group of patients, receipt of surgery (1996: 13%, 2010: 7%; $p = 0.05$) and radiation (1996: 57%, 2010: 47% p=0.01) decreased significantly (data not shown). Bivariate analyses indicated that chemotherapy administration, the most commonly administered modality of treatment in this patient group, increased significantly over time (1996: 36%; 2010: 51%; $p = <0.01$; Table 3). A significant temporal increase in chemotherapy was still observed after adjustment for other covariates. Multivariate analysis also indicated that receipt of chemotherapy was less likely among older patients (≥80 vs <70: OR: 0.26; 95% CI: 0.15–0.45) and patients with more advanced disease (stage IV vs. IIIB: OR: 0.51; 95% CI: 0.36–0.71); being married was associated with a higher likelihood of receiving chemotherapy (OR: 1.84; 95% CI: 1.35–2.51). Receipt of chemotherapy was also associated with receipt of radiation and targeted therapy.

The utilization of specific systemic (e.g., chemotherapy and targeted therapy) agents varied with time (Table 4). Among stage IIIB/IV patients who received systemic therapy, etoposide administration decreased from 32% in 1996 to 5% in 2010 ($p = <0.01$). Cisplatin administration also decreased, from 35% in 1996 to 18% in 2010 ($p = <0.01$). Use of carboplatin increased from 50% in 1996 to 73% in 2010 ($p = <0.01$) while docetaxel increased from 2% in 1996 to 13% in 2010. The 2005 and 2010 data also provided an opportunity to examine the uptake of more recently developed targeted therapies. In this span of 5 years, the percentage of patients receiving pemetrexed increased from 6% to 38% ($p = <0.01$) and those receiving bevacizumab increased from 4% to 22% ($p = <0.01$).

Survival by Stage at Diagnosis

Among stage I/II patients, median survival did not change significantly during the early study period (1996: 51 months, 2005: 64 months; p=0.75; data not shown); length of follow-up was not sufficient to determine the median survival for patients diagnosed in 2010. Furthermore, year of diagnosis was not associated with all-cause mortality using bivariate Cox proportional hazard regression. During multivariate analyses, all-cause mortality was

found to be significantly higher among older patients [70–79 and ≥80 vs. <70: Hazard Ratio (HR): 1.60, 95% CI: 1.17–2.19 and HR:1.76; 95% CI: 1.19–2.61, respectively]; patients who had any Medicaid, Medicare only and no or unknown insurance, patients with COPD (HR: 1.56; 95% CI: 1.16–2.11) and patients with large cell tumors (vs. squamous cell: HR: 1.69; 95% CI: 1.02–2.78; Table 5). All-cause mortality was significantly lower among females (HR: 0.73; 95% CI: 0.56–0.95); Hispanic patients (vs. NHW: HR: 0.58; 95% CI: 0.35–0.97) and patients who had surgery (HR: 0.30; 95% CI: 0.20–0.46).

Median survival among stage IIIA patients increased from 11 months in 1996 to 23 months in 2010 ($p < 0.01$, data not shown). Year of diagnosis was, however, not associated with all-cause mortality based on bivariate Cox proportional hazard regression. Among the stage IIIA patients, during multivariate analysis, all-cause mortality was significantly higher among Hispanic patients (vs. NHW: HR: 2.19; 95% CI: 1.41–3.41) and among patients with Medicare only (vs. other insurance: HR: 1.63; 95% CI: 1.01–2.64; Table 5). All-cause mortality was significantly lower among patients who had surgery (HR: 0.45; 95% CI: 0.30–0.66).

Among stage IIIB/IV patients, median survival increased from 4 months in 1996 to 5 months in 2005 and 2010 ($p<0.01$; data not shown). Multivariate analyses indicated that all-cause mortality was significantly higher among patients with carcinoma, not otherwise specified (vs. squamous cell: HR: 1.44; 95% CI: 1.18–1.77) and lower among patients diagnosed in 2005 (vs. 1996: HR: 0.83; 95% CI: 0.69–0.99; Table 5). Receipt of each treatment modality was also associated with lower all-cause mortality (radiation: HR: 0.76, 95% CI: 0.66–0.88; surgery: HR: 0.46, 95% CI: 0.34–0.61; chemotherapy: HR: 0.43, 95% CI: 0.37–0.50 and targeted therapy: HR: 0.57, 95% CI: 0.46–0.70).

Discussion

Our results elucidate trends in treatment and survival of NSCLC patients diagnosed in 1996, 2005 and 2010. During the study period, regardless of stage, utilization of systemic therapy increased, while utilization of surgery and radiation therapy remained stable for stage I/II and IIIA patients and decreased for stage IIIB/IV patients. Receipt of therapy was also found to vary by patient sociodemographics, most notably older patients were less likely to receive stage appropriate treatment. Finally, although median survival was observed to improve over time the temporal difference for stage I/II patients was not significant and although significant the one-month increase in median survival for stage IIIB/IV patients, which was in agreement with the experience of the vast majority of lung cancer patients diagnosed in the SEER areas,[21] was in reality minimal.

Few previous studies have examined trends in administration of chemotherapy, radiation, and surgery in NSCLC patients, particularly those treated in the United States. The American College of Surgeons estimated that 71.7% of stage I and 62.2% of stage II patients diagnosed in 2001 received surgery,[12] which appears to be in agreement with our findings. A recent analysis that examined treatment patterns among Medicare patients diagnosed with metastatic NSCLC between 2001–2009 also reported 45% received chemotherapy and 55% received radiation.[22] Our findings show similar results regarding chemotherapy

administration in stage IIIB/IV patients; however, radiation utilization was notably lower in our patient population. The discrepancies in radiation usage may be due to different inclusion criteria (e.g., metastatic vs. stage IIIB/IV; age 20+y vs. 65+y) and/or study periods.

Differences in receipt of surgery and chemotherapy were also examined with respect to patient sociodemographics. Receipt of either treatment was associated with patient age at diagnosis, even after accounting for other potential factors. Patients over the age of 70 were significantly less likely to receive treatment. Though the risks of post-operative complications along with higher mortality rates have traditionally made elderly patients poor candidates for surgical intervention,[23–25] recent evidence has indicated that after accounting for other risk factors, such as performance status, older patients may show outcome benefits equal to those of younger patients.[26] Thus, it has been argued that age alone should not be a contraindication to undergoing tumor resection. The benefits of chemotherapy treatment for late stage elderly patients are not as well-defined;[27] however, a recent study by Koyi et al. again suggests performance status, not age, should be the main determinant of treatment.[28] Additional sociodemographic factors were associated with receipt of stage-specific treatment. Receipt of surgery was found to be significantly less likely among patients with public insurance (e.g., Medicare only or any Medicaid), which is consistent with prior studies.[13, 14] Furthermore, having any Medicaid, Medicare only and no/unknown insurance was found to be associated with poorer survival among stage I/II patients. These latter findings highlight the impact that variations in access to care can have on cancer outcomes.

Notably fewer patient characteristics were found to be associated with receipt of chemotherapy among late stage patients. Patients diagnosed during the later years of the study (2005, 2010) were significantly more likely to receive chemotherapy, likely due to the improved effectiveness of newly approved agents such as permetrexed and bevacizumab and improvements to care delivery.[7] Patients who were married were also more likely to receive chemotherapy, which is consistent with previously published studies in other cancers.[29, 30] However, insurance status and race/ethnicity, both factors that significantly affected receipt of surgery among stage I/II patients, were not associated with receipt of chemotherapy among stage IIIB/IV patients. In addition to sociodemographic characteristics, significant temporal variation in the administration of specific chemotherapeutic agents were observed. In particular, between 1996 and 2010 the use of cisplatin decreased while the use of carboplatin increased, which likely reflects the increased awareness of cisplatin toxicities compared with carboplatin[31] and the increased availability of carboplatin after generic versions were introduced in the mid-2000's.[32]

A limitation of this study is its observational nature; therefore, the findings should be interpreted with caution, particularly the observation that treatments were associated with better survival as this may have resulted because patients receiving the treatments had better performance status and were more likely to have longer survival regardless of treatment. Survival was also assessed from the time of diagnosis and there is typically a time lag between diagnosis and treatment. When analyses were restricted to patients who survived at least two months post-diagnosis, the Cox proportional HR point estimates were attenuated (e.g., stage IIIB/IV chemotherapy HR: 0.53 and targeted therapy HR: 0.69, data not shown). However, the inferences regarding the survival benefits of treatment remained unchanged.

Thus, an immortal time bias cannot fully explain the observed results. It is possible though that advancements in staging procedures may have resulted in stage migration, which may explain some of the observed improvements in survival. Although Charlson score was included as a covariate, information on performance status, which may have influenced treatment and/or survival was unavailable. Similarly, although ever smoking status was included as a covariate, more detailed information was not available; thus, residual confounding associated with smoke exposure cannot be ruled out. Patient and physician preference with regard to treatment was also not known. A particular strength of this study was the large population-based sample of patients treated throughout the United States, which provided the opportunity to assess “real world” disparities associated with NSCLC treatment and survival.

In conclusion, these results demonstrate trends in the administration of surgery and chemotherapy among early and late stage NSCLC patients, respectively. Administration of chemotherapy increased significantly between 1996 and 2010, with notable changes in the usage of specific agents such as carboplatin and cisplatin, while surgery did not vary significantly over time. Age and insurance status were associated with receipt of treatment and survival. Although these findings indicate that improvements in NSCLC treatment and survival have been made over the past two decades, these findings also highlight that there is still room for improvement.

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References

1. American Cancer Society. Cancer Facts & Figures. Atlanta: American Cancer Society; 2015.
2. National Comprehensive Cancer Network. Clinical Practice Guidelines in Oncology: Non-Small Cell Lung Cancer v1.1996. 1996
3. National Comprehensive Cancer Network. Clinical Practice Guidelines in Oncology: Non-Small Cell Lung Cancer v2.2005. 2005
4. National Comprehensive Cancer Network. Clinical Practice Guidelines in Oncology: Non-Small Cell Lung Cancer v2.2010. 2010
5. Non-small Cell Lung Cancer Collaborative Group. Chemotherapy in non-small cell lung cancer: a meta-analysis using updated data on individual patients from 52 randomised clinical trials. Bmj. 1995; 311:899–909. [PubMed: 7580546]
6. Schiller JH, Harrington D, Belani CP, et al. Comparison of four chemotherapy regimens for advanced non-small-cell lung cancer. N Engl J Med. 2002; 346:92–98. [PubMed: 11784875]
7. Thomas A, Liu SV, Subramaniam DS, Giaccone G. Refining the treatment of NSCLC according to histological and molecular subtypes. Nat Rev Clin Oncol. 2015; 12:511–526. [PubMed: 25963091]
8. Cykert S, Dilworth-Anderson P, Monroe MH, et al. Factors associated with decisions to undergo surgery among patients with newly diagnosed early-stage lung cancer. Jama. 2010; 303:2368–2376. [PubMed: 20551407]

9. Esnaola NF, Gebregziabher M, Knott K, et al. Underuse of Surgical Resection for Localized, Non–Small Cell Lung Cancer Among Whites and African Americans in South Carolina. Ann Thorac Surg. 2008; 86:220–227. [PubMed: 18573427]
10. Hardy D, Liu CC, Xia R, et al. Racial disparities and treatment trends in a large cohort of elderly black and white patients with nonsmall cell lung cancer. Cancer. 2009; 115:2199–2211. [PubMed: 19365824]
11. Greenberg ER, Chute CG, Stukel T, et al. Social and Economic Factors in the Choice of Lung Cancer Treatment. N Engl J Med. 1988; 318:612–617. [PubMed: 2830514]
12. Little AG, Gay EG, Gaspar LE, Stewart AK. National survey of non-small cell lung cancer in the United States: epidemiology, pathology and patterns of care. Lung Cancer. 2007; 57:253–260. [PubMed: 17451842]
13. Groth SS, Al-Refaie WB, Zhong W, et al. Effect of insurance status on the surgical treatment of early-stage non-small cell lung cancer. Ann Thorac Surg. 2013; 95:1221–1226. [PubMed: 23415239]
14. Slatore CG, Au DH, Gould MK. An official American Thoracic Society systematic review: insurance status and disparities in lung cancer practices and outcomes. Am J Respir Crit Care Med. 2010; 182:1195–1205. [PubMed: 21041563]
15. Howlader, NNA.; Krapcho, M.; Garshell, J.; Neyman, N.; Altekruse, SF.; Kosary, CL.; Yu, M.; Ruhl, J.; Tatalovich, Z.; Cho, H.; Mariotto, A.; Lewis, DR.; Chen, HS.; Feuer, EJ.; Cronin, KA. SEER Cancer Statistics Review, 1975–2010. Bethesda, MD: National Cancer Institute; 2013.
16. Basche M, Kelly K. Treatment of non-small-cell lung cancer in older persons. Oncology (Williston Park). 2003; 17:31–39. discussion 43-34, 47-38. [PubMed: 12599930]
17. Charlson ME, Pompei P, Ales KL, MacKenzie CR. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. J Chronic Dis. 1987; 40:373–383. [PubMed: 3558716]
18. MPCe. , editor. Lyon, France: 2007. Cancer Incidence in Five Continents. al.]
19. Division of Cancer Prevention and Control NCI. , editor. 1993. SEER Program: Comparative Staging Guide for Cancer.
20. Greene, FL.; Page, DL.; Fleming, ID., et al., editors. AJCC Cancer Staging Manual Sixth Edition. American Joint Committee on Cancer; 2002.
21. National Cancer Institute, DCCPS, Surveillance Research Program, Surveillance Systems Branch; Surveillance, Epidemiology, and End Results (SEER) Program (www.seer.cancer.gov) SEER*Stat Database: Incidence - SEER 18 Regs Research Data + Hurricane Katrina Impacted Lousiana Cases, Nov 2015 Sub (1973–2013) - Linked To County Attributes - Total U.S., 1969–2014 Counties. based on the November 2015 submission [released April 2016]
22. Davis KL, Goyal RK, Able SL, Brown J, Li L, Kaye JA. Real-world treatment patterns and costs in a US Medicare population with metastatic squamous non-small cell lung cancer. Lung Cancer. 2015; 87:176–185. [PubMed: 25532680]
23. Iwamoto K, Ichiyama S, Shimokata K, Nakashima N. Postoperative pneumonia in elderly patients: incidence and mortality in comparison with younger patients. Intern Med. 1993; 32:274–277. [PubMed: 8358115]
24. Shiono S, Yoshida J, Nishimura M, et al. Risk factors of postoperative respiratory infections in lung cancer surgery. J Thorac Oncol. 2007; 2:34–38. [PubMed: 17410007]
25. Rivera C, Falcoz PE, Bernard A, Thomas PA, Dahan M. Surgical management and outcomes of elderly patients with early stage non-small cell lung cancer: a nested case-control study. Chest. 2011; 140:874–880. [PubMed: 21436251]
26. Palma DA, Tyldesley S, Sheehan F, et al. Stage I non-small cell lung cancer (NSCLC) in patients aged 75 years and older: does age determine survival after radical treatment? J Thorac Oncol. 2010; 5:818–824. [PubMed: 20521349]
27. Maione P, Rossi A, Sacco PC, et al. Treating advanced non-small cell lung cancer in the elderly. Ther Adv Med Oncol. 2010; 2:251–260. [PubMed: 21789138]
28. Koyi H, Hillerdal G, Andersson O, Kolbeck KG, Liv P, Branden E. Chemotherapy Treatment of Elderly Patients (>/=70 Years) with Non-Small Cell Lung Cancer: A Seven-Year Retrospective

Study of Real-Life Clinical Practice at Karolinska University Hospital, Sweden. Lung Cancer Int. 2015; 2015:317868. [PubMed: 26316949]

29. Potosky AL, Harlan LC, Kaplan RS, Johnson KA, Lynch CF. Age, Sex, and Racial Differences in the Use of Standard Adjuvant Therapy for Colorectal Cancer. J Clin Oncol. 2002; 20:1192–1202. [PubMed: 11870160]
30. Harlan LC, Clegg LX, Trimble EL. Trends in Surgery and Chemotherapy for Women Diagnosed With Ovarian Cancer in the United States. J Clin Oncol. 2003; 21:3488–3494. [PubMed: 12972525]
31. Kelly K, Crowley J, Bunn PA Jr, et al. Randomized phase III trial of paclitaxel plus carboplatin versus vinorelbine plus cisplatin in the treatment of patients with advanced non--small-cell lung cancer: a Southwest Oncology Group trial. J Clin Oncol. 2001; 19:3210–3218. [PubMed: 11432888]
32. Azzoli CG, Kris MG, Pfister DG. Cisplatin versus carboplatin for patients with metastatic non-small-cell lung cancer--an old rivalry renewed. J Natl Cancer Inst. 2007; 99:828–829. [PubMed: 17551137]

Highlights

- Between 1996 and 2010 use of systemic therapy increased significantly, regardless of stage.
- Older patients (≥70 vs. <70) were less likely to receive surgery and chemotherapy.
- Median survival improved significantly among III–IV patients.
- However, among IIIB/IV patients median survival increased only from 4 to 5 months.

Table 1

Characteristics of non-Small Cell Lung Cancer Patients by Year of Diagnosis, Patterns of Care (N=3,318)

	1996	2005	2010	
	(N=906)	(N=1,061)	(N=1,351)	
Characteristic	**N[1] (%)[2]**	**N[1] (%)[2]**	**N[1] (%)[2]**	***p*[3]**
Sex				
Male	498 (56)	560 (53)	681 (53)	0.67
Female	408 (44)	501 (47)	670 (47)	
Age at diagnosis, years				
<70	574 (59)	609 (51)	800 (55)	<0.01
70–79	259 (31)	312 (32)	354 (28)	
≥80	73 (10)	140 (16)	197 (17)	
Race/ethnicity				
non-Hispanic white	416 (84)	335 (75)	364 (74)	0.64[4]
non-Hispanic black	303 (11)	300 (12)	345 (12)	
non-Hispanic other	0	225 (8)	364 (8)	
Hispanic	187 (5)	201 (6)	278 (7)	
Health insurance				
Other (Private/HMO/VA)	584 (72)	604 (65)	776 (64)	<0.01
Medicaid, any	141 (9)	253 (14)	315 (16)	
Medicare only	128 (15)	155 (17)	182 (16)	
None/Unknown	53 (4)	49 (3)	78 (4)	
Marital status				
Married	468 (57)	558 (56)	646 (47)	<0.01
Not married/Unknown	438 (43)	503 (44)	705 (53)	
COPD				
No	297 (37)	339 (36)	478 (42)	0.22
Yes	609 (63)	722 (64)	873 (58)	
Charlson comorbidity score[5]				
0	702 (78)	797 (75)	936 (71)	0.02
1	173 (19)	209 (19)	328 (23)	
≥2	31 (3)	55 (7)	87 (7)	
Smoking History				
Never Smoker	69 (7)	168 (11)	247 (12)	<0.01
Ever Smoker	762(86)	812 (80)	1036 (83)	
Unknown	75 (7)	81 (9)	68(5)	
Tumor Characteristics				
Stage[6]				
I/II	245 (31)	270 (28)	321 (26)	0.01

	1996	2005	2010	
	(N=906)	(N=1,061)	(N=1,351)	
Characteristic	**N[1] (%)[2]**	**N[1] (%)[2]**	**N[1] (%)[2]**	***p*[3]**
IIIA	112 (12)	84 (7)	117 (8)	
IIIB/IV	549 (57)	707 (65)	913 (66)	
Histology				
Squamous cell	245 (25)	231 (21)	327 (28)	<0.01
Adenocarcinoma	377 (45)	484 (43)	721 (49)	
Carcinoma, NOS	213 (23)	298 (30)	262 (20)	
Large cell	71 (7)	48 (5)	41 (3)	

[1] Unweighted number of patients

[2] Weighted percentage of patients

[3] X^2 across years

[4] X^2 across 2005/2010 only

[5] Charlson comorbidity score, excluding lung cancer and COPD from the calculation.

[6] American Joint Committee on Cancer (1996: 3rd Edition; 2005 and 2010: 6th Edition)

COPD: Chronic Obstructive Pulmonary Disease; NOS: not otherwise specified; VA: Veteran Affairs

Table 2

Factors Associated with Receipt of Surgery in Stage I/II non-Small Cell Lung Cancer Patients Diagnosed in 1996, 2005, and 2010, Patterns of Care (N=836)

Characteristic	N[1]	%[2]	*p*[3]	OR[4] (95% CI)
Year of diagnosis				
1996	188	78.8	0.18	
2005	201	70.6		
2010	237	68.5		
Sex				
Male	277	67.6	0.10	
Female	349	76.0		
Age at diagnosis, years				
<70	402	84.7	<0.01	1.00
70–79	169	70.5		0.31 (0.16 – 0.63)
≥80	55	38.2		0.04 (0.02 – 0.10)
Race/ethnicity				
non-Hispanic white	236	71.4	<0.01	1.00
non-Hispanic black	155	64.4		0.56 (0.23 – 1.37)
non-Hispanic other	105	80.2		2.05 (0.78 – 5.37)
Hispanic	130	84.7		1.38 (0.49 – 3.86)
Health insurance				
Other (Private/HMO/VA)	457	78.0	<0.01	1.00
Medicaid, any	78	46.5		0.14 (0.05 – 0.40)
Medicare only	70	59.7		0.34 (0.14 – 0.78)
None/Unknown	21	58.0		0.38 (0.07 – 2.12)
Marital status				
Not Married	276	66.1	0.05	1.00
Married	350	76.1		0.94 (0.47 – 1.88)
COPD				
No	389	79.1	<0.01	1.00
Yes	237	63.4		0.70 (0.37 – 1.33)
Charlson comorbidity score[5]				
0	475	73.3	0.25	
1	234	72.8		
≥2	18	43.0		
Smoking history				
Never	91	85.6	0.02	1.00
Ever Unknown	499 36	71.9 48.5		0.30 (0.03 – 2.94) 0.13 (0.01 – 2.66)
Stage[6]				

Characteristic	N[1]	%[2]	*p*[3]	OR[4] (95% CI)
I	514	73.5	0.25	
II	112	65.5		
Histology				
Squamous	159	55.6	<0.01	1.00
Adenocarcinoma	332	86.2		2.92 (1.38 – 6.20)
Carcinoma, NOS	110	67.9		1.32 (0.56 – 3.14)
Large	25	81.1		6.11 (1.96 – 19.00)
Radiation				
No	561	89.0	<0.01	1.00
Yes	65	24.4		0.03 (0.01 – 0.06)
Systemic therapy				
No	499	75.0	0.05	1.00
Yes	127	62.0		1.03 (0.50 – 2.16)

[1] Unweighted number of Stage I/II patients receiving surgery

[2] Weighted percentage of Stage I/II patients receiving surgery

[3] Bivariate X^2

[4] Estimated odds ratio of receiving surgery, adjusted for variables found to be significant during bivariate analyses.

[5] Charlson comorbidity score, excluding lung cancer and COPD from the calculation.

[6] American Joint Committee on Cancer (1996: 3rd Edition; 2005 and 2010: 6th Edition)

CI: Confidence Interval; COPD: Chronic Obstructive Pulmonary Disease; OR: Odds Ratio; NOS: not otherwise specified; VA: Veteran Affairs

Table 3

Factors Associated with Receipt of Chemotherapy in Stage IIIB/IV non-Small Cell Lung Cancer Patients Diagnosed in 1996, 2006, and 2010, Patterns of Care (n = 2,169)

Characteristic	N[1]	%[2]	p[3]	OR[4] (95% CI)
Year of Diagnosis				
1996	186	36.1	<0.01	1.00
2005	368	48.6		2.04 (1.39 – 2.98)
2010	464	51.2		2.03 (1.40 – 2.94)
Age at diagnosis, years				
<70	740	56.5	<0.01	1.00
70–79	230	43.1		0.71 (0.50 – 1.01)
≥80	48	21.1		0.26 (0.15 – 0.45)
Sex				
Male	541	46.3	0.57	
Female	477	48.4		
Race/ethnicity				
non-Hispanic white	316	47.6	0.91	
non-Hispanic black	288	45.9		
Non-Hispanic other	213	48.0		
Hispanic	201	45.5		
Health insurance				
Other (Private/HMO/VA)	629	50.6	0.06	
Medicaid, any	212	45.5		
Medicare only	115	36.8		
None/Unknown	62	46.5		
Marital status				
Not Married	442	38.2	<0.01	1.00
Married	576	56.2		1.84 (1.35 – 2.51)
COPD Status				
No	736	49.3	0.13	
Yes	282	43.6		
Charlson comorbidity score[5]				
0	773	50.4	<0.01	1.00
1	190	35.1		0.72 (0.50 – 1.02)
≥2	55	47.8		0.67 (0.44 – 1.02)
Smoking History				
Never	179	50.2	0.01	1.00
Ever Unknown	786 53	48.6 27.9		0.99 (0.64–1.54) 0.34 (0.14–0.81)

Characteristic	N[1]	%[2]	p[3]	OR[4] (95% CI)
Stage[6]				
IIIB	277	54.0	0.02	1.00
IV	741	44.9		0.51 (0.36 – 0.71)
Histology				
Squamous cell	199	48.0	0.39	
Adenocarcinoma	513	48.8		
Carcinoma, NOS	249	42.6		
Large cell	57	54.5		
Radiation				
No	392	38.4	<0.01	1.00
Yes	626	56.5		1.94 (1.41 – 2.67)
Surgery				
No	927	47.0	0.56	
Yes	91	50.4		
Targeted Therapy				
No	794	43.2	<0.01	1.00
Yes	224	75.8		3.71 (2.13 – 6.45)

[1] Number of stage IIIB/IV patients receiving chemotherapy

[2] Weighted percentage of Stage IIIB/IV patients receiving chemotherapy

[3] Bivariate X^2

[4] Estimated odds ratio of receiving chemotherapy, adjusted for variables found to be significant during bivariate analyses.

[5] Charlson comorbidity score, excluding lung cancer and COPD from the calculation.

[6] American Joint Committee on Cancer (1996: 3rd Edition; 2005 and 2010: 6th Edition)

CI: Confidence Interval; COPD: Chronic Obstructive Pulmonary Disease; OR: Odds Ratio; NOS: not otherwise specified; VA: Veteran Affairs

Table 4

Frequency of Systemic Therapy by Specific Agent Administration in Stage[1] IIIB/IV non-Small Cell Lung Cancer Patients by Year of Diagnosis, Patterns of Care (n = 1098).

	1996		2005		2010		
Systemic Therapy	**N[2]**	**%[3]**	**N[2]**	**%[3]**	**N[2]**	**%[3]**	***P*[4]**
Bevacizumab	-	-	24	4	99	22	<0.01
Carboplatin	92	50	278	72	351	73	<0.01
Cisplatin	71	35	55	14	103	18	<0.01
Docetaxel	**	2	86	17	78	13	<0.01
Erlotinib	-	-	69	14	124	17	0.43
Etoposide (VP16)	65	32	26	5	43	5	<0.01
Gemcitabine	-	-	85	19	92	21	0.62
Paclitaxel (Taxol)	55	28	181	50	209	42	<0.01
Pemetrexed	-	-	22	6	187	38	<0.01
Vinorelbine	27	18	24	4	22	5	0.01

[1] American Joint Committee on Cancer (1996: 3rd Edition; 2005–2010: 6th Edition)

[2] Unweighted number of patients receiving the systemic therapy agent.

[3] Weighted percentage of patients receiving the systemic therapy agent.

[4] X^2 across years.

** Cell size less than 5, results masked for confidentiality.

- Agent not assessed.

Table 5

Factors Associated with All-Cause Mortality among non-Small Cell Lung Cancer Patients Diagnosed in 1996, 2005, and 2010 by Stage, Patterns of Care

	Stage[1]		
	I/II	**IIIA**	**IIIB/IV**
Characteristic	**HR**[2] **(95% CI)**	**HR**[2] **(95% CI)**	**HR**[2] **(95% CI)**
Year of Diagnosis			
1996			1.00
2005			0.83 (0.69 – 0.99)
2010			0.88 (0.74 – 1.05)
Age at diagnosis, years			
<70	1.00		1.00
70–79	1.60 (1.17 – 2.19)		1.10 (0.93 – 1.30)
≥80	1.76 (1.19 – 2.61)		1.07 (0.85 – 1.34)
Sex			
Male	1.00		1.00
Female	0.73 (0.56 – 0.95)		0.88 (0.76 – 1.01)
Race/ethnicity			
non-Hispanic white	1.00	1.00	
non-Hispanic black	1.11 (0.83 – 1.47)	1.24 (0.85–1.79)	
non-Hispanic other	0.73 (0.48 – 1.11)	1.08 (0.59 – 1.97)	
Hispanic	0.58 (0.35 – 0.97)	2.19 (1.41 – 3.41)	
Health insurance			
Other (Private/HMO/VA)	1.00	1.00	1.00
Medicaid, any	1.64 (1.07 – 2.54)	1.06 (0.63 – 1.76)	0.96 (0.81 – 1.15)
Medicare only	1.56 (1.08 – 2.25)	1.63 (1.01 – 2.64)	1.22 (0.99 – 1.50)
None/Unknown	2.19 (1.28 – 3.73)	1.96 (0.96 – 3.99)	1.21 (0.88 – 1.66)
COPD			
No	1.00	1.00	
Yes	1.56 (1.16 – 2.11)	1.41 (0.98–2.02)	
Charlson comorbidity score[3]			
0	1.00		
1	1.25 (0.90 – 1.72)		
≥2	1.52 (0.89 – 2.58)		
Smoking History			
Never			1.00
Ever			1.15 (0.92 – 1.45)
Unknown			0.75 (0.51 – 1.09)
Histology			

	Stage[1]		
	I/II	**IIIA**	**IIIB/IV**
Characteristic	**HR[2] (95% CI)**	**HR[2] (95% CI)**	**HR[2] (95% CI)**
Squamous	1.00		1.00
Adenocarcinoma	0.85 (0.60 – 1.19)		1.04 (0.86 – 1.26)
Carcinoma, NOS	0.76 (0.52 – 1.09)		1.44 (1.18 – 1.77)
Large	1.69 (1.02 – 2.78)		1.22 (0.85 – 1.75)
Radiation			
No	1.00		1.00
Yes	0.99 (0.62 – 1.57)		0.76 (0.66 – 0.88)
Surgery			
No	1.00	1.00	1.00
Yes	0.30 (0.20 – 0.46)	0.45 (0.30–0.66)	0.46 (0.34 – 0.61)
Chemotherapy			
No			1.00
Yes			0.43 (0.37 – 0.50)
Targeted Therapy			
No			1.00
Yes			0.57 (0.46 – 0.70)
Systemic Therapy			
No	1.00		
Yes	1.39 (0.99 – 1.95)		

[1] American Joint Committee on Cancer (1996: 3rd Edition; 2005 and 2010: 6th Edition)

[2] Estimated Cox Proportional Hazards Ratio for all-cause mortality, adjusted for variables found to be significant during bivariate analyses.

[3] Charlson comorbidity score, excluding lung cancer and COPD from the calculation.

CI: Confidence Interval; COPD: Chronic Obstructive Pulmonary Disease; HR: Hazard Ratio; NOS: not otherwise specified; VA: Veteran Affairs