Published in final edited form as:
Lung Cancer. 2012 December ; 78(3): 245–252. doi:10.1016/j.lungcan.2012.09.008.

Patterns and Predictors of First-line Chemotherapy Use among Adults with Advanced Non-small Cell Lung Cancer in the Cancer Research Network

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Abstract

Background—Relatively low rates of chemotherapy receipt have been observed in older patients diagnosed with advanced non-small cell lung cancer (NSCLC) in SEER-Medicare-based studies. However, little is known about variation in first-line NSCLC chemotherapy use in younger patients, health maintenance organization (HMO)-based settings, and for high-cost, novel agents, such as bevacizumab and erlotinib.

Methods—A cohort of 6,614 stage IIIB/IV NSCLC patients aged >21 years diagnosed between 2000 and 2007 was identified at four HMOs that participate in the Cancer Research Network (CRN). Demographic, comorbidity, tumor characteristics, and chemotherapy treatment data were included in logistic regression models to identify factors associated with chemotherapy receipt and tests of association examined secular and age-specific variation in first-line chemotherapy regimens.

Results—Within 120 days of diagnosis, 3,612 (55%) patients received chemotherapy; increasing from 52% of patients diagnosed in 2000 to 59% in 2007 ($p<0.001$). Receipt was significantly higher for patients aged <65 years (64% versus 46% in ≥65) and was inversely related to stage and

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Notes The funders did not have any involvements in the design of the study; the collection, analysis, and interpretation of the data; the writing of the article; or the decision to submit the article for publication.

Conflict of Interest There is no conflict of interest by any of the authors of this paper.

comorbidites (all p<0.001). Carboplatin and paclitaxel were received most frequently. Erlotinib and bevacizumab use in the later years of the study was associated with a significant change in distributions of first-line chemotherapies (p<0.001).

Conclusions—For patients alive 30 days post diagnosis, chemotherapy use was higher in the aged population (>65 years) than previously published estimates, and higher still in among younger patients. Chemotherapy use increased over the observation period, and the mix of first-line therapies used changed substantially over time. Of note, novel, high cost treatments were used in first-line therapy prior to FDA approval, increasing significantly throughout the study period.

These findings demonstrate the utility of HMO CRN data to augment SEER-Medicare to conduct comparative effectiveness research related to chemotherapy use and the use of specific agents, especially among younger patients.

Keywords

HMO; chemotherapy; Non-small cell lung cancer; advanced stage; Erlotinib; bevacizumab

1. Introduction

Lung cancer is the leading cause of cancer deaths, accounting for 26% and 29% of female and male cancer deaths, respectively [1]. The majority of incident cancer cases are diagnosed at late stage and approximately two-thirds of all non-small cell lung cancer (NSCLC) cases are ≥65 years [2]. Various chemotherapy regimens, mostly platinum-based doublets with and without novel agents, have been shown to prolong survival by upwards of 3 months in patients with advanced (stage IIIB-IV) NSCLC, but often at considerable costs. [3;4] SEER-Medicare data linked studies suggest that only 25% - 38% of older patients diagnosed with advanced NSCLC receive chemotherapy [3;5]. It is unknown if treatment rates are similar in younger patients or for those receiving care in a health maintenance organization (HMO). Furthermore, few studies exist that describe first-line chemotherapy that includes oral medications (i.e., those covered by Medicare Part D) or examine utilization rates and trends over time.

Generalizable data regarding treatment utilization patterns for patients diagnosed with advanced NSCLC, which include patients younger than those captured in SEER-Medicare, and for patients that receive care outside of a fee-for-service setting, are needed to inform both clinicians and policymakers and to conduct comparative effectiveness research on treatment options commonly used in community-based oncology practices. This study extends the work of Lang et al [5] and bridges the gap in the literature on patterns of chemotherapy use in advanced NSCLC patients across all adult ages and for patients receiving care in an HMO setting. Using data derived from four HMOs that participate in the National Cancer Institute (NCI)-funded Cancer Research Network (CRN) [6;7], we examine the proportion of advanced NSCLC patients that received first-line chemotherapy. In addition, we examine variation in the ten most frequently used chemotherapy agents and regimens (used either as single agents or in combination) by age group, among the patients receiving treatment, and the changes in the distribution of first-line chemotherapy regimens over time.

2. Methods

2.1. Study setting

This was a retrospective cohort study to assess chemotherapy treatment among advanced NSCLC patients conducted within four non-profit HMOs (Colorado, Northern California, and Northwest Regions of Kaiser Permanente, and Group Health Cooperative). Each HMO

is a member of the NCI-funded CRN and provides comprehensive health services to its members, primarily through closed-panel delivery models by salaried physicians. In each HMO, the majority of ambulatory cancer care is delivered in plan-owned facilities and events are captured using Epicare based electronic medical records (EMR). This project was approved by the Institutional Review Boards of the four participating HMOs.

2.2. Data sources

The primary data source for this analysis was the CRN's Virtual Data Warehouse (VDW). As described in detail elsewhere, the VDW is a standardized data model that was developed for research use, in which each HMO maintains their data locally, but a programmer at one site can write a data-extraction program that can be run at other sites.[7;8]. Within the VDW, the Virtual Tumor Registry (VTR) contains data consistent with the North American Association of Central Cancer Registries standards [9]. VTR data are obtained from manual reviews of cancer patients' medical charts by trained abstractors and include coded clinical data associated with inpatient and outpatient events, date of diagnosis, first-course treatment (surgery, radiotherapy, chemotherapy, etc), tumor characteristics, etc. VDW diagnosis and procedure files include coded diagnoses and procedures associated with inpatient and outpatient encounters or events including cancer treatment related surgery, radiotherapy, and chemotherapy that are derived from EMRs and other claims databases. Codes are based on International Classification of Diseases, 9th Revision, Clinical Modification (ICD-9-CM), Healthcare Common Procedure Coding System (HCPCS), and the Fourth Edition of the Common Procedure Terminology codes (CPT-4). The VDW pharmacy files capture national drug code (NDC) based prescription drugs dispensed from both outpatient pharmacies and infusion centers. The VDW Census files include measures of socioeconomic status (e.g., median family income, education) where patients' residential addresses are mapped to census block data using geocoding software. Death data are derived from the VTR, membership data, state (CA, CO, WA) level death datasets, and data from the Social Security Administration.

2.3. Sample selection

The study sample included patients identified in the VTR as aged ≥21 years, diagnosed with stage IIIb/IV NSCLC between 01/01/2000 and 12/31/2007, and followed through 2008. Patients were excluded if they had any previously diagnosed cancers, non-pathologically confirmed lung cancer diagnosis, were not enrolled in the HMO, or did not survive at least one month past diagnosis.

2.4. Identification of chemotherapy

We have previously demonstrated that the CRN VDW files provide a valid and reliable source (relative to gold standard chart audited data) of chemotherapy treatments [7;10]. In this analysis we employed the same methods described in Ritzwoller et al [7], using chemotherapy tables that are available on the CRN website (http://crn.cancer.gov/resources/codes.html) to identify first-course chemotherapy. These tables contain over 2,000 NDC and 300 procedure and diagnosis treatment-related codes. All codes in these tables were examined for the study sample.

2.5. Outcome measures

The primary outcome measure is the proportion of advanced NSCLC patients receiving first-line chemotherapy. A distinction was made between patients with generic codes for receipt of chemotherapy and those receiving identifiable chemotherapy (by product name, NDC, or HCPC code). We examined the distribution of the ten most frequently used identifiable chemotherapy agents, as single agents or in combination, by age category (<65

vs. > 65 years). We also examined the distribution of first line therapy by singlet, doublet, and triplet regimen categories, by year, over the course of the study period. Finally we identified the diffusion over time of novel agents, including erlotinib (Tarceva®) and bevacizumab (Avastin®), which entered the market during the study period. First-line chemotherapy was defined as initiation of systemic chemotherapy within 120 days of NSCLC diagnosis. Additional chemotherapy agents received within 8 days of the first agent were considered to be components of the same regimen. We based singlet, doublet, and triplet (or more) designation on the number of chemotherapy products within each identified regimen. The date of treatment (index date) was defined as the first date a patient received any chemotherapy. Patients were followed from their diagnosis date until death, disenrollment from the HMO, or December 31, 2008, whichever came first.

2.6. Data analysis/statistical methods

Descriptive statistics were computed to characterize patients and chemotherapy regimens received. We calculated the percentages of patients who received (and did not receive) chemotherapy by HMO, age group, sex, race/ethnicity, median neighborhood family income, median neighborhood educational attainment, stage at diagnosis, tumor grade, year of diagnosis, and modified Charlson comorbidity score [11].

The association between patient characteristics and receipt of any chemotherapy was evaluated using univariate and multivariate logistic regression models adjusting for HMO, age groups, gender, race/ethnicity, neighborhood education (or median neighborhood family income), stage at diagnosis, tumor grade, year of diagnosis, and modified Charlson comorbidity score. Odds ratios and confidence intervals were generated to measure the strength of the association for each factor. Using methods described by Allison [12], we conducted sensitivity analyses by testing interaction effects between year of diagnosis and patient age, year of diagnosis and HMO, and age and HMO. We also estimated separate models by age category (<65 vs. >65 years). Customary residual and effect statistics were examined to assess model fit and evaluate for outliers. Statistical significance of differences in the distributions by age categories or over time was tested with the chi-square test. All analyses were performed using SAS 9.1 (SAS Institute Inc., Cary, NC).

3. Results

Of 8,516 patients diagnosed with stage IIIB or IV NSCLC between 2000 and 2007, 6,614 (77%) patients met study inclusion criteria (Figure 1). There were 834 cases excluded because they did not survive for thirty days after diagnosis.

Overall, 3,612 (54.6%) patients received chemotherapy within 120 days of diagnosis (Figure 1) This study sample was used in the analyses described in Tables 1 and 2. Of the included patients, 38% were under 65 years and this did not vary by stage (data not shown). Significant variation was found by age at diagnosis, race/ethnicity, and year of diagnosis at the HMO level (data not shown). HMO B had younger patients and more patients diagnosed in 2007 relative to the other HMOs. The distribution of Hispanic patients in HMOs A and C differed significantly from either HMOs B or D.

Chemotherapy use increased from 51% for patients diagnosed in 2000 to 59% in 2007. Sixty-eight percent of patients <65 years received chemotherapy while 46% of patients ≥65 years received chemotherapy ($p < 0.0001$). While more males than females were diagnosed with advanced cancer, equal proportions (55%) received chemotherapy. Unadjusted, univariate findings indicate that patients residing in census tracts with the highest education or income, with fewer comorbidities, diagnosed with stage IIIB vs. stage IV, or treated later in the observation period were more likely to have received chemotherapy. In addition in the

unadjusted models, Hispanics and Asian/Pacific Islander patients were more likely to have received chemotherapy. The likelihood of having received chemotherapy was lower for patients in HMO B and C relative to HMO A.

Results from the fully adjusted multivariate models (Table 2) confirm that the likelihood of having received chemotherapy was inversely related to age, number of comorbidities, and higher stage. Adjusting for all other characteristics, the likelihood of receiving chemotherapy declines in each age category; specifically, patients >80 years were 90% less likely to have received chemotherapy relative to patients <55 years. Patients with three or more comorbidities (relative to 0 or 1), or those diagnosed with stage IV disease (relative to IIIB) were 39% and 31% less likely to have received chemotherapy, respectively. However, no significant differences were associated with gender or race/ethnicity of the patient. Due to collinearity between income and education, only education proxies were included in the final model.

Patients residing in census tracts where the proportion of adults with a college education were in the 60th or 80th quintiles were 38% and 48% more likely to have received chemotherapy than lower quintiles, respectively. Those diagnosed in later years (2005-2007) of the study were significantly more likely to have received chemotherapy. Specifically, the odds of having received chemotherapy for patients diagnosed in 2007 were 62% higher than for patients diagnosed in 2000. In multivariate models the differences in the likelihood of receiving chemotherapy by HMO also persist. However, interactions between year of diagnosis and patient age were not significant. However, the interaction between age and HMO B was significant ($p < 0.0001$) in all models tested. When similar models were estimated in samples limited to patients <65 or >65 years, significant variation for this HMO persisted; though only for the sample of patients <65 years.

Of the treated patients, 3,458 (96% who were comparable in terms of baseline and demographic characteristics to the overall sample receiving chemotherapy) received an identifiable first-line regimen (i.e. where the specific product could be ascertained from NDC, HCPC codes, or product name), and comprised the study sample used in the final analyses describing the distribution of first-line therapies (Tables 3 and Figure 2 and 3). Among these patients, doublet chemotherapy was most common for first-line treatment and used in 77% of the patients (Figure 2). Overall distribution of first-line chemotherapy differed significantly for patients <65 vs. > 65 years ($p < 0.0001$) (Table 3). Carboplatin was the most frequently used chemotherapy agent, either as a singlet or in combination. Carboplatin-paclitaxel was the most common doublet for patients in both age categories. Four percent of first-line regimens in patients <65 years was triplet bevacizumab-carboplatin-paclitaxel (making it the 5th most common regimen in this age category), but only 1.7% for patients ≥65 years (making it the 10th most common regimen in this age category). The same four regimens (carboplatin/paclitaxel, cisplatin/etoposide, carboplatin/gemcitabine, and carboplatin) are at the top of the distribution list for both age categories, but for patients <65 years **(**relative to >65 years**)** there is a slightly larger proportion receiving cisplatin/etoposide (7.7% vs 6.4%), and a slightly smaller proportion receiving carbopaltin alone. Erlotinib was the 8th most frequently used regimen in patients <65 years but 7th most in patients ≥ 65 years.

While the proportion of patients receiving chemotherapy increased over time, the distribution of the receipt of singlet, doublet, triplet also changed over the course of the observation period (Figure 3). Doublets containing cisplatin or carboplatin plus a taxane (docetaxel/paclitaxel) were the most common first-line chemotherapy regimens across all study years. However, use of doublet therapy declined from a high of 87% for patients diagnosed in 2002 to 65% in 2007. During this same period, use of singlet therapy increased

from a low of 12% (2002) to 23% in 2007. From 2000 to 2004, platinums (cisplatin or carboplatin) comprised the most singlet agents used. However from 2005 forward, erlotinib became the most common singlet agent. More striking was the increase found in triplet use that occurred after 2005. By 2007, the triplet carboplatin-paclitaxel-bevaizumab comprised 11% of all first-line treatment. Additional details regarding the distribution of specific regimens, by age category and year, are noted in supplementary data (Appendix A).

4. Discussion

This retrospective analysis of data from four CRN HMOs evaluating the patterns and factors associated with first-line chemotherapy receipt in patients with incident, advanced NSCLC is the first of its kind and represents a number of contributions to the existing literature. First, for patients diagnosed between 2000 and 2007, we found that the proportion of patients who received first-line chemotherapy was higher in the HMO setting than that reported in published SEER-Medicare data among all age categories but particularly among patients aged <65 years. Prior SEER-Medicare estimates of NSCLC patients ≥65 years reported rates that ranged from 28%-41% with an inverse relationship between age and receipt of chemotherapy [3;5].

Second, while we found differences between education, comorbidity, stage and year of diagnosis and receipt of chemotherapy, we found no differences by gender or race/ethnicity in our adjusted models. Our former findings are consistent with four other studies that have evaluated utilization of chemotherapy in patients with NSCLC [3;5;13;14]. These studies reported that several other factors were associated with receipt of chemotherapy including stage, socioeconomic measures (income and education census proxies), number of comorbidities, and year of diagnosis; all similar to our findings. However, our later results are not consistent with earlier studies where differences by gender and race/ethnicity were found in adjusted models. It is possible that the integrated health system models of the HMOs described here allows patients to navigate the healthcare system more easily and that those with higher education may have an even easier time navigating.

Third, our study is the first to use a large non-SEER-Medicare cohort to describe the distribution of first-line regimens (at the agent or product level) over time and between age categories. Contrary to potential stereotypes of managed care performing “cookie cutter” medicine, there was significant variation in the number of regimens used and the likelihood of receiving chemotherapy at the individual HMO level. While the regimens represented do appear to be evidence-based, the overall variability likely suggests that guideline—or pathway-based care is not ubiquitous in the study HMOs during this time period. Consistent with much of the published literature on the relative age related toxicities and effectiveness of many the chemotherapy agents described here [15] as noted in Table 3, significant differences were noted in distribution of the various regimens by age category. The difference in receipt of chemotherapy at the individual HMO level may represent a number of factors including differences in oncologist practice-style, patient preferences, or subtle differences in data availability. Differences by site do exist in tumor registry data collection; HMO B in this study receives all cancer diagnoses regardless of enrollment status in the HMO or treatment location at the time of diagnosis, which may inadvertently lead to greater identification of incident cancer cases without associated internal EMR events or claims based utilization data.

Finally, and perhaps the most significant finding, our study is one of first to profile the use of first-line monoclonal antibodies and targeted oral chemotherapies (including erlotinib) in HMO practices. Specifically, secular changes in use and in the distribution of first-line regimens that we observed were directly attributable to increasing use of newer and more

high-cost agents. The antiangiogenic monoclonal antibody bevacizumab is an expensive, infused, antineoplastic agent that was initially approved by the FDA in 2004 for metastatic colorectal cancer. In October 2006, bevacizumab received a label extension for administration in combination with carboplatin-paclitaxel (CP) for first-line treatment of advanced lung cancer.[16] Our findings suggest that use of the triplet combination that includes CP-bevacizumab emerged prior to the label extension for lung cancer use. Nevertheless, the largest increase in use came in 2007 after the label extension. Given recent findings by Zhu et al [17], uncertainty exists with respect to whether this trend will continue.

Erlotinib is an expensive, oral tyrosine kinase inhibitor of the EGFR receptor enzymatic intracellular domain. It was approved by the FDA in late 2004 for advanced or metastatic NSCLC after first-line therapy failure and then approved in 2010 as maintenance treatment after four cycles of platinum-based first-line chemotherapy [18-20]. While tumor markers or site specific factors including EGFR mutation status were not collected or available in the tumor registries during the observation period, our study found that 152 patients (2.3%) of our cohort diagnosed between 2005 and 2007 received first-line therapy with erlotinib, even though it has not received FDA approval for first-line use. Consistent with the findings presented at the 2007 ASCO meeting [18;19], we hypothesize that first-line use of erlotinib may have occurred, and may have increased over the last 5 years, in a select group of patients including women with adenocarcinoma, those with limited smoking history, and those found to have an EGFR mutation and without KRAS mutations. Further study is needed to test this hypothesis.

While our study contributes important information regarding the patterns and use of chemotherapy treatments for patients diagnosed with stage IIIB/IV NSCLC in HMO settings, it is not without limitations. First, this is a retrospective, observational study that does not provide clear information regarding the choice for or against treatment. In addition, we did not include measures of performance status—a key clinical measure needed to assess chemotherapy appropriateness [21]. Future studies may include this information, as well as assess adherence to evidence based recommended chemotherapy guidelines [11;22] and investigate patient-reported measures of preferences and outcomes. Consistent with methods described by Zhu et al [17], we excluded patients who died within 30 days of diagnosis, which may be potentially biasing toward healthier patients. Finally, the data used in this study was limited to data captured through 2008. Given the dynamic nature of drug discoveries and recent clinical trial findings, contemporary data are needed to further assess diffusion of these agents. Additional research is also needed related to use of erlotinib, bevacizumab and other novel, and often expensive, agents to determine the impact on survival and costs for adult patients diagnosed with advanced NSCLC, who are treated in off-trial and in HMO settings.

In conclusion, this study highlights results from previously unavailable data for patients <65 years, receiving care in an HMO setting, and receiving novel oral and intravenous agents for the first-line treatment of advanced NSCLC. Future studies can use HMO CRN data to perform chemotherapy specific comparative effectiveness research, complementing and extending SEER-Medicare studies.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

Funding for this research was provided by NCI Grant No. RC2 CA148185, Building CER Capacity: Aligning CRN, CMS, and State Resources to Map Cancer Care, Co-PIs: Jane C. Weeks, MD and Debra P. Ritzwoller, PhD; NCI

Grant No. R01 CA114204, Medical Care Burden of Cancer: System and Data Issues, PI: Mark C. Hornbrook, PhD; and NCI Cooperative Agreement No. U19 CA79689, Increasing Effectiveness of Cancer Control Interventions (Cancer Research Network), PI: Edward H. Wagner, MD.

The following staff members provided data processing support for this study: KP Northwest: Jenny Stabb, KP Northern California: Karl Huang; Group Health: Arvind Ramaprasan. We would like to acknowledge the contributions of Drs. Jane Weeks and Deborah Schrag for their comments and suggestions associated with earlier drafts of this manuscript.

References

1. Siegel R, Naishadham D, Jemal A. Cancer statistics, 2012. CA Cancer J Clin. 2012; 62(1):10–29. [PubMed: 22237781]
2. American Cancer Society. [Accessed 3-20-12] Lung Cancer (Non-Small Cell). 2010. Available at: http://www.cancer. org/acs/groups/cid/documents/webcontent/003115-pdf. pdf
3. Ramsey SD, Howlader N, Etzioni RD, Donato B. Chemotherapy use, outcomes, and costs for older persons with advanced non-small-cell lung cancer: evidence from surveillance, epidemiology and end results-Medicare. J Clin Oncol. 2004; 22(24):4971–4978. [PubMed: 15611512]
4. Fojo T, Grady C. How much is life worth: cetuximab, non-small cell lung cancer, and the $440 billion question. J Natl Cancer Inst. 2009; 101(15):1044–1048. [PubMed: 19564563]
5. Lang K, Marciniak MD, Faries D, Stokes M, Buesching D, Earle C, et al. Trends and predictors of first-line chemotherapy use among elderly patients with advanced non-small cell lung cancer in the United States. Lung Cancer. 2009; 63(2):264–270. [PubMed: 18649969]
6. Li EC, DeMartino J. Preliminary report: the development of the NCCN Comparative Therapeutic Index as a clinical evaluative process for existing data in oncology. J Natl Compr Canc Netw. 2010; 8(Suppl 5):S1–S9.
7. Ritzwoller DP, Carroll N, Delate T, O'Keeffe-Rossetti M, Fishman PA, Loggers ET, et al. Validation of Electronic Data on Chemotherapy and Hormone Therapy Use in HMOs. Med Care. Apr 23.2012 [epub ahead of print].
8. Hornbrook MC, Hart G, Ellis JL, Bachman DJ, Ansell G, Greene SM, et al. Building a virtual cancer research organization. J Natl Cancer Inst Monogr. 2005; (35):12–25. [PubMed: 16287881]
9. North American Association of Central Cancer Registries. [Accessed 8-26-11] NAACCR Strategic Management Plan. 2011. http://www.naaccr.org/Home.aspx
10. Delate T, Bowles EJ, Pardee R, Wellman RD, Habel LA, Yood MU, et al. Validity of Eight Integrated Healthcare Delivery Organizations' Administrative Clinical Data to Capture Breast Cancer Chemotherapy Exposure. Cancer Epidemiol Biomarkers Prev. Apr; 2012 21(4):637–680. [Epub 2012 Feb 15].
11. Wang S, Wong ML, Hamilton N, Davoren JB, Jahan TM, Walter LC. Impact of Age and Comorbidity on Non-Small-Cell Lung Cancer Treatment in Older Veterans. J Clin Oncol. 2012
12. Allison, P. Logistic Regression Using the SAS System. 1st ed. SAS Institute; Cary, NC: 1999.
13. Potosky AL, Saxman S, Wallace RB, Lynch CF. Population variations in the initial treatment of non-small-cell lung cancer. J Clin Oncol. 2004; 22(16):3261–3268. [PubMed: 15310770]
14. Earle CC, Venditti LN, Neumann PJ, Gelber RD, Weinstein MC, Potosky AL, et al. Who gets chemotherapy for metastatic lung cancer? Chest. 2000; 117(5):1239–1246. [PubMed: 10807806]
15. Rajeswaran A, Trojan A, Burnand B, Giannelli M. Efficacy and side effects of cisplatin- and carboplatin-based doublet chemotherapeutic regimens versus non-platinum-based doublet chemotherapeutic regimens as first line treatment of metastatic non-small cell lung carcinoma: a systematic review of randomized controlled trials. Lung Cancer. 2008; 59(1):1–11. [PubMed: 17720276]
16. National Cancer Institute. [Accessed 3-20-12] Cancer Drug Information: FDA approval for Bevacizumab. 2012. Available at: http://www.cancer gov/cancertopics/druginfo/fda-bevacizumab#Anchor-NSCLC
17. Zhu J, Sharma DB, Gray SW, Chen AB, Weeks JC, Schrag D. Carboplatin and paclitaxel with vs without bevacizumab in older patients with advanced non-small cell lung cancer. JAMA. 2012; 307(15):1593–1601. [PubMed: 22511687]

18. Herbst RS, Prager D, Hermann R, Fehrenbacher L, Johnson BE, Sandler A, et al. TRIBUTE: a phase III trial of erlotinib hydrochloride (OSI-774) combined with carboplatin and paclitaxel chemotherapy in advanced non-small-cell lung cancer. J Clin Oncol. 2005; 23(25):5892–5899. [PubMed: 16043829]
19. Gatzemeier U, Pluzanska A, Szczesna A, Kaukel E, Roubec J, De RF, et al. Phase III study of erlotinib in combination with cisplatin and gemcitabine in advanced non-small-cell lung cancer: the Tarceva Lung Cancer Investigation Trial. J Clin Oncol. 2007; 25(12):1545–1552. [PubMed: 17442998]
20. Cataldo VD, Gibbons DL, Perez-Soler R, Quintas-Cardama A. Treatment of non-small-cell lung cancer with erlotinib or gefitinib. N Engl J Med. 2011; 364(10):947–955. [PubMed: 21388312]
21. Salloum RG, Smith TJ, Jensen GA, Lafata JE. Using claims-based measures to predict performance status score in patients with lung cancer. Cancer. 2011; 117(5):1038–1048. [PubMed: 20957722]
22. National Comprehensive Cancer Network. Non-small cell lung cancer. Practice guidelines in oncology (Version 3.2011). 2011 (1-7-2011 to 1-20-2011).

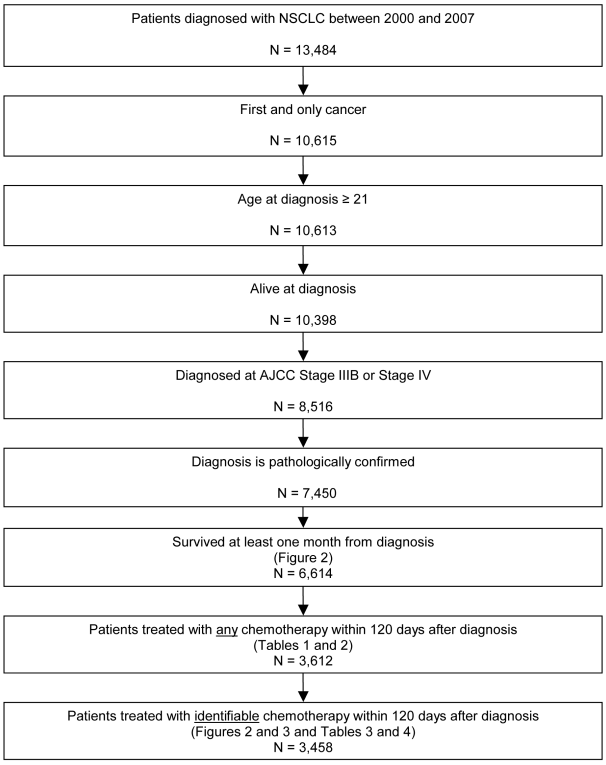

Fig. 1.
Flow of patients with Stage IIIB/IV NSCLC who received first–line chemotherapy from identification to sample inclusion.

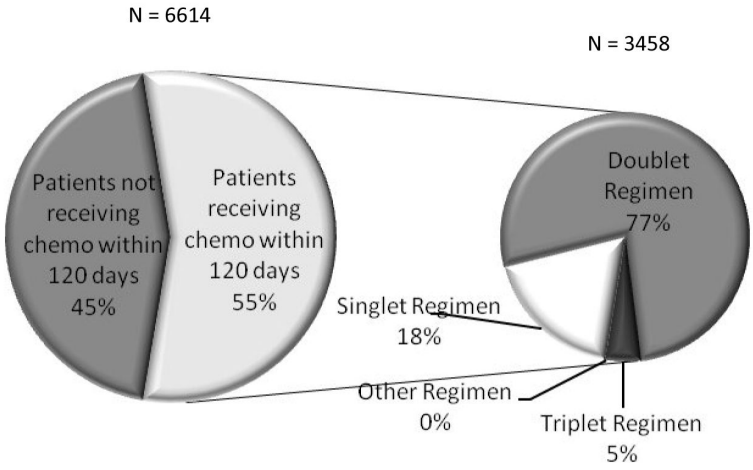

Fig. 2.
Proportion of NSCLC patients receiving chemotherapy

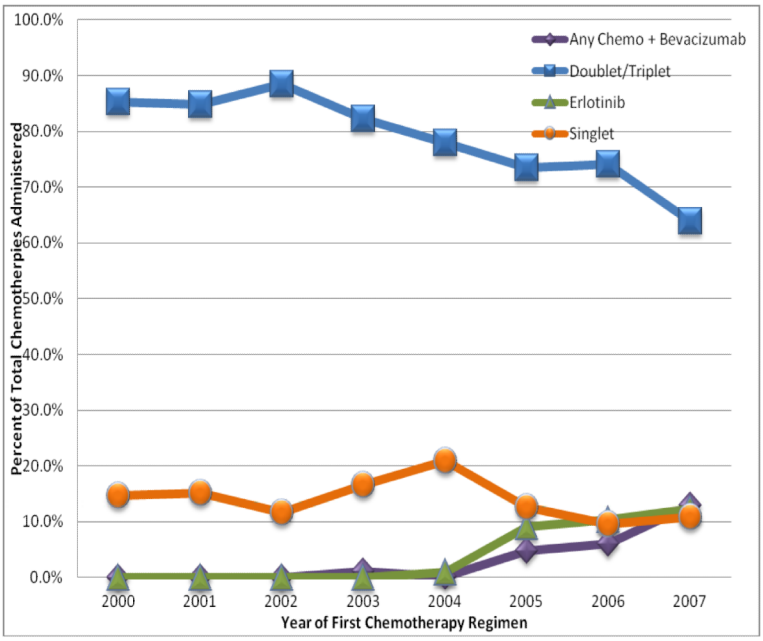

Fig. 3.
Distribution of chemotherapy regimens for stage IIB/IV NSCLC patients diagnosed in 2000 through 2007.

Table 1

Characteristics for stage IIIB/IV NSCLC patients and proportion with receipt of any chemotherapy

Patient Characteristics	Percent of Patients with Characteristic N= 6,614	Percent of patients who received chemotherapy with characteristic N = 3,612	Effects of patient characteristics on receipt of any first-line chemotherapy within 120 days of diagnosis		
			OR	95% CI	P
Age at diagnosis, years					
< 55	12.9	73.4	Ref		
55 – 64	25.0	65.8	0.70	0.580 to 0.837	0.0001
65 – 69	18.0	61.4	0.58	0.475 to 0.697	< .0001
70 – 74	17.5	49.1	0.35	0.289 to 0.423	< .0001
75 – 79	14.2	43.0	0.27	0.224 to 0.333	< .0001
80 +	12.4	23.9	0.11	0.091 to 0.142	< .0001
Age at diagnosis, years					
< 65	37.8	68.4	Ref		
65 +	62.2	46.2	0.40	0.358 to 0.441	< .0001
Gender					
Female	47.4	54.5	Ref		
Male	52.6	54.7	1.01	0.917 to 1.114	0.8265
Race Ethnicity					
White	75.5	53.4	Ref		
Hispanic	6.1	58.3	1.22	0.994 to 1.500	0.0571
Black	7.5	56.4	1.13	0.936 to 1.358	0.2066
Asian/Pacific Islander	8.6	62.5	1.45	1.215 to 1.736	< .0001
Other race	2.3	49.7	0.86	0.624 to 1.188	0.3638
% college educated (census tract quintile)					
1 (lowest)	20.5	51.8	Ref		
2	19.6	52.5	1.03	0.882 to 1.196	0.7337
3	20.2	53.7	1.08	0.926 to 1.254	0.3319
4	20.3	56.5	1.21	1.039 to 1.407	0.0141
5 (highest)	19.4	58.7	1.32	1.135 to 1.545	0.0003
Median income (census					

Patient Characteristics	Percent of Patients with Characteristic N= 6,614	Percent of patients who received chemotherapy with characteristic N = 3,612	Effects of patient characteristics on receipt of any first-line chemotherapy within 120 days of diagnosis		
			OR	95% CI	P
tract quintile)					
1 (lowest)	20.8	51.5	Ref		
2	19.6	50.4	0.96	0.823 to 1.115	0.5818
3	20.5	53.9	1.10	0.948 to 1.281	0.2049
4	19.5	56.3	1.22	1.043 to 1.416	0.0123
5 (highest)	19.7	61.1	1.48	1.269 to 1.725	< .0001
Modified Charlson comorbidity score					
0	44.3	58.7	Ref		
1	25.6	56.7	0.92	0.818 to 1.042	0.1981
2	9.8	53.7	0.82	0.689 to 0.969	0.0205
3+	20.3	43.5	0.54	0.475 to 0.617	< .0001
AJCC Stage at Diagnosis					
III	28.1	57.9	Ref		
IV	71.9	53.3	0.83	0.747 to 0.927	0.0009
Tumor Grade					
Well-moderately differentiated	12.9	54.8	Ref		
Poorly differentiated/undifferentiated	26.8	53.4	0.95	0.802 to 1.113	0.4968
Unknown	60.2	55.1	1.01	0.874 to 1.176	0.8601
Year of Diagnosis					
2000	11.5	51.1	Ref		
2001	12.2	49.6	0.94	0.771 to 1.146	0.5388
2002	12.3	49.6	0.94	0.771 to 1.146	0.5390
2003	12.7	55.5	1.19	0.981 to 1.454	0.0776
2004	13.1	54.7	1.15	0.949 to 1.402	0.1524
2005	13.1	58.4	1.34	1.104 to 1.634	0.0032
2006	12.6	59.0	1.38	1.131 to 1.680	0.0015
2007	12.5	58.2	1.33	1.092 to 1.624	0.0046

Patient Characteristics		Percent of Patients with Characteristic N= 6,614	Percent of patients who received chemotherapy with characteristic N = 3,612	Effects of patient characteristics on receipt of any first-line chemotherapy within 120 days of diagnosis		
				OR	95% CI	P
HMO						
	A		56.6	Ref		
	B		43.7	0.59	0.508 to 0.694	< .0001
	C	49.6		0.75	0.628 to 0.905	0.0025
	D	56.2		0.98	0.832 to 1.159	0.8313

Table 2

Adjusted characteristics for stage IIIB/IV NSCLC patients associated with receipt of any chemotherapy

Patient Characteristics N=3,612	Effects of patient characteristics on receipt of any first-line chemotherapy within 120 days of diagnosis adjusted for all variables noted below		
	Odds Ratio	**95% CI**	**P**
Age at diagnosis, Years			
< 55	Ref		
55 – 64	0.70	0.582 to 0.845	0.0002
65 – 69	0.56	0.463 to 0.687	< .0001
70 – 74	0.34	0.283 to 0.419	< .0001
75 – 79	0.27	0.216 to 0.326	< .0001
80 +	0.10	0.080 to 0.126	< .0001
Gender			
Female	Ref		
Male	1.09	0.978 to 1.201	0.1218
Race Ethnicity			
White	Ref		
Hispanic	1.09	0.875 to 1.361	0.4382
Black	0.90	0.739 to 1.104	0.3202
Asian/Pacific Islander	1.06	0.872 to 1.28	0.5706
Other race	1.07	0.729 to 1.573	0.7280
% College Educated (Census Tract Quintile)			
1 (lowest)	Ref		
2	1.13	0.963 to 1.336	0.1319
3	1.09	0.931 to 1.287	0.2749
4	1.38	1.169 to 1.621	0.0001
5 (highest)	1.48	1.255 to 1.754	< .0001
Modified Charlson Comorbidity Score			
0	Ref		
1	0.99	0.870 to 1.129	0.8901
2	0.99	0.820 to 1.187	0.8877
3+	0.61	0.531 to 0.704	< .0001
AJCC Stage at Diagnosis			
III	Ref		
IV	0.69	0.617 to 0.780	< .0001
Tumor Grade			
Well-moderately differentiated	Ref		
Poorly differentiated/undifferentiated	0.94	0.792 to 1.125	0.5199
Unknown	1.05	0.895 to 1.231	0.5505
Year of Diagnosis			

Patient Characteristics N=3,612		Effects of patient characteristics on receipt of any first-line chemotherapy within 120 days of diagnosis adjusted for all variables noted below		
		Odds Ratio	**95% CI**	**P**
	2000	Ref		
	2001	0.98	0.789 to 1.203	0.8108
	2002	1.01	0.816 to 1.242	0.9523
	2003	1.30	1.054 to 1.604	0.0142
	2004	1.37	1.109 to 1.685	0.0034
	2005	1.55	1.253 to 1.905	< .0001
	2006	1.58	1.281 to 1.958	< .0001
	2007	1.62	1.311 to 2.009	< .0001
HMO				
	A	Ref		
	B	0.54	0.457 to 0.642	< .0001
	C	0.73	0.584 to 0.903	0.0040
	D	0.89	0.739 to 1.061	0.1874

** Interaction between Health Plan and age not significant at 0.1564

** Interaction between Year of Diagnosis and age not significant at 0.7730

Table 3

Ten most frequent first-line chemotherapy regimens by age group*

< 65 years of age N= 1649		**65 years of age and older N= 1809**	
Carboplatin – Paclitaxel	55.7%	Carboplatin – Paclitaxel	51.1%
Cisplatin – Etoposide	7.7%	Cisplatin – Etoposide	6.4%
Carboplatin – Gemcitabine	4.5%	Carboplatin – Gemcitabine	6.1%
Carboplatin	4.4%	Carboplatin	5.1%
Bevacizumab - Carboplatin – Paclitaxel	4.4%	Carboplatin – Docetaxel	4.3%
Carboplatin – Docetaxel	2.6%	Cisplatin – Gemcitabine	4.3%
Cisplatin – Gemcitabine	2.5%	Erlotinib	2.4%
Erlotinib	2.3%	Carboplatin – Etoposide	2.4%
Carboplatin – Etoposide	1.8%	Vinorelbine	2.3%
Vinorelbine	1.5%	Bevacizumab - Carboplatin – Paclitaxel	1.7%
Other Treatment	12.6%	Other Treatment	13.9%

*Chi-Square difference between proportions: $p < 0.0001$