Referral and Treatment Patterns Among Patients With Stages III and IV Non-Small-Cell Lung Cancer

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Abstract

Purpose: Little is known about how referrals to different cancer specialists influence cancer care for non-small-cell lung cancer (NSCLC). Among Medicare enrollees, we identified factors of patients and their primary care physician that were associated with referrals to cancer specialists, and how the types of cancer specialists seen correlated with delivery of guideline-based therapies (GBTs).

Methods: Data from patients with stages III and IV NSCLC included in the SEER-Medicare database were linked to their physicians in the American Medical Association Masterfile database. Using logistic regression, we (1) identified patient and physician factors that were associated with referrals to cancer specialists (medical oncologists, radiation oncologists, and surgeons); (2) identified the types of referral to cancer specialists that predicted greater likelihood of receiving GBT (per National Comprehensive Cancer Network guidelines).

Results: A total of 28,977 patients with NSCLC diagnosed from January 1, 2000 to December 31, 2005 met eligibility criteria. Younger age, white race, higher income, and primary physician specialty other than family practice predicted higher likelihood of referrals to medical oncologists ($P < .01$ for all predictors). Seeing the three types of cancer specialists predicted higher likelihood of GBT (stage IIIA: odds ratio [OR] = 20.6; $P < .001$; IIIB: OR = 77.2; $P < .001$; and IV: OR = 1.2; $P = .011$), compared with seeing a medical oncologist only. Use of GBTs increased over the study period (42% to 48% from 2000 to 2005; $P < .001$).

Conclusion: Referrals to all types of cancer specialists increased the likelihood of treatment with standard therapies, particularly in stage III patients. However, racial and income disparities still prevent optimal referrals to cancer specialists.

Introduction

Lung cancer is a common and serious disease, with more than 221,000 new cases and 157,000 deaths nationwide in 2011.¹ Non-small-cell lung cancer (NSCLC) comprises approximately 85% of lung cancer cases, and 75% of NSCLC cases are diagnosed at stages III and IV.¹⁻³ Treatments for stage III NSCLC include combinations of surgery, radiotherapy, and chemotherapy, with cure rates of 10% to 25%.⁴⁻⁶ Treatment for stage IV NSCLC consists primarily of palliative chemotherapy, with palliative radiation therapy or surgery used to control symptomatic distant tumor sites, including bone and brain metastasis.⁷⁻¹¹ Although lung cancer treatments are provided by cancer specialists, including medical oncologists, radiation oncologists, and surgeons, most patients diagnosed with NSCLC first present to other health care providers, who subsequently refer them to cancer specialists.^{12,13} The manner in which newly diagnosed NSCLC patients are referred to specialists and how such referrals ultimately influence care are important but understudied aspects of the quality of care provided to these patients. In addition, because treatments for stage III and IV NSCLC may involve multiple modalities, it is important to understand whether referral to particular cancer specialists influences the likelihood that a patient with NSCLC receives the array of services that are recommended by treatment guidelines, on the basis of stage at diagnosis.

To address these issues, we conducted a retrospective study using the SEER-Medicare database. The study had the following goals: (1) to identify factors influencing the likelihood of referrals to cancer specialists among patients with stage III and IV NSCLC; (2) to describe the initial treatments delivered to these patients; (3) To identify how referrals to particular cancer specialists correlate with delivery of guideline-based therapies for stages III and IV NSCLC.

Methods

Patient Population

The study included patients in the SEER-Medicare database with histologically or cytologically proven stages IIIA, IIIB and IV NSCLC diagnosed from January 1, 2000, to December 31, 2005. The SEER-Medicare database captures 94% of all Medicare enrollees diagnosed with cancer within the 16 SEER registries existing in the study period, providing patient data on sociodemographic and tumor characteristics, as well as longitudinal data on health care resource utilization from Medicare claims.¹⁴ The SEER registries cover 26% of the US population, providing a nationally representative sample of lung cancer cases.¹⁵ We included patients who were 66 years or older at diagnosis in order to determine noncancer comorbidity that could influence referrals and care, based on 12 months of Medi-

care claims preceding the cancer diagnosis.¹⁶ Patients had to have complete Medicare part A and B claims available (ie, patients enrolled in HMOs were excluded). We excluded patients diagnosed with previous or concurrent cancers, patients enrolled in Medicare as a result of end-stage renal disease or disability, patients who died within 2 months of diagnosis, patients whose month of diagnosis was unknown, and patients whose initial physician could not be identified.

Patient Data Collection

SEER records provided information on patient histology (adenocarcinoma, squamous cell carcinoma, large-cell carcinoma, or NSCLC not otherwise specified) and stage according to the American Joint Committee on Cancer (AJCC) sixth edition. For a relatively small number of patients ($N = 1,961$), only SEER historical staging information was available. For these patients, we defined the SEER stage “regional” as AJCC stage IIIB, and “distant” as AJCC stage IV. We assigned patients to their census geographic area (northeast, midwest, west, and south) on the basis of SEER registry areas. From the SEER-Medicare database, we obtained patient sociodemographic variables, in addition to treatment information up to 6 months after diagnosis based on the Healthcare Common Procedure Coding System, International Classification of Diseases ninth revision, and revenue center codes included in Medicare claims. We defined surgical treatments as codes for lobectomy, sleeve lobectomy, bi-lobectomy, and pneumonectomy. Radiation therapy included all codes for external beam radiation therapy. Because these codes do not specify the site irradiated (eg, chest, brain, bones) or the indication for radiation (curative *v* palliative), we assumed that radiation therapy was given to the chest with curative intent in patients with stage III disease and that patients with stage IV received palliative radiation therapy to symptomatic metastatic sites.¹⁷ We based chemotherapy treatments on all chemotherapy administration codes and on specific codes for cisplatin, carboplatin, gemcitabine, etoposide, paclitaxel, docetaxel, vinblastine, vinorelbine, and bevacizumab.¹⁸ The study received approval from the institutional review board.

Initial Physician Data

We developed an algorithm to identify the physician who was initially involved in the management of the patient’s NSCLC (Appendix Figure A1, online only). We identified these physicians using Unique Physician Identification Numbers (UPIN) that were included in claims for imaging studies in the time period near to the diagnosis of NSCLC (from 12 weeks before diagnosis to 6 weeks after diagnosis). Because SEER reports only the month and year of diagnosis, we set the date of diagnosis as the first day of the month. In order to capture studies that were performed before the diagnosis, we included imaging study claims up to 6 weeks after the set date of diagnosis. The first round of the algorithm captured the computed tomography (CT) scan of the chest taken closest to the time of diagnosis (94% of the final cohort of patients). If no claims were found, the second round of the algorithm captured CT scans of the

abdomen or CT scans or magnetic resonance imaging (MRI) of the brain, whichever was closest to diagnosis, assuming these tests were the initial work-up for lung cancers diagnosed through distant metastatic sites (5% of patients). If no claims were found, the third round of the algorithm captured claims for nuclear bone scans (1% of patients). The use of positron emission tomography (PET) scans was not frequent in the study period, and we did not include this imaging modality in the algorithm.

To determine physician specialty and other relevant physician characteristics, we linked the UPINs captured by the algorithm to the UPINs included in the American Medical Association (AMA) Masterfile database. The AMA Masterfile database includes member and nonmember physician (MDs and doctors of oncology [Dos]) information collected since 1906, and represents a validated data source of individual physician characteristics for linking with Medicare claims.^{19,20} Physician data included age, sex, office geographic location, MD versus DO degree, receipt of the AMA Physician Recognition Award, country of medical school graduation, primary specialty, years since graduation from medical school, primary type of practice (eg, direct patient care *v* administrative), and employment setting (eg, solo practice *v* group practice).

Referral to Cancer Specialists

We defined cancer specialists as medical oncologists or hematologists-oncologists (hereafter medical oncologists), radiation oncologists, thoracic surgeons, and general surgeons. We based referral episodes on claims for outpatient and inpatient visits that occurred after the initial imaging study or cancer diagnosis (whichever was first) and on all treatment claims up to 6 months after diagnosis. We linked the UPINs contained in these claims to the AMA Masterfile to identify the primary specialty of each cancer specialist. We also identified referrals to pulmonologists before referrals to cancer specialists on the basis of UPINs for outpatient or inpatient visit claims billed by pulmonologists.

Definition of Guideline-Based Therapy

Guideline-based therapies were defined using the current version of the National Comprehensive Cancer Network (NCCN) practice guidelines.⁷ For broad treatment categories used in this study, (surgery, radiation, and chemotherapy), the current NCCN recommendations are the same as during the study period. Appendix Table A1 (online only) provides the stage-specific treatment recommendations endorsed by NCCN. For stage IIIA, these recommendations included different combinations and sequences of chemotherapy, radiation, and surgery; for stage IIIB, the NCCN recommends concurrent chemoradiotherapy or chemotherapy followed by radiation; and for stage IV, chemotherapy alone or with palliative radiation for symptomatic metastatic sites.⁷

Statistical Analyses

We used uni- and multivariable multilevel mixed logistic regression models to test associations of patient and initial physician characteristics with referrals to (1) medical oncologists

(because chemotherapy is indicated for stages III and IV NSCLC) and (2) all cancer specialists (medical oncologists, radiation oncologists, and thoracic or general surgeons, because seeing all cancer specialist could potentially enhance adherence to standard therapies). We used the initial physician UPIN as a random-effect variable to account for patient clustering around the same initial physician (1.6 patients per physician on average). We entered all covariates that were statistically significant at a *P* value less than .05 in univariable analysis into the final multivariable model. We omitted the initial physician age and office geographic area from the final models as a result of collinearity with years of graduation from medical school and patient geographical area, respectively.

We used a multivariable logistic model to identify types of referrals to cancer specialists that were associated with higher likelihood of receipt of guideline-based therapies, stratified by stage, and adjusted for patient-specific factors. We used χ^2 tests to test the association of patient stage with receipt of guideline-based therapies, and tested all models for potential interactions. *P* values less than .05 were considered statistically significant.

To evaluate the effect of calendar time on referral and treatment trends, we added year of diagnosis as a discrete variable into all multivariable models. For the referral models, we assumed a fixed effect for each study period year relative to the reference year (2000). For the guideline-based therapy model, we tested the individual effect of each year of diagnosis relative to the year of 2000.

Results

The SEER-Medicare database included 157,638 patients with stages III and IV NSCLC diagnosed from January 1, 2000, to December 31, 2005. We excluded 3,360 patients as a result of a lack of identifiable initial physician data in Medicare claims or in the AMA Masterfile. After applying all eligibility criteria, the final study cohort included 28,977 patients (Appendix Figure A2, online only).

Appendix Table A2 (online only) describes the characteristics of patients and their initial physicians (*N* = 18,605). Mean patient age was 76 years; 53% were male, 83% were white, and 51% had stage IV NSCLC. Initial physician mean age was 49 years; 86% were male, 55% had internal medicine or family practice as their primary specialty, 75% have been in practice for 15 years or more, and 90% worked primarily with patient care. Of the 1,204 (4%) patients who had no referrals to any cancer specialists, mean age was 79 years, 78% were white, 49% were male, 38% had no comorbidities, and 49% had stage IV NSCLC.

Within 6 months from diagnosis, 24,462 patients (84%) saw at least a medical oncologist, and 9,053 patients (31%) saw all cancer specialists (medical oncologists, radiation oncologists, and thoracic or general surgeons). Of 14,870 patients with stage IV NSCLC, 88% saw at least a medical oncologist and 54% received guideline-based therapies (chemotherapy alone in 24% and chemotherapy plus palliative radiotherapy in 30% patients). Of 4,371 patients with stage IIIA, 41% saw all cancer

specialists, 19% saw a medical oncologist plus a radiation therapist, 16% saw a medical oncologist plus a surgeon, and 45% received a combination of therapies that are consistent with guideline recommendations (chemoradiotherapy in 35%, chemotherapy plus surgery in 4%, and trimodality therapy in 6%). Of 9,376 patients with stage IIIB, 18% saw a medical oncologist and a radiation therapist, 32% saw all cancer specialists, and 30% received guideline-based therapies (chemoradiotherapy; Table 1). Although patients with stages IIIA and IIIB were more likely to see all types of cancer specialists than stage IV patients (41% and 32% *v* 28%, *P* < .001), patients with stages IIIA and IIIB were less likely to receive care consistent with guidelines than stage IV patients (45% and 30% *v* 54%, *P* < .001).

In the multivariable model, patients were less likely to see a medical oncologist if they were older, black, had higher comorbidities, or had initially seen a family practice physician versus a general internist. Patients were more likely to see a medical oncologist if they lived in areas of higher income, had stage IV versus IIIA or IIIB, were diagnosed in later study years, or were referred to a pulmonologist first (Table 2).

Patients were less likely to see all cancer specialists if they were older, black, female, had higher comorbidities, or if their initial physician graduated from a US medical school, was female, was a pulmonologist, worked in a teaching hospital, or worked in a government hospital (Veterans Affairs and other federally funded hospitals). Patients were more likely to see all cancer specialists if they had stage IIIA or IIIB versus IV; lived in areas other than the West; if their initial physician was an oncologist, general or thoracic surgeon; or if their initial physician graduated from medical school within 10 to 14 years before the date of diagnosis (Appendix Table A3, online only).

Patients with stage IIIA and IIIB NSCLC were more likely to receive guideline-based therapies if they saw a medical oncologist and radiation oncologist, compared with seeing a medical oncologist only. Stage III patients who saw all types of cancer specialists had the highest likelihood of receiving guideline-based therapies (Table 3).

Stage IV patients were less likely to receive guideline-based therapies if they saw a medical oncologist and radiation oncologist, compared with those who saw a medical oncologist alone (Table 3). Those who saw both a radiation therapist and a medical oncologist were more likely to be treated with radiation alone than those who saw only an oncologist (45% versus 3%, *P* < .001). Compared with seeing a medical oncologist alone, stage IV patients who saw all 3 specialties were slightly more likely to receive guideline-based therapies if the surgeon was a general surgeon, but not a thoracic surgeon. This difference is partly explained by a higher frequency of surgery among stage IV patients who saw a thoracic surgeon compared with those who saw a general surgeon (7% versus 1%, *P* < .001).

Patient referrals to medical oncologists steadily increased over the study period, from 81% in 2000 to 87% in 2005 (odds ratio = 1.1; *P* < .001 for each subsequent year; Table 2).

Table 1. Patterns of Referral to Cancer Specialists and Treatments, by Stage

Stage, Referral, and Treatment	No.	%
Stage IIIA		
Referral type		
Oncology and radiation oncology	831	19.0
Oncology and surgery (thoracic or general)	710	16.2
Oncology, radiation oncology, and surgery	1,784	40.9
Other specialty combinations*	917	20.9
No referrals	129	3.0
Total	4,371	100.0
Treatments		
Chemotherapy and radiotherapy	1,513	34.6
Chemotherapy and surgery	181	4.1
Chemotherapy, radiotherapy, and surgery	269	6.2
Other treatment combinations†	1,849	42.3
No treatment	559	12.8
Total	4,371	100.0
Stage IIIB		
Referral type		
Oncology and radiation oncology	1,709	17.6
Oncology, radiation oncology, and surgery	3,089	31.7
Other specialty combinations‡	4,451	45.7
No referrals	487	5.0
Total	9,736	100.0
Treatments		
Chemotherapy and radiotherapy	2,937	30.2
Chemotherapy, radiotherapy, and surgery	187	1.9
Other treatment combinations§	4,525	46.5
No treatment	2,087	21.4
Total	9,736	100.0
Stage IV		
Referral type		
Oncology with or without other specialties	13,013	87.5
Other specialties without oncology	1,268	8.5
No referrals	589	4.0
Total	14,870	100.0
Treatments		
Chemotherapy alone	3,645	24.5
Chemotherapy and radiotherapy	4,437	29.8
Other treatment combinations¶	3,954	26.6
No treatment	2,834	19.1
Total	14,870	100.0

* Includes referrals to a single specialty (oncology, radiation oncology, or surgery), radiation oncology plus general surgery or thoracic surgery.

† Includes single modality treatments (chemotherapy alone, radiation alone, or surgery alone), or radiation plus surgery.

‡ Includes referrals to a single specialty (oncology, radiation oncology, or surgery), oncology plus general or thoracic surgery, or radiation oncology plus general or thoracic surgery.

§ Includes single modality treatments (chemotherapy alone, radiation alone, or surgery alone), chemotherapy plus surgery, or radiation plus surgery.

|| Includes referrals to a single specialty other than oncology (radiation oncology, general surgery, or thoracic surgery), or radiation oncology plus general or thoracic surgery.

¶ Includes radiation alone, surgery alone, chemotherapy plus surgery, radiation plus surgery, or chemotherapy plus radiation plus surgery.

Referrals to all three types of cancer specialists remained relatively constant over time, varying from 32% in 2000 to 30% in 2005 (odds ratio = 1.00; $P = .536$; Appendix Table A3).

Stage III patients diagnosed in 2004 and 2005 were more likely to receive guideline-based therapies than patients diagnosed in 2000. Stage IV patients diagnosed between 2003 and 2005 were more likely to receive guideline-based therapies than those diagnosed in 2000 (Table 3).

Discussion

Using a nationally representative claims database for Medicare patients, we identified factors associated with referral to cancer specialists and types of treatment received (in relation to recommendations) for patients with stages III and IV NSCLC. Our study suggests that most patients (84%) will see at least a medical oncologist, whereas 31% will see all cancer specialists. Patients who saw a medical oncologist, a radiation oncologist, and a surgeon had the highest likelihood of receiving treatments endorsed by the NCCN guidelines, a finding that was particularly relevant in patients with stage III NSCLC.

Patients diagnosed in more recent years were more likely to see medical oncologists and to receive recommended therapies. This increasing trend in adoption of evidence-based practices suggests improvements in supportive care, lower surgical morbidity, and increased dissemination of guideline recommendations through scientific events and multimedia tools, including Web-enabled electronic health records.

Several observational studies have shown that 45% to 90% of patients with NSCLC are referred to cancer specialists, and 20% to 65% receive recommended therapies for their disease stage.^{12,21-29} A common finding in these studies is that patients who are older or have a lower socioeconomic status are less likely to see cancer specialists and/or receive recommended cancer therapies, including surgery for early-stage or chemotherapy for advanced-stage NSCLC.

Consistent with these observations, our study showed a lower likelihood of referrals to medical oncologists in patients who were older, black, or lived in lower income areas. In addition, patients seen initially by family practice physicians were statistically less likely to see medical oncologists. These findings indicate that sociodemographic characteristics still represent access barriers to specialty care for NSCLC and that some general practitioners are not fully aware of the role of chemotherapy for stages III and IV NSCLC.³⁰ Health care systems need to promote efforts that increase access to specialty care so that only medical factors and patient preferences determine the receipt of cancer therapy modalities.

Patients with stages IIIA and IIIB NSCLC were more likely to see all types of cancer specialists compared with stage IV patients (40% and 32% *v* 28%, respectively), and yet patients with stage III disease were less likely to receive guideline-based therapies than stage IV patients (45% and 30% *v* 54%, respectively). These differences could be partly explained by the higher complexity and toxicity of standard multimodality therapy for stage III compared with palliative chemotherapy for stage IV disease, which could result in a lower adherence to

Table 2. Multivariate Logistical Regression Analysis of Patient and Initial Physician Characteristics With Referrals to Medical Oncologists

Characteristic	Referred*		Unadjusted <i>P</i>	Adjusted OR	95% CI	Adjusted <i>P</i>
	No.	%				
Patients (N = 28,977)						
Age, years†			< .001	0.94‡	0.93 to 0.94	< .001
Mean	75					
SD	6					
Race/ethnicity			.010			
White	20,490	85		Reference		
Black	1,891	81		0.79	0.69 to 0.90	< .001
Hispanic	857	84		0.96	0.79 to 1.17	.691
Asian	1,147	84		0.96	0.81 to 1.14	.633
American Indian/Alaska Native	55	82		0.91	0.45 to 1.84	.790
Unknown	22	69		0.34	0.14 to 0.81	.015
Sex			.535			
Male	12,974	85				
Female	11,488	84				
Stage			< .001			
IV	13,013	88		Reference		
IIIA	3,585	82		0.65	0.59 to 0.72	< .001
IIIB	7,864	81		0.64	0.59 to 0.70	< .001
Region			.307			
West	9,492	83				
Northeast	5,726	87				
Midwest	4,020	87				
South	5,224	82				
Household income§			< .001			
Lower tertile	7,847	82		Reference		
Medium tertile	8,110	84		1.18	1.08 to 1.29	< .001
Higher tertile	8,403	87		1.48	1.35 to 1.62	< .001
Unknown	102	85		1.61	0.91 to 2.83	.101
Charlson index			< .001			
0	11,163	86		Reference		
1-2	10,326	83		0.83	0.77 to 0.90	< .001
> 2	2,008	81		0.74	0.65 to 0.84	< .001
Unknown	965	82		0.62	0.52 to 0.74	< .001
Year of diagnosis			< .001			
2000	3,598	81		Reference		
2001	3,807	83		1.11		< .001
2002	3,995	84				
2003	4,369	84			1.08 to 1.13	
2004	4,379	87				
2005	4,314	87				
Initial Physicians (N = 18,605)						
Degree			.081			
MD	22,671	84				
DO	1,791	86				
AMA Physician Recognition Award			.096			
No	22,783	84				
Yes	1,679	86				

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Table 2. (Continued)

Characteristic	Referred*		Unadjusted <i>P</i>	Adjusted OR	95% CI	Adjusted <i>P</i>
	No.	%				
US medical school			.194			
Yes	18,084	84				
No	6,378	85				
Primary specialty			< .001			
Internal medicine	9,114	84		Reference		
Family practice	4,298	83		0.87	0.78 to 0.96	.008
Pulmonology	2,975	83		0.88	0.78 to 1.00	.053
Emergency medicine	1,206	83		0.85	0.72 to 1.01	.062
Cardiology	1,116	84		1.04	0.87 to 1.24	.674
Oncology	1,046	100		N/A		N/A
General surgery	551	84		0.93	0.73 to 1.19	.581
Thoracic surgery	329	84		0.94	0.68 to 1.29	.690
Other	3,827	85		0.99	0.89 to 1.11	.865
Sex			.791			
Male	21,459	84				
Female	3,003	84				
Years since graduation			.332			
0-9	2,282	85				
10-14	3,188	86				
≥ 15	18,992	84				
Type of practice			.662			
Direct patient care	22,309	84				
Administration	188	82				
Teaching	173	80				
Research	181	82				
Not active during study period	1,556	85				
Unknown	55	79				
Employment setting			.833			
Self-employed/solo	6,449	84				
Group practice¶	13,992	85				
Medical school	237	85				
Government hospital (VA/non-VA)	1,142	81				
Nongovernment hospital	755	84				
Other/unknown	1,887	85				
Pulmonology after initial physician			< .001			
No	9,748	83		Reference		
Yes	14,714	85		1.20	1.12 to 1.29	< .001
Initial physician random-effect coefficient				0.83	0.73 to 0.94	< .0001
Total referred to oncologist	24,462	84				

Abbreviations: AMA, American Medical Association; DO, doctor of oncology; OR, odds ratio; SD, standard deviation; VA, Veterans Affairs.

* Percentages in parentheses indicate row proportions of patients referred to medical oncologists (as opposed to those not referred) for each category level.

† Among patients who saw medical oncologists.

‡ Odds ratio shows the effect of 1-year increase in age on the odds of referral to medical oncologist.

§ Median household income at the census tract or Zip code level.

¶ We assumed a fixed effect for each subsequent year on referral to medical oncologists.

¶¶ Group practice refers to two or more physicians working in the same clinic other than health maintenance organizations.

guideline-recommended treatments in stage III compared with stage IV. In addition, other factors not accounted for in the study could have influenced the differences observed in treatment adherence, including performance status, patient prefer-

ences, and other clinical characteristics not available in the SEER-Medicare database (eg, pulmonary function test results).

Several limitations apply to our study. Factors that could influence referrals and care that are not available in the SEER-

Table 3. Multivariate Logistic Regression Analysis of Patterns of Referral to Cancer Specialists and Treatment With Guideline-Based Therapies by Stage (adjusted for patient age, race, sex, household income, comorbidity, country region, and diagnosis year)

Referral Type	Guideline-Based Therapy		Odds Ratio	95% CI	P
	No.*	%			
Stage IIIA					
Oncology	27	10.4	Reference		
Oncology and radiotherapy	475	57.1	13.4	8.7 to 20.7	< .001
Oncology and thoracic surgery	150	27.9	2.7	1.7 to 4.3	< .001
Oncology and general surgery	23	13.4	1.2	0.6 to 2.1	.629
Oncology, radiotherapy, thoracic surgery	804	66.0	14.8	9.7 to 22.7	< .001
Oncology, radiotherapy, general surgery	390	68.9	20.6	13.1 to 32.2	< .001
Nononcology referrals† or no referrals (n = 0)	94	12.0	1.2	0.7 to 1.9	.461
Stage IIIB					
Oncology	24	2.2	Reference		
Oncology and radiotherapy	892	52.2	50.4	33.2 to 76.6	< .001
Oncology and thoracic surgery	47	3.7	1.5	0.9 to 2.5	.099
Oncology and general surgery	33	4.6	2.1	1.2 to 3.5	.009
Oncology, radiotherapy, thoracic surgery	1,045	54.3	47.5	31.3 to 72.0	< .001
Oncology, radiotherapy, general surgery	745	64.0	77.2	50.5 to 118.2	< .001
Nononcology referrals† or no referrals (n = 1)	151	8.1	4.3	2.8 to 6.7	< .001
Stage IV					
Oncology	1,367	57.9	Reference		
Oncology and radiotherapy	1,867	50.5	0.6	0.6 to 0.7	< .001
Oncology and Thoracic surgery	824	62.3	1.1	0.9 to 1.3	.205
Oncology and general surgery	997	68.6	1.6	1.4 to 1.8	< .001
Oncology, radiotherapy, thoracic surgery	1,162	61.3	0.9	0.8 to 1.1	.257
Oncology, radiotherapy, general surgery	1,500	65.7	1.2	1.0 to 1.3	.011
Nononcology referrals† or no referrals (n = 88)	365	19.7	0.2	0.1 to 0.2	< .001
Time-trend analysis: Stage III patients‡					
Year of diagnosis					
2000	782	33.3	Reference		
2001	745	31.3	0.9	0.8 to 1.1	.245
2002	813	33.0	1.0	0.9 to 1.2	.624
2003	896	34.4	1.1	0.98 to 1.2	.111
2004	859	39.1	1.4	1.3 to 1.6	< .001
2005	805	38.1	1.3	1.2 to 1.5	< .001
Time-trend analysis: Stage IV patients‡					
Year of diagnosis					
2000	1,084	51.8	Reference		
2001	1,152	51.6	1.0	0.9 to 1.1	.789
2002	1,214	53.5	1.1	1.0 to 1.3	.101
2003	1,469	57.1	1.3	1.1 to 1.4	< .001
2004	1,551	54.8	1.2	1.0 to 1.3	.009
2005	1,612	56.2	1.3	1.2 to 1.5	< .001

* Percentages refer to rows.

† Nononcology referrals include thoracic surgery, general surgery, or radiation therapy, alone or in combination.

‡ Time-trend analyses were performed as part of the same multivariate model, but with a simplified stage variable (III v IV, instead of IIIA/IIIB/IV).

Medicare database, including performance status, could have influenced the associations we found for referrals and treatments in this study. Treatment and referral data relied on claim codes and are therefore subject to unverifiable errors. Our algo-

rithm to identify initial physicians has not been validated. Current claims for radiation therapy do not allow the distinction between treatments delivered with curative and those delivered with palliative intent, and this may have biased our estimates of

receipt of guideline-based therapies. We did not explore associations of referrals or treatment patterns with overall survival, because substantial selection bias would probably prevent an accurate interpretation of survival outcomes.

In conclusion, our study suggests that sociodemographic disparities still prevent access to cancer specialists for patients with advanced NSCLC, and patients who see medical oncologists, radiation oncologists, and surgeons have the highest likelihood of receiving therapies endorsed by guidelines, particularly those with stage III NSCLC. As providers strive to improve quality of care, efforts should focus on decreasing disparities in access and elucidating other reasons for suboptimal therapy in patients appropriately referred to lung cancer specialists, including patient preferences and clinical characteristics.

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References

1. Siegel R, Ward E, Brawley O, et al: Cancer statistics, 2011: The impact of eliminating socioeconomic and racial disparities on premature cancer deaths. *CA Cancer J Clin* 61:212-236, 2011
2. Govindan R, Page N, Morgensztern D, et al: Changing epidemiology of small-cell lung cancer in the United States over the last 30 years: Analysis of the Surveillance, Epidemiologic, and End Results database. *J Clin Oncol* 24:4539-4544, 2006
3. Nair A, Klusmann MJ, Jogeesvaran KH, et al: Revisions to the TNM staging of non-small cell lung cancer: Rationale, clinicoradiologic implications, and persistent limitations. *Radiographics* 31:215-238, 2011
4. Albain KS, Swann RS, Rusch VW, et al: Radiotherapy plus chemotherapy with or without surgical resection for stage III non-small-cell lung cancer: A phase III randomised controlled trial. *Lancet* 374:379-386, 2009
5. van Meerbeeck JP, Kramer GW, Van Schil PE, et al: Randomized controlled trial of resection versus radiotherapy after induction chemotherapy in stage IIIA-N2 non-small-cell lung cancer. *J Natl Cancer Inst* 99:442-450, 2007
6. Curran WJ Jr, Paulus R, Langer CJ, et al: Sequential vs. concurrent chemoradiation for stage III non-small cell lung cancer: Randomized phase III trial RTOG 9410. *J Natl Cancer Inst* 103:1452-1460, 2011
7. National Comprehensive Cancer Network: Non-Small Cell Lung Cancer version 2.2012, NCCN guidelines, NCCN, 2011. <http://www.nccn.org>
8. NSCLC Meta-Analyses Collaborative Group: Chemotherapy in addition to supportive care improves survival in advanced non-small-cell lung cancer: A systematic review and meta-analysis of individual patient data from 16 randomized controlled trials. *J Clin Oncol* 26:4617-4625, 2008
9. Sandler A, Gray R, Perry MC, et al: Paclitaxel-carboplatin alone or with bevacizumab for non-small-cell lung cancer. *N Engl J Med* 355:2542-2550, 2006
10. Reck M, von Pawel J, Zatlouk P, et al: Overall survival with cisplatin-gemcitabine and bevacizumab or placebo as first-line therapy for nonsquamous non-small-cell lung cancer: Results from a randomised phase III trial (AVAiL). *Ann Oncol* 21:1804-1809, 2010
11. Shepherd FA, Rodrigues Pereira J, Ciuleanu T, et al: Erlotinib in previously treated non-small-cell lung cancer. *N Engl J Med* 353:123-132, 2005
12. Earle CC, Neumann PJ, Gelber RD, et al: Impact of referral patterns on the use of chemotherapy for lung cancer. *J Clin Oncol* 20:1786-1792, 2002
13. Beatty S, Stevens W, Stevens G, et al: Lung cancer patients in New Zealand initially present to secondary care through the emergency department rather than by referral to a respiratory specialist. *N Z Med J* 122:33-41, 2009
14. Potosky AL, Riley GF, Lubitz JD, et al: Potential for cancer related health services research using a linked Medicare-tumor registry database. *Med Care* 31:732-748, 1993
15. National Cancer Institute: SEER program overview, National Cancer Institute, 2011. <http://seer.cancer.gov/>
16. Deyo RA, Cherkin DC, Ciol MA: Adapting a clinical comorbidity index for use with ICD-9-CM administrative databases. *J Clin Epidemiol* 45:613-619, 1992
17. Hayman JA, Abrahamse PH, Lakhani I, et al: Use of palliative radiotherapy among patients with metastatic non-small-cell lung cancer. *Int J Radiat Oncol Biol Phys* 69:1001-1007, 2007
18. Warren JL, Harlan LC, Fahey A, et al: Utility of the SEER-Medicare data to identify chemotherapy use. *Med Care* 40:55-61, 2002
19. Baldwin LM, Adamache W, Klabunde CN, et al: Linking physician characteristics and Medicare claims data: Issues in data availability, quality, and measurement. *Med Care* 40:82-95, 2002
20. Jang TL, Bekelman JE, Liu Y, et al: Physician visits prior to treatment for clinically localized prostate cancer. *Arch Intern Med* 170:440-450, 2010
21. Ramsey SD, Howlader N, Etzioni RD, et al: 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* 22:4971-4978, 2004
22. Li X, Butts C, Fenton D, et al: Utilization of oncology services and receipt of treatment: A comparison between patients with breast, colon, rectal, or lung cancer. *Ann Oncol* 22:1902-1909, 2011
23. Podnos YD, Borneman TR, Koczywas M, et al: Symptom concerns and resource utilization in patients with lung cancer. *J Palliat Med* 10:899-903, 2007

24. Vinod SK, O'Connell DL, Simonella L, et al: Gaps in optimal care for lung cancer. *J Thorac Oncol* 3:871-879, 2008
25. Vinod SK, Simonella L, Goldsbury D, et al: Underutilization of radiotherapy for lung cancer in New South Wales, Australia. *Cancer* 116:686-694, 2010
26. Wang J, Kuo YF, Freeman J, et al: Increasing access to medical oncology consultation in older patients with stage II-IIIa non-small-cell lung cancer. *Med Oncol* 25:125-132, 2008
27. Winget M, Stanger J, Gao Z, et al: Predictors of surgery and consult with an oncologist for adjuvant chemotherapy in early stage NSCLC patients in Alberta, Canada. *J Thorac Oncol* 4:629-634, 2009
28. Earle CC, Venditti LN, Neumann PJ, et al: Who gets chemotherapy for metastatic lung cancer? *Chest* 117:1239-1246, 2000
29. Dalton SO, Frederiksen BL, Jacobsen E, et al: Socioeconomic position, stage of lung cancer and time between referral and diagnosis in Denmark, 2001-2008. *Br J Cancer* 105:1042-1048, 2011
30. Wassenaar TR, Eickhoff JC, Jarzemyk DR, et al: Differences in primary care clinicians' approach to non-small cell lung cancer patients compared with breast cancer. *J Thorac Oncol* 2:722-728, 2007

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Appendix

Table A1. CAM Therapies: General Types and Specific Therapies

Type of CAM Therapy	Specific Therapies
Special diet	Lacto-ovo vegetarian (no meat) Vegan (no meat, dairy, eggs) Macrobiotic Gerson's diet treatment Other (list)
Psychotherapy	Social worker Psychologist Psychiatrist Support group Other (list)
Movement/PT	Exercise Yoga Tai chi Chi gong Chiropractic/osteopathic Massage Other (list)
Mind/body	Imagery/visualization Hypnosis Meditation Biofeedback Massage therapy Reiki Energy healing/therapeutic touch Journaling Music therapy Other (list)
Spiritual practices	Prayer Prayer/spiritual healing (by others) Other (list)
Dietary supplements	Multivitamins/minerals Vitamin E Vitamin C Soy supplement (isoflavones, pills) Echinacea Garlic (pill form) Selenium Saw palmetto Green tea (EGCG, pills) Coenzyme Q10 St. John's wort Melatonin Essiac Mistletoe (Isador)

Continued on next page

Table A1. (Continued)

Type of CAM Therapy	Specific Therapies
	Milk thistle
	PC SPES
	Laetrile
	Shark cartilage
	Bovine cartilage (Catrx)
	Other (list)
Additional therapies	Homeopathy
	Ayurvedic remedies
	Bioelectro-magnetic therapies
	Acupuncture
	Folk remedies
	Other (list)

Abbreviations: CAM, complementary and alternative medicine; EGCG, epigallocatechin gallate; PC SPES, herbal supplement promoted for prostate health, containing the herbs *crysanthemum morifolium*, *ganoderma lucidum*, *glycyrrhiza glabra*, *isatis indigotica*, *panax pseudoginseng*, *rabdosis rubescens*, *scutellaria baicalensis*, and *serenoa repens*; recalled in 2012 after prescription medications found in product; PT, physical therapy.

Appendix

Table A1. Treatment Recommendations for Stage III and IV Non–Small-Cell Lung Cancer Endorsed by the National Comprehensive Cancer Network Guidelines

Stage IIIA	T3 N1 M0	Surgery followed by chemotherapy with or without postoperative radiation (the latter only if positive margins)
	T1-T3 N2 M0	Neoadjuvant chemotherapy followed by surgery Neoadjuvant chemotherapy followed by surgery and postoperative radiation (if positive margins) Neoadjuvant chemoradiation followed by surgery Definitive concurrent chemoradiation Sequential chemotherapy followed by radiation (if borderline performance status)
Stage IIIB	T4 any N M0	Definitive concurrent chemoradiation Sequential chemotherapy followed by radiation (if borderline performance status)
	Any T N3 M0	Definitive concurrent chemoradiation Sequential chemotherapy followed by radiation (if borderline performance status)
Stage IV	Any T any N M1	Chemotherapy alone
		Chemotherapy and palliative radiation

Recommendations are based on the American Joint Committee on Cancer 6th Edition Staging System.

Table A2. Patient and Initial Physician Characteristics

Characteristic	No.	%
Patients (N = 28,977)		
Age, years		75.6
Mean		6.1
SD		
Sex		
Male	15,346	53.0
Female	13,631	47.0
Race/ethnicity		
White	24,161	83.4
Black	2,336	8.1
Hispanic	1,021	3.5
Asian	1,360	4.7
American Indian/Alaskan Native	67	0.2
Unknown	32	0.1
SEER registry area		
San Francisco-Oakland	974	3.4
Connecticut	2,151	7.4
Detroit	2,539	8.8
Hawaii	409	1.4
Iowa	2,064	7.1
New Mexico	497	1.7
Seattle/Puget Sound	1,666	5.8
Utah	401	1.4
Atlanta	777	2.7
San Jose	614	2.1
Los Angeles	1,867	6.4
Rural Georgia	91	0.3
Greater California	5,025	17.3
Kentucky	3,041	10.5
Louisiana	2,449	8.5
New Jersey	4,412	15.2

Continued on next page

Table A2. (Continued)

Characteristic	No.	%
2004	5,030	17.4
2005	4,982	17.2
Initial Physicians (N = 18,605)		
Median annual household income, \$*		
Lower tertile	≤ 36,600	
Medium tertile	36,601-52,700	
Higher tertile	52,701-200,000	
Charlson comorbidity score		
0	12,949	44.7
1-2	12,380	42.7
> 2	2,469	8.5
Unknown	1,179	4.1
Stage		
IIIA	4,371	15.1
IIIB	9,736	33.6
IV	14,870	51.3
Year of diagnosis		
2000	4,442	15.3
2001	4,610	15.9
2002	4,737	16.3
2003	5,176	17.9
Age, years		
Mean	49.4	
SD	9.9	
Sex		
Male	15,899	85.5
Female	2,706	14.5
Degree		
MD	17,258	92.8
DO	1,347	7.2
AMA Physician Recognition Award		
Yes	1,308	7.0
No	17,297	93.0
US medical school graduate		
Yes	13,856	74.5
No	4,749	25.5
Primary medical specialty		
Internal medicine	6,713	36.1
Family practice	3,543	19.0
Pulmonology	1,304	7.0
Emergency medicine	1,170	6.3
Cardiology	973	5.2
Hematology-oncology or oncology	652	3.5
General surgery	527	2.8
Thoracic surgery	244	1.4
Other/unknown	3,479	18.7

Continued on next page

Table A2. (Continued)

Characteristic	No.	%
Office geographic region		
West	7,183	38.6
Northeast	3,853	20.7
Midwest	2,708	14.6
South	3,830	20.6
Unknown	1,031	5.5
Years since graduation from medical school†		
0-9	2,074	11.1
10-14	2,599	14.0
≥ 15	13,932	74.9
Type of primary practice		
Direct patient care	16,822	90.4
Administrative	154	0.8
Medical teaching	164	0.9
Medical research	138	0.7
Not currently active	1,276	6.9
Unknown	51	0.3
Practice setting		
Self-employed/solo	4,755	25.6
Group‡	10,440	56.1
HMO	23	0.1
Teaching hospital	223	1.2
VA/non-VA government hospital	991	5.3
Nongovernment hospital	578	3.1
Other or unknown	1,595	8.6

Abbreviations: AMA, American Medical Association; DO, doctor of oncology; HMO, health maintenance organization; SD, standard deviation; VA, Veterans Affairs.

* Household income at the census tract or Zip code level.

† At the time of initiation of study period (January 1, 2000).

‡ Group practice includes two or more physicians working in the same clinic, excluding HMOs.

Table A3. Univariable and Multivariable Logistic Regression Analysis of Patient and Initial Physician Characteristics With Referrals to All Cancer Specialists (medical oncologists, radiation oncologists, and thoracic or general surgeons)

Characteristic	Referred*		Unadjusted <i>P</i>	Adjusted OR	95% CI	Adjusted <i>P</i>
	No.	%				
Patients (N = 28,977)						
Age, years†			< .001	0.94‡	0.94 to 0.95	< .001
Mean	74					
SD	5					
Race/ethnicity			< .001			
White	7,718	32		Reference		
Black	690	30		0.79	0.72 to 0.87	< .001
Hispanic	274	27		0.90	0.77 to 1.05	.169
Asian	344	25		0.97	0.85 to 1.12	.691
American Indian/Alaska Native	22	33		1.34	0.78 to 2.30	.292
Unknown	5	16		0.42	0.15 to 1.13	.087
Sex			< .001			
Male	4,945	32		Reference		
Female	4,108			0.95	0.90 to 0.99	.040
Stage		30	< .001			
IV	4,180	28		Reference		
IIIA	1,784	41		1.86	1.73 to 2.01	< .001
IIIB	3,089	32		1.27	1.20 to 1.35	< .001
Region			< .001			
West	2,923	26		Reference		
Northeast	2,201	34		1.53	1.42 to 1.64	< .001
Midwest	1,756	38		1.84	1.70 to 2.00	< .001
South	2,173	34		1.44	1.34 to 1.56	< .001
Household income§			.608			
Lower tertile	2,973	31				
Medium tertile	3,009	31				
Higher tertile	3,035	31				
Unknown	36	30				
Charlson index			< .001			
0	4,193	32		Reference		
1-2	3,841	31		0.92	0.87 to 0.98	.006
> 2	688	28		0.78	0.70 to 0.86	< .001
Unknown	331	28		0.72	0.63 to 0.83	< .001
Year of diagnosis			.188			
2000	1,417	32		Reference		
2001	1,433	31		1.00		.536
2002	1,488	31				
2003	1,634	32			0.99 to 1.02	
2004	1,572	31				
2005	1,509	30				
Initial Physicians (N = 18,605)						
Degree			.180			
MD	8,372	31				
DO	681	33				

Continued on next page

Table A3. (Continued)

Characteristic	Referred*		Unadjusted <i>P</i>	Adjusted OR	95% CI	Adjusted <i>P</i>
	No.	%				
AMA Physician Recognition Award			.473			
No	8,427	31				
Yes	626	32				
US medical school			.028			
Yes	2,422	32		Reference		
No	6,631	31		0.93	0.87 to 0.99	.026
Primary specialty			< .001			
Internal medicine	3,316	31		Reference		
Family practice	1,614	31		0.98	0.90 to 1.06	.549
Pulmonology	1,002	28		0.84	0.77 to 0.92	< .001
Emergency medicine	408	28		1.00	0.88 to 1.15	.962
Cardiology	405	31		1.01	0.88 to 1.15	.881
Oncology	358	34		1.17	1.01 to 1.36	.031
General surgery	317	48		2.15	1.81 to 2.55	< .001
Thoracic surgery	192	49		2.01	1.61 to 2.52	< .001
Other	1,441	32		1.08	1.00 to 1.18	.048
Sex			.002			
Male	8,021	32		Reference		
Female	1,032	29		0.92	0.84 to 0.99	.048
Years since graduation			.020			
0-9	776	29		Reference		
10-14	1,179	32		1.13	1.01 to 1.27	.040
≥ 15	7,098	31		1.10	1.00 to 1.21	.055
Type of practice			.697			
Direct patient care	8,248	31				
Administration	73	31				
Teaching	58	27				
Research	54	25				
Not active during study period	602	33				
Unknown	18	26				
Employment setting			.010			
Self-employed/solo	2,459	32		Reference		
Group practice¶	5,181	31		0.95	0.89 to 1.01	.094
Medical school	74	26		0.74	0.55 to 0.99	.039
Government hospital (VA/non-VA)	397	28		0.81	0.71 to 0.93	.003
Nongovernment hospital	282	31		0.91	0.77 to 1.07	.268
Other/unknown	660	30		0.89	0.80 to 1.00	.048
Pulmonology after initial physician			.281			
No	3709	32				
Yes	5,344	31				
Initial physician random-effect coefficient				0.40	0.31 to 0.53	< .001
Total referred to all specialists	9,053	31				

* Percentages in parenthesis indicate row proportions of patients referred to all cancer specialists (as opposed to those not referred) for each category level.

† Among patients who saw all types of cancer specialists.

‡ Odds ratio shows the effect of 1-year increase in age on the odds of referral to all cancer specialists.

§ Median household income at the census tract or Zip code level.

¶ We assumed a fixed effect for each subsequent year on referral to all cancer specialists.

¶ Group practice refers to two or more physicians working in the same clinic other than health maintenance organizations.

Figure A1. Algorithm to identify physicians initially involved in the management of non-small-cell lung cancer cases (initial physician). CT, computed tomography; MRI, magnetic resonance imaging.

Figure A2. Flow chart of patient selection criteria. UPIN, universal physician identification number.