Disparities in Receiving Guideline-Concordant Treatment for Lung Cancer in the United States

Erik F. Blom^{1,2*}, Kevin ten Haaf¹, Douglas A. Arenberg², and Harry J. de Koning¹

¹Department of Public Health, Erasmus MC, University Medical Center Rotterdam, Rotterdam, the Netherlands; and ²Division of Pulmonary and Critical Care Medicine, University of Michigan, Ann Arbor, Michigan

ORCID ID: 0000-0002-2016-5668 (E.F.B.).

Abstract

Rationale: The level of adherence to lung cancer treatment guidelines in the United States is unclear. In addition, it is unclear whether previously identified disparities by racial or ethnic group and by age persist across all clinical subgroups.

Objectives: To assess the level of adherence to the minimal lung cancer treatment recommended by the National Comprehensive Cancer Network guidelines (guideline-concordant treatment) in the United States, and to assess the persistence of disparities by racial or ethnic group and by age across all clinical subgroups.

Methods: We evaluated whether 441,812 lung cancer cases in the National Cancer Database diagnosed between 2010 and 2014 received guideline-concordant treatment. Logistic regression models were used to assess possible disparities in receiving guideline-concordant treatment by racial or ethnic group and by age across all clinical subgroups, and whether these persist after adjusting for patient, tumor, and health care provider characteristics.

Results: Overall, 62.1% of subjects received guideline-concordant treatment (range across clinical subgroups = 50.4–76.3%). However, 21.6% received no treatment (range = 10.3–31.4%) and 16.3% received less intensive treatment than recommended (range = 6.4–21.6%). Among the most common less intensive treatments for all

subgroups was “conventionally fractionated radiotherapy only” (range = 2.5–16.0%), as was “chemotherapy only” for nonmetastatic subgroups (range = 1.2–13.7%), and “conventionally fractionated radiotherapy and chemotherapy” for localized non-small-cell lung cancer (5.9%). Guideline-concordant treatment was less likely with increasing age, despite adjusting for relevant covariates (age ≥ 80 yr compared with < 50 yr: adjusted odds ratio = 0.12, 95% confidence interval = 0.12–0.13). This disparity was present in all clinical subgroups. In addition, non-Hispanic black patients were less likely to receive guideline-concordant treatment than non-Hispanic white patients (adjusted odds ratio = 0.78, 95% confidence interval = 0.76–0.80). This disparity was present in all clinical subgroups, although statistically nonsignificant for extensive disease small-cell lung cancer.

Conclusions: Between 2010 and 2014, many patients with lung cancer in the United States received no treatment or less intensive treatment than recommended. Particularly, elderly patients with lung cancer and non-Hispanic black patients are less likely to receive guideline-concordant treatment. Patterns of care among those receiving less intensive treatment than recommended suggest room for improved uptake of treatments such as stereotactic body radiation therapy for subjects with localized non-small-cell lung cancer.

Keywords: lung neoplasms; guideline adherence; physicians' practice patterns; healthcare disparities.

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Correspondence and requests for reprints should be addressed to Erik F. Blom, M.D., Erasmus MC, University Medical Center Rotterdam, Department of Public Health, P.O. Box 2040, Internal postal address Na-2401, 3000CA Rotterdam, the Netherlands. E-mail: e.f.blom@erasmusmc.nl.

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An estimated 142,670 persons will die of lung cancer in the United States in 2019, making it the leading cause of cancer-related deaths (1). Reflecting the large burden to society, lung cancer treatment is an important topic of medical research. A recent bibliometric analysis identified a total of 32,161 studies published on lung cancer between 2004 and 2013, of which 36% focused on treatments (2). Clinical practice guidelines, which can be considered the basis for measures of quality of care, compile the available evidence and expert consensus (3).

However, literature indicates that the minimal treatment recommended in these guidelines (i.e., guideline-concordant treatment) may not be provided to all patients with lung cancer in the United States (4). Furthermore, there is evidence that specific subgroups are less likely than others to receive guideline-concordant treatment. For example, the proportion of cases that receive guideline-concordant treatment is lower for more advanced stages (4). Also, disparities by racial or ethnic group have been described. For example, black patients are less likely to receive surgical treatment for localized non-small-cell lung cancer (L-NSCLC; stages I–II) than white patients (5–10). In addition, elderly patients with lung cancer are less likely to receive guideline-concordant treatment, despite controlling for comorbidity (4, 9, 10). However, comparability and generalizability of the available literature are limited, because often only one specific subset of clinical cases is examined (5, 11), relatively small sample sizes are used (8, 10), different methodologies are applied (5, 7), or the data cover different timespans (5, 7). Thus, it is unclear whether disparities in receiving guideline-concordant treatment by racial or ethnic group and by age persist, and whether these are similar across clinical subgroups of lung cancer in the United States.

Therefore, the first aim of this study was to assess the level of adherence to predefined, stage-specific, guideline-concordant treatment for each clinical subgroup of patients with lung cancer in a large U.S. dataset. The second aim was to assess whether previously identified disparities in receiving guideline-concordant treatment by racial or ethnic group and by age persist across all clinical subgroups of lung cancer. Some of the results of this study have been

previously reported in the form of an abstract (12).

Methods

Data

We used the U.S. National Cancer Database (NCDB) to extract a cohort of 441,812 patients diagnosed with lung cancer between 2010 and 2014 (see Figure E1 in the online supplement). The NCDB, established in 1989, is a nationwide, facility-based, comprehensive clinical surveillance resource oncology dataset that currently captures 70% of all newly diagnosed malignancies in the United States annually, from more than 1,500 affiliated facilities. The NCDB records the first course of treatment, defined as all methods of treatment recorded in the treatment plan and administered to the patient before disease progression or recurrence. Analysis of individual-level NCDB data was performed on site at the University of Michigan Medical School.

To assess the generalizability of the NCDB data to the general U.S. population, we compared baseline characteristics to a cohort of patients with lung cancer from the population-based Surveillance, Epidemiology, and End Results (SEER) dataset (13). A detailed version of the methods, including the rationale for case selection, data cleaning, and the analysis of the SEER dataset, is available online (see supplemental METHODS and Tables E1 and E2). This study was deemed exempt by the Institutional Review Board of the University of Michigan.

Definition of Guideline-Concordant Treatment

Two main lung cancer types can be distinguished: NSCLC and small-cell lung cancer (SCLC), with the majority presenting as NSCLC. Because SCLC is clinically more aggressive than NSCLC, clinical guidelines provide specific treatment recommendations for clinical subgroups of lung cancer type and stage at diagnosis. For each of these clinical subgroups, we assessed whether guideline-concordant treatment was received, defined as the minimal first course treatment these patients should receive according to the National Comprehensive Cancer Network guidelines (14, 15).

Although surgery is still recommended as the primary minimal treatment for

L-NSCLC (stages I–II), stereotactic body radiation therapy (SBRT) is now recommended as an alternative treatment to surgery for patients with L-NSCLC (14). SBRT delivers high-dose radiation to a specific target in only a few fractions and provides local tumor control rates of up to 90% with moderate toxicity (16, 17). Therefore, both surgery and SBRT were considered guideline-concordant treatment for L-NSCLC. The minimal recommended treatment for locally advanced NSCLC (LA-NSCLC; stage III) and limited-disease SCLC (LD-SCLC; stages I–III) depends on operability (14, 15). If operable, the minimal recommendation is surgery combined with chemotherapy. However, the majority of patients with LA-NSCLC and those with LD-SCLC are inoperable, in which case the minimal recommendation is a combination of radiotherapy and chemotherapy. Therefore, both treatment combinations were considered guideline concordant for LA-NSCLC and LD-SCLC. For advanced NSCLC (A-NSCLC; stage IV) and extensive disease SCLC (ED-SCLC; stage IV), the minimally recommended treatment is chemotherapy (14, 15). As we assessed the minimal recommended treatment for each clinical subgroup, additional treatments were allowed beside guideline-concordant treatment (e.g., radiotherapy for bone metastases beside chemotherapy in A-NSCLC). A summary of the treatment combinations that were considered guideline concordant for each clinical subgroup can be found in Table E3.

Because the most frequently used SBRT schemes in the United States comprise a total dose of 45 Gray or more over 1–5 fractions (18–20) and the U.S. billing code for SBRT includes a maximum of 5 fractions (14), SBRT was defined as thoracic radiotherapy with a total radiation dose of 45 Gray or more delivered in 5 fractions or less. There were no restrictions on radiation dose or fractionation for stages other than L-NSCLC. Chemotherapy included the use of targeted therapies. We were not able to separately assess the use of immunotherapy agents in these data, because their use was not recommended in the evaluated time period (see supplemental METHODS).

Statistical Analysis

For each clinical subgroup, we assessed the proportion of cases that received guideline-concordant treatment, less intensive treatment than recommended (defined as

treatment that was not guideline concordant), and no treatment. We used clinical stage at diagnosis for creating clinical subgroups, because pathological stage can only be known after the outcome of interest (initial treatment) has occurred. For the groups of patients who received guideline-concordant treatment and less intensive treatment than recommended, we separately assessed which mutually exclusive combinations of surgery, SBRT, conventionally fractionated radiotherapy (CRT; defined as all radiotherapy other than SBRT), chemotherapy (including targeted therapy), and other treatment (including immunotherapy and experimental treatments) were received.

To identify whether previously identified disparities in receiving guideline-concordant treatment by racial or ethnic group and by age persist, we fitted a logistic regression model with receipt of guideline-concordant treatment as binary outcome and racial or ethnic group and age as independent variables. We further adjusted this model for several covariates that could be associated with racial or ethnic group and age, and also affect receiving guideline-concordant treatment. Based on previous literature, we included sex (9), health insurance status (21), Charlson comorbidity score (22), facility type (11), and stage at diagnosis (4). We further included histology, because squamous cell carcinomas are often located centrally (23), potentially making them more difficult to surgically resect. Finally, we included hospital volume, because it is a well-established indicator of quality of care (24). The derivation and composition of these variables is detailed in the supplemental METHODS.

To identify whether disparities by racial or ethnic group and by age extend across all clinical subgroups, we also fitted a separate model for each clinical subgroup. For clinical subgroups with multiple guideline-concordant treatment combinations, we fitted a separate model for each treatment combination. For example, two separate models were fitted for L-NSCLC: one with SBRT as binary outcome and one with surgery as binary outcome. These models were adjusted for the same covariates as the overall model.

All analyses were performed using R software version 3.4.1 (25). The base-R glm function was used to fit the logistic regression models. We used multiple imputation to address missing data, using three imputations (26). Multicollinearity

was assessed by calculating generalized variance inflation factors (27).

Results

Patient Characteristics

Baseline characteristics of the 441,812 included patients are shown in Table 1. When comparing these with lung cancer cases in the population-based SEER registry, we found only very small differences in sex, age, racial or ethnic group, health insurance status, histology, and stage at diagnosis (Table E4).

Adherence to Guideline-Concordant Treatment

The proportion of cases that received guideline-concordant treatment within each clinical subgroup was stable between 2010 and 2014 (Figure E2). As shown in Table 2, 62.1% of all cases diagnosed between 2010 and 2014 received guideline-concordant treatment (range = 50.4% in A-NSCLC to 76.3% in L-NSCLC). However, 16.3% received less intensive treatment than recommended (range = 6.4% in ED-SCLC to 21.6% in LA-NSCLC), and 21.6% received no treatment (range = 10.3% in L-NSCLC to 31.4% in A-NSCLC).

Patterns of Care among Patients that Received Guideline-Concordant Treatment

Among L-NSCLC cases that received guideline-concordant treatment, “surgery only” was received most frequently (49.1%), followed by “surgery and chemotherapy” (11.4%), and “SBRT only” (10.0%) (Table 3). In every other clinical subgroup, “CRT and chemotherapy” was most common (range = 25.9% in A-NSCLC to 63.5% in LD-SCLC). Among subjects with LA-NSCLC and LD-SCLC, “surgery, CRT, and chemotherapy” was also used (7.4% and 2.6%, respectively), as was “surgery and chemotherapy” (4.4% and 2.4%, respectively). Among subjects with A-NSCLC and ED-SCLC, “chemotherapy only” was common (19.5% and 35.0%, respectively).

Patterns of Care among Patients that Received Less Intensive Treatment Than Recommended

“CRT only” was among the most commonly received less-intensive-than-recommended therapies for each clinical subgroup, as was “chemotherapy only” for subgroups other

than A-NSCLC and ED-SCLC (Table 3). Most common among L-NSCLC were “CRT only” (6.1%), “CRT and chemotherapy” (5.9%), and “chemotherapy only” (1.2%). Among subjects with LA-NSCLC and LD-SCLC, the most commonly received less-intensive-than-recommended treatments were “CRT only” (8.7% and 2.5%, respectively) and “chemotherapy only” (7.9% and 13.7%, respectively). “CRT only” was the most common among metastatic subgroups A-NSCLC (16.0%) and ED-SCLC (5.8%).

Disparities in Receiving Guideline-Concordant Treatment

As can be seen in Table 4, the odds of receiving guideline-concordant treatment decreased with advancing age (for those aged ≥ 80 yr compared with those aged < 50 yr: odds ratio [OR] = 0.14, 95% confidence interval [CI] = 0.13–0.14). This association remained present after adjusting for covariates (for those aged ≥ 80 yr compared with those aged < 50 yr: adjusted OR [aOR] = 0.12; 95% CI = 0.12–0.13). In addition, the association between age and receiving guideline-concordant treatment was consistent across clinical subgroups, with a notable exception in L-NSCLC (Table E5). In L-NSCLC, advancing age was associated with a decreased odds of receiving surgery (for those aged ≥ 80 yr compared with those aged < 50 yr: aOR = 0.06; 95% CI = 0.05–0.06). However, the odds of receiving SBRT for L-NSCLC increased with advancing age (for those aged ≥ 80 yr compared with those aged < 50 yr: aOR = 18.39; 95% CI = 14.09–23.99).

Compared with non-Hispanic white patients, non-Hispanic black patients (OR = 0.82; 95% CI = 0.81–0.84) and Hispanic patients (OR = 0.87; 95% CI = 0.84–0.90) were less likely to receive guideline-concordant treatment. This association remained present after adjusting for covariates (non-Hispanic black patients: aOR = 0.78; 95% CI = 0.76–0.80; Hispanic patients: aOR = 0.94; 95% CI = 0.90–0.98). On the other hand, non-Hispanic Asian patients were more likely to receive guideline-concordant treatment after adjusting for covariates (aOR = 1.09; 95% CI = 1.04–1.15). However, results for non-Hispanic Asian patients and Hispanic patients varied within clinical subgroups (Table E5). For example, within the subgroup of L-NSCLC, both non-Hispanic

Table 1. Characteristics of patients in the National Cancer Database diagnosed with non-small-cell lung cancer or small-cell lung cancer in the years 2010–2014

	Overall (N = 441,812)	NSCLC (n = 375,832)	SCLC (n = 65,980)
Patient characteristics			
Sex, n (%)			
Male	228,519 (51.7)	196,454 (52.3)	32,065 (48.6)
Female	213,293 (48.3)	179,378 (47.7)	33,915 (51.4)
Age at diagnosis, n (%)			
<50 yr	22,328 (5.1)	19,224 (5.1)	3,104 (4.7)
50–54 yr	33,619 (7.6)	27,968 (7.4)	5,651 (8.6)
55–59 yr	50,955 (11.5)	42,054 (11.2)	8,901 (13.5)
60–64 yr	62,839 (14.2)	51,902 (13.8)	10,937 (16.6)
65–69 yr	75,298 (17.0)	62,838 (16.7)	12,460 (18.9)
70–74 yr	71,798 (16.3)	60,983 (16.2)	10,815 (16.4)
75–79 yr	58,053 (13.1)	50,616 (13.5)	7,437 (11.3)
≥80 yr	66,922 (15.1)	60,247 (16.0)	6,675 (10.1)
Racial or ethnic group, n (%)			
Non-Hispanic white	349,842 (79.2)	294,833 (78.4)	55,009 (83.4)
Non-Hispanic black	48,060 (10.9)	42,799 (11.4)	5,261 (8.0)
Non-Hispanic Asian	9,483 (2.1)	8,741 (2.3)	742 (1.1)
Hispanic	12,081 (2.7)	10,587 (2.8)	1,494 (2.3)
Other	2,806 (0.6)	2,441 (0.6)	365 (0.6)
Unknown	19,540 (4.4)	16,431 (4.4)	3,109 (4.7)
Health insurance status, n (%)			
Private	117,168 (26.5)	99,666 (26.5)	17,502 (26.5)
Medicare	256,740 (58.1)	219,916 (58.5)	36,824 (55.8)
Medicaid	34,278 (7.8)	28,118 (7.5)	6,160 (9.3)
Other government insurance	7,023 (1.6)	5,928 (1.6)	1,095 (1.7)
No insurance	18,112 (4.1)	15,009 (4.0)	3,103 (4.7)
Unknown	8,491 (1.9)	7,195 (1.9)	1,296 (2.0)
Charlson comorbidity score, n (%)			
0	24,687 (55.9)	211,483 (56.3)	35,404 (53.7)
1	130,577 (29.6)	110,304 (29.3)	20,273 (30.7)
≥2	64,348 (14.6)	54,045 (14.4)	10,303 (15.6)
Health care provider characteristics			
Facility type, n (%)			
Academic	140,344 (31.8)	121,914 (32.4)	18,430 (27.9)
Nonacademic	298,618 (67.6)	251,260 (66.9)	47,358 (71.8)
Unknown	2,850 (0.6)	2,658 (0.7)	192 (0.3)
Hospital volume, median (IQR)	524 (302–861)	533 (304–871)	500 (288–837)
Tumor characteristics			
Histology*, n (%)			
Adenocarcinoma	192,943 (43.7)	192,943 (51.3)	—
Squamous cell	98,848 (22.4)	98,848 (26.3)	—
Other non-small cell	84,041 (19.0)	84,041 (22.4)	—
Small cell	65,980 (14.9)	—	65,980 (100.0)
Clinical stage at diagnosis, n (%)			
IA	62,694 (14.2)	61,123 (16.3)	1,571 (2.4)
IB	26,984 (6.1)	26,049 (6.9)	935 (1.4)
IIA	17,456 (4.0)	15,898 (4.2)	1,558 (2.4)
IIB	15,199 (3.4)	14,300 (3.8)	899 (1.4)
IIIA	57,989 (13.1)	48,881 (13.0)	9,108 (13.8)
IIIB	34,088 (7.7)	26,941 (7.2)	7,147 (10.8)
IV	227,402 (51.5)	182,640 (48.6)	44,762 (67.8)

Definition of abbreviations: IQR = interquartile range; NSCLC = non-small-cell lung cancer; SCLC = small-cell lung cancer.

*NSCLC is subdivided into three distinct histology categories, whereas SCLC is considered a separate disease category.

Asian patients and Hispanic patients were more likely to receive surgery than non-Hispanic white patients (non-Hispanic Asian patients: aOR = 1.23; 95% CI = 1.10–1.37; Hispanic patients: aOR = 1.24; 95% CI = 1.13–1.36), but less likely to receive SBRT (non-Hispanic

Asian patients: aOR = 0.51; 95% CI = 0.43–0.62; Hispanic patients: aOR = 0.47; 95% CI = 0.40–0.56). In addition, non-Hispanic Asian patients with A-NSCLC were more likely to receive chemotherapy (aOR = 1.25; 95% CI = 1.18–1.34).

Discussion

To our knowledge, this study is the first to investigate adherence to guideline-concordant treatment, as well as disparities by racial or ethnic group and by age in a uniform manner for all clinical

Table 2. Receipt of guideline-concordant treatment among patients with lung cancer by clinical subgroup

Clinical Subgroup	<i>n</i>	Guideline-Concordant Treatment* <i>n</i> (%)	Less Intensive Treatment than Recommended† <i>n</i> (%)	No Treatment <i>n</i> (%)
Overall	441,812	274,338 (62.1)	72,155 (16.3)	95,319 (21.6)
L-NSCLC	117,370	89,503 (76.3)	15,741 (13.4)	12,126 (10.3)
LA-NSCLC	75,822	45,774 (60.4)	16,412 (21.6)	13,636 (18.0)
A-NSCLC	182,640	92,119 (50.4)	33,227 (18.2)	57,294 (31.4)
LD-SCLC	21,218	14,765 (69.6)	3,927 (18.5)	2,526 (11.9)
ED-SCLC	44,762	32,177 (71.9)	2,848 (6.4)	9,737 (21.8)

Definition of abbreviations: A-NSCLC = advanced non-small-cell lung cancer (stage IV); ED-SCLC = extensive disease small-cell lung cancer (stage IV); L-NSCLC = localized non-small-cell lung cancer (stages I–II); LA-NSCLC = locally advanced non-small-cell lung cancer (stage III); LD-SCLC = limited-disease small-cell lung cancer (stages I–III).

*Guideline-concordant treatment was defined as the minimal treatment patients should receive according to the National Comprehensive Cancer Network guidelines. Hence, additional treatment was allowed beside guideline-concordant treatment. We considered guideline-concordant treatment to be either surgery or stereotactic body radiation therapy for L-NSCLC; either radiotherapy and chemotherapy or surgery and chemotherapy for LA-NSCLC; chemotherapy for A-NSCLC; either radiotherapy and chemotherapy or surgery and chemotherapy for patients with LD-SCLC; and chemotherapy for patients with ED-SCLC.

†Less intensive treatment than recommended was defined as treatment that was not guideline concordant.

subgroups of lung cancer, including SCLC.

Adherence to Guideline-Concordant Treatment

We show that, overall, the level of adherence to guideline-concordant treatment among patients with lung cancer in the United States is only 62.1%, and varies across clinical subgroups. The rate of guideline-concordant treatment was highest for L-NSCLC. This makes sense, as treatment for L-NSCLC is potentially curative and therefore offers the most obvious benefits. The rate of guideline-concordant treatment was lowest for A-NSCLC.

A possible explanation for this finding could be a lack of referral to medical oncologists among patients with A-NSCLC. A recent study reported that only 54% of stage IIIB–IV NSCLC cases triaged at the British Columbia Cancer Agency were assessed by a medical oncologist (28). Another study found that one of the most common reasons for not referring patients to a medical oncologist or prescribing chemotherapy was the patient's preference against treatment (29). Some patients with incurable disease fear that chemotherapy side-effects may negatively affect their quality of life (30). Perhaps this could influence their willingness to accept chemotherapy. However, chemotherapy for advanced disease has been shown to improve quality of life, symptom control, and survival compared with best supportive care (31). Therefore, discussing a patient's possible fears of chemotherapy and the potential health

benefits could be an important step toward increasing the uptake of chemotherapy.

Compared with our results, Wang and colleagues (4) reported even lower rates of guideline-concordant treatment among 20,511 NSCLC cases diagnosed between 2003 and 2008. In their study, the proportion that received guideline-concordant treatment was 51% among subjects with L-NSCLC, 35% among subjects with LA-NSCLC, and 27% among subjects with A-NSCLC. The difference compared with our study is likely due to patient selection, as Wang and colleagues included only veterans aged 65 years or older.

Within the group that received guideline-concordant treatment, our data show that most L-NSCLC cases received surgery, whereas SBRT and other modalities were used much less frequently. In contrast, most cases in the potentially operable clinical subgroups LA-NSCLC and LD-SCLC did not receive surgery as guideline-concordant treatment.

In our data, 16.3% of cases received less intensive treatment than recommended. The patterns of care among these cases provide important clues toward improvements in clinical care. For example, the frequent use of "CRT only", "CRT and chemotherapy", and "chemotherapy only" among L-NSCLC suggests that the uptake of SBRT among inoperable cases may still be lagging. Among subjects with LA-NSCLC and those with LD-SCLC, the most common forms of less-intensive-than-recommended treatment were "CRT only" and "chemotherapy only". These findings

suggest room for improvement in the uptake of multimodality treatments, such as "CRT and chemotherapy" and "surgery and chemotherapy", for these subgroups. The frequent use of "CRT only" among A-NSCLC and ED-SCLC subgroups suggests room for an increased uptake of chemotherapy among these metastatic subgroups.

Finally, 21.6% of cases in our study received no treatment. This is consistent with findings in a smaller study among 6,662 lung cancer cases in the Kaiser Permanente Southern California tumor registry diagnosed between 2008 and 2013 (22). In that study, rates of nontreatment ranged from 9% among stage 0–II (compared with 10.3% among L-NSCLC in our study) to 34% among stage IV (compared with 31.4% among A-NSCLC in our study).

Disparities in Receiving Guideline-Concordant Treatment

In our study, advancing age was strongly associated with the odds of receiving guideline-concordant treatment across all clinical subgroups. These findings are in line with the conclusions of an earlier study (4). This association persisted after adjusting for factors that could influence fitness for surgery, such as comorbidity, histology, and stage, as well as health care provider characteristics. Other studies also reported a lower likelihood of lung cancer surgery among older patients, although these findings cannot be directly compared with ours due to the use

Table 3. Patterns of care among patients with lung cancer by clinical subgroup

Clinical Subgroup/Treatment Received*	n (%)
L-NSCLC	
Guideline-concordant treatment	
Surgery only	57,605 (49.1)
Surgery and chemotherapy	13,359 (11.4)
SBRT only	11,740 (10.0)
Surgery, CRT, and chemotherapy	4,405 (3.8)
Surgery and CRT	1,562 (1.3)
Less intensive treatment than recommended	
CRT only	7,129 (6.1)
CRT and chemotherapy	6,953 (5.9)
Chemotherapy only	1,465 (1.2)
LA-NSCLC	
Guideline-concordant treatment	
CRT and chemotherapy	36,108 (47.6)
Surgery, CRT, and chemotherapy	5,580 (7.4)
Surgery and chemotherapy	3,335 (4.4)
Less intensive treatment than recommended	
CRT only	6,577 (8.7)
Chemotherapy only	6,008 (7.9)
Surgery only	2,676 (3.5)
A-NSCLC	
Guideline-concordant treatment	
CRT and chemotherapy	47,370 (25.9)
Chemotherapy only	35,620 (19.5)
CRT, chemotherapy, and other treatment	2,970 (1.6)
Chemotherapy and other treatment	2,715 (1.5)
Less intensive treatment than recommended	
CRT only	29,219 (16.0)
LD-SCLC	
Guideline-concordant treatment	
CRT and chemotherapy	13,477 (63.5)
Surgery, CRT, and chemotherapy	545 (2.6)
Surgery and chemotherapy	514 (2.4)
Less intensive treatment than recommended	
Chemotherapy only	2,917 (13.7)
CRT only	534 (2.5)
Surgery only	340 (1.6)
ED-SCLC	
Guideline-concordant treatment	
CRT and chemotherapy	15,671 (35.0)
Chemotherapy only	15,658 (35.0)
Less intensive treatment than recommended	
CRT only	2,597 (5.8)

Definition of abbreviations: A-NSCLC = advanced non-small-cell lung cancer (stage IV); CRT = conventionally fractionated radiotherapy, defined as all radiotherapy other than stereotactic body radiation therapy; ED-SCLC = extensive disease small-cell lung cancer (stage IV); L-NSCLC = localized non-small-cell lung cancer (stages I-II); LA-NSCLC = locally advanced non-small-cell lung cancer (stage III); LD-SCLC = limited-disease small-cell lung cancer (stages I-II); SBRT = stereotactic body radiation therapy, defined as thoracic radiotherapy with a dose of ≥ 45 Gray in ≤ 5 fractions.

*All mutually exclusive combinations of treatment modalities (i.e., all combinations of surgery, SBRT, CRT, chemotherapy, and other treatment) were assessed. However, for each clinical subgroup, only those treatment combinations that were more prevalent than 1% are reported in this table.

of different age groups and methods (9, 10, 32). Although we confirm the lower likelihood of receiving surgery for elderly L-NSCLC cases, we also show that the likelihood of receiving SBRT strongly increases with advancing age. These results indicate that SBRT is indeed used as an alternative guideline-concordant treatment for L-NSCLC cases that have

contraindications for surgery. However, especially in other clinical subgroups, efforts should be made to ensure that elderly patients receive the minimal recommended treatment.

Racial or ethnic group was also associated with the odds of receiving guideline-concordant treatment in both the adjusted and unadjusted analyses. Earlier

research among U.S. patients with lung cancer had already shown that black patients are less likely to receive surgery for L-NSCLC (5–10, 33) and chemotherapy for A-NSCLC (33, 34). Our current study shows that disparities by racial or ethnic group persist and extend to every clinical subgroup of NSCLC. Furthermore, we show that Hispanic patients are also less likely to receive guideline-concordant treatment in general, but more likely to receive surgery for L-NSCLC. In an earlier study, McCann and colleagues (35) offer a possible explanation for racial disparities. They reported that, although surgery was offered to black and white patients with lung cancer at the same rate, black patients declined surgery more often. Their study showed no statistically significant difference in insurance between the groups, and results were corrected for preoperative pulmonary function, tumor stage, and comorbidity. Furthermore, Lin and colleagues (36) reported that negative surgical beliefs, fatalism, and mistrust among racial minorities can partly explain why black patients are less likely to receive guideline-concordant treatment. More research is needed to identify the underlying reasons for such beliefs and mistrust and to test strategies to overcome any barriers to delivery of guideline-concordant treatment.

Strengths and Limitations

A major strength of this study is the very large sample size, combined with the extensive treatment data available in the NCDB. The linked SEER-Medicare database, which also contains detailed treatment variables, may be biased toward older individuals, as it mainly includes patients aged 65 years or older. In contrast, the NCDB data used for our study included patients with lung cancer aged 18 years or older.

There are several potential limitations to our study. The first is the hospital-based nature of the data, which captures only cases diagnosed and treated in Commission on Cancer-affiliated hospitals. However, these hospitals together treat 70% of incident cancer cases in the United States. Furthermore, we compared baseline characteristics to a cohort of patients captured by the smaller, but population-based, SEER database and found only small differences. Therefore, our results are likely generalizable to the U.S. population.

Table 4. Effect of age and racial or ethnic group on the odds of receiving guideline-concordant treatment for lung cancer

	Age							Racial or Ethnic Group					
	<50 yr	50-54 yr	55-59 yr	60-64 yr	65-69 yr	70-74 yr	75-79 yr	≥80 yr	Non-Hispanic White	Non-Hispanic Black	Non-Hispanic Asian	Hispanic	Other
No. of subjects	22,328	33,619	50,955	62,839	75,298	71,798	58,053	66,922	365,922†	50,256†	9,958†	12,682†	2,995†
No. events	17,710	25,242	36,765	43,702	50,822	44,959	31,977	23,161	229,378†	29,206†	6,344†	7,529†	1,881†
Event risk	0.79	0.75	0.72	0.70	0.67	0.63	0.55	0.35	0.63†	0.58†	0.64†	0.59†	0.63†
Crude OR (95% CI)*	Reference	0.79 (0.75-0.82)	0.68 (0.65-0.70)	0.60 (0.57-0.62)	0.54 (0.52-0.56)	0.44 (0.42-0.45)	0.32 (0.31-0.33)	0.14 (0.13-0.14)	Reference	0.82 (0.81-0.84)	1.04 (1.00-1.09)	0.87 (0.84-0.90)	1.00 (0.93-1.09)
Adjusted OR (95% CI)*	Reference	0.76 (0.73-0.79)	0.63 (0.60-0.65)	0.53 (0.51-0.55)	0.48 (0.47-0.50)	0.39 (0.37-0.40)	0.28 (0.27-0.29)	0.12 (0.12-0.13)	Reference	0.78 (0.76-0.80)	1.09 (1.04-1.15)	0.94 (0.90-0.98)	0.94 (0.86-1.03)

Definition of abbreviations: CI = confidence interval; OR = odds ratio.

*The crude and adjusted ORs are from the pooled regression model based on all three imputed datasets. Adjusted ORs are adjusted for sex, insurance status, Charlson comorbidity score, treating facility type, hospital volume, histology, and clinical stage at diagnosis. Variance inflation factors were ≤ 2 for all covariates, indicating that multicollinearity was limited.

[†]The number of subjects, number of events, and event risks for racial or ethnic group are based on the mean values across the three imputed datasets.

Second, our data include only the first course of treatment. Nevertheless, we were able to define guideline-concordant treatment as the minimal recommended treatment. Although the focus of this article was therefore the issue of receiving less intensive treatment than recommended, we acknowledge that receiving more intensive treatment than recommended could potentially also be an issue. However, for most clinical subgroups, the NCDB data does not contain sufficient clinical variables to assess whether each possible combination of surgery, radiotherapy, chemotherapy, and other treatment was more intensive than recommended. For example, radiotherapy is not recommended as a minimal treatment for A-NSCLC, but may still be prescribed as symptomatic treatment for painful bone metastases. Nevertheless, we were able to assess that 10.4% of stage I NSCLC cases received adjuvant or neoadjuvant chemotherapy, which could provide an indication of the extent to which overtreatment occurs. In addition, 2.9% of A-NSCLC cases received surgery. Future studies should focus more in depth on the severity and consequences of receiving more intensive treatment than recommended for lung cancer.

Third, the data did not include several clinical variables that may affect the choice of treatment. Smoking cessation after the diagnosis of lung cancer has been associated with reduced all-cause mortality (37) and a reduced risk of hospital death and pulmonary complications after surgery (38). Therefore, active smokers may have been less likely to receive surgery. However, guidelines state that surgery should not be denied to patients only due to smoking (14). Pulmonary function and performance score may have also influenced the likelihood of receiving surgery (39). Although our correction for comorbidities may have partially accounted for these factors, the Charlson score is an aggregate measure that does not account for all possible comorbidities. Another factor that we could not fully account for using the NCDB data is socioeconomic status, although we were able to include insurance status. We addressed the absence of these clinical variables by assessing multiple guideline-concordant treatments for some clinical subgroups. For instance, both SBRT and surgery were regarded guideline-concordant treatments for L-NSCLC. However, this carries the

implicit assumption that, when the nonsurgical treatment was given, the patient was indeed medically inoperable.

Fourth, we used the official cut-off of 5 fractions in our definition of SBRT, whereas some institutions use schemes with up to 10 fractions (19). However, using a cut-off of 10 fractions would only increase the use of SBRT among L-NSCLC in our dataset from 10.4 to 10.9%.

Fifth, hospital-based data, such as those from the NCDB, could potentially be clustered by hospital. However, in an exploratory analysis using the data before multiple imputation, incorporating clustering by hospital identification had a negligible effect on the estimates of the overall regression model (data not shown). Given that the effect of clustering by hospital is therefore likely small, we did not incorporate clustering by hospital in our final models.

Finally, we were not able to take patient preferences into account. Hence, we cannot draw firm conclusions on the underlying causes of the identified disparities by racial or ethnic group and by age.

Conclusions

We show that many patients with lung cancer in the United States do not receive guideline-concordant treatment. Efforts should be made to decrease the proportion of cases that receive no treatment or less intensive treatment than recommended. Specifically, patterns of care among those receiving less intensive treatment than recommended suggest room for an improved uptake of SBRT among L-NSCLC, multimodality therapy among LA-NSCLC and LD-SCLC subgroups, and chemotherapy among those with metastatic disease (A-NSCLC and ED-SCLC). Furthermore,

we show that elderly patients and non-Hispanic black patients are less likely to receive guideline-concordant treatment across most clinical subgroups of lung cancer, despite adjusting for relevant patient, tumor, and health care provider characteristics. This knowledge may be used to target interventions for improving the rate of lung cancer cases that receive guideline-concordant treatment and to reduce disparities. ■

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References

- 1 Siegel RL, Miller KD, Jemal A. Cancer statistics, 2019. *CA Cancer J Clin* 2019;69:7–34.
- 2 Aggarwal A, Lewison G, Idir S, Peters M, Aldige C, Boerckel W, *et al*. The state of lung cancer research: a global analysis. *J Thorac Oncol* 2016; 11:1040–1050.
- 3 Benson AB III, Brown E. Role of NCCN in integrating cancer clinical practice guidelines into the healthcare debate. *Am Health Drug Benefits* 2008;1:28–33.
- 4 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;30:1447–1455.
- 5 Bach PB, Cramer LD, Warren JL, Begg CB. Racial differences in the treatment of early-stage lung cancer. *N Engl J Med* 1999;341: 1198–1205.
- 6 Fry WA, Menck HR, Winchester DP. The National Cancer Data Base report on lung cancer. *Cancer* 1996;77:1947–1955.
- 7 Esnaola NF, Gebregziabher M, Knott K, Finney C, Silvestri GA, Reed CE, *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;86:220–226. [Discussion, p. 227.]
- 8 Check DK, Albers KB, Uppal KM, Suga JM, Adams AS, Habel LA, *et al*. Examining the role of access to care: racial/ethnic differences in receipt of resection for early-stage non-small cell lung cancer among integrated system members and non-members. *Lung Cancer* 2018; 125:51–56.
- 9 Balekian AA, Wisnivesky JP, Gould MK. Surgical disparities among patients with stage I lung cancer in the National Lung Screening Trial. *Chest* 2019;155:44–52.
- 10 Cykert S, Dilworth-Anderson P, Monroe MH, Walker P, McGuire FR, Corbie-Smith G, *et al*. Factors associated with decisions to undergo surgery among patients with newly diagnosed early-stage lung cancer. *JAMA* 2010;303:2368–2376.
- 11 Bott MJ, Patel AP, Verma V, Crabtree TD, Morgensztern D, Robinson CG, *et al*. Patterns of care in hilar node-positive (N1) non-small cell lung cancer: a missed treatment opportunity? *J Thorac Cardiovasc Surg* 2016;151:1549–1558.e2.
- 12 Blom E, Ten Haaf K, Arenberg D, De Koning H. MA18.06 Patterns of lung cancer care in the United States: developments and disparities [abstract]. *J Thorac Oncol* 2018;13:S420.
- 13 National Cancer Institute. Surveillance, Epidemiology, and End Results (SEER) Program. SEER*Stat Database: Incidence-SEER 18 Regs Research Data + Hurricane Katrina Impacted Louisiana Cases, Nov 2016 Sub (1973-2014 varying)-Linked To County Attributes-Total U.S., 1969-2015 Counties. 2017 Apr [accessed 2017 Oct 17]. Available from: www.seer.cancer.gov.
- 14 National Comprehensive Cancer Network. Clinical Practice Guidelines in Oncology: non-small cell lung cancer version 5.2017. Plymouth Meeting, PA: National Comprehensive Cancer Network. 2017 Mar 16 [accessed 2017 Apr 20]. Available from: https://www.nccn.org/professionals/physician_gls/pdf/nscl.pdf.
- 15 National Comprehensive Cancer Network. Clinical Practice Guidelines in Oncology: Small Cell Lung Cancer Version 3.2017. 2017 Feb 23 [accessed 2017 Apr 20]. Available from: https://www.nccn.org/professionals/physician_gls/pdf/scl.pdf.
- 16 Baumann P, Nyman J, Hoyer M, Wennberg B, Gagliardi G, Lax I, *et al*. Outcome in a prospective phase II trial of medically inoperable stage I non-small-cell lung cancer patients treated with stereotactic body radiotherapy. *J Clin Oncol* 2009;27:3290–3296.
- 17 Timmerman R, Paulus R, Galvin J, Michalski J, Straube W, Bradley J, *et al*. Stereotactic body radiation therapy for inoperable early stage lung cancer. *JAMA* 2010;303:1070–1076.
- 18 Guckenberger M, Andratschke N, Dieckmann K, Hoogeman MS, Hoyer M, Hurkmans C, *et al*. ESTRO ACROP consensus guideline on implementation and practice of stereotactic body radiotherapy for peripherally located early stage non-small cell lung cancer. *Radiother Oncol* 2017;124:11–17.
- 19 Videtic GMM, Donington J, Giuliani M, Heinzerling J, Karas TZ, Kelsey CR, *et al*. Stereotactic body radiation therapy for early-stage non-small cell lung cancer: executive summary of an ASTRO evidence-based guideline. *Pract Radiat Oncol* 2017;7:295–301.
- 20 Pan H, Rose BS, Simpson DR, Mell LK, Mundt AJ, Lawson JD. Clinical practice patterns of lung stereotactic body radiation therapy in the United States: a secondary analysis. *Am J Clin Oncol* 2013;36: 269–272.
- 21 Groth SS, Al-Refaie WB, Zhong W, Vickers SM, Maddaus MA, D'Cunha J, *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.
- 22 Gould MK, Munoz-Plaza CE, Hahn EE, Lee JS, Parry C, Shen E. Comorbidity profiles and their effect on treatment selection and survival among patients with lung cancer. *Ann Am Thorac Soc* 2017; 14:1571–1580.

- 23 Kumar V, Abbas AK, Fausto N. Robbins and Cotran pathologic basis of disease. Philadelphia: Elsevier Saunders; 2005.
- 24 Birkmeyer JD, Stukel TA, Siewers AE, Goodney PP, Wennberg DE, Lucas FL. Surgeon volume and operative mortality in the United States. *N Engl J Med* 2003;349:2117–2127.
- 25 R Foundation for Statistical Computing. R: a language and environment for statistical computing [computer program], version 3.4.1. Vienna, Austria: R Foundation for Statistical Computing; 2017.
- 26 Van Buuren S, Groothuis-Oudshoorn K. MICE: multivariate imputation by chained equations in R. *J Stat Softw* 2011;45:1–68.
- 27 Fox J, Weisberg S. An R companion to applied regression. Thousand Oaks, CA: SAGE Publications; 2011.
- 28 Noonan K, Tong KM, Laskin J, Melosky B, Sun S, Murray N, *et al*. Referral patterns in advanced non–small cell lung cancer: impact on delivery of treatment and survival in a contemporary population based cohort. *Lung Cancer* 2014;86:344–349.
- 29 Ko JJ, Tudor R, Li H, Liu M, Skolnik K, Boland WK, *et al*. Reasons for lack of referral to medical oncology for systemic therapy in stage IV non-small-cell lung cancer: comparison of 2003–2006 with 2010–2011. *Curr Oncol* 2017;24:e486–e493.
- 30 Passik SD, Kirsh KL, Rosenfeld B, McDonald MV, Theobald DE. The changeable nature of patients' fears regarding chemotherapy: implications for palliative care. *J Pain Symptom Manage* 2001;21:113–120.
- 31 Non-Small Cell Lung Cancer Collaborative Group. Chemotherapy and supportive care versus supportive care alone for advanced non–small cell lung cancer. *Cochrane Database Syst Rev* 2010;(5):CD007309.
- 32 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.
- 33 Hardy D, Liu CC, Xia R, Cormier JN, Chan W, White A, *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.
- 34 Earle CC, Venditti LN, Neumann PJ, Gelber RD, Weinstein MC, Potosky AL, *et al*. Who gets chemotherapy for metastatic lung cancer? *Chest* 2000;117:1239–1246.
- 35 McCann J, Artinian V, Duhaime L, Lewis JW Jr, Kvale PA, DiGiovine B. Evaluation of the causes for racial disparity in surgical treatment of early stage lung cancer. *Chest* 2005;128:3440–3446.
- 36 Lin JJ, Mhango G, Wall MM, Lurshurchachai L, Bond KT, Nelson JE, *et al*. Cultural factors associated with racial disparities in lung cancer care. *Ann Am Thorac Soc* 2014;11:489–495.
- 37 Parsons A, Daley A, Begh R, Aveyard P. Influence of smoking cessation after diagnosis of early stage lung cancer on prognosis: systematic review of observational studies with meta-analysis. *BMJ* 2010;340:b5569.
- 38 Mason DP, Subramanian S, Nowicki ER, Grab JD, Murthy SC, Rice TW, *et al*. Impact of smoking cessation before resection of lung cancer: a Society of Thoracic Surgeons General Thoracic Surgery Database study. *Ann Thorac Surg* 2009;88:362–370. [Discussion, pp. 370–371.]
- 39 Zhang R, Lee SM, Wigfield C, Vigneswaran WT, Ferguson MK. Lung function predicts pulmonary complications regardless of the surgical approach. *Ann Thorac Surg* 2015;99:1761–1767.