

Patterns of Care and Survival in Stage III NSCLC Among Black and Latino Patients Compared With White Patients

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Abstract

In the present National Cancer Database analysis, black and Latino men with stage III non–small-cell lung carcinoma had worse socioeconomic characteristics than white patients; however, only black patients were less likely to receive guideline concordant care. When accounting for various demographic, disease, and treatment factors, black and Latino patients had improved and equivalent overall survival compared with white patients. This paradoxical finding could potentially be explained by genetic differences between cohorts.

Background: Race and socioeconomic status have continued to affect the survival and patterns of care of patients with non–small-cell lung cancer (NSCLC). However, data evaluating these associations in patients with stage III disease remain limited. Therefore, we investigated the patterns of care and overall survival (OS) of black and Latino patients with locally advanced NSCLC compared with white patients, using the National Cancer Database. **Materials and Methods:** All patients with stage III NSCLC from 2004 to 2013 who had undergone external beam radiotherapy (RT) alone, RT with chemotherapy (bimodality), or RT with chemotherapy followed by surgery (trimodality) were analyzed within the National Cancer Database according to race (n = 113,945). Univariate associations among the demographic, disease, and treatment characteristics within the 3 cohorts were assessed using χ^2 tests. The OS between cohorts were analyzed using the log-rank test and multivariate Cox proportional hazards regression. **Results:** The black and Latino patients were younger at diagnosis, had lower median household incomes, and were less likely to be insured than were the white patients. The black patients were more likely to receive RT alone (19.3% vs. 18%; $P < .001$) and less likely to have undergone concurrent chemo-RT (53.6% vs. 56.1%; $P < .001$) compared with the white patients. Black patients had improved OS ($P < .001$). In contrast, the Latino patients had survival equivalent to that of the white patients ($P = .920$). **Conclusions:** Despite epidemiologic differences and a propensity for less aggressive treatment, black patients with locally advanced NSCLC had better OS than white patients and Latino patients had equivalent outcomes. Additional research is needed to elucidate this finding, perhaps focusing on biological differences among the cohorts.

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Keywords: Black patients, Disparities, Latino disparities, Locally advanced non-small-cell lung cancer, Population-based analysis

Introduction

A number of population-based studies have been recently reported on non–small-cell lung cancer (NSCLC).¹⁻³ However,

limited data have addressed the effects of race on the patterns of care and oncological outcomes in a modern patient cohort with potentially curative, locally advanced NSCLC (LA-NSCLC). Of all

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patients with NSCLC, 22% will present with stage III disease,⁴ and, despite advances in treatment paradigms, the 5-year overall survival (OS) has remained poor, ranging from 19% to 36%.⁵ Stage III NSCLC has typically been treated with a combination of radiotherapy (RT) and platinum-based chemotherapy,^{6,7} given definitively or neoadjuvantly before surgical resection.⁸ However, even with the improvements in survival during the past several decades, black patients have still had a greater incidence of NSCLC, have been more likely to present with advanced disease, and have been reported to be at an increased risk of death compared with other races.⁹

Although the consequences of NSCLC disparities have been well-documented in black patients,⁹⁻¹³ the effects in the Latino population remain unclear. Some studies have suggested that Latino patients have improved OS compared with non-Hispanic white patients,^{14,15} despite presenting with more advanced disease¹⁶ and being less likely to undergo definitive treatment.¹⁴ We, therefore, performed a population-based analysis using the National Cancer Database (NCDB) to evaluate the relationships among race, patterns of care, and OS for patients with stage III NSCLC, focusing on black and Latino patients compared with white patients.

Materials and Methods

Data Source

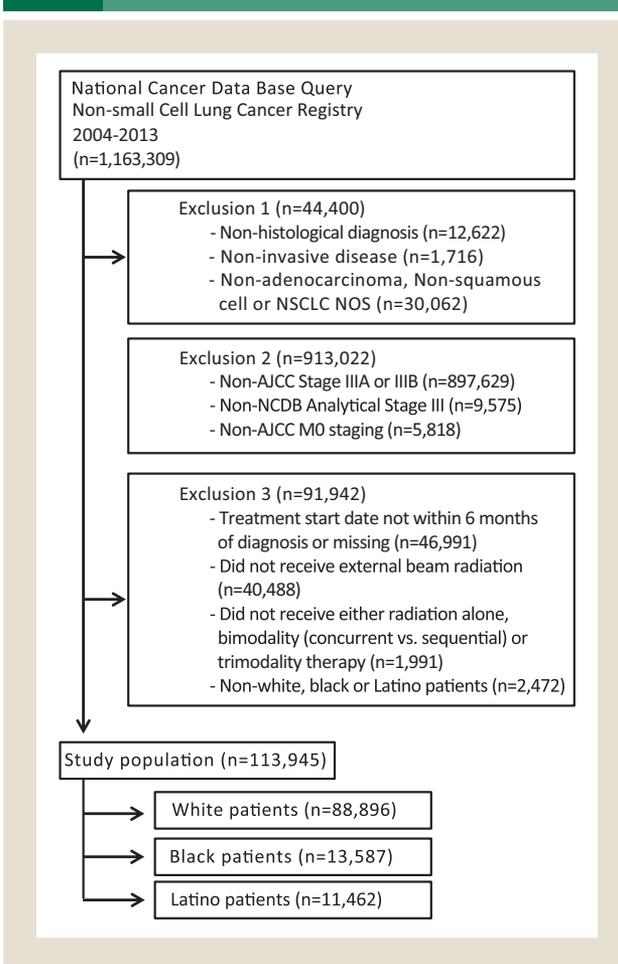
The NCDB is an oncology database that contains hospital registry data from > 1500 Commission on Cancer–accredited facilities and is cosponsored by the American College of Surgeons and the American Cancer Society. Developed in 1989, it is one of the largest cancer databases in the world and represents > 70% of newly diagnosed cancer cases in the United States.¹⁷

Patient Selection and Study Variables in NCDB

The American College of Surgeons and the American Cancer Society provided permission to obtain and analyze the NCDB NSCLC data set (2004-2013), and our study required no additional local or central institutional review board approval. Patients with biopsy-proven, NCDB analytic stage III (American Joint Committee on Cancer, 7th edition staging) NSCLC treated within 6 months of diagnosis with either external beam RT alone or concurrent chemo-RT with (trimodality) or without (bimodality) surgical resection were included in the present analysis (Figure 1). Patients were defined as having received concurrent chemotherapy and RT versus sequential if they had started both treatment modalities within 14 days of each another. Race as categorized in the present study and reported in the NCDB were white, black, or Latino. Patients who had been reported as black or white but had identified with Latino ethnicity were analyzed in the Latino group.

Demographic data (Table 1) included median income derived from the zip code of residence at the diagnosis, percentage (in quartiles) of patients with no high school degree (also derived from the patient's zip code of residence), and treatment facility type. The treatment facilities included academic/research centers (including National Cancer Institute–designated facilities), community center programs, comprehensive community centers, and integrated cancer network programs. Facility type was classified using the Commission on Cancer accreditation criteria. The Charlson-Deyo

Figure 1 CONSORT (Consolidated Standards of Reporting Trials) Diagram of Exclusion Criteria and Final Study Population for Analysis



Abbreviations: AJCC = American Joint Committee on Cancer; NCDB = National Cancer Database; NOS = not otherwise specified; NSCLC = non–small-cell lung cancer.

comorbidity index, as reported in the NCDB, is a weighted score derived from the sum of the comorbid conditions mapped from reported patient-specific secondary diagnosis codes, with values of 0, 1, or 2 indicating levels of increasing comorbidity burden.

Statistical Analysis

All statistical analyses were performed using SPSS Statistics, version 21 (IBM Corp, Armonk, NY), and tests of statistical significance were 2-sided. Univariate associations between each demographic, disease, and treatment characteristic within the 3 cohorts were assessed using χ^2 tests. This was repeated for both black versus white patients and as Latino versus non–Latino white patients. Binary logistic regression with forward modeling selection was used to analyze the predictors for guideline concordant care (GCC) versus non–GCC according to stage and stratified by race for multivariate analysis (MVA). For stage IIIA disease, GCC was limited to sequential and concurrent bimodality therapy and trimodality treatment. For patients with stage IIIB, GCC included sequential or concurrent chemo-RT. The variables analyzed for predictors of OS and treatment selection included

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Table 1 Patient, Disease, and Treatment Characteristics in the 3 Cohorts (n = 113,945)^a

Characteristic	White Patients	Black Patients	Latino Patients	P Value
Sex				.245, .116
Male	50,874 (57.2)	7848 (57.8)	6648 (58.0)	
Female	38,022 (42.8)	5739 (42.2)	4814 (42.0)	
Age, y				<.001, <.001
Median	68	64	67	
Range	18-90	21-90	19-90	
Age group				<.001, <.001
≤60 y	23,193 (26.1)	5442 (40.1)	3242 (28.3)	
>60 y	65,703 (73.9)	8145 (59.9)	8220 (71.7)	
% No HS degree				<.001, <.001
≥29%	13,072 (14.7)	5503 (40.5)	2315 (20.2)	
20%-28.9%	22,471 (25.3)	4157 (30.6)	3158 (27.6)	
14%-14.9%	22,551 (25.4)	1901 (14.0)	2860 (25.0)	
<14%	27,261 (30.7)	1562 (11.5)	2762 (24.0)	
Missing	3541 (3.9)	464 (3.4)	367 (3.2)	
Median income				<.001, <.001
<\$30,000	10,918 (12.3)	5324 (39.2)	2157 (18.8)	
\$30,000-\$35,999	17,538 (19.7)	2881 (21.2)	2435 (21.2)	
\$36,000-\$45,999	26,906 (30.3)	2963 (21.8)	3302 (28.8)	
≥\$46,000	29,998 (33.7)	1959 (14.4)	3204 (28.0)	
Missing	3536 (4.0)	460 (3.4)	364 (3.2)	
Insurance				<.001, <.001
Private	26,286 (29.6)	3713 (27.3)	3361 (29.5)	
Medicare	51,985 (58.5)	6408 (47.2)	6314 (55.1)	
Medicaid	4793 (5.4)	2004 (14.7)	913 (8.0)	
Other government	1823 (2.0)	262 (1.9)	215 (1.8)	
No insurance	2834 (3.2)	897 (6.6)	431 (3.6)	
Missing	1175 (1.3)	303 (2.3)	228 (2.0)	
Facility location				<.001, <.001
Northeast	17,684 (19.9)	2014 (14.8)	2139 (18.7)	
South	20,354 (22.9)	4740 (34.9)	1824 (15.9)	
Midwest	43,250 (48.7)	6251 (46.0)	6734 (58.5)	
West	7206 (8.1)	497 (3.7)	699 (6.3)	
Missing	402 (0.5)	85 (0.6)	66 (0.6)	
Facility type				<.001, <.001
Academic/research	22,766 (25.6)	5702 (42.0)	3362 (29.3)	
Community/other	13,050 (14.7)	1459 (10.7)	1471 (12.8)	
Comprehensive community center	46,964 (52.8)	5299 (39.0)	5693 (49.7)	
Integrated network	5714 (6.4)	1042 (7.7)	870 (7.6)	
Missing	402 (0.5)	85 (0.6)	66 (0.6)	
Residence				<.001, .001
Metropolitan	65,150 (73.3)	11,607 (85.4)	8586 (74.9)	
Urban	17,819 (20.0)	1473 (10.8)	2145 (18.7)	
Rural	2540 (2.9)	156 (1.2)	347 (3.0)	
Missing	3387 (3.8)	351 (2.6)	384 (3.4)	
Charlson-Deyo score				<.001, <.001
0	55,274 (62.2)	8447 (62.2)	7383 (64.4)	
1	24,034 (27.0)	3531 (26.0)	2842 (24.8)	
2	9588 (10.8)	1609 (11.8)	1237 (10.8)	

Table 1 Continued

Characteristic	White Patients	Black Patients	Latino Patients	P Value
Histologic type				<.001, <.001
Adenocarcinoma	28,546 (32.1)	4504 (33.1)	3630 (31.7)	
Squamous cell	37,427 (42.1)	5283 (38.9)	4624 (40.3)	
NSCLC NOS	18,733 (21.1)	3130 (23.0)	2573 (22.4)	
Other	4190 (4.7)	670 (4.9)	635 (5.5)	
T stage				<.001, <.001
Tx	3943 (4.4)	525 (3.9)	525 (4.6)	
≤T2	37,884 (42.6)	5206 (38.3)	4736 (41.3)	
≥T3	46,651 (45.5)	7816 (57.5)	6172 (53.8)	
Missing	418 (0.5)	40 (0.3)	29 (0.3)	
N stage				.034, .001
Nx	2783 (3.1)	410 (3.0)	430 (3.8)	
≤N1	14,481 (16.3)	2264 (16.7)	1822 (15.9)	
N2	53,846 (60.6)	8074 (59.4)	6856 (59.8)	
N3	17,786 (20.0)	2839 (20.9)	2354 (20.5)	
Overall stage				<.001, <.001
IIIA	47,910 (53.9)	6839 (50.3)	5870 (51.2)	
IIIB	40,986 (46.1)	6748 (49.7)	5592 (48.8)	
Time to treatment, d				<.001, .66
Median	28	31	28	
Range	0-180	0-180	0-178	

Abbreviations: HS = high school; NOS = not otherwise specified; NSCLC = non-small-cell lung cancer.
^aP values reported using χ^2 comparisons between black versus white and Latino versus white patients, respectively.

age (> 60 vs. ≤ 60 years), race (black vs. white vs. Latino), sex, median income in quartiles (<\$30,000 vs. \$30,000-\$35,999 vs. \$36,000-\$45,999 vs. >\$46,000), percentage with no high school diploma (≥29% vs. 20%-28.9% vs. 14%-19.9% vs. < 14%), patient area of residence (metropolitan vs. urban vs. rural), insurance status (none vs. government vs. private), region of treatment (Northeast vs. South vs. Midwest vs. West), facility type as listed previously, Charlson-Deyo comorbidity index score, histologic type (adenocarcinoma vs. squamous cell vs. NSCLC, not otherwise specified [NOS], vs. other), T stage (Tx vs. ≤ T2 vs. ≥ T3) and N stage (Nx vs. ≤ N1 vs. N2 vs. N3).

The Kaplan-Meier product limit method with the log-rank test was used to estimate OS, stratified by race, treatment type, and age. Cox regression analysis with forward model selection was used for MVA in predicting OS, using the stated variables and treatment type (RT alone, sequential bimodality, concurrent bimodality, or trimodality therapy). First-order interactions between race and the other variables were also analyzed, using the Cox regression proportional hazards model, keeping the main effects in the model. These interactions were limited between black and white patients, focusing on age, sex, comorbidities, median income quartiles, insurance status, stage (IIIA vs. IIIB), and treatment type.

Results

Cohorts and Patterns of Care

A total of 113,945 patients were included in the present study (Figure 1). The baseline patient demographic and treatment characteristics for black (n = 13,587), white (n = 88,896), and Latino

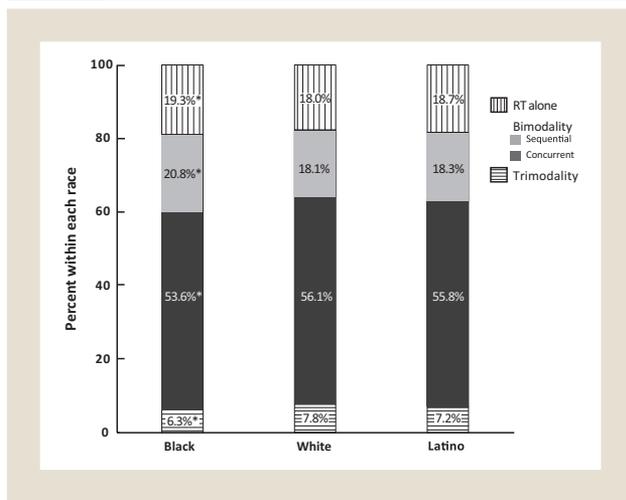
(n = 11,462) patients are summarized in Table 1. Considering the data only for living patients at the time the NCDB had been last updated in the 3 cohorts, the median interval (35 months) to the last follow-up examination was identical for the black and white patients (P = .641). In contrast, it was significantly longer for the Latino patients than for the white patients (41 and 35 months, respectively; P < .001). Approximately 74% of the entire study population had undergone bimodality therapy; however, black patients were less likely to have received concurrent chemotherapy compared with white patients (53.6% vs. 56.1%; P < .001; Figure 2). In contrast, the Latino patients had treatment patterns similar to those of white patients (P = .056).

Predictors for Treatment Selection

The statistically significant variables that predicted for GCC as stratified by overall stage (IIIA vs. IIIB) are summarized in Table 2. Evaluation of the factors that were important for stage IIIA GCC on MVA revealed that the most significant covariates were age and insurance status, with older age (age, > 60 years) predicting for a 60% chance of not receiving GCC and government insurance or no insurance coverage predicting for a greater chance of non-GCC by ~50% and ~35%, respectively. Race was also important for treatment selection for patients with stage IIIA NSCLC. Black patients were 11% less likely to have received appropriate treatment. For stage IIIB disease, older age, insurance status, and increasing comorbidity burden were, again, among the major predictors of GCC. Race was not an independent predictor for GCC for patients with stage IIIB disease. The predictors for GCC were further

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Figure 2 Stacked Bar Graph Showing Patterns of Care in Black, White, and Latino Patients With Stage III Non–Small-cell Lung Cancer. *Statistically Significant Difference Compared With White Patients Using χ^2 Test. Significance Associated With Treatment Paradigm Differences Between Black and White Patients Was $P < .001$, With $P = .056$ Calculated Between Latino and White Patients



stratified by stage and race (Supplemental Table 1; available in the online version).

Overall Survival

When stratified by race, black patients had a better median survival of 15.4 months (3-year OS, 25%) compared with a median survival of 14.4 months (3-year OS, 22.9%) in white patients (unadjusted hazard ratio [HR], 0.939; 95% confidence interval [CI], 0.919-0.959; $P < .001$; Figure 3A). In contrast, the Latino patients had median survival estimates that were indistinguishable statistically from those of the white patients (14.4 months; 3-year OS, 22.8%; unadjusted HR, 1.00; 95% CI, 0.980-1.02; $P < .884$). To assess the effect of any selection bias, OS was also evaluated in the 46,991 patients initially excluded because their treatment had not been initiated within 6 months of diagnosis (Figure 1). The black patients continued to have a survival advantage compared with white patients when considering this population alone ($n = 46,991$; unadjusted HR, 0.941; 95% CI, 0.927-0.957; $P < .001$) or when combined with the entire cohort who had started treatment within 6 months ($n = 117,648$; unadjusted HR, 0.935; 95% CI, 0.915-0.955; $P < .001$). We also evaluated the group that had not undergone external beam RT ($n = 40,488$; Figure 1). In that setting, black patients had OS equivalent to that of the white group (unadjusted HR, 1.015; 95% CI, 0.997-1.053; $P = .447$). However, the black patients continued to have improved OS when this population was combined with the entire cohort who had received external beam RT ($n = 155,260$; unadjusted HR, 0.956; 95% CI, 0.938-0.973; $P < .001$).

When accounting for various socioeconomic, disease, and treatment characteristics on MVA using the original exclusion criteria (Figure 1), black race remained associated with a decreased risk of death. The most significant predictor of OS on MVA was treatment

Table 2 Factors Predicting for Guideline Concordant Versus Non–Guideline Concordant Care^a

Covariate	OR	95% CI	P Value
Stage IIIA^b			
Age	0.387	0.360-0.417	<.001
Sex (favoring females)	0.911	0.871-0.954	
Charlson-Deyo score	0.824	0.799-0.850	<.001
Race			
White	Reference	Reference	NA
Black	0.893	0.828-0.962	.003
Latino	0.959	0.888-1.036	.287
Insurance status			
Private	Reference	Reference	NA
Government	0.489	0.458-0.522	<.001
No insurance	0.644	0.547-0.758	<.001
Median income			
≥\$46,000	Reference	Reference	NA
<\$30,000	0.832	0.772-0.897	<.001
\$30,000-\$35,999	0.837	0.783-0.896	<.001
\$36,000-\$45,999	0.913	0.861-0.969	.003
Residence			
Rural	Reference	Reference	NA
Metropolitan	0.798	0.691-0.921	.002
Urban	0.931	0.803-1.078	.338
Histologic type			
Adenocarcinoma	Reference	Reference	NA
Squamous cell	0.715	0.677-0.755	<.001
NSCLC NOS	0.723	0.677-0.772	<.001
Other	0.880	0.782-0.990	.033
T stage	0.885	0.849-0.924	<.001
N stage	1.156	1.099-1.216	<.001
Facility location			
West	Reference	Reference	NA
Northeast	1.280	1.165-1.407	<.001
South	1.370	1.249-1.502	<.001
Midwest	1.352	1.241-1.473	<.001
Stage IIIB^c			
Age	0.613	0.579-0.648	<.001
Sex (favoring females)	0.916	0.877-0.957	<.001
Charlson-Deyo score	0.803	0.779-0.827	<.001
Insurance status			
Private	Reference	Reference	NA
Government	0.894	0.791-1.010	.073
No insurance	0.672	0.637-0.709	<.001
No HS degree, %			
<14	Reference	Reference	NA
≥29	0.863	0.809-0.921	<.001
20-28.9	0.916	0.864-0.972	.004
14-14.9	0.972	0.916-1.032	.360
Residence			
Rural	Reference	Reference	NA
Metropolitan	0.805	0.702-0.924	.002

Covariate	OR	95% CI	P Value
Urban	0.887	0.770-1.023	.099
Histologic type			
Adenocarcinoma	Reference	Reference	NA
Squamous cell	0.859	0.815-0.905	<.001
NSCLC NOS	0.914	0.860-0.970	.003
Other	0.798	0.720-0.884	<.001
T stage	0.744	0.715-0.775	<.001
N stage	1.342	1.309-1.376	<.001
Facility type			
Integrated network	Reference	Reference	NA
Academic/research	0.829	0.754-0.913	<.001
Community/other	0.971	0.875-1.078	.582
Comprehensive community program	0.914	0.835-1.001	.054
Facility location			
West	Reference	Reference	NA
Northeast	0.829	0.754-0.913	<.001
South	0.971	0.875-1.078	.582
Midwest	0.887	0.770-1.023	.099

Abbreviations: HS = high school; NA = not applicable; NOS = not otherwise specified; NSCLC = non-small-cell lung cancer.

^aBinary logistic regression with forward modeling selection was used to predict treatment selection on multivariate analysis; results are listed from the final logistic regression model, with the odds ratio presented adjusted for each another.

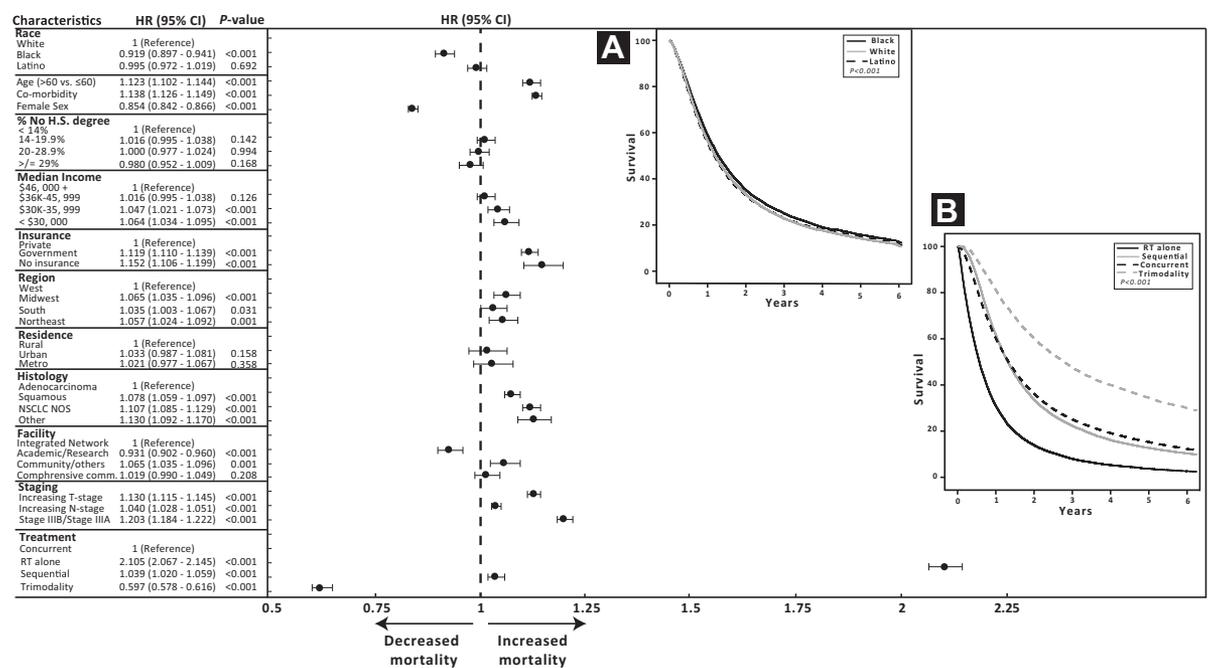
^bSample size for stage IIIA analysis was 60,619.

^cSample size for stage IIIB analysis was 53,326.

modality. Trimodality therapy was associated with an estimated median survival of 33.5 months compared with RT alone (6.8 months), sequential bimodality treatment (15.7 months), and concurrent bimodality treatment (15.8 months), an association that remained significant on MVA. When stratified by treatment modality and race, black patients continued to have better OS compared with white patients receiving RT alone or bimodality treatment (Figure 4A,B). However, this survival benefit was lost when patients receiving only trimodality therapy were analyzed (Figure 4C). The Latino patients had OS rates indistinguishable from those of white patients, regardless of treatment modality. Histologic type was also significant for clinical outcomes, with nonadenocarcinoma tumors predicting for inferior OS (Figure 3). When both race and histologic type were considered, black patients with adenocarcinoma retained an OS advantage compared with white patients (Figure 4D). This survival benefit remained statistically significant but was attenuated for squamous cell carcinoma (Figure 4E) and NSCLC, NOS (Figure 4F). The Latino patients had OS that was identical to that of white patients, irrespective of histologic type.

Older age was likewise associated with an increased risk of mortality on MVA. Although black patients were younger at diagnosis than were white patients, no statistically significant difference was noted in OS when stratified by race for patients aged < 60 years (Supplemental Figure 1; available in the online version). However, black patients still had improved OS compared with white patients in the older population (age, > 60 years; Supplemental Figure 1; available in the online version). No significant difference was seen in

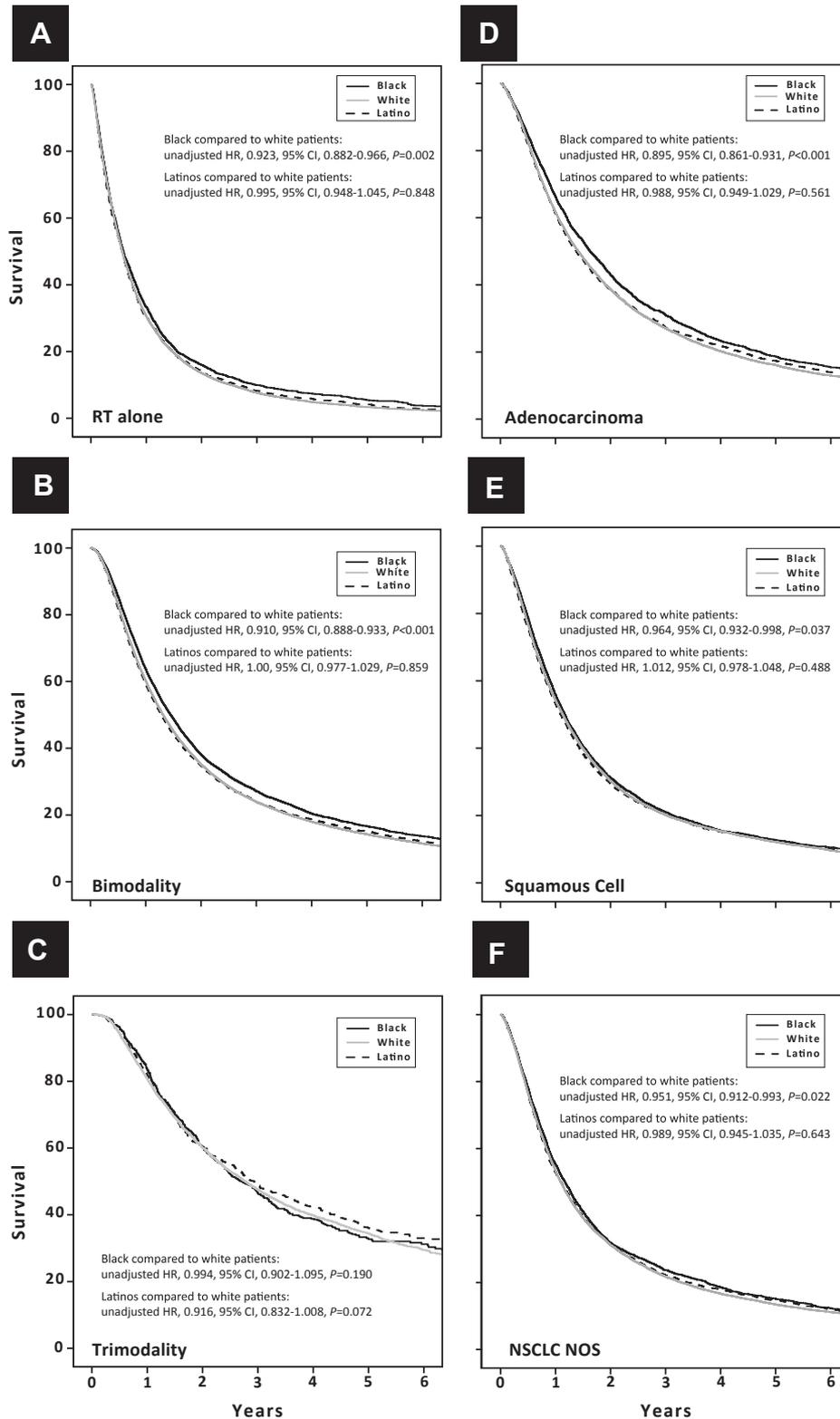
Figure 3 Forest Plot Depicting Hazard Ratios (HRs) and 95% Confidence Intervals (CIs) of Certain Socioeconomic, Disease, and Treatment Characteristics Important for Survival From Multivariate Analysis, With HRs Presented Adjusted for Each Another. Kaplan-Meier Curves of Overall Survival Stratified by (Inset A) Race and (Inset B) Treatment Modality



Abbreviations: H.S. = high school; NSCLC NOS = non-small-cell lung cancer, not otherwise specified; RT = radiotherapy.

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Figure 4 Kaplan-Meier Overall Survival Curves Stratified by Treatment Modality, Histologic Type, and Race. (A) Radiotherapy (RT) Alone; (B) Bimodality; (C) Trimodality; (D) Adenocarcinoma; (E) Squamous Cell Carcinoma; and (F) Non-Small-cell Lung Cancer, Not Otherwise Specified (NSCLC NOS)



Abbreviations: CI = confidence interval; HR = hazard ratio.

OS for the older or younger patients comparing the Latino and white groups.

First-order interactions between race (black vs. white patients) and certain variables are summarized in [Supplemental Table 2](#) (available in the online version). Significant interactions between race and age and race and treatment were also found. In both cases, black race was no longer associated with an OS advantage when the interaction term for age or treatment was considered in the analysis. Interactions among race, comorbidity, income, and insurance status were also present. In all these examples, the black population continued to have superior OS compared with white patients; however, this survival was largely driven by the least favorable groups. For example, black patients with no insurance had a greater OS advantage compared with white patients with no insurance, in contrast to the results from a comparison of the 2 races with private or government insurance ([Supplemental Figure 1](#) and [Supplemental Table 2](#); available in the online version). A similar pattern was also appreciated for median income and Charlson comorbidity index. Race and sex were independent covariates with no interactions seen on OS ([Supplemental Table 2](#); available in the online version).

Discussion

The disparities associated with LA-NSCLC described in the reported data have typically compared black and white populations, with black patients having a greater incidence and mortality rate accompanying the lung cancer diagnosis.^{9-11,13,18} In contrast, although the Latino patients were more likely to have a diagnosis of more advanced disease than white patients, their OS using Surveillance, Epidemiology, and End Results (SEER) Program^{15,16} data and retrospective studies¹⁴ was found to be slightly superior. However, lung cancer survival in the Latino population should be carefully considered, because artificial OS inflation secondary to incomplete follow-up data and an underestimation of cancer death has been common.^{16,19} In our analysis, the Latino patients had a significantly longer follow-up period compared with the white patients. Nonetheless, in our assessment, the Latino patients with stage III NSCLC had indistinguishable OS from that of the white population, which was not surprising given that Latino men were equally likely to be considered for GCC and more locally aggressive trimodality therapy, despite having less favorable socioeconomic characteristics.

Latino patients constitute a heterogeneous ethnic group, and the probability of mortality differences among the subgroups are important elements to consider, given the unique immigration patterns and cultural differences among the countries of origin.²⁰⁻²³ One limitation of the present analysis was the lack of country-specific outcomes. In the present NCDB group, 90% of the Latino population had an unknown country of origin, limiting the statistical power of the analysis. To accurately compare OS and limit bias, a complete death evaluation is critical. Future studies that include the Latino population with NSCLC should take great care in collecting data from meaningful cohorts (ie, foreign-born or not, birthplace, and country of origin) to ensure an accurate survival representation for this diverse ethnic group.

In contrast, black patients with lung cancer have been consistently shown to have worse OS compared with the white population.^{13,18,24-26} This disparity has been attributed to various complex socioeconomic interactions,^{24,27} access to care,^{13,28} and biological

differences between the 2 groups.^{29,30} In the present study, the black population was also less likely to receive GCC for stage IIIA disease ([Table 2](#)) or more locally aggressive treatment ([Figure 2](#)), a trend that has been described in other reports.^{9,26,31-33} Bach et al²⁶ reported a SEER analysis of early-stage, resectable NSCLC and found that the rate of surgical resection was 12.7% lower for black patients than for their white counterparts, which translated to a detriment in 5-year OS for the black cohort (26.4% vs. 34.1%).

In addition to race, other socioeconomic factors can significantly affect the treatment selection for patients with NSCLC. Greenberg et al³⁴ reported a population-based study from 2 rural states. They found that younger, privately insured patients with NSCLC who were married were more likely to receive aggressive treatment.³⁴ This trend was also reflected in a more recent SEER analysis evaluating elderly patients with NSCLC. In that analysis, older black patients and those with a lower median income had greater disparities in the receipt of care compared with white patients in a higher income quartile.³² The discrepancies in treatment found in our study could have resulted, in part, from differences in staging between black and white patients, because black patients presented with larger primary tumors and more advanced disease ([Table 1](#)). As seen for stage IIIB disease, increasing T stage was associated with a 20% to 30% decrease in receiving appropriate treatment for all races ([Supplemental Table 1](#); available in the online version).

Other institutional studies have shown equivalent survival between the 2 races for early-stage NSCLC^{35,36} and LA-NSCLC,^{31,33,37} especially in the context of equivalent access to health care. A number of prospective studies of NSCLC have also reported equivalent outcomes between black and white patients.³⁸⁻⁴⁰ For example, a subset analysis from the PointBreak study, evaluated survival of black and white patients with stage IIIB/IV NSCLC. Although black patients presented with more advanced disease, no OS difference was found between the 2 races in either treatment arm (HR, 1.125; $P = .525$).⁴⁰ Furthermore, a meta-analysis that included 9 prospective NSCLC Radiation Therapy Oncology Group trials reported a pooled HR between white and nonwhite patients, with no statistically significant difference in survival (HR, 1.01; 95% CI, 0.84-1.20).³⁸ This suggests that with similar treatment standards, black patients will have indistinguishable survival compared with white patients. However, only the patients with the most favorable characteristics will be enrolled in clinical trials, such as those who are young, with an excellent performance status and an ideal social support system.⁴¹ Using a population-based approach can give a more generalized account of the treatments received and outcomes of patients with NSCLC.

In the present study, after accounting for various socioeconomic, disease, and treatment characteristics, black patients with LA-NSCLC had an ~8% OS advantage compared with the white patients. To explain this paradoxical finding, we studied OS stratified by various covariates. Black patients tended to be younger than white patients at diagnosis. Also, although they continued to have improved OS compared with the white cohort in the older subgroup (age, > 60 years), this advantage disappeared in the younger population (age, ≤ 60 years). A similar trend was seen when OS was stratified by treatment modality, with black patients continuing to have markedly improved OS compared with the white group when receiving RT alone and bimodality therapy ([Figure 4A,B](#)), an association that

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disappeared when trimodality therapy was evaluated (Figure 4C). We also observed that the survival advantage with black patients was largely driven by the most socioeconomic disadvantaged subgroups such as those with no insurance or with poor comorbidity status (Supplemental Table 2; available in the online version). This improvement in OS with older age, more comorbidities, and less aggressive treatment might, in part, be attributed to a “stage migration” phenomenon.⁴²⁻⁴⁴ Black patients have been less likely to be selected for more aggressive treatment. Also, it is possible that those black patients with more “favorable” disease characteristics have been inadvertently compared with white patients who had had “less favorable” attributes. Even with the survival advantage seen with trimodality therapy, an inherent selection bias for which we could not account for was likely present in the present analysis. It was assumed that these patients represented the most advantageous of the entire cohort across races—young patients with minimal nodal disease, good insurance, and higher incomes—and, hence, the equivalent OS seen when stratified by race.

Another possible explanation for the paradoxical improvement in survival seen with the black patients could, in part, have been the result of more favorable tumor biology. Initial studies have suggested that black patients have a lower incidence of *EGFR* and *KRAS* mutations than white patients,^{29,30,45,46} both of which have been associated with improved outcomes. Newer data from Araujo et al^{47,48} suggested that black Americans have the same incidence of *EGFR* and *KRAS* mutations as white patients.^{47,48} A similar biomolecular explanation for the improved survival of black patients was also proposed in the Veterans Affairs NSCLC study by Ganti et al.⁴⁹ They also reported that African Americans had a lower risk of death compared with white patients (HR, 0.94; $P < .001$).⁴⁹ In the present study, when stratified by histologic type, black patients with adenocarcinoma had improved OS compared with white patients, an effect that was lost for squamous cell carcinoma or NSCLC, NOS. To assess this hypothesis, it is important that future analyses explore tumor mutational data in a cohort of uniformly treated patients.⁵⁰

Conclusions

Despite the disparities seen in socioeconomic characteristics and treatment modalities between black and white patients, black patients with LA-NSCLC had improved survival compared with white patients. Future work should examine possible biomolecular tumor differences between the 2 cohorts to explain this contradictory outcome. The Latino patients had OS identical to that of white patients, with equivalent patterns of care. However, ethnic diversity within this group, as shown in previous studies, could potentially affect this assessment.

Clinical Practice Points

- Disparities in lung cancer have been well-documented when comparing black and white patients, with black patients having a greater incidence, often presenting with more advanced disease, less likely to receive GCC, and greater mortality.
- The effects of lung cancer disparities in the Latino population remain ambiguous, with conflicting data reported.

- Despite the disparities seen in socioeconomic characteristics and treatment modalities between black and white patients, black patients with stage III NSCLC had improved survival compared with white patients.
- In contrast, Latino patients were equally likely to have received the standard of care and had equivalent survival compared with the white patients.
- Future work should examine possible genetic differences between the 2 cohorts to explain this contradictory outcome.

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Supplemental Data

Supplemental tables and figure accompanying this article can be found in the online version at <https://doi.org/10.1016/j.clcc.2019.02.015>.

Disclosure

The authors declare that they have no competing interests.

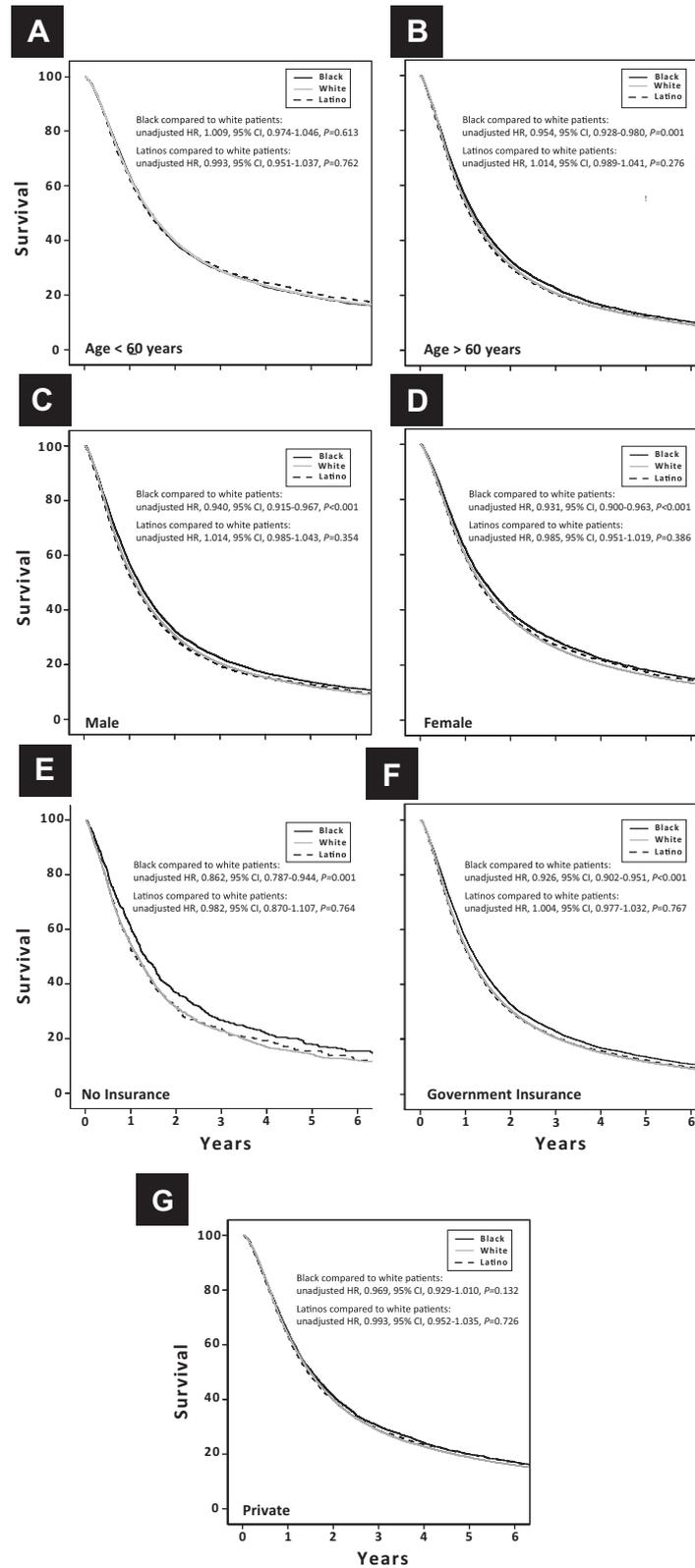
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Supplemental Figure 1 Kaplan-Meier Overall Survival Curves Stratified by Age, Sex, Insurance Status, and Race. (A) Age ≤ 60 Years; (B) Age > 60 Years; (C) Male; (D) Female; (E) No Insurance; (F) Government Insurance; and (G) Private Insurance



Abbreviations: CI = confidence interval; HR = hazard ratio.

Supplemental Table 1 Factors Predicting for Guideline Concordant Versus Non-Guideline Concordant Care Stratified by Race and Stage^a

Covariate	White			Black			Latino		
	OR	95% CI	P Value	OR	95% CI	P Value	OR	95% CI	P Value
Stage IIIA^b									
Age	0.386	0.353-0.421	<.001	0.415	0.351-0.491	<.001	0.356	0.282-0.451	<.001
Sex	0.900	0.854-0.947	<.001	NA	NA	NA	0.854	0.737-0.990	.036
Charlson-Deyo score	0.823	0.795-0.852	<.001	0.860	0.786-0.940	.001	0.782	0.708-0.864	<.001
Insurance status									
Private	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
Government	0.479	0.445-0.516	<.001	0.489	0.458-0.522	<.001	0.488	0.398-0.597	<.001
No insurance	0.696	0.569-0.853	<.001	0.561	0.401-0.785	<.001	0.689	0.406-1.168	.167
Median income									
≥\$46,000	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
<\$30,000	0.882	0.790-0.985	.026	Ref	Ref	Ref	Ref	Ref	Ref
\$30,000-\$35,999	0.861	0.788-0.941	.001	Ref	Ref	Ref	Ref	Ref	Ref
\$36,000-\$45,999	0.904	0.841-0.972	.006	Ref	Ref	Ref	Ref	Ref	Ref
No HS degree									
<14%	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
≥29%	0.885	0.799-0.980	.019	Ref	Ref	Ref	Ref	Ref	Ref
20%-28.9%	0.988	0.911-1.071	.769	Ref	Ref	Ref	Ref	Ref	Ref
14%-14.9%	1.008	0.937-1.085	.827	Ref	Ref	Ref	Ref	Ref	Ref
Residence									
Rural	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
Metropolitan	0.772	0.658-0.905	.001	Ref	Ref	Ref	Ref	Ref	Ref
Urban	0.906	0.770-1.065	.230	Ref	Ref	Ref	Ref	Ref	Ref
Histologic type									
Adenocarcinoma	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
Squamous cell	0.723	0.679-0.769	<.001	0.637	0.543-0.748	<.001	0.727	0.610-0.866	<.001
NSCLC NOS	0.726	0.674-0.782	<.001	0.646	0.533-0.782	<.001	0.790	0.639-0.977	.030
Other	0.934	0.815-1.070	.323	0.746	0.533-1.044	.087	0.708	0.507-0.991	.044
T stage	0.876	0.835-0.918	<.001	Ref	Ref	Ref	Ref	Ref	Ref
N stage	1.167	1.102-1.235	<.001	1.169	1.013-1.350	.033	Ref	Ref	Ref
Facility location									
West		Ref	Ref	Ref	Ref	Ref		Ref	Ref
Northeast	1.227	1.107-1.361	<.001	1.835	1.274-2.644	.001	1.327	0.978-1.800	.069
South	1.338	1.208-1.481	<.001	1.489	1.065-2.081	.020	1.876	1.358-2.591	<.001
Midwest	1.304	1.187-1.432	<.001	1.352	0.972-1.881	.074	1.936	1.461-2.567	<.001
Stage IIIB^c									
Age	0.625	0.585-0.668	<.001	0.606	0.531-0.693	<.001	0.531	0.445-0.632	<.001
Sex (favoring females)	0.915	0.871-0.962	<.001	Ref	Ref	Ref	Ref	Ref	Ref
Charlson-Deyo score	0.813	0.785-0.842	<.001	0.771	0.710-0.838	<.001	0.775	0.706-0.850	<.001
Insurance status									
Private	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
Government	0.659	0.619-0.701	<.001	0.726	0.627-0.840	<.001	0.715	0.606-0.844	<.001
No insurance	0.844	0.730-0.977	.023	1.094	0.827-1.446	.530	0.943	0.641-1.388	.766
Median income									
≥\$46,000	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
<\$30,000	Ref	Ref	Ref	Ref	Ref	Ref	0.723	0.592-0.883	.001
\$30,000-\$35,999	Ref	Ref	Ref	Ref	Ref	Ref	0.881	0.722-1.075	.212
\$36,000-\$45,999	Ref	Ref	Ref	Ref	Ref	Ref	0.939	0.785-1.124	.492

Disparities in Stage III NSCLC

Supplemental Table 1 Continued

Covariate	White			Black			Latino		
	OR	95% CI	P Value	OR	95% CI	P Value	OR	95% CI	P Value
No HS degree									
<14%	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
≥29%	0.875	0.808-0.947	.001	Ref	Ref	Ref	Ref	Ref	Ref
20%-28.9%	0.934	0.874-0.999	.046	Ref	Ref	Ref	Ref	Ref	Ref
14%-14.9%	0.986	0.923-1.052	.663	Ref	Ref	Ref	Ref	Ref	Ref
Residence									
Rural	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
Metropolitan	0.808	0.694-0.940	.006	Ref	Ref	Ref	0.773	0.514-1.163	.217
Urban	0.891	0.762-1.042	.147	Ref	Ref	Ref	1.030	0.676-1.569	.891
Histologic type									
Adenocarcinoma	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
Squamous cell	0.870	0.820-0.924	<.001	0.818	0.706-0.947	.007	Ref	Ref	Ref
NSCLC NOS	0.905	0.844-0.969	.004	0.896	0.761-1.056	.190	Ref	Ref	Ref
Other	0.809	0.718-0.911	<.001	0.727	0.552-0.958	.024	Ref	Ref	Ref
T stage	0.737	0.703-0.771	<.001	0.795	0.708-0.892	<.001	0.745	0.656-0.846	<.001
N stage	1.365	1.327-1.405	<.001	1.264	1.179-1.355	<.001	1.282	1.190-1.381	<.001
Facility type									
Integrated network	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
Academic/research	0.829	0.754-0.913	<.001	Ref	Ref	Ref	0.697	0.514-1.163	.014
Community/other	0.971	0.875-1.078	.582	Ref	Ref	Ref	0.931	0.671-1.294	.671
Comprehensive community program	0.914	0.835-1.001	.054	Ref	Ref	Ref	0.807	0.613-1.064	.128
Facility location									
West	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
Northeast	1.211	1.096-1.337	<.001	Ref	Ref	Ref	1.129	0.847-1.505	.407
South	1.263	1.145-1.393	<.001	Ref	Ref	Ref	1.676	1.231-2.281	.001
Midwest	1.250	1.143-1.367	<.001	Ref	Ref	Ref	1.474	1.134-1.917	.004

Abbreviations: HS = high school; NA = not applicable; NOS = not otherwise specified; NSCLC = non-small-cell lung cancer; Ref = reference.

^aBinary logistic regression with forward modeling selection was used to predict treatment selection on multivariate analysis; results listed from final logistic regression model, with ORs presented adjusted for each another.

^bSample size for stage IIIA analysis was 44,585, 6396, and 5498 for white, black, and Latino patients, respectively.

^cSample size for stage IIIB analysis was 37,905, 6260, and 5173 for white, black, and Latino patients, respectively.

Supplemental Table 2 First-order Interactions Between Race and Other Covariates^{a, b}

Covariate	HR	95% CI	P Value
Age	1.319	1.296-1.343	<.001
Race	1.011	0.975-1.047	.564
Interaction term	0.944	0.799-0.850	.011
Sex	0.841	0.828-0.854	<.001
Race	0.940	0.915-0.967	<.001
Interaction term	0.991	0.948-1.035	.669
Charlson-Deyo	1.188	1.175-1.201	<.001
Race	0.955	0.930-0.980	.001
Interaction term	0.958	0.929-0.987	.006
Median income	0.950	0.943-0.957	<.001
Race	0.858	0.817-0.902	<.001
Interaction term	1.023	1.003-1.044	.026
Stage	1.303	1.283-1.323	<.001
Race	0.900	0.872-0.929	<.001
Interaction term	1.066	1.021-1.112	.004
Insurance	0.795	0.783-0.807	<.001
Race	0.823	0.782-0.867	<.001
Interaction term	1.099	1.058-1.143	<.001
Treatment	0.825	0.819-0.830	<.001
Race	0.978	0.940-1.018	.271
Interaction term	0.972	0.955-0.990	.002

Abbreviations: CI = confidence interval; HR = hazard ratio.

^aCox regression proportion hazard model used to determine interactions, keeping the main effects in the model.

^bOnly black and white patients were considered for the analysis (n = 102,483).