

Race, Socioeconomic Status, and Survival: A Pathway Analysis in Metastatic Non-Small-Cell Lung Cancer

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Research Article

Keywords: Non-Small-Cell Lung Cancer, Health Disparities, Socioeconomic Status, SEER-Medicare, Health Equity

Posted Date: September 30th, 2026

DOI: <https://doi.org/10.21203/rs.3.rs-11003408/v1>

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Additional Declarations: No competing interests reported.

Abstract

Purpose

Black patients with advanced cancer experience persistent disparities in overall survival. We evaluated the sequential pathway linking race, neighborhood socioeconomic status (nSES), complexity of presentation at diagnosis, systemic treatment receipt, and survival.

Methods

We conducted a retrospective cohort analysis using the SEER-Medicare data (2016–2019) of Black and White patients aged ≥ 65 diagnosed with stage IV NSCLC. Pathway analysis was performed using a series of logistic, ordinal, and Cox proportional hazard models to assess how race interacts with nSES to influence comorbidity burden, stage at diagnosis, receipt of first-line systemic treatment, and mortality.

Results

Lower nSES was strongly associated with baseline comorbidity (low vs. high nSES: aOR = 1.59, 95% CI: 1.41–1.81). Non-receipt of systemic therapy was driven by low nSES (low nSES: aOR = 1.78, 95% CI: 1.55–2.05) and high comorbidity (NCI score > 1 : aOR = 2.04, 95% CI: 1.79–2.33), rather than race independently (aOR = 1.11, $p = 0.200$). Non-treatment was the strongest predictor of overall mortality (aHR = 3.69, 95% CI: 3.46–3.92). In the fully adjusted model, the survival disparity for Black relative to White patients was attenuated (aHR = 0.95, 95% CI: 0.86–1.04, $p = 0.300$).

Conclusion

Observed survival disparities between Black and White patients were accounted for by sequential differences in nSES, complexity of presentation at diagnosis, and systemic treatment receipt. Policy interventions targeting upstream socioeconomic deprivations and supportive care models for complex patients are essential to achieve health equity.

Introduction

Lung cancer is the leading cause of cancer-related deaths in the U.S., responsible for approximately one in five cancer deaths, and claims more lives than colon, breast, and prostate cancers combined [1]. About 80–85% of all lung cancer cases are non-small cell lung cancer (NSCLC), and almost half of these cases are not diagnosed until a late stage when the survival rate is only 6% [1, 2]. The burden of cancer is substantial for all patients, but some racial and ethnic groups experience higher levels of burden, especially for underrepresented minority groups living in the US [2, 3]. Black patients have 16% lower 5-year NSCLC survival rates compared to White individuals, are 19% less likely to receive surgical

treatment, and 12% more likely not to receive any treatment [3]. A better understanding of the survival outcomes of Black versus White patients with lung cancer, especially metastatic NSCLC (mNSCLC), is paramount.

Prior literature has demonstrated that Black patients with mNSCLC frequently present at a more advanced stage, have higher levels of comorbidity, and receive less systemic treatment compared to White patients, contributing to reduced overall survival [4, 5]. However, other factors, specifically neighborhood socioeconomic status (nSES), may be an important underlying driver of these survival disparities, reflecting a partial effect of structural racism and emphasizing that race is not a biological trait but rather a social construct shaped by systemic inequities [6].

This led us to theorize that nSES may have a relationship with race and survival [7]. nSES, recognized as a fundamental cause of racial disparities and also known for its intertwined relationship with race, may further drive the observed differences in receipt of systemic treatment [8–14]. Differences in neighborhood quality and community conditions may partially result from residential segregation by race, and there could be multiple pathways through which differences in nSES could negatively impact patients' access to care, smoking behaviors, and diet [8–14].

The objective of this study was to evaluate the relationship between nSES, presentation characteristics at diagnosis (comorbidity and AJCC stage), receipt of systemic treatment, and overall survival among Black and White patients with mNSCLC, with a focus on the potential mediating role of nSES.

Materials and Methods

Data source and study design

This is a retrospective cohort, observational analysis of the SEER-Medicare database from 2016–2019. SEER-Medicare reflects the linkage of two large population-based data sources that provide detailed information on Medicare beneficiaries with cancer and are updated biennially. SEER collects cancer incidence data, including patient demographics, primary tumor site, tumor morphology, stage at diagnosis, and first course of treatment, from population-based cancer registries that cover approximately 47.9% of the U.S. population [15]. Medicare claims collect data for Medicare Part A, B, and D enrollees from the time a person becomes eligible for Medicare until their death. An index date for this study was defined as the date of the first observed diagnosis of mNSCLC. The research protocol was approved by the Institutional Review Board of the University of Minnesota.

Conceptual framework & hypothesis

We developed a conceptual framework, illustrating how patient race, presentation at diagnosis (e.g., AJCC stage, comorbidity), and receipt of systemic treatment work together to influence survival disparities in Black patients relative to White patients. A conceptual framework is shown in Fig. 1. We

hypothesized that structural racism, partially reflected in Black patients' greater likelihood of residing in lower-SES neighborhoods, would be associated with more adverse presentation characteristics at mNSCLC diagnosis, resulting in a decreased likelihood of receiving systemic treatment and, thus, reduced survival outcomes.

Study cohort

Our study population consisted of individuals who were (1) ≥ 65 years of age at diagnosis, (2) had at least 1 SEER record claim with International Classification of Disease for Oncology 3rd Edition (ICD-O-3) site codes for NSCLC, i.e., excluding any ICD-O morphology codes for small-cell-lung cancer or neuroendocrine lung cancer, (3) were diagnosed with AJCC stage IV (metastatic), (4) had known month of diagnosis, (5) were not diagnosed at autopsy or on the death certificate, (6) did not have more than one cancer simultaneously diagnosed within the 12 months before or after the index date, (7) had ≥ 12 months of Medicare coverage before diagnosis (to allow for comorbidity assessment), (8) had ≥ 3 months of a continuous fee-for-service Medicare A and B coverage after the index date or until death to identify systemic therapy receipt (if any), and ≥ 3 months of a continuous fee-for-service Medicare D coverage after the index date to rule out any targeted therapy for known driver mutations that were prescribed through Part D, and (9) were either identified as Black or White according to SEER. Patients receiving targeted therapy post diagnosis were excluded as a proxy for those with driver mutations, who typically respond favorably. This allowed the analysis to focus on patients more likely to receive immunotherapy with or without standard chemotherapy. A flow chart of included individuals is presented in Supplementary Fig. 1.

Study measures

The primary outcome variable, overall survival (OS), was defined as the time from the date of metastatic diagnosis to the date of death. Patients who were alive at the end of the study period were censored using their last observed date in the data. Race was classified as either Black or White, and ethnicity was categorized as Hispanic or non-Hispanic [16]. Covariates included demographic variables (age, sex, and SEER region), the Yost neighborhood socioeconomic status (nSES) index, presentation characteristics (National Comorbidity Index [NCI] score, metastatic stage, NSCLC histology, and tumor size), and treatment variables (receipt of systemic therapy post-diagnosis and within 3 months). Detailed classifications, index components, and coding definitions for all variables are provided in the Supplementary Methods S1.

Assessment and statistical analyses

We conducted a series of logistic, ordinal regression, and Cox proportional hazard models to assess the relationship between nSES, presentation characteristics at diagnosis (i.e., comorbidity, AJCC stage), receipt of systemic treatment, and OS between Black and White patients with mNSCLC. To test the

influence of structural racism, we treated nSES, NCI comorbidity, stage, and receipt of systemic treatment as part of the pathway rather than confounders, following prior literature on racism's downstream effects [17]. Rather than adjusting for all of these variables simultaneously in a single model, we created a series of five sequential models revealing the chain effect of racism through each variable in the pathway (see Supplementary Methods S2 for full model specifications).

Continuous variables were summarized using medians and quartiles and compared between Black and White patients with mNSCLC using t-tests. Categorical variables were summarized using proportions and compared using Chi-square tests. Odds ratios (ORs) for logistic regression and hazard ratios (HRs) from Cox proportional hazard models were reported. A two-sided p-value ≤ 0.05 was considered statistically significant. All analyses were performed in R Studio, version 4.1.3.

Results

Baseline characteristics

A total of 8,562 patients met the eligibility criteria (Supplementary Fig. 1; 9.6% were Black, 90.4% were White, and the median age was 76.3 years (interquartile range [IQR], 65–104) (Table 1). On average, Black patients were diagnosed with mNSCLC at a younger age compared to White patients (28.5% vs. 20.6% in the 65–69 years old group, 25.5% vs. 32.2% in the 80 + years old group; $p < 0.001$). More Black patients reported in SEER were from the Southern US region (44.1%), whereas more White patients were from the Western US region (37.7%; $p < 0.001$). Almost 50% of Black patients, compared to 17.3% of White patients, were from neighborhoods with low nSES status ($p < 0.001$).

Table 1
Baseline Characteristics of Black and White patients diagnosed with mNSCLC in SEER-Medicare database (2016–2019)

Age at diagnosis groups	Overall (N = 8562)	Black patients (N = 821, 9.6%)	White patients (N = 7741, 90.4%)	P-value
65–69	1828 (21.4%)	234 (28.5%)	1594 (20.6%)	< 0.001
70–74	2127 (24.8%)	212 (25.8%)	1915 (24.7%)	
75–79	1907 (22.3%)	166 (20.2%)	1741 (22.5%)	
80+	2700 (31.5%)	209 (25.5%)	2491 (32.2%)	
Sex				
Male	4215 (49.2%)	423 (51.5%)	3792 (49.0%)	0.178
Female	4347 (50.8%)	398 (48.5%)	3949 (51.0%)	
Ethnicity				
Hispanic	454 (5.3%)	8 (1.0%)	446 (5.8%)	< 0.001
Non-Hispanic	8108 (94.7%)	813 (99.0%)	7295 (94.2%)	
SEER region ^a				
Northeast	1786 (20.9%)	128 (15.6%)	1658 (21.4%)	< 0.001
Midwest	1178 (13.8%)	137 (16.7%)	1041 (13.4%)	
South	2482 (29.0%)	362 (44.1%)	2120 (27.4%)	
West	3116 (36.4%)	194 (23.6%)	2922 (37.7%)	
Yost nSES index ^b				
Low	1730 (20.2%)	394 (48.0%)	1336 (17.3%)	< 0.001
Moderate	3168 (37.0%)	280 (34.1%)	2888 (37.3%)	
High	3485 (40.7%)	129 (15.7%)	3356 (43.4%)	
Unknown	179 (2.1%)	18 (2.2%)	161 (2.1%)	
Year of diagnosis				
2017	3072 (35.9%)	292 (35.6%)	2780 (35.9%)	0.308
2018	2692 (31.4%)	276 (33.6%)	2416 (31.2%)	

Age at diagnosis groups	Overall (N = 8562)	Black patients (N = 821, 9.6%)	White patients (N = 7741, 90.4%)	P-value
2019	2798 (32.7%)	253 (30.8%)	2545 (32.9%)	
NSCLC histology ^c				
Squamous	1716 (20.0%)	192 (23.4%)	1524 (19.7%)	0.0418
Adenocarcinoma	5014 (58.6%)	462 (56.3%)	4552 (58.8%)	
Others	1832 (21.4%)	167 (20.3%)	1665 (21.5%)	
Tumor size				
< 3 cm	1751 (20.5%)	147 (17.9%)	1604 (20.7%)	0.0456
[3–5) cm	2088 (24.4%)	184 (22.4%)	1904 (24.6%)	
≥ 5 cm	2779 (32.5%)	294 (35.8%)	2485 (32.1%)	
Unknown	1944 (22.7%)	196 (23.9%)	1748 (22.6%)	
NCI comorbidity score				
0	2790 (32.6%)	200 (24.4%)	2590 (33.5%)	< 0.001
(0–1]	3537 (41.3%)	305 (37.1%)	3232 (41.8%)	
> 1	1774 (20.7%)	228 (27.8%)	1546 (20.0%)	
Unknown	461 (5.4%)	88 (10.7%)	373 (4.8%)	
AJCC stage				
IV	3560 (41.6%)	332 (40.4%)	3228 (41.7%)	0.49
IVA	2548 (29.8%)	239 (29.1%)	2309 (29.8%)	
IVB	2454 (28.7%)	250 (30.5%)	2204 (28.5%)	
Systemic treatment received at any time post-diagnosis ^d				
Systemic treatment received	3947 (46.1%)	330 (40.2%)	3617 (46.7%)	< 0.001
No systemic treatment received	4615 (53.9%)	491 (59.8%)	4124 (53.3%)	
Systemic treatment received within 3 months post-diagnosis				

Age at diagnosis groups	Overall (N = 8562)	Black patients (N = 821, 9.6%)	White patients (N = 7741, 90.4%)	P-value
Received <i>within</i> 3 months	1042 (12.2%)	221 (67%)	2684 (74.2%)	0.0043
Received <i>after</i> 3 months	2905 (33.9%)	109 (33%)	933 (25.8%)	
At least 1 primary care visit 12 months prior to diagnosis				
No	1391 (16.2%)	228 (27.8%)	1163 (15.0%)	< 0.001
Yes	7171 (83.8%)	593 (72.2%)	6578 (85.0%)	
At least 1 lung cancer screening 12 months prior to diagnosis				
No	6426 (75.1%)	636 (77.5%)	5790 (74.8%)	0.101
Yes	2136 (24.9%)	185 (22.5%)	1951 (25.2%)	
Follow-up (months)				
Mean (SD)	7.31 (8.07)	6.68 (7.26)	7.38 (8.15)	0.0101
Median [Min, Max]	3.93 [0.0331, 36.2]	4.00 [0.0331, 36.2]	3.93 [0.0992, 36.2]	
<i>nSES</i> neighborhood socioeconomic status, <i>NCI</i> National Comorbidity Index, <i>AJCC</i> American Joint Committee on Cancer.				
^a SEER region: Northeast (CT, MA, NJ, NY), Midwest (IO, MI- Detroit), South (GA, KY, LA), West (Alaska Natives, CA, HI, ID, NM, UT, WA- Seattle/ Puget Sound)				
^b Yost nSES index: Derived from Yost ACS 2013_2017 quintile index by SEER definition Low (index = 1), Moderate (index = 2,3), High (index = 4,5)				
^c NSCLC histology: "Others" include adenosquamous carcinoma of lung, salivary gland type tumor of lung, other epithelial tumors of lung, large cell carcinoma of lung				
^d Systemic therapy: Immunotherapy, Chemotherapy, or Both				

Black patients had higher comorbidity scores at baseline (27.8% vs. 20% with NCI score > 1; $p < 0.001$) and slightly larger tumor size (35.8% vs. 32.1% with tumors ≥ 5 cm; $p = 0.045$). Squamous cell carcinoma was more frequently reported in Black patients compared to White patients (23.4% vs. 19.7%; $p = 0.04$). Among Black patients, 59.8% did not receive any form of systemic treatment, compared to 53.3% among White patients ($p < 0.001$), and they were less likely to receive treatment within 3 months of diagnosis (p

= 0.004). Black patients also had lower primary care utilization in the year leading to diagnosis (72.2% vs. 85%; $p < 0.001$). There were no statistically significant differences in sex, year of diagnosis, stage, and lung cancer screening.

Sequential pathway analysis of survival disparities

To elucidate the mechanisms underlying racial disparities in overall survival, sequential multivariable logistic and Cox proportional hazards regression models were evaluated (Table 2).

Table 2
Sequential Multivariable Models Testing the Pathway from Race to Survival

Variables	Outcomes				
	Model 1: nSES*	Model 2b: NCI comorbidity score	Model 3b: AJCC stage	Model 4d: Not receiving treatment	Model 5d: OS
	aOR (95% CI)	aOR (95% CI)	aOR (95% CI)	aOR (95% CI)	aHR (95% CI)
Race					
White					
Black	3.87 (3.32– 4.53)***	1.44 (1.25– 1.68)***	1.06 (0.89– 1.20)	1.11 (0.94– 1.32)	0.95 (0.86– 1.04)
Age group at diagnosis					
65–69					
70–74	0.83 (0.73– 0.95)**	1.17 (1.04– 1.34)**	0.95 (0.85– 1.09)	1.11 (0.97– 1.27)	1.01 (0.93– 1.10)
75–79	0.79 (0.7– 0.91)***	1.62 (1.43– 1.84)***	0.88 (0.81– 1.04)	1.42 (1.24– 1.64)***	0.96 (0.88– 1.05)
80+	0.69 (0.61– 0.79)***	1.96 (1.74– 2.21)***	0.72 (0.72– 0.91)***	2.94 (2.57– 3.37)***	1.04 (0.96– 1.13)
SEER region					
Northeast	Ref				
Midwest	4.80 (4.13– 5.60)***	0.92 (0.80– 1.07)	1.61 (1.24– 1.67)***	1.18 (1.00– 1.39)*	1.02 (0.93– 1.12)
South	10.18 (8.87– 11.7)***	0.83 (0.73– 0.95)**	1.29 (1.09– 1.41)***	1.30 (1.13– 1.50)***	0.95 (0.88– 1.04)
West	2.37 (2.09– 2.71)***	0.76 (0.68– 0.86)***	1.22 (1.05– 1.32)**	1.12 (0.99– 1.28)	0.88 (0.82– 0.95)***
Yost nSES index					
High					

Variables	Outcomes				
	Model 1: nSES*	Model 2b: NCI comorbidity score	Model 3b: AJCC stage	Model 4d: Not receiving treatment	Model 5d: OS
	aOR (95% CI)	aOR (95% CI)	aOR (95% CI)	aOR (95% CI)	aHR (95% CI)
Moderate		1.23 (1.12– 1.36)***	0.99 (0.90– 1.10)	1.33 (1.19– 1.48)***	1.04 (0.97– 1.11)
Low		1.59 (1.41– 1.81)***	0.81 (0.75– 0.96)*	1.78 (1.55– 2.05)***	1.04 (0.96– 1.13)
NCI comorbidity score					
0					
(0–1]				1.13 (1.02– 1.26)*	1.26 (1.18– 1.35)***
> 1				2.04 (1.79– 2.33)***	1.35 (1.26– 1.46)***
AJCC stage					
IV					
IVA				0.89 (0.80– 1.00)*	0.78 (0.73– 0.84)***
IVB				0.96 (0.86– 1.08)	1.13 (1.05– 1.20)***
Systemic treatment received at any time post-diagnosis					
Yes					
No					3.69 (3.46– 3.92)***

Variables	Outcomes				
	Model 1: nSES*	Model 2b: NCI comorbidity score	Model 3b: AJCC stage	Model 4d: Not receiving treatment	Model 5d: OS
	aOR (95% CI)	aOR (95% CI)	aOR (95% CI)	aOR (95% CI)	aHR (95% CI)
<p><i>aOR</i> adjusted odds ratio, <i>aHR</i> adjusted hazard ratio, <i>CI</i> confidence interval, <i>nSES</i> neighborhood socioeconomic status, <i>NCI</i> National Comorbidity Index, <i>AJCC</i> American Joint Committee on Cancer. All models are adjusted for age at diagnosis and SEER region. *$p < 0.05$, **$p < 0.01$, ***$p < 0.001$.</p>					
<p>† Model Selection Note: This table presents the primary specifications for each step along the conceptual pathway:</p>					
Model 1 (race → nSES; low or moderate nSES as a comparison group, and high nSES as a reference group; 179 missing observations of nSES were excluded from all regressions)					
Model 2b (race + nSES → comorbidity; NCI score = (0–1] or > 1 as a comparison group, and NCI score = 0 as a reference group)					
Model 3b (race + nSES → stage; Stage = IVA or IVB as a comparison group, and Stage = IV as a reference group)					
Model 4d (race + nSES + presentation characteristics → receipt of systemic treatment; outcome was modelled as no treatment receipt)					
Model 5d (full pathway → overall survival).					
Complete step-by-step model iterations showing sequential attenuation (Models 2a, 3a, 4a–4c, and 5a–5c), are provided in Supplementary Tables 2–5.					

Upstream Determinants: Socioeconomic Status, Comorbidity, and Stage (Models 1–3b)

In baseline models examining clinical presentation, Black patients exhibited significantly higher odds of presenting with multi-comorbidity compared to White patients (aOR = 1.44, 95% CI: 1.25–1.68, $p < 0.001$; Model 2b). However, lower nSES was independently and strongly associated with increased comorbidity burden (Low nSES: aOR = 1.59, 95% CI: 1.41–1.81, $p < 0.001$). In Model 3b, after controlling for age, geographic region, and nSES, the association between Black race and advanced stage at diagnosis was

attenuated to non-significance (aOR = 1.06, 95% CI: 0.89–1.20, $p = 0.620$), whereas lower nSES remained an independent risk factor for advanced stage presentation (Low nSES: aOR = 0.81, 95% CI: 0.75–0.96, $p = 0.010$).

Determinants of Systemic Treatment Non-Receipt (Model 4d)

In the fully adjusted treatment model (Model 4d), race was not an independent predictor of going untreated (aOR = 1.11, 95% CI: 0.94–1.32, $p = 0.200$). Instead, non-receipt of systemic therapy was primarily driven by lower neighborhood socioeconomic status, multimorbidity, and stage at presentation. Compared to patients residing in high nSES neighborhoods, those living in moderate nSES (aOR = 1.33, 95% CI: 1.19–1.48, $p < 0.001$) and low nSES areas (aOR = 1.78, 95% CI: 1.55–2.05, $p < 0.001$) demonstrated significantly higher odds of remaining untreated. Pre-existing comorbidity also strongly predicted non-treatment, with odds increasing sequentially for patients with NCI scores of 1 (aOR = 1.13, 95% CI: 1.02–1.26, $p = 0.02$) and > 1 (aOR = 2.04, 95% CI: 1.79–2.33, $p < 0.001$). Relative to the general Stage IV reference group, patients with Stage IVA disease had slightly lower odds of going untreated (aOR = 0.89, 95% CI: 0.80–1.00, $p = 0.046$), whereas Stage IVB presentation showed no significant difference in treatment non-receipt (aOR = 0.96, 95% CI: 0.86–1.08, $p = 0.500$).

Full Pathway of Overall Survival Disparities (Model 5d)

In the final multivariable Cox proportional hazards model incorporating the entire conceptual pathway (Model 5d), the mortality hazard for Black relative to White patients was completely attenuated (aHR = 0.95, 95% CI: 0.86–1.04, $p = 0.300$). Non-receipt of systemic treatment emerged as the single strongest independent predictor of all-cause mortality (aHR = 3.69, 95% CI: 3.46–3.92, $p < 0.001$), followed by high comorbidity burden (aHR = 1.35, 95% CI: 1.26–1.46, $p < 0.001$) and more advanced stage at diagnosis (Stage IVB; aHR = 1.13, 95% CI: 1.05–1.20, $p < 0.001$).

Discussion

In this study, we found that nSES significantly mediated the relationship between race and survival in mNSCLC. Our findings suggest that structural factors may drive the underlying relationship between race and reduced survival as reflected in Black patients' greater likelihood of residing in lower-SES neighborhoods, which was associated with more adverse presentation characteristics at diagnosis, resulting in a decreased likelihood of receiving systemic treatment and, thus, reduced survival outcomes. Addressing disparities in nSES, comorbidity burden, and access to systemic treatment is vital for survival improvements for Black patients in this population.

Upstream Socioeconomic Drivers and Presentation Complexity

Our pathway analysis highlights the critical role of neighborhood-level socioeconomic deprivation in shaping clinical presentation at diagnosis. Lower nSES was independently associated with an increased burden of pre-existing comorbidities (Model 2b) and advanced stage at presentation (Model 3b). Crucially, adjusting for nSES attenuated the racial disparity in stage at diagnosis to non-significance (aOR 1.06, 95% CI: 0.89–1.20), indicating that socioeconomic disadvantage—rather than biological or racial differences—drives late-stage presentation. Patients residing in socioeconomically deprived neighborhoods can face compounding barriers, including reduced healthcare access, insurance fragmentation, and financial toxicity, which frequently delay symptom evaluation and diagnostic workups until disease progression or acute complications occur.

Multiple structural pathways stemming from low nSES—including limited access to preventive care, higher smoking prevalence, and nutritional insecurity—might contribute to this elevated comorbidity burden [8–14]. As noted by Parsons et al. (2024), patients living in areas with lower educational attainment, higher income inequality, and fewer hospitals providing cancer treatment faced longer travel hours [18]. Thus, the impact of structural racism on patient health is largely channeled through nSES and further compounded through pre-existing disease burdens [18–21].

Treatment Non-Receipt as the Primary Actionable Mechanism

Non-receipt of guideline-concordant systemic therapy emerged as the single largest independent predictor of overall mortality in our cohort, conferring a nearly fourfold increase in the risk of death (aHR = 3.69, 95% CI: 3.46–3.92), yet Black patients were significantly less likely to receive treatment compared to White patients. First, this treatment effect makes sense in light of our cohort, diagnosed between 2017 and 2019, when immunotherapy was approved as the first-line standard of care for mNSCLC, offering improved survival benefits over chemotherapy [22]. We speculate that the adoption of immunotherapy increased during this period, and that Black patients might receive less immunotherapy compared to White patients, following other real-world observational studies [23–34].

Second, interestingly, in the fully adjusted treatment model (Model 4d), race was not an independent predictor of remaining untreated (aOR 1.11, 95% CI: 0.94–1.32, $p = 0.200$). Sequential adjustment showed that the race odds ratio attenuated from 1.39 to 1.18 upon adding nSES (Supplementary Table 4-Model 4b), and further to non-significance when clinical presentation factors were included (Model 4d), indicating that neighborhood deprivation and clinical complexity act jointly to constrain treatment access. While nSES appeared to influence presentation characteristics, its effect alone did not fully explain treatment disparities; likewise, presentation characteristics alone were insufficient. Residual effects not captured by one factor may be reflected in the other; therefore, both nSES and presentation characteristics must be considered together, as they reflect distinct yet interconnected dimensions of structural and clinical vulnerability that together drive inequities in access to systemic treatment.

Finally, non-receipt of therapy was primarily driven by lowest neighborhood SES (aOR = 1.78, 95% CI: 1.55–2.05) and high comorbidity burden (NCI > 1: aOR = 2.04, 95% CI: 1.79–2.33), as well as older age

(80 + years: aOR = 2.94). This finding aligns with the previously reported association between the presence of comorbidities and a lower likelihood of receiving cancer-recommended therapies [35–37]. For instance, Rios et al. (2017) reported that among patients with invasive NSCLC stages I through IV, those with higher comorbidity scores were less likely to receive chemotherapy, surgical, and radiation treatment [36]. Given that patients diagnosed with lung cancer tend to have certain comorbid conditions, it is possible that the impact of comorbid conditions could be exacerbated in Black populations, influencing their ability to receive treatment and overall prognosis [35, 38–40].

Policy and Clinical Implications

This nuance is essential for policy and clinical interpretation: lower rates of systemic therapy among Black patients are not primarily explained by explicit clinical bias at the moment of treatment decision-making, but rather by the disproportionate burden of pre-existing comorbidities and complex clinical presentations that stem from structural inequity. When patients present with severe medical frailty or acute presentation delays, clinicians may deem systemic chemotherapy unsafe or contraindicated, inadvertently locking patients into a trajectory of non-treatment and reduced survival.

Addressing these disparities, therefore, requires tackling systemic inequities in healthcare access and socioeconomic conditions through upstream interventions that focus on improving access to routine healthcare and screening, as well as financial support and transportation, particularly in underserved and marginalized communities. Furthermore, the impact of comorbidities versus treatment on survival disparities needs careful consideration. Although treatment may provide survival benefits, comorbidities may shape physicians' decisions about the intensity of recommended cancer treatment and their evaluation of patients' socioeconomic status to assess the adequacy of social support, housing, and recovery resources post-treatment. Therefore, further research should emphasize the importance of complementing statistical interpretations with additional perspectives, including social and treatment aspects, to comprehensively understand these disparities.

An important strength of our study is the in-depth analyses using our conceptual framework to explore the relationships between our variables, specifically presentation characteristics at diagnosis and treatment, along with the addition of nSES to reflect the impact of racism. There were also limitations. We did not conduct a formal mediation analysis to partition indirect versus direct effects. Also, the definition of race used in our analyses likely reflects a combination of the effects of physical phenotype, parental physical phenotype, and genetic background [41, 42]. However, this information is not contained in SEER-Medicare, so we included nSES in our analyses to reflect the impact of racism. While race itself cannot be altered, the effects of racism and the resulting lower nSES can be.

Conclusion

In conclusion, our findings highlight that racial disparities in mNSCLC survival are largely driven by differences in presentation characteristics at diagnosis, socioeconomic context, and access to systemic treatment, underscoring the need for upstream interventions that improve early detection, comorbidity

management, and equitable delivery of care. Future research should delve into the specific comorbidities affecting different racial groups and explore the underlying clinical and social determinants driving these health differences, such as neighborhood conditions and community qualities. While mitigating comorbidities is crucial, improving access to timely and effective mNSCLC treatments is also imperative for achieving optimal patient outcomes.

Declarations

Funding

The authors declare that no funds, grants, or other support were received during the preparation of this manuscript.

Competing interests

The authors have no relevant financial or non-financial interests to disclose.

Ethics approval

This study is a retrospective observational analysis of de-identified population-based data from the SEER-Medicare database. The research protocol was reviewed and approved by the Institutional Review Board (IRB) of the University of Minnesota.

Consent to participate & consent to publish

Individual patient consent was waived by the Institutional Review Board because the study involved secondary analysis of existing, fully de-identified administrative claims data from the SEER-Medicare linked database.

Data availability

The data that support the findings of this study are available from the National Cancer Institute (NCI) and the Centers for Medicare & Medicaid Services (CMS), but restrictions apply to the availability of these data, which were used under a Data Use Agreement for the current study. Data are available upon reasonable request and with permission/approval from NCI and CMS. Instructions for obtaining these data are available at <https://healthcaredelivery.cancer.gov/seermedicare/obtain/>.

Author contributions

All authors contributed to the study conception and design. Conceptualization, Methodology, Investigation, Writing- Original draft preparation was performed by TD. Conceptualization, Methodology, Writing- Reviewing and Editing, Resources, Validation, and Supervision was performed by DS, HP, AC, EH, and JS. All authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

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Figures

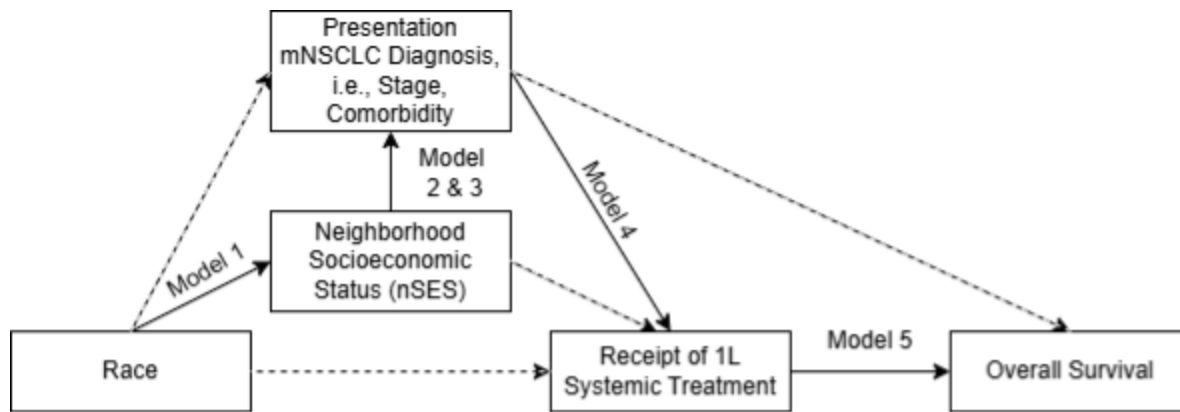


Figure 1

Conceptual Framework

Note: Solid arrows indicate the full pathway from race to overall survival

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