ORIGINAL ARTICLE

Impact of Socioeconomic Factors on Overall Survival in SCLC

Logan Roof, MD,* Wei Wei, MS, Katherine Tullio, MS, Nathan A. Pennell, MD, PhD, James P. Stevenson, MD

Department of Hematology & Medical Oncology, Cleveland Clinic Taussig Cancer Institute, Cleveland, Ohio

Received 30 March 2022; revised 31 May 2022; accepted 8 June 2022
Available online - 18 June 2022

ABSTRACT

Objectives: To determine how the incidence and demographics of SCLC have changed over time and to evaluate whether patient demographics, disease presentation, and treatment characteristics affect patient outcomes.

Methods: We identified patients with SCLC in the National Cancer Database from 2004 to 2016. Differences in demographics, disease, and treatment characteristics were assessed by year of diagnosis using chi-square test. The effect of age, race, insurance status, income, distance to treatment center, and education level on overall survival (OS) was evaluated by multivariable Cox proportional hazard model.

Results: Patients diagnosed after 2010 were significantly older, more frequently treated at academic centers, had more comorbidities, had government payer insurance, had more stage IV disease, and lived further from treatment centers. More females, African Americans, patients without high school diplomas, and those from rural areas were diagnosed after 2010. In patients diagnosed between 2004 and 2010, 5-year OS was 6.8% (95% confidence interval: 6.6–6.9), and after 2010, 5-year OS was 8.7% (95% confidence interval: 8.5–8.9), despite an increase in stage IV disease in the latter group. Older patients, males, Caucasians, patients with stage IV disease, those with government primary payer insurance, and those from rural areas had significantly worse OS. Patients without comorbidities and treated at academic centers had significantly better OS. OS significantly increased with community income and education level.

Conclusions: Despite improvement in OS, disparities were noted in demographics which may complicate patient and provider access to health care resources, including rural communities, distance to academic centers, income, insurer, and education level. Efforts to affect these variables will improve outcomes for patients with SCLC.

Keywords: Small cell lung cancer; Outcomes; Socioeconomic factors; Healthcare disparities

Introduction

SCLC accounts for approximately 13% of all lung cancer diagnoses in the United States.[1] Cigarette smoking is a known substantial risk factor for the development of SCLC.[2,3] This disease is generally thought to carry a poor prognosis; however, it is important to note that stages I to III disease can be treated with curative intent. The demographics of this disease have evolved over time; for example, in the 1970s, 28% of patients with SCLC were female, whereas in the early 2000s, 50% of patients were female. Some of the differences in incidence and demographics are thought to be related to changes in the rates of smoking over time, but this likely does not explain all the observed changes.[4,5] There has been a paucity of data regarding updates in incidence, prevalence, and patient demographics in SCLC since the

*Corresponding author.

Disclosure: The authors declare no conflict of interest.

Address for correspondence: Logan Roof, MD, Department of Hematology & Medical Oncology, Cleveland Clinic Taussig Cancer Institute, 10201 Carnegie Avenue, CA Building, CA 6, Cleveland, OH 44106. E-mail: roofl@ccf.org

Cite this article as: Roof L, Wei W, Tullio K, Pennell NA, Stevenson JP. Impact of socioeconomic factors on overall survival in SCLC. *JTO Clin Res Rep*. 2022;3:100360.

ISSN: 2666-3643

https://doi.org/10.1016/j.jtocrr.2022.100360

early 2000s. A recent article investigated the demographic and treatment characteristics associated with outcomes in limited-stage SCLC, however, did not include patients with extensive-stage disease.[6] Given recent treatment advances, the impact that demographic factors have on patient outcomes for SCLC requires further evaluation. In this study, we determine how the demographics of SCLC have changed over time and evaluate whether patient demographics, disease presentation, and the treatment they receive affect patient outcomes for limited- and extensive-stage SCLC.

Materials and Methods

Data Source

The National Cancer Database (NCDB) is a database that captures more than 70% of all new cancers occurring in the United States. This nationally recognized database is jointly sponsored by the American College of Surgeons and the American Cancer Society. Deidentified data from accredited hospitals are collected to analyze and track patients' neoplastic diseases, treatments, and outcomes.[7,8] A formal data request was placed to access the NCDB data for this study.

Patient Selection

We studied a total of 262,049 patients diagnosed with having SCLC in the NCDB between 2004 and 2016. These patients were identified using the International Classification of Diseases codes. Clinical staging was defined according to the seventh and eighth American Joint Committee on Cancer TNM staging systems.[9,10] Patients with incomplete follow-up were excluded. For the purpose of our analysis, we divided these patients into two groups based on their date of diagnosis: those diagnosed between 2004 and 2010 and those diagnosed between 2011 and 2016. There were 137,253 cases of SCLC diagnosed in the NCDB between 2004 and 2010 and 124,796 cases diagnosed between 2011 and 2016. We collected the following clinical and biological data from the NCDB: Charlson comorbidity index, primary site of tumor, histologic subtype, grade, and stage of tumor, patient performance status, month and year of diagnosis, presence of metastatic disease, time from diagnosis to treatment, treatment facility type and location, radiation therapy (RT) received, surgery received, systemic therapy days from diagnosis, and vital status. Charlson comorbidity index was defined as previously published and analyzed as 0 or greater than or equal to 1. Tumor grade was characterized as poorly differentiated, undifferentiated, or anaplastic, well or moderately differentiated, or unknown. Stage was categorized as stages I to III, stage IV, or unknown. Patient performance status was defined by the Eastern Cooperative Oncology Group scale as previously published. Time-to-treatment was defined as days from diagnosis to first treatment received (surgery, RT, systemic therapy). Facility type was categorized into academic/research center and nonacademic programs (including community cancer programs, comprehensive community cancer programs, and integrated cancer networks). An academic/research institution was defined as participating in postgraduate medical education in at least four fields, with more than 500 newly diagnosed cancer cases per year. Vital status was defined as alive or dead at the time of analysis. The variables extracted are further described in the NCDB Participant User File data dictionary.[11]

We collected the following demographic and socioeconomic data from the NCDB: patient age, sex, race, zip code, distance to treatment center, primary payer insurance, education level, community income, and whether patients reside in a rural, metropolitan, or urban location. Age at diagnosis was categorized as less than 65 years old or more than or equal to 65 years old. Sex was defined as male or female for the purposes of this analysis. Race/ethnicity was categorized into African American, Asian, Caucasian, Hispanic, unknown, and other. Distance to the treatment center was defined as the distance in miles between the patients' residence and the hospital that reported the case. Insurance was categorized as government primary payer insurance (Medicare and Medicaid), private, unknown, and not insured. Education level was divided into quartiles of the population without a high school diploma, in groups with more than 17.6%, 10.9% to 17.5%, 6.3% to 10.8%, and less than 6.3% of people aged 25 years or older in the patients' residence zip code area without a high school diploma. Median community income was divided into less than $40,000, $40 to $50,000, $50 to $63,000, and more than $63,000. Residence area was categorized as metropolitan, urban, rural, and unknown based on the typology published by the U.S. Department of Agriculture Economic Research Service.[11]

Statistical Analysis

Patient characteristics were summarized using median and range for continuous variables and frequencies and percentages for categorical variables. Chi-square test was used to compare patient characteristics between year of diagnosis groups. Wilcoxon ranked sum test was used to compare distance to treatment center and time-to-treatment between year groups. Overall survival (OS) was calculated from diagnosis to death or last follow-up. OS was estimated by Kaplan-Meier method and compared by log-rank test. A multivariable Cox model without model selection was used to associate patient characteristics with OS. All tests were two sided, and

Table 1. Annual Incidence of SCLC in the NCDB

Patients Diagnosed With SCLC in NCDB 2004-2016

Year of Diagnosis	n
2004	18,675
2005	19,064
2006	19,395
2007	19,664
2008	20,227
2009	20,082
2010	20,146
2011	20,160
2012	20,510
2013	20,709
2014	20,962
2015	21,500
2016	20,955

NCDB, National Cancer Database.

p values of 0.05 or less were considered statistically significant. Statistical analysis was carried out using SAS Studio 3.7 (SAS Institute, Cary, NC) and R version 4 (R Foundation, Vienna, Austria).

Results

Patient Characteristics

A total of 262,049 patients diagnosed with having SCLC between 2004 and 2016 was included in our analysis. There was a median follow-up time of 33.1 months for all patients, with a range of 0.1 to 181.7 months of follow-up time. As noted in Table 1, there were no major changes in incidence of SCLC in the time frame studied.

We found statistically significant differences in patient characteristics between those diagnosed with having SCLC between 2004 and 2010 and those diagnosed between 2011 and 2016. As illustrated in Table 2, patients diagnosed after 2010 were significantly older, were more frequently female, had more comorbidities, and more often had stage IV disease at diagnosis ($p < 0.0001$ for all). As found in Table 3, those diagnosed after 2010 were more frequently treated at academic centers and had more of each of the following: RT, chemotherapy, and immunotherapy (IO) ($p < 0.0001$ for all). There was no significant change in the rates of surgery ($p = 0.09$). As found in Table 4, patients diagnosed after 2010 lived significantly further away from their treatment center ($p < 0.0001$). There was no significant difference in the time-to-treatment ($p = 0.95$) between the two groups.

OS Analyses

The median OS of all patients was 8.51 months (95% confidence interval [CI]: 8.48–8.54) with a 5-year OS of 7.6% (95% CI: 7.5–7.7). There was significant improvement in OS between these time frames, with a 5-year OS for patients diagnosed between 2004 and 2010 of 6.8% (95% CI: 6.6–6.9) and a 5-year OS for patients diagnosed between 2011 and 2016 of 8.7% (95% CI: 8.5–8.9), with p value less than 0.0001.

We noted certain factors to be associated with survival that suggest a role in prognosis and outcomes based on multivariable Cox model results. As found in Table 5, patients with significantly worse OS were older, male, Caucasian, had government primary payer insurance, and were from rural areas ($p < 0.0001$ for all). As found in Table 6, patients diagnosed after 2010 and with fewer comorbidities had significantly better OS ($p < 0.0001$ for both). In addition, we found that OS increased by residence area level of education and by mean community income ($p < 0.0001$).

Disease stage and treatment-related factors also affected survival in these patients. The interaction term between stage and treatment was significant; therefore, we did subgroup analyses by year and disease stage. Accordingly, patients with stage IV disease had worse OS than patients who were diagnosed at an earlier stage ($p < 0.0001$). Improvement in OS was noted in those treated at academic centers, those who were able to undergo surgery for their disease, and in patients who received RT, chemotherapy, and IO alone or in combination; each of these factors was individually significant ($p < 0.0001$ for all). Table 7 represents a summary of the multivariable Cox proportional hazard model for OS from diagnosis. Year of diagnosis and stage had significant interaction with other factors; therefore, subgroup analyses were carried out by year group and stage. Staging and treatment findings are found in Figures 1 to 3. Treatment was evaluated by stage (stages I–III or limited-stage versus stage IV or extensive-stage SCLC), as those who had surgery and radiation may be of earlier stage than those who did not receive either treatment modality. Figure 1 reveals OS by stage and whether the patients received surgery for their disease; OS was best in patients with early stage disease who underwent surgery and worst for patients with stage IV disease who did not undergo surgery. Figure 2 reveals OS by stage and whether patients received RT for their disease; similarly, patients with limited stage disease who received RT had the best OS and patients with extensive stage disease who did not receive RT had the worst OS. Figure 3 reveals OS by stage and whether patients received chemotherapy; again, it is found that patients with early stage disease receiving chemotherapy had the best OS and patients with stage IV disease who were unable to receive chemotherapy had the worst OS. All findings from Figures 1 to 3 were statistically significant ($p < 0.0001$).

Table 2. Patient Demographic/Socioeconomic Factors Diagnosed in 2011 to 2016 Versus 2004 to 2010

		Dx 2004-2010 n = 137,253	Dx 2011-2016 n = 124,796	Pts Dx 2011-2016 Vs. Dx 2004-2010
Factor	Category	n (%)	n (%)	*p* Value
Age	<65	54,987 (40.06)	48,187 (38.61)	<0.0001
	≥65	82,266 (59.94)	76,609 (61.39)	
Sex	Female	70,141 (51.1)	64,870 (51.98)	<0.0001
	Male	67,112 (48.9)	59,926 (48.02)	
Race/ethnicity	African American	9972 (7.27)	9791 (7.85)	<0.0001
	Asian	1310 (0.95)	1518 (1.22)	
	Caucasian	121,501 (88.52)	109,235 (87.53)	
	Hispanic	2786 (2.03)	2947 (2.36)	
	Others	1684 (1.23)	1305 (1.04)	
Insurance	Government	89,225 (65.01)	87,507 (70.12)	<0.0001
	Not insured	5191 (3.78)	4417 (3.54)	
	Private	39,795 (28.99)	30,637 (24.55)	
Residence area	Metropolitan	106,376 (77.5)	96,513 (77.34)	0.004
	Rural	3375 (2.46)	3208 (2.57)	
	Urban	23,705 (17.27)	22,160 (17.76)	

Note: *p* values by chi-square test.
Dx, diagnosed; Pts, patients.

Table 3. Patient Clinical/Biological Factors Diagnosed in 2011 to 2016 Versus 2004 to 2010

		Dx 2004-2010 n = 137,253	Dx 2011-2016 n = 124,796	Pts Dx 2011-2016 Vs. Dx 2004-2010
Factor	Category	n (%)	n (%)	*p* Value
Charlson-Deyo score	0	78,123 (56.92)	66,757 (53.49)	<0.0001
	≥1	59,130 (43.08)	58,039 (46.51)	
Cancer center type	Academic/research	34,609 (25.22)	34,171 (27.38)	<0.0001
	Others	102,644 (74.78)	90,625 (72.62)	
Stage	Stages I-III	47,248 (34.42)	41,696 (33.41)	<0.0001
	Stage IV	73,851 (53.81)	78,187 (62.65)	
Surgery	No	132,503 (96.54)	120,533 (96.58)	0.09
	Yes	4450 (3.24)	3896 (3.12)	
Radiation therapy	No	70,820 (51.6)	62,173 (49.82)	<0.0001
	Yes	63,525 (46.28)	59,580 (47.74)	
Chemotherapy	No	35,692 (26)	31,577 (25.3)	<0.0001
	Yes	99,031 (72.15)	90,973 (72.9)	
Immunotherapy	No	136,043 (99.12)	123,902 (99.28)	<0.0001
	Yes	299 (0.22)	669 (0.54)	

Note: *p* values by chi-square test.
Dx, diagnosed; Pts, patients.

Table 4. Summary of Distance to Treatment Center and Time-to-Treatment by Year of Diagnosis

	Year of Dx	n	Min	Median	Max	*p* Value
Distance to Treatment Center (miles)	2004-2010	134,998	0	8.6	4786.9	<0.0001
	2011-2016	118,613	0	9.6	3814.6	
Time-to-Treatment (d)	2004-2010	105,900	0	13	3697	0.95
	2011-2016	97,729	0	14	1130	

Note: p values by Wilcoxon ranked sum test.
Dx, diagnosed; Max, maximum; Min, minimum.

Discussion

Our analysis of these data revealed several interesting differences in patient, disease, and treatment characteristics over time. Our key findings are that patients diagnosed after 2010 were significantly older, more frequently treated at academic centers, had more comorbidities, had government payer insurance, had more stage IV disease, and lived further from treatment

Table 5. Factors Leading to a Worse Overall Survival in All Patients With SCLC Diagnosed Between 2004 and 2016

Factor	Level	Total N	Median Survival in mo (95% CI)	Rate at 5 y (95% CI)	*p* Value
Age	<65 y	103,174	10.48 (10.41-10.55)	0.105 (0.102-0.107)	<0.0001
	≥65 y	158,875	7.13 (7.06-7.2)	0.058 (0.056-0.059)	
Sex	Female	135,011	9.3 (9.26-9.4)	0.091 (0.09-0.093)	<0.0001
	Male	127,038	7.79 (7.72-7.82)	0.06 (0.059-0.061)	
Race/ethnicity	African American	19,763	9.2 (9.03-9.4)	0.087 (0.082-0.091)	<0.0001
	Asian	2828	9.79 (9.13-10.18)	0.11 (0.097-0.124)	
	Caucasian	230,736	8.44 (8.38-8.48)	0.074 (0.073-0.075)	
	Hispanic	5733	8.74 (8.44-9.07)	0.105 (0.097-0.115)	
	Others	1301	9.17 (8.34-9.95)	0.094 (0.078-0.114)	
Primary payer insurance	Government	176,732	7.59 (7.52-7.62)	0.063 (0.062-0.064)	<0.0001
	Not insured	9608	8.31 (8.11-8.54)	0.079 (0.074-0.086)	
	Private	70,432	10.81 (10.71-10.87)	0.108 (0.106-0.111)	
Residence area	Metropolitan	202,889	8.51 (8.48-8.57)	0.078 (0.076-0.079)	<0.0001
	Rural	6583	8.25 (7.98-8.48)	0.06 (0.054-0.066)	
	Urban	45,865	8.48 (8.38-8.57)	0.071 (0.068-0.074)	
Stage	I-III	88,944	14.36 (14.23-14.49)	0.16 (0.157- 0.163)	<0.0001
	IV	143,934	6.21 (6.14-6.28)	0.024 (0.024-0.025)	

Note: p values by log-rank test.
CI, confidence interval; Dx, diagnosed.

Table 6. Factors Leading to a Better Overall Survival in All Patients With SCLC Diagnosed Between 2004 and 2016

Factor	Level	Total N	Median Survival in mo (95% CI)	Rate at 5 y (95% CI)	*p* Value
Year of Dx	2004-2010	130,912	8.41 (8.34-8.48)	0.068 (0.066-0.069)	<0.0001
	2011-2016	124,796	8.61 (8.54-8.67)	0.087 (0.085-0.089)	
Charlson-Deyo	0	144,880	9.59 (9.53-9.66)	0.088 (0.086-0.09)	<0.0001
	≥1	117,169	7.1 (7.0-7.16)	0.061 (0.06-0.063)	
Median community income	<40,000	57,221	8.11 (8.02-8.21)	0.07 (0.067-0.072)	<0.0001
	40,000-50,000	65,788	8.34 (8.25-8.44)	0.069 (0.067-0.071)	
	50,000-63,000	59,557	8.4 (8.31-8.5)	0.072 (0.069-0.074)	
	≥63,000	67,973	8.77 (8.67-8.84)	0.077 (0.075-0.079)	
No high school degree quartiles	≥17.6%	57,607	8.25 (8.15-8.34)	0.073 (0.071-0.075)	<0.0001
	10.9-%-7.5%	76,040	8.31 (8.25-8.41)	0.07 (0.068-0.072)	
	6.3%-10.8%	71,200	8.51 (8.41-8.57)	0.073 (0.071-0.075)	
	<6.3%	46,335	8.64 (8.54-8.74)	0.073 (0.071-0.076)	
Treatment center type	Academic	68,780	9.13 (9.07-9.23)	0.089 (0.087-0.092)	<0.0001
	Nonacademic	193,269	8.28 (8.25-8.34)	0.071 (0.07-0.073)	
Surgery	No	253,036	8.28 (8.25-8.31)	0.068 (0.067-0.069)	<0.0001
	Yes	8346	26.38 (25.49-27.3)	0.316 (0.306-0.327)	
Chemotherapy	No	67,269	1.48 (1.45-1.51)	0.033 (0.031-0.034)	<0.0001
	Yes	190,004	10.68 (10.61-10.71)	0.091 (0.089-0.092)	
Radiation therapy	No	132,993	5.45 (5.39-5.52)	0.039 (0.038-0.04)	<0.0001
	Yes	123,105	12.06 (11.99-12.16)	0.117 (0.115-0.119)	
Immunotherapy	No	259,945	8.48 (8.44-8.51)	0.075 (0.074,0.077)	<0.0001
	Yes	968	10.97 (10.61,11.4)	0.074 (0.055,0.10)	

Note: *p* values by log-rank test.
CI, confidence interval; Dx, diagnosed.

centers. More females, African Americans, patients without high school diplomas, and those from rural areas were diagnosed after 2010. Older patients, males, Caucasians, patients with stage IV disease, those with government primary payer insurance, and those from rural areas had significantly worse OS. Patients without comorbidities and treated at academic centers had significantly better OS. OS significantly increased with community income and education level. The most notable and reassuring finding was that survival for patients diagnosed after 2010 was significantly better than those diagnosed between 2004 and 2010. This occurred despite more stage IV diagnoses during this time frame, likely most affected by more routine use of positron emission tomography/computed tomography (PET/CT) scans at diagnosis. Just as with NSCLC, greater staging accuracy of SCLC allows identification of patients who may benefit from combined modality therapy,

Table 7. Summary of Multivariable Cox Proportional Hazard Model for OS From Diagnosis

		2004–2010						2011–2016					
		Stages I–III			Stage IV			Stages I–III			Stage IV		
Factor	Comparison	Hazard ratio	95% CI	*p* value	Hazard ratio	95% CI	*p* value	Hazard ratio	95% CI	*p* value	Hazard ratio	95% CI	*p* value
Age	18–29 vs. ≥60	0.78	0.372–1.638	0.5118	0.722	0.455–1.147	0.1674	0.381	0.123–1.18	0.0943	0.449	0.26–0.775	0.0041
	30–39 vs. ≥60	0.683	0.565–0.826	<0.0001	0.715	0.625–0.818	<0.0001	0.611	0.471–0.792	0.0002	0.833	0.704–0.986	0.0339
	40–49 vs. ≥60	0.735	0.7–0.771	<0.0001	0.854	0.824–0.886	<0.0001	0.768	0.714–0.826	<0.0001	0.93	0.889–0.973	0.0018
	50–59 vs. ≥60	0.809	0.787–0.833	<0.0001	0.906	0.887–0.926	<0.0001	0.81	0.783–0.838	<0.0001	0.897	0.878–0.916	<0.0001
Sex	Female vs. male	0.846	0.829–0.863	<0.0001	0.87	0.857–0.884	<0.0001	0.834	0.814–0.854	<0.0001	0.877	0.864–0.891	<0.0001
Race/ethnicity	African American vs. Caucasian	0.94	0.904–0.978	0.0023	0.937	0.908–0.967	<0.0001	0.864	0.825–0.905	<0.0001	0.857	0.831–0.884	<0.0001
	Asian vs. Caucasian	0.845	0.764–0.935	0.0011	0.783	0.72–0.853	<0.0001	0.94	0.842–1.049	0.2661	0.835	0.775–0.9	<0.0001
	Hispanic vs. Caucasian	0.893	0.828–0.963	0.0034	0.852	0.806–0.901	<0.0001	0.863	0.791–0.942	0.001	0.705	0.668–0.745	<0.0001
	Others vs. Caucasian	0.92	0.794–1.066	0.2681	0.925	0.826–1.037	0.1803	0.816	0.686–0.971	0.0221	0.868	0.777–0.969	0.012
Insurance	Government vs. private	1.27	1.24–1.302	<0.0001	1.201	1.178–1.223	<0.0001	1.22	1.184–1.258	<0.0001	1.123	1.102–1.146	<0.0001
	Not insured vs. private	1.154	1.087–1.225	<0.0001	1.166	1.12–1.214	<0.0001	1.184	1.096–1.278	<0.0001	1.12	1.073–1.169	<0.0001
Community median income	40K vs. >63K	1.077	1.036–1.12	0.0002	1.028	0.998–1.06	0.0689	1.082	1.032–1.134	0.0011	1.173	1.138–1.21	<0.0001
	40–50K vs. >63K	1.056	1.021–1.091	0.0016	1.017	0.991–1.043	0.2098	1.049	1.008–1.092	0.0197	1.095	1.067–1.124	<0.0001
	50–63K vs. >63K	1.043	1.011–1.075	0.008	1.042	1.018–1.067	0.0007	1.026	0.989–1.065	0.1664	1.09	1.064–1.116	<0.0001
No high school degree quartiles	≥17.6% vs. <6.3%	0.991	0.951–1.032	0.6474	0.982	0.952–1.013	0.248	0.959	0.913–1.007	0.0962	0.863	0.836–0.891	<0.0001
	10.9%–17.5% vs. <6.3%	1.001	0.966–1.037	0.9752	0.988	0.962–1.016	0.4084	0.994	0.953–1.038	0.7956	0.932	0.907–0.958	<0.0001
	6.3%–10.8% vs. <6.3%	1.008	0.976–1.041	0.6235	0.983	0.959–1.007	0.1621	1.003	0.965–1.043	0.8637	0.962	0.939–0.987	0.0026
Residence area	Metro vs. urban	1.045	1.017–1.074	0.0016	1.023	1.001–1.045	0.0418	0.998	0.965–1.032	0.9073	0.986	0.965–1.008	0.2
	Rural vs. urban	1.087	1.017–1.163	0.0147	1.027	0.974–1.082	0.3301	0.991	0.914–1.073	0.8187	1.066	1.011–1.125	0.0188
Charlson-Deyo	0 vs. ≥1	0.8	0.784–0.817	<0.0001	0.812	0.799–0.825	<0.0001	0.835	0.815–0.855	<0.0001	0.835	0.822–0.848	<0.0001
Center type	Academic vs. non-academic	0.952	0.93–0.975	<0.0001	0.952	0.935–0.97	<0.0001	0.949	0.923–0.976	0.0002	0.946	0.93–0.963	<0.0001
Surgery	No vs. yes	3.001	2.875–3.132	<0.0001	1.667	1.524–1.822	<0.0001	3.533	3.347–3.73	<0.0001	1.386	1.253–1.533	<0.0001
Radiation therapy	No vs. yes	1.736	1.695–1.778	<0.0001	1.24	1.22–1.26	<0.0001	2.045	1.985–2.106	<0.0001	1.379	1.356–1.402	<0.0001
Chemotherapy	No vs. yes	1.734	1.685–1.784	<0.0001	2.772	2.723–2.822	<0.0001	1.684	1.628–1.743	<0.0001	3.117	3.06–3.175	<0.0001
Immunotherapy	No vs. yes	1.097	0.891–1.351	0.3831	1.183	1.008–1.388	0.0395	1.441	1.082–1.919	0.0124	1.229	1.119–1.35	<0.0001

CI, confidence interval; OS, overall survival.

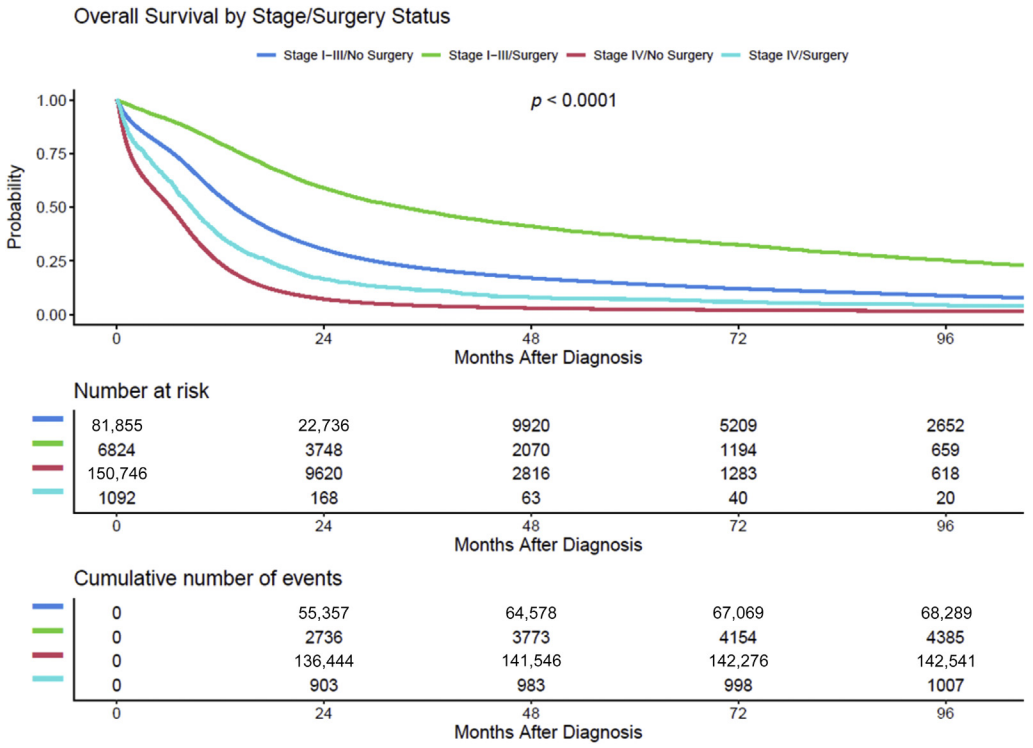

Figure 1. OS by stage/surgery status for all patients diagnosed in 2004 to 2016. OS, overall survival.

including surgical resection in some cases. This promising difference in survival seems to also be linked to more patients receiving treatment at academic centers, greater receipt of RT, chemotherapy, IO, and improvement in supportive care measures. Since 2016, IO has become a standard of care for the treatment of extensive-stage SCLC, and further improvements in OS will occur as treatment advances for this disease continue to develop. Results of the IMpower 133 trial of first-line atezolizumab plus chemotherapy in extensive-stage SCLC were published in 2018, with atezolizumab gaining Food and Drug Administration approval in combination with carboplatin and etoposide for the first-line treatment of adult patients with extensive-stage SCLC in 2019.[12] Subsequently, the CASPIAN trial of durvalumab plus platinum-etoposide versus platinum-etoposide in first-line treatment of extensive-stage SCLC was published in 2019, with durvalumab attaining Food and Drug Administration approval with etoposide and either carboplatin or cisplatin as first-line treatment of patients with extensive-stage SCLC in 2020.[13] A recently published update to the CASPIAN trial revealed that three times more patients were estimated to be alive at three years when receiving treatment with durvalumab plus platinum-etoposide versus platinum-etoposide alone, with most patients still receiving durvalumab at the time of data cutoff. This helps solidify the role for durvalumab plus platinum-etoposide as first-line standard of care therapy for patients with extensive-stage SCLC.[14] As these data mature and are processed and collected in the NCDB in the next several years, we will have significantly more information regarding IO and outcomes in patients with SCLC.

Despite these promising findings, an issue of great concern is that patients from rural communities, at a further distance to an academic center, with lower income, with government primary payer insurance, and with lower residence area education level had significantly worse survival. We suspect that these differences in survival rates may be due to patient and provider limitations in access to health care resources and subspecialist care. It is worth noting that patients who live in rural areas have higher rates of smoking and both lung cancer incidence and mortality when compared with patients who live in urban areas.[15] Additional studies have found that access to low-dose CT screening, which can detect lung cancer at earlier, more treatable stages, is lower in rural areas than in urban areas.[16,17] Studies have also found that lower education level is associated with increased ever and current smoking prevalence, including the use of electronic cigarettes, across all racial and ethnic groups.[18] It has been revealed that patients with Medicaid and other public insurance are significantly less likely to receive certain standard treatments as compared with patients with the same disease who are privately insured.[19] Clinical trial access is also most certainly affected by these barriers to care.

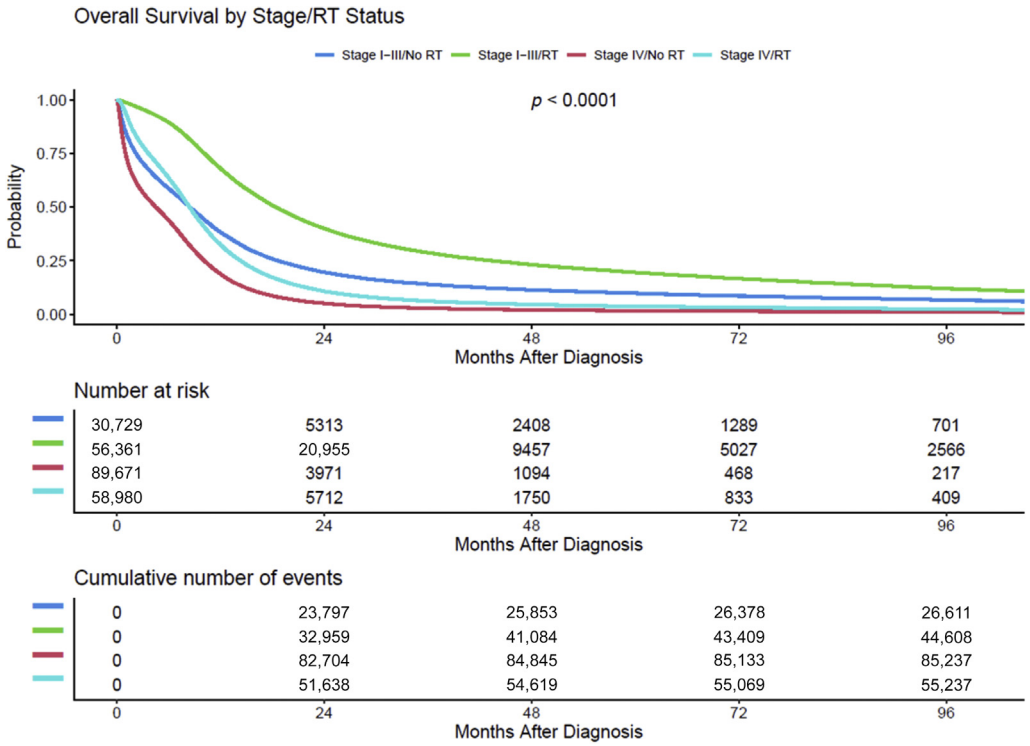

Figure 2. OS by stage/RT status for all patients diagnosed in 2004 to 2016. OS, overall survival; RT, radiation therapy.

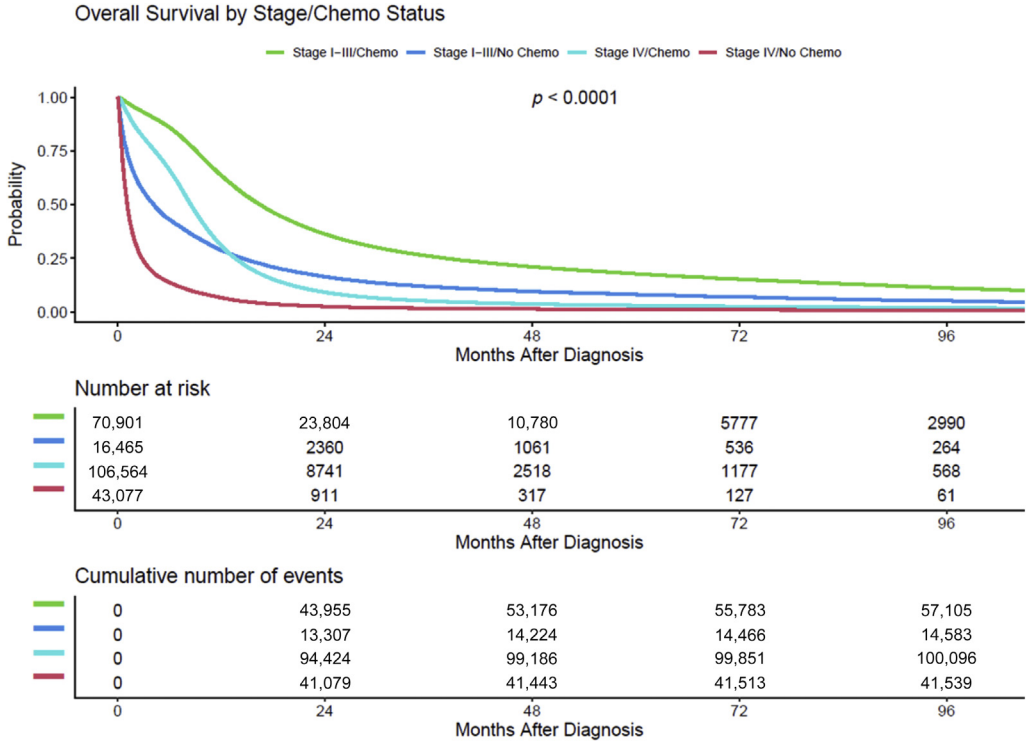

Figure 3. OS by stage/chemo status for all patients diagnosed in 2004 to 2016. Chemo, chemotherapy; OS, overall survival.

We believe that there is a complex interplay of these factors and that disparities noted in these key demographics may correspond with access to health care resources. We feel strongly that focused health care outreach programs will lead to improved outcomes in these populations. Examples include expansion of

broadband access and telehealth resources, academic center outreach and affiliation with rural cancer centers, and perhaps most importantly, improved primary care access, resulting in greater awareness of screening and prevention resources, such as low-dose chest CT scans and smoking cessation programs.

On the basis of the efforts of the National Lung Screening Trial Research Team, more patients are being screened for lung cancer with low-dose CT imaging. More patients are being identified as having lung cancer, and these cancers are being found at earlier stages, leading to improved outcomes for these patients.[20] The recent NELSON trial findings may lead to changes that will increase the population that is eligible for lung cancer CT screening, and thereby help to identify more patients with earlier stage disease.[21] It is unclear what impact these screening guidelines may have on patients with SCLC, as this disease is often found in later stages and can progress rapidly. One study found that lung cancer screening with low-dose CT did not improve survival in patients with SCLC owing to higher cumulative tobacco consumption and more advanced stage disease being identified at the time of screening.[22] Ongoing studies of these outreach efforts and their clinical benefit are needed. Over time, there has been increased usage of guidelines, such as the National Comprehensive Cancer Network, in patient care. Adherence to such published guidelines will improve the consistency of care between academic and community centers and improve patient outcomes. Health care provider access to guideline-based care resources is of paramount importance in improving survival in patients from rural communities or otherwise unable to access care at academic institutions.

The principal strength of this study is the use of a large clinical oncology database which is sourced through hospital registry data collected in more than 1500 Commission on Cancer–accredited treatment facilities. These data are representative of a contemporary Western population. The data in the NCDB undergoes extensive audits annually to ensure its validity.

The main limitation of our findings is that a very large patient population was studied and included in the analysis, such that even small differences in patient characteristics and outcomes were able to be detected and to have statistical significance. Another limitation inherent in the NCDB is that there is no patient-level detail regarding individual therapies used, including types of systemic therapies received and molecular markers.[23,24] Overall, it is important to note the advantages and potential shortcomings of any large database for the purpose of clinical research studies and to tailor the hypothesis accordingly before collecting and analyzing data. We feel that our questions were appropriate for study using the NCDB.

Lessons from the coronavirus disease 2019 pandemic have revealed that telehealth is feasible, can spearhead outreach efforts in many communities, and can also lead to improved health care outcomes. Studies have revealed that numerous patients from disadvantaged backgrounds do have access to telehealth resources and that such technology has improved their health care utilization.[25–27] We need these efforts to continue to alleviate the disparities present in these medically underserved demographic groups leading to poorer outcomes in not only SCLC, but also other common malignancies.

CRediT Authorship Contribution Statement

Logan Roof: Conceptualization, Data curation, Investigation, Methodology, Project administration, Visualization, Roles/Writing—original draft, Writing—review and editing.

Wei Wei: Data curation, Formal analysis, Software, Validation.

Katherine Tullio: Data curation, Project administration.

Nathan A. Pennell: Supervision, Writing—review and editing.

James P. Stevenson: Conceptualization, Project administration, Supervision, Writing—review and editing.

References

1. Govindan R, Page N, Morgensztern D, et al. Changing epidemiology of small-cell lung cancer in the United States over the last 30 years: analysis of the surveillance, epidemiologic, and end results database. *J Clin Oncol*. 2006;24:4539–4544.
2. Jemal A, Thun MJ, Ries LA, et al. Annual report to the nation on the status of cancer, 1975–2005, featuring trends in lung cancer, tobacco use, and tobacco control. *J Natl Cancer Inst*. 2008;100:1672–1694.
3. Alberg AJ, Samet JM. Epidemiology of lung cancer. *Chest*. 2003;123(1 suppl):21S–49S.
4. Travis WD. Advances in neuroendocrine lung tumors. *Ann Oncol*. 2010;21(suppl 7):vii65–vii71.
5. Travis WD, Brambilla E, Nicholson AG, et al. The 2015 World Health Organization Classification of Lung Tumors: impact of genetic, clinical and radiologic advances since the 2004 classification. *J Thorac Oncol*. 2015;10:1243–1260.
6. Zhou K, Shi H, Chen R, et al. Association of race, socioeconomic factors, and treatment characteristics with overall survival in patients with limited-stage small cell lung cancer. *JAMA Netw Open*. 2021;4:e2032276.
7. Menck HR, Cunningham MP, Jessup JM, et al. The growth and maturation of the National Cancer Database. *Cancer*. 1997;80:2296–2304.
8. Winchester DP, Stewart AK, Phillips JL, Ward EE. The National Cancer Database: past, present, and future. *Ann Surg Oncol*. 2010;17:4–7.

9. Edge S, Byrd DR, Compton CC, et al. *AJCC Cancer Staging Manual*. 7th ed. New York, NY: Springer; 2010.
10. Amin MB, Edge SB, Greene FL, et al. *AJCC Cancer Staging Manual*. 8th ed. New York, NY: Springer; 2017.
11. National Cancer Database. Cancer programs American College of Surgeons. https://www.facs.org/-/media/files/quality-programs/cancer/ncdb/puf_data_dictionary_2018.ashx. Accessed November 9, 2021.
12. Horn L, Mansfield AS, Szczęsna A, et al. IMpower133 study group. First-line atezolizumab plus chemotherapy in extensive-stage small-cell lung cancer. *N Engl J Med*. 2018;379:2220–2229.
13. Paz-Ares L, Dvorkin M, Chen Y, et al. CASPIAN investigators. Durvalumab plus platinum-etoposide versus platinum-etoposide in first-line treatment of extensive-stage small-cell lung cancer (CASPIAN): a randomised, controlled, open-label, phase 3 trial. *Lancet*. 2019;394:1929–1939.
14. Paz-Ares L, Chen Y, Reinmuth N, et al. Durvalumab, with or without tremelimumab, plus platinum-etoposide in first-line treatment of extensive-stage small-cell lung cancer: 3-year overall survival update from CASPIAN. *ESMO Open*. 2022;7:100408.
15. Nguyen-Grozavu FT, Pierce JP, Sakuma KK, et al. Widening disparities in cigarette smoking by race/ethnicity across education level in the United States. *Prev Med*. 2020;139:106220.
16. Odahowski CL, Zahnd WE, Eberth JM. Challenges and opportunities for lung cancer screening in rural America. *J Am Coll Radiol*. 2019;16:590–595.
17. Rohatgi KW, Marx CM, Lewis-Thames MW, Liu J, Colditz GA, James AS. Urban-rural disparities in access to low-dose computed tomography lung cancer screening in Missouri and Illinois. *Prev Chronic Dis*. 2020;17:E140.
18. Wang G, Wu L. Healthy people 2020: social determinants of cigarette smoking and electronic cigarette smoking among youth in the United States 2010–2018. *Int J Environ Res Public Health*. 2020;17:7503.
19. Maguire FB, Morris CR, Parikh-Patel A, et al. Disparities in systemic treatment use in advanced-stage non-small cell lung cancer by source of health insurance. *Cancer Epidemiol Biomarkers Prev*. 2019;28:1059–1066.
20. National Lung Screening Trial Research Team, Aberle DR, Adams AM, et al. Reduced lung-cancer mortality with low-dose computed tomographic screening. *N Engl J Med*. 2011;365:395–409.
21. de Koning HJ, van der Aalst CM, de Jong PA, et al. Reduced lung-cancer mortality with volume CT screening in a randomized trial. *N Engl J Med*. 2020;382:503–513.
22. Silva M, Galeone C, Sverzellati N, et al. Screening with low-dose computed tomography does not improve survival of small cell lung cancer. *J Thorac Oncol*. 2016;11:187–193.
23. Boffa DJ, Rosen JE, Mallin K, et al. Using the National cancer database for outcomes research: a review. *JAMA Oncol*. 2017;3:1722–1728.
24. Jairam V, Park HS. Strengths and limitations of large databases in lung cancer radiation oncology research. *Transl Lung Cancer Res*. 2019;8(suppl 2):S172–S183.
25. Hirko KA, Kerver JM, Ford S, et al. Telehealth in response to the COVID-19 pandemic: implications for rural health disparities. *J Am Med Inform Assoc*. 2020;27:1816–1818.
26. Flores Garcia J, Reid M, Raymond J. Feasibility of shared telemedicine appointments for low SES adolescents and young adults with T1D. *Diabetes*. 2018;67(suppl 1):1325.
27. Kichloo A, Albosta M, Dettloff K, et al. Telemedicine, the current COVID-19 pandemic and the future: a narrative review and perspectives moving forward in the USA. *Fam Med Community Health*. 2020;8:e000530.