The impact of social determinants of health on textbook oncological outcomes and overall survival in locally advanced non–small cell lung cancer

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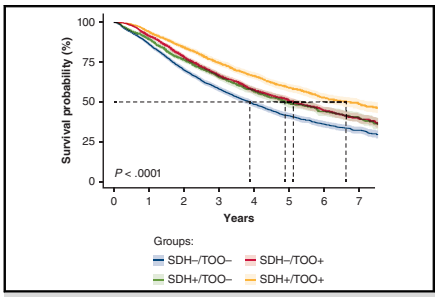
ABSTRACT

Objectives: Textbook oncological outcome (TOO) is a composite metric for surgical outcomes, including non–small cell lung cancer (NSCLC). We hypothesized that social determinants of health (SDH) can affect both the attainment of TOO and the overall survival (OS) in surgically resected NSCLC patients with pathological nodal disease.

Methods: We queried the National Cancer Database (2010-2017) for preoperative therapy-naïve lobectomies for NSCLC with tumor size <7 cm and pathologic N1/N2. Socioeconomic factors comprised SDH scores, where SDH negative (−) was considered if SDH ≥2 (disadvantage); otherwise, SDH was positive (+). TOO+ was defined as R0 resection, ≥5 lymph nodes resected, hospital stay <75th percentile, no 30-day mortality, adjuvant chemotherapy initiation ≤3 months, and no unplanned readmission. If one of these parameters was not achieved, the case was considered TOO−.

Results: Of 11,274 patients, 48% of cases were TOO+ and 38% were SDH+. A total of 15% of patients were SDH− and were less likely (adjusted odds ratio, 0.85; 95% confidence interval [CI], 0.78-0.92) to achieve TOO+ than patients with SDH+. After accounting for confounders, patients with TOO+ had 22% lower overall mortality than patients with TOO− (adjusted hazard ratio, 0.78; CI, 0.73-0.82). In contrast, SDH− remained an independently significant risk factor, reducing survival by 24% compared with SDH+ (adjusted hazard ratio, 1.24; CI, 1.17-1.32). The impact of SDH on OS was significant for both patients with TOO+ and TOO−: SDH+/TOO+ had the best OS and SDH−/TOO− had the worst OS.

Conclusions: SDH score has a significant association with TOO achievement and TOO-driven overall posttreatment survival in patients with lobectomy-resected NSCLC with postoperative pathologic N1/N2 nodal metastasis. Addressing SDH is important to optimize care and long-term survival of this patient population. (JTCVS Open 2023;16:888-906)



Association of textbook outcomes (TOO) and social determinants of health (SDH) on survival.

CENTRAL MESSAGE

Social determinants of health are independent factors impacting achievement of textbook oncologic outcome and overall survival of non–small cell lung cancer with N1/N2 nodal metastasis.

PERSPECTIVE

In addition to standard clinical and pathologic factors that define textbook oncologic outcomes, social determinants of health (SDH) factors affect survival of patients with locally advanced non–small cell lung cancer. Strategies to support sociogeographic disadvantaged patients with locally advanced NSCLC throughout their care may improve their overall survival.

See Discussion on page 907.

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Received for publication Feb 27, 2023; revisions received Sept 1, 2023; accepted for publication Sept 5, 2023; available ahead of print Oct 23, 2023.

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2666-2736

https://doi.org/10.1016/j.xjon.2023.09.013

Abbreviations and Acronyms

aHR = adjusted hazard ratio
aOR = adjusted odds ratio
CDCI = Charlson-Deyo comorbidity index
CI = confidence interval
FPL = federal poverty level
HR = hazard ratio
MIS = minimally invasive surgery
NCDB = National Cancer Database
NSCLC = non–small cell lung cancer
OS = overall survival
SDH = social determinants of health
TOO = textbook oncological outcomes

Textbook oncological outcome (TOO) is a multidimensional composite outcome metric representing the most desirable outcome for patients following curative-intent surgical resection of a primary cancer. TOO is used for colorectal, upper gastrointestinal, and aneurysm surgery and has recently been explored in non–small cell lung cancer (NSCLC).[1-3] In NSCLC, TOO mandates surgical R0 resection, adequate lymph node resection for pathologic examination, timely receipt adjuvant therapy when indicated, and no prolonged length of hospital stay, 30-day mortality, reintervention, unplanned readmission, or major complications. Previous studies of stage I NSCLC demonstrated that TOO metrics were associated with superior overall survival (OS).[4] Similarly, patients with TOO have significantly better OS in stage II NSCLC.[1-3]

Potentially resectable locally advanced lung cancer, including hilar/mediastinal lymph node metastasis, confirmed either pre- or postoperatively, requires comprehensive multimodal evaluation and induction or adjuvant systemic therapy with cytotoxic agents, immunotherapy with immune checkpoint inhibitors, targeted molecular therapy, or thoracic radiation where appropriate.[5-8] Having access to care and adequate socioeconomic resources increases the likelihood of receipt of the prescribed therapy. Although clinical–pathological parameters form the basis of TOO determination, little is known about the impact of sociogeographic status, which combines social and geographic elements on the achievement of TOO and TOO-associated OS.

Socioeconomic status metrics, such as household income, have been previously demonstrated to affect NSCLC treatment options and outcomes.[9,10] More recently, social determinants of health (SDH) is used as a broader population-level metric that includes not only factors representing social-economic status but also other important sociogeographical factors, such as education level, area of residence, and hospital access.[10-12] Socioeconomic disadvantages have been associated with lower-quality care and suboptimal outcomes, including increased lung cancer mortality.[13-16] There are limited data, however, regarding the association of SDH with TOO, in general, and survival outcomes in surgically resected NSCLC in particular. In this study, we aimed to determine (1) the rate of achieving TOO in relation to SDH scores, (2) the association between SDH and TOO, and (3) the association between SDH and TOO-driven OS.

METHODS

Data Source

The data used in the study are derived from a deidentified 2017 National Cancer Database (NCDB) participant user data file. NCDB is a hospital-based cancer registry that is a joint program of the American College of Surgeons Commission on Cancer and the American Cancer Society. The University of Miami Miller School of Medicine's institutional review boards deemed this study exempt from review because the data were deidentified.

Study Population

This study included adult (≥18 years) patients with adenocarcinoma or squamous cell carcinoma surgically treated with lobectomy (2010-2017). Inclusion criteria included tumor size <7 cm and postoperative pathologic N1 and/or N2 nodal metastasis in patients who underwent lobectomy (Surveillance, Epidemiology, and End Results codes: 30, 33). Exclusion criteria included tumor size of ≥7 cm, neoadjuvant therapy, palliative surgery, those who did not receive surgery due to contraindications (patient risk factor or oncologist recommendation), patients with reported metastasis, unknown stage, or unreported follow-up status.

Study Outcomes and Covariates

The primary outcome was the achievement of TOO (TOO+) or failure to achieve TOO (TOO–). TOO was defined by the following criteria: a complete (R0) resection of the primary cancer, sufficient lymph node dissection (sampling of ≥5 lymph nodes), no prolonged hospital stay (≤75th percentile per year [mean, 7.4 ± 0.5 days]), no unplanned hospital readmission after discharge, no 30-day mortality, and initiating adjuvant chemotherapy ≤3 months of diagnosis when indicated. The secondary outcome was OS, which was measured as the time from diagnosis to the date of last contact or death (from any cause).

SDH included ZIP code–level median income (<100% federal poverty level [FPL], 100%-150% FPL, or >150% FPL based on 2016 US Census data), metropolitan statistical area (metropolitan, urban, or rural), education level (based on a percentage of ZIP code holding high school degree), and hospital type within 250 miles of patients' residence.

The SDH score was created using an item response analysis, where one point was awarded for each of the following factors based on a Cox regression model: median income (<100% FPL), rural place of residence, less than high school education, and community hospitals within 250 miles from patient's residence. Each factor was evaluated individually, and once the data showed a negative impact of that factor on survival (Table E1), it was assigned a number. Then, the total number from all factors was aggregated to calculate a broader SDH score (0-4). A sociogeographic disadvantage was assumed for patients with SDH scores of >2 (labeled as SDH–). In contrast, a score of 0 to 1 denotes being sociogeographic advantaged (SDH+).

Other variables of interest included demographics (age, sex, race, and/or ethnicity, grouped into Hispanic and non-Hispanic [White, Black, Asian, or other]), Charlson–Deyo comorbidity index (CDCI), facility type (academic, integrated, comprehensive, and community), and facility

lung cancer surgical volume (categorized into low [≤27/year], moderate [28-87/year], and high [88-202/year] by the quartile yearly case volume, with an additional category of "very high" [>203/year] based on the top 5% percentile).

Statistical Analysis

Descriptive statistics were used to summarize patient characteristics as means (± standard deviation) after normality assessment for continuous variables and frequencies (%) for categorical variables. Wilcoxon rank sum test and Pearson χ^2-squared or Fisher exact tests were used to determine the significance of differences in patients who were TOO+ and TOO–.

Uni- and multivariable logistic regression analyses estimated the likelihood of TOO achievement. The Kaplan–Meier method estimated OS, which was compared between different variables by using the log-rank test. Uni- and multivariable Cox proportional hazards regression analyses were used to evaluate the association between patient characteristics and survival. The adjustment was made for relevant factors including TOO, SDH, and facility-related variables after z score transformation for continuous variables, data imputation (by random forest), variables correlation (by variance inflation factor), and proportional hazards assumption assessment (by Schoenfeld residuals). The SDH variable reference was changed from SDH+ to SDH– in a different model to better demonstrate the results of SDH advantage. A subanalysis of the SDH score categorized into 3 groups was performed to highlight the effect of accumulating sociogeographical disadvantages in NSCLS population.

Two-sided *P* values were reported along with 95% confidence interval (CI) levels. All statistical analyses were performed with R software (R version 4.2.2 [2022-10-31 ucrt] with 'gtsummary,' 'missRanger,' and 'survminer' packages, along with their dependencies).[17-19]

RESULTS

Study Cohort Overview

A total of 11,274 patients eligible for this study were identified from the NCDB between 2010 and 2017. The mean age was 68 ± 10 years. Greater proportions of patients were female (57%) and non-Hispanic White (84%), whereas Black, Hispanic, and Asian patients accounted for 8.8%, 3.0%, and 3.3% of the sample size, respectively. Among SDH factors, 36% of patients lived in areas with income >150% FPL, 33% lived in areas with high educational attainment, and 84% lived in metropolitan areas. There were 61% of patients with Medicare or other government insurance, 32% had private insurance, and 7.1% had Medicaid or noninsured (Table 1). Overall, 47.8% of the entire study cohort achieved TOO+ status. Low numeric SDH scores of 0-1 (SDH+) were observed in 38% of patients. Correlating SDH+ status with achieving TOO+, significantly more patients with SDH+ were TOO+ (2163/4136, 52%) compared with only 45% (3060/6814) of the SDH– cohort ($P < .001$). Clinical stage I NSCLC accounted for 66% of patients (n = 7386), equally distributed between TOO– and TOO+ categories (TOO–: 51%, n = 3765 vs TOO+: 49%, n = 3621). Clinical stage II accounted for 35% (n = 3869) of the entire study cohort (TOO–: 54%, n = 2106 vs TOO+: 46%, n = 1763); and the population present with a higher stage II SDH– (64%, n = 2401) than SDH+ (36%, n = 1358) (Table E2). After pathologic staging, N1 lymph nodes accounted for 65% (n = 7366) of patients and N2 accounted for 34% (n = 3908), with no significant difference between TOO+ and TOO– status ($P = .965$). Pulmonary resections were more frequently performed at academic/research programs and integrated network cancer programs (37% and 16%, respectively) than at community programs (47.5%). More resections were performed at moderate- or low-volume centers (51% and 23%, respectively) versus 21% and 5.3% at high- and very high-volume centers, respectively. Achieving TOO+ status was greater in academic/integrated network cancer center programs than in community programs (50% vs 45%, $P < .001$). Open thoracotomy for lobectomy was performed in 58% of the entire cohort whereas a minimally invasive approach was used in 42% of cases (31% with video-assisted thoracoscopic surgery and 11% with robotic surgery). Adjuvant chemotherapy was given in 70% of cases, with 75% of therapies initiated ≤3 months of diagnosis.

Primary Outcome: TOO

Unadjusted factors adversely associated with TOO+ (odds ratio <1 and $P < .05$) by univariable analysis are shown in Table 2. These include SDH– (sociogeographic disadvantage), Black, government insurance (particularly Medicaid and noninsured status), increasing CDCI, nonacademic/research medical facilities, lobectomy by open thoracotomy, and low-volume hospitals. After adjusting for important variables in a multivariable model, SDH–, Black race, government insurance, increasing CDCI, lobectomy by open thoracotomy, and low-volume hospitals remained independent factors adversely affecting TOO+. SDH– was associated with a 15% reduction of TOO+ achievement (adjusted odds ratio [aOR], 0.85; CI, 0.78-0.92, $P < .001$) (Table 2). After changing the reference group to SDH–, SDH+ was associated with an 18% increase of TOO+ achievement (aOR, 1.18; CI, 1.09-1.28, $P < .001$). Female sex and academic/research program were positively associated with TOO+ by univariate analysis but not by multivariate modeling. Granular analysis of the impact of SDH– aggregate scores on TOO+ showed that scores of 2 or 3-4 decreased TOO+ by 15% (aOR, 0.85; CI, 0.77-0.93) to 21% (aOR, 0.79; CI, 0.71-0.88, $P < .001$), respectively, when compared with that of SDH score of 0-1 (SDH+) (Table E4).

Secondary Outcomes: OS

Overall, there were 5196 deaths at the last follow-up. The 1- and 5-year survival of this entire cohort was 90% (CI, 80%-90%) and 49% (CI, 48%-50%). In patients with TOO+, the 1- and 5-year OS was 92% (CI, 92%-93%) and 54% (CI, 53%-56%) and median survival was 5.7 years (CI, 5.5-6.0). For the TOO– cohort, 1-year and 5-year survival rates were 87% (86%-88%) and 44% (42%-46%) and median survival was 4.2 years (CI, 4.0-4.3) (Figure 1,

TABLE 1. Demographics of NSCLC with pathologic nodal disease stratified based on TOO achievement

Characteristic	Overall N = 11,274*	TOO– N = 5879*	TOO+ N = 5395*	*P* value†
Age at diagnosis, y	67 (10)	67 (10)	67 (10)	.2
Age, y (groups)				**.002**
<60	2549 (23%)	1301 (51%)	1248 (49%)	
60-69	3904 (35%)	2016 (52%)	1888 (48%)	
70-79	3714 (33%)	2022 (54%)	1692 (46%)	
80+	1107 (9.8%)	540 (49%)	567 (51%)	
Sex				**.010**
Male	4829 (43%)	2586 (54%)	2243 (46%)	
Female	6445 (57%)	3293 (51%)	3152 (49%)	
Race/ethnicity				**<.001**
Hispanic	333 (3.0%)	181 (54%)	152 (46%)	
Non-Hispanic				
White	9440 (84%)	4848 (51%)	4592 (49%)	
Black	988 (8.8%)	610 (62%)	378 (38%)	
Asian	369 (3.3%)	172 (47%)	197 (53%)	
Other	87 (0.8%)	39 (45%)	48 (55%)	
Unknown	57	29	28	
Education				**<.001**
High	3682 (33%)	1786 (49%)	1896 (51%)	
Low	7592 (67%)	4093 (54%)	3499 (46%)	
Income level				**<.001**
>150% FPL	3681 (36%)	1699 (46%)	1982 (54%)	
100%-150% FPL	4678 (46%)	2508 (54%)	2170 (46%)	
<100% FPL	1792 (18%)	1072 (60%)	720 (40%)	
Unknown	1123	600	523	
Patient location				>.9
Metropolitan	9221 (84%)	4763 (83%)	4458 (85%)	
Urban	1531 (14%)	854 (15%)	677 (13%)	
Rural	198 (1.8%)	110 (1.9%)	88 (1.7%)	
Unknown	324	152	172	
SDH score (3 groups)				**<.001**
0-1	4136 (38%)	1973 (48%)	2163 (52%)	
2	3817 (35%)	2028 (53%)	1789 (47%)	
3-4	2997 (27%)	1726 (58%)	1271 (42%)	
Unknown	324	152	172	
TNM clinical stage				**<.001**
Stage 1	7386 (66%)	3765 (51%)	3621 (49%)	
Stage 2	3869 (34%)	2106 (54%)	1763 (46%)	
Unknown	19	8	11	
LN pathologic stage				>.9
N1	7366 (65%)	3840 (52%)	3526 (48%)	
N2	3908 (35%)	2039 (52%)	1869 (48%)	
Charlson/Deyo score				**<.001**
0	6056 (54%)	2950 (49%)	3106 (51%)	
1	3564 (32%)	1952 (55%)	1612 (45%)	
2	1198 (11%)	708 (59%)	490 (41%)	
3+	456 (4.0%)	269 (59%)	187 (41%)	
Insurance				**<.001**
Medicaid/not insured	798 (7.1%)	495 (62%)	303 (38%)	
Medicare/other government	6829 (61%)	3639 (53%)	3190 (47%)	
Private insurance	3547 (32%)	1700 (48%)	1847 (52%)	
Unknown	100	45	55	

(Continued)

TABLE 1. Continued

Characteristic	Overall N = 11,274*	TOO– N = 5879*	TOO+ N = 5395*	*P* value†
Facility type				**<.001**
Academic	4147 (37%)	2022 (49%)	2125 (51%)	
Integrated	1789 (16%)	946 (53%)	843 (47%)	
Community	5279 (47%)	2890 (55%)	2389 (45%)	
Unknown	59	21	38	
Hospital volume				**<.001**
Very high	597 (5.3%)	239 (40%)	358 (60%)	
High	2337 (21%)	1078 (46%)	1259 (54%)	
Low	2646 (23%)	1579 (60%)	1067 (40%)	
Moderate	5694 (51%)	2983 (52%)	2711 (48%)	
Surgical approach				**<.001**
Open/unspecified	6561 (58%)	3632 (55%)	2929 (45%)	
Robotic/VATS	4713 (42%)	2247 (48%)	2466 (52%)	
Postoperative radiotherapy	2042 (19%)	1165 (57%)	877 (43%)	**<.001**
Unknown	279	151	128	
Postoperative chemotherapy	7862 (70%)	4334 (55%)	3528 (45%)	**<.001**
Unknown	392 (3.5%)	168 (43%)	224 (57%)	
Chemotherapy after 3 mo	2823 (25%)	2823 (100%)	0 (0%)	**<.001**

Statistically significance is denoted in bold. *TOO*, Textbook outcomes; *FPL*, federal poverty level; *NA*, not available; *SDH*, social determinants of health; *TNM*, tumor, node, and metastasis staging system; *LN*, lymph node; *VATS*, video-assisted thoracic surgery. *n (%); mean (SD). †Wilcoxon rank sum test; Pearson χ^2 test; Fisher exact test.

A). For patients who were SDH+, the 1- and 5-year OS was 91% (CI, 91%-92%) and 54% (CI, 52%-56%) with a median survival of 5.8 years (CI, 5.5-6.1). For the SDH– group, 1- and 5-year OS was 88% (87%-89%) and 45% (44%-47%), respectively, and median survival was 4.3 years (CI, 4.2-4.5) (Figure 1, *B*). The impact of SDH on patients with TOO+ is shown in Figure 2, *A*; patients who were SDH+ had improved 1-, 5-year, and median survival as compared with the SDH– cohort. While TOO– was associated with decreased 1-, 5-year, and median survival, those of the SDH+ cohort had improved OS (Figure 2, *B*). Finally, a combination of SDH+ and TOO+ had the best survival estimates of 94% (CI, 93%-95%) and 59% (CI, 56%-61%), at 1 and 5 years, respectively, with a median survival of 6.6 years (CI, 6.0-7.5). In contrast, SDH– and TOO– had the worst survival estimates of 86% (CI, 85%-87%) and 41% (CI, 40%-43%) at 1 and 5 years, respectively, with the median survival being 3.9 years (CI, 3.7-4.1), $P < .001$ (Figure 2, *C*). Table 3 summarizes the survival data of the entire cohort and subgroups. Kaplan–Meier analyses for individual SDH score components are presented in Figures E1-E4. In our subanalysis of SDH with 3 groups (Table E4, Figure E5), patients with high SDH score of 3-4 (significant sociogeographic disadvantages SDH– subgroup) had 1.9 years shorter median survival time than those with SDH+ score 0-1 (3.9 years [CI, 3.7-4.1] vs 5.8 years [CI, 5.5-6.1], respectively); an SDH score of 2 (intermediate sociogeographic disadvantages SDH– subgroup) had a median survival of 4.7 years (4.7 [CI, 4.5-5.0])

Table 4 summarizes the univariate and multivariate Cox regression analyses of factors associated with mortality over time of our study cohort. Unadjusted Cox analyses demonstrated a positive association between SDH+ (hazard ratio [HR], 0.76, CI, 0.72-0.81, $P < .001$) and TOO+ (HR, 0.73, CI, 0.69-0.77, $P < .001$) and better overall OS. Other factors associated with better OS include non-White race (Asian race had the best OS [Figure E6]), private insurance, minimally invasive surgery, no underlying comorbidity (CDCI = 0), surgical years, academic programs, and non–low-volume facilities. Poor OS was associated with advanced age, nonprivate insurance, CDCI >0, minimally invasive converted to open surgery, and lymph-vascular invasion. SDH score of 3-4 (significant sociogeographic disadvantages SDH– subgroup) increased mortality by 48% (HR, 1.48; CI, 1.39-1.59, $P < .001$) versus SDH score of 0-1 (SDH+ subgroup) (Table E4).

After adjustment for relevant patient and tumor characteristics, as well as SDH and facility-related variables, multivariable Cox regression modeling demonstrated that SDH– was associated with a 24% decreased OS (adjusted hazard ratio [aHR], 1.24; CI, 1.17-1.32, $P < .001$), while SDH+ was associated with a 20% increased OS (aHR, 0.80; CI, 0.78-0.85, $P < .001$). TOO+ was associated with a 22% increased OS (aHR, 0.78; 0.73-0.82, $P < .001$). Although most variables from the unadjusted model remained significant, facility type ($P > .05$), Black race ($P = .10$), or high-volume facility ($P = .3$) were no longer significantly associated with OS; however, very high-volume remained significant, increasing OS by 31%

TABLE 2. Uni- and multivariable logistic regression analyses demonstrating factors associated with TOO in patients with NSCLC with pathologic nodal disease

Characteristic	Univariable module			Multivariable module		
	OR	95% CI	*P* value	aOR	95% CI	*P* value
SDH–	0.75	0.70-0.81	**<.001**	0.85	0.78-0.92	**<.001**
Age (z score)*	0.97	0.94-1.01	.12	0.97	0.92-1.02	.2
Female sex	1.10	1.02-1.19	**.010**	1.07	0.99-1.15	.10
Race/ethnicity						
White	–	–		–	–	
Black	0.65	0.57-0.75	**<.001**	0.69	0.60-0.80	**<.001**
Asian	1.21	0.98-1.49	.074	1.16	0.93-1.43	.2
Hispanic	0.89	0.71-1.10	.3	0.92	0.74-1.16	.5
Other	1.30	0.85-2.00	.2	1.30	0.84-2.01	.2
Insurance						
Private insurance	–	–		–	–	
Medicare/other government	0.81	0.74-0.88	**<.001**	0.86	0.78-0.95	**.003**
Medicaid/not insured	0.56	0.48-0.66	**<.001**	0.63	0.54-0.74	**<.001**
Charlson/Deyo score						
0	–	–		–	–	
1	0.78	0.72-0.85	**<.001**	0.80	0.73-0.87	**<.001**
2	0.66	0.58-0.75	**<.001**	0.70	0.61, 0.79	**<.001**
3+	0.66	0.54-0.80	**<.001**	0.72	0.59-0.87	**<.001**
Minimally invasive surgery						
Open/unspecified	–	–		–	–	
MIS	1.45	1.34-1.57	**<.001**	1.38	1.27-1.50	**<.001**
MIS converted	0.87	0.73-1.03	.11	0.86	0.72-1.02	.086
Years of surgery (z score)	0.95	0.92-0.99	**.006**	0.91	0.88-0.95	**<.001**
Lymph-vascular invasion						
Not present	–	–		–	–	
Present	0.97	0.90-1.04	.4	0.93	0.86-1.01	.69
Academic/research program	1.24	1.15-1.34	**<.001**	0.98	0.89-1.07	.6
Hospital volume						
Low	–	–	–	–	–	
Moderate	1.34	1.23-1.48	**<.001**	1.29	1.16-1.43	**<.001**
High	1.73	1.54-1.93	**<.001**	1.59	1.40-1.80	**<.001**
Very high	2.22	1.85-2.66	**<.001**	1.93	1.57-2.36	**<.001**

Statistically significance is denoted in bold. *OR*, Odds ratio; *CI*, confidence interval; *aOR*, adjusted odds ratio; *SDH*, social determinants of health; *MIS*, minimally invasive surgery (video-assisted thoracoscopy or robotic). *z-score transformation = (value – mean)/standard deviation.

(aHR, 0.69; CI, 0.59-0.81, $P < .001$) compared with low-volume facilities (Table 4). High SDH score of 3-4 increased mortality by 32% (aHR, 1.32; CI, 1.22-1.42, $P < .001$) versus that of the SDH+ subgroup (score of 0-1) (Table E4).

DISCUSSION

In this cohort of patients with locally advanced NSCLC, we find that sociogeographic status—indicated by SDH score—has an important association with both textbook outcomes and survival. SDH+ increased TOO likelihood by 18%, whereas SDH– decreased it by 15%. TOO+, which was achieved in 48% of the study cohort, was associated with a 22% increase in OS, whereas SDH– was associated with a 24% decrease in OS. The sociogeographic disadvantage was better demonstrated by classifying patients into 3 groups in our subanalysis, showing that a significant sociogeographic disadvantage (score of 3-4) was associated with a 21% decrease in TOO and a 32% decrease in OS compared with SDH+ subgroup (score of 0-1) (Table E4). These results reiterated some of the known disparities in cancer survival related to SDH at the individual level which emphasized the sociogeographic influence on optimal outcomes.[12] In NSCLC with N1/N2 nodal metastasis, vulnerable patient population groups living in areas with limited income, limited education, rural locations, and areas with limited access to specialized cancer care settings are at increased risk of poor perioperative

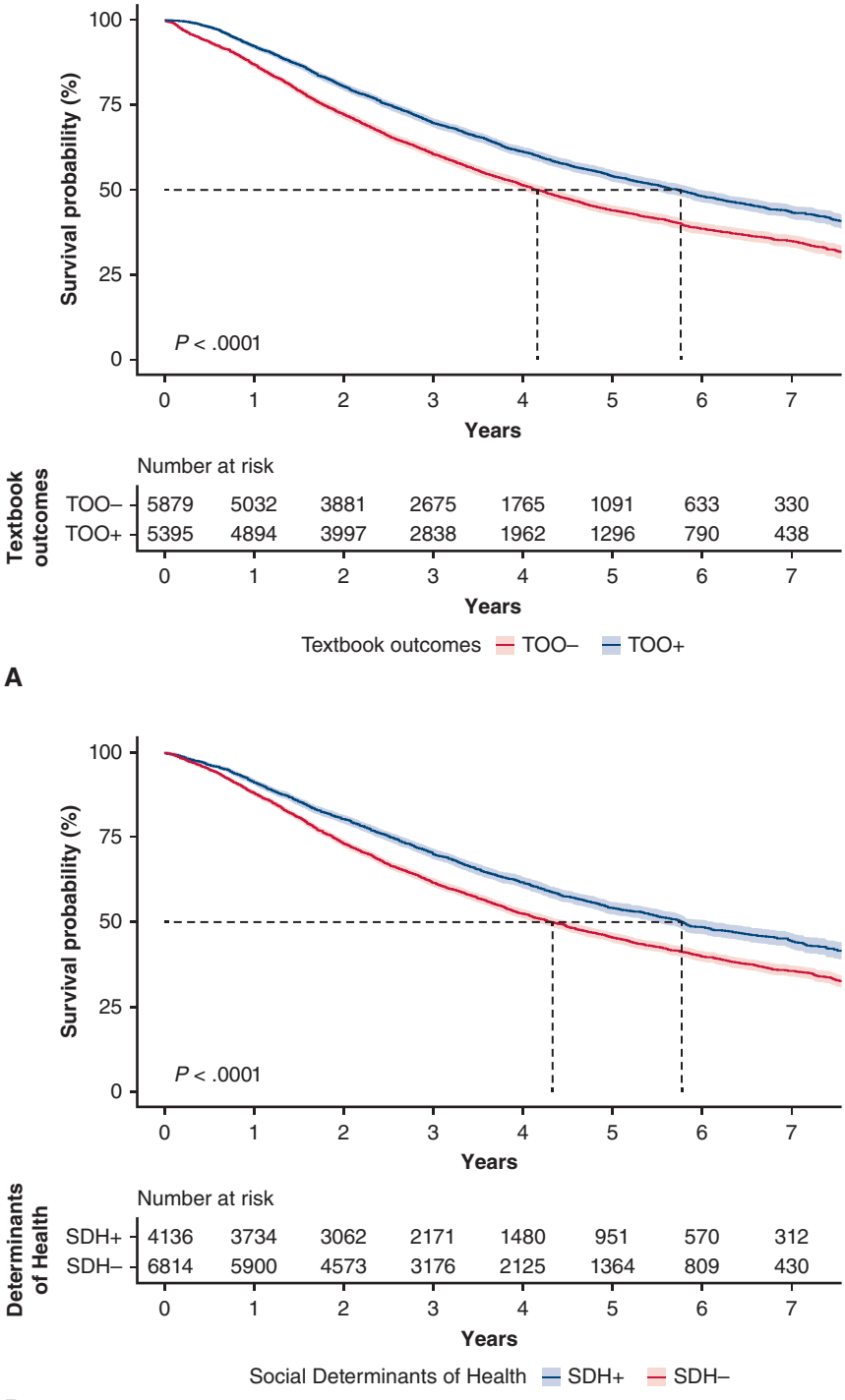


FIGURE 1. Kaplan–Meier curves (survival estimate with 95% confidence interval) comparing N1/N2 non–small cell lung cancer survival based on (A) textbook oncological outcomes (*TOO*) with TOO+ (*purple*) and TOO– (*red*); and (B) social determinants of health (*SDH*) with SDH+ (*blue*) and SDH– (*red*).

outcomes and long-term mortality. Our model was robust enough to discriminate SDH– factors (low income, low level of education, rural location of residence, community hospital within 250 miles of residence) association with outcomes, as well as the magnitude of sociogeographic disadvantages (subanalysis with 3 groups).

The overall 5-year survival rate of locally advanced NSCLC was 49%, which did not differ significantly from

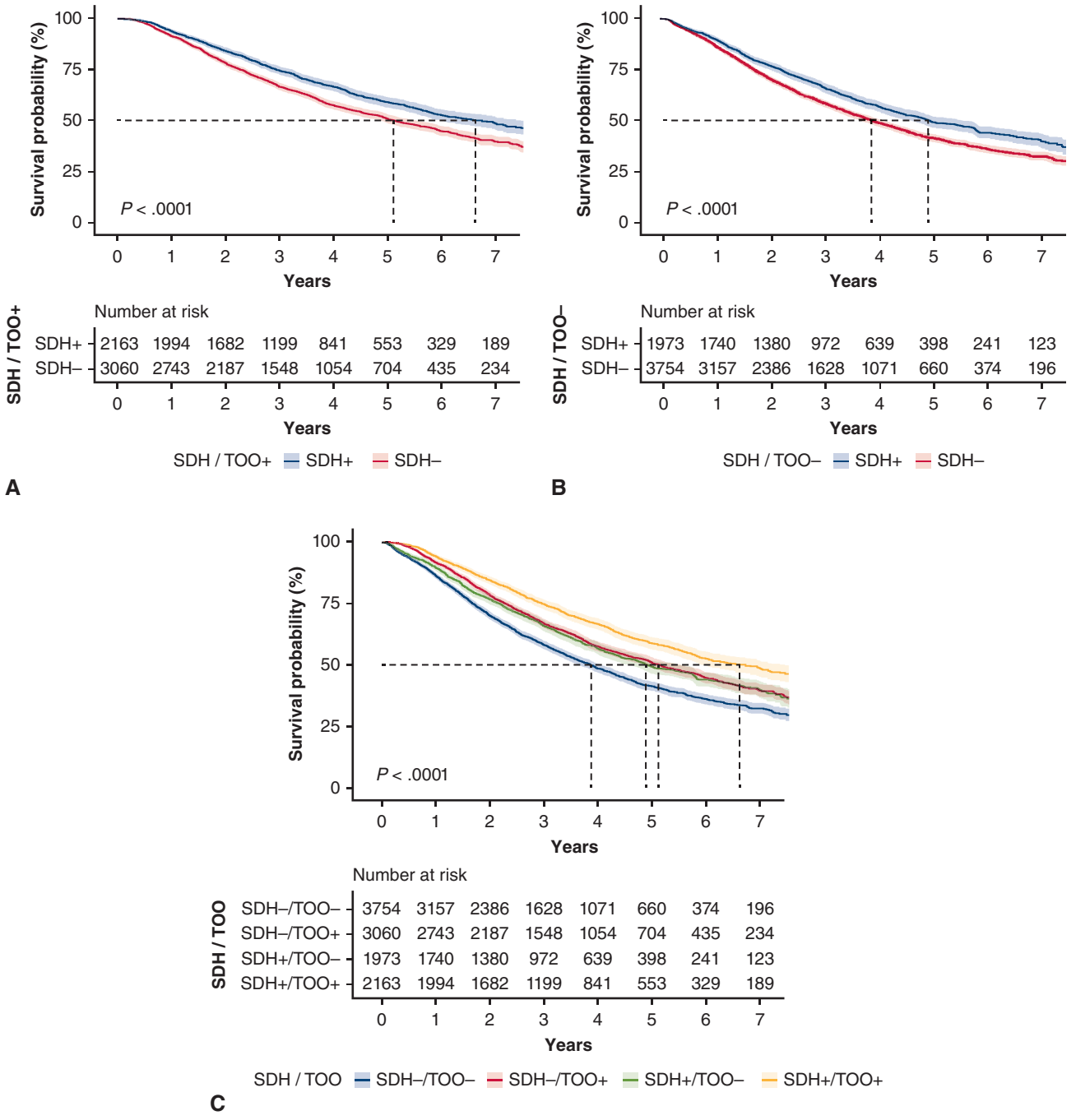


FIGURE 2. Kaplan–Meier curves (survival estimates with 95% confidence interval) demonstrating the impact of (A) SDH on overall survival of TOO+ (*blue*: SDH+ and *red*: SDH–); (B) SDH on the overall survival of patients with TOO–(*blue*: SDH+ and *red*: SDH–); and (C) combination of SDH and TOO. *SDH*, Social determinants of health; *TOO*, textbook oncological outcomes.

the 47.5% survival estimates reported 2 decades ago.[20] Identifying factors that influence better survival of locally advanced NSCLC cancers managed by multimodal approaches may aid in the development of care strategies and advocacy for patients based on their race/ethnicity/socioeconomic status with augmentation of resources for appropriate access. To better understand the contribution of SDH to TOO and OS disparities at the population level, we constructed an SDH numeric score based on nonclinical and nonbiological factors. The greater the numeric score indicative of social/geographic/economic disadvantages, the less likely TOO was achieved, which indicates that

TABLE 3. 1- and 5-year survival and median survival time for patients with NSCLC with pathologic nodal disease

Characteristic	1-y (%) with 95% CI	5-y (%) with 95% CI	Median survival*
Overall	90% (89%, 90%)	49% (48%, 50%)	4.8 (4.7, 4.9)
SDH			
SDH+	91% (91%, 92%)	54% (52%, 56%)	5.8 (5.5, 6.1)
SDH–	88% (87%, 89%)	45% (44%, 47%)	4.3 (4.2, 4.5)
TOO			
TOO+	92% (92%, 93%)	54% (53%, 56%)	5.7 (5.5, 6.0)
TOO–	87% (86%, 88%)	44% (42%, 46%)	4.2 (4.0, 4.3)
SDH/TOO			
SDH–/TOO–	86% (84%, 87%)	41% (39%, 43%)	3.9 (3.7, 4.1)
SDH–/TOO+	91% (90%, 92%)	51% (49%, 53%)	5.2 (4.9, 5.6)
SDH+/TOO–	89% (88%, 91%)	49% (46%, 52%)	4.9 (4.6, 5.5)
SDH+/TOO+	94% (93%, 95%)	59% (56%, 61%)	6.6 (6.0, 7.5)

SDH, Social determinants of health; *TOO*, textbook oncological outcomes. *Years.

despite the demographic and tumor characteristics of the patient, insurance coverage, or hospital expertise, disadvantaged patients have poor surgical outcomes. Interestingly, even when TOO was not achieved, SDH+ cohort had better OS (Figure 2, *B*). Furthermore, SDH+/TOO+ and SDH+/TOO– patient populations have survival curves superimposed on each other and lie in between those of the best (SDH+/TOO+) and the worst (SDH-/TOO–) subgroups (Figure 2, *C*).

Although such a composite SDH score has not yet been reported to our knowledge, similar associations with diagnosis and outcomes have been established for sociogeographic indices consisting of median income, educational attainment, and geographic settings in NSCLC and other cancers.[9,11,21] Previous reports examining the association between socioeconomic status and lung cancer incidence, treatment intensity, and survival focus on income- and education-related variables.[11,22,23] Indeed, poor income ($\leq$150% FPL) was associated with 30% of decreased OS, similar to the 34% increase of mortality reported in patients with income <$20,000 compared with $60,000 (HR, 1.34; CI, 1.16-1.55, $P < .001$).[23] In our study, we also found an effect of education on survival similar to the reported association previously established in stage IA-IIB NSCLC, where unadjusted middle education had a 23% decreased likelihood of mortality (HR, 0.77; CI, 0.71-0.83, $P < .001$) similar to the 22% decreased likelihood of mortality in our study (Table 4).[11] Geographic settings were also components of the SDH score that influenced NSCLC outcomes. A previous analysis incorporating area deprivation index and rurality revealed that socioeconomic status deprivation, but not rurality, was associated with higher lung cancer prevalence and mortality.[24] However, in our cohort we find patients living in rural areas have a 30% decreased likelihood of OS, manifesting in long-term outcomes (landmark time analysis in Table E1). Thus, future studies should focus on sociogeographic disadvantages to explore SDH complex and the disadvantages affecting patients with cancer where they live, work, and learn. By considering hospital access within patients' reach, we find that the availability of only community hospitals within 250 miles adversely affected survival. Our landmark time analysis reveals that lack of access to secondary and tertiary hospitals manifested its effect more profoundly on survival <90 days (HR, 1.44; CI, 1.09-1.89, $P = .010$). Geographic distance from specialized hospitals imposes an increased travel burden. Traveling long distances to access proper health services carries benefits that may outweigh the costs by enabling more patients to receive optimal treatment.[25] The composite score allows us to account for distance with income, which may impede the ability to travel.[26] To mitigate this disparity, a previous study suggested combining initial diagnostics locally with coordination and continuity of care at referral facilities.[27]

Our study holds significant implications for clinical practice. While the elements comprising SDH scores are not immediately modifiable for transitioning from SDH– to the advantageous SDH+ during the perioperative period, it is essential to acknowledge that the detrimental impact of SDH– factors affects both patients who are TOO– and TOO+. Policymakers should ensure equitable access to surgery and multimodality therapy to ensure equity of care for patients with locally advanced NSCLC. Moreover, thoracic care providers, including surgeons, can strategically allocate resources to mitigate this impact. For instance, involving social workers and case managers to offer social support and promoting adherence to prescribed care regimens in the preoperative and postoperative phases could indirectly counter the effects of SDH–. In addition, surgeons can directly enhance outcomes by optimizing TOO+ achievement irrespective of SDH status. This approach underscores the potential for targeted interventions and underscores the surgeon's role in driving positive treatment outcomes.

TABLE 4. Uni- and multivariable Cox regression analyses demonstrating factors associated with mortality over time in patients with NSCLC with pathologic nodal disease

Characteristic	Univariable module			Multivariable module		
	HR	95% CI	*P* value	aHR	95% CI	*P* value
SDH–	1.31	1.24-1.39	**<.001**	1.24	1.17-1.32	**<.001**
TOO+	0.73	0.69-0.77	**<.001**	0.78	0.73-0.82	**<.001**
Age (z score)	1.27	1.23-1.31	**<.001**	1.23	1.19-1.28	**<.001**
Female sex	0.70	0.67-0.74	**<.001**	0.74	0.70-0.79	**<.001**
Race/ethnicity						
White	–	–		–	–	
Black	0.88	0.80-0.97	**.013**	0.92	0.83-1.02	.12
Asian	0.60	0.50-0.72	**<.001**	0.67	0.56- 0.80	**<.001**
Hispanic	0.81	0.68-0.97	**.023**	0.79	0.66-0.95	**.012**
Other	0.63	0.44-0.90	**.012**	0.71	0.49-1.02	.066
Insurance						
Private insurance	–	–	–	–	–	
Medicare/other government	1.53	1.44-1.63	**<.001**	1.15	1.07-1.24	**<.001**
Medicaid/not insured	1.27	1.13-1.43	**<.001**	1.27	1.13-1.44	**<.001**
Charlson/Deyo score						
0	–	–	–	–	–	
1	1.20	1.13-1.28	**<.001**	1.14	1.07-1.21	**<.001**
2	1.43	1.31-1.56	**<.001**	1.26	1.15-1.38	**<.001**
3+	1.77	1.55-2.01	**<.001**	1.50	1.31-1.70	**<.001**
MIS						
Open/unspecified	—	—		—	—	
MIS	0.84	0.80-0.90	**<.001**	0.91	0.86-0.97	**.004**
MIS converted	1.13	1.00-1.27	**.046**	1.14	1.01-1.28	**.037**
Years of surgery (z score)	0.93	0.91-0.96	**<.001**	0.94	0.91-0.97	**<.001**
Academic/research program	0.78	0.74-0.83	**<.001**	0.89	0.84-0.96	**.001**
Lymph-vascular Invasion						
Not present	—	—		—	—	
Present	1.33	1.26-1.41	**<.001**	1.34	1.27-1.41	**<.001**
Hospital volume						
Low	—	—		—	—	
Moderate	0.87	0.82-0.93	**<.001**	0.93	0.87-0.99	**.028**
High	0.83	0.76-0.90	**<.001**	0.96	0.87-1.05	.3
Very high	0.59	0.51-0.68	**<.001**	0.69	0.59-0.81	**<.001**

Statistically significance is denoted in bold. Z score transformation = (value – mean)/standard deviation. *HR*, Hazard ratio; *CI*, confidence interval; *aHR*, adjusted hazard ratio; *SDH*, social determinants of health; *TOO*, textbook oncological outcomes; *MIS*, minimally invasive surgery (video-assisted thoracoscopy or robotic).

Previous studies have reported the benefits of minimally invasive surgery (MIS),[1] where MIS increased TOO likelihood by 47%; our study indicates that MIS effect on TOO decreased from 45% to 38% after adjusting for SDH and other variables. Interestingly, conversion to open surgery did not affect TOO but mortality risk was increased by 13%. This is consistent with a previous study indicating inferior outcomes in NSCLC.[28] Hospital volume in the top 5th percentile decreased mortality risk by 31%, and increased TOO likelihood by 93% as compared to low-volume hospitals. This highlights the role of surgeon competence and experience, as disadvantaged patients may lack access to facilities with NSCLC volume and proper MIS experience. Our previous analysis indicates that lymph node yield was significantly higher for MIS approaches,[29] which in turn may influence TOO.[1]

Numerous biological factors, including lung function, smoking status, obesity, cardiovascular disease, diabetes, and renal function, have implications for overall survival in patients with NSCLC.[30,31] However, the relationship between these biological risk factors and SDH remains inadequately characterized. Although it is plausible that patients with sociogeographic disadvantage indicators (SDH scores) may have more pronounced medical comorbidities that hinder treatment outcomes, the precise extent of the influence of these biological factors on the observed

SDH-driven overall survival in both TOO+ and TOO– cases remains speculative.

Our findings also support previous observations related to the important role of race on cancer outcomes and survival. Black patients were 31% less likely to achieve TOO than White patients. When OS was assessed, there was no significant difference in Black patients' survival after accounting for SDH score and other important variables. In contrast, Asian patients had 33% better OS and Hispanics had 21% better OS than non-Hispanic White patients (Figure E6). This remains to be further studied.

In future research, we advocate for an extensive exploration of surgical outcomes and SDH relationships, encompassing validation of the SDH metric's relevance and consistent association with outcomes in a distinct NSCLC patient cohort. Moreover, integrating the SDH metric score into a predictive model with established individual risk factors, such as smoking history, underlying lung quality, obesity, and other health conditions, and leveraging machine learning to explore interactions between these factors and SDH, could yield deeper insights.

Limitations

Our study's strengths included analysis of long-term survival and a large sample size; potential limitations include hospital-based cases included in the NCDB versus a potentially greater number of cases that might have been captured in a more inclusive database such as SEER. This may introduce a selection bias, particularly patients' disadvantages based on SDH, as the choice of hospitals depends on various factors. Furthermore, NCDB may underestimate readmission rates, one of TOO parameters, as it captures readmissions to the same hospital. TOO parameters differ based on the databases used in each study, which may not be captured by NCDB.[1-3] In our study, we defined lymph node evaluation as $\geq$5 rather than 10.[32] In addition, NCDB does not have granular data to explain the reason for delayed chemotherapy initiation. SDH impact on OS has speculative reasoning. Furthermore, SDH estimation based on zip codes may not reflect individual status; thus, a broader concept should be studied, such as sociodemographic disparities (encompassing ethnicity, marital status, family size, and other social, economical, and demographic attributes). Finally, the lack of longitudinal treatment data, recurrence, and complication-specific data limits our ability to assess disease-free survival.

FUTURE DIRECTIONS

Building upon the study findings and reviewer feedback, we identified promising avenues for future research:

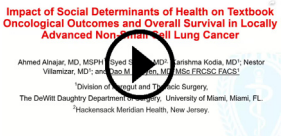
1. Validating and refining the SDH score. This includes using SDH for another NSCLC cohort as well as potentially customizing it for individual patients and incorporating preventable variables; making it more actionable for NSCLC.
2. Exploring interactions between SDH components and clinical factors using advanced machine-learning predictive models. Previously proven to illustrate the combined impact of variables.[33]
3. Considering SDH in longitudinal and multilevel analysis to track patients and the dynamic nature of SDH could identify prevention measures and meaningful community collaboration and education.
4. Collaborating with local cancer communities at the grassroots level, similar to previous initiative,[34,35] for improved NSCLC outcomes.
5. Since clinical trials remain the gold standard for assessing the effectiveness of interventions, future trials may address SDH factors to improve patient outcomes.
6. Developing educational programs for timely screening and referrals of disadvantaged patients.

CONCLUSIONS

In conclusion, although surgical treatment for patients with locally advanced NSCLC achieved TOO+ well, nonclinical and nonbiological SDH factors also independently impact the ability to achieve TOO+ and OS. This study highlights the importance of SDH on TOO-driven OS. Our analysis elucidates the value of an SDH score in successfully identifying patients with increased mortality risk despite adequate initial treatment. There remain key health care access and sociodemographic disparities to be studied under the SDH paradigm in addition to optimal therapy when treating NSCLC. Future research fosters discussions on SDH, contributing to effective health disparities management.

Webcast

You can watch a Webcast of this AATS meeting presentation by going to: https://www.aats.org/resources/the-impact-of-social-determinants-of-health-on-textbook-oncological-outcome-and-overall-survival-of-patients-with-locally-advanced-non-small-cell-lung-cancer.



Conflict of Interest Statement

The authors reported no conflicts of interest.

The *Journal* policy requires editors and reviewers to disclose conflicts of interest and to decline handling or reviewing manuscripts for which they may have a conflict

of interest. The editors and reviewers of this article have no conflicts of interest.

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Key Words: lung cancer, survival, equity, disparities, textbook outcomes

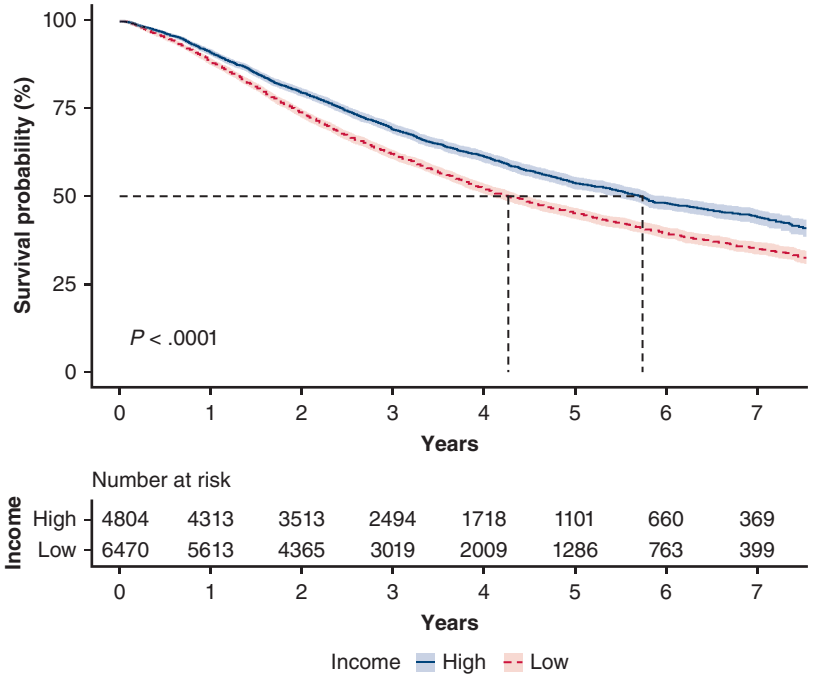

FIGURE E1. Income levels and survival (Kaplan–Meier curves, 95% CI).

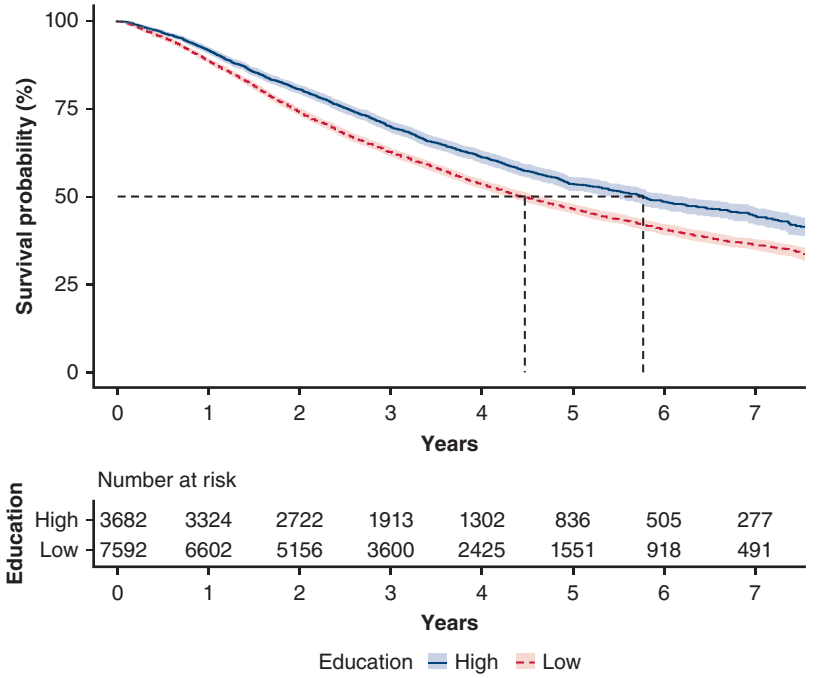

FIGURE E2. Education levels and survival (Kaplan–Meier curves, 95% CI).

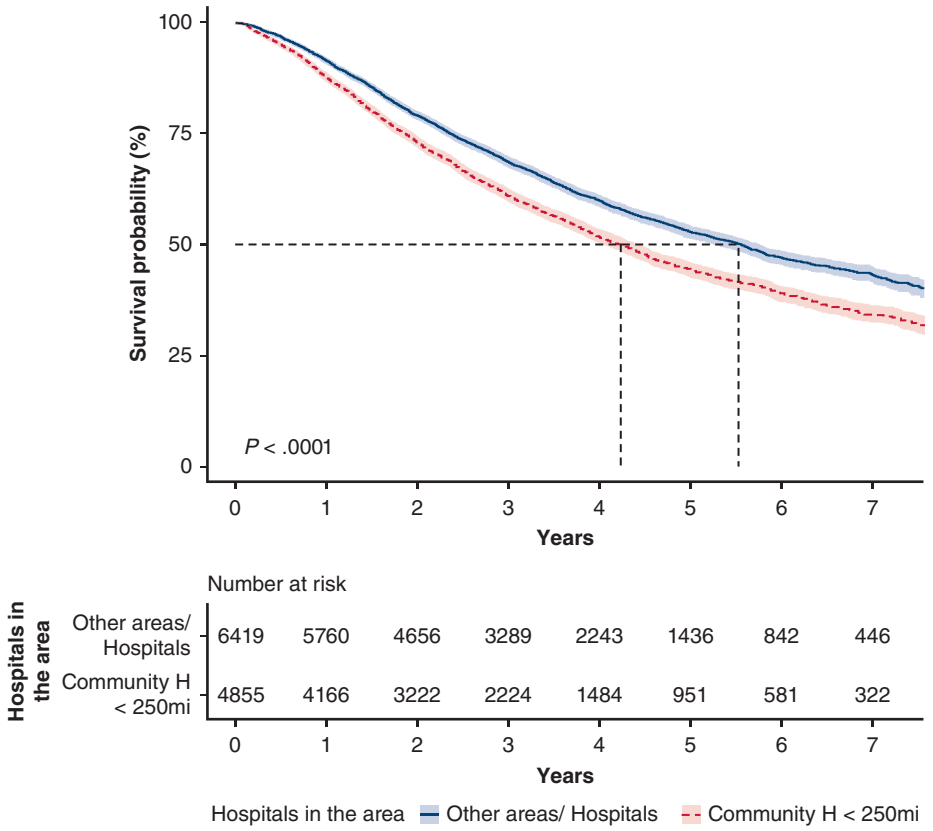

FIGURE E3. Hospital access and survival (Kaplan–Meier curves, 95% CI).

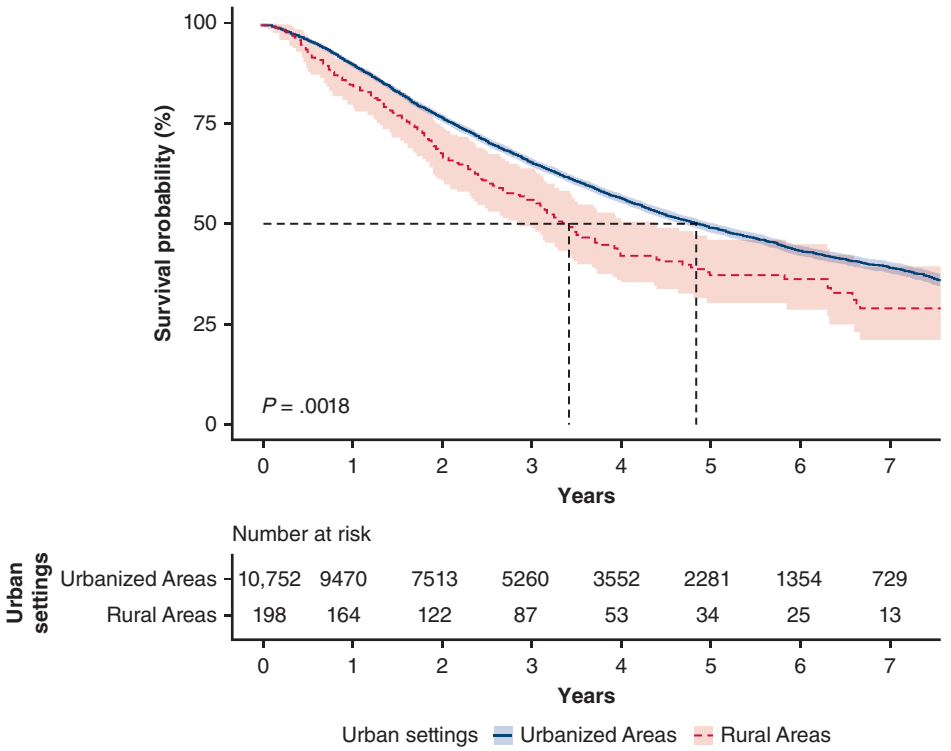

FIGURE E4. Urban settings and survival (Kaplan–Meier curves, 95% CI).

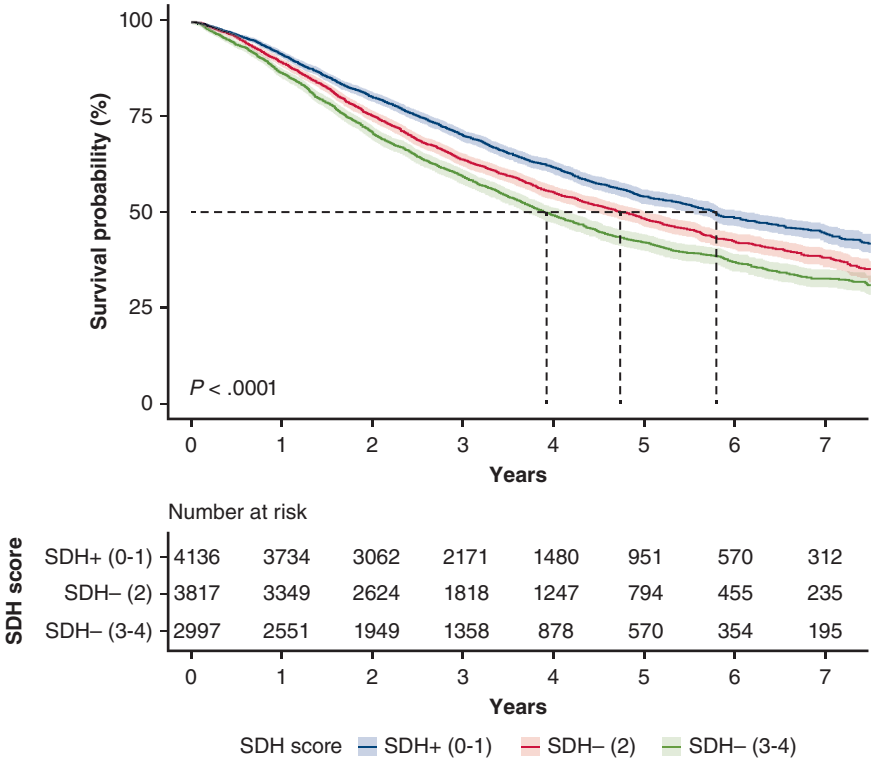

FIGURE E5. Social determinants of health (*SDH*) score and survival (3 groups, Kaplan–Meier curves, 95% CI).

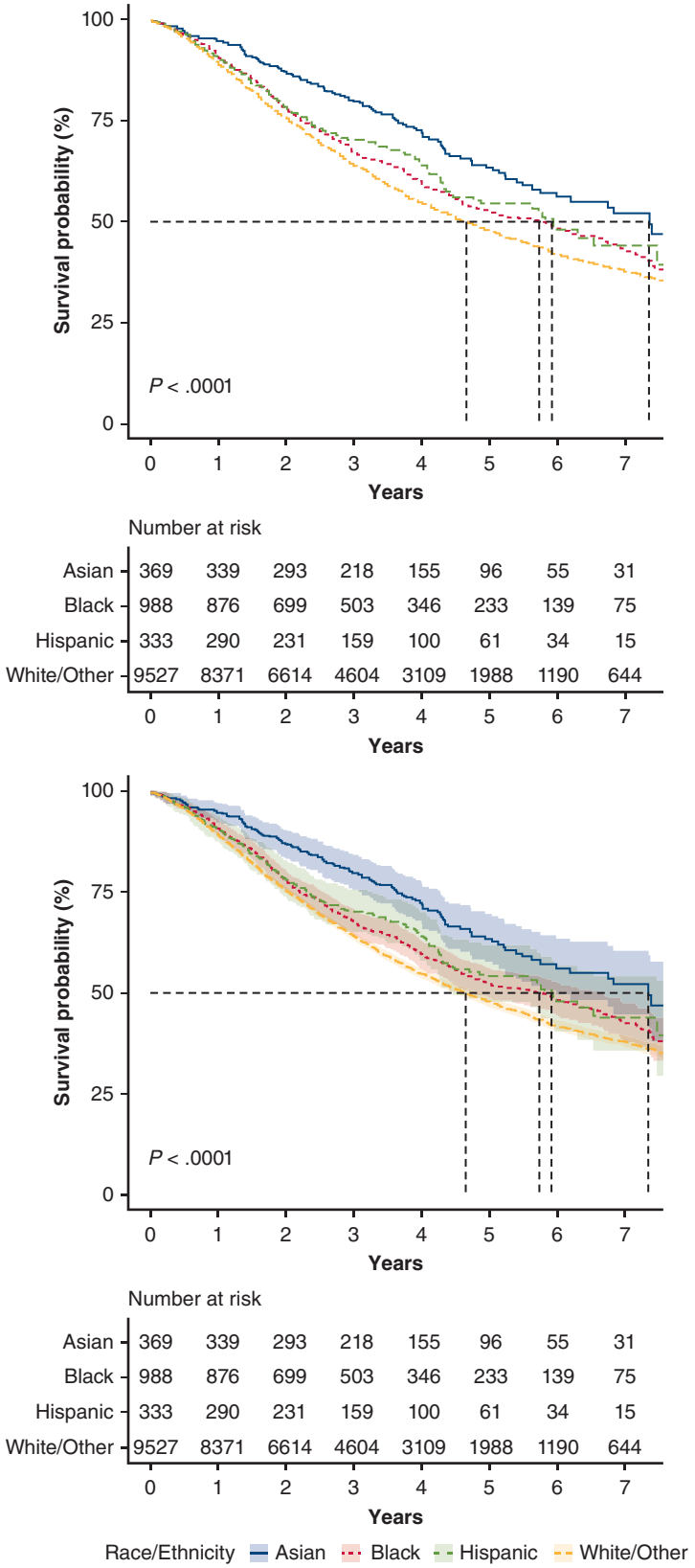

FIGURE E6. Race and ethnicity and survival (*upper*: Kaplan–Meier curve; *lower*: Kaplan–Meier curve with 95% CI).

TABLE E1. SDH composite score variables and their independent association with overall, short-, and long-term survival

Characteristic	Overall			<3-mo survival			3-mo+ survival		
	HR	95% CI	*P* value	HR	95% CI	*P* value	HR	95% CI	*P* value
Poor income	1.30	1.23-1.37	<**.001**	0.95	0.72-1.25	.7	1.30	1.23-1.38	<**.001**
Low education	1.28	1.20-1.36	<**.001**	0.98	0.72-1.32	.9	1.27	1.19-1.35	<**.001**
Community hospitals <250 mi	1.29	1.22-1.36	<**.001**	1.44	1.09-1.89	**.010**	1.27	1.20-1.34	<**.001**
Rural areas	1.35	1.12-1.62	**.002**	0.86	0.32-2.30	.8	1.36	1.12-1.65	**.002**

HR, Hazard ratio; *CI*, confidence interval; *SDH*, social determinants of health.

TABLE E2. Demographics of NSCLC with pathologic nodal disease stratified based on SDH score

Characteristic	N = 11,274*	SDH+ N = 4136*	SDH– N = 6814*	*P* value†
Age at diagnosis, y	67 (10)	68 (10)	67 (10)	**<.001**
Age, y (groups)				**<.001**
<60	2549 (23%)	834 (34%)	1640 (66%)	
60-69	3904 (35%)	1422 (37%)	2381 (63%)	
70-79	3714 (33%)	1419 (40%)	2173 (60%)	
80+	1107 (9.8%)	461 (43%)	620 (57%)	
Sex				**.029**
Male	4829 (43%)	1719 (37%)	2977 (63%)	
Female	6445 (57%)	2417 (39%)	3837 (61%)	
Race/ethnicity				**<.001**
Hispanic	333 (3.0%)	94 (28%)	237 (72%)	
White	9440 (84%)	3597 (39%)	5561 (61%)	
Black	988 (8.8%)	210 (22%)	755 (78%)	
Asian	369 (3.3%)	184 (51%)	177 (49%)	
Other	87 (0.8%)	33 (39%)	51 (61%)	
Unknown	57	18	33	
Education				**<.001**
High	3682 (33%)	3290 (92%)	283 (7.9%)	
Low	7592 (67%)	846 (11%)	6531 (89%)	
Income level				**<.001**
>150% FPL	3681 (36%)	2801 (79%)	756 (21%)	
100%-150% FPL	4678 (46%)	226 (5.0%)	4326 (95%)	
<100% FPL	1792 (18%)	15 (0.9%)	1731 (99%)	
Unknown	1123	1094	1	
Patient location				**<.001**
Metropolitan	9221 (84%)	3847 (42%)	5374 (58%)	
Urban	1531 (14%)	263 (17%)	1268 (83%)	
Rural	198 (1.8%)	26 (13%)	172 (87%)	
Unknown	324			
Textbook outcomes				**<.001**
TOO–	5879 (52%)	1973 (34%)	3754 (66%)	
TOO+	5395 (48%)	2163 (41%)	3060 (59%)	
TNM clinical stage				**.009**
Stage 1	7386 (66%)	2775 (39%)	4397 (61%)	
Stage 2	3869 (34%)	1358 (36%)	2401 (64%)	
Unknown	19	3	16	
LN pathologic stage				.078
N1	7366 (65%)	2663 (37%)	4500 (63%)	
N2	3908 (35%)	1473 (39%)	2314 (61%)	
Charlson/Deyo score				**<.001**
0	6056 (54%)	2419 (41%)	3458 (59%)	
1	3564 (32%)	1195 (34%)	2272 (66%)	
2	1198 (11%)	371 (32%)	798 (68%)	
3+	456 (4.0%)	151 (35%)	286 (65%)	
Insurance				**<.001**
Medicaid/not insured	798 (7.1%)	197 (25%)	589 (75%)	
Medicare/other government	6829 (61%)	2505 (38%)	4121 (62%)	
Private insurance	3547 (32%)	1404 (41%)	2038 (59%)	
Unknown	100	30	66	
Facility type				**<.001**
Academic	4147 (37%)	2040 (51%)	1950 (49%)	
Community	5279 (47%)	1211 (23%)	3971 (77%)	

(Continued)

TABLE E2. Continued

Characteristic	N = 11,274*	SDH+ N = 4136*	SDH– N = 6814*	*P* value†
Integrated	1789 (16%)	860 (50%)	860 (50%)	
Unknown	59	25	33	
Hospital volume				**<.001**
High	2337 (21%)	1084 (48%)	1184 (52%)	
Low	2646 (23%)	720 (28%)	1871 (72%)	
Moderate	5694 (51%)	2037 (37%)	3531 (63%)	
Very high	597 (5.3%)	295 (56%)	228 (44%)	
Surgical approach				**<.001**
Open/unspecified	6561 (58%)	2175 (34%)	4219 (66%)	
Robotic/VATS	4713 (42%)	1961 (43%)	2595 (57%)	
Postoperative radiotherapy				.6
No	8953 (79%)	3264 (38%)	5419 (62%)	
Unknown	279 (2.5%)	100 (36%)	174 (64%)	
Yes	2042 (18%)	772 (39%)	1221 (61%)	
Postoperative chemotherapy				**.027**
No	3020 (27%)	1049 (36%)	1886 (64%)	
Unk	392 (3.5%)	137 (37%)	229 (63%)	
Yes	7862 (70%)	2950 (39%)	4699 (61%)	
Chemotherapy after 3 mo	2823 (25%)	966 (35%)	1782 (65%)	**.001**

SDH, Social determinants of health; *FPL*, federal poverty level; *TOO*, textbook oncological outcomes; *TNM*, tumor, node, and metastasis staging system; *LN*, lymph node; *VATS*, video-assisted thoracic surgery. *n (%); mean (SD). †Pearson χ^2 test; Wilcoxon rank sum test.

TABLE E3. SDH score (3 groups) effect on TOO and survival

	Univariable module			Multivariable module		
TOO	**OR**	**95% CI**	***P* value**	**aOR***	**95% CI**	***P* value**
SDH score (3 groups)						
0-1	–	–	–	–	–	
2	0.78	0.72-0.85	**<.001**	0.85	0.77- 0.93	**<.001**
3-4	0.66	0.60-0.72	**<.001**	0.79	0.71- 0.88	**<.001**
Survival	**HR**	**95% CI**	***P* value**	**aHR**	**95% CI**	***P* value**
SDH score (3 groups)						
0-1	–	–	–	–	–	
2	1.24	1.16-1.33	**<.001**	1.23	1.15-1.32	**<.001**
3-4	1.48	1.39-1.59	**<.001**	1.32	1.22- 1.42	**<.001**

TOO, Textbook oncological outcomes; *OR*, odds ratio; *CI*, confidence interval; *aOR*, adjusted odds ratio; *SDH*, social determinants of health; *HR*, hazard ratio; *aHR*, adjusted hazard ratio. *Adjusted analysis by patient, operative, and hospital variables.