

# The impact of Social Determinants of Health on Management of Stage I Non-Small Cell Lung Cancer

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## **Abstract**

The impact of Social Determinants of Health on Management of Stage I Non-Small Cell Lung Cancer

## **Background**

Social Determinants of Health (SDOH) can be important contributors in health care outcomes. We hypothesized that certain SDOH independently impact the management and outcomes of stage I Non-Small Cell Lung Cancer (NSCLC).

## **Study Design**

Patients with clinical stage I NSCLC were identified from the National Cancer Database. The impact of SDOH factors on utilization of surgery, perioperative outcomes and overall survival were examined, both in bivariate and multivariable analyses.

## **Results**

A total of 236,140 patients were identified. In multivariate analysis, SDOH marginalization were associated with less frequent use of surgery, lower 5-year survival and, in surgical patients, more frequent use of open surgery and lower 90-day postoperative survival.

## **Conclusion**

SDOH disparities have a significant impact in the management and outcomes of stage I NSCLC. We identified SDOH patient groups particularly impacted by such disparities, in which higher utilization of surgery and minimally invasive approaches may lead to improved outcomes.

**Keywords:** Social Determinants; Disparities; marginalization, Lung Cancer; Under-resources; Healthcare Outcomes; Surgery.

## ***Introduction***

Lung cancer remains the leading cause of cancer-related deaths worldwide.<sup>1</sup> Despite overall advances in the management of lung cancer in all stages of disease, there is increasing evidence of outcome dissimilarities between different patient populations based on multiple social determinants of health (SDOH), such as income, education and race.<sup>2-6,35,36</sup> Several reasons have been proposed to explain these dissimilarities, including limited access to care, limited understanding of the disease process and financial or cultural constraints<sup>35,36</sup> in therapeutic decision making.<sup>7-12</sup> Most studies to date have examined the effect of racial disparities<sup>13-15</sup> and insurance status<sup>16, 17</sup> to overall lung cancer survival. The current study attempts to examine the effects of SDOH specifically to management of early stage Non-Small Cell Lung cancer (NSCLC)

## ***Patients and Methods***

The National Cancer Data Base (NCDB) is a large de-identified database operated by the Commission on Cancer and sponsored by the American College of Surgeons. It captures nearly 70% of cancer patients from over 1500 participating facilities in the United States.<sup>18</sup> This study was exempt from review by the Indiana University School of Medicine Institutional Review Board.

We queried the NCDB for patients diagnosed with clinical stage I NSLCC between January 1, 2010, and December 31, 2015, as there has been a change in the tumor staging system. Also, after January 1, 2010, the NCDB started capturing minimally invasive surgery data.<sup>39</sup> Patients with incomplete data (such as lack of histologic confirmation, treatment details and long-term outcomes) were excluded. The primary outcome measures were: utilization of surgery as first mode of treatment<sup>39</sup> and long-term overall survival (OS). Secondary outcomes were: utilization of minimally invasive surgery and 90-day mortality after surgery in those patients who underwent surgery. The following social determinants of health (SDOH) were

examined: income (using the quartiles of the median income from 2016 American Community Survey adjusted for the 2016 inflation for the patient's zip code at the time of diagnosis), education level (using the quartiles of the percent of adults 25 or older who did not graduate from high school for the patient's zip code from 2016 American Community Survey), patient insurance status and "urbanicity" level (using the typology published by the USDA Economic Research Service). In the former two variables we compared the outcomes between the highest and the lowest quartiles; the insurance variable had the following categories: Uninsured, Medicaid, Private and Medicare, with the first two (uninsured and Medicaid) considered the ones representing inequity. The "urbanicity" variable included Urban, Metropolitan and Rural categories.<sup>39</sup> The statistical analysis included bivariate analysis as well as non-parametric Kruskal-Wallis equality-of-populations rank test for non-normal continuous outcomes. To mitigate the effect of confounding patient, facility and disease factors, we performed multivariable analyses of all outcomes. The other outcomes studied were binary and hence we fitted multivariable logistic regressions. The included factors in the multivariable models were: patient age, gender,<sup>40</sup> Charlson-Deyo comorbidity index,<sup>37,38</sup> race (White vs non-White), income, education level, location of residence (metropolitan, urban or rural), type of treatment facility (academic or not), "crowfly" distance between patient's residence and treatment facility, tumor size and, for the Cox proportional hazard analysis, the inclusion of surgery as first treatment. To account for the correlation of patients treated at the same facility we also examined the standard error using cluster variance, facility ID being the clustering variable. We did a bivariate analysis of predicting mortality by no surgery and found that the risk of dying was more in patients who did not receive surgery. The significance of all SDOH were examined at p-value  $\leq 0.01$  and 99% confidence intervals were reported. All statistical analyses were performed in Stata software Version 14.2 (Stata Corporation, College Station, TX).

## **Results**

A total of 236,140 patients were identified. Their demographic information is shown in Table 1. The results of bivariate analysis between SDOH and the examined outcomes are included in Table 2. Overall, patients with SDOH marginalization had the lowest proportion of surgery utilization and lowest long-term median overall survival. Patients with under-resources going through surgery also had lower minimally invasive surgery utilization and lower rates of 90-day survival after surgery. The only exception to this finding was patients with Medicare insurance, who had similar outcomes to those with Medicaid or no insurance at all in all but one category (proportion of open surgery, where uninsured patients were the sole outliers).

The results of the multivariate analyses are seen in Table 3 for the primary outcomes and Table 4 for the secondary outcomes. Although additional risk factors were identified, the examined SDOH remained significant in all categories. While their impact varied depending on the outcomes, the most impactful effects were seen in the following categories: a. lower utilization of surgery in uninsured, Medicaid or low-income patients, b. lower utilization of minimally invasive surgery in uninsured or low-income patients, c. increased risk for postoperative mortality in uninsured, Medicaid, low income or low education patients and d. lower long-term overall survival in uninsured, Medicaid or low-income patients. Of note, the worse outcomes seen for Medicare patients compared to Medicaid and uninsured patients in bivariate analysis were in fact reversed after multivariate analysis, as shown in Tables 3 and 4.

In a separate survival analysis including only patients who underwent surgery, open surgery was a significant risk factor for long-term mortality (Hazard ratio 1.07, 99% CI 1.03 – 1.10).

## **Discussion**

An increasing body of literature has pointed out that disparities in socioeconomic factors have a significant impact on the care of patients with lung cancer.<sup>19-22</sup> In most studies the main focus of analysis has been on race and insurance status and their effects on the overall

population of patients with NSCLC. In addition, patients with lower socioeconomic status have a lower chance of getting any therapy at all for lung cancer.<sup>23-25</sup> It has been previously shown that African American patients with early stage lung cancer are less likely to undergo surgery.<sup>11</sup> In the current study, we sought to analyze the specific effect of social determinants of health, including income, education and population density (“urbanicity”) on the overall management and outcomes of stage I NSCLC. Unlike prior trials, we chose to focus on a subset of patients where therapeutic interventions have the highest potential for a curative outcome – and where perhaps actionable information on equity gaps might be most consequential.

Our findings suggest that SDOH exert a negative impact on many steps in the patient’s journey from treatment to survivorship. With respect to treatment choices in this patient cohort, we noted a significant negative effect of SDOH marginalization. While the comparison between surgical resection and stereotactic radiation is not a focus of this analysis, adherence to the current standard of care (i.e. surgical resection) was seen in a significantly lower proportion of patients with lower income and education levels, rural patients as well as patients with Medicaid or uninsured status. The reasons for this discrepancy are undoubtedly multiple, and possible include difficulties with access, provider bias and medical eligibility; however, it is also quite possible that socially disadvantaged may lead patient decision-making towards short-term goals (avoiding time off work and income disruption or avoiding travel to specialized treatment centers) in favor of possible long-term benefits (survival advantage after surgery).

Discrepancies in type of treatment extended even in patients receiving surgery: underprivileged patients were much less likely to undergo minimally-invasive surgery. The short-term benefits of minimally invasive approaches in early stage lung cancer have been demonstrated in multiple studies<sup>26-28</sup> and include lower postoperative mortality, shorter hospital stay, faster recovery and return to normal activities. Once again, several factors may explain this disadvantage, including selection of regional community hospitals for care that might not offer this option.<sup>29, 30</sup> A recent report<sup>31</sup> that rural populations may have limited access to thoracic surgeons could perhaps

provide an explanation for this finding and, in combination with our findings, may provide basis for future workforce considerations.

It should be noted, that these short-term benefits, and specifically earlier return to work, may exacerbate some of the biases against surgical therapy in this population. In essence, SDOH marginalization may act synergistically in creating gaps in care.

We also observed significantly worse postoperative outcomes in under-served patients in SDOH, specifically 90-day mortality. As confirmed by multivariate analysis these outcomes are affected by several other factors, in addition to insurance status, income and education levels. It should be noted however that the effect of these SDOH may be exacerbated further by the fact that an additional risk factor for postoperative mortality, namely open surgery, was also seen more frequently in underprivileged populations in our study.

Finally, we discovered that insurance status (specifically uninsured or Medicaid status) low-income status and low-education status were independent risk factors for long-term overall mortality in stage I NSCLC patients. Since the NCDB does not include cancer-specific mortality data, it is difficult to know whether this effect is related to gaps in the cancer care these patients received or to inequities in their overall care, which have been also shown to impact overall survival.<sup>32-34</sup>

One additional observation from our analysis involves the effect of SDOH factors other than the primary ones studied, specifically race and rural residence. Similarly, to other reports, African Americans had a significantly lower chance of receiving surgery for stage I NSCLC, but this didn't translate to a long-term survival disadvantage. Whether racial disparities impact care independently of income and education levels will need to be studied further.

The current study has certain limitations, primarily dictated by the available data in the NCDB. In addition to the lack of cancer-specific mortality, the database does not include detailed information on medical comorbidities, history of smoking, pulmonary function testing

and functional performance status, conditions that might affect the decision to pursue surgical therapy in stage I NSCLC as well as subsequent outcomes.

### ***Conclusion***

SDOH negatively impact the management and outcomes of patients with Stage I NSCLC. While this effect extends across multiple steps along the patient's journey, the most significant findings that may be amenable to intervention include lower utilization of surgery in uninsured, Medicaid, rural or low-income patients and lower utilization of minimally invasive surgery in uninsured, rural or low-income patients. Healthcare providers, healthcare institutions and policy makers may incorporate the findings of this study to affect decision making about patient care and health care planning.

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## Tables

Table 1: Patient Demographics

<b>Characteristics</b>	<b>Number of Patients n(%)</b>
<b>Total</b>	<b>236,140</b>
<b>Gender</b>	
Female	129,574 (54.9)
Male	106,566 (45.1)
<b>Age (median , IQR*)</b>	71 (IQR 13)
<b>Race</b>	
White	207,508 (87.9)
African American	20,609(8.7)
Other	8,023(3.4)
<b>Charlson Deyo Comorbidity Index</b>	
0	124,659 (52.8)
1	71,249 (30.2)
2	27,707 (11.7)
≥3	12,525 (5.3)
<b>Insurance</b>	
Uninsured	3,158 (1.4)
Medicaid	10,672 (4.7)
Medicare	160,302 (70.2)
Private	54,352 (23.8)
<b>Urban vs Rural</b>	
Metropolitan	190,506 (82.7)
Urban	35,110 (15.2)
Rural	4,729 (2.1)
<b>Type of facility</b>	
Academic	86,838 (36.8)
Non-academic	149,302 (63.23)
<b>Distance in miles from treating facility (median, IQR*)</b>	10.6 (IQR 21.2)

\*IQR=Interquartile Range

Table 2: Bivariate Analysis

	Surgery performed in stage I NSCLC (%)	Proportion of open surgery (%)	90-day mortality (%)	Median Survival, Stage I pts (months)
<b>Insurance status</b>				
Uninsured	68.4*	61.7	2.4*	71.2
Medicaid	67.1*	56.5	2.4*	60.9
Private	78.2	54.6	1.6	87.2
Medicare	59.8	53.6	3.7	50
<b>Income Quartile</b>				
Lowest Quartile	59.7	60.5	3.7	51
Highest Quartile	68.8	49.5	2.4	66.7
<b>High school graduation quartile</b>				
Lowest Quartile	61.4	58.8	3.6	54.4
Highest Quartile	67.6	49.8	2.4	65
<b>Urbanicity</b>				
Rural	60.9*	63.0	3.3*§	50.7*
Urban	61.4*	60.3	3.5§	52*
Metropolitan	64.5	53.1	2.9*	60.3

All results significant at  $p < 0.001$ , except in pairs denoted with \* or § (where  $p = \text{NS}$ )

Table 3: Multivariate Analysis: Primary Outcomes (**bold** denotes  $p < 0.0001$ ). Ratios over 1 signify a positive association with the respective outcome (i.e. increasing value)

Variables	No Surgery		Overall Mortality	
	Adjusted Odds		Hazard	
	ratio	99% CI	ratio	99% CI
<b>Age</b>	<b>1.07</b>	(1.07 - 1.07)	<b>1.03</b>	1.03 - 1.04
<b>Gender</b>				
Female vs Male	<b>0.95</b>	(0.93 - 0.97)	<b>0.67</b>	0.65 - 0.69
<b>Race</b>				
African American vs White	<b>1.34</b>	(1.29 - 1.41)	0.97	0.92 - 1.03
Other vs White	<b>0.76</b>	(0.71 - 0.82)	<b>0.66</b>	0.60 - 0.73
<b>Facility type</b>				
Academic vs Nonacademic	<b>0.86</b>	(0.84 - 0.87)	<b>0.90</b>	(0.87 - 0.93)
<b>Charlson Deyo CI</b>				
0 (reference)				
1	<b>0.73</b>	(0.71 - 0.75)	<b>1.23</b>	(1.19 - 1.27)
2	<b>0.89</b>	(0.86 - 0.93)	<b>1.45</b>	(1.38 - 1.51)
≥3	<b>1.20</b>	(1.14 - 1.26)	<b>1.80</b>	(1.69 - 1.92)
<b>Insurance</b>				
Medicaid vs Uninsured	1.01	(0.90 - 1.14)	1.11	(0.96 - 1.28)
Private vs Uninsured	<b>0.50</b>	(0.44 - 0.55)	<b>0.74</b>	(0.65 - 0.84)
Medicare vs Uninsured	<b>0.60</b>	(0.54 - 0.67)	<b>0.86</b>	(0.76 - 0.98)
Private vs Medicaid	<b>0.49</b>	0.46 - 0.52)	<b>0.73</b>	(0.69 - 0.77)
Medicare vs Medicaid	<b>0.59</b>	(0.56 - 0.63)	<b>0.85</b>	(0.80 - 0.89)
<b>Income</b>				
Lowest Quartile (reference)				
Highest Quartile	<b>0.67</b>	(0.64 - 0.71)	<b>0.82</b>	(0.78 - 0.87)
<b>High School Education</b>				
Lowest Quartile (reference)				
Highest Quartile	<b>0.93</b>	(0.88 - 0.97)	<b>0.92</b>	(0.87 - 0.97)



Variables	No Surgery		Overall Mortality	
	Adjusted Odds		Hazard	
	ratio	99% CI	ratio	99% CI
<b>Surgery (No vs Yes)</b>	NA		<b>1.07</b>	(1.03 - 1.10)
<b>Tumor Size (in mm<sup>**</sup>)</b>	<b>NA</b>		<b>1.01</b>	(1.01 - 1.01)
<b>Urbanicity</b>				
Metropolitan (reference)				
Urban	1.06	(0.97 - 1.15)	<b>1.06</b>	(1.02 - 1.11)
Rural	<b>1.06</b>	(1.02 - 1.10)	1.07	(0.96 - 1.18)

<sup>\*\*</sup> Each mm increase in size, the hazard ratio increases by 1%

Table 4: Secondary outcomes (surgery patients only) – **bold** denotes  $p < 0.0001$ . Ratios over 1 signify a positive association with the respective outcome (i.e. increasing value)

Variables	Open Surgery		90 Day Mortality after Surgery	
	Adjusted Odds ratio	99% CI	Adjusted Odds ratio	99% CI
<b>Age</b>	1.00	(0.99 - 1.00)	<b>1.05</b>	(1.04 - 1.06)
<b>Gender</b>				
Female vs Male	<b>0.90</b>	(0.87 - 0.93)	<b>0.55</b>	(0.50 - 0.61)
<b>Race</b>				
African American vs White	1.05	(0.99 - 1.11)	0.87	(0.72 - 1.04)
Other vs White	<b>0.87</b>	(0.83 - 0.93)	<b>0.60</b>	(0.43 - 0.82)
<b>Facility type</b>				
Academic vs Nonacademic	<b>0.60</b>	(0.59 - 0.62)	<b>0.79</b>	(0.71 - 0.87)
<b>Charlson Deyo CI</b>				
0 (reference)				
1	<b>0.95</b>	(0.92 - 0.98)	<b>1.12</b>	(1.01 - 1.25)
2	0.97	(0.93 - 1.02)	<b>1.38</b>	(1.21 - 1.58)
≥3	<b>0.88</b>	(0.82 - 0.94)	<b>1.65</b>	(1.37 - 1.99)
<b>Insurance</b>				
Medicaid vs Uninsured	<b>0.81</b>	(0.71 - 0.93)	0.97	(0.61 - 1.54)
Private vs Uninsured	<b>0.81</b>	(0.72 - 0.92)	<b>0.61</b>	(0.40 - 0.93)
Medicare vs Uninsured	<b>0.78</b>	(0.70 - 0.88)	0.81	(0.53 - 1.22)
Private vs Medicaid	1.00	(0.93 - 1.07)	<b>0.63</b>	(0.49 - 0.82)
Medicare vs Medicaid	0.96	(0.89 - 1.03)	0.83	(0.65 - 1.07)
<b>Income</b>				
Lowest Quartile (reference)				
Highest Quartile	<b>0.74</b>	(0.70 - 0.79)	<b>0.74</b>	(0.62 - 0.87)
<b>High School Education</b>				
Lowest Quartile (reference)				
Highest Quartile	0.92	(0.87 - 0.97)	<b>0.81</b>	(0.67 - 0.96)
<b>Open (No vs Yes)</b>	NA		<b>1.46</b>	(1.33 - 1.61)
<b>Tumor Size (1mm)</b>	NA		<b>1.01</b>	(1.01 - 1.01)
<b>Urbanicity</b>				
Metropolitan (reference)				

Urban	<b>1.16</b>	(1.11 - 1.22)	0.99	(0.87 - 1.13)
Rural	<b>1.25</b>	(1.12 - 1.39)	0.94	(0.69 - 1.29)

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**Précis:** Using data from the National Cancer Database, we demonstrated that disparities in social determinants of health impacted negatively both the care provided and the outcomes of patients with stage I non-small cell lung cancer.