How Do Social Factors Explain Outcomes in Non–Small-Cell Lung Cancer Among Hispanics in California? Explaining the Hispanic Paradox

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ABSTRACT

Purpose

Hispanics in the United States have lower age-adjusted mortality resulting from non–small-cell lung cancer (NSCLC) compared with non-Hispanic whites (NHWs). The purpose of this study was to evaluate individual, clinical, and neighborhood factors in survival among Hispanics with NSCLC.

Patients and Methods

We performed a retrospective analysis of NHWs and Hispanics with NSCLC between 1998 and 2007 in the California Cancer Registry (follow-up to December 2009). Kaplan-Meier curves depict survival by nativity for Hispanics with NSCLC. Cox proportional hazards models estimated hazard of mortality by race with adjustment for individual (age, sex, marital status), clinical (histologic grade, surgery, irradiation, chemotherapy), and neighborhood factors (neighborhood socioeconomic status, ethnic enclave).

Results

We included 14,280 Hispanic patients with NSCLC. Foreign-born Hispanics had 15% decreased risk of disease-specific mortality resulting from NSCLC compared with NHWs (hazard ratio [HR], 0.85; 95% CI, 0.83 to 0.88) after adjustment for individual, clinical, and neighborhood factors. After adjustment for individual factors, compared with US-born Hispanics, foreign-born Hispanics had 10% decreased risk of disease-specific mortality (HR, 0.90; 95% CI, 0.87 to 0.96). Clinical and neighborhood factors slightly moderated the survival benefit for foreign-born patients. A modestly more pronounced survival advantage was seen for foreign-born Hispanics living in low socioeconomic and high Hispanic enclave neighborhoods as compared with US-born Hispanics (HR, 0.86; 95% CI, 0.81 to 0.90).

Conclusion

Foreign-born Hispanics with NSCLC have a decreased risk of disease-specific mortality compared with NHWs and US-born Hispanics with NSCLC. Neighborhood factors slightly moderate this survival advantage. This survival advantage is slightly more pronounced in lower socioeconomic and higher Hispanic enclave neighborhoods.

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INTRODUCTION

Studies have demonstrated that Hispanics have 50% lower lung cancer mortality rates than non-Hispanic whites (NHWs)¹⁻⁵; however, Hispanics are more likely to be diagnosed at advanced stages^{1-4,6} and less likely to receive treatment.^{7,8} Relatively lower cancer mortality among US Hispanics is consistent with the so-called Hispanic paradox, referring to better health relative to NHWs despite disadvantages in socioeconomic status (SES).⁹⁻¹¹

Reasons for the observed NSCLC mortality paradox among US Hispanics have not been identified. In other health outcomes, the so-called immigrant paradox (ie, tendency of foreign-born to outlive native-born populations despite lower SES) has been evaluated,^{10,12,13} with the suggestion that the Hispanic

paradox may hold true only for the foreign born.¹⁴ One recent study using SEER data demonstrated the survival advantage persists for US Hispanics, despite nativity.⁶ However, this study excluded Hispanic patients with unknown birthplaces, despite previous findings that those with unknown birthplaces are more likely to be US born and alive; thus, exclusion can bias survival statistics.¹⁵⁻¹⁹ Differential emigration, or possibility of noncapture of mortality outcomes among Hispanics who migrate to their native countries, also does not explain the disparity in mortality.^{9,13,20-22} The extent to which the immigrant paradox influences NSCLC mortality has not been examined.

Another proposed mechanism for the Hispanic paradox is culturally rooted protection in the form of greater community support after diagnosis; increased social support is associated with improved cancer

Table 1. Demographic and Clinical Characteristics for Hispanics With NSCLC in California by Nativity, 1988 to 2007*

Characteristic	US Born (n = 7,206; %)	Foreign Born (n = 7,074; %)	P
Sex			< .001
Male	55.1	62.0	
Female	44.9	38.0	
Age at diagnosis, years			< .001
< 60	26.8	26.6	
60 to 69	33.1	27.7	
≥ 70	40.1	45.7	
Marital status at diagnosis			< .001
Married	55.3	58.1	
Never married	11.5	12.8	
Previously married	30.6	26.3	
Unknown	2.6	2.9	
Disease stage			< .001
Localized	16.0	12.6	
Regional	21.8	19.0	
Advanced	55.3	60.1	
Unknown	6.8	8.4	
Histology			.058
Adenocarcinoma	40.7	41.7	
Bronchioalveolar	4.3	5.2	
Large cell	7.5	7.7	
Mixed	2.0	1.7	
Squamous	24.2	22.7	
Other non-small cell	9.3	9.1	
Undifferentiated/other	11.9	11.9	
Grade			.0035
1	4.4	4.6	
2	15.8	14.1	
3	35.0	33.6	
4	5.6	5.6	
Unknown	39.3	42.1	
Surgery			< .001
Yes	25.1	19.9	
No	74.7	79.9	
Unknown	0.2	0.1	
Irradiation			< .001
Yes	46.7	41.9	
No	53.2	58.1	
Unknown	0.1	0.0	
Chemotherapy			.0151
Yes	36.7	36.5	
No	61.2	60.7	
Unknown	2.1	2.8	
Neighborhood SES, quintile			< .001
1 (lowest)	25.5	39.7	
2	25.6	24.4	
3	21.7	16.5	
4	16.4	12.0	
5	10.8	7.5	
Ethnic enclave, quintile			< .001
1 (lowest)	10.7	4.2	
2	14.9	8.5	
3	19.1	13.0	
4	26.8	24.9	
5	28.5	49.4	
Neighborhood SES plus ethnic enclave			< .001
High SES, low enclave	34.2	20.6	
High SES, high enclave	14.8	15.3	

(continued in next column)

Table 1. Demographic and Clinical Characteristics for Hispanics With NSCLC in California by Nativity, 1988 to 2007* (continued)

Characteristic	US Born (n = 7,206; %)	Foreign Born (n = 7,074; %)	P
Low SES, low enclave	10.5	5.1	
Low SES, high enclave	40.6	58.9	

Abbreviations: NSCLC, non-small-cell lung cancer; SES, socioeconomic status.
*Follow-up through December 31, 2009.

survival.²³⁻²⁶ Among particular populations, specifically Hispanics and Asians/Pacific Islanders (As/Pis), this protective effect may operate through ethnic enclaves. Ethnic enclaves are geographic units with dense social networks and widely held cultural norms, practices, and infrastructures for social advancement.²⁷⁻²⁹ These environments are health promoting because residents share community attitudes about health and behaviors.²⁷⁻²⁹ However, ethnic enclaves also have attributes that worsen health because they are of lower SES with less access to medical care²⁹ and greater access to ethnic foods, which may be either healthier or less healthy than conventional foods.³⁰ Previous work has demonstrated the mixed influence of ethnic enclaves on cancer incidence and survival for Hispanics and As/Pis.³¹⁻³⁴ In NSCLC specifically, one SEER study found that Hispanics living in census tracts with relatively higher percentages of Hispanics—one component of the definition of Hispanic enclave—were more likely to be diagnosed at advanced stages.³⁵ For Hispanic patients with NSCLC, the joint impact of nativity, neighborhood ethnic enclave, and neighborhood SES on survival has not been studied.

Therefore, we aimed to better understand the Hispanic paradox in NSCLC by comparing survival among foreign-born Hispanics, US-born Hispanics, and NHWs. We further aimed to investigate clinical and neighborhood factor influences on outcomes from NSCLC for Hispanics. We hypothesized that foreign-born Hispanics would have better survival rates than NHWs and US-born Hispanics, but survival advantage would be moderated by residence in ethnic enclaves. We used California Cancer Registry (CCR) data enhanced with nativity, neighborhood-level ethnic enclave, and SES data. This study was motivated by our belief that better understanding of the influence of social factors can facilitate identification of protective factors for NSCLC outcomes.

PATIENTS AND METHODS

We obtained CCR data (comprising three SEER registries) on all California residents diagnosed with NSCLC (International Classification of Diseases for Oncology [third edition] site codes C34.0 to C34.9) between years 1988 and 2007. These histologic codes were designated as NSCLC: 8010, 8012, 8013, 8020, 8046, 8050 to 8052, 8070 to 8078, 8140, 8141, 8143, 8147, 8250 to 8255, 8260, 8310, 8430, 8480, 8481, 8490, 8560, and 8570 to 8575. We excluded patients with small-cell lung cancer (8041 to 8045) and carcinoid (8240) or neuroendocrine tumors (8246). Patient characteristics included age, residential address at diagnosis, sex, race, Hispanic ethnicity,³⁶ place of birth, marital status, SEER summary stage (localized, regional, distant), histologic subtype (adenocarcinoma, bronchioloalveolar carcinoma, squamous cell, large cell, mixed histology, other non-small cell, or undifferentiated), and first-course treatment (surgery, irradiation, chemotherapy). We included patients with NSCLC whose ethnicity was classified as NHW or Hispanic/Latino regardless of race. Classification of Hispanic ethnicity, which is believed to underascertain Hispanics, was improved by application of the North American Association of Central Cancer Registries Hispanic identification algorithm.³⁶ We did not further classify Hispanics by country of origin, because of a high proportion (> 40%) of missing data; however, 84% of California Hispanics are of Mexican

origin, and 9% are of Central American origin.³⁶ We excluded 2,137 Hispanics and 16,796 NHWs who were recorded as having negative or zero survival and 365 Hispanics who had unknown ethnic enclave.

Cancer registry or death certificate data on birthplace, used to determine nativity (US v foreign born) were available for 90.8% of patients; we previously found this information to be highly accurate.^{15,16} For 9.2% of patients with unknown birthplace, the first five digits of each patient's Social Security number (SSN), which indicate year of issuance, were used with date of birth to calculate age of issuance to impute nativity based on validated methods.^{15,37,38} Imputed nativity based on age of SSN issuance, compared with self-reported nativity, has 81% sensitivity and 80% specificity for classifying foreign birthplace when Hispanic patients who received their SSNs at age ≥ 20 years are imputed as foreign born and those who received their SSNs at age < 20 years are imputed as US born.³¹ This age cut point was determined by comparison with self-reported nativity from interviews with 1,227 Hispanic patients³¹ and maximization of the area under the receiver-operating characteristic curve.

Patients' addresses at diagnosis were geocoded using a parcel-based method and linked to census block group–level composite index of SES incorporating 1990 (for those diagnosed from 1988 to 1995) and 2000 (for those diagnosed from 1996 onward) US Census data on education, occupation, unemployment, household income, poverty, rent, and house values.^{10,39,40} Cancer registries do not collect data on individual-level patient SES.

Ethnic enclave composite index was developed through principal components analysis and includes 1990 and 2000 US Census block group–level data on percent linguistically isolated, percent linguistically isolated who speak Spanish, percent speaking limited English, percent Spanish speaking who speak limited English, percent recent immigrants, percent Hispanic, and percent foreign born.^{31–33} Neighborhood measures were classified into quintiles based on distributions across California.

Survival time, in months, was defined as time from diagnosis to whichever of the following occurred first: death resulting from any cause (overall survival) or from lung cancer (specific survival), date of last known contact, or end of study follow-up (December 31, 2009). Sensitivity analyses were conducted that conservatively assumed all foreign-born Hispanics who were last noted as being alive and had a date of last known contact > 24 months before the study end date had died as a result of lung cancer. χ^2 test of independence was used to test statistical significance of differences in individual-, clinical-, and neighborhood-level variables between Hispanic and NHW patients. To assess independent influence of race/ethnicity, neighborhood SES, and neighborhood enclave status while adjusting for other known risk factors (eg, sex, stage, and treatment modalities), multivariable stage-stratified Cox proportional hazards models estimated hazard ratios (HRs) with 95% CIs for overall and lung cancer–specific mortality. Survival models were adjusted for block group clustering. Numbers of patients per block group were too small to warrant multilevel analyses. We tested the proportionality assumption through a thorough analysis of scaled Schoenfeld residuals.⁴¹ Statistical

analyses were performed using SAS software (version 9.3; SAS Institute, Cary, NC). A *P* value less than .05 was considered significant. All statistical tests were two sided. The study was approved by the Stanford University Institutional Review Board.

RESULTS

There were 14,280 Hispanic patients with NSCLC included in the study. Fifty percent were foreign born (Table 1). A higher proportion of foreign-born (60.1%) than US-born patients (55.3%) had advanced disease, and adenocarcinoma was the most common histologic subtype. The majority of patients did not receive treatment, with slightly higher nonreceipt among the foreign born than US born for surgery and irradiation. Foreign-born Hispanics were more likely to live in the lowest SES neighborhoods and highest Hispanic enclaves. Kaplan-Meier unadjusted overall and lung cancer–specific survival showed a trend toward improved survival among NHWs with NSCLC compared with foreign-born and US-born Hispanics (Fig 1).

Unadjusted logistic regression models demonstrated that foreign-born patients were 40% more likely than US-born patients to be diagnosed with advanced versus localized disease, 25% more likely to be diagnosed with advanced than regional disease, and 12% more likely to be diagnosed with regional versus localized disease (data not shown). In fully adjusted models for age, sex, year of diagnosis, marital status, and neighborhood SES/ethnic enclave, for some stages, foreign-born patients were less likely to receive (first-course) treatment as compared with US-born patients. Specifically, compared with US-born patients, foreign-born men were 22% less likely to receive surgery and 10% less likely to undergo irradiation for distant-stage disease; foreign-born women were 34% less likely to receive chemotherapy, 22% less likely to undergo irradiation for localized disease, and 23% less likely to undergo irradiation for distant disease (data not shown).

Compared with NHWs, foreign-born Hispanics had an 8% decreased relative risk of overall mortality after adjustment for individual factors (age, stage, sex, year of diagnosis, marital status) and treatment (HR, 0.92; 95% CI, 0.90 to 0.95; Table 2). After further adjustment (neighborhood SES $\times$ ethnic enclave), foreign-born Hispanics had a 10% lower relative risk of death (HR, 0.90; 95% CI, 0.88 to 0.93), whereas US-born Hispanics had the same survival as NHWs (HR, 1.00; 95% CI, 0.97 to 1.02). These findings were more pronounced in cancer-specific mortality

Fig 1. Kaplan-Meier survival curves of (A) overall and (B) cancer-specific survival among non-Hispanic whites and Hispanics with non-small-cell lung cancer by nativity, California, 1988 to 2007, with follow-up through December 31, 2009.

Table 2. Cox Proportional Hazards Models for Mortality for NHWs and Hispanics With NSCLC in California by Nativity, 1988 to 2007*

Model No.†	Overall Mortality						Cancer-Specific Mortality					
	NHWs (n = 137,321) HR	US Born (n = 7,206)		Foreign Born (n = 7,074)		NHWs (n = 141,060) HR	US Born (n = 7,206)		Foreign Born (n = 7,074)		Sensitivity (n = 7,074)‡	
		HR	95% CI	HR	95% CI		HR	95% CI	HR	95% CI	HR	95% CI
Overall												
1	1.0	1.04	1.01 to 1.06	0.98	0.96 to 1.01	1.0	1.31	1.00 to 1.06	0.92	0.90 to 0.95	0.96	0.94 to 0.99
2	1.0	1.01	0.99 to 1.04	0.92	0.90 to 0.95	1.0	1.00	0.98 to 1.03	0.87	0.84 to 0.89	0.90	0.88 to 0.93
3	1.0	1.00	0.97 to 1.02	0.90	0.88 to 0.93	1.0	0.99	0.97 to 1.02	0.85	0.83 to 0.88	0.89	0.86 to 0.91
Men												
1	1.0	1.04	1.01 to 1.08	1.03	0.99 to 1.07	1.0	1.05	1.01 to 1.09	1.01	0.97 to 1.05	1.01	0.97 to 1.05
2	1.0	1.02	0.99 to 1.06	1.00	0.96 to 1.04	1.0	1.03	0.99 to 1.06	0.97	0.94 to 1.02	0.97	0.94 to 1.02
3	1.0	1.01	0.97 to 1.04	0.98	0.95 to 1.02	1.0	1.02	0.98 to 1.05	0.97	0.93 to 1.01	0.96	0.93 to 1.01
Women												
1	1.0	1.00	0.96 to 1.03	0.96	0.92 to 1.00	1.0	0.93	0.90 to 0.96	0.91	0.87 to 0.95	0.95	0.91 to 1.00
2	1.0	0.93	0.90 to 0.96	0.91	0.87 to 0.95	1.0	0.87	0.84 to 0.90	0.86	0.82 to 0.90	0.90	0.86 to 0.94
3	1.0	0.91	0.88 to 0.94	0.89	0.85 to 0.93	1.0	0.85	0.82 to 0.89	0.85	0.81 to 0.89	0.89	0.85 to 0.93

Abbreviations: HR, hazard ratio; NHW, non-Hispanic white; NSCLC, non-small-cell lung cancer; SES, socioeconomic status.

*Follow-up through December 31, 2009.

†Model 1: adjusted for age, sex, stage, histology, year of diagnosis, and marital status; model 2: model 1 adjusted for surgery, irradiation, and chemotherapy; model 3: model 2 adjusted for neighborhood SES/ethnic enclave.

‡Of 834 censored foreign-born Hispanics (431 men, 403 women), if follow-up > 24 months (124 men, 89 women), event was assumed.

models. When stratified by men and women, comparable patterns were only seen for foreign-born women for all-cause and cause-specific survival. Table 2 demonstrates that in sensitivity analyses, the statistically significant HRs for foreign-born Hispanics relative to NHWs shifted toward the null but remained statistically significant.

Table 3 compares survival between foreign- and US-born Hispanics and demonstrates that foreign-born Hispanics had 9% lower relative risk of overall mortality (HR, 0.91; 95% CI, 0.88 to 0.95) and 13% lower mortality resulting from NSCLC compared with US-born Hispanics (HR, 0.87; 95% CI, 0.83 to 0.90) after adjustment for individual, clinical, and neighborhood factors. Similar effects were seen for

Hispanic men and women. Sensitivity analyses conducted for lung cancer-specific survival showed that HRs remained statistically significant for men but not for women.

Stratified results by neighborhood SES × ethnic enclave demonstrated that foreign-born Hispanics experienced improved survival independent of neighborhood composition (Table 4). However, a modestly more pronounced survival advantage was seen for foreign-born Hispanics living in low SES neighborhoods with high enclave status as compared with US-born Hispanics living in those neighborhoods (HR, 0.86; 95% CI, 0.81 to 0.90). These effect associations were more pronounced for men than women. Consistently across all

Table 3. Cox Proportional Hazards Models for Mortality in Hispanics With NSCLC in California by Nativity, 1988 to 2007*

Model No.†	Overall Mortality			Cancer-Specific Mortality				
	US Born (n = 7,206) HR	Foreign Born (n = 7,074)		US Born (n = 7,206) HR	Foreign Born (n = 7,074)		Sensitivity (n = 7,074)‡	
		HR	95% CI		HR	95% CI	HR	95% CI
Overall								
1	1.0	0.95	0.92 to 0.99	1.0	0.90	0.87 to 0.94	0.94	0.91 to 0.98
2	1.0	0.92	0.89 to 0.96	1.0	0.87	0.84 to 0.91	0.91	0.88 to 0.95
3	1.0	0.91	0.88 to 0.95	1.0	0.87	0.83 to 0.90	0.90	0.87 to 0.94
Men								
1	1.0	0.96	0.92 to 1.00	1.0	0.89	0.85 to 0.94	0.93	0.89 to 0.98
2	1.0	0.92	0.88 to 0.96	1.0	0.86	0.81 to 0.90	0.89	0.85 to 0.94
3	1.0	0.91	0.87 to 0.97	1.0	0.85	0.81 to 0.89	0.88	0.84 to 0.93
Women								
1	1.0	0.95	0.88 to 1.00	1.0	0.92	0.86 to 0.97	0.96	0.90 to 1.02
2	1.0	0.93	0.88 to 0.98	1.0	0.91	0.85 to 0.96	0.95	0.89 to 1.01
3	1.0	0.92	0.87 to 0.97	1.0	0.90	0.84 to 0.95	0.94	0.88 to 1.00

Abbreviations: HR, hazard ratio; NSCLC, non-small-cell lung cancer; SES, socioeconomic status.

*Follow-up through December 31, 2009.

†Model 1: adjusted for age, sex, stage, histology, year of diagnosis, and marital status; model 2: model 1 adjusted for surgery, irradiation, and chemotherapy; model 3: model 2 adjusted for neighborhood SES/ethnic enclave.

‡Of 834 censored foreign-born Hispanics (431 men, 403 women), if follow-up > 24 months (124 men, 89 women), event was assumed.

Table 4. Cox Proportional Hazards Models for Mortality in Hispanics With NSCLC in California by Nativity, Stratified by Neighborhood SES and Enclave*

SES/Enclave	Overall Mortality			Cancer-Specific Mortality		
	US Born HR	Foreign Born HR	95% CI	US Born HR	Foreign Born HR	95% CI
Overall						
High SES						
Low enclave	1.0	0.91	0.85 to 0.97	1.0	0.87	0.81 to 0.94
High enclave	1.0	0.94	0.86 to 1.03	1.0	0.89	0.81 to 0.99
Low SES						
Low enclave	1.0	0.89	0.78 to 1.02	1.0	0.88	0.76 to 1.02
High enclave	1.0	0.91	0.87 to 0.96	1.0	0.86	0.81 to 0.90
Men						
High SES						
Low enclave	1.0	0.90	0.84 to 0.97	1.0	0.85	0.78 to 0.93
High enclave	1.0	0.93	0.85 to 1.03	1.0	0.87	0.79 to 0.97
Low SES						
Low enclave	1.0	0.89	0.77 to 1.02	1.0	0.86	0.74 to 1.01
High enclave	1.0	0.91	0.86 to 0.96	1.0	0.84	0.79 to 0.89
Women						
High SES						
Low enclave	1.0	0.91	0.84 to 0.99	1.0	0.90	0.82 to 0.99
High enclave	1.0	0.94	0.85 to 1.04	1.0	0.92	0.83 to 1.03
Low SES						
Low enclave	1.0	0.90	0.78 to 1.03	1.0	0.91	0.78 to 1.06
High enclave	1.0	0.92	0.86 to 0.98	1.0	0.88	0.82 to 0.95

NOTE. Models adjusted for age, sex, marital status, year of diagnosis, stage, histology, surgery, irradiation, chemotherapy, and neighborhood SES/ethnic enclave. Abbreviations: HR, hazard ratio; NSCLC, non-small-cell lung cancer; SES, socioeconomic status.

*Follow-up through December 31, 2009.

models, there was an independent protective association for women, more recent year of diagnosis, younger age, married status, receipt of chemotherapy, receipt of surgery, and bronchioloalveolar carcinoma and adenocarcinoma histologic subtypes.

DISCUSSION

In this population-based study of Hispanic patients in California with NSCLC, we evaluated the influence of individual, clinical, and neighborhood factors on survival. We found that relative to NHWs, foreign-born Hispanics had improved survival from NSCLC, whereas US-born Hispanics had equivalent survival, after adjusting for both individual and clinical factors. Among foreign-born men, greater rates of loss to follow-up may explain some of the survival benefit observed. Despite having more advanced disease at diagnosis and lower likelihood of treatment, foreign-born Hispanics had improved survival compared with US-born Hispanics.

Furthermore, neighborhood SES and ethnic enclave slightly moderated the survival benefit among foreign-born relative to US-born Hispanics, such that survival differences were slightly more pronounced in low SES and high enclave neighborhoods. This result is in contrast to findings in breast cancer showing that Hispanics living in low SES and high enclave neighborhoods were more likely to present with late stages of breast cancer and have higher rates of mortality compared with Hispanics living in high SES, low enclave neighborhoods.³² These patterns in breast cancer may reflect screening differences such that less acculturated Hispanics have lower screening rates compared with more acculturated individuals.⁴²⁻⁴⁴ For cancers that are historically not screenable, the implications and positive association of segregated populations may hold true. As lung cancer screening becomes widespread,⁴⁵⁻⁴⁸ it will be interesting to see how stage and survival patterns change. Our findings indicate that enclave plays an important protective role for foreign-born Hispanics with NSCLC and are consistent with findings on gastric cancer incidence among Hispanics in California.⁴⁹

Our primary finding of better survival among foreign-born compared with US-born Hispanics is also consistent with studies of NSCLC mortality as well as of other cancer types.^{1,12,50} Foreign-born Hispanics, despite having lower SES, have been shown to have better health outcomes than US-born Hispanics. The tendency for foreign-born Hispanics to have improved outcomes despite lower SES and access to medical care is consistent with other studies that have evaluated the Hispanic paradox. These observations could be a result of true health advantage resulting from more favorable health behaviors among foreign-born populations as compared with US-born Hispanics. Studies demonstrate that US-born Hispanics are more likely to be assimilated to US dietary lifestyles and more likely to participate in behaviors, such as smoking, that are associated with poorer health outcomes.⁵¹⁻⁵³ These explanations, however, do not fully explain the survival advantage for foreign-born Hispanics.

As we have demonstrated in our study, social factors may also play a role. Prior research on the role of social capital has demonstrated that immigrants living in neighborhood enclaves tend to have more advantageous health behaviors and better access to medical care if they are surrounded by support systems. Many immigrant populations follow a trajectory of settling into highly segregated enclaves and then, with passage of time, assimilate into less isolated neighborhoods.^{54,55} Although initial isolation may have detriment for some health outcomes that benefit from access to screening, such as cervical and breast cancers,^{27,56} the social support in a neighborhood enclave is also protective, in that populations retain some cultural and behavioral norms that may be advantageous with respect to the incidence and mortality of some cancers. Additionally, selective migration, or immigration of healthier individuals, may also play a role in the better outcomes seen among foreign-born populations compared with US-born populations.^{14,57} This phenomenon alone, however, does not explain the better health outcomes of foreign-born Hispanics.⁵⁸ Our neighborhood enclave variable suggests that coethnic social support may play a role in the survival advantage among foreign-born relative to US-born Hispanics with NSCLC in those neighborhoods.

Although there are few studies that have evaluated the influence of Hispanic ethnicity on lung cancer survival,^{1-3,59} our study is consistent with these investigations. However, some studies have found mixed results regarding the influence of nativity status on survival from NSCLC. Some studies have demonstrated a protective effect for immigrant patients in other disease states, whereas other studies, including a recent

study by Saeed et al,⁶ have shown no survival advantage for Hispanic immigrants compared with US-born populations with NSCLC. Although our study investigates the same years as Saeed et al, our populations are different. First, the sample in our population was relatively ethnically homogeneous (mainly Mexican Hispanics), whereas the Saeed et al population was more heterogeneous; it represented the entire US Hispanic population. Additionally, our distributions of foreign-born and US-born patients are quite different. In the analysis of Saeed et al, only 14% of patients were considered foreign born, and 85.8% were considered US born, as compared with our study population, in which 50% of patients were foreign born. It is unclear from this previous study how nativity status was determined.^{6,19} There are limitations to using SEER for classification of nativity because birthplace data are incomplete for up to one third of Hispanic patients,⁶⁰ although only 10% of those in our study population had missing birthplace. Furthermore, birthplace information is more likely to be incomplete for those who are US born and alive,^{16,37} and this differential incompleteness has implications on the validity of survival analyses comparing US-born and foreign-born patients. The distribution of foreign-born and US-born patients in our study population closely reflects national data; approximately 55% of US Hispanics in the general population are US born.⁶¹ In our study, to overcome issues associated with nonrandomly missing registry birthplace data, we used a validated method to impute nativity in cancer registry data using patients' SSNs.⁵⁶ Although we did not further classify Hispanics by native country, given a high proportion of patients with missing information and that a large proportion of Hispanics in California are of Mexican origin, future studies should investigate whether the findings are generalizable to other Hispanic subgroup populations.

Our analysis is the first to our knowledge to evaluate the influence of individual, clinical, and neighborhood factors on survival from NSCLC for Hispanic patients using population-based data. The limitations of our study include that we had first-course treatment data but no details on type of chemotherapy or secondary treatments received. Additionally, we lacked recurrence or disease progression information and did not have individual-level SES or acculturation to separately evaluate these

factors. Cancer registry data on Hispanic ethnicity could be subject to misclassification^{61,62}; however, accuracy was enhanced through our use of North American Association of Central Cancer Registries Hispanic identification algorithm.³⁶ Additionally, analysis of lung cancer–specific deaths is subject to inaccuracy of underlying cause of death code, although classification of lung cancer on death certificates has previously been found to be 90% accurate.⁶³ Lastly, we had no information on smoking status. Some authors have suggested the role of smoking in differences in mortality between Hispanics and NHWs.^{52,64–69} Although studies indicate that foreign-born Hispanics are less likely to smoke than US-born Hispanics,^{67,69} none have demonstrated an influence on survival after diagnosis of lung cancer.

In conclusion, despite advanced stage at diagnosis, lower likelihood of treatment, and greater likelihood of living in low SES neighborhoods, foreign-born Hispanics had improved survival after NSCLC than US-born Hispanics and NHWs. The survival benefit among foreign-born Hispanics was slightly more pronounced among patients in low SES and high enclave neighborhoods. Further research focusing on particular attributes of foreign-born populations, particularly those living in lower SES and high enclave neighborhoods, may better clarify reasons for the paradox and help improve outcomes in NSCLC.

AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

The author(s) indicated no potential conflicts of interest.

AUTHOR CONTRIBUTIONS

Conception and design: Manali I. Patel, Heather A. Wakelee
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Data analysis and interpretation: All authors
Manuscript writing: All authors
Final approval of manuscript: All authors

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