DISPARITIES IN GUIDELINE-CONCORDANT TREATMENT AND SURVIVAL AMONG BORDER COUNTY RESIDENTS WITH GASTRIC CANCER

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Executive MPH Program, Applied Epidemiology Track

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Michelle Ju, MD 7/22/21

Approval Sheet

DISPARITIES IN GUIDELINE-CONCORDANT TREATMENT AND SURVIVAL AMONG BORDER COUNTY RESIDENTS WITH GASTRIC CANCER

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Abstract Cover Page

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By

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B.A., Washington University in St. Louis, 2012

M.D., University of Washington Medical School, 2016

Thesis Committee Chair: Michael Kramer, PhD, MMSc

An abstract of

A thesis submitted to the Faculty of the

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2021

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Background: Previous studies have shown health disparities among US-Mexico border county (BC) residents. However, the impact of BC residence on gastric cancer treatment and survival outcomes is unknown. Our study compares receipt of guideline-concordant care (GCC) and survival for gastric cancer patients by BC status.

Methods: We conducted a retrospective review of adult Non-Hispanic White and Hispanic patients with gastric adenocarcinoma diagnosed between 2004-2017 in the Texas Cancer Registry. Chi-square tests were used to compare categorical group differences, with pooled t-tests used to compare group means. The impact of BC residence on likelihood of receiving GCC was assessed with logistic regression. Overall survival was estimated using the Kaplan-Meier method and compared with log-rank tests.

Results: Our cohort consisted of 12,514 patients (15% BC). Overall, 45% of non-border county (NBC) residents received GCC vs 35% of BC residents ($p<0.0001$). After adjusting for age, race, stage, and insurance status, BC patients remained significantly less likely to receive GCC (OR 0.68, 95% CI 0.60-0.78). BC residence was associated with increased hazard of all-cause mortality after accounting for age, race, stage, poverty index, and treatment receipt (HR 1.11, 95% CI 1.04-1.18). BC residents had significantly worse overall survival for localized and regional disease.

Conclusions: BC residents with gastric cancer have worse survival outcomes than NBC residents. This significant survival disparity is likely related to receipt of suboptimal care among BC residents as demonstrated by lower likelihood of GCC. Further studies are needed to identify specific contributing mechanisms to improve healthcare equity.

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Chapter I: Literature Review

1. GASTRIC CANCER

Gastric Cancer Epidemiology and Risk Factors

Gastric cancer is the fifth most common cancer worldwide and the fourth leading cause of cancer deaths (1). In 2020, over one million new cases of gastric cancer were diagnosed globally, resulting in an estimated 769,000 deaths (equating to 1 in every 13 deaths worldwide). Rates are two-fold higher among men than women and most commonly affects individuals in the 6th decade of life or later. Although gastric cancer is usually reported as a single entity, it can be classified into two distinct subtypes based on topography: cardia stomach cancer, or tumors involving the upper stomach, and non-cardia stomach cancer, or tumors involving the lower stomach. These entities differ significantly in terms of epidemiologic patterns, risk factors for disease development, and tumor biology.

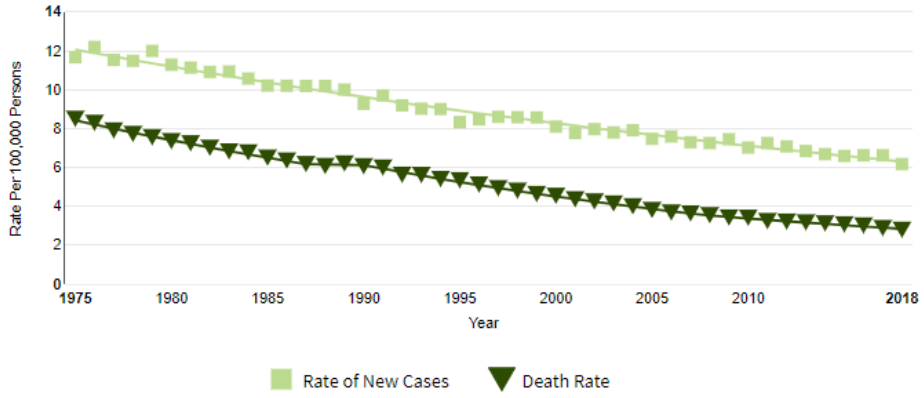
Chronic infection with *Helicobacter pylori* is the main risk factor for the development of non-cardia gastric cancer (2, 3). Over half of the global population is infected with *H. pylori*, and geographic variation in infection prevalence correlates fairly well with that of gastric cancer incidence (4). However, less than 5% of individuals infected with *H.* pylori will go on to develop cancer, likely due to differences in bacterial and host genetics, age of infection acquisition, and environmental factors (5). Additional risk factors for non-cardia gastric cancer include alcohol consumption, smoking, consumption of foods preserved via salting, diets high in processed meats or grilled meats/fish, as well as low fruit intake (6). In contrast, cardia gastric cancer is linked to excess body weight and gastroesophageal reflux disease (7).

Gastric Cancer Incidence and Mortality Trends Within the United States

In the US, gastric cancer accounts for 1.4% of all new cancer cases diagnosed each year. In 2021, an estimated 26,560 individuals will be diagnosed with gastric cancer (8).

Approximately 11,180 deaths will result from gastric cancer (1.8% of all cancer deaths). Over the past decade, the incidence of gastric cancer has declined by around 1.5% per year (9). Mortality rates are also declining. For much of the early 20th century, gastric cancer was the leading cause of cancer deaths in the United States. Today, it is the 15th leading cause of cancer-related deaths. Age-adjusted death rates have been falling on average 2.1% per year between 2009-2018 (9).

Figure 1: Gastric Cancer New Cases and Deaths in the U.S.; Trends from 1975-2018 (9)



Disparities in Gastric Cancer Incidence and Mortality Among US Hispanics

Although overall gastric cancer incidence and mortality in the US is declining, significant racial/ethnic disparities exist. Gastric cancer disproportionally affects Hispanics compared to non-Hispanic whites (10). Gastric cancer incidence among Hispanic men is over 60% higher than among non-Hispanic white men. Among Hispanic women, the incidence rate is double the rate seen in non-Hispanic white women. Additionally, Hispanics have twice the gastric cancer incidence and mortality compared to non-Hispanics (11). Hispanic patients are also diagnosed at younger ages, present with more advanced disease, and have a higher proportion of diffuse-type cancers compared with non-Hispanic Whites (12-15). Improving understanding of gastric cancer

among Hispanics and reducing outcome disparities is a critical issue as the US Hispanic population is projected to triple by 2050, from 42 million to 128 million (16).

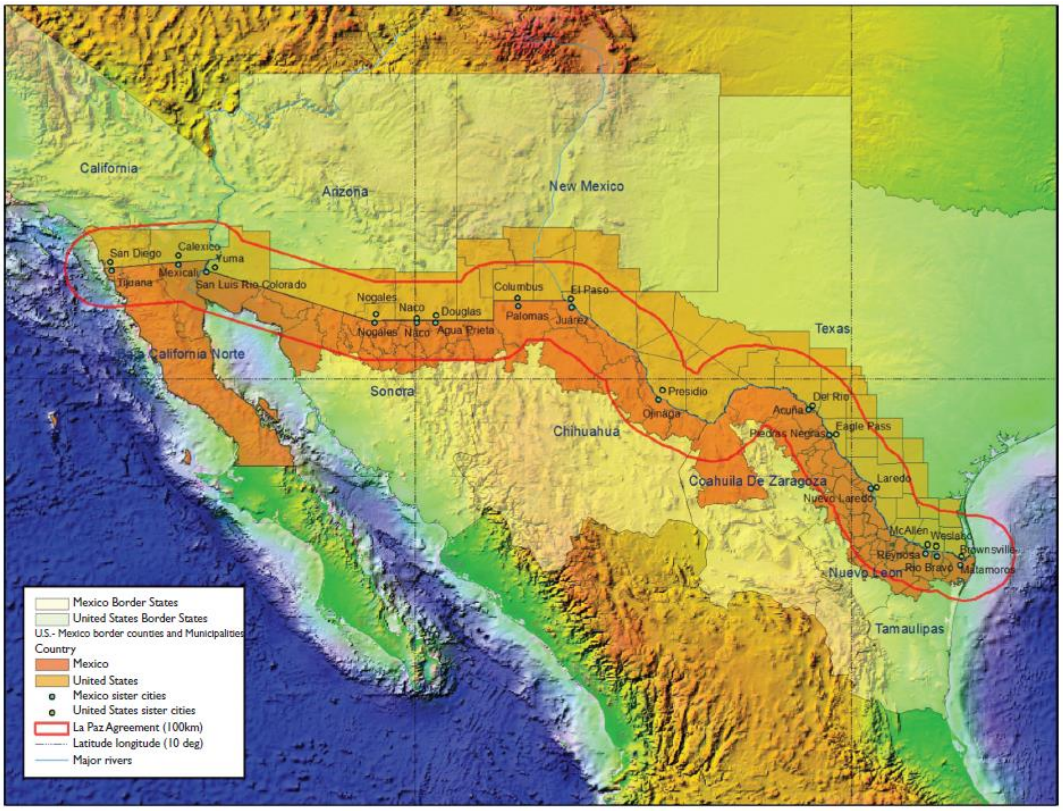
Figure 2: Disparities in Gastric Cancer Incidence and Mortality (11)

2. THE UNITED-STATES MEXICO BORDER REGION

Overview

The United States-Mexico border stretches 2,000 miles from the Gulf of Mexico to the Pacific Ocean. While defined in part by the Rio Grande River, the border has no other natural boundaries. Defined in the La Paz Agreement of 1983 as the area 100 kilometers north and south of the US-Mexican border, this area includes counties in Arizona, California, New Mexico, and Texas (17). According to the 2000 US Census, more than 6.5 million people resided in the 44 US border counties; by 2025, the population is expected to double (18). Two of the fastest-growing border metropolitan areas in the United States, Laredo and McAllen, are both located in the state of Texas. With the exception of San Diego County, Hispanics and Non-Hispanic Whites represent more than 95% of the border population (19).

Figure 3: United States-Mexico Border Region (20)



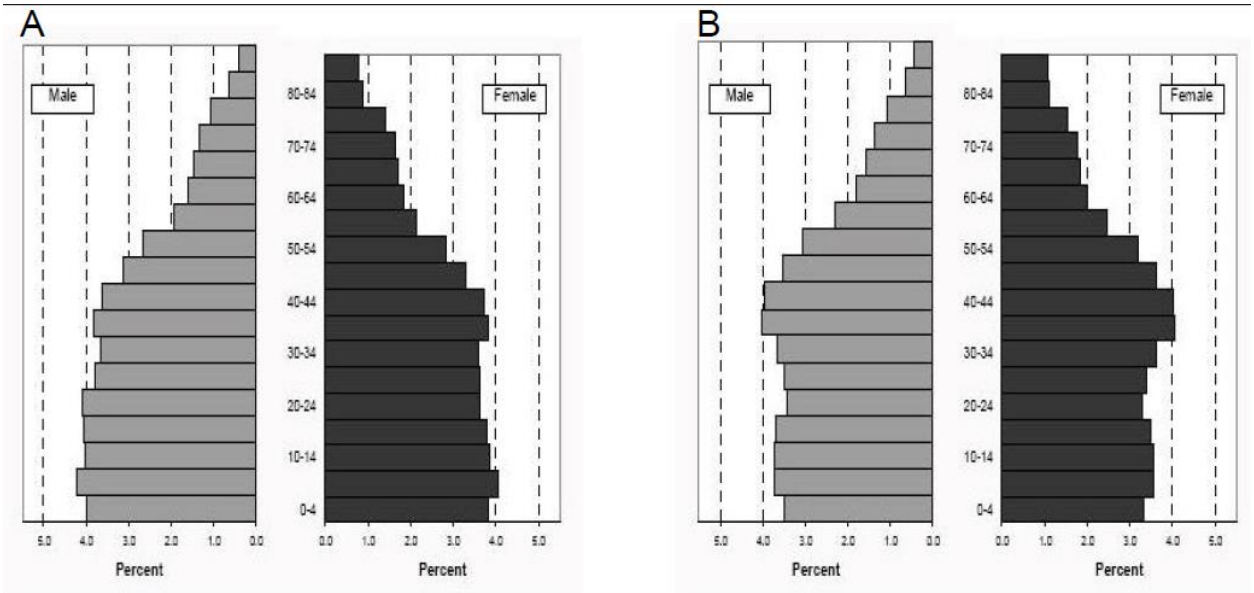
The border region represents a complex milieu of people, languages, cultures, and traditions. The border is difficult to characterize, with stark contrasts of wealth versus poverty, dense urban areas versus rural desert landscapes. These complex and seemingly contradictory factors characterize the lives of those who live in the border. This social, cultural, economic, and political context provides the backdrop for the health and well-being of US-Mexico border residents (19).

Age Distribution

Overall, the age distribution of border residents is younger than that of the overall US population. However, the border age distribution is affected by three major trends:

1. Movement of retirees to the border region increases the proportion of elderly.
2. Migration of work-seeking individuals increases the working-age population.
3. The high birth rate in many border counties leads to a relatively large proportion of children.

Figure 4A: Population Pyramid, US-Mexico Border, 2000 and Figure 4B: Population Pyramid, United States, 2000 (21)



Race and Ethnicity

Race/ethnicity contribute in important ways to the overall health status of the border region. The high proportion of Hispanics residing in the border region means that a substantial part of the population may be predisposed to certain diseases, such as hypertension and diabetes (22). Incidence for certain cancers, such as cervical cancer and gastrointestinal cancers (including stomach, liver, and colon/rectum) are also higher (23, 24). Many Hispanics living in

the border region suffer from a lack of health insurance, low levels of income and education, and limited English language skills, all of which represent barriers to adequate healthcare (19).

Socioeconomic Status

The US-Mexico border region population is typically characterized as having low socioeconomic status with regard to poverty, income level, and educational attainment. Poverty is high within the border region. In 1999, the proportion of the US-Mexico border population living below the poverty level was over 50% higher than for the US as a whole (20% vs 12%). The highest percentage of those living in poverty is in Starr County, Texas (51%) (21). These socioeconomic disadvantages are particularly evident among Hispanic border residents.

Barriers to Healthcare and Health Disparities in the US-Mexico Border Region

US-Mexico border residents face multiple significant barriers to healthcare. Low income can significantly limit ability to access health care. Particularly, border families whose income is above Medicaid income limits, but not high enough to readily afford private health insurance, are often unable to pay for out of pocket healthcare costs (25). Healthcare facilities and physicians are also less likely to locate in poor areas. This is reflected by the fact that multiple US border counties do not have a single physician, let alone a clinic or hospital (26).

Rapid population growth presents additional challenges to ensuring an adequate supply of health resources. Population growth is outpacing growth of health personnel, equipment, and supplies. Many US border counties are rural and sparsely populated. Residents in these ultra-rural counties may live large distances from healthcare facilities and specialized care.

These circumstances result in significant health disparities. If the border region were made into the 51st state, it would rank second in death rates due to hepatitis and third in deaths related to diabetes (21). Previous studies have also shown higher mortality rates for certain cancers including breast, prostate, lung, colorectal, skin, and gynecologic cancers (27, 28).

Statement of the Problem

Texas has one of the higher state gastric cancer incidence rates in the US at 6.4 per 100,000. Approximately 10% of Texas' population resides within a Texas-Mexico border county. Previous studies have shown significant health disparities among residents of border counties. However, the impact of border county residence on gastric cancer treatment and survival outcomes remains unstudied. In the US, Hispanics have twice the gastric cancer incidence and mortality compared to non-Hispanics (29). The predominance of Hispanic residents in the border region makes understanding disparities in treatment patterns and outcomes of gastric cancer particularly poignant to study.

Purpose of the Thesis

The purpose of this study is to characterize clinical differences in gastric cancer presentation among Non-Hispanic Whites/Hispanics living in border counties vs non-border counties, and to compare receipt of guideline-concordant cancer care and survival. This will be done utilizing a retrospective review of the Texas Cancer Database. I hypothesize that border county residents will have worse stage-specific survival after gastric cancer diagnosis, and that these survival differences can be attributed to differential receipt of guideline-concordant care.

Chapter II: Journal Article

I was involved in all aspects of this project including conceptualization of the study, data cleaning, analysis, development of figures/tables, and preparation of the final manuscript. The intended target journal for first submission is JCO Oncology Practice.

ABSTRACT

Background:

Previous studies have shown health disparities among US-Mexico border county (BC) residents. However, the impact of BC residence on gastric cancer treatment and survival outcomes is unknown. Our study compares receipt of guideline-concordant care (GCC) and survival for gastric cancer patients by BC status.

Methods: We conducted a retrospective review of adult Non-Hispanic White and Hispanic patients with gastric adenocarcinoma diagnosed between 2004-2017 in the Texas Cancer Registry. Chi-square tests were used to compare categorical group differences, with pooled t-tests used to compare group means. The impact of BC residence on likelihood of receiving GCC was assessed with logistic regression. Overall survival was estimated using the Kaplan-Meier method and compared with log-rank tests.

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Conclusions: BC residents with gastric cancer have worse survival outcomes than NBC residents. This significant survival disparity is likely related to receipt of suboptimal care among BC residents as demonstrated by lower likelihood of GCC. Further studies are needed to identify specific contributing mechanisms to improve healthcare equity.

INTRODUCTION

The US-Mexico border region is a unique, dynamic area where multiple cultures integrate and interconnect across geopolitical boundaries. Defined in the La Paz Agreement of 1983 as the area 100 kilometers north and south of the US-Mexican border, this area includes counties in Arizona, California, New Mexico, and Texas.(17) According to the 2000 US Census, more than 6.5 million people resided in the 44 US border counties; by 2025, the population is expected to double.(18) Two of the fastest-growing border metropolitan areas in the United States, Laredo and McAllen, are both located in the state of Texas. With the exception of San Diego County, Hispanics and Non-Hispanic Whites represent more than 95% of the border population.(19)

Border county residents face high poverty rates, complex barriers to accessing health care, multiple socioeconomic, cultural, and environmental challenges, and a complex regulatory/political environment. These circumstances result in significant health disparities. If the border region were made into the 51st state, it would rank second in death rates due to hepatitis and third in deaths related to diabetes.(21) Previous studies have also shown higher mortality rates for certain cancers including breast, prostate, lung, colorectal, skin, and gynecologic cancers.(27, 28) However, the impact of border county residence on gastric cancer survival outcomes remains unstudied. In the US, Hispanics have twice the gastric cancer incidence and mortality compared to non-Hispanics.(29) The predominance of Hispanic residents in the border region makes understanding disparities in treatment patterns and outcomes of gastric cancer particularly poignant to study.

We hypothesize that border county residents will have worse stage-specific survival after gastric cancer diagnosis, and that these survival differences can be attributed to differential

receipt of guideline-concordant care. We conducted a retrospective review of the Texas Cancer Registry to characterize clinical differences in gastric cancer presentation among Non-Hispanic Whites/Hispanics living in border counties vs non-border counties, and to compare receipt of guideline-concordant cancer care and survival.

METHODS

Our study was approved by the Institutional Review Board of the University of Texas Southwestern Medical Center. We queried the Texas Cancer Registry (TCR) for Non-Hispanic White and Hispanic adult patients with gastric adenocarcinoma diagnosed between 2004-2017. The TCR is a statewide database of demographic, clinical, hospital, and socioeconomic data on all incident cancer cases diagnosed in the state of Texas.(30) By legislative mandate, all providers treating patients with a primary diagnosis of cancer are required to report clinical encounters, resulting in a case completeness of >98%. We chose not to capture Black and Asian/Pacific Islander patients in this study due to very low numbers of gastric cancer cases (N<12) in border county residents. Patients with in-situ or unknown SEER summary stage were excluded. [Figure 1]

The Texas Department of State Health Services border area is defined as the area within 100 kilometers of the Rio Grande in the La Paz Agreement of 1986, which includes 32 Texas counties and Mexico.(31) Patients were categorized into border county (BC) and non-border county (NBC) groups based on Federal Information Processing System (FIPS) codes for the county a patient resided in at the time of diagnosis, as provided by the TCR. FIPS codes are numbers which uniquely identify geographic areas that are assigned by the National Institute of Standards and Technology (NIST). We defined guideline-concordant care based on NCCN

guidelines as receipt of surgery for localized stage, surgery and chemotherapy for regional stage, and chemotherapy for metastatic stage. Staging was determined based off the SEER summary stage variable provided by the TCR, which documents the stage at initial diagnosis or treatment of the reported tumor. Poverty index was based on neighborhood poverty levels from the 2010 American Community Survey results as determined by the census tract of the diagnosis address. The TCR stratifies poverty index into quartiles, with the highest quartile being ≥20%.

Chi-square tests were used to compare categorical differences between BC and NBC groups. Pooled t-tests were used to compare group means. Logistic regression was performed to assess the impact of BC residence on the likelihood of receiving guideline-concordant care. Multicollinearity among covariates included in the multivariable logistic regression model was tested using correlation coefficients and variance inflation factor (VIF) values. No evidence of severe multicollinearity was found, with all VIFs <2.7. The fully adjusted model included BC residence, age, race, stage, and insurance status.

Overall survival was estimated using the Kaplan-Meier method and compared using log-rank tests. A multivariable Cox-regression model was used to assess the impact of BC status on survival and included the following covariates in addition to the variable of interest: age, race, stage, poverty index, receipt of chemotherapy, and receipt of surgery. For all covariates in the model, the proportionality of hazards assumption was tested using plots of Kaplan–Meier survival curve with predicted survival curve, log-log of survival curve plotted as −ln[−ln(survival)] vs ln(analysis time), and scatter plots of Schoenfeld residuals obtained after fitting the Cox-regression model. The proportional hazards assumption was found to be satisfied. All tests were two-sided and performed at the 5% significance level. Statistical analysis was performed utilizing SAS 9.4 (SAS Institute, Cary, NC).

RESULTS

Demographics by Border County Residence

After applying exclusions, our final study cohort consisted of 12,514 patients, 15% of whom were border county residents. For all races/ethnicities, those living in the BC were, on average, older at the time of diagnosis (mean age 66 vs 65; $p<0.0001$). [Table 1] While the male: female ratio in NBC was approximately 2:1 (63% male vs 37% female), similar to the worldwide distribution,(32) the ratio was 1.3:1 in BC (57% male vs 43% female; $p<0.0001$). Consistent with known Texas BC demographics, BC residents were predominantly Hispanic (88%),(33) more often uninsured (12% vs 9% NBC; $p<0.0001$),(34) and poorer (77% living in neighborhoods with poverty index $\geq$20% vs 30% NBC; $p<0.0001$).(21) There were no significant differences in the clinical presentation of gastric cancer in BC vs NBC among NHW patients. [Table 2] However, Hispanics residing in BC tended to be older (mean age 66 vs 61; $p<0.0001$), more often presented with localized disease (32% vs 24%; $p<0.0001$), and with distal tumors (24% pylorus/antrum vs 22%; $p<0.05$) than Hispanics living in NBC. [Table 3].

Overall Survival by Border County Residence

For all stages combined, BC residents had significantly worse overall survival (OS) than NBC residents (median OS 11 months vs 12 months; $p<0.05$). [Figure 2A] When stage-specific survival was compared, BC residents had worse OS for localized and regional disease, but survival differences for metastatic disease were not significant. Median OS for BC residents with localized disease was 34 months vs 52 months for NBC ($p<0.001$). [Figure 2B] For regional disease, median OS was 13 months for BC vs 18 months for NBC ($p<0.0001$). [Figure 2C]

Median OS for BC residents with metastatic disease was 5 months compared with 6 months for NBC residents; however, this difference was not statistically significant. [Figure 2D] After adjusting for age, race, stage, poverty index, and receipt of treatment (surgery and chemotherapy), living in a BC continued to be associated with worse OS (HR 1.11, 95% CI 1.04-1.18).

Differences in Receipt of Guideline-Concordant Treatment between Border and Non-Border County Residents

We subsequently examined the receipt of guideline-concordant treatment as an explanatory mechanism for observed survival differences. Overall, 45% of NBC residents received guideline-concordant care vs 36% of BC residents ($p<0.0001$). For those with localized disease, 43% of NBC residents received surgical resection (SEER program surgery codes 30-52), while only 35% of BC residents underwent surgery ($p<0.0001$). [Table 4] The low rate of surgical resection among patients with localized disease may partially be explained by increasing adoption of novel endoscopic therapies for early-stage cancers.(35) Local tumor excision (SEER program site specific surgery codes 26-27) was received by 11% of patients with localized disease (N=405 of 3,602 total). The incidence of local excision did not differ significantly by border county status (11.5% NBC vs 10.1% NBC; p=NS).

Approximately 36% of NBC patients with regional disease received surgery and chemotherapy compared with 29% of NBC residents ($p<0.05$). While a higher proportion of BC patients with regional disease received surgery only (27% vs 21% NBC), this difference was not statistically significant. Among patients receiving both chemotherapy and surgery, 18% of BC residents received neoadjuvant therapy vs 43% of NBC residents ($p<0.0001$). BC patients with

metastatic disease also less often received chemotherapy than NBC patients (41% vs 53%; $p<0.0001$).

In comparing NHW only, BC residents less often received surgery for localized disease (30% vs 40%; $p<0.01$), but no significant differences in treatment patterns for regional or metastatic disease were observed. [Table 5] Similar to NHW, Hispanic BC residents also less often received surgery for localized disease (36% vs 48%; $p<0.0001$). However, rates of chemotherapy receipt for metastatic disease were also lower among Hispanics living in BC (40% vs 52% NBC; $p<0.0001$). After adjusting for age, race, stage, and insurance status, BC residents were significantly less likely to receive guideline-concordant cancer care (OR 0.68, 95% CI 0.60-0.78).

DISCUSSION

Despite having more favorable tumor factors than NBC residents, patients living in BC experienced worse survival after gastric cancer diagnosis. These survival differences result in part from disparities in receipt of guideline-concordant cancer care. The diagnosis, staging, and treatment of gastric cancer is complex and requires multidisciplinary coordination to achieve optimal care.(36, 37) This coordination is difficult even under ideal circumstances, and access barriers to specialized cancer care, or even healthcare in general, can result in inferior patient outcomes. Border county residents face significant difficulties in accessing healthcare resulting from lack of healthcare infrastructure and social determinants of health such as medical literacy/language barriers, financial difficulties, logistical issues such as transportation, and discrimination. This results in suboptimal gastric cancer care and worse survival outcomes for BC residents.

If the US-Mexico border region were considered to be the 51st state, it would rank last in access to healthcare.(21) Nearly 1 in 5 adults living in the border region do not have adequate access to healthcare and reported being unaware of where they can go to seek care. Lack of healthcare access is more severe among Hispanics living in BC, who were more than 3 times as likely as NHW living in BC to report not having a place to go to receive healthcare services (32% vs 10%).(25) Health care deserts are defined as a populated region more than 60 minutes away from the nearest acute-care hospital. The state of Texas has a heavy burden of health care deserts, with 159 of the state's 254 counties having no general surgeons, 121 having no medical specialists, and 35 having no doctors at all.(38) The border region is particularly affected. The entire Texas-Mexico border region is served by 25 hospitals distributed across 6 of the 32 border counties.(26) Based on 2020 population estimates,(39) this results in 2.2 hospital beds per 1,000 population in BC, compared to an average of 2.3 per 1,000 population across the state.(40)

Of these 25 hospitals in the Texas border region, 84% (N=21) have inpatient surgery capabilities and just 40% (N=10) have oncology services.(26) Among the 10 hospitals offering oncology services, only 3 offer both chemotherapy and radiotherapy, while the remaining offer radiotherapy only (N=1) or chemotherapy only (N=6). Six of these hospitals are Commission-on-Cancer (CoC) accredited, concentrated within El Paso and Webb counties.(41) There are a total of 64 CoC facilities in Texas. The closest NCCN member institution/NCI-designated cancer center is over 350 miles driving distance from the Texas-Mexico border.(42, 43) Extremely limited availability of cancer care within the Texas border region points to systemic difficulties with receiving gastric cancer treatments for BC residents. Increasing the workforce of oncologists practicing in rural/urban underserved areas, as well as creative partnerships with

existing cancer centers such as outreach clinics, virtual tumor boards, and telemedicine visits are key strategies for closing this treatment availability gap.

Even when cancer care is available, BC residents face additional difficulties in utilizing healthcare services. Among Texas border residents ages 18-64, 9.8% speak English “not at all”, and 10.4% speak “not well.” In the ages 65+ population, which is the main demographic diagnosed with gastric cancer, these rates increase to 18.4% who speak English “not at all” and 13.3% “not well.” This is in contrast to 11% of the overall Texas 65+ population with limited English proficiency (speak English “less than very well”).(44) Previous studies have established that patients with limited English fluency are at high risk for lower quality care due to communication barriers.(45-47)

Limited English fluency patients diagnosed with cancer may be particularly impacted by communication barriers, as cancer care conversations often involve complex, confusing, and emotionally-laden discussions. Poor quality communication is significantly correlated with worse patient acceptance of, and adherence to, recommended treatments.(48) A 2016 survey conducted by the American Hospital Association of over 4,500 hospitals found that only 56% offered some type of linguistic/translation services, a modest increase of 2% from a survey conducted 5 years prior.(49) Yet, 97% of physicians see at least some patients who do not speak English or have limited English proficiency.(50) These statistics highlight the need for an overhaul of current healthcare system practices to have language services be a required part of providing high-quality healthcare.

BC residents may also face increased discrimination which negatively impacts the quality of care they receive. An estimated two-thirds of clinicians have implicit bias against Hispanics, with 51% having moderate to strong bias.(51) Oncologist implicit bias predicts less patient

confidence in the treatments recommended and lower likelihood of completing therapies.(52) Higher implicit bias is also associated with increased patient difficulty in remembering the content of cancer care discussions. Thus, implicit racial bias is likely an important source of disparities in receipt of guideline-concordant cancer care among BC residents, over 88% of whom are Hispanic.(53) Low socioeconomic status patients have also been shown to be at risk for receiving less thorough/accurate clinical assessments and guideline-concordant treatments as a result of provider biases,(54-56) and 23% of BC residents live under the Federal Poverty Line.(34)

Increasing the diversity of border region healthcare providers is an important strategy in reducing disparities. Currently, only 47% of Texas physicians providing direct patient care in border areas are Hispanic, and 35% are NHW.(25) However, the vast majority of BC residents are Hispanic. A systematic review on the effects of racial concordance between providers and physicians found an association with improved communication, information-giving, partnership building, and patient participation.(57) Cultural sensitivity and bias training, as well as a focus on engaging in higher quality communication with racially discordant patients by focusing on improving patient-centeredness, partnership building, and patient engagement, is also key.

Our study had several limitations. While the TCR captures treatment receipt and treatment sequencing data, the completeness is limited. Presumably, some proportion of patients with treatment receipt captured as “unknown” did indeed receive guideline-concordant care, which may have resulted in underestimation. We were also unable to ascertain specific reasons why guideline-concordant treatment was not received. The issue of proper staging for localized/regional disease is also a potential confounder for survival outcomes. If BC residents are less likely to be properly staged than NBC residents, this could be an explanation for

observed differences in GCC receipt and survival. Our finding of a significantly higher proportion of localized disease among BC residents suggests that understaging may be more commonly experienced in this group. Additionally, it is known that BC residents may travel to Mexico to receive care. In one study, up to 37% of Texas BC residents reported having visited Mexico for doctors' appointments.(58) Treatments received in Mexico would not be captured in the TCR. However, a high prevalence of usage of healthcare services in Mexico by Texas BC residents would be further suggestive of unmet needs in health care on the US side of the border.(58) Despite these limitations, our study highlights critical gastric cancer treatment and survival disparities among border county residents and the need for systematic reform to improve healthcare equity.

CONCLUSION

BC residents with gastric cancer have worse survival outcomes after gastric cancer diagnoses than NBC residents. This significant survival disparity is related to receipt of suboptimal care among BC residents as demonstrated by lower likelihood of guideline-concordant therapies. This is a major health equity issues that may potentially be related to systemic bias. Further studies are needed to identify specific contributing mechanisms to lower receipt of guideline-concordant care among BC residents to improve healthcare equity and outcomes for all Texas gastric cancer patients.

Figure 1: Flow Diagram

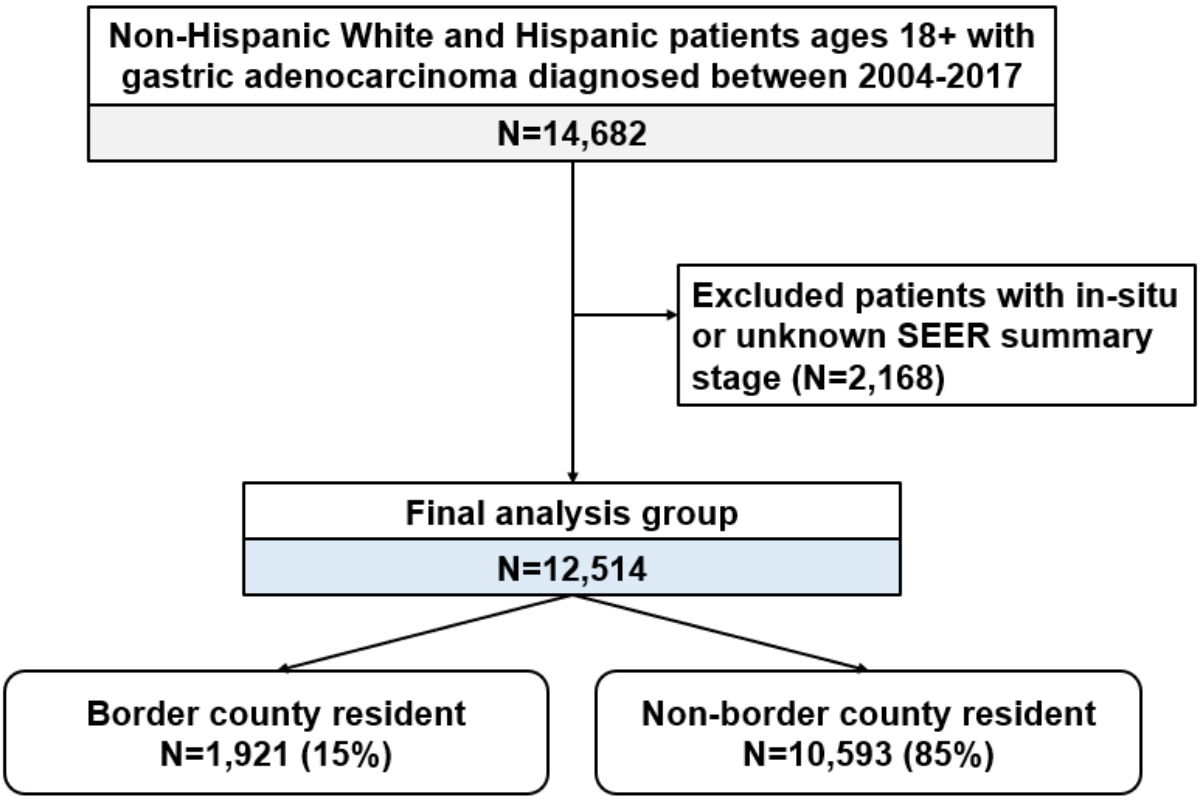
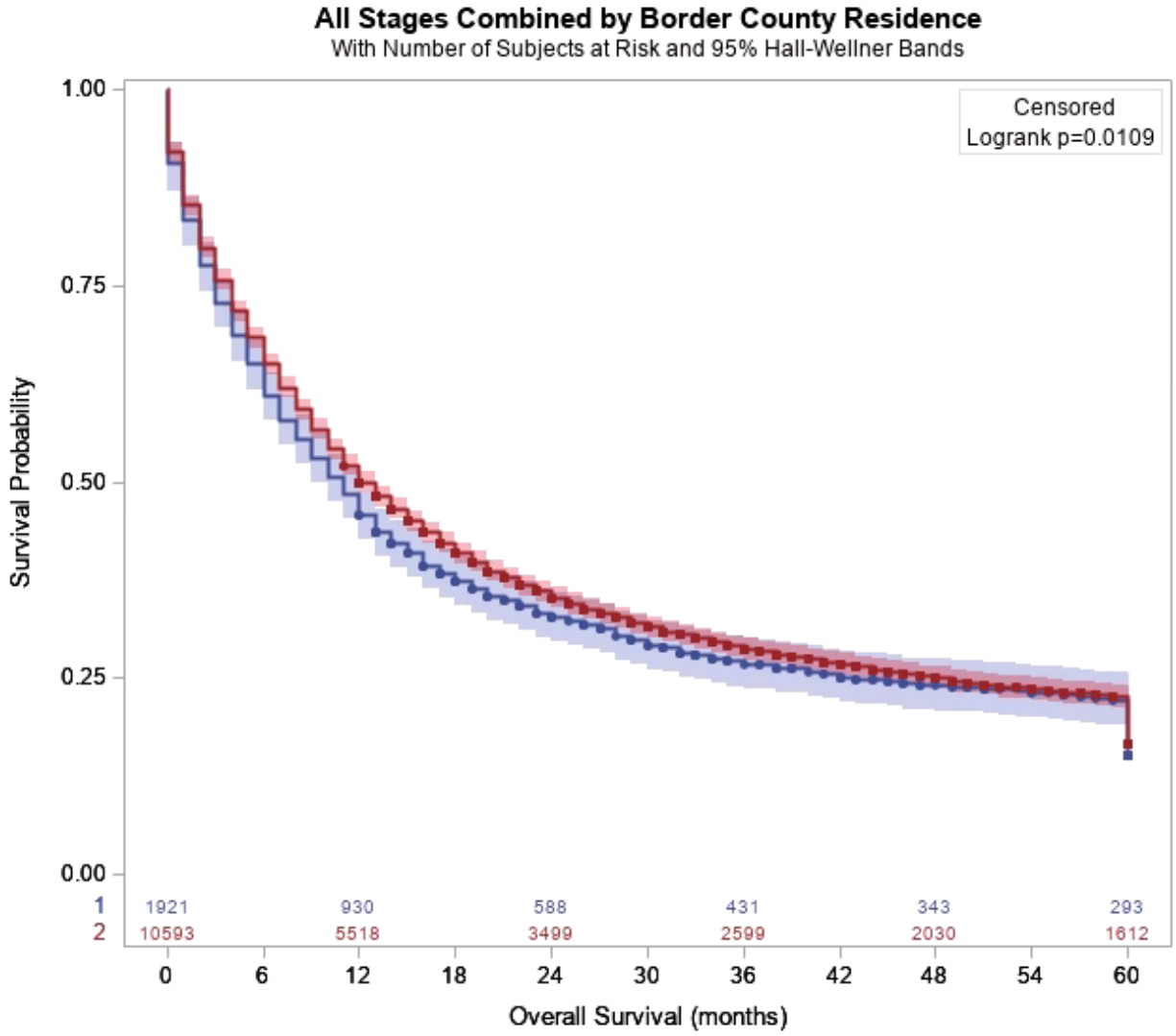


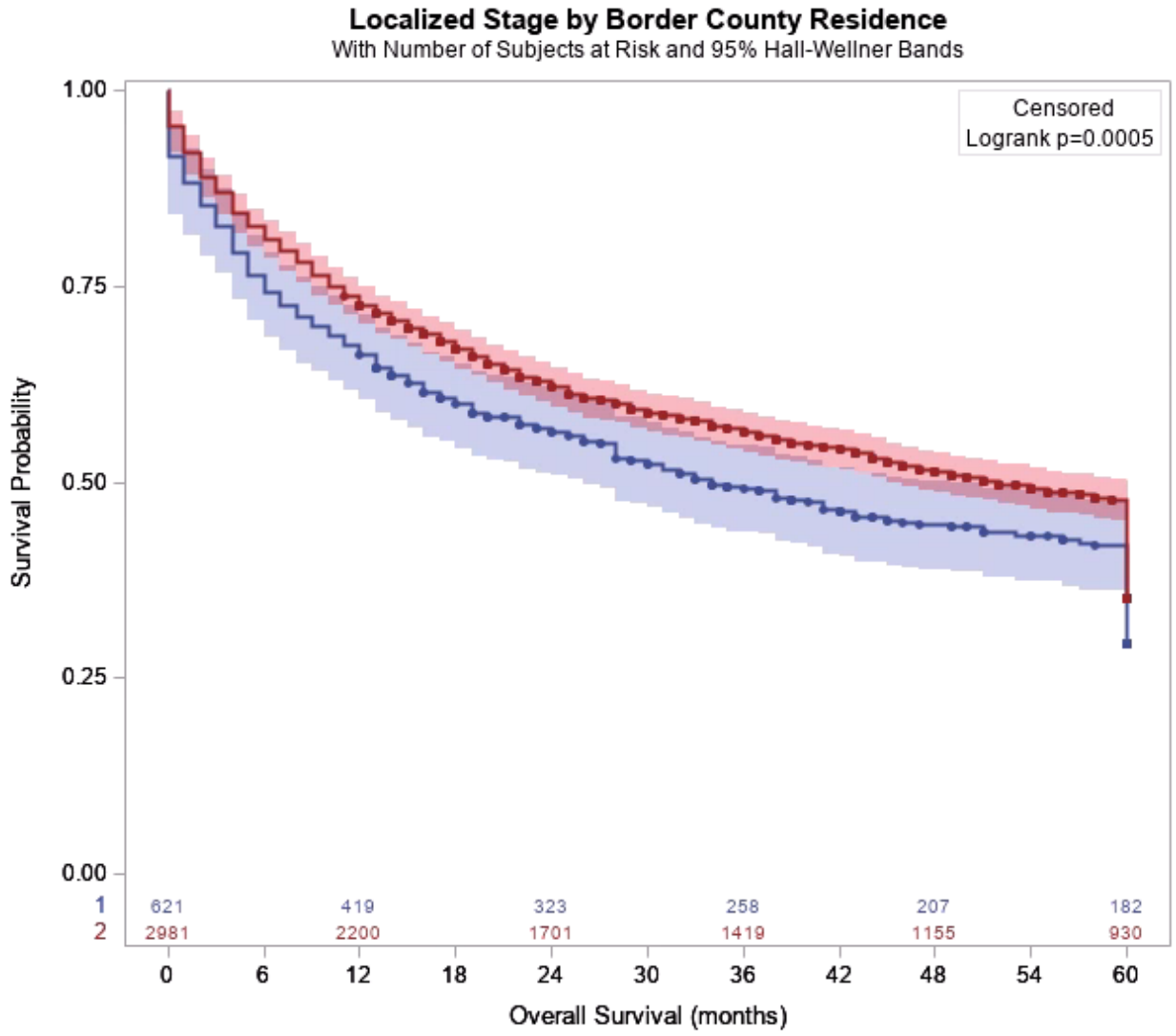
Figure 2: Overall Survival Comparison by Border County Residence

a) All Stages Combined



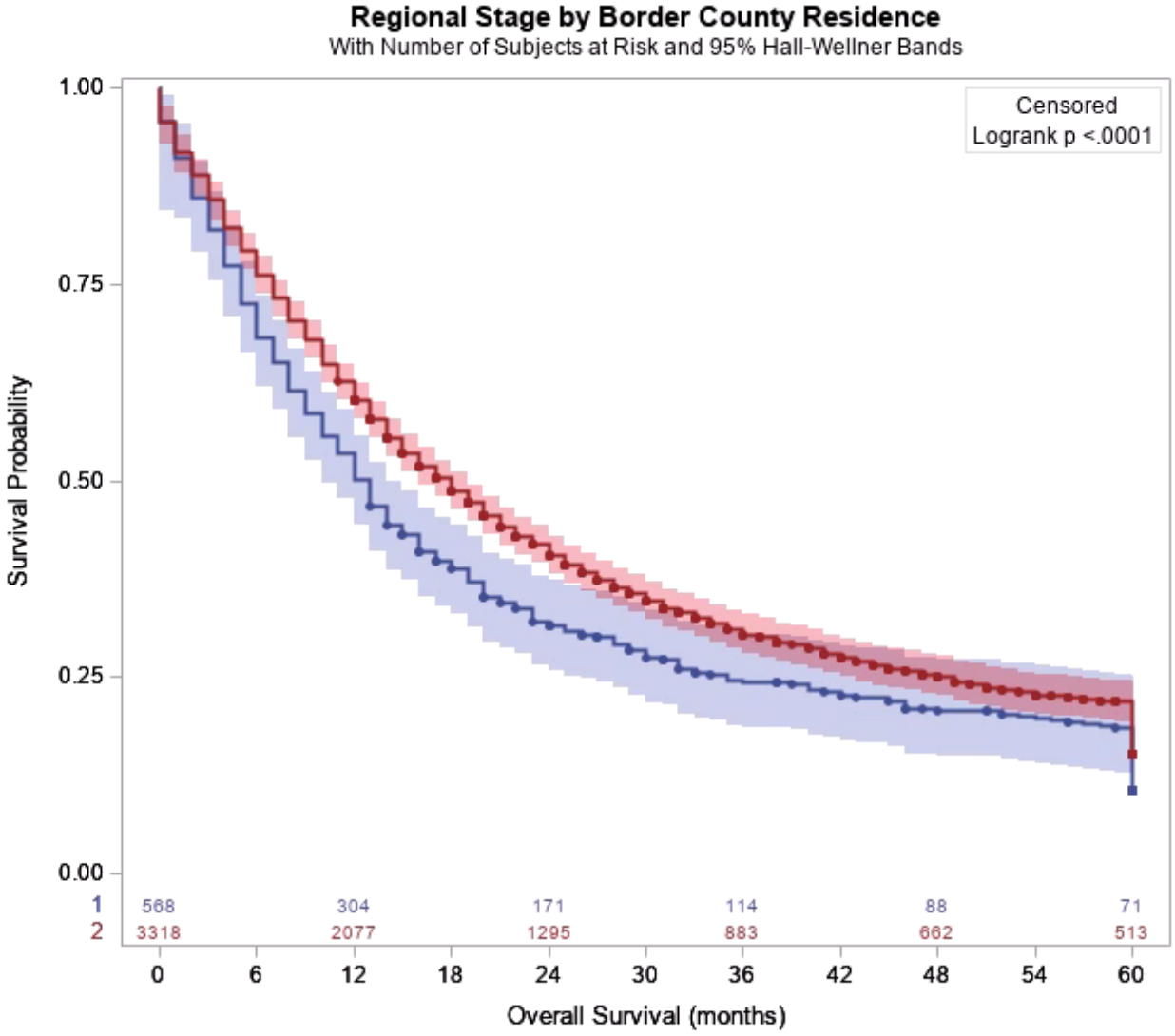
	Subjects	Event	Censored	Median Survival	95% CL	
'Border county resident'	1921	1541	380	11	10	12
'Non border county resident'	10593	8324	2269	12	12	13

b) Localized



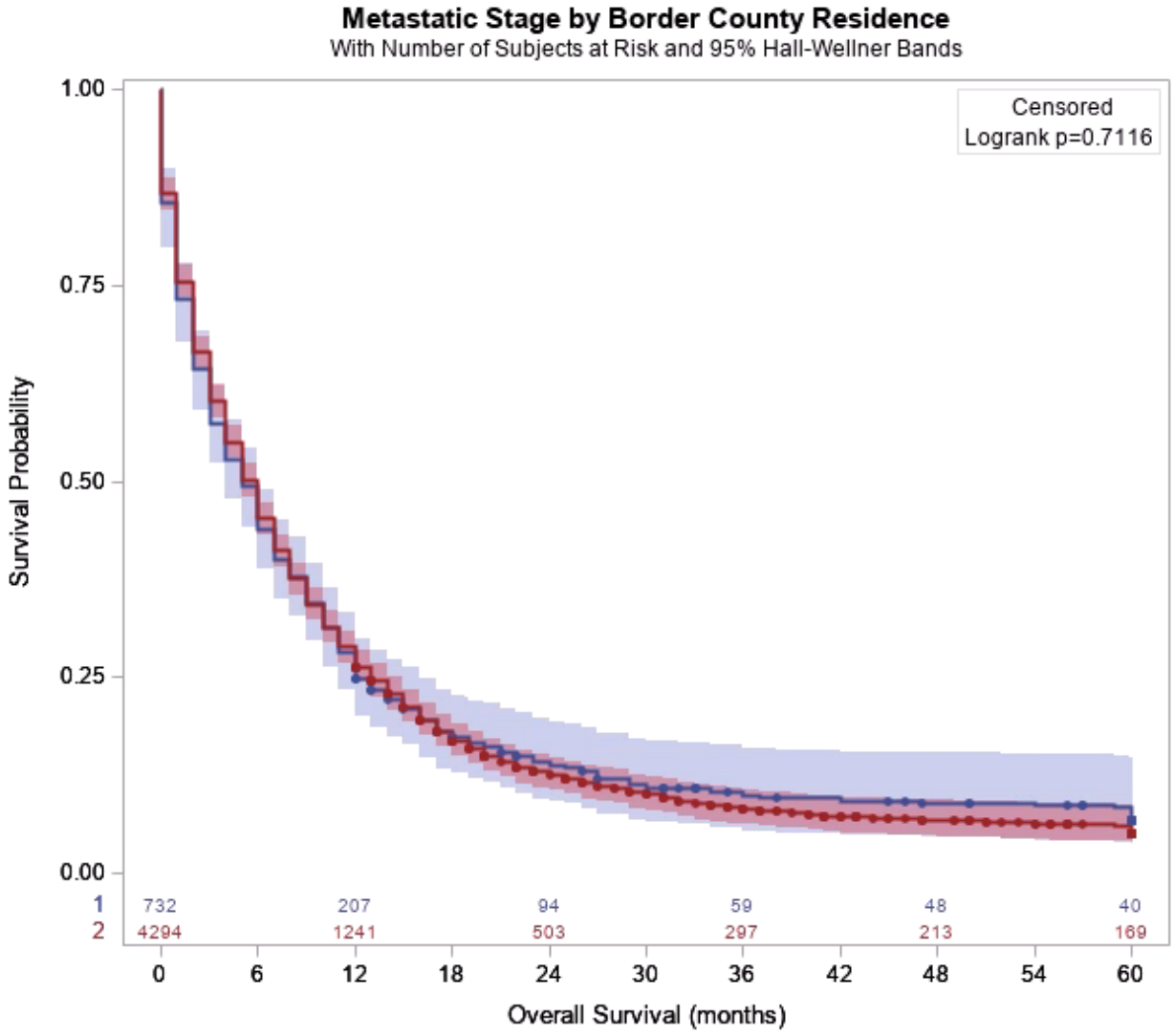
	Subjects	Event	Censored	Median Survival	95%	CL
'Border county resident'	621	397	224	34	28	43
'Non border county resident'	2981	1705	1276	52	47	58

c) Regional



	Subjects	Event	Censored	Median Survival	95%	CL
'Border county resident'	568	476	92	13	11	14
'Non border county resident'	3318	2630	688	18	17	19

d) Metastatic



	Subjects	Event	Censored	Median Survival	95%	CL
'Border county resident'	732	668	64	5	4	6
'Non border county resident'	4294	3989	305	6	5	6

Table 1: Demographics by Border County Residence Status; All Races/Ethnicities

		Non-border county resident N=10,593	Border county resident N=1,921	p-value
		Mean (std dev)		
Age at Diagnosis		65.0 (13.9)	66.4 (13.9)	<0.0001
		N (%)		
Age Group at Diagnosis	<50 years	1,476 (13.9%)	248 (12.9%)	NS
	50+ years	9,117 (86.1%)	1,673 (87.1%)	
Sex	Female	3,940 (37.2%)	832 (43.3%)	<0.0001
	Male	6,653 (62.8%)	1,089 (56.7%)	
Race/Ethnicity	Non-Hispanic White	6,764 (63.9%)	241 (12.6%)	<0.0001
	Hispanic	3,829 (36.2%)	1,680 (87.5%)	
Insurance Status	Uninsured	909 (8.6%)	224 (11.7%)	<0.0001
	Private	2,686 (25.4%)	326 (17.0%)	
	Medicaid	381 (3.6%)	109 (5.7%)	
	Medicare	4,055 (38.3%)	748 (38.9%)	
	Other gov.	240 (2.3%)	53 (2.8%)	
	Unknown	2,322 (21.9%)	461 (24.0%)	
Poverty Index[ǂ]	0-5%	1,565 (14.8%)	15 (0.8%)	<0.0001
	5-9.9%	2,142 (20.2%)	90 (4.7%)	
	10-19.9%	3,717 (35.1%)	334 (17.4%)	
	20-100%	3,149 (29.7%)	1,478 (76.9%)	
	Unknown	20 (0.2%)	4 (0.2%)	
Birth Country	Non-USA	1,181 (11.2%)	606 (31.6%)	<0.0001
	USA	6,485 (61.2%)	803 (41.8%)	
	Unknown	2,927 (27.6%)	512 (26.7%)	
Stage at Diagnosis	Localized	2,981 (28.2%)	621 (32.3%)	<0.01
	Regional	3,318 (31.3%)	568 (29.6%)	
	Metastatic	4,294 (40.5%)	732 (38.1%)	
Tumor Location	Pylorus	243 (2.3%)	68 (3.5%)	<0.0001
	Antrum	1,492 (14.1%)	375 (19.5%)	
	Body	957 (9.0%)	271 (14.1%)	
	Cardia	3,556 (33.6%)	285 (14.8%)	
	Fundus	458 (4.3%)	100 (5.2%)	
	Greater curve NOS	345 (3.3%)	78 (4.1%)	
	Lesser curve NOS	673 (6.4%)	135 (7.0%)	
	NOS	2,869 (27.1%)	610 (31.8%)	

ǂ Code for neighborhood poverty level based on the census tract of diagnosis address.

Table 2: Demographics by Border County Residence Status; Non-Hispanic Whites

		Non-border county resident N=6,764	Border county resident N=241	p-value
		Mean (std dev)		
Age at Diagnosis		67.2 (12.8)	68.5 (12.8)	NS
		N (%)		
Age Group at Diagnosis	<50 years	608 (9.0%)	21 (8.7%)	NS
	50+ years	6,156 (91.0%)	220 (91.3%)	
Sex	Female	2,295 (33.9%)	85 (35.3%)	NS
	Male	4,469 (66.1%)	156 (64.7%)	
Insurance Status	Uninsured	264 (3.9%)	12 (5.0%)	<0.001
	Private	1,731 (25.6%)	49 (20.3%)	
	Medicaid	125 (1.9%)	5 (2.1%)	
	Medicare	2,932 (43.4%)	97 (40.3%)	
	Other gov.	185 (2.7%)	18 (7.5%)	
	Unknown	1,527 (22.6%)	60 (24.9%)	
Poverty Index	0-5%	1,293 (19.1%)	5 (2.1%)	<0.0001
	5-9.9%	1,706 (25.2%)	19 (7.9%)	
	10-19.9%	2,453 (36.3%)	66 (27.4%)	
	20-100%	1,300 (19.2%)	151 (62.7%)	
	Unknown	12 (0.2%)	---	
Birth Country	Non-USA	242 (3.6%)	22 (9.1%)	<0.0001
	USA	4,796 (70.9%)	154 (63.9%)	
	Unknown	1,726 (25.5%)	65 (27.0%)	
Stage at Diagnosis	Localized	2,058 (30.4%)	88 (36.5%)	NS
	Regional	2,087 (30.9%)	67 (27.8%)	
	Metastatic	2,619 (38.7%)	86 (35.7%)	
Tumor Location	Pylorus	115 (1.7%)	5 (2.1%)	NS
	Antrum	773 (11.4%)	35 (14.5%)	
	Body	508 (7.5%)	24 (10.0%)	
	Cardia	3,028 (44.8%)	82 (34.0%)	
	Fundus	269 (4.0%)	12 (5.0%)	
	Greater curve NOS	170 (2.5%)	7 (2.9%)	
	Lesser curve NOS	315 (4.7%)	10 (4.2%)	
	NOS	1,586 (23.5%)	66 (27.4%)	

Table 3: Demographics by Border County Residence Status; Hispanics

		Non-border county resident N=3,829	Border county resident N=1,680	p-value
		Mean (std dev)		
Age at Diagnosis		61.2 (15.0)	66.2 (14.0)	<0.0001
		N (%)		
Age Group at Diagnosis	<50 years	868 (22.7%)	227 (13.5%)	<0.0001
	50+ years	2,961 (77.3%)	1,453 (86.5%)	
Sex	Female	1,645 (43.0%)	747 (44.5%)	NS
	Male	2,184 (57.0%)	933 (55.5%)	
Insurance Status	Uninsured	645 (16.9%)	212 (12.6%)	<0.0001
	Private	955 (24.9%)	277 (12.6%)	
	Medicaid	256 (6.7%)	104 (6.2%)	
	Medicare	1,123 (29.3%)	651 (38.8%)	
	Other gov.	55 (1.4%)	35 (2.1%)	
	Unknown	795 (20.8%)	401 (23.9%)	
Poverty Index	0-5%	272 (7.1%)	10 (0.6%)	<0.0001
	5-9.9%	436 (11.4%)	71 (4.2%)	
	10-19.9%	1,264 (33.0%)	268 (16.0%)	
	20-100%	1,849 (48.3%)	1,327 (79.0%)	
	Unknown	8 (0.2%)	4 (0.2%)	
Birth Country	Non-USA	939 (24.5%)	584 (34.8%)	<0.0001
	USA	1,689 (44.1%)	649 (38.6%)	
	Unknown	1,201 (31.4%)	447 (26.6%)	
Stage at Diagnosis	Localized	923 (24.1%)	533 (31.7%)	<0.0001
	Regional	1,231 (32.2%)	501 (29.8%)	
	Metastatic	1,675 (43.8%)	646 (38.5%)	
Tumor Location	Pylorus	128 (3.3%)	63 (3.8%)	<0.05
	Antrum	719 (18.8%)	340 (20.2%)	
	Body	449 (11.7%)	246 (14.6%)	
	Cardia	528 (13.8%)	203 (12.1%)	
	Fundus	189 (4.9%)	88 (5.2%)	
	Greater curve NOS	175 (4.6%)	71 (4.2%)	
	Lesser curve NOS	358 (9.4%)	125 (7.4%)	
	NOS	1,283 (33.5%)	544 (32.4%)	

Table 4: Treatment Patterns by Stage and Border County Residence

			All Races/Ethnicities N (%)		
			Non-border county resident N=10,593	**Border county resident N=1,921**	**p-value**
Localized Disease N=3,602	Surgical resection	No	1,570 (52.7%)	348 (56.0%)	<0.0001
		Yes	1,272 (42.7%)	218 (35.1%)	
		Unknown	139 (4.7%)	55 (8.9%)	
Regional Disease N=3,886	Treatment received	Surgery only	694 (20.9%)	154 (27.1%)	NS
		Chemo only	621 (18.7%)	81 (14.3%)	<0.01
		Surgery + chemo	1186 (35.7%)	162 (28.5%)	<0.05
		Unknown	817 (24.6%)	171 (30.1%)	---
	Chemotherapy/surgery sequence (in patients receiving both treatments)	Adjuvant	496 (42.0%)	86 (54.1%)	<0.0001
		Neoadjuvant	418 (35.4%)	21 (13.2%)	
		Peri-operative	86 (7.3%)	8 (5.0%)	
		Unknown	181 (15.3%)	44 (27.7%)	
Metastatic Disease N=5,026	Chemotherapy	No	1,641 (38.2%)	348 (47.5%)	<0.0001
		Yes	2,259 (52.6%)	300 (41.0%)	
		Unknown	394 (9.2%)	84 (11.5%)	
			Non-Hispanic Whites N (%)		
			Non-border county resident N=6,764	**Border county resident N=241**	**p-value**
Localized Disease N=2,146	Surgical resection	No	1,127 (54.8%)	51 (58.0%)	<0.01
		Yes	831 (40.4%)	26 (29.5%)	
		Unknown	100 (4.9%)	11 (12.5%)	
Regional Disease N=3,886	Treatment received	Surgery only	430 (20.6%)	12 (17.9%)	NS
		Chemo only	406 (19.5%)	18 (26.9%)	NS
		Surgery + chemo	734 (34.2%)	18 (26.9%)	NS
		Unknown	517 (24.8%)	19 (28.4%)	---
Metastatic Disease N=2,705	Chemotherapy	No	984 (37.6%)	36 (41.9%)	NS
		Yes	1,395 (53.3%)	42 (48.8%)	
		Unknown	240 (9.2%)	8 (9.3%)	
			Hispanics N (%)		
			Non-border county resident N=3,829	**Border county resident N=1,680**	**p-value**
Localized Disease N=1,456	Surgical resection	No	443 (48.0%)	297 (55.7%)	<0.0001
		Yes	441 (47.8%)	192 (36.0%)	
		Unknown	39 (4.2%)	44 (8.3%)	

Regional Disease N=1,732	Treatment received	Surgery only	264 (21.4%)	142 (28.3%)	NS
		Chemo only	215 (17.5%)	63 (12.6%)	<0.01
		Surgery + chemo	272 (22.1%)	79 (15.8%)	NS
		Unknown	480 (39.0%)	217 (43.3%)	---
Metastatic Disease N=2,321	Chemotherapy	No	657 (39.2%)	312 (48.3%)	<0.0001
		Yes	864 (51.6%)	258 (39.9%)	
		Unknown	154 (9.2%)	76 (11.8%)	

Chapter III: Conclusions

Border county residents are significantly less likely to receive guideline-concordant gastric cancer care compared with those living in non-border counties. Subsequently, border residents experienced worse survival outcomes. These significant disparities likely stem from healthcare access barriers and systemic bias.

Among Texas border residents ages 18-64, 9.8% speak English "not at all", and 10.4% speak "not well." In the 65+ population, which is the main demographic diagnosed with gastric cancer, these rates increase to 18.4% who speak English "not at all" and 13.3% "not well." This is in contrast to 11% of the overall Texas 65+ population with limited English proficiency (speak English "less than very well") (44). Previous studies have established that patients with limited English fluency are at high risk for lower quality care, including higher rates of misdiagnoses, medical errors, and serious adverse events due to communication barriers (45-47). Limited English fluency patients diagnosed with cancer may be particularly impacted by communication barriers, as cancer care conversations often involve complex, confusing, and emotionally-laden discussions. Poor quality communication is significantly correlated with worse patient acceptance of, and adherence to, recommended treatments (48).

A qualitative study of interpreters working in oncology departments identified system-level barriers and underutilization of trained interpreters as major factors that interfere with the provision of quality cancer care for limited English fluency patients. On a systems level, it was noted that non-English proficient patients were often given written materials in English due to a lack of translated information. Patients then needed to find somebody who reads English to explain the information to them; however, interpreters often did not have extra allotted time to translate written materials, and patients may not have easy access to anyone else who is able to do so (59). Patient-specific themes such as limited knowledge of interpreter services (e.g., being

concerned about extra charges, not knowing services are available), fear of appearing incompetent/ignorant, and privacy concerns emerged as reasons for underutilization of interpreters. Provider-specific themes included refusing interpreters in an effort to save time during patient encounters, and overestimating patients' language mastery or perceived understanding of interactions.

In a 2004 survey of 272 hospitals, only 39% reported collecting any kind of data on the preferred language/English proficiency of patients (60, 61). A 2016 survey conducted by the American Hospital Association of over 4,500 hospitals found that only 56% offered some type of linguistic/translation services, a modest increase of 2% from a survey conducted 5 years prior (49). Yet, 97% of physicians see at least some patients who do not speak English or have limited English proficiency (50). These statistics highlight the need for an overhaul of current healthcare system practices to have language services be a required part of providing high-quality health care. The importance of combatting language-access issues also needs to be integrated into healthcare students' and physicians' education. A 2017 study of medical and nursing students published by the Association of American Medical Colleges found that students were taught to value efficiency over effective communication and the learning environment did not support or emphasize high-quality care for patients with limited English proficiency (62). Policies should be developed to mandate the availability of in-house or virtual translation services at all healthcare centers.

Border residents also face additional barriers to accessing health care services beyond language. The border states of Texas and New Mexico have historically reported two of the highest uninsured rates in the nation. Although health insurance status is a critical determinant of healthcare access, even those with health insurance may be unable to afford needed health care

because of high out-of-pocket costs for deductibles/co-payments. In the border region, approximately 1 out of 20 adults reported not receiving health care because they could not afford it (25). Additionally, between 2000-2003, nearly 1 in 5 adults living in the border region did not have adequate access to health care and reported being unaware of where they could go to seek care. Hispanics living in the border region were more than 3 times more likely than non-Hispanic whites to report not having a place to go to receive healthcare services (31.9% vs 10.0%) (25).

These findings suggest a few crucial areas that need to be addressed in order to improve access to health care in the US-Mexico border. Firstly, healthcare providers must be given the necessary infrastructure and resources to provide affordable, quality care to those who cannot afford it. Secondly, the BC population needs to be provided with resources and information on how to effectively access health care at all levels, and community health workers/non-governmental organizations should be leveraged to fill gaps. Thirdly, systematic efforts to train, attract, and retain practitioners practicing in rural and urban underserved areas such as the US-Mexico border are needed. This will require cooperation between public health professionals, health care providers, and the government.

The impact on current attitudes toward immigration policies, immigrants, and discriminatory/racist rhetoric on health seeking behaviors also cannot be ignored. In our BC cohort, over 31% of patients were foreign-born. A qualitative study published in 2019 of community health workers in Texas found a growing fear of interacting with health and social services among both documented and undocumented Hispanic residents and their families (63). The study also found that social networks were spreading warnings of avoiding certain healthcare facilities due to fear of discrimination and/or being reported to ICE by staff, further limiting access to care in communities where access is already strained.

Finally, the role of provider bias toward racial minorities must be discussed. While provider explicit racial bias tends to be rather low, implicit bias is high among healthcare professionals (64). Approximately two-thirds of clinicians had implicit bias against Hispanics, with 51% having moderate to strong bias (51). Oncologists implicit bias predicts less patient confidence in the treatments recommended and lower likelihood of completing therapies (52). Higher implicit bias is also associated with increased patient difficulty in remembering the content of cancer care discussions. Thus, implicit racial bias is likely an important source of racial disparities in receipt of guideline-concordant cancer care. A systematic review on the effects of found that racial concordance between providers and physicians was associated with improved communication across the following domains: satisfaction, information-giving, partnership building, patient participation, positive and negative affect/talk, length of visit/time and talk-time ratio (57). Increasing the diversity of our healthcare providers to allow for more racial concordant physician-patient interactions is likely an important aspect of reducing disparities. Cultural sensitivity and bias training, as well as a focus on engaging in higher quality communication with racially discordant patients by focusing on improving patient-centeredness, partnership building, and patient engagement, is also key.

In conclusion, border county residents with gastric cancer are less likely to receive guideline-concordant care, likely as a result of multiple factors including access barriers, living in areas of healthcare deserts, and bias. This is a major health equity issue. Further studies are needed to identify the specific contributing mechanisms, and relative weight of, various factors which limit receipt of quality cancer care among US-Mexico border county residents. This is an important area of future research to improve healthcare equity and outcomes for all gastric cancer patients. Lessons learned and public health programs/policies developed to target gastric

cancer care improvement can also be applied to other areas of health disparities among border residents.

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