Original Article Open Access

Archives Of Breast Cancer

DOI: 10.32768/abc.1582986193-725

Influence of Ethnicity and Birthplace on Breast Cancer Clinical Features, Treatment, and Survival Among Texas Women

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ARTICLE INFO

Received:
21 April 2026
Revised:
16 July 2026
Accepted:
27 July 2026

Keywords:
breast neoplasms, radiotherapy, health care disparities, ethnicity, birthplace

ABSTRACT

Background: The influence of nativity on cancer outcomes has been described across several malignancies, but its role in breast cancer remains unclear. We examined whether birthplace is associated with differences in presentation, treatment, and mortality among women diagnosed with invasive breast cancer in Texas.

Methods: We performed a retrospective cohort study using the Texas Cancer Registry, including 290 656 women diagnosed with primary invasive breast cancer between 1995 and 2018. Demographic, clinical, treatment, and mortality data were analyzed. Missing birthplace data were addressed using multiple imputation. Associations were evaluated using χ^2 or Fisher exact tests, and multivariable logistic regression was used to identify factors associated with all-cause mortality.

Results: Foreign-born Hispanic and Asian women were more likely to present with metastatic disease at diagnosis compared to their US-born counterparts (Hispanic: 4.7% vs 2.7%; Asian: 3.3% vs 2.1%). Asian women demonstrated higher rates of radiation therapy use regardless of nativity. In multivariable analyses, foreign-born Hispanic (OR, 1.482; 95% CI, 1.419-1.548; $P < .001$) and foreign-born Asian women (OR, 1.172; 95% CI, 1.058-1.299; $P = .002$) had significantly higher odds of all-cause mortality compared to US-born non-Hispanic white women.

Conclusion: Birthplace was associated with differences in breast cancer presentation, treatment patterns, and mortality outcomes.

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INTRODUCTION

Breast cancer is the most common cancer diagnosis and the second leading cause of cancer death among US women overall, including non-Hispanic white (NHW) and Asian women. Notably, however, it remains the leading cause of cancer death specifically for US Hispanic women.[1-3]

An increase in immigration to the US has spurred research into the association between birthplace and incidence and mortality of various malignancies. Determining a patient's birthplace for epidemiologic research is complicated by the fact that this variable is often missing from electronic medical records (EMRs).[4,5] Multiple imputation strategies such as those presented by Montealegre *et al.* can be employed to effectively handle missing nativity data.

Birthplace has been shown to be associated with survival after diagnosis and with the incidence of malignancies such as cervical, colon, and prostate cancer, as well as Hodgkin lymphoma.[6-9] Breast cancer has also been examined, but mixed results have been reported.

For example, while some studies report lower breast cancer incidence and mortality rates among foreign-born Hispanic and Asian women compared to their US-born counterparts, others have found the opposite association.[10-16] However, a consensus exists that foreign-born Hispanic and Asian women have a greater likelihood of late-stage disease and a more adverse risk factor profile at diagnosis compared to US-born women of the same ethnicities.[10,14-16]

Because there is an increase in the number of foreign-born women residing in states such as Texas, it is especially pertinent to define the association of birthplace with breast cancer diagnosis, prognosis, and treatment. Our goal, therefore, was to determine any significant differences in presentation, clinical features, treatment, and survival for US-born Hispanic, foreign-born Hispanic, US-born Asian, foreign-born Asian, and NHW women diagnosed with invasive breast cancer in Texas. We conducted a retrospective cohort study of women in the Texas Cancer Registry (TCR) with a diagnosis of first primary invasive breast cancer between 1995 and 2018.

METHODS

Study design, setting, and reporting

Adult women diagnosed with primary invasive breast cancer between 1995 and 2018 were identified from the Texas Cancer Registry. The TCR is a statewide, population-based registry that systematically collects and maintains data on all cancer cases diagnosed in Texas. Eligible patients included women with localized, regional, or distant disease. Patients with unknown stage, grade, receptor status, ethnicity, and/or birthplace were retained and included in the analyses. Vital status data were censored on December 31, 2018. Vital status was available for all patients and coded as alive or deceased at the censoring point. Therefore, no patients were excluded due to missing vital status. The final study cohort consisted of 290 656 women.

This study used de-identified registry data from the Texas Cancer Registry. Given the use of de-identified secondary data and the absence of direct human contact, the Texas Department of State Health Services IRB waived review and did not require informed consent.

Data collection

Variables were selected a priori based on clinical relevance and prior literature. Demographic and clinical variables, including pathology, receptor status (estrogen receptor [ER], progesterone receptor [PR], and human epidermal growth factor receptor 2 [HER2]), treatment, and vital status were extracted. Treatment variables included radiation therapy, chemotherapy, hormone therapy, surgery (breast-conserving or mastectomy), and combinations of these modalities. According to the TCR, vital status reflects all-cause mortality.

Statistical Analysis

Accounting for missing birthplace data

Missing data for birthplace, a key demographic variable, were addressed using multiple imputation via fully conditional specification under a Markov chain Monte Carlo (MCMC) framework, assuming data were missing at random (MAR). Multiple imputation was performed only for missing birthplace data. For other categorical covariates with unavailable information, "Unknown" or "No/Unknown" values were retained and analyzed as separate categories, as applicable. These observations were not excluded, and no additional imputation procedures were performed for these covariates.

Assessing multiple imputation strategy

To assess the robustness of the imputation strategy, two separate χ^2 tests were conducted. First, birthplace and mortality distributions before and after imputation were compared. Second, associations between missing birthplace data and observed demographic, clinical, treatment, and outcome variables were evaluated to assess the plausibility of the missing at random (MAR) assumption. To further assess the plausibility of the MAR assumption, multivariable logistic regression was performed using missing birthplace data as the outcome variable (1 = missing birthplace; 0 = observed birthplace). Predictor variables included observed demographic, clinical, treatment, and outcome-related characteristics available in the registry, including age group, histology, stage at diagnosis, tumor grade, radiation treatment, chemotherapy, hormone therapy, and vital status. This analysis was used to determine whether missing birthplace data could be explained by measured variables incorporated into the imputation model. Associations between missing birthplace data and observed variables were interpreted as supporting the plausibility of the MAR framework. Receiver operating characteristic (ROC) analysis was performed as an additional sensitivity assessment using predicted probabilities from logistic regression models before and after imputation.

Complete-case analysis of birthplace data

Patient demographic and clinical characteristics were summarized using frequencies and percentages. Unadjusted associations between categorical variables and mortality were initially evaluated using χ^2 or Fisher exact tests, as appropriate. Univariable logistic regression analyses were subsequently performed to further evaluate the unadjusted association between each candidate predictor and mortality. Variables with $P < .20$ in the univariable logistic regression analyses were considered for inclusion in the multivariable logistic regression model. Multivariable logistic regression was used to evaluate birthplace as the main factor associated with mortality, after controlling for demographic characteristics and other clinically relevant variables. Results of univariable and multivariable logistic regression analyses are presented as odds ratios (ORs) and 95% confidence intervals (CIs). The final multivariable logistic regression model included ethnicity/birthplace cohort, age group, tumor grade, census tract poverty indicator, stage, receipt of radiation, receipt of chemotherapy, and receipt of hormone therapy. Receptor status and surgery were examined descriptively but were not included in the final adjusted model. Receptor status was incompletely captured for most years of the registry and, therefore, had excessive missing data, precluding inclusion in the multivariable model. Surgery was omitted from the final adjusted model because surgical status was known for nearly 80% of patients; moreover, since surgery is the mainstay

of breast cancer treatment, our analytic focus was on adjuvant therapies. The follow-up time and date of last contact were not available in the analytic dataset; therefore, time-to-event analyses, including Cox proportional hazards regression and Kaplan-Meier estimation, could not be performed. Mortality status at the censoring point was analyzed as a binary outcome using multivariable logistic regression. Statistical significance was defined as $P < .05$. Statistical analyses were performed using IBM SPSS Statistics for Windows, version 29.0 (IBM Corp., Armonk, NY, USA), and R version 4.4.1 (R Foundation for Statistical Computing, Vienna, Austria).

Patient and public involvement

It was not appropriate or possible to involve patients or the public in the design, conduct, reporting, or dissemination plans of this research, as this study was a retrospective analysis of previously collected data.

RESULTS

Patient Characteristics

The majority of patients were aged 40 to 64 years at diagnosis (152 071; 52.3%), had ductal carcinoma (202 776; 69.8%), grade 2 disease (101 067; 34.8%), and were born in the US (269 066; 92.6%) (Table 1). Notably, exact patient age was not available, as age was categorized as younger than 40 years, aged 40 to 64 years, or 65 years and older. While most patients were aged 40 to 64 years, 5.6% (n = 16 404) were younger than 40 years and 42.0% (n = 122 181) were 65 years and older.

Multiple Imputation

Associations between birthplace and mortality were examined before and after multiple imputation using χ^2 tests. Before imputation, the analysis was restricted to patients with observed birthplace data (n = 127 481). In this complete-case subset, mortality was observed in 35.1% of US-born individuals and 37.3% of foreign-born individuals. After multiple imputation, the analysis included the full cohort (N = 290 656), and mortality was observed in 17.4% of US-born individuals and 24.5% of foreign-born individuals. Patients with missing birthplace data differed systematically from those with observed birthplace data, explaining the change in crude mortality after inclusion of the full cohort. All P values were < .001.

Separate analyses were performed to assess the plausibility of the MAR assumption. Missing birthplace data demonstrated significant associations with age, histology, stage at diagnosis, tumor grade, treatment variables, and vital status (all $P < .001$), suggesting that missing birthplace data were related to measured patient and disease characteristics available in the registry. In a subsequent multivariable logistic regression model using missing birthplace data as the outcome, several observed variables remained significantly associated with missing birthplace data, supporting the plausibility of the MAR framework used for multiple imputation. For example, distant-stage disease remained strongly associated with mortality in both analyses (complete-case OR, 15.15; imputed OR, 15.37), suggesting the preservation of major inferential relationships following imputation.

The area under the curve (AUC) for the complete-case model was 0.711 (95% CI, 0.708-0.714), while the model based on the imputed dataset demonstrated an AUC of 0.767 (95% CI, 0.764-0.769). This apparent increase in discrimination likely reflects the larger analytic sample and reduced complete-case selection bias after imputation rather than a true improvement in predictive performance. Therefore, ROC findings (Figure 1) should be interpreted as supporting the preservation of model behavior following imputation rather than the formal validation of imputation accuracy.

Clinical Presentation and Disease Course

Foreign-born Hispanic (4.7%) and foreign-born Asian women (3.3%) had significantly higher rates of metastatic disease at presentation compared to their US-born counterparts (2.7% and 2.1%, respectively). We observed marginally higher rates of grade 3 disease among foreign-born Hispanic (35.7%) and foreign-born Asian women (32.6%) compared to their US-born counterparts; however, these rates were substantially higher when foreign-born Hispanic and foreign-born Asian women were compared to US-born NHW women (27.5%). Overall, the proportions of all patients recorded as having hormone receptor-negative disease (estrogen receptor-negative and progesterone receptor-negative), including patients with unknown receptor status in the denominators, were 1.0% among Hispanic women, 1.3% among Asian women, and 0.6% among NHW women, pooling across birthplace.

Treatment Modalities and Outcomes

All candidate variables met the prespecified $P < .20$ criterion in the univariable logistic regression analyses; the final adjusted model excluded receptor status and surgery, as described in Methods. Table 2 shows the unadjusted and adjusted associations between the examined predictors and mortality. Surgery was examined descriptively and was not included in the adjusted model. Descriptive treatment patterns for patients with localized and regional disease are presented in Figure 2A and B. The reported proportions receiving radiation were higher among Asian women (25.7%) than among Hispanic (22.3%) and NHW women (24%), regardless of birthplace. Most notably, foreign-born Hispanic (OR, 1.482; 95% CI, 1.419-1.548; $P < .001$) and foreign-born Asian women (OR, 1.172; 95% CI, 1.058-1.299; $P = .002$) had significantly increased odds of all-cause mortality compared to US-born NHW women (Table 2).

DISCUSSION

This single-state analysis of adult women with primary invasive breast cancer provides valuable insights into the influence of birthplace and ethnicity on clinical features, treatment patterns, and outcomes. At diagnosis, we observed the highest proportion of metastatic disease among foreign-born Hispanic

Table 1. Clinical Features of Breast Cancer by Ethnicity and Birthplace Among Women Diagnosed With Breast Cancer in Texas, 1995-2018 (N = 290 656)

Characteristic	Hispanic US-born	Hispanic foreign-born	Asian US-born	Asian foreign-born	NHW US-born	NHW foreign-born	*P* value
Age, n (%)							<.001
<40 years	4703 (9.4)	1372 (10.4)	584 (11.2)	270 (11.3)	8999 (4.2)	476 (7.9)	
40–64 years	29 572 (59.4)	7858 (59.5)	3509 (67.0)	1535 (64.3)	106 048 (49.6)	3549 (59.2)	
≥65 years	15 547 (31.2)	3975 (30.1)	1143 (21.8)	583 (24.4)	98 961 (46.2)	1972 (32.9)	
Stage at diagnosis, n (%)							<.001
Localized	13 620 (27.3)	2869 (21.7)	1722 (32.9)	485 (20.3)	69 063 (32.3)	1478 (24.6)	
Regional	7902 (15.9)	2375 (18.0)	788 (15.0)	294 (12.3)	29 886 (14.0)	713 (11.9)	
Distant	1337 (2.7)	619 (4.7)	111 (2.1)	79 (3.3)	5471 (2.6)	140 (2.3)	
Unknown	26 963 (54.1)	7342 (55.6)	2615 (49.9)	1530 (64.1)	109 558 (51.2)	3666 (61.1)	
Histology, n (%)							<.001
Ductal	35 272 (70.8)	9355 (70.8)	3906 (74.6)	1738 (72.8)	148 368 (69.3)	4137 (69.0)	
Lobular	3354 (6.7)	799 (6.1)	270 (5.2)	129 (5.4)	17 770 (8.3)	611 (10.2)	
Mixed/other	11 196 (22.5)	3051 (23.1)	1060 (20.2)	521 (21.8)	47 870 (22.4)	1249 (20.8)	
Grade, n (%)							<.001
Grade 1	6511 (13.1)	1329 (10.1)	771 (14.7)	290 (12.1)	38 618 (18.0)	1068 (17.8)	
Grade 2	15 994 (32.1)	3896 (29.5)	1861 (35.5)	716 (30.0)	76 463 (35.7)	2137 (35.6)	
Grade 3	17 271 (34.7)	4712 (35.7)	1673 (32.0)	778 (32.6)	58 858 (27.5)	1614 (26.9)	
Unknown	10 046 (20.2)	3268 (24.7)	931 (17.8)	604 (25.3)	40 069 (18.7)	1178 (19.6)	
Receptor status, n (%)							<.001
Negative	487 (1.0)	139 (1.1)	75 (1.4)	27 (1.1)	1291 (0.6)	39 (0.7)	
Positive[a]	11425 (22.9)	3069 (23.2)	1510 (28.8)	707 (29.6)	54310 (25.4)	1637 (27.3)	
Unknown	37910 (76.1)	9997 (75.7)	3651 (69.7)	1654 (69.3)	158407 (74)	4321 (72.1)	

[a] Receptor positive indicates patients who had single or double positive receptor status or received hormones.

(4.7%) and foreign-born Asian women (3.3%) (Table 1). Additionally, Asian women were more likely to receive radiation therapy as part of their treatment regimen, regardless of birthplace (Figure 2A and B). Most notably, foreign-born Hispanic and foreign-born Asian women had significantly increased odds of all-cause mortality compared to their US-born counterparts (Table 2).

Previous research by Montealegre *et al.* highlighted significant gaps in birthplace data within cancer registries, with birthplace data missing for up to 49% of patients with prostate cancer and slightly lower rates for cervical (31%) and colorectal cancer (39%).[5] In our study, birthplace data were missing for 56.1% of patients. They demonstrated that multiple imputation strategies could detect foreign-born status with a sensitivity ≥90% and specificity ≥86%.[5]

Our findings of more advanced disease at diagnosis among foreign-born Hispanic and foreign-born Asian women align with prior studies. For example, Kouri *et al.* reported lower rates of stage I disease in foreign-born Hispanics compared to US-born Hispanics and NHW women.[15] Similarly, a meta-analysis by Herbach *et al.* showed that foreign-born women were less likely to present with localized disease compared to native-born women across eight cohorts, including five studies using US-born women as the comparison group.[17]

Hormone receptor status is a critical factor in breast cancer management. While we found no significant differences based on birthplace, the proportions of all patients recorded as having hormone receptor-negative disease (estrogen and progesterone receptor-negative) were higher among Hispanic (1.0%) and Asian women (1.3%) than among NHW women (0.6%), with patients of unknown receptor status included in the denominators. This is consistent with a study of women aged 50 years and older that reported higher odds of estrogen receptor-negative/progesterone receptor-negative breast cancer in several Asian and Hispanic subgroups compared with NHW women.[18]

In our analysis of treatment regimens—including breast-conserving surgery (BCS) with radiation, mastectomy with radiation, BCS without radiation/unknown radiation status, and mastectomy without radiation/unknown radiation status—we observed that Asian women, regardless of birthplace, were more likely to receive radiation therapy compared to Hispanic and NHW women. This finding contrasts with an earlier California study of localized breast carcinoma, which reported higher rates of mastectomy or omission of radiation after BCS among Chinese women compared with NHW women.[19] These discrepancies may reflect geographical differences in treatment practices and highlight the need for further investigation.

Importantly, foreign-born Hispanic and foreign-born Asian women in our study faced significantly

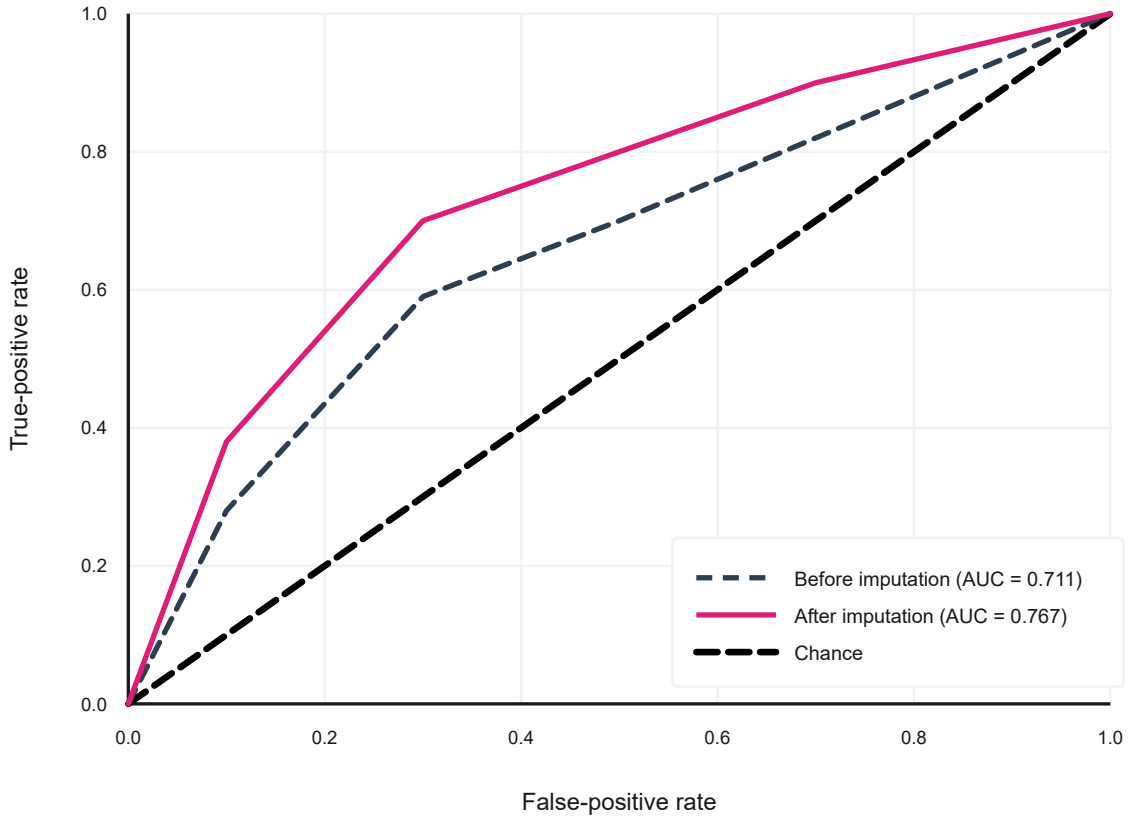


Figure 1. Receiver Operating Characteristic Curves Before and After Multiple Imputation
Receiver operating characteristic curves compare discrimination before and after multiple imputation (AUC, 0.711 vs 0.767); the diagonal line indicates chance discrimination. The higher post-imputation AUC supports preservation of model behavior in the larger imputed analytic sample but does not formally validate imputation accuracy. Abbreviations: AUC, area under the curve; ROC, receiver operating characteristic.

increased odds of all-cause mortality compared to US-born NHW women. Gomez *et al.* similarly reported higher mortality rates among foreign-born Asian women.[16] Likewise, Kouri *et al.* found that foreign-born Hispanic women were more likely to present with advanced disease and receive suboptimal treatment regimens, contributing to increased mortality rates.[15]

Several factors may contribute to the observed differences in presentation and outcomes based on birthplace. Prior studies have demonstrated that foreign-born populations may experience barriers to timely cancer screening, diagnosis, and treatment due to reduced access to health care systems, lack of insurance coverage, language barriers, and socioeconomic disparities.[15,17] Differences in breast cancer risk factors may also play a role. Variations in obesity prevalence, breastfeeding practices, reproductive patterns, and contraceptive use across populations have previously been associated with differences in breast cancer incidence and outcomes.[20-22] Delayed presentation and reduced access to follow-up care may partially explain the higher rates of metastatic disease and mortality observed among foreign-born Hispanic and Asian women in our cohort.

These findings underscore the association of birthplace with clinical presentation and outcomes, while ethnicity appears to be associated with receptor status and treatment approaches. This study represents the first analysis to examine the influence of birthplace on breast cancer presentation, treatment, and outcomes in this population, offering a novel perspective on these disparities. However, several limitations must be acknowledged. First, although the plausibility of the MAR assumption was assessed using observed demographic, clinical, treatment, and outcome characteristics, MAR remains an untestable assumption and residual bias due to unmeasured mechanisms cannot be excluded. However, model variables included in the imputation and analytic models were selected a priori based on clinical relevance, prior literature, and availability within the data registry to preserve important relationships and minimize potential bias due to omitted measured factors. Second, we acknowledge that logistic regression provides a simplified assessment of mortality. Because the date of last follow-up was not available in the analytic

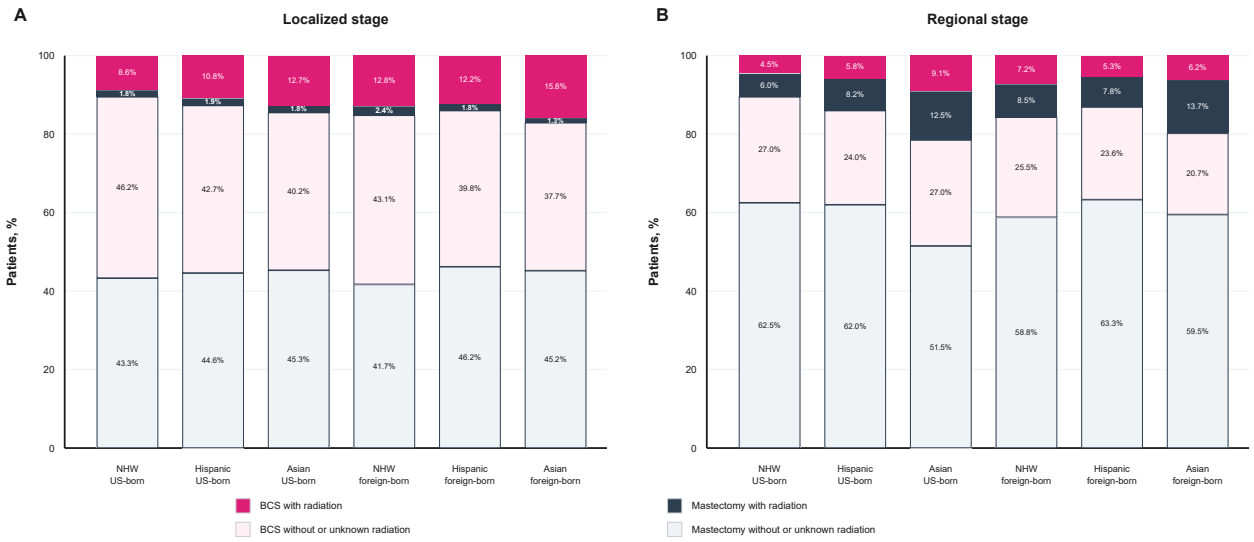


Figure 2. Treatment Modality by Ethnicity, Birthplace, and Disease Stage
Stacked bars show the proportions of patients receiving breast-conserving surgery (BCS) with radiation, mastectomy with radiation, BCS without or with unknown radiation status, and mastectomy without or with unknown radiation status, stratified by ethnicity and birthplace. A, Localized-stage disease. B, Regional-stage disease. Colors are used consistently across panels for treatment categories. Abbreviations: BCS, breast-conserving surgery; NHW, non-Hispanic white; US, United States.

dataset, survival analyses accounting for time-to-event could not be performed. Logistic regression was, therefore, used to evaluate factors associated with mortality status as a binary endpoint. Finally, external validation was not performed and would be required to assess the generalizability of our findings.

CONCLUSION

Our results suggest that birthplace is significantly associated with the clinical presentation of breast cancer and all-cause mortality, while ethnicity is associated with receptor status and treatment patterns. Addressing these disparities through culturally tailored interventions and equitable access to care will be essential for improving breast cancer outcomes in diverse populations.

ETHICAL CONSIDERATIONS

This study used de-identified individual-level registry data from the Texas Cancer Registry. Given the use of de-identified secondary data and the absence of direct human contact, the Texas Department of State Health Services IRB waived review and did not require informed consent.

DATA AVAILABILITY

The authors will provide the raw data and programming code upon reasonable request.

CONFLICT OF INTERESTS

There are no conflicts of interest to declare.

FUNDING

This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

ACKNOWLEDGMENTS

Texas cancer data have been provided by TCR, the Cancer Epidemiology and Surveillance Branch, Texas Department of State Health Services, 1100 West 49th Street, Austin, TX 78756. Data from TCR are supported by the following: Cooperative Agreement No. 1NU58DP007140 from the Centers for Disease Control and Prevention (CDC), Contract No. 75N91021D00011 from the National Cancer Institute's Surveillance, Epidemiology, and End Results (SEER) Program, and the Cancer Prevention and Research Institute of Texas (CPRIT).

AI DISCLOSURE

Generative AI was not used in the production of this manuscript.

AUTHOR CONTRIBUTIONS

ANC: Conceptualization, Methodology, Data curation, Formal analysis, Writing – original draft. MHA: Methodology, Software, Formal analysis, Data curation, Writing – review & editing. NBA: Conceptualization, Methodology, Data curation, Writing – review & editing. RP: Formal analysis, Writing – review & editing. ML: Conceptualization, Methodology, Formal analysis, Writing – review & editing, Supervision.

Table 2. Logistic Regression Model Predicting All-Cause Mortality

Characteristic	Unadjusted OR (95% CI)	*P* value	Adjusted OR (95% CI)	*P* value
Ethnicity				
NHW US-born	Reference	NA[a]	Reference	NA[a]
Hispanic US-born	0.890 (0.867-0.914)	<.001	0.739 (0.718-0.761)	<.001
Asian US-born	0.349 (0.314-0.388)	<.001	0.340 (0.304-0.379)	<.001
NHW foreign-born	0.709 (0.658-0.764)	<.001	0.700 (0.647-0.757)	<.001
Hispanic foreign-born	1.955 (1.880-2.032)	<.001	1.482 (1.419-1.548)	<.001
Asian foreign-born	1.336 (1.213-1.471)	<.001	1.172 (1.058-1.299)	.002
Age				
<40 years	Reference	NA[a]	Reference	NA[a]
40–64 years	0.704 (0.677-0.732)	<.001	0.877 (0.841-0.914)	<.001
≥65 years	0.845 (0.812-0.879)	<.001	1.215 (1.163-1.269)	<.001
Grade				
Grade 1	Reference	NA[a]	Reference	NA[a]
Grade 2	2.303 (2.209-2.401)	<.001	2.005 (1.921-2.092)	<.001
Grade 3	4.743 (4.554-4.940)	<.001	3.633 (3.482-3.790)	<.001
Grade unknown	6.470 (6.206-6.744)	<.001	5.007 (4.797-5.225)	<.001
Census tract poverty indicator				
0-5%	Reference	NA[a]	Reference	NA[a]
5.1-9.9%	1.127 (1.094-1.161)	<.001	1.090 (1.057-1.125)	<.001
10-19.9%	1.320 (1.284-1.356)	<.001	1.221 (1.186-1.257)	<.001
20-100%	1.469 (1.427-1.512)	<.001	1.288 (1.246-1.330)	<.001
Unknown	1.618 (1.054-2.484)	.028	1.450 (0.926-2.271)	.104
Stage				
Local	Reference	NA[a]	Reference	NA[a]
Regional	3.554 (3.442-3.670)	<.001	3.026 (2.926-3.129)	<.001
Distant	20.619 (19.564-21.731)	<.001	15.371 (14.555-16.233)	<.001
Unknown	2.451 (2.386-2.517)	<.001	2.114 (2.057-2.173)	<.001
Radiation received				
Yes	Reference	NA[a]	Reference	NA[a]
No/unknown	1.699 (1.639-1.761)	<.001	1.507 (1.449-1.567)	<.001
Chemotherapy received				
Yes	Reference	NA[a]	Reference	NA[a]
No/unknown	0.604 (0.592-0.616)	<.001	0.736 (0.719-0.753)	<.001
Hormones received				
Yes	Reference	NA[a]	Reference	NA[a]
No/unknown	1.532 (1.495-1.570)	<.001	1.299 (1.264-1.335)	<.001

[a] NA indicates not applicable.
Abbreviations: CI, confidence interval; OR, odds ratio.

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How to Cite This Article

Chavana AN, Almekdash MH, Alam NB, Pettit R, Ludwig M. Influence of Ethnicity and Birthplace on Breast Cancer Clinical Features, Treatment, and Survival Among Texas Women. Arch Breast Cancer. 2026; 13(4):434-441. doi: 10.32768/abc.1582986193-725
Available from: https://www.archbreastcancer.com/index.php/abc/article/view/1320