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Worse Breast Cancer Outcomes for Southern Nevadans, Filipina and Black Women

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Abstract

Background—Breast cancer is the second deadliest cancer for women in the demographically unique mountainous west state of Nevada. This study aims to accurately characterize breast cancer survival among the diverse women of the flourishing Silver State.

Methods—Nevada Central Cancer Registry data was linked with the National Death Index and the Social Security Administration Masterfile. Overall five-year cause-specific survival, survival stratified by race/ethnicity, and stage-specific survival stratified by region of Nevada were calculated. Adjusted hazard ratios were computed with Cox proportional hazards regression.

Results—11,111 cases of breast cancer were diagnosed from 2003–2010. Overall 5-year breast cancer survival in Nevada was 84.4%, significantly lower than the US, at 89.2%. Black and Filipina women had a higher risk of death than white women.

Discussion—Poor survival in the racially and ethnically diverse Las Vegas metropolitan area, with a large foreign-born population, drives Nevada's low overall survival. System-wide changes are recommended to reduce the racial/ethnic disparities seen for black and Filipina women and improve outcomes for all.

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Compliance with Ethical Standards

Research involving human participants and/or animals

This article does not contain any studies with human participants or animals performed by any of the authors.

Author identifying information is located on title page.

Disclosure of potential conflicts of interest

The first author declares that he/she has no conflict of interest.

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Keywords

breast cancer; survival; Nevada; Filipinos; Blacks

Background

Breast cancer was the most common type of new cancer diagnosed in women in the United States (US) in 2015. It was the second most deadly cancer after lung, accounting for an estimated 40,290 deaths [1]. The lifetime risk for an American woman of developing breast cancer is 12.3%; the incidence and mortality risk increase with age [1]. Survival from breast cancer varies considerably by the stage of the tumor when diagnosed, with 99% relative 5-year survival in women with localized tumors but only 26% for those with distant stage disease [1]. Tumor size, histological type, and estrogen receptor status are also significant pathological factors in predicting survival [1].

Largely due to increases in screening and improvements in treatment, mortality rates have declined overall by 36% since their peak in 1989 [1]. Yet, the gains have not been realized uniformly across all racial/ethnic groups of women in the US. While historically white women have had the highest breast cancer incidence, as of 2012, rates of black and white women have converged [2]. Along with an increasing incidence trend, black women bear a disproportionate share of the mortality burden; their death rates from breast cancer in 2012 were 42% higher than rates in white women [1].

The Mountain West state of Nevada, with a 2015 estimated population of 2.9 million [3], ranks poorly on many health outcome measures, including cancer [4–6]. Few studies have examined breast cancer specifically in Nevada. Two recent cancer reports, Cancer in Nevada [6] and the Nevada State Cancer Plan 2016–2020 [7], both highlighted the need for improvement in the Nevada Cancer Surveillance system in order to better quantify outcomes, especially survival. This study partially addresses those limitations by using enhanced Nevada Cancer Registry data to present age-adjusted 5-year survival for breast cancer. We aim to analyze breast cancer survival among Nevada's diverse women, examining differences by race/ethnicity as well as region of residence in Nevada. This accurate characterization of the determinants of breast cancer survival in Nevada women should help set priorities not only for future research but also for appropriate public health and clinical interventions.

Methods

Nevada Central Cancer Registry (NCCR) data were obtained for women diagnosed with a first primary invasive breast cancer from the years 2003–2010. Breast cancer codes C50.0 – C50.9 from the International Classification of Diseases for Oncology, third edition (ICD-O-3) were included. The NCCR routinely links deaths records from the Office of Vital Records at the Nevada State Division of Public and Behavioral Health. For the first time in Nevada, we made linkages with the National Death Index as well as the Social Security Administration Masterfile in order to get accurate survival data by minimizing the number of missing deaths.

Demographic variables that were analyzed for impact on survival included gender, age, race/ethnicity, and Nevada region. International age standard survival classification categories were used to form 5 age groups: 15–44, 45–54, 55–64, 65–74, and 75+. Mutually exclusive racial/ethnic categories used were: non-Hispanic white (white), non-Hispanic black (black), Hispanic, American Indian, Filipino, and other Asian (Chinese, Japanese, Korean, Indian, and others). Filipinos were considered separately from other Asians as they account for 67% of Nevada's overall Asian population [8]. Nevada regions were broken into three distinct categories: Southern, which includes 2.1 million residents of Clark County; Northwestern, which includes 0.6 million residents of Douglas, Lyon, Storey, and Washoe Counties as well as Carson City; and Rural, with 0.2 million residents dispersed through the remaining eleven Nevada counties: Churchill, Elko, Esmeralda, Eureka, Humboldt, Lincoln, Lander, Mineral, Nye, Pershing, and White Pine.

Pathological factors, identified at stage of diagnosis, were also included in the study. Surveillance, Epidemiology and End Results (SEER) staging categories (localized, regional, or distant), estrogen-receptor (ER) status (positive or negative), and tumor grade 1, 2 or 3 (well, moderately, or poorly differentiated, respectively), were analyzed for prognostic significance.

Two social factors were included in the study, insurance status and socioeconomic status (SES). Insurance information was classified into four categories: Medicare, private insurance, Medicaid, and no insurance. Estimates for SES were based on ecological zip code data for the residence of each cancer patient. Zip codes were classified by proportion of persons living in poverty according to 2011 US Census Bureau data. Three categories were used: high, medium, and low SES, defined as having less than 5%, between 5–10%, and over 10% poverty in the population living in that zip code.

Population-based five-year cause-specific overall survival was calculated for the entire state, as well as survival stratified by race/ethnicity, and stage-specific survival stratified by Nevada region. We used the life table method adjusted for age, according to the International Cancer Survival Standard [9] to enable comparison between Nevada and the United States survival estimates, using 2003–2010 SEER data. Cause-specific survival time was measured in months from the date of diagnosis until the date of death or, if not found as deceased, the date of last mortality linkage as of Dec 31, 2012, whichever occurred first. For censored observations, the presumed alive assumption was used. Patients diagnosed at autopsy only or by death certificate were excluded, as well as cases with a negative or missing survival period.

Univariate analyses to determine significant prognostic factors were performed using the log-rank test. Then, three Cox proportional hazards regression models for multivariate survival analysis were constructed, adjusting for age in the first model; age, race/ethnicity, insurance status, SES, and region of NV in the second model; and in model three, adjusting for all second model variables plus stage, ER status, and grade of tumor. Hazard ratios and their corresponding 95% confidence intervals (CI) were computed to calculate risk of death specifically from breast cancer. A visual inspection of the log (–log) plot of the survival

distribution for each independent variable showed no significant violations of the proportional hazards assumption.

The study was approved by the University of Nevada, Las Vegas Institutional Review Board.

Results

There were 11,111 cases of breast cancer identified from 2003–2010 in the Nevada Central Cancer Registry. Most cases were from Southern Nevada (68%) among women with private insurance (45%). Almost one-third of all cases occurred in women under age 55. Tumors were predominantly ER positive (59%) and localized (59%). (Table I)

Overall five-year age-adjusted survival in Nevada was 84.4%, significantly lower than the US proportion of 89.2% based on the SEER-17 catchment area for the same time period (Table II). Within the state, survival in Northwestern Nevada (88.2%; CI: 86.9–89.5) was significantly higher than in Southern Nevada (83.0%; CI: 82.1–83.9); the rural survival estimate was also low (84.3%; CI 81.4–87.2) (Table II). By race/ethnicity, survival was highest for Asian (non-Filipina) women, at 89.5%. Filipinas and blacks showed a disadvantage in survival compared to all other racial/ethnic groups analyzed, at 76.6% and 76.0% respectively (Table II). In stage-specific survival by region, Southern Nevada had consistently lower survival than Northwestern Nevada, although only significant at the localized stage (where cases are most numerous), 93.1% compared to 95.7%. Compared to the overall US, Southern Nevada had significantly lower survival at all stages, localized, regional, and distant, while Northwestern Nevada did not differ significantly at any stage (Table III).

In a Cox model controlling only for age, black and Filipina women had significantly higher risk of death than white women, hazard ratio (HR) 1.78 and HR 1.47, respectively. After fully adjusting for all covariates, only black women retained a significantly higher risk than white women. (HR 1.29; CI: 1.08–1.54). (Table IV) Women from Southern Nevada with breast cancer had a 16% higher risk of death than women from Northwestern Nevada, even after controlling for all demographic, social, and pathological factors. Stage at diagnosis was the most influential risk factor. Patients diagnosed at distant stage had 17.7 times higher risk of death than those diagnosed at localized stage. Negative estrogen receptor status also conferred a risk 1.78 times higher than positive ER status (Table IV).

Discussion

Only a few studies have characterized any cancer outcomes in Nevada. This is the first to use enhanced registry data, accurately portraying the breast cancer burden. Unique in its demographic features, Nevada is the seventh largest US state in terms of square miles [3], but has only two major metropolitan centers and is otherwise sparsely populated in its rural and frontier areas [10]. Nevada is racially and ethnically diverse, with a higher percentage of Hispanics (28%), Asians/Pacific Islanders (9%), and American Indian/Alaskan Natives (2%) than the US average [3]. Non-Hispanic blacks account for 9% of Nevada's population, and the remaining 52% are non-Hispanic white. Notably, almost one in five Nevadans is foreign born, higher than the US average of 13% [3]. This study adds to the growing body of

literature on breast cancer survival disparities for blacks, as well as Filipinas. Moreover, we present evidence of a significant breast cancer survival disparity between two urban regions of the state, separated by over 400 miles of desert terrain [10].

Overall 5-year survival from breast cancer for Nevada women is lower than the US average. Poor survival in the populous Southern region, including the Greater Las Vegas Metropolitan area, almost entirely explains this geographic disparity between Nevada and the US, as survival in the Northwestern Reno-Sparks Metropolitan area and the US is not dissimilar. Within the state, we also find racial/ethnic disparities, with survival disadvantages for black and Filipina women.

Previous studies have demonstrated a breast cancer survival disadvantage for black women, with many factors converging to partially explain the disparity [11]. Black women are more likely to have aggressive tumors, including the triple negative molecular subtype [2, 11–15]. Although not able to fully track all of the molecular subtypes due to inadequate reporting to the Nevada Registry, we did find that black women had a smaller proportion of ER-positive tumors than white women, 51% compared to 60%. (Data not shown.) ER-positive tumors are slower growing, less aggressive, and receptive to hormonal therapies, including tamoxifen, aromatase inhibitors, luteinizing hormone-releasing hormones, and fulvestrant [1]. Additionally, as seen in other studies, our study showed that black women were diagnosed at later stages, but that controlling for tumor factors only attenuated without eliminating the survival disadvantage [11, 16]. Other potentially contributing factors to explain the survival disparity between black and white women include differences in mammography screening [17], higher proportions of obesity [11], delays in treatment after diagnosis [18,19], and differences in treatment received. Black women, much less likely to get treatment according to standard care guidelines, have a lower likelihood of mastectomy [20], radiation after surgery [21, 22], and hormone therapy among those eligible [19]. We ran separate analyses that included binomial YES/NO treatment variables for surgery and chemotherapy, but found they were not significant survival predictors. Our fully adjusted Cox models showed a persistent breast cancer survival disadvantage for black women in Nevada.

On the other hand, the Filipina disparity seen in our study was attributable to stage at diagnosis. In the model only adjusted for age, Filipina women had worse survival than white women, a surprising finding since Asian women are characterized by relatively high survival [1], as seen in our non-Filipina (other) Asian group. After adjusting for social factors, the Filipina survival disadvantage was somewhat attenuated. This was not unexpected; compared to the US average, Filipinos are better educated, more likely to work professional jobs, and have higher incomes [23, 24]. On the other hand, Filipinas are also more likely than other Asian groups to be obese [23], which is linked to lower breast cancer survival [25]. A few other studies, mostly conducted in California where detailed demographic data on Asian subpopulations is collected, have looked at survival by Asian subgroup, and found that Filipina women had the worst breast cancer survival among Asians [26, 27]. However, similar to what was revealed by Cox model 3 in our study, Lin et al. (2002) found that after controlling for stage, Filipina survival was no worse than other groups [28]. Higher proportions of late stages of diagnosis among Filipinas accounted for their relative survival disadvantage in Nevada.

The strongest predictor of breast cancer survival in Nevada women was stage at diagnosis, which has been linked to mammography screening [29]. Nevada is in the lowest quartile for state mammography rates. In 2010, 73% of Nevada's women aged 50 years reported having a mammogram within the past 2 years, compared to the US average of 80% [30]. Yet, controversy exists regarding mammography. The extent to which nation-wide improvements over time in breast cancer survival can be attributed to treatment improvements or increases in mammography is unclear [31]. Studies have shown significant overdiagnosis of early stage breast cancer, and only minimal decreases in late-stage diagnoses [31]. Interestingly, black women have high rates of self-reported mammography nationally [30], and Filipinas have been found to have the highest mammography screening rates among Asians [23]. Nonetheless, careful examination of actual mammography rates by race/ethnicity in Nevada women is warranted [32] to determine if increased screening among disadvantaged groups is advisable to decrease diagnoses at later stages, which would improve overall breast cancer survival.

Some research has shown that access to primary care better predicts late stage at diagnosis than mammography rates [13, 33]. Unfortunately, Nevada also ranks poorly in per population general and family practice physician rates, 22 per 100,000 in 2012 compared to the US average of 31 per 100,000 [34]. In fact, Nevada's overall physician-to-population rank among US states is 47th. However, within Nevada, these shortages are primarily seen in the South [34].

In 2012, Southern Nevada had only 217 medical doctors (MD) per 100,000, compared to the national average of 327 per 100,000 [34]. Yet, Washoe County, comprising the largest proportion of the Northwestern population in our study, has a per capita MD rates similar to the US, at 336 per 100,000 [34]. This shortage of physicians is likely a contributing factor to the survival disadvantage seen for patients in Southern Nevada. Moreover, while previous studies have demonstrated a positive association between treatment by oncology specialists and breast cancer survival [35, 36], Southern Nevada in 2012 had only 65% of the US average number of physician specialists per capita [34].

Another likely reason for the region of Southern Nevada driving the survival disadvantage seen in the state is the lack of a public medical school in Southern Nevada, which is the largest major metropolitan area in the US without one [37]. Better breast cancer survival outcomes have been associated with hospitals that have research activity and teaching status [38–40]. Patients who are uninsured and/or on Medicaid were more likely to get adjuvant chemotherapy in teaching hospitals than community hospitals [19], and patients with small breast cancer tumors in teaching hospitals fared better than those in non-teaching hospitals [38]. While Southern Nevada does have one large teaching hospital, the state overall ranks 46th in residency and fellowship programs, partially due to having just one public medical school, located in Northwestern Nevada [34]. Fortunately, Southern Nevada will soon have its own medical school, attracting experts to the state, with all of the associated benefits, including enhanced research and clinical trial opportunities, grant funding, increases in residency and fellowship programs, and ultimately, an increase in physicians. Hopefully, this will serve to bridge the survival disparity between Northwestern and Southern Nevada that is also seen with other cancers [6].

Our results may suffer from a degree of residual confounding. For example, not knowing HER2/neu receptor status meant we could not establish the triple negative cancers, known to be more common among black women. Screening rates specific to each racial/ethnic group in Nevada are not available. Lacking individual level data on obesity and on other comorbidities, we were unable to adjust for these in our study, which may have affected our final estimates. However, since our outcome was cancer-specific survival and we adjusted for stage at diagnosis, the potential effect of these variables was reduced. Some of the populations analyzed had low numbers, potentially leading to imprecise estimates. It is also possible that apparent cancer survival benefits attributed to immigrant populations may be artifactual, as these populations have more missed deaths, especially given the presumed alive method for censoring [41]. Lastly, our SES measure is ecological rather than individual, and may not be totally accurate for each individual case.

Conclusion

Overall survival in Nevada is lower than average, with significant disparities between racial/ethnic groups and by region. Black and Filipina women have a survival disadvantage compared to white women. While the Filipina disadvantage seems determined by the stage at diagnosis distribution, that is not the case for the disadvantage among Black women. By region, Northwestern Nevada has survival outcomes similar to the US average, while women with breast cancer in Southern Nevada are significantly disadvantaged. Undoubtedly, system-wide changes will be needed to see large overall gains in patient survival in Nevada. The new University of Nevada Las Vegas School of Medicine (SOM) will be poised to play an important role in these changes by increasing the number and quality of medical professionals including researchers who will have a diverse population to draw from in conducting clinical trials in populous Southern Nevada. Additionally, the SOM can lead the public health community in embarking upon research driven, culturally appropriate quality improvement initiatives across the entire continuum of breast cancer care, including expanding access to primary care, providing patient education, monitoring mammography screening by race/ethnicity, and increasing treatment according to guidelines for all patients. This study provides an important baseline for characterizing breast cancer survival in all Nevada women. Nevada's goal must be to keep the incidence of breast cancer relatively low, while increasing survival rates for women who do get breast cancer, thus averting some of the 380 breast cancer deaths [4] that occur each year among Nevada's diverse women.

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Table I**Breast Cancer in Nevada 2003–2010**

	N	%
DEMOGRAPHIC FACTORS		
<i>Age</i>		
16–44 years old	1314	11.8
45–54 years old	2327	20.9
55–64 years old	2980	26.8
65–74 years old	2551	23.0
75+ years	1939	17.5
<i>Race/ethnicity</i>		
Non-Hispanic White	8562	77.1
Non-Hispanic Black	714	6.4
Hispanic	1005	9.0
American Indian	63	0.6
Filipino	261	2.3
Asian Other	335	3.0
Other/Unknown	171	1.5
<i>Nevada Region</i>		
Northwestern NV	2832	25.5
Southern NV	7575	68.2
Rural NV	704	6.3
SOCIAL FACTORS		
<i>Insurance Status</i>		
Medicare	3302	29.7
No Insurance	261	2.3
Medicaid	601	5.4
Private Insurance	4994	44.9
Unknown	1953	17.6
<i>Socioeconomic Status</i>		
High	2749	24.7
Intermediate	4195	37.8
Low	3978	35.8
Unknown	189	1.7
PATHOLOGICAL FACTORS		
<i>SEER Stage</i>		
Localized	6508	58.6
Regional	3210	28.9
Distant	570	5.1
Unstaged/Unknown	823	7.4
<i>Estrogen Receptors</i>		
ER Positive	6568	59.1

	N	%
ER Negative	1803	16.2
Unknown	2740	24.7
<i>Tumor Grade</i>		
Well differentiated	2167	19.5
Moderately differentiated	4142	37.3
Poorly differentiated	3394	30.5
Unknown	1408	12.7

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Table II

5-Year Age-Adjusted ^{*} Survival Estimates for Nevada by Race/ethnicity and by Region, and for SEER-17, 2003–2010.

	Survival	95% CI
Overall US (SEER-17)	89.2%	(89.1 – 89.4)
Overall Nevada	84.4%	(83.7 – 85.2)
<i>Nevada by Region</i>		
Northwestern Nevada	88.2%	(86.9 – 89.5)
Southern Nevada	83.0%	(82.1 – 83.9)
Rural	84.3%	(81.4 – 87.2)
<i>Nevada by Race/ethnicity</i>		
Non-Hispanic White	85.1%	(84.2 – 85.9)
Non-Hispanic Black	76.0%	(72.6 – 79.4)
Hispanic	84.0%	(81.9 – 86.2)
American Indian	83.2%	(73.7 – 92.6)
Filipino	76.6%	(71.3 – 82.0)
Other Asian	89.5%	(85.5 – 93.6)

^{*} Adjusted according to International Cancer Survival Standard

Table III

5-Year Age-Adjusted* Stage-Specific Survival Estimates for Nevada by Region and for SEER-17, 2003–2010.

	Survival	95% CI
Localized Stage		
Overall US (SEER-17)	96.4%	–(96.3 – 96.5)
Overall Nevada	94.0%	(93.4 – 94.6)
Northwestern NV	95.7%	(94.6 – 96.8)
Southern NV	93.1%	(92.3 – 93.9)
Rural NV	96.0%	(93.9 – 98.0)
Regional Stage		
Overall US (SEER-17)	85.9%	(85.7 – 86.2)
Overall Nevada	81.0%	(79.6 – 82.5)
Northwestern NV	83.7%	(81.1 – 86.3)
Southern NV	79.8%	(78.0 – 81.7)
Rural NV	82.0%	(76.3 – 87.8)
Distant Stage		
Overall US (SEER-17)	36.4%	(35.6 – 37.1)
Overall Nevada	28.1%	(23.6 – 32.6)
Northwestern NV	40.1%	(29.2 – 50.9)
Southern NV	25.8%	(20.7 – 30.9)
Rural NV	22.7%	(5.00 – 40.5)

* Adjusted according to International Cancer Survival Standard

Table IV

Risk of Death from Breast Cancer among Nevada Women

	*Model 1				† Model				‡ Model 3			
	HR	CI	p-value		HR	CI	p-value		HR	CI	p-value	
Race/Ethnicity												
Non-Hispanic White	Ref.	-	-		Ref.	-	-		Ref.	-	-	
Non-Hispanic Black	1.78	(1.50–2.11)	>.001		1.55	(1.31–1.85)	>.001		1.29	(1.08–1.54)	.004	
Hispanic	1.00	(0.83–1.20)	.967		0.82	(0.68–0.99)	.040		0.83	(0.69–1.00)	.053	
American Indian	1.19	(0.64–2.22)	.587		1.00	(0.53–1.85)	.976		1.28	(0.68–2.40)	.440	
Filipino	1.47	(1.10–1.97)	.009		1.41	(1.05–1.89)	.022		1.18	(0.88–1.59)	.270	
Asian Other	1.05	(0.78–1.41)	.744		1.04	(0.78–1.40)	.783		1.09	(0.81–1.47)	.568	
Other/Unknown	0.68	(0.42–1.09)	.111		0.50	(0.31–0.81)	.005		0.38	(0.24–0.62)	>.001	
Insurance Status												
Medicare	Ref.	-	-		Ref.	-	-		Ref.	-	-	
Private Insurance					0.89	(0.77–1.02)	.101		0.94	(0.82–1.09)	.417	
Medicaid					1.68	(1.35–2.08)	>.001		1.33	(1.07–1.64)	.009	
No Insurance					2.80	(2.16–3.61)	>.001		1.43	(1.10–1.85)	.008	
Unknown					1.81	(1.58–2.07)	>.001		1.17	(1.01–1.35)	.039	
Nevada Region												
Northwestern NV	Ref.	-	-		Ref.	-	-		Ref.	-	-	
Southern Nevada					1.40	(1.24–1.59)	>.001		1.16	(1.02–1.32)	.022	
Rural Nevada					1.23	(0.98–1.55)	.070		0.94	(0.75–1.19)	.617	
Stage												
Localized									Ref.	-	-	
Regional									3.13	(2.72–3.56)	>.001	
Distant									17.72	(15.16–20.70)	>.001	
Unknown									6.14	(5.13–7.35)	>.001	
Estrogen Receptors												
ER Positive									Ref.	-	-	
ER Negative									1.78	(1.55–2.05)	>.001	

	*Model 1			†Model 2			‡Model 3		
	HR	CI	p-value	HR	CI	p-value	HR	CI	p-value
Unknown							1.28	(1.13–1.46)	>.001
<i>Grade of Tumor</i>									
Grade 1							Ref.	-	-
Grade 2							1.98	(1.55–2.53)	>.001
Grade 3							3.62	(2.84–4.61)	>.001
Unknown							3.80	(2.95–4.90)	>.001

Cox Proportional Hazards Models

* Model 1 was adjusted for age

†Model 2 was adjusted for age, race/ethnicity, insurance status, SES, and region of NV

‡Model 3 was adjusted for model 2 variables plus stage, ER status, and grade of tumor