

Survival Differences in Chinese Versus White Women With Breast Cancer in the United States: A SEER-Based Analysis

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PURPOSE The affect of race on breast cancer prognosis is not well understood. We compared crude and adjusted breast cancer survival rates of Chinese women versus White women in the United States.

METHODS We conducted a cohort study of Chinese and White women with breast cancer diagnosed between 2004 to 2015 in the SEER 18 registries database. We abstracted information on age at diagnosis, tumor size, grade, lymph node status, receptor status, surgical treatment, receipt of radiotherapy and chemotherapy, and death. We compared crude breast cancer–specific mortality between the two ethnic groups. We calculated adjusted hazard ratios (HRs) in a propensity-matched design using the Cox proportional hazards model. $P < .05$ was considered statistically significant.

RESULTS There were 7,553 Chinese women (1.8%) and 414,618 White women (98.2%) with stage I-IV breast cancer in the SEER database. There were small differences in demographics, nodal burden, and clinical stage between Chinese and White women. Ten-year breast cancer–specific survival was 88.8% for Chinese women and 85.6% for White women (HR, 0.73; 95% CI, 0.67 to 0.80; $P < .0001$). In a propensity-matched analysis among women with stage I–IIIC breast cancer, the HR was 0.71 (95% CI, 0.62 to 0.81; $P < .0001$). Annual mortality rates in White women exceeded those in Chinese women for the first 9 years after diagnosis.

CONCLUSION Chinese women in the United States have superior breast cancer–specific survival compared with White women. The reason for the observed difference is not clear. Differences in demographic and tumor features between Chinese and White women with breast cancer may contribute to the disparity, as may the possibility of intrinsic biologic differences.

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INTRODUCTION

The basis for racial and ethnic disparities observed in breast cancer survival is not well understood. Several studies have reported lower breast cancer survival rates among Black women compared with White women,¹⁻³ but less is known regarding outcomes in other ethnic groups, including Chinese women. One can compare the survival rates in China with those of Chinese women in other countries or compare survival rates by ethnic group within a given country. In the National Central Cancer Registry of China, between 2003 and 2005, the 5-year survival for all women with breast cancer was 73.0%—much lower than the crude survival of women with breast cancer in Australia (89%), Europe (82%), Hong Kong (85.2%), and the United States (90%).^{4,5}

The relatively poor survival among women in China, compared with women in Hong Kong or Western countries, may be a consequence of a later disease

stage at diagnosis, inadequate cancer care, or intrinsically more aggressive breast cancers. The extent of screening in a given country will also affect the stage at which diagnosis is made and, ultimately, survival. If the disparity were due to the result of inadequate treatment or delayed diagnosis, one might expect to see better survival among Chinese women in the United States compared with women in China. On the other hand, if there were intrinsic biologic differences that render breast cancers in Chinese women more aggressive, then we might observe worse outcomes in Chinese women in the United States than in a comparable group of White women (ie, those with similar stage at presentation and equal access to care). We compared survival rates in the United States for Chinese and White women with breast cancer in the SEER database whose disease was diagnosed between 2004 and 2015. We compared both crude and adjusted survival rates, matched for age and year of diagnosis, demographic factors, clinical presentation, and treatment.

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CONTEXT

Key Objective

To determine if there is a survival difference between Chinese and White women with breast cancer. Prior reports of survival in Chinese compared with White women with breast cancer have not demonstrated a difference.

Knowledge Generated

In a propensity-matched analysis comparing Chinese and White women with breast cancer diagnosed between 2004 and 2015 in the SEER database, we found that Chinese women had significantly better 10-year breast cancer–specific survival compared with White women (hazard ratio, 0.73). Crude annual mortality rates in White women exceeded those in Chinese women for the first 9 years after diagnosis.

Relevance

This study raises the possibility that superior survival in Chinese women with breast cancer may be influenced by underlying host or tumor factors or intrinsic biologic differences in tumor type.

METHODS

We used SEER*Stat statistical software, version 8.3.6 (National Cancer Institute, Bethesda, MD) to conduct a case-listing session and retrieved all cases of Chinese and White women with first primary invasive breast cancer in the SEER 18 registries research database (November 2016 submission). Our inclusion criteria were women with American Joint Committee on Cancer (AJCC) stage I-IV breast cancer diagnosed from 2004 to 2015. Exclusion criteria included a previous history of breast cancer; women with tumors that were not infiltrating ductal, lobular, or mixed histology; and women who were lost to or had no follow-up (Fig 1). This study was exempted from review by the Women's College Hospital research ethics board, because patient informed consent was not required. We adhered to the "Strengthening the Reporting of Observational Studies in Epidemiology Statement" guidelines for reporting observational studies.⁶

For each case, we retrieved patient demographics, including marital status and neighborhood median household income. Breast cancer characteristics included year of diagnosis, laterality, tumor size (T stage) and grade, nodal status (N stage), AJCC stage, and receptor status (ie, estrogen receptor [ER], progesterone receptor [PR], and HER2/neu receptor). Treatment details included the type of breast surgery received (ie, lumpectomy, mastectomy), chemotherapy (yes or no), and radiotherapy (yes or no). Information on endocrine therapy was not available.

Chinese and White women were compared for demographic, pathologic, and treatment variables and differences were assessed using standardized differences. Our primary outcome was death from breast cancer. We extracted information on survival time from the variable "survival time months." The SEER*Stat program estimates survival time by subtracting the date of diagnosis from the date of last contact (study cutoff).

Matching

We conducted a matched analysis, adjusting for clinical presentation and treatments. Women were matched on the year of diagnosis and age at diagnosis (both within 2 years), tumor grade, T and N stages, AJCC stage, ER and HER2 status (positive, negative, or unknown), and propensity score. The propensity score accounted for marital status, household income, tumor size, PR status, and surgical procedure. Median household income and tumor size were treated as continuous variables and modeled as a natural cubic spline. Caliper matching was performed by matching participants who were within 0.2 times the standard deviation of their propensity score.⁷ A standardized difference > 0.1 was considered a meaningful imbalance between comparison groups.⁸ Variable distributions for the matched cohorts are presented in Table 1.

Statistical Analysis

Using the Kaplan-Meier method, we first estimated crude cumulative breast cancer–specific mortality and survival rates for Chinese and White women with stage I-IV breast cancer. Patients were followed from the date of diagnosis until the end of follow-up, death from breast cancer or another cause, or loss to follow-up. We calculated annual mortality rates for women for each year of follow-up until 12 years postdiagnosis. For our propensity-matched analysis, we further excluded women with missing data and women with bilateral or stage IV disease (Fig 1). We calculated HRs using the Cox proportional hazards model in SAS, version 9.4 (SAS Institute, Cary, NC). A log-rank test was used to compare differences between groups using the Kaplan-Meier method. For all HRs, 95% confidence limits were generated. *P* values were two-tailed with a level of significance set at $< .05$.

RESULTS

Between 2004 and 2015, there were 7,553 Chinese women (1.8%) and 414,618 White women (98.2%) listed in the SEER database as having been diagnosed with stage

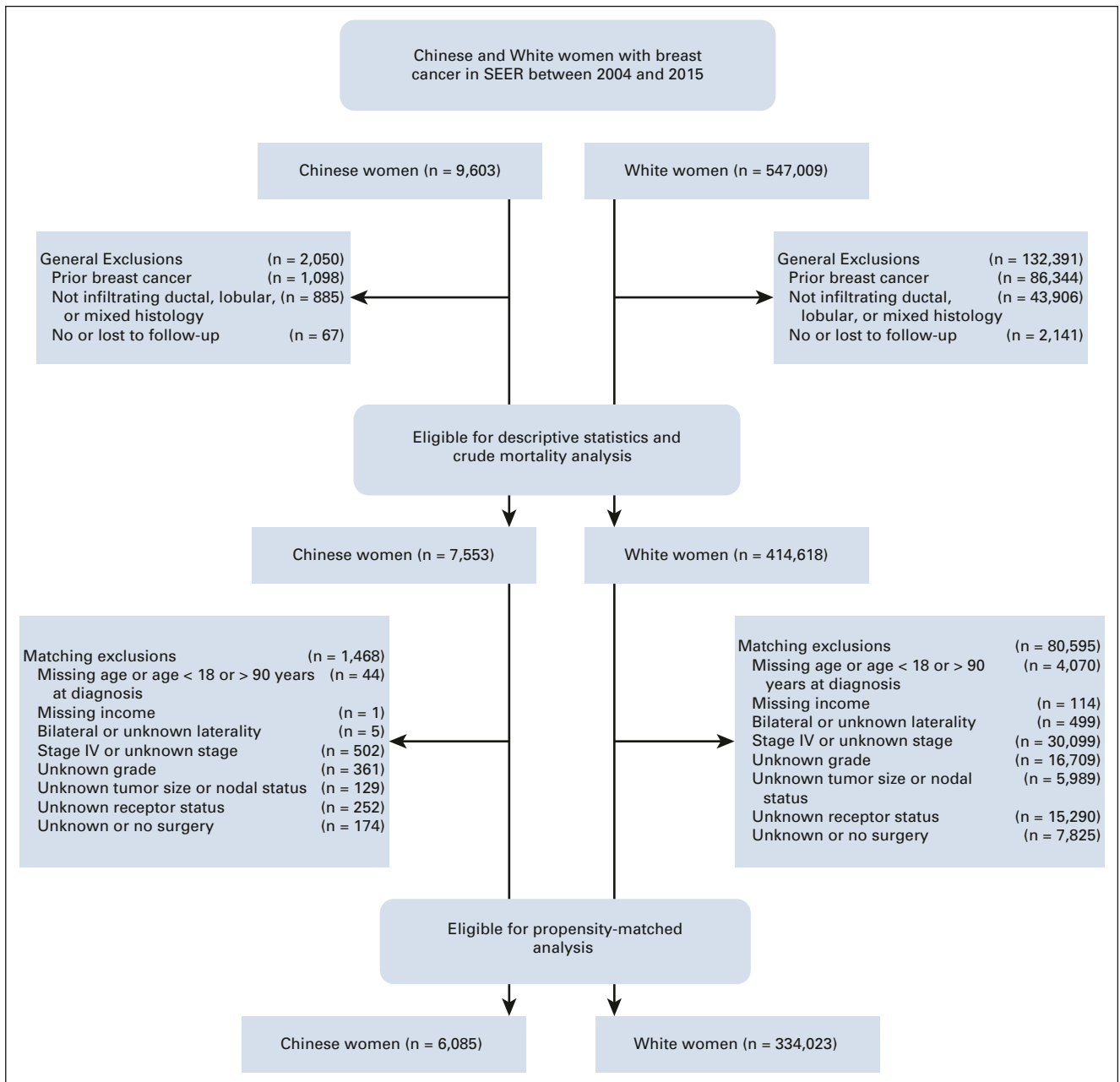


FIG 1. CONSORT diagram.

I-IV breast cancer. Their characteristics are compared in Table 2. Chinese women were younger on average at diagnosis than White women (56.3 years v 60.8 years; $P < .0001$). A greater proportion of Chinese women were married than White women (68.7% v 57.4%). The mean annual household income was slightly higher for Chinese women than for White women.

The mean tumor size and nodal status were similar for Chinese and White women, but small differences were noted. At presentation, 47.1% of White women and 46.6% of Chinese women had stage I disease, 15.4% of White women and 13.1% of Chinese women had stage III or

IV disease, and 32.7% of White women and 31.9% of Chinese women had positive lymph nodes. A greater proportion of White women had grade 1 tumors compared with Chinese women (21.2% v 16.9%; $P < .0001$). A greater percentage of Chinese women had HER2-positive tumors compared with White women (10.5% v 7.4%; $P < .0001$).

There were small differences in treatment received. A greater proportion of White women had lumpectomy than Chinese women (54.6% v 47.8%; $P < .0001$). A greater proportion of White women received radiotherapy than Chinese women (51.6% v 47.2%; $P < .0001$). Among

TABLE 1. Baseline Characteristics of Chinese and White Women with Stage I-IIIc Breast Cancer (Matched Analysis)

Parameter	Chinese	White	P
No. of patients	5,650 (50.0)	5,650 (50.0)	
Year range of diagnosis			.74
2004-2006	1,138 (20.1)	1,122 (19.9)	
2007-2009	1,420 (25.1)	1,436 (25.4)	
2010-2012	1,457 (25.8)	1,417 (25.1)	
2013-2015	1,635 (28.9)	1,675 (29.6)	
Age at diagnosis, mean	56.4 (12.5)	56.4 (12.4)	.97
Marital status			.31
Married	3,919 (69.4)	4,003 (70.8)	
Never married	698 (12.4)	640 (11.3)	
Widowed	482 (8.5)	475 (8.4)	
Divorced	379 (6.7)	351 (6.2)	
Unknown	172 (3.0)	181 (3.2)	
Annual household income, mean (USD)	53,554 (10,408)	53,473 (10,711)	.68
Tumor size, mean, cm	2.0 (1.5)	2.0 (1.5)	.78
Tumor grade			1.0
I	1,063 (18.8)	1,063 (18.8)	
II	2,675 (47.3)	2,675 (47.3)	
III	1,912 (33.8)	1,912 (33.8)	
Nodal status (N stage)			1.0
N0	3,965 (70.2)	3,965 (70.2)	
N1	1,325 (23.5)	1,325 (23.5)	
N2	268 (4.7)	268 (4.7)	
N3	92 (1.6)	92 (1.6)	
Clinical stage			1.0
I	2,932 (51.9)	2,932 (51.9)	
II	2,249 (39.8)	2,249 (39.8)	
III	469 (8.3)	469 (8.3)	
ER status			1.0
Positive	4,756 (84.2)	4,756 (84.2)	
Negative	894 (15.8)	894 (15.8)	
PR status			.94
Positive	4,079 (72.2)	4,089 (72.4)	
Negative	1,523 (27.0)	1,516 (26.8)	
Unknown	48 (0.8)	45 (0.8)	
HER2 status			1.0
Positive	494 (8.7)	494 (8.7)	
Negative	2,598 (46.0)	2,598 (46.0)	
Not Available	2,558 (45.3)	2,558 (45.3)	
Surgery			.46
Lumpectomy	3,111 (55.1)	3,150 (55.8)	
Mastectomy	2,539 (44.9)	2,500 (44.2)	
Follow-up time, mean, years	5.8 (3.4)	5.9 (3.3)	.86

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TABLE 1. Baseline Characteristics of Chinese and White Women with Stage I-IIIc Breast Cancer (Matched Analysis) (Continued)

Parameter	Chinese	White	P
Radiotherapy			.004
Positive	2,952 (52.2)	3,052 (54.0)	
Negative	2,587 (45.8)	2,449 (43.3)	
Unknown	111 (2.0)	149 (2.6)	
Chemotherapy			.002
Yes	2,476 (43.8)	2,644 (46.8)	
No or unknown	3,174 (56.2)	3,006 (53.2)	
Vital status			< .0001
Alive	5,179 (91.7)	5,026 (89.0)	
Died of breast cancer	237 (4.2)	327 (5.8)	
Died of other cancer	64 (1.1)	71 (1.3)	
Died of cardiac condition	64 (1.1)	87 (1.5)	
Died of other diseases	55 (1.0)	85 (1.5)	
Unknown death cause	51 (0.9)	54 (1.0)	

NOTE. Data reported as No. (%) or mean (standard deviation).
Abbreviations: ER, estrogen receptor; PR, progesterone receptor.

those who had a lumpectomy, 75.8% of Chinese women and 74.3% of White women had radiotherapy. A slightly greater proportion of Chinese women received chemotherapy than White women (43.8% v 41.2%; $P < .0001$). Among those with stage II-III disease, 65.9% of Chinese women versus 62.7% of White women received chemotherapy.

Among women with stage I-IV breast cancer, the crude 10-year breast cancer–specific survival was 88.8% for Chinese women, compared with 85.6% for White women. The cumulative mortality from breast cancer at 11 years of follow-up was 13.9% for Chinese women and 17.3% for White women (crude HR, 0.73; 95% CI, 0.67 to 0.80; $P < .0001$; Fig 2A). In the first 9 years after diagnosis, annual mortality rates were higher for White women than for Chinese women. Following the first 9 years after diagnosis, the annual mortality rate for Chinese women exceeded that of White women (Fig 3).

In the propensity-matched analysis, we generated 5,650 matched pairs after excluding women with missing data and women with bilateral or stage IV breast cancer. The two groups were similar for age and year of diagnosis, stage, grade, and ER and HER2 status (Table 1). In the matched analysis, the cumulative mortality rate from breast cancer after 11 years of follow-up was 8.9% for Chinese women and 11.9% for White women ($P = .0002$; Fig 2B). The adjusted HR was 0.71 (95% CI, 0.62 to 0.81) and was similar to the crude HR of 0.73 (95% CI, 0.67 to 0.80). The adjusted HR was 0.78 (95% CI, 0.56 to 1.08) for ER-negative breast cancer and 0.67 (95% CI, 0.54 to 0.84) for ER-positive breast cancer. Moreover, Chinese women had better survival than White women in subgroups defined by age of diagnosis, tumor grade, stage, and nodal status

(Table 3). The largest survival differences between the two ethnic groups were observed for stage I cancer (HR, 0.57; 95% CI, 0.36 to 0.90) and for node-negative cancer (HR, 0.61; 95% CI 0.46 to 0.82).

DISCUSSION

We found that Chinese women diagnosed with breast cancer in the United States between 2004 and 2015 had significantly better survival rates than White women with breast cancer. Over a 10-year follow-up, Chinese women with breast cancer experienced a 30% lower annual rate of death than a comparable group of White women with breast cancer. After adjustment for size, nodal status, tumor grade, and ER status, the crude and adjusted HRs were almost identical.

There were demographic and clinical differences between Chinese and White women with breast cancer in the SEER database that could explain the survival difference, but the differences were small. From 2004 to 2015, a greater proportion of White women had more advanced nodal (N2 or N3) and clinical stage (III and IV) disease than Chinese women. A greater proportion of Chinese women than White women received chemotherapy. Chinese women also had a higher household income, which suggests greater socioeconomic status and access to care. Although these differences are not quantitatively large, these several small differences in standard oncologic-outcome determinants may contribute to the small mortality difference observed at 10 years in our study.

We also measured initiation of systemic therapy and not completion. It is possible that Chinese women in the SEER database were more likely than White women to complete prescribed therapy. Although we did not have information on endocrine therapy that may have been prescribed to the

TABLE 2. Baseline Characteristics of Chinese and White Women With Breast Cancer (All Stages)

Parameter	Chinese	White	P ^a
No. of patients	7,553	414,618	
Year of diagnosis			< .0001
2004-2006	1,495 (19.8)	95,731 (23.1)	
2007-2009	1,857 (24.6)	102,923 (24.8)	
2010-2012	1,966 (26.0)	105,512 (25.4)	
2013-2015	2,235 (29.6)	110,452 (26.6)	
Age at diagnosis, mean, years	56.3 (13.1)	60.8 (13.6)	< .0001
Marital Status			< .0001
Married	5,188 (68.7)	238,013 (57.4)	
Never married	948 (12.6)	51,471 (12.4)	
Widowed	659 (8.7)	58,351 (14.1)	
Divorced	488 (6.5)	47,468 (11.4)	
Unknown	270 (3.6)	19,315 (4.7)	
Annual household income, mean, USD	53,981 (10,989)	47,548 (11,507)	< .0001
Tumor size, mean, cm	2.3 (2.7)	2.3 (2.2)	.87
< 1	1,407 (18.6)	79,619 (19.2)	.0001
1-2	2,560 (33.9)	144,688 (34.9)	
2-3	1,588 (21.0)	81,269 (19.6)	
3-5	1,101 (14.6)	57,174 (13.8)	
> 5	559 (7.4)	34,816 (8.4)	
Unknown	338 (4.5)	17,052 (4.1)	
Tumor grade			< .0001
I	1,276 (16.9)	87,874 (21.2)	
II	3,265 (43.2)	176,362 (42.5)	
III	2,590 (34.3)	129,980 (31.3)	
Unknown	422 (5.6)	20,402 (4.9)	
Nodal status (N stage)			< .0001
N0	5,047 (66.8)	271,090 (65.4)	
N1	1,774 (23.5)	97,412 (23.5)	
N2	417 (5.5)	24,162 (5.8)	
N3	221 (2.9)	14,176 (3.4)	
Unknown	94 (1.2)	7,778 (1.9)	
Clinical stage			< .0001
I	3,522 (46.6)	195,081 (47.1)	
II	2,757 (36.5)	141,246 (34.1)	
III	779 (10.3)	47,834 (11.5)	
IV	215 (2.8)	16,332 (3.9)	
Unknown	280 (3.7)	14,125 (3.4)	
ER status			.0001
Positive	5,937 (78.6)	331,375 (79.9)	
Negative	1,366 (18.1)	67,844 (16.4)	
Unknown	250 (3.3)	15,399 (3.7)	

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TABLE 2. Baseline Characteristics of Chinese and White Women With Breast Cancer (All Stages) (Continued)

Parameter	Chinese	White	P ^a
PR status			.0001
Positive	5,078 (67.2)	285,804 (68.9)	
Negative	2,164 (28.7)	110,075 (26.5)	
Unknown	311 (4.1)	18,739 (4.5)	
HER2 status			< .0001
Positive	795 (10.5)	30,771 (7.4)	
Negative	3,136 (41.5)	172,366 (41.6)	
Not available	3,352 (44.4)	198,654 (47.9)	
Unknown	270 (3.6)	12,827 (3.1)	
Surgery			< .0001
Lumpectomy	3,608 (47.8)	226,450 (54.6)	
Mastectomy	3,490 (46.2)	160,241 (38.6)	
No surgery	409 (5.4)	25,832 (6.2)	
Unknown	46 (0.6)	2,095 (0.5)	
Radiotherapy			< .0001
Yes	3,567 (47.2)	214,038 (51.6)	
No	3,848 (50.9)	189,909 (45.8)	
Unknown	138 (1.8)	10,671 (2.6)	
Chemotherapy			< .0001
Yes	3,305 (43.8)	170,983 (41.2)	
No or unknown	4,248 (56.2)	243,635 (58.8)	
Follow-up time, mean, years	5.6 (3.4)	5.7 (3.5)	.04
Vital status			< .0001
Alive	6,686 (88.5)	333,250 (80.4)	
Died of breast cancer	529 (7.0)	40,238 (9.7)	
Died of other cancer	85 (1.1)	8,440 (2.0)	
Died of cardiac condition	105 (1.4)	13,103 (3.2)	
Died of other diseases	72 (1.0)	11,230 (2.7)	
Unknown death cause	76 (1.0)	8,357 (2.0)	

NOTE. Data reported as No. (%) or mean (standard deviation).

Abbreviations: ER, estrogen receptor; PR, progesterone receptor.

^aContinuous variables were assessed by *t* tests and Mann-Whitney tests; categorical variables were assessed by χ^2 tests.

women, we used ER and PR status as a surrogate of receiving endocrine therapy. Chinese women in the ER-positive and stage I tumor subgroups had better survival than did White women; this may be due in some part to differences in treatment compliance and completion.

Our data do not suggest more frequent screening among Chinese compared with White women in the United States: the mean size of cancers at diagnosis in both groups was the same. If breast cancer screening was more prevalent among Chinese women, we would expect a smaller tumor size at diagnosis and a higher proportion of stage I cancers.⁹

It is also possible that the observed survival differences may reflect differences in underlying comorbid illnesses (eg,

obesity, diabetes, cardiovascular disease). Several reports in different populations have demonstrated worse oncologic outcomes in women with significant comorbid disease.¹⁰⁻¹² In our study, 3.2% of White women died of cardiac disease compared with 1.4% of Chinese women, suggesting a higher prevalence of cardiovascular disease in White women. In addition, 2.7% of White women died of other (noncardiac) diseases, compared with 1.0% of Chinese women.

Another consideration is that inherent genetic predisposition may improve the survival of Chinese women with breast cancer. Although several consortia have published on genetic variation that predicts survival in patients with breast cancer, no specific genetic markers have been

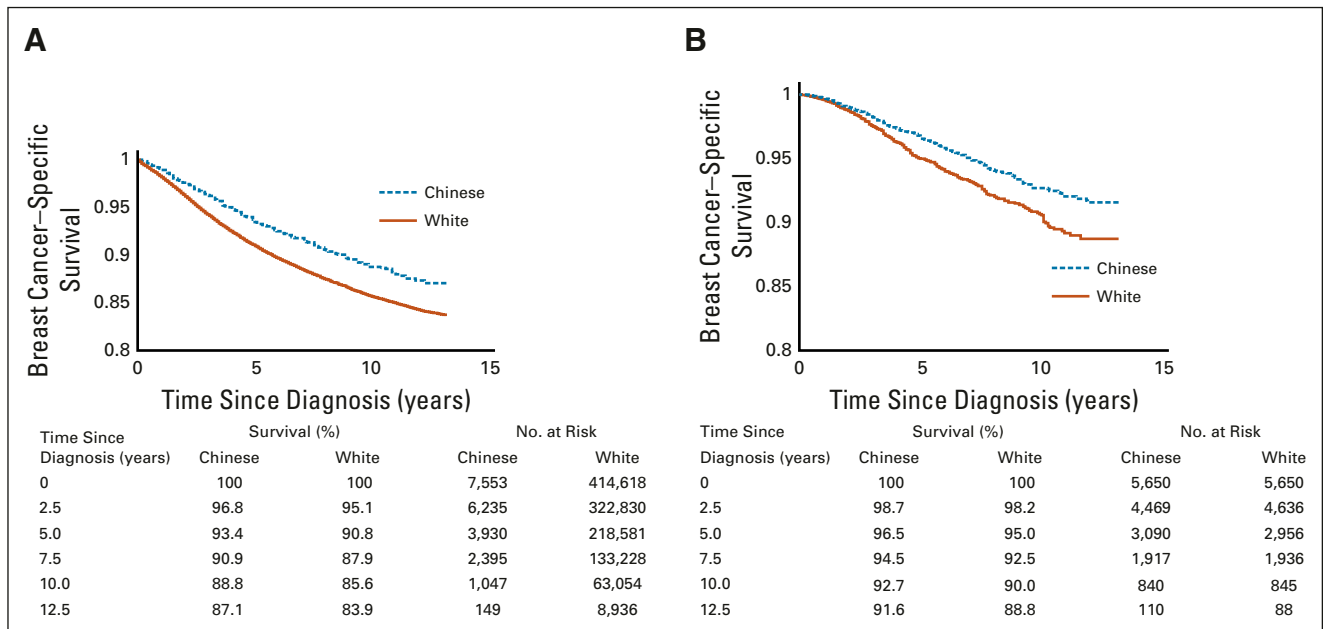


FIG 2. Breast cancer–specific survival. (A) Crude and (B) adjusted propensity-matched Kaplan-Meier curves for Chinese versus White women with breast cancer in the SEER database from 2004 to 2015.

identified that predict differences in survival metrics according to race.¹³⁻¹⁶ There is limited evidence that genomic mutations in Chinese women with breast cancer differ significantly from those in White women, such as an increased prevalence of *TP53* and *AKT1* mutations,⁴ which may translate into differences in oncologic outcomes.

To better understand differences in mortality, we considered both incidence and case-fatality rates. Between 2003 and 2011, breast cancer mortality in the United States was reported at 9.9 per 100,000 for Chinese women and 23.3 per 100,000 for White women.¹⁷ The age-adjusted breast cancer incidence of Chinese and White women in the

United States between 2009 and 2011 was 82.8 and 134.4 per 100,000, respectively.¹⁸ WHO GLOBOCAN 2018 reports age-adjusted breast cancer incidence and mortality rates for breast cancer for China and the United States. In 2018, breast cancer incidence was 36.1 and 84.9 per 100,000 for China and the United States, respectively.¹⁹ Breast cancer mortality in 2018 was 8.8 and 12.7 per 100,000 for China and the United States, respectively.¹⁹ From the different databases, we can appreciate that the lower mortality observed in Chinese women in the United States compared with White women can be accounted for by a combination of both lower breast cancer incidence rates and better survival rates (Table 4). It is notable that the women in China experienced a similar mortality rate to Chinese women in the United States, despite having a much higher case-fatality rate. There are two possible explanations. The conventional interpretation is that as women emigrate from China to the United States, the cancer incidence increases as a consequence of adopting a Western lifestyle, including a change in diet, exercise, and reproductive patterns. However, this increased incidence is offset by a better survival, presumably as a result of improved access to care, including earlier detection and timely and appropriate therapy. An alternate interpretation is that the excess of cancers diagnosed per 100,000 women is because of increased screening and other methods of early detection in the United States, and screening largely identifies indolent cancers that contribute little to the total number of deaths (ie, overdiagnosis). It is also a possibility that in China, the incidence is under-reported but all the deaths from breast cancer are captured.

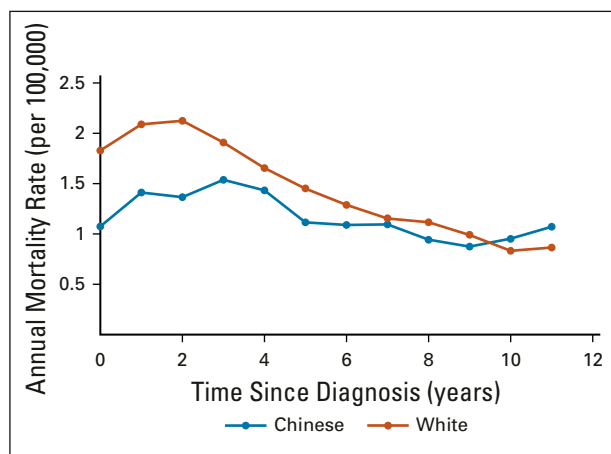


FIG 3. Crude annual breast cancer–specific mortality rates of Chinese versus White women with breast cancer in the SEER database from 2004 to 2015.

TABLE 3. Adjusted Hazard Ratios for Breast Cancer–Specific Death in Chinese Versus White Women With Stage I-IIIc Breast Cancer (Matched Analysis)

Parameter	Hazard Ratio (95% CI)	P
Overall	0.705 (0.617 to 0.806)	< .0001
Age at diagnosis, years		
≤ 50	0.731 (0.544 to 0.982)	.038
> 50	0.689 (0.542 to 0.876)	.002
Tumor grade		
I/II	0.753 (0.552 to 1.026)	.07
III	0.680 (0.539 to 0.858)	.0012
Disease stage		
I	0.569 (0.360 to 0.897)	.015
II	0.688 (0.532 to 0.888)	.004
III	0.836 (0.595 to 1.174)	.30
Nodal stage		
N0	0.612 (0.456 to 0.822)	.001
N1-N3	0.776 (0.610 to 0.987)	.039
Estrogen-receptor status		
Positive	0.672 (0.536 to 0.843)	.0006
Negative	0.780 (0.563 to 1.082)	.14

Previous reports of survival in Chinese women and (non-Hispanic) White women with breast cancer in the SEER registry did not demonstrate a difference, including a 1988-2008 report (HR, 0.98; 95% CI, 0.91 to 1.05),²⁰ a 1991-2007 report (HR, 0.96; 95% CI, 0.87 to 1.05),²¹ and a 1991-2011 report (HR, 0.90; 95% CI, 0.83 to 0.99).²² One SEER analysis from 1990 to 2009 reported that Chinese women with breast cancer had significantly better overall survival (HR, 0.68; 95% CI, 0.63 to 0.74) but similar breast cancer-specific survival (HR, 0.90; 95% CI, 0.81 to 1.0) than White women.²³ Our study findings differ from those of these earlier reports in several respects, including a larger and more recent cohort and a longer follow-up period. We focused on one cancer site (breast cancer) and one ethnic group (Chinese women); previous studies were much more wide ranging. We conducted a detailed analysis of a single end point (breast cancer–specific survival). Our study is a direct comparison of Chinese and White women with breast cancer treated in the same health care system.

We adjusted for prognostic factors, demographic factors, and clinical factors. This matched approach is a contemporary statistical approach to analyzing observational data. Our study avoids the limitations of comparing Chinese women in China with Western women, where study differences may be accounted for by different health care systems and cultural barriers facing women in China, such as access to care, fatalism of cancer, and reliance on traditional medicine.⁴

There are limitations to our study.²⁴ Information on endocrine therapy is not collected in the SEER database. The possibility of differential rates of endocrine therapy compliance might potentially confound our mortality analysis, but this should only affect women with ER-positive cancers. The race effect was present in both ER-positive and ER-negative subgroups but was less pronounced (and non-significant) in ER-negative cancers. We have data on chemotherapy initiation, but data on completion of treatment are not included. Radiation therapy is under-reported in the SEER database.²⁵ In addition, a large proportion of the US population does not self-identify as a single race and thus not all Chinese women with breast cancer may have been captured. We also could not differentiate between Chinese women who were born in China and those who were born in the United States.^{26,27} The treatment assignment was not random. Thus, there may be latent confounding in that treatment decisions were associated with other favorable prognostic factors related to demographic, clinical, or tumor factors that are not included in our matched analysis.

We observed that after 9 years postdiagnosis, the annual mortality rates for Chinese women begin to exceed that of White women with breast cancer. We believe this may be a manifestation of our previously reported general relationship between the risk of dying from breast cancer and the distribution of times to death; that is, patient cohorts with an inherently low risk of dying have a prolonged time to death and many deaths are delayed. For example, the clinical course of low-risk ER-positive breast cancer is inherently unpredictable, with death as likely to equally occur at year 3 and year 20.²⁸ The latent period when the tumor remains dormant until it is reactivated may vary by ethnicity.

TABLE 4. Comparison of Incidence, Mortality and Case-Fatality Rates of Chinese Versus White Women With Breast Cancer

Population Location	Mortality (per 100,000/year [ref])	Incidence (per 100,000/year [ref])	Case Fatality (% of case patients who died of breast cancer [ref])
China	8.8 ^a (2018) ¹⁹	36.1 ^a (2018) ¹⁹	27.0 (1997-2001) ⁵
Chinese in United States	9.9 ^b (2003-2011) ¹⁷	82.8 ^b (2009-2011) ¹⁸	13.9 ^c (2004-2015)
White in United States	23.3 ^b (2003-2011) ¹⁷	134.4 ^b (2009-2011) ¹⁸	17.3 ^c (2004-2015)

Abbreviation: ref, reference number.

^aAge-adjusted to the world standard population.

^bAge-adjusted to the US standard population.

^cCurrent study.

In the current study, Chinese women experienced a median time to death approximately 1 year later than White women; 78% of deaths occurred in White women, whereas 74% of deaths occurred in Chinese women before 5 years postdiagnosis. Therefore, we propose that a longer period of tumor dormancy for Chinese than for White women may account for the observation that the annual mortality rates cross after 9 years, but it will be necessary to follow the cohort longer to confirm this.

In summary, we observed a 30% lower annual rate of death among Chinese women with breast cancer

compared with White women with breast cancer in the SEER database. This was observed in both the crude data and a propensity-matched analysis. The lower mortality rate from breast cancer in Chinese women in the United States reflects a combination of lower incidence and better survival. The difference in breast cancer-specific survival between Chinese and White women may be a consequence of differences in biologic aggressiveness, but we cannot rule out residual differences in patient demographics, comorbidity, and tumor characteristics.

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AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

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