

Ethnic differences in breast cancer in Hawai'i: age, stage, hormone receptor status, and survival

Abstract: Previous examinations of breast cancer and survival in Hawai'i's 5 major ethnic groups have found that Native Hawaiian women have the highest breast cancer mortality rates. Although ethnic disparities in survival are reduced when age and stage at diagnosis are controlled for statistically, prior studies could not explain ethnic variation in survival among women who were diagnosed at the same stage. We examined variations in breast tumor characteristics for a multiethnic sample of 4,583 women diagnosed in 1990-1997 by stage and age group and extended previous multivariate analyses by adding a new prognostic variable: estrogen receptor (ER) and progesterone receptor (PR) status. Logistic regression was used to examine the influence of age, stage, and hormone status on 5-year survival. With a few exceptions, greater proportions of Native Hawaiian women were diagnosed both in later stages of disease and at earlier ages compared to women of other ethnicities, and smaller proportions of Native Hawaiians survived 5 years post diagnosis in each stage and age group. Surprisingly, greater proportions of Native Hawaiian women in all age groups had ER/PR positive tumors, which is a prognostic indicator for better, not worse, survival. Native Hawaiian women had an increased risk of death and Japanese women had an increased chance of survival after controlling for age, stage, and ER/PR status. Future studies should examine other reasons for better survival of Japanese women and worse survival of Native Hawaiian women, including socioeconomic status, access to health insurance, adequacy of recommended screening frequency, co-morbid conditions, treatment appropriateness and compliance, and genetic markers of tumor aggressiveness. **Key Words:** Asian Americans, mortality, Native Hawaiians, Pacific Islander Americans, vulnerable populations

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Introduction

Hawai'i is a natural laboratory for the study of specific Asian and Pacific Islander ethnic groups, for which data often are aggregated¹. The state's 5 major ethnic groups include Caucasians (25%), Japanese (25%), Chinese (5%), Filipino (17%), and Native Hawaiian (22%); the latter are the state's indigenous people who trace their ancestry to the Polynesians inhabiting the islands prior to Western contact in 1778.

Previous examinations of breast cancer and survival in Hawai'i's 5 major ethnic groups have found that Native Hawaiian women have the highest breast cancer mortality rates^{2,3}. Prior research also suggests that Native Hawaiian,

Filipino, and Caucasian women are significantly more likely to be diagnosed with late-stage breast cancer than Chinese and Japanese women, and that as much as 44% of the ethnic variation in breast cancer survival is attributable to differences in stage at diagnosis. Although ethnic disparities in survival are reduced when age and stage at diagnosis are controlled for statistically, prior studies could not explain ethnic variation in survival among women who were diagnosed at the same stage. Among localized cases, Japanese women had the lowest mortality risk, nearly half that of Native Hawaiian and Caucasian women, and nearly one-third that of Filipino women. Among regional and distant cases, Japanese women had half the mortality risk of Native Hawaiian women^{2,3}. The aims of this study were to further look at within-stage variation and to extend previous analyses by examining another prognostic variable: estrogen receptor (ER) and progesterone receptor (PR) status.

ER and PR status is used to inform breast cancer treatment, and women whose tumors have two positive receptors (ER+PR+) usually have a better prognosis than women whose tumors have two negative receptors (ER-PR-) ^{4,5}. Although we could not locate studies that examined data on ER/PR status in Native Hawaiian women with breast cancer, other studies have found that some minority women tend to have higher rates of ER-PR- tumors^{4,9}. This paper presents a cross-ethnic comparison of age and stage at diagnosis, ER/PR status, and 5-year survival among women diagnosed with breast cancer in Hawai'i in 1990-1997. Logistic regression was used to determine if ethnicity was a significant predictor of stage at diagnosis and 5-year survival after controlling for other variables.

Methods

Study Population. A total of 6,455 female breast cancer cases were diagnosed in Hawai'i between January 1, 1990

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and December 31, 1997, as identified through the Surveillance, Epidemiology, and End Results (SEER) program. We eliminated cases with missing age, stage, and ER/PR data, as well as cases lost to follow up less than 5 years post diagnosis. Because our study was designed to examine ethnic differences, we limited our analysis to subjects in Hawai'i's 5 major ethnic groups. The final sample included 4,583 cases: Native Hawaiian (n = 720, 15.7%); Filipino (n = 448, 9.8%); Japanese (n = 1,713, 37.4%); Chinese (n = 332, 7.2%); and Caucasian (n = 1,370, 29.9%).

Variables. The main variable of interest was ethnicity. Other variables were age at diagnosis, stage, TNM (a staging variable), ER/PR status, and 5-year survival. TNM was calculated from the extent-of-disease (EOD) code included in the SEER registry. This 7-category staging variable (0, I, IIa, IIb, IIIa, IIIb, and IV) is determined by tumor size (T), lymph node involvement (N), and extent of metastasis (M) according to the American Joint Committee on Cancer (AJCC) guidelines for breast carcinomas¹⁰, and is used by clinicians in making treatment recommendations. Stage 0 refers to noninvasive or *in situ* breast cancer. Stage I cancers include tumors less than 2 cm in diameter that do not appear to have spread beyond the breast. Stage II refers to tumors that are larger than 2 cm (Stage IIa) and/or have spread to the lymph nodes under the arm on the same side as the breast cancer (Stage IIb). Stage III refers to a locally advanced breast cancer. A Stage IIIa cancer is larger than 5cm (over 2 inches) and/or has spread to the lymph nodes or surrounding tissue. Stage IIIb is a cancer of any size that has spread to the skin, chest wall, or the internal mammary lymph nodes, which are located beneath the breast and inside the chest. In our analysis, Stages IIIa and IIIb were combined due to the small sample size. A Stage IV breast cancer is one that, regardless of its size, has metastasized (spread) to different sites.

Information about ER and PR status is provided in the SEER registry, from which we created a 3-category variable combining ER and PR status: ER-PR-, ER or PR negative (including ER+PR- and ER-PR+), and ER+PR+. To examine 5-year survival, each case was classified as expired (from any cause of death), alive, or lost to follow up based on SEER registry data on vital status, diagnosis date, and last active date.

Analysis. SPSS (Statistical Package for Social Sciences) software was used to manage and analyze data¹¹. ANOVA and chi-square statistics were used to test for ethnic differences across our variables of interest, including age groups (<40, 40-49, 50-59, 60-69, and 70+). Binary logistic regression was used to examine the relative strength of predictors of regional/distant cancer (age, ER/PR status, and ethnicity) and predictors of 5-year survival (TNM, age, ER/PR status, and ethnicity). When used as categorical predictors, Cauca-

sian women served as the reference category for ethnicity, ER-PR- was the reference category for ER/PR status, and TNM 0 was the reference category for TNM.

Results

Bivariate analysis

Table 1 describes each ethnic group in terms of age, stage, hormone receptor status, and 5-year survival. The age at diagnosis for the 4,385 cases ranged from 27 to 100, with a mean age of 60.23. Ethnic comparison suggested a significantly lower mean age at diagnosis for Filipino and Native Hawaiian women, compared with Caucasian women, and a significantly higher mean age at diagnosis for Chinese and Japanese women. More specifically, the mean age of diagnosis for Japanese women was 3 years older than for Caucasians and 5 years older than for Native Hawaiians. Age-group distributions were also significantly different, with greater proportions of younger women and smaller proportions of older women in the Native Hawaiian group compared with other ethnic groups.

Significant ethnic variations were seen for TNM, with greater proportions of Japanese women diagnosed at early stages, and greater proportions of Native Hawaiian and Filipino women diagnosed at late stages. Specifically, data show that between 1990 and 1997, 71.0% of Japanese women were diagnosed at TNM 0 or I compared with only 55.7% of Native Hawaiian women; while only 7.8% of Japanese women were diagnosed at TNM III or IV compared with 16.4% of Native Hawaiian women. For all stages combined, 67.2% of Native Hawaiian women were ER+PR+, compared to 59.7% to 65.4% in other groups. Finally, 25.3% of the Native Hawaiian sample was classified as expired within 5 years of diagnosis, compared to 12.6% to 18.7% in other groups.

Shown in Table 2 are ethnic differences in the proportion of women surviving 5 years post diagnosis by age group, TNM, and ER/PR status. These data confirm ethnic disparities in survival among women in the same age group and with the same TNM and ER/PR status. In every age stratum, fewer Hawaiians were alive at the end of 5 years compared to most other ethnic groups. Significant differences were found in the three older age groups (50-59, 60-69, and 70+), in which the percent of surviving Hawaiian women was 10 to 20 percentage points lower than the percent of surviving Japanese women. Also, Native Hawaiians had the smallest or second smallest proportion of survivors at each TNM; differences were statistically significant for TNM I, III, and IV. For example, at TNM III, only 40.8% of Native Hawaiian women were alive after 5 years, compared to 64.0% of

Previous examinations of breast cancer and survival in Hawai'i's five major ethnic groups have found that Native Hawaiian women have the highest breast cancer mortality rates.

Table 1. Mean age, age group, stage, TNM, ER/PR status, and survival at 5 years, by ethnicity, for women diagnosed with breast cancer in Hawai`i, 1990-1997. n = 4,583

	Caucasian	Chinese	Japanese	Filipino	Native Hawaiian	Total
N (%)	1,370 (29.9)	332 (7.2)	1,713 (37.4)	448 (9.8)	720 (15.7)	4,583 (100)
Mean Age of Diagnosis^{***}	59.89	61.74	62.51	55.69	57.06	60.23
Age Group^{***}						
27-39	94 (6.9)	20 (6.0)	65 (3.8)	40 (8.9)	60 (8.3)	279 (6.1)
40-49	279 (20.4)	54 (16.3)	246 (14.4)	126 (28.1)	143 (19.9)	848 (18.5)
50-59	294 (21.5)	64 (19.3)	312 (18.2)	111 (24.8)	186 (25.8)	967 (21.1)
60-69	302 (22.0)	89 (26.8)	538 (31.4)	104 (23.2)	208 (28.9)	1,241 (27.1)
70+	401 (29.3)	105 (31.6)	552 (32.2)	67 (15.0)	123 (17.1)	1,248 (27.2)
TNM^{***}						
0	222 (16.7)	62 (19.6)	357 (21.4)	74 (17.2)	104 (15.2)	819 (18.5)
I	581 (43.8)	153 (48.4)	829 (49.6)	178 (41.3)	276 (40.5)	2,017 (45.6)
IIa	273 (20.6)	54 (17.1)	293 (17.5)	89 (20.6)	135 (19.8)	844 (19.1)
IIb	138 (10.4)	25 (7.9)	103 (6.2)	47 (10.9)	91 (13.3)	404 (9.1)
III	112 (8.4)	22 (7.0)	89 (5.3)	43 (10.0)	76 (11.1)	342 (7.7)
IV	44 (3.2)	16 (4.8)	42 (2.5)	17 (3.8)	38 (5.3)	157 (3.4)
ER/PR^{**}						
ER-PR-	226 (18.9)	58 (20.1)	232 (15.8)	94 (23.7)	112 (17.4)	722 (18.1)
ER+ or PR+	234 (19.6)	55 (19.1)	278 (18.9)	66 (16.6)	99 (15.4)	732 (18.3)
ER+PR+	736 (61.5)	175 (60.8)	962 (65.4)	237 (59.7)	432 (67.2)	2,542 (63.6)
Status at 5 years^{***}						
Expired	256 (18.7)	52 (15.7)	216 (12.6)	83 (18.5)	182 (25.3)	789 (17.2)
Alive	1,114 (81.3)	280 (84.3)	1,497 (87.4)	365 (81.5)	538 (74.7)	3,794 (82.8)

^a See definitions for TNM stages in the methods section of the text.

^b Because ER/PR tests are not performed on TNM 0 cases, we excluded them from the denominator when calculating percentages of women with tumors in each ER/PR category. Denominators upon which these percentages are based were: Caucasian 1,196; Chinese 288; Japanese 1,472; Filipino 397; Native Hawaiian 643; and total 3,996.

^{**} p < 0.01 ^{***} p < 0.001

Japanese women. At TNM IV, only 5.3% of Native Hawaiian women were alive after 5 years, compared to 26.2% of Japanese women. Even among ER+PR+ women, who should have had the most favorable prognosis, significant differences were found in survival, with only 78.2% of Native Hawaiian women alive after 5 years, compared to 89.8% of Japanese women.

Ethnic differences by age group are shown in Table 3. With few exceptions, Native Hawaiian women in all age groups had the smallest proportions of TNM 0 or I tumors and the largest proportions with ER/PR positive tumors. Significant differences in TNM were found for all age groups except the <40 years group. Significant differences in ER/PR status were detected in the 40-49 and 50-59 groups. Despite the positive prognosis associated with ER+PR+ status, fewer Hawaiians were alive at the end of 5 years compared to other ethnic groups; and significant differences were found in the oldest three age groups.

Ethnic differences by TNM stage are shown in Table 4. Mean age of diagnosis for Native Hawaiians was youngest or second youngest (to Filipino), and percent alive at 5 years was lowest for Native Hawaiians within each TNM group,

although not all differences were significant. When comparing within TNM group, ethnic differences in proportions of women with ER+PR+ tumors were not significant.

Multivariate analysis of stage at diagnosis

Logistic regression was used to determine the effect of age, ER/PR status, and ethnicity on being diagnosed with late-stage breast cancer (TNM III or IV) vs. early-stage breast cancer (TNM 0, I, or II). The effects of age alone (Model 1), age and ER/PR status (Model 2), and age, ER/PR, and ethnicity (Model 3) are shown in Table 5. Based on the comparison of the -2 log likelihood (a statistic that measures goodness of fit) for each model, adding ER/PR status and ethnicity improve the model significantly. Findings suggest that being diagnosed with a late-stage breast cancer was associated with being younger when diagnosed, having an ER-PR- tumor, and being Native Hawaiian. Being diagnosed with an early-stage cancer was associated with being older when diagnosed, having a tumor with positive ER and/or PR receptors, and being Japanese or Chinese.

Table 2. Percent of 5-year survivors in each ethnic group, by age group, TNM stage, and ER/PR status, (women diagnosed with breast cancer in Hawai'i, 1990-1997, n = 4,583

	Caucasian	Chinese	Japanese	Filipino	Native Hawaiian	Total
N (%)	1,370 (29.9)	332 (7.2)	1,713 (37.4)	448 (9.8)	720 (15.7)	4,583 (100)
Age Group						
27-39	85 (90.4)	15 (75.0)	60 (92.3)	34 (85.0)	48 (80.0)	242 (86.7)
40-49	246 (88.2)	49 (90.7)	223 (90.7)	106 (84.1)	121 (84.6)	745 (87.9)
50-59 ^{***}	251 (85.4)	56 (87.5)	278 (89.1)	93 (83.8)	136 (73.1)	814 (84.2)
60-69 ^{***}	258 (85.4)	76 (85.4)	489 (90.9)	87 (83.7)	148 (71.2)	1,058 (85.3)
70+ ^{***}	274 (68.3)	84 (80.0)	447 (81.0)	45 (67.2)	85 (69.1)	935 (74.9)
TNM^a						
0	206 (92.8)	53 (85.5)	341 (95.5)	70 (94.6)	95 (91.3)	765 (93.4)
I ^{**}	511 (88.0)	143 (93.5)	765 (92.3)	164 (92.1)	238 (86.2)	1,821 (90.3)
Ila	225 (82.4)	42 (77.8)	246 (84.0)	77 (86.5)	111 (82.2)	701 (83.1)
Ilb	101 (73.2)	22 (88.0)	77 (74.8)	33 (70.2)	61 (67.0)	294 (72.8)
III [*]	57 (50.9)	13 (59.1)	57 (64.0)	19 (44.2)	31 (40.8)	177 (51.8)
IV ^{**}	14 (31.8)	7 (43.8)	11 (26.2)	2 (11.8)	2 (5.3)	36 (22.9)
ER/PR						
ER- & PR- ^{**}	164 (72.6)	39 (67.2)	170 (73.3)	71 (75.5)	62 (55.4)	506 (70.1)
ER+ or PR+ ^{***}	180 (76.9)	48 (87.3)	236 (84.9)	46 (69.7)	68 (68.7)	578 (79.0)
ER+ & PR+ ^{***}	610 (82.9)	156 (89.1)	864 (89.8)	201 (84.8)	338 (78.2)	2,169 (85.3)
ER/PR not done for in situ	160 (92.0)	37 (84.1)	227 (94.2)	47 (92.2)	70 (90.9)	541 (92.2)

^a See definitions for TNM stages in the Methods section of the text.

^{*} *p* < 0.05 ^{**} *p* < 0.01 ^{***} *p* < 0.001

Table 3. Tumor characteristics by ethnicity by age group (women diagnosed with breast cancer in Hawai'i, 1990-1997, n = 4,583)

	Caucasian	Chinese	Japanese	Filipino	Native Hawaiian	Total
N (%)	1,370 (29.9)	332 (7.2)	1,713 (37.4)	448 (9.8)	720 (15.7)	4,583 (100)
Age Group 27-39						
	(n= 94)	(n=20)	(n=65)	(n=40)	(n=60)	(n=279)
TNM 0-I ^a	41 (43.6)	6 (30.0)	36 (55.4)	20 (50.0)	24 (40.0)	127 (45.5)
ER+PR+	45 (47.9)	8 (40.0)	31 (40.0)	18 (45.0)	32 (53.3)	134 (48.0)
Alive	85 (90.4)	15 (75.0)	60 (92.3)	34 (85.0)	48 (80.0)	242 (86.7)
Age Group 40-49						
	(n=279)	(n=54)	(n=246)	(n=126)	(n=143)	(n=848)
TNM 0-I ^{a*}	158 (56.6)	37 (68.5)	159 (64.6)	72 (57.1)	74 (51.7)	500 (59.0)
ER+PR+ [*]	137 (49.1)	30 (55.6)	141 (57.3)	72 (57.1)	88 (61.5)	468 (55.2)
Alive	246 (88.2)	49 (90.7)	223 (90.7)	106 (84.1)	121 (84.6)	745 (87.9)
Age Group 50-59						
	(n=294)	(n=64)	(n=312)	(n=111)	(n=186)	(n=967)
TNM 0-I ^{a***}	180 (61.2)	39 (60.9)	213 (68.3)	59 (53.2)	86 (56.2)	577 (59.7)
ER+PR+ ^{**}	154 (52.4)	35 (54.7)	159 (51.0)	55 (49.5)	108 (58.1)	511 (52.8)
Alive ^{**}	251 (85.4)	56 (87.5)	278 (89.1)	93 (83.8)	136 (73.1)	814 (84.2)
Age Group 60-69						
	(n=301)	(n=89)	(n=538)	(n=104)	(n=208)	(n=1,240)
TNM 0-I ^{a***}	186 (61.6)	59 (66.3)	385 (71.6)	60 (57.7)	116 (55.8)	806 (64.9)
ER+PR+	169 (56.0)	43 (48.3)	321 (59.7)	58 (55.8)	123 (59.1)	714 (57.5)
Alive ^{***}	258 (85.4)	76 (85.4)	489 (90.9)	87 (83.7)	148 (71.2)	1,058 (85.3)
Age Group 70+						
	(n=401)	(n=105)	(n=552)	(n=67)	(n=123)	(n=1,248)
TNM 0-I ^{a**}	238 (59.4)	74 (70.5)	393 (71.2)	41 (61.2)	80 (65.0)	826 (66.2)
ER+PR+	231 (57.6)	59 (56.2)	310 (56.2)	34 (50.7)	81 (65.9)	715 (57.3)
Alive ^{***}	274 (68.3)	84 (80.0)	447 (81.0)	45 (67.2)	85 (69.1)	935 (74.9)

^a See definitions for TNM stages in the methods section of the text.

^{*} *p* < .05 ^{**} *p* < .01 ^{***} *p* < .001

Table 4. Tumor characteristics by ethnicity by TNM^a stage, women diagnosed with breast cancer in Hawai'i, 1990-1997, n = 4,583

	Caucasian	Chinese	Japanese	Filipino	Native Hawaiian	Total
N (%)	1,370 (29.9)	332 (7.2)	1,713 (37.4)	448 (9.8)	720 (15.7)	4,583 (100)
TNM 0^a	(n=222)	(n=62)	(n=357)	(n=74)	(n=104)	(n=819)
Mean age [*]	58.18	63.19	60.95	56.64	57.07	59.27
ER+PR+	31 (14.0)	11 (17.7)	74 (20.7)	10 (13.5)	20 (19.2)	145 (17.8)
Alive	206 (92.8)	56 (93.0)	341 (95.5)	70 (94.6)	95 (91.3)	765 (93.4)
TNM I^a	(n=581)	(n=153)	(n=829)	(n=178)	(n=276)	(n=2,017)
Mean age [*]	61.36	63.06	64.01	56.07	59.62	61.87
ER+PR+	380 (65.4)	100 (65.4)	575 (69.4)	119 (66.9)	203 (73.6)	1,377 (68.3)
Alive ^{**}	511 (88.0)	143 (93.5)	756 (92.3)	164 (92.1)	238 (86.2)	1,821 (90.3)
TNM IIa^a	(n=273)	(n=54)	(n=293)	(n=89)	(n=135)	(n=844)
Mean age [*]	59.09	58.44	61.68	55.00	54.93	58.83
ER+PR+	160 (58.6)	34 (63.0)	193 (65.9)	49 (55.1)	89 (65.9)	525 (62.2)
Alive	225 (82.4)	45 (83.3)	246 (84.0)	77 (86.5)	111 (82.2)	707 (83.1)
TNM IIb^a	(n=138)	(n=25)	(n=103)	(n=47)	(n=91)	(n=404)
Mean age	55.39	54.16	58.17	52.62	55.29	55.75
ER+PR+	72 (55.2)	12 (46.0)	57 (55.3)	26 (55.3)	57 (62.6)	224 (55.4)
Alive	57 (50.9)	22 (88.0)	77 (74.8)	33 (70.2)	61 (67.0)	294 (72.8)
TNM III^a	(n=112)	(n=22)	(n=89)	(n=43)	(n=76)	(n=342)
Mean age [*]	62.73	61.91	63.80	57.95	57.36	61.16
ER+PR+	70 (62.5)	9 (40.9)	44 (49.4)	24 (55.8)	45 (59.2)	192 (56.1)
Alive [*]	57 (50.9)	13 (59.1)	57 (64.0)	19 (44.2)	31 (40.8)	177 (51.8)
TNM IV^a	(n=44)	(n=16)	(n=42)	(n=17)	(n=38)	(n=157)
Mean age [*]	60.93	66.25	64.07	54.069	58.34	60.94
ER+PR+	23 (52.3)	9 (56.3)	19 (45.2)	(52.9)	18 (47.4)	78 (49.7)
Alive ^{**}	14 (31.8)	7 (43.8)	11 (26.3)	2 (11.8)	2 (5.3)	36 (22.9)

^a See definitions for TNM stages in the methods section of the text.

^{*} $p < .05$ ^{**} $p < .01$

Multivariate analysis of 5-year survival

Logistic regression also was used to determine the effect of age, TNM, ER/PR status, and ethnicity on 5-year survival (Table 6). Each of 4 models was evaluated with and without ethnicity as a covariate. Model 1a included age and TNM; Model 1b included these variables plus ethnicity. Model 2a included age, TNM, and ER/PR status; Model 2b added ethnicity. Model 3a included age, TNM, ER/PR status, and the cross-product of age and stage; Model 3b added ethnicity. Model 4a included age, TNM, ER/PR status, the cross-product of age and stage, and the cross-product of ER/PR status and stage; Model 4b added ethnicity. In all models, Native Hawaiian women were significantly less likely to be alive after 5 years, while Japanese women were significantly more likely to be alive. Based on -2 log likelihood values, each model was improved by adding ethnicity as a covariate. In addition, the models improved with the addition of each new variable, with Model 4b providing the best fit.

Discussion

Even with the addition of ER/PR status, this study found that ethnic differences in breast cancer survival exist in Hawai'i, albeit, as others have found, these differences are reduced by statistically controlling for age and stage^{2,3}.

Although research suggests that ER+PR+ tumors are associated with better prognosis and that they occur with less frequency in minority women compared to Whites^{4,9}, Japanese and Native Hawaiian women appear to be exceptions. Our study confirmed findings from 2 separate analyses of 90,000+ cases of breast cancer from 11 SEER registries in the US that determined that ER+PR+ tumors occur with similar frequency in Japanese and Hawaiian women as in Caucasian women (66-67% for Japanese, 68-69% for Hawaiians, and 64-67% for Caucasians vs. 48-52% for African Americans)^{4,5}.

We also found that, along with age and ethnicity, ER/PR status was a predictor of stage at diagnosis, with women

Table 5. Odds ratios (OR) and 95% confidence intervals (CI) for diagnosis of TNM III or IV^a, adjusting for age, ER/PR status, and ethnicity; women diagnosed with breast cancer in Hawai'i, 1990-1997. n = 4,583

	Model 1 OR (95% CI)	Model 2 OR (95% CI)	Model 3 OR (95% CI)
Age at diagnosis	0.99 (0.98-0.99) ^{***}	0.99 (0.98-0.99) ^{***}	0.99 (0.98-0.99) ^{***}
ER/PR status^b			
ER+ or PR+		0.68 (0.55-0.83) ^{***}	0.69 (0.56-0.85) ^{***}
ER+ and PR+		0.56 (0.57-0.66) ^{***}	0.56 (0.47-0.66) ^{***}
Ethnicity^b			
Chinese			0.76 (0.59-0.99) [*]
Japanese			0.65 (0.55-0.76) ^{***}
Filipino			1.01 (0.80-1.27)
Native Hawaiian			1.24 (1.02-1.50) ^{**}
-2 Log Likelihood	6,058.01	5,386.01	5,329.54
Chi-square Model 1 vs. 2		672.0 ^{***}	
Chi-square comparing Models 2 vs. 3			56.5 ^{***}

^a See definitions for TNM stages in the methods section of the text.

^b The reference group for ER/PR status is ER-PR- and the reference group for ethnicity is Caucasian.

^{*} $p < .05$ ^{***} $p < .001$

Table 6. Adjusted odds ratios (OR) and 95% confidence intervals (CI) for 5-year survival in women diagnosed with breast cancer in Hawai'i, 1990-1997. n=4,583

Model	Adjustment variables by model							
	1a	1b	2a	2b	3a	3b	4a	4b
Description	age and TNM	age, TNM, ethnicity	age, TNM, ER/PR	age, TNM, ER/PR, ethnicity	age, TNM, ER/PR, age*TNM	age, TNM, ER/PR, age*TNM, ethnicity	age, TNM, ER/PR, age*TNM, ER/PR*TNM	age, TNM, ER/PR, age*TNM, ER/PR*TNM, ethnicity
		OR 95% CI		OR 95% CI		OR 95% CI		OR 95% CI
Caucasian ^a		1.00		1.00		1.00		1.00
Chinese		1.31 (.91-1.90)		1.36 (.94-2.00)		1.37 (.94-1.98)		1.39 (.96-2.02)
Japanese		1.49 ^{***} (1.20-1.85)		1.50 ^{***} (1.20-1.90)		1.49 ^{***} (1.19-1.86)		1.51 ^{***} (1.21-1.89)
Filipino		0.91 (.67-1.25)		0.93 (.68-1.27)		0.93 (.68-1.28)		0.93 (.68-1.28)
Hawaiian		0.68 ^{**} (.53-.86)		0.65 ^{***} (.51-.83)		0.65 ^{***} (.51-.84)		0.66 ^{***} (.51-.84)
-2 Log Likelihood	3452.87	3411.94	3391.99	3348.27	3363.89	3320.93	3355.40	3311.47
Chi-square for Models a vs. b		40.93 ^{***}		43.72 ^{***}		42.96 ^{***}		43.93 ^{***}

^a Reference group

^{**} $p < 0.01$ ^{***} $p < 0.001$

with ER+ and/or PR+ tumors less likely to be diagnosed with late-stage disease. In an analysis of 112,582 women, Chu et al. also found that stage-at-diagnosis patterns appear to be affected by ER/PR status, age, and ethnicity. In general, ER+PR+ tumors are associated with TNM I diagnoses, and ER-PR- tumors are associated with TNM II diagnoses. However, they found a number of exceptions, including the fact that Japanese and Native Hawaiians with ER-PR- tumors were more likely to be diagnosed at later ages than Whites with ER-PR- tumors. The discovery of these and other exceptions led these investigators to suggest that, within ethnic groups, ER/PR status may further divide breast cancer patients into two or more subgroups with unique tumor characteristics⁵. In another analysis of multiple SEER sites, Miller found that ER/PR status did not change Caucasian-Japanese-Hawaiian differences in being diagnosed with regional or distant breast cancer once variables representing socio-economic status (SES) were considered⁶. Taken together, these studies suggest that further investigation into the significance of ER/PR status for each ethnic group is warranted.

Focusing on survival, we confirmed that, regardless of stage, fewer Hawaiian women survive 5 years after diagnosis than Japanese women^{2,4}. Particularly, higher mortality for *in situ* cancer among Native Hawaiians may indicate that Native Hawaiian women have co-morbid medical conditions that jeopardize overall health status, as *in situ* tumors should be metastasizing in less than 2% of cases. Individuals with more severe levels of co-morbidity have worse survival, both directly and indirectly, as severe co-morbidities reduce options for treatment and ability to tolerate treatment^{13,14}. Cross-ethnic comparisons of health status in Hawai'i have demonstrated relatively high rates of obesity, heart disease, diabetes, and lung disease among Native Hawaiians. These data also show that Japanese residents have the best health status and longest life expectancy in the state^{14,15}. This suggests that studying Japanese Americans may provide clues for improving the health status of all US residents, and investigators in Hawai'i may want to use Japanese Americans, rather than Caucasians, as the dominant comparison group.

A number of investigators believe that ethnic disparities in morbidity and mortality reflect differential access to services, and they call for equal quality health care for all Americans¹⁶⁻¹⁹. In support of this theory, several researchers have included measures of socio-economic status (SES) in their analyses and have found that ethnic differences in survival are reduced when SES and insurance status were controlled for statistically^{17,18}. This theory could partially explain lower survival rates among Native Hawaiian women with breast cancer, as Native Hawaiians have the highest rates of poverty, underemployment, and underinsurance of Hawai'i's 5 major ethnic groups^{14,20}. Also, some Native Hawaiians have reported discrimination in health care^{14,20}. For example, in focus groups with cancer survivors affiliated with Native Hawaiian health centers, 25% of participants

recounted having their cancer symptoms disregarded by their physicians, including several women who brought breast lumps to the attention of their physicians and were told that they were "too young to have cancer" (these women were in their 20s and 30s when diagnosed) and/or to "lay off caffeine"²¹.

Hawai'i-based research by Maskarinec and colleagues also supports this view. To study the impact of insurance on survival of women diagnosed with breast cancer in Hawai'i, they merged SEER data with health-insurance claims data. Among women with insurance, ethnic differences in survival were very similar once age and stage were controlled for statistically¹⁷. At least 2 investigators who have compared survival differences of Caucasian and African American women with breast cancer have reached this same conclusion^{17,18}. On the other hand, 2 separate studies of military populations found that, despite equal access to cancer screening and treatment services through Department of Defense facilities, Black women with breast cancer still had lower rates of 5-year survival than White women even after controlling for known prognostic factors (including, in one study, family history, tobacco/alcohol use, and waiting time between diagnosis and treatment)^{22,23}.

Another possible reason for survival disparities may be access to treatment. Looking specifically at cancer treatment in Hawai'i, analyses of SEER data have found that few differences exist among ethnic groups in prescribed treatment regimes^{4,12}. Future studies should examine patient compliance with recommended treatment, and may need to gather data through review of medical records and claims, rather than relying on SEER registry data.

In addition to more research on differential access to and compliance with treatment, some investigators feel that research on the biological aggressiveness of tumors is warranted, especially when considering evidence of younger age, later stage at diagnosis, and worse survival within age and stage strata for minority women compared to Caucasian women^{4,17,24,25}. Researchers are investigating the prognostic value of various biomarkers of gene expression²⁶⁻³⁰, and advances in tumor microarray analysis technology promise to speed discoveries in this area.

Summary

Native Hawaiian women have the poorest rates of breast cancer survival of Hawai'i's major ethnic groups, even after controlling for age, stage, and ER/PR status. Future studies should examine other factors associated with differential outcomes, including reasons for better survival of Japanese women and worse survival of Native Hawaiian women, such as co-morbidities, SES, treatment appropriateness and compliance, and genetic markers of tumor aggressiveness.

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