Differences in Breast Cancer Hormone Receptor Status and Histology by Race and Ethnicity among Women 50 Years of Age and Older[1]

Christopher I. Li,[2] Kathleen E. Malone, and Janet R. Daling

Fred Hutchinson Cancer Research Center, Division of Public Health Sciences, Seattle, Washington 98109-1024

Abstract

Numerous studies have demonstrated differences in certain biological breast cancer characteristics associated with survival, including hormone receptor status and histology, among women of different racial and ethnic groups. However, women classified as "Asian or Pacific Islanders" or "Hispanic whites" represent heterogeneous populations, and few studies have separately evaluated subgroups of these populations with respect to these breast tumor characteristics. Using data obtained from 11 cancer registries that participate in the Surveillance, Epidemiology, and End Results (SEER) Program, the tumor characteristics of 93,317 women in whom invasive breast cancer was diagnosed from 1992 to 1998 were compared by race and ethnicity using unconditional and polytomous logistic regression. The study consisted of 75,978 non-Hispanic whites, 6,915 African Americans, 203 Native Americans, 5,750 Asians/Pacific Islanders, and 4,471 Hispanic whites. Eight Asian/Pacific Islander and four Hispanic white subgroups were also analyzed separately. Relative to non-Hispanic whites, African Americans, Native Americans, Filipinos, Chinese, Koreans, Vietnamese, Indians/Pakistanis, Mexicans, South/Central Americans, and Puerto Ricans living in the United States had 1.4- to 3.1-fold elevated risks of presenting with estrogen receptor-negative/progesterone receptor-negative breast cancer. Numerous differences by histological type, including lobular, ductal/lobular, mucinous, comedocarcinoma, tubular, and medullary histologies, were also observed by race/ethnicity. Breast cancer tumor characteristics differ by race/ethnicity in the United States. Both biological and lifestyle factors likely contribute to these findings. Our results may explain, to some extent, the differences in breast cancer stage and survival observed by race/ethnicity. Understanding the factors underlying these differences may provide further insight into breast cancer etiology in different populations.

Introduction

African American (1–6), Hispanic (1, 2, 6–9), Native American (7, 10), Hawaiian, and Filipino (1, 11, 12) women living in the United States are more likely to be diagnosed with advanced stages of breast cancer and to have poorer survival after diagnosis compared with non-Hispanic whites. Alternatively, Japanese and Chinese women have been shown either to be no different with respect to breast cancer stage and survival (1) or to actually present with less advanced stages and to have better survival compared with non-Hispanic whites (11, 12). Various explanations for these findings have been postulated including differences in sociodemographic, cultural, and behavioral characteristics. With respect to African Americans, some studies have shown that differences in insurance coverage and socioeconomic status (13, 14) do not explain the observed differences in stage, whereas other studies find that, after adjusting for factors such as socioeconomic status, income, stage, and breast cancer treatments, differences in survival are no longer observed (15–17).

These stage and survival differences may also be related to the differential expression of breast tumor characteristics that have been independently shown to be related to mortality. Specifically, hormone receptor-negative breast tumors (18–20) are associated with poorer survival, whereas tumors that have a lobular histology are associated with better survival (21). Previous studies suggested that African Americans are more likely to have ER[3]-negative, PR-negative (5, 22), and medullary (4, 6) breast tumors, and less likely to have tumors with a lobular histology (23). Whether or not Hispanic women are more likely to have ER-negative and PR-negative breast tumors remains unclear with one study showing that they do (6) and two others showing that they do not (22, 24). Overall, there are few studies that have explored the relationship between race/ethnicity and breast tumor characteristics, and those that have, have been limited by studying women living in single geographic regions, by their sample sizes, and in their abilities to assess women in different racial/ethnic subgroups.

Using data from 11 population-based tumor registries in the United States, we assessed the relationship between race/ethnicity, using 17 separate categories, and risk of invasive breast carcinoma by hormone receptor status and histological type among women 50 years of age and older.

Materials and Methods

Women 50 years of age and older with diagnoses of invasive breast cancer made between 1992 and 1998 were identified through 11 population-based cancer registries in the United

Received 8/24/01; revised 3/22/02; accepted 4/3/02.
The costs of publication of this article were defrayed in part by the payment of page charges. This article must therefore be hereby marked *advertisement* in accordance with 18 U.S.C. Section 1734 solely to indicate this fact.
[1] Supported by Contract N01 CN 05230 from the National Cancer Institute, NIH.
[2] To whom requests for reprints should be addressed, at Fred Hutchinson Cancer Research Center, Division of Public Health Sciences; 1100 Fairview Avenue North, MP 381, P. O. Box 19024, Seattle, Washington 98109-1024. Phone: (206) 667-4630; Fax: (206) 667-5948, E-mail: cili@fhcrc.org.

[3] The abbreviations used are: ER, estrogen receptor; PR, progesterone receptor; SEER, Surveillance, Epidemiology, and End Results (survey); NOS, not otherwise specified; OR odds ratio; CI, confidence interval; ICD-O, International Classification of Diseases for Oncology.

States that participate in the National Cancer Institute's SEER Program. The study was limited to women 50 years of age and older because hormone receptor status is known to differ by menopausal status (25), and in the absence of information on menstrual history, 50 years of age has been shown to be a reasonable proxy for defining menopause (26). The year 1992 was chosen as the starting point for this analysis because this was the year when two registries were added to the SEER program, those serving the urban areas surrounding Los Angeles and San Jose, California, both of which contain racially and ethnically diverse populations. The other SEER registries that were used include those serving the states of Connecticut, Hawaii, Iowa, New Mexico, and Utah and the urban areas surrounding Atlanta, Georgia; Detroit, Michigan; San Francisco-Oakland, California; and Seattle, Washington. The principal sources of data used by SEER are patients' medical records. It is estimated that >95% of all incident cancer cases in the populations under surveillance are ascertained. Further operational details and methods used by the SEER program are provided elsewhere (27).

A total of 95,523 women whose breast cancer diagnosis was their first primary cancer diagnosis of any type recorded at their registry were eligible for this study. Subjects were excluded if their cancer was diagnosed at autopsy ($n = 33$), if their race was classified as "other" ($n = 159$) or "unknown" ($n = 611$), or if their Hispanic ethnicity was classified as either "Spanish surname only" (meaning that the only evidence of a woman's Hispanic origin was her surname or maiden name) or "unknown" ($n = 1,360$). In addition, to make our race/ethnicity categories mutually exclusive, 31 African American women, 1 Native American woman, and 11 Asians/Pacific Islanders who were also categorized as being Hispanic were excluded leaving a total of 93,317 subjects.

Our primary exposure of interest was race/ethnicity. Beginning in 1988, in addition to categorizing "race/ethnicity" as white, black, Native American/Alaskan Native, Chinese, Japanese, Filipino, and Hawaiian, SEER added categories for Koreans, Asian Indians/Pakistanis, and Vietnamese among others. Of the 5,750 Asian/Pacific Islanders included in this study, 127 were of less common Asian/Pacific Islander races, including Thai, Laotian, Tongan, and so forth; and 239 were classified as being other or NOS Asian/Pacific Islanders. These 366 women were grouped together and classified as other/NOS Asians/Pacific Islanders. In 1988, SEER also added information about "Spanish surname or origin" specifically coding whether individuals were Mexican, Puerto Rican, Cuban, South or Central American (except Brazil), other specified Spanish/Hispanic Origin (includes European), and Spanish/Hispanic NOS. We used these expanded categorizations in our analyses (although, because of the small number of Cubans ($n = 117$), we merged them with the 2,534 women of other/NOS Spanish/Hispanic origin). Given these categorizations, our study consisted of 75,978 non-Hispanic whites, 6,915 African Americans, 203 Native Americans, 5,750 Asians/Pacific Islanders, and 4,471 Hispanic whites.

In addition to age and year of diagnosis, SEER also provides information on: ER status, PR status, and histology. Moreover, information on the following tumor characteristics, which we evaluated as potential confounders or effect modifiers of the relationship between race/ethnicity and ER status, PR status, and histology, is available: American Joint Committee on Cancer (AJCC) stage, size, number of positive lymph nodes, number of lymph nodes examined, and tumor grade. In addition, surgical and radiation treatment information is available. Although information on marital status is provided, data regarding other sociodemographic factors such as income and health insurance status are not.

ORs were calculated as an estimate of the relative risk to evaluate the association between ER status, PR status, and histological type and different racial/ethnic groups. Non-Hispanic whites served as the reference group because they represented over 80% of our total study population. Using Stata 6.0 for Windows (Stata Corporation, College Station, TX) statistical software, unconditional logistic regression was performed to compute ORs and 95% CIs (28) and to evaluate the effects of confounding and modifying factors on the association between race/ethnicity and ER status and PR status. A factor was considered to be a confounder if it changed our estimates by more than 10%. None of the potential confounders or effect modifiers listed above were found to confound or modify the relationships that we assessed. In addition, histology was not a confounder of the relationships that we observed between hormone receptor status and race/ethnicity, and hormone receptor status was not a confounder of the relationship between histology and race/ethnicity. However, all analyses were adjusted for age at diagnosis (as a categorical variable), year at diagnosis (as a continuous variable), and SEER registry. Unconditional logistic regression was used to assess the association between race/ethnicity and ER status and PR status among women with a known hormone receptor status. Women whose hormone receptor status was classified as borderline, not assessed, or unknown were considered to have an unknown status. Polytomous logistic regression was used to evaluate the association between race/ethnicity and ER/PR status and histology. In these polytomous models the baseline categories used were ER-positive/PR-positive and ductal histology (defined using ICD-O code 8500), respectively. The other histologies that we assessed, were classified using ICD-O codes, as follows: lobular (8520), ductal-lobular (8522), mucinous (8480), comedocarcinoma (8501), adenocarcinoma (8140), tubular (8211 and 8201), and medullary (8510). These analyses were also adjusted for age at diagnosis, year at diagnosis, and SEER registry.

Results

Table 1 presents a comparison of various characteristics by race/ethnicity. Non-Hispanic white women tended to have later diagnosis ages compared with women of other races/ethnicities, although this may reflect the fact that the non-Hispanic white population is on average older than the other populations. African-American women most frequently came from the Atlanta, Detroit, and Los Angeles registries; Native Americans from New Mexico and Seattle/Puget Sound; Asian Americans/Pacific Islanders from Hawaii, Los Angeles, and San Francisco/Oakland; and Hispanic whites from Los Angeles and New Mexico. African Americans, Native Americans, and Hispanic whites were somewhat more likely to present with tumors that had a more advanced stage, were larger, and had more positive lymph nodes compared with non-Hispanic whites and Asians/Pacific Islanders. Of note, ER status was borderline, not assessed, or unknown for 19.3% of non-Hispanic whites, 28.5% of African Americans, 16.8% of Native Americans, 17.3% of Asians/Pacific Islanders, and 27.8% of Hispanic whites.

Tables 2 and 3 present age, diagnosis year, and SEER registry-adjusted risks of breast tumors for each race/ethnicity by hormone receptor status. Compared with non-Hispanic whites, African Americans, Native Americans, Asians/Pacific Islanders, and Hispanic whites all had 1.2- to 2.2-fold elevations in their risks of ER-negative, PR-negative, and ER-negative/PR-negative tumors, with African Americans having

Table 1 Comparison of various characteristics among 93,317 subjects of different races/ethnicities

Characteristic	Race/Ethnicity									
	Non-Hispanic white		African American		Native American		Asian/Pacific Islander		Hispanic white	
	n = 75,978	%	*n* = 6,915	%	*n* = 203	%	*n* = 5,750	%	*n* = 4,471	%
Demographics										
Age at diagnosis, yr										
50–59	20,566	27.1	2,391	34.6	102	50.3	2,145	37.3	1,628	36.4
60–69	21,874	28.8	2,120	30.7	53	26.1	1,891	32.9	1,483	33.2
70–79	21,871	28.8	1,664	24.1	37	18.2	1,324	23.0	971	21.7
≥80	11,667	15.4	740	10.7	11	5.4	390	6.8	389	8.7
Diagnosis year										
1992	10,497	13.8	943	13.6	39	19.2	678	11.8	699	15.6
1993	10,409	13.7	904	13.1	25	12.3	680	11.8	653	14.6
1994	10,523	13.9	947	13.7	31	15.3	685	11.9	573	12.8
1995	10,775	14.2	1,002	14.5	22	10.8	812	14.1	611	13.7
1996	10,857	14.3	1,009	14.6	36	17.7	846	14.7	620	13.9
1997	11,574	15.2	1,054	15.2	28	13.8	1,031	17.9	625	14.0
1998	11,343	14.9	1,056	15.3	22	10.8	1,018	17.7	690	15.4
Registry										
Atlanta	3,758	5.0	1,080	15.6	5	2.5	35	0.6	32	0.7
Connecticut	9,899	13.0	470	6.8	2	1.0	29	0.5	148	3.3
Detroit	9,387	12.4	2,108	30.5	3	1.5	60	1.0	31	0.7
Hawaii	870	1.2	14	0.2	8	3.9	2,144	37.3	5	0.1
Iowa	9,302	12.2	88	1.3	2	1.0	14	0.2	26	0.6
Los Angeles	13,606	17.9	2,001	28.9	9	4.4	1,550	27.0	2,300	51.4
New Mexico	2,817	3.7	48	0.7	104	51.2	18	0.3	811	18.1
San Francisco/Oakland	8,452	11.1	823	11.9	7	3.5	1,107	19.3	557	12.5
San Jose	4,253	5.6	82	1.2	4	2.0	456	7.9	417	9.3
Seattle	10,051	13.2	195	2.8	54	26.6	305	5.3	58	1.3
Utah	3,583	4.7	6	0.1	5	2.5	32	0.6	86	1.9
Tumor characteristics										
AJCC stage[a]										
I	40,440	53.2	2,700	39.1	97	47.8	2,967	51.6	1,856	41.5
II	27,099	35.7	2,891	41.8	70	34.5	2,169	37.7	1,962	43.9
III	4,794	6.3	728	10.5	20	9.9	364	6.3	373	8.3
IV	3,645	4.8	596	8.6	16	7.9	250	4.4	280	6.3
Grade										
1	11,715	15.4	688	10.0	19	9.4	768	13.4	532	11.9
2	27,095	35.7	1,888	27.3	75	37.0	2,094	36.4	1,439	32.2
3	20,174	26.6	2,453	35.5	54	26.6	1,706	29.7	1,452	32.5
4	1,804	2.4	146	2.1	9	4.4	135	2.4	118	2.6
Unknown	15,190	20.0	1,740	25.2	46	22.7	1,047	18.2	930	20.8
Size										
<2.0	43,533	57.3	2,957	42.8	102	50.3	3,160	55.0	2,003	44.8
2.0–4.9	24,354	32.1	2,658	38.4	75	37.0	1,931	33.6	1,799	40.2
≥5.0+	5,641	7.4	978	14.1	19	9.4	530	9.2	503	11.3
Unknown	2,450	3.2	322	4.7	7	3.5	129	2.2	166	3.7
No. of positive LNs										
0	41,254	54.3	2,986	43.2	91	44.8	3,323	57.8	2,217	49.6
1	6,507	8.6	635	9.2	20	9.9	449	7.8	390	8.7
2–4	6,628	8.7	706	10.2	22	10.8	529	9.2	464	10.4
≥5	5,953	7.8	689	10.0	23	11.3	502	8.7	497	11.1
None examined	15,225	20.0	1,805	26.1	45	22.2	906	15.8	861	19.3
Unknown	411	0.5	94	1.4	2	1.0	41	0.7	33	0.9
No. of LNs examined										
1–10	16,847	22.2	1,318	19.1	37	18.2	1,244	21.6	848	19.0
11–20	32,955	43.4	2,772	40.1	90	44.3	2,533	44.1	1,991	44.5
≥20	9,947	13.1	870	12.6	27	13.3	980	17.0	701	15.7
None examined	15,232	20.1	1,805	26.1	45	22.2	906	15.8	864	19.3
Unknown	70	0.1	8	0.1	0	0.0	6	0.1	7	0.2
ER status										
Positive	49,807	65.6	3,283	47.5	121	59.6	3,662	63.7	2,429	54.3
Negative	11,536	15.2	1,668	24.1	49	24.1	1,091	19.0	795	17.8
Borderline	422	0.6	45	0.7	2	1.0	28	0.5	19	0.4
Not assessed	3,578	4.7	559	8.1	16	7.9	244	4.2	252	5.6
Unknown	10,635	14.0	1,360	19.7	15	7.9	725	12.6	976	21.8
PR status										
Positive	41,086	54.1	2,653	38.4	100	49.3	3,123	54.3	1,999	44.7
Negative	18,070	23.8	2,100	30.4	66	62.5	1,525	26.5	1,132	25.3

Table 1 Continued

Characteristic	Race/Ethnicity									
	Non-Hispanic white		African American		Native American		Asian/Pacific Islander		Hispanic white	
	n = 75,978	%	*n* = 6,915	%	*n* = 203	%	*n* = 5,750	%	*n* = 4,471	%
Borderline	649	0.9	72	1.0	4	2.0	40	0.7	24	0.5
Not assessed	4,407	5.8	670	9.7	17	8.4	308	5.4	298	6.7
Unknown	11,766	15.5	1,420	20.5	16	7.9	754	13.1	1,018	22.8
Histology										
Ductal	53,545	70.5	4,858	70.3	143	70.4	4,364	75.9	3,086	69.0
Lobular	7,277	9.6	437	6.3	12	5.9	259	4.5	320	7.2
Ductal/lobular	4,508	5.9	323	4.7	10	4.9	196	3.4	243	5.4
Comedocarcinoma	1,304	1.7	176	2.6	9	4.4	158	2.8	100	2.2
Mucinous	2,054	2.7	198	2.6	3	1.5	198	3.4	114	2.6
Adenocarcinoma	1,428	1.9	181	2.6	4	2.0	106	1.8	133	3.0
Tubular	1,506	2.0	59	0.9	1	0.5	57	1.0	68	1.5
Medullary	522	0.7	152	2.2	6	3.0	67	1.2	74	1.7
Other/unknown	3,834	5.1	531	7.7	15	7.4	345	6.0	333	7.5

[a] AJCC, American Joint Committee on Cancer; LN, lymph node.

the highest risk of ER-negative/PR-negative tumors. Although overall there was a 40% elevation in risk of ER-negative/PR-negative tumors among Asian/Pacific Islanders, this increase appeared limited to 1.4- to 3.1-fold elevations in the risk of such tumors among Filipinos, Chinese, Hawaiians, Koreans, Vietnamese, and Asian Indians/Pakistanis. Among Hispanic whites, Mexicans, South/Central Americans, and Puerto Ricans had 1.5- to 1.7-fold elevated risks of ER-negative/PR-negative tumors.

Table 4 presents risks of different breast cancer histologies by race and ethnicity adjusted for age, year of diagnosis, and SEER registry. Compared with non-Hispanic whites, each subgroup had 20–70% reductions in risk of lobular and/or ductal/lobular carcinoma (except for Native Americans, Hawaiians, Indians/Pakistanis, and Puerto Ricans). Among African Americans, Native Americans, Asians/Pacific Islanders, and Hispanic Whites, 1.3- to 3.4-fold increases in risk of mucinous carcinoma were observed. However, the increased risk among Asians/Pacific Islanders appeared limited to Filipino and Chinese women, whereas the increased risk among Hispanic whites seemed to be limited to Mexicans and South/Central Americans. African American and Chinese women had 20 and 50% elevations in their risk of comedocarcinoma, respectively. A 1.5- to 2.4-fold increase in the risk of adenocarcinoma was limited to African Americans, Vietnamese, Mexicans, and South/Central Americans; and 40–80% reductions in risk of tubular carcinoma were seen among African Americans, Japanese, Filipinos, Chinese, Hawaiians, and Hispanic whites. Finally, 1.5- to 7.7-fold elevations in risk of medullary carcinoma were seen among African Americans, Native Americans, Filipinos, Chinese, Mexicans, and Puerto Ricans, with Puerto Ricans having the highest risk.

Discussion

Our findings are generally consistent with the few published studies in this area. With respect to hormone receptor status, our results are similar in magnitude and direction to previous findings that African-American women have greater risks of ER-negative (29), PR-negative (4–6), ER-positive/PR-negative, ER-negative/PR-positive, and ER-negative/PR-negative (22) breast tumors. Fewer studies have looked at other racial/ethnic groups with one finding that white Hispanic women have greater risks of ER-negative and PR-negative breast tumors (6), whereas other groups have not (4, 23). Also, one study found that Asians were more likely than non-Hispanic whites to have ER-negative/PR-negative breast tumors (30). Even fewer studies have reported on differences in breast cancer histologies by race/ethnicity. African Americans and Hispanic whites do appear to have decreased risks of lobular carcinoma and increased risks of medullary carcinoma compared with non-Hispanic whites (4, 22, 23), and one study that examined Asian/Pacific Islanders also found that they had a lower risk of lobular carcinoma, although this reduction in risk was not significant (23). Joslyn *et al.* (4), also reported that African Americans were less likely to have ductal/lobular and tubular tumors.

Again, these studies were all limited in their ability to assess risk among different Asians/Pacific Islanders and Hispanic whites of different origins and in the geographic regions studied. Thus, in this study of women living in 11 geographic regions, we expand on what has been reported, *i.e.*, that Native Americans, Filipinos, Chinese, Koreans, Vietnamese, Indians/Pakistanis, Mexicans, South/Central Americans, and Puerto Ricans (in addition to African Americans) living in the United States have elevated risks of being diagnosed with ER-negative/PR-negative tumors, which are tumors known to be associated with poorer survival (18–20). Furthermore, we document differences with respect to histology, with African Americans, Native Americans, all Asian/Pacific Islander subtypes (except for Hawaiians and Indians/Pakistanis), and all Hispanic white subtypes (except for Puerto Ricans) having decreased risks of lobular carcinoma, which is a histological subtype that may be associated with a better prognosis (21), than the most common histological type of breast cancer, ductal carcinoma. Overall, compared with non-Hispanic whites, differences were seen in at least five of the seven histological subtypes analyzed for African Americans, Filipinos, Chinese, Mexicans, and South/Central Americans.

A potential limitation of this study is that our exposure of interest, race/ethnicity, was determined via medical record reviews. However, information on race was classified as other or unknown, and ethnicity was classified as Spanish surname only or unknown, whether Spanish/Hispanic or not, for only 2130 women, representing 2.3% of the eligible study population. With respect to Asians/Pacific Islanders, only 239 women, representing 4.2% of this population, were classified as being of a NOS Asian/Pacific Islander race. An inability to categorize

Table 2 Relative risks of ER-negative and PR-negative breast cancer by race and ethnicity

Race/Ethnicity	ER status						PR status					
	Positive		Negative		OR[a]	95% CI	Positive		Negative		OR	95% CI
	n	%	*n*	%			*n*	%	*n*	%		
Non-Hispanic white	49,807	81.2	11,536	18.8	1.0	(ref)	41,086	69.5	18,070	30.6	1.0	(ref)
African American	3,283	66.3	1,668	33.7	2.1[b]	1.9–2.2	2,653	55.8	2,100	44.2	1.7[b]	1.6–1.8
Native American	121	71.2	49	28.8	1.7[b]	1.2–2.3	100	60.2	66	39.8	1.4[b]	1.0–2.0
Asian/Pacific Islander (PI)	3,662	77.1	1,091	23.0	1.4[b]	1.2–1.5	3,123	67.2	1,525	32.8	1.2[b]	1.1–1.3
Japanese	1,311	80.0	327	20.0	1.2[b]	1.0–1.3	1,132	70.2	480	29.8	1.0	0.9–1.1
Filipino	795	75.6	256	24.4	1.3[b]	1.2–1.6	656	64.5	361	35.5	1.3[b]	1.1–1.4
Chinese	686	77.1	204	22.9	1.4[b]	1.1–1.6	579	66.6	290	33.4	1.2[b]	1.0–1.4
Hawaiian	359	80.7	86	19.3	1.0	0.8–1.4	316	72.2	122	27.9	0.9	0.7–1.1
Korean	108	60.7	70	39.3	2.6[b]	1.9–3.6	88	51.2	84	48.8	2.1[b]	1.6–2.9
Vietnamese	90	67.2	44	32.8	2.0[b]	1.4–2.9	78	59.1	54	40.9	1.6[b]	1.1–2.2
Indian/Pakistani	89	72.4	34	27.6	1.5[b]	1.0–2.3	77	62.6	46	37.4	1.3	0.9–1.9
Other Asian/PI	224	76.2	70	23.8	1.3	1.0–1.7	197	69.1	88	30.9	1.0	0.8–1.3
Hispanic White	2,429	75.3	795	24.7	1.4[b]	1.3–1.5	1,999	63.9	1,132	36.2	1.3[b]	1.2–1.4
Mexican	583	74.5	200	25.5	1.5[b]	1.2–1.7	490	65.3	261	34.8	1.2[b]	1.0–1.4
South/Central American	243	70.4	102	29.6	1.7[b]	1.3–2.1	196	59.9	131	40.1	1.5[b]	1.2–1.9
Puerto Rican	61	70.1	26	29.9	1.7[b]	1.1–2.7	53	60.9	34	39.1	1.3	0.9–2.1
Other Hispanic	1,542	76.8	467	23.3	1.3[b]	1.1–1.4	1,260	64.1	706	35.9	1.2[b]	1.1–1.4

[a] All ORs are adjusted for age at diagnosis, year of diagnosis, and SEER registry using polytomous logistic regression in which the reference (ref) race/ethnicity is non-Hispanic whites, the baseline ER status is ER positive, and the baseline PR status is PR positive.
[b] $P < 0.05$.

Table 3 Relative risks of different ER/PR breast cancer profiles by race and ethnicity

Race/Ethnicity	ER/PR status													
	ER+/PR+		ER+/PR−		OR[a]	95% CI	ER−/PR+		OR		ER−/PR−		OR	95% CI
	n	%	*n*	%			*n*	%			*n*	%		
Non-Hispanic white	39,376	66.9	8,299	14.1	1.0	(ref)	1,545	2.6	1.0	(ref)	9,604	16.3	1.0	(ref)
African American	2,465	52.3	638	13.5	1.2[b]	1.1–1.3	171	3.6	1.5[b]	1.3–1.8	1,441	30.6	2.2[b]	2.1–2.4
Native American	94	57.3	21	12.8	1.0	0.6–1.7	5	3.1	1.5	0.6–3.7	44	26.8	1.8[b]	1.3–2.6
Asian/Pacific Islander (PI)	2,948	63.8	608	13.2	1.0	0.9–1.1	163	3.5	1.2[b]	1.0–1.5	904	19.6	1.4[b]	1.2–1.5
Japanese	1,075	67.0	210	13.1	0.9	0.7–1.0	53	3.3	1.1	0.8–1.6	267	16.6	1.1	1.0–1.3
Filipino	614	60.7	147	14.5	1.1	0.9–1.4	39	3.9	1.3	0.9–1.8	211	20.9	1.4[b]	1.2–1.6
Chinese	545	63.2	120	13.9	1.0	0.8–1.3	31	3.6	1.3	0.9–1.9	167	19.4	1.4[b]	1.1–1.6
Hawaiian	299	69.1	50	11.6	0.8	0.5–1.0	15	3.5	1.0	0.6–1.8	69	15.9	1.0	0.7–1.3
Korean	80	46.5	22	12.8	1.3	0.8–2.1	8	4.7	2.0	1.0–4.2	62	36.1	3.1[b]	2.2–4.3
Vietnamese	74	56.1	14	10.6	0.9	0.5–1.6	4	3.0	1.2	0.4–3.4	40	30.3	2.1[b]	1.5–3.1
Indian/Pakistani	75	61.0	14	11.4	0.9	0.5–1.6	2	1.6	0.6	0.1–2.4	32	26.0	1.6[b]	1.1–2.5
Other Asian/PI	186	65.5	31	10.9	0.8	0.6–1.2	11	3.9	1.3	0.7–2.5	56	19.7	1.2	0.9–1.6
Hispanic White	1,876	60.3	461	14.8	1.1[b]	1.0–1.3	111	3.6	1.3[b]	1.1–1.6	662	21.3	1.4[b]	1.3–1.6
Mexican	463	61.8	92	12.3	0.9	0.7–1.2	26	3.5	1.2	0.8–1.8	168	22.4	1.5[b]	1.2–1.8
South/Central American	177	54.6	52	16.1	1.4[b]	1.0–1.9	16	4.9	1.8[b]	1.0–3.0	79	24.4	1.7[b]	1.3–2.3
Puerto Rican	49	57.0	11	12.8	1.0	0.5–1.9	3	3.5	1.3	0.4–4.3	23	26.7	1.7[b]	1.1–2.9
Other Hispanic	1,187	60.8	306	15.7	1.2[b]	1.0–1.3	66	3.4	1.3[b]	1.0–1.7	392	20.1	1.3[b]	1.2–1.5

[a] All ORs are adjusted for age at diagnosis, year of diagnosis, and SEER registry using polytomous logistic regression in which the reference (ref) race/ethnicity is non-Hispanic whites and the baseline ER/PR status is ER-positive/PR-positive.
[b] $P < 0.05$.

Hispanic whites into subgroups was a more important problem, because 2534 women, representing 56.7% of this population, were classified as being of an other or NOS Spanish/Hispanic origin. This inability to subcategorize the majority of Hispanic whites could bias our results with respect to these subgroups either toward or away from the null. Additionally, because we evaluated 17 different racial/ethnic groups and, hence, a large number of associations, some of the statistically significant relationships that we identified could have been attributable to chance.

Another limitation of this study was our lack of information regarding other factors that may be associated with hormone receptor status and histology. Specifically, data on hormonal, reproductive, anthropometric, and lifestyle factors were unavailable. These factors could contribute to the differences that we observed, because nulliparity/late age at first live birth, early age at menarche, and higher body mass indices have been associated with an increased risk of developing an ER-positive tumor, but a decreased risk of developing an ER-negative tumor (18, 31–33). However, with respect to hormone receptor status,

Table 4 Relative risks of different breast cancer histological types by race and ethnicity

Race/Ethnicity	Histology													
	Lobular (n = 9,902)		Ductal/lobular (n = 6,990)		Mucinous (n = 3,011)		Comedocarcinoma (n = 2,798)		Adenocarcinoma (n = 2,397)		Tubular (n = 2,072)		Medullary (n = 1,589)	
	OR[a]	95% CI	OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI
Non-Hispanic white	1.0	(ref)	1.0	(ref)	1.0	(ref)	1.0	(ref)	1.0	(ref)	1.0	(ref)	1.0	(ref)
African American	0.6[b]	0.6–0.7	0.7[b]	0.6–0.8	1.3[b]	1.1–1.5	1.2[b]	1.0–1.4	1.5[b]	1.2–1.7	0.5[b]	0.4–0.6	3.0[b]	2.5–3.7
Native American	0.7	0.4–1.2	0.8	0.4–1.6	3.4[b]	1.7–6.9	0.6	0.2–1.9	0.9	0.3–2.5	0.2	0.03–1.4	4.7[b]	2.0–11.0
Asian/Pacific Islander (PI)	0.5[b]	0.4–0.5	0.5[b]	0.4–0.6	1.8[b]	1.4–2.1	1.3[b]	1.1–1.5	1.1	0.9–1.4	0.3[b]	0.3–0.5	1.7[b]	1.3–2.3
Japanese	0.6[b]	0.5–0.7	0.4[b]	0.3–0.6	1.3	0.9–1.9	1.1	0.8–1.4	0.9	0.6–1.4	0.5[b]	0.3–0.7	1.5	0.9–2.6
Filipino	0.4[b]	0.3–0.5	0.5[b]	0.4–0.7	2.1[b]	1.6–2.9	1.4	1.0–1.9	1.3	0.9–1.9	0.2[b]	0.1–0.4	1.7[b]	1.1–2.8
Chinese	0.4[b]	0.3–0.5	0.5[b]	0.4–0.7	2.0[b]	1.4–2.9	1.5[b]	1.1–2.0	1.2	0.8–1.8	0.2[b]	0.1–0.5	1.8[b]	1.1–3.2
Hawaiian	0.9	0.6–1.3	0.6	0.3–1.1	1.0	0.4–2.3	1.7	1.0–2.8	0.8	0.3–1.8	0.3[b]	0.1–0.8	0.6	0.1–2.7
Korean	0.3[b]	0.1–0.6	0.3[b]	0.1–0.7	1.9	0.9–3.9	0.9	0.4–2.2	1.7	0.7–3.8	0.3	0.1–1.2	2.4	1.0–5.8
Vietnamese	0.4[b]	0.2–0.9	0.5	0.3–1.1	1.9	0.9–4.2	1.2	0.5–2.9	2.4[b]	1.1–5.2	0.4	0.1–1.8	1.4	0.3–5.7
Indian/Pakistani	0.6	0.3–1.2	1.2	0.7–2.1	1.6	0.7–4.0	1.5	0.6–3.7	1.2	0.4–3.8	0.6	0.1–2.3	1.6	0.4–6.9
Other Asian/PI	0.5[b]	0.3–0.8	0.5[b]	0.3–0.9	1.2	0.6–2.5	1.4	0.8–2.5	0.7	0.3–1.8	0.5	0.2–1.2	1.4	0.5–3.7
Hispanic white	0.7[b]	0.6–0.8	0.7[b]	0.6–0.8	1.3[b]	1.0–1.6	1.0	0.8–1.2	1.6[b]	1.3–1.9	0.7[b]	0.5–0.9	2.2[b]	1.7–2.8
Mexican	0.8[b]	0.6–1.0	0.7[b]	0.6–0.9	1.5[b]	1.0–2.1	1.0	0.7–1.5	2.2[b]	1.6–3.0	0.7	0.5–1.2	2.0[b]	1.2–3.2
South/Central American	0.6[b]	0.4–0.8	0.8	0.6–1.1	1.6	1.0–2.7	1.0	0.5–1.7	2.1[b]	1.3–3.4	0.6	0.3–1.3	1.8	0.9–3.6
Puerto Rican	0.8	0.4–1.6	0.8	0.4–1.9	1.4	0.4–4.5	1.1	0.3–3.4	2.2	0.8–5.9	0.5	0.1–3.6	7.7[b]	3.5–16.9
Other Hispanic	0.7[b]	0.6–0.9	0.7[b]	0.5–0.8	1.1	0.8–1.4	0.9	0.7–1.2	1.2	1.0–1.6	0.6[b]	0.5–0.9	2.1[b]	1.5–2.9

[a] All ORs are adjusted for age at diagnosis, year of diagnosis, and SEER registry using polytomous logistic regression in which the reference (ref) race/ethnicity is non-Hispanic whites and the baseline histology is ductal (n = 89,556).
[b] $P < 0.05$.

these factors may not play an important role because a study evaluating the risk of ER-positive tumors among whites and blacks found that blacks were still more likely than whites to have ER-negative tumors even after adjusting for age, reproductive factors, body mass index, use of alcohol and tobacco, socioeconomic status, and health care access and use (29).

An additional concern is that hormone receptor assays and the classifications of tumor histologies were not conducted in a centralized location. This, and the fact that, relative to the other groups, African Americans and Hispanic whites had greater proportions of unknown data with respect to hormone receptors status, may bias our results. However, with respect to the first issue, it is unlikely that different practices across institutions could entirely account for our findings, particularly because the study is limited to a finite recent time period in which hormone receptor assays have been routinely used in the assessment of breast carcinomas and in which, histological classifications of breast tumors have not undergone major revisions. What is also reassuring is that our distributions of hormone receptor status and histology are quite comparable with other published results with respect to non-Hispanic white, African-American, and Hispanic white women (22).

In summary, our findings suggest that relative to non-Hispanic white women, women of certain races/ethnicities living in the United States, including African Americans, Native Americans, Filipinos, Chinese, Koreans, Vietnamese, Indians/Pakistanis, Mexicans, South/Central Americans, and Puerto Ricans, have greater risks of presenting with breast cancers the characteristics of which are associated with a poorer prognosis. A combination of biological, genetic, environmental, and lifestyle differences across these populations are likely to account for these variations. Thus, rather than an independent risk factor for particular hormone receptor profiles and histologies, race/ethnicity is more likely to be a marker for other risk factors associated with such outcomes. Nevertheless, it may be important to explore how the impact of breast cancer risk factors vary by race/ethnicity because some of these factors have been independently associated with breast cancers with certain hormone receptor expression profiles and histologies. For example, the use of hormone replacement therapy (HRT) is associated with an increased risk of tumors with a lobular histology (34, 35). Although it is known that the use of HRT is more common among non-Hispanic whites than it is among African American women, whether or not this difference alone could explain our results is uncertain. In addition, as others have also suggested (6), findings such as ours may partly explain the more advanced stages and poorer survival experienced by different racial/ethnic groups, including African Americans, Native Americans, Mexicans, and Puerto Ricans. Although both hormone receptor status and histology may be fairly crude measures of biological differences of breast tumors across races/ethnicities, important differences were identified here that will hopefully encourage the research of how other biological factors, including genetic and molecular markers, may further explain the observed variations in stage and survival across races/ethnicities and provide greater insight into breast cancer etiology in different populations.

References

1. Hsu, J. L., Glaser, S. L., and West, D. W. Racial/ethnic differences in breast cancer survival among San Francisco Bay Area women. J. Natl. Cancer Inst. (Bethesda), *89:* 1311–1312, 1997.

2. Boyer-Chammard, A., Taylor, T. H., and Anton-Culver, H. Survival differences in breast cancer among racial/ethnic groups: a population-based study. Cancer Detect. Prev., *23:* 463–473, 1999.

3. Chevarley, F., and White, E. Recent trends in breast cancer mortality among white and black US women. Am. J. Public Health, *87:* 775–781, 1997.

4. Joslyn, S. A., and West, M. M. Racial differences in breast carcinoma survival. Cancer (Phila.), *88:* 114–123, 2000.

5. Elmore, J. G., Moceri, V. M., Carter, D., and Larson, E. B. Breast carcinoma tumor characteristics in black and white women. Cancer (Phila.), *83:* 2509–2515, 1998.

6. Elledge, R. M., Clark, G. M., Chamness, G. C., and Osborne, C. K. Tumor biologic factors and breast cancer prognosis among white. Hispanic, and black women in the United States. J. Natl. Cancer Inst. (Bethesda), *86:* 705–712, 1994.

7. Frost, F., Tollestrup, K., Hunt, W. C., Gilliland, F., Key, C. R., and Urbina, C. E. Breast cancer survival among New Mexico Hispanic. American Indian, and non-Hispanic White women (1973–1992). Cancer Epidemiol. Biomark. Prev., *4:* 861–866, 1996.

8. Zaloznik, A. J. Breast cancer stage at diagnosis: Caucasians versus Hispanics. Breast Cancer Res. Treat., *42:* 121–124, 1997.

9. Bentley, J. R., Delfino, R. J., Taylor, T. H., Howe, S., and Anton-Culver, H. Differences in breast cancer stage at diagnosis between non-Hispanic white and Hispanic populations. San Diego County 1988–1993. Breast Cancer Res. Treat., *50:* 1–9, 1998.

10. Sugarman, J. R., Dennis, L. K., and White, E. Cancer survival among American Indians in western Washington state (United States). Cancer Causes Control, *5:* 440–448, 1994.

11. Meng, L., Maskarinec, G., and Wilkens, L. Ethnic differences and factors related to breast cancer survival in Hawaii. Int. J. Epidemiol., *26:* 1151–1158, 1997.

12. Meng, L., Maskarinec, G., and Lee, J. Ethnicity and conditional breast cancer survival in Hawaii. J. Clin. Epidemiol., *50:* 1289–1296, 1997.

13. Roetzheim, R. G., Pal, N., Tennant, C., Voti, L., Ayanian, J. Z., Schwabe, A., and Krischer, J. P. Effects of health insurance and race on early detection of cancer. J. Natl. Cancer Inst., *91:* 1409–1415, 1999.

14. Lannin, D. R., Matthews, H. F., Mitchell, J., Swanson, M. S., Swanson, F. H., and Edwards, M. S. Influence of socioeconomic and cultural factors on racial differences in late-stage presentation of breast cancer. J. Am. Med. Assoc., *279:* 1801–1807, 1998.

15. Yood, M. U., Johnson, C. C., Blount, A., Abrams, J., Wolman, E., McCarthy, B. D., Raju, U., Nathanson, D. S., Worsham, M., and Wolman, S. R. Race and differences in breast cancer survival in a managed care population. J. Natl. Cancer Inst. (Bethesda), *91:* 1487–1491, 1999.

16. Perkins, P., Cooksley, C. D., and Cox, J. D. Breast cancer: is ethnicity an independent prognostic factor for survival? Cancer (Phila.), *78:* 1241–1247, 1996.

17. Ansell, D., Whitman, S., Lipton, R., and Cooper, R. Race, income, and survival from breast cancer at two public hospitals. Cancer (Phila.), *72:* 2974–2978, 1993.

18. McGuire, W. L., and Clark G. M. Prognostic factors and treatment decisions in axillary-node-negative breast cancer. N. Engl. J. Med., *326:* 1756–1761, 1992.

19. Clahsen, P. C., van de Velde, C. J. H., Ducal. C, Pallud, C., Mandard, A. M., Delobelle-Deroide, A., van den Broek, L., and van de Vijver, M. J. The utility of mitotic index, oestrogen receptor and Ki-67 measurements in the creation of novel prognostic indices for node-negative breast cancer. Eur. J. Surg. Oncol., *25:* 356–363, 1999.

20. Mauri, F. A., Maisonneuve, P., Caffo, O., Veronese, S., Aldovini, D., Ferrero, S., Cozzaglio, F., Dalla Palma, P., Galligioni, E., and Barbareschi, M. Prognostic value of estrogen receptor status can be improved by combined evaluation of p53. Bcl2 and PgR expression: an immunohistochemical study on breast carcinoma with long-term follow-up. Int. J. Oncology, *15:* 1137–1147, 1999.

21. Du Toit, R. S., Locker, A. P., Ellis, I. O., Elston, C. W., Nicholson, R. I., Robertson, J. F. R., and Blamey, R. W. An evaluation of differences in prognosis, recurrence patterns and receptor status between invasive lobular and other invasive carcinomas of the breast. Eur. J. Surg. Oncol., *17:* 251–257, 1991.

22. Gapstur, S. M., Dupuis, J., Gann, P., Collila, S., and Winchester, D. P. Hormone receptor status of breast tumors in black. Hispanic, and non-Hispanic white women: an analysis of 13,239 cases. Cancer (Phila.), *77:* 1465–1471, 1996.

23. Klonoff-Cohen, H. S., Schaffroth, L. B., Edelstein, S. L., Molgaard, C., and Saltzstein, S. L. Breast cancer histology in Caucasians, African Americans, Hispanics, Asians, and Pacific Islanders. Ethnicity Health, *3:* 189–198, 1998.

24. Weiss, S. E., Tartter, P. I., Ahmed, S., Brower, S. T., Brusco, C., Bossolt, K., Amberson, J. B., and Bratton, J. Ethnic differences in risk and prognostic factors for breast cancer. Cancer (Phila.), *76:* 268–274, 1995.

25. Anderson, W. F., Chu, K. C., Chatterjee, N., Brawley, O., and Brinton, L. A. Tumor variants by hormone receptor expression in white patients with node-negative breast cancer from the Surveillance, Epidemiology, and End Results database. J. Clin. Oncol., *19:* 18–27, 2001.

26. Morabia, A., and Flandre, P. Misclassification bias related to definition of menopausal status in case-control studies of breast cancer. Int. J. Epidemiol., *21:* 222–228, 1992.

27. Young, J. L., Jr., Percy, C., and Asire, A. J. (eds). Surveillance, Epidemiology, and End Results: incidence and mortality, 1973–77. Natl. Cancer Inst. Monogr., *57:* 1–1082, 1981.

28. Breslow, N. E., and Day, N. E. The Analysis of Case-Control Studies. Lyon, France: IARC, 1980.

29. Chen, V. W., Correa, P., Kurman, R. J., Wu, X-C., Eley, J. W., Austin, D., Muss, H., Hunter, C. P., Redmond, C., Sobhan, M., Coates, R., Reynolds, P., Herman, A. A., and Edwards, B. K. Histological characteristics of breast carcinoma in blacks and whites. Cancer Epidemiol. Biomark. Prev., *3:* 127–135, 1994.

30. Pegoraro, R. J., Karnan, V., Nirmul, D., and Joubet, S. M. Estrogen and progesterone receptors in breast cancer among women of different racial groups. Cancer Res., *46:* 2117–2120, 1986.

31. Potter, J. D., Cerhan, J. R., Sellers, T. A., McGovern, P. G., Drinkard, C., Kushi, L. R., and Folsom, A. R. Progesterone and estrogen receptors and mammary neoplasia in the Iowa Women's Health Study: how many kinds of breast cancer are there?. Cancer Epidemiol. Biomark. Prev., *3:* 319–326, 1995.

32. Enger, S. M., Ross, R. K., Paganini-Hill, A., Carpenter, C. L., and Bernstein, L. Body size, physical activity, and breast cancer hormone receptor status: results from two case-control studies. Cancer Epidemiol. Biomark. Prev., *9:* 681–687, 2000.

33. Huang, W. Y., Newman, B., Millikan, R. C., Schell, M. J., Hulka, B. S., and Moorman, P. G. Hormone-related factors and risk of breast cancer in relation to estrogen receptor and progesterone receptor status. Am. J. Epidemiol., *151:* 703–714, 2000.

34. Li, C. I., Weiss, N. S., Stanford, J. L., and Daling, J. R. Hormone replacement therapy in relation to risk of lobular and ductal breast cancer in middle-aged women. Cancer (Phila.), *88:* 2570–2577, 2000.

35. Chen, C-L., Weiss, N. S., Newcomb, P., Barlow, W., and White, E. Hormone replacement therapy in relation to breast cancer. J. Am. Med. Assoc., *287:* 734–742, 2002.