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Racial and ethnic differences in risk of second primary cancers among breast cancer survivors

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Abstract

Purpose—Disparities exist in breast cancer (BC) outcomes between racial/ethnic groups in the United States. Reasons for these disparities are multifactorial including differences in genetics, stage at presentation, access to care and socioeconomic factors. Less is documented on racial/ethnic differences in subsequent risk of second primary cancers (SPC). The purpose of this study is to evaluate the risk of SPC among different racial/ethnic groups of women with BC.

Methods—Retrospective cohort of 134,868 Non-Hispanic White (NHW), 17,484 Black, 18,034 Hispanic and 19,802 Asian/Pacific Islander (API) women with stages I–III BC in twelve Surveillance, Epidemiology and End Results Program registries between 2001–2010. Standardized incidence ratios (SIR), 95% confidence intervals (CI) and absolute excess risks were calculated by comparing incidence of SPC in the cohort to incidence in the general population for specific cancer sites by race/ethnicity and stratified by index BC characteristics.

Results—All women were at increased risks of second primary BC and acute myeloid leukemia (AML), with higher risk among more advanced stage index BC. Black and API women had higher SIRs for AML [4.86 (95% CI 3.05–7.36) and 5.00 (95% CI 3.26–7.32) respectively] which remained elevated among early-stage (I) BC cases.

Conclusions—Women with a history of invasive BC have increased risk of SPC, most notable for second primary BC and AML. These risks for secondary cancers differ by race/ethnicity. Studies evaluating possible genetic and biobehavioral mechanisms underlying these differences

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Conflict of interest

The authors declare that they have no conflict of interest.

are warranted. Strategies for BC adjuvant treatment and survivorship care may require further individualization with consideration given to race/ethnicity.

Keywords

Breast cancer; Second primary cancer; Racial/ethnic disparities; Survivorship; Surveillance

INTRODUCTION

Breast cancer (BC) is the most commonly diagnosed cancer in women regardless of race or ethnicity [1], and there are an estimated 2.9 million BC survivors in the United States [2]. Increased acceptance and implementation of screening mammography have resulted in more women being diagnosed with early-stage disease [3]. Combined with improvements in adjuvant treatment, relative survival for women diagnosed with BC is 89% at 5 years after diagnosis [4]. With greater potential survivorship years post-BC, these women remain at ongoing risks of recurrence, complications from their initial treatment, and development of second cancers [5].

Previous studies describe racial and ethnic health disparities in BC with respect to utilization of screening mammography, stage and size of tumors at diagnosis, tumor biology, adequate receipt of appropriate BC treatment, underlying comorbidities, and socioeconomic factors [6–9]. Consequently, Black and Hispanic women consistently have lower 5-year cause-specific survival rates, 77.5% and 83.8% respectively. Less has been reported, however, about differences in risk of second primary cancers by racial and ethnic groups [4].

Risk factors for second malignancies after BC are multifactorial and can include side effects from treatment for the initial cancer, normal aging, lifestyle and environmental factors, and genetic susceptibility [5]. Clinically, the identification of patients who are at increased risk of experiencing subsequent malignancies is important for optimizing treatment and may help identify those who would benefit from enhanced surveillance or tailored survivorship care [10]. If identified, vulnerable populations may benefit from further efforts targeted at improving access to and delivery of quality cancer care and prevention [11,12].

The purpose of this study was to evaluate differences in risk of second primary cancers between Non-Hispanic White, Black, Hispanic, and Asian/Pacific Islander women diagnosed with invasive BC in the Surveillance, Epidemiology and End Results (SEER) registries between 2001 and 2010.

PATIENTS AND METHODS

Study Population and Data Sources

We conducted a retrospective cohort study of women diagnosed with a first primary invasive, stages I-III BC between January 1, 2001 and December 31, 2010 identified through twelve population-based cancer registries in the U.S. that participate in the National Cancer Institute's SEER Program – those serving the geographic areas of San Francisco-Oakland, Connecticut, Detroit, Hawaii, Iowa, New Mexico, Seattle-Puget Sound, Utah, Atlanta, San Jose-Monterey, Los Angeles, and Rural Georgia. SEER ascertains and follows

demographic and tumor-specific information including age at diagnosis, stage, vital status, and diagnoses of multiple primary cancers in these individuals. Further details and methods used by the SEER Program are provided elsewhere [13].

Index First Primary Breast Cancer Cases

A total of 190,188 women ages 20 years and older with invasive, stages I–III BC documented in SEER as their first primary cancer diagnosis (no history of cancer before index diagnosis) that received cancer-directed surgery were included in this study. Women were excluded if their cancer was diagnosed at autopsy, if their race was classified as other or unknown and if their Hispanic ethnicity was classified as either “Spanish surname only” or unknown. To further restrict race and ethnicity categories to be mutually exclusive, 93 Black women and 38 Asian/Pacific Islander women who were also categorized as being Hispanic were excluded.

The primary exposure of interest was race and ethnicity. We used SEER-coded categories of race and ethnicity to classify study participants. Asian/Pacific Islander women included those coded to be Chinese, Japanese, Filipino, Hawaiian, Korean, Vietnamese, Thai, Laotian, Tongan, and Asian Indian and Pakistani, among others. Women classified as “other” or “not otherwise specified (NOS) Asian/Pacific Islander” were also grouped with the above women to compose the 19,802 Asian/Pacific Islander women included in the study. The SEER registries also document information on “Spanish surname or origin,” specifically coding whether individuals were Mexican, Puerto Rican, Cuban, South or Central American (except Brazil), other specified Spanish or Hispanic origin (includes European), or Spanish or Hispanic NOS. We used these categorizations in our analyses to classify women into mutually exclusive categories of Non-Hispanic White, Black, Hispanic White (henceforth referred to as “Hispanic”), and Asian/Pacific Islander.

We ascertained data for this cohort of BC survivors from the SEER registries, including: age at diagnosis, year of diagnosis, American Joint Committee on Cancer (AJCC) stage [14], estrogen receptor (ER) status, progesterone receptor (PR) status, tumor size, and lymph node status. Information on type of surgery and receipt of radiation treatment was obtained, but data on adjuvant chemotherapy and adjuvant hormonal therapy were not available. Data regarding other socioeconomic factors, such as income and health insurance status, were also not available. Women included were required to have cancer-directed surgery documented in SEER, classified as mastectomy (radical or total) or breast-conserving surgery (less than total mastectomy: segmental mastectomy, lumpectomy, quadrectomy, tylectomy, wedge resection, nipple resection, excisional biopsy, or partial mastectomy NOS).

Second Primary Cancer Cases

Women were followed from date of index BC diagnosis to the first of a second primary cancer, death, or end of the study period (December 2012). All second primary cancers were diagnosed among index BC cases between 2001 and 2010 within the included SEER registries. Definitions for second primary cancer were based on established SEER criteria, [13] requiring a second primary malignancy subsequent to the index BC to not be

documented as a metastasis in the clinical record and must be located in a site with a different International Classification of Diseases for Oncology third edition (ICD-O-3) code; or if the second malignancy is of the same site as the index cancer (i.e., second primary BC) then the tumor must be diagnosed more than one year after the index BC. All other second primary tumors identified within the 6-month period after the index BC diagnosis were considered synchronous tumors and excluded.

Statistical Analysis

Using SEER*Stat statistical software version 8.1.5 frequency and multiple primary-standardized incidence ratio (MP-SIR) modules [15], we estimated standardized incidence ratios (SIR) and 95% confidence intervals (CI) by comparing the observed occurrence of second primary cancers after first primary BC to the occurrence that would be expected based on cancer incidence rates in the general population of the SEER ascertainment areas. The MP-SIR module calculates expected sex-specific incidence rates and person-years at risk for second cancer stratified by 5-year age intervals and 5-year calendar-time intervals. Numbers of expected cancers were calculated by multiplying stratum-specific person-years at risk and corresponding stratum-specific incidence rates and then summing these products across strata. Therefore, the sex-specific SIRs presented are effectively adjusted for age, calendar year, and geographic location (registry). For each case group defined by race/ethnicity (Non-Hispanic White, Black, Hispanic, and Asian/Pacific Islander), we calculated RRs for “all sites” (i.e., all second primary cancer sites excluding non-melanoma skin cancer) as well as site-specific SIRs. We also conducted stratified sub-analyses to estimate race/ethnicity-specific RR by index BC AJCC stage, tumor size, lymph node status, and ER/PR status for second primary acute myeloid leukemia (AML). To account for the multiple comparisons made between race/ethnicity and risk of SPC, P values <0.001 were considered statistically significant. We also estimated the absolute excess risk for second primary cancers. Excess risk was calculated as the number of observed cases minus the number of expected cases divided by person-years at risk. Estimates of excess risk are presented per 10,000 person-years at risk.

RESULTS

Descriptive characteristics by race/ethnicity are summarized in Table 1. Of the 190,188 women diagnosed with first primary BC included in the analysis, 70.9% were Non-Hispanic White, 9.2% were Black, 9.5% were Hispanic, and 10.4% were Asian/Pacific Islander. Median age at diagnosis was highest for Non-Hispanic White women (60 years) and tended to be lower for women of other racial/ethnic groups (54–56 years). Black and Hispanic women were more often diagnosed with a first primary BC that was AJCC stage II or III, ER(–)/PR(–), ≥ 1 cm in tumor size, and have positive lymph node status. Greater proportions of Asian/Pacific Islander women received radical or total mastectomy and radiation.

Overall risk of second primary cancer of any anatomic site, including secondary BC, was significantly elevated among Non-Hispanic White (SIR=1.08, 95% CI 1.06–1.10), Black (SIR=1.47, 95% CI 1.38–1.56) and Asian/Pacific Islander (SIR=1.51, 95% CI 1.42–1.61) women but not Hispanic women (SIR=1.04, 95% CI 0.97–1.11) (Table 2). Risk of second

primary BC was significantly increased in all racial/ethnic groups (Non-Hispanic White, SIR=1.17, 95% CI 1.12–1.21; Black, SIR=2.16, 95% CI 1.96–2.36; Hispanic, SIR=1.39, 95% CI 1.24–1.54; Asian/Pacific Islander, RR=1.80, 95% CI 1.62–2.00). Risk of second primary AML was also elevated among all four racial/ethnic groups ranging from a two-fold increased risk (95% CI, 1.92–2.76) among Non-Hispanic White women to five-fold increased risk (95% CI, 3.26–7.32) among Asian/Pacific Islander women. Some associations were not consistent across race/ethnicity. In particular, the risk for second primary lung and bronchus cancers was highest among Asian/Pacific Islander women (SIR=1.29, 95% CI 1.04–1.59) but lower among Hispanic women (SIR=0.63, 95% CI 0.49–0.81). Asian/Pacific Islander women also had an increased risk of ovarian cancer (SIR=1.52, 95% CI 1.02–2.19), whereas no such increased ovarian cancer risk was observed in other racial/ethnic groups. Lower than expected incidence of cervical cancer was observed in all groups but was only statistically significant in Non-Hispanic White women (SIR=0.55, 95% CI 0.39–0.75) and Hispanic women (SIR=0.32, 95% CI 0.07–0.94).

Absolute excess risks of site-specific second primary cancers by race/ethnicity are reported in Table 3. Excess risk of second primary cancers differed greatly between racial/ethnic groups. For second primary BC, absolute excess risk was higher among Black and Asian/Pacific Islander women (33.3 and 17.2 cases per 10,000 person-years, respectively) compared to Non-Hispanic White and Hispanic women (5.7 and 11.7 cases per 10,000 person-years, respectively). Absolute excess risk of second primary AML was low, reflecting the less frequent occurrence of this malignancy; although excess risk was similarly higher among Black and Asian/Pacific Islander women (2.4 and 2.3 cases per 10,000 person-years, respectively) compared to Non-Hispanic White and Hispanic women (1.1 and 1.0 cases per 10,000 person-years, respectively).

Second Primary AML

Risk estimates for second primary AML by AJCC stage are shown in Figure 1. Findings suggested that risk of developing second primary AML was elevated for all racial/ethnic groups at any stage, although these estimates were not significant for Non-Hispanic White and Hispanic women with stage I index BC (SIR=1.28, 95% CI 0.91–1.74 and SIR=1.48, 95% CI 0.40–3.80, respectively). Black and Asian/Pacific Islander women were at statistically significant increased risk of second primary AML following an index BC of any stage. Sub-analyses also showed that other tumor characteristics indicating more advanced disease and/or those more likely to be treated with radiation and chemotherapy, such as lymph node-positive and ER(–)/PR(–) BC, were associated with significantly increased risk of second primary AML (Online Resource 1).

DISCUSSION

To our knowledge, this large population-based study is the first to evaluate racial/ethnic differences in risk of second primary cancers among invasive BC survivors between 2001 and 2010. Consistent with existing literature [16–20], our analysis demonstrates that BC survivors across all racial/ethnic backgrounds were frequently at increased risks of second primary BC and AML, with the greatest risk in more advanced stage index BC. Our study

also suggests that Black and Asian/Pacific Islander women have increased relative risk and excess risk of AML that remains elevated even among early-stage (Stage I) invasive BC cases.

This is one of the few studies to report differences in risk of second primary cancers based on racial/ethnic background, and many different explanations should be considered including biologic, pathologic, treatment-related, socioeconomic, environmental and behavioral mechanisms. Our findings are hypothesis generating, and understanding the reasons for these differences in risk could have important ramifications. Further studies to identify conceptually and empirically meaningful pathways for an increased risk of secondary cancers among breast cancer survivors of varied racial/ethnic backgrounds is the next step. Specifically, understanding the unique cancer risk among specific breast cancer populations could help to identify possible genetic markers, guide treatment decisions in the adjuvant setting, improve surveillance and prevent future malignancies. If the reasons for these differential risks are better defined, the decision-making process around adjuvant chemotherapy or survivorship care could be tailored to decrease the risk of future malignancies.

Other large population studies have demonstrated the same association of advanced BC stage with increased risk of AML, due to known toxicities of chemotherapeutic agents [21–23]. Additional studies report a risk of myelodysplastic syndrome (MDS) and AML post-BC to be associated with radiotherapy [24] and with younger age [25] and higher stage [26] at index BC diagnosis, which would also correlate with higher likelihood of receiving adjuvant chemotherapy. In line with previous studies, we found that all patients despite racial/ethnic background have increased risk of AML with increasing BC stage, but Black and Asian/Pacific Islander women demonstrated a non-trivial degree of elevated risk even among the Stage I cases. In subgroup analyses, we observed that women with Stage III, lymph node-positive, larger tumor size, and/or hormone receptor-negative disease also had the greatest risk of second primary AML. This supports the hypothesis that these secondary malignancies in women who were more likely to be treated aggressively for their primary invasive cancer are therapy-related. Future studies on risk of MDS/AML with use of specific chemotherapy agents and differences in utilization of chemotherapy may be important to clarify the role of race/ethnicity in therapy-related malignancies risk post-BC.

Considering race/ethnicity as a risk factor for secondary malignancies has potentially wide implications for not only curative-intent treatment but also survivorship care. BC therapies commonly used in the curative setting include radiation, adjuvant chemotherapy and hematopoietic growth factors. Some commonly used chemotherapy agents, anthracyclines and topoisomerase II inhibitors are known to subsequently increase risk for AML [27, 28]. Therapy-related AML often has a poor prognosis and is lethal, particularly for racial/ethnic minority patients [29–31]. Controversy remains as to whether granulocyte colony-stimulating factors (G-CSF) used following myeloablative, dose dense chemotherapeutic regimens confer a significant leukemic risk for patients [32, 18]. Additional studies among BC survivors with detailed information on adjuvant chemotherapy treatment, administration of G-CSF and long-term follow up are warranted to fully understand the benefits and potential risks of therapy-related myeloid neoplasms by race/ethnicity.

A few other studies have observed racial/ethnic differences in risk of second primary BC, but differ from our study in many ways. Unlike our study of invasive BC, other studies have investigated women with index ductal carcinoma in situ (DCIS) [33–35]. For example, Liu et al [35] examined the risk of second breast tumors by race/ethnicity among 102,489 women diagnosed with primary DCIS between 1988 and 2009 from 18 SEER registries. They identified 2,925 women who developed ipsilateral breast tumors and 3,723 who developed contralateral breast tumors. Compared to Non-Hispanic White women, Black (RR=1.46; 95% CI 1.29–1.65), and Hispanic (RR=1.18, 95% CI 1.03–1.36) women had higher ipsilateral breast tumor risk after adjusting for age at diagnosis, treatment, and tumor grade, size and histology. Contralateral breast tumor risk was also increased among Black (RR=1.21, 95% CI 1.08–1.36) and Asian/Pacific Islander (RR=1.16, 95% CI 1.02–1.31) women. Differences in risk of second primary breast tumors after DCIS by race/ethnicity persisted even after accounting for pathological features and index treatments. They conclude that further studies are required to investigate reasons for this higher risk. Among 100 matched Black and White women with DCIS, Stark et al [36] also reported greater risk of subsequent invasive BC among Black women, finding that differences in stage at presentation, treatments received or histopathological characteristics did not account for racial/ethnic differences in risk of second primary BC.

Genetic or biologic attributes in each race/ethnicity group could explain the observed distribution of second primary cancer risk in our study [37]. However, differences in socioeconomic and healthcare utilization patterns, rather than a biologic mechanism [38] should also be considered. Patients of any race with lower socioeconomic status tend to present with worse tumor pathologic factors and higher stage of disease [39]. For Black women, some studies [40–43] suggest that low socioeconomic status, income, and differences in treatment explain poorer outcomes following BC; but others [44, 45] describe little or no effect of these factors. Other causes that could impact racial/ethnic differences in second primary cancer risk include differences in treatment regimens, the prevalence of obesity [46], higher stage at index BC diagnosis due to differences in mammography use [47, 48, 38] and adherence to adjuvant therapy or surveillance mammography after first primary BC [49]. Given the conflicting and mixed results on race/ethnicity in relation to BC outcomes, it is possible a combination of biologic, socioeconomic, behavioral, and lifestyle factors are influencing second primary cancer risk. Therefore, understanding these differences with future research could have major implications and importance in the continued improvement of BC survivorship care for women of some racial/ethnic backgrounds, such as Black and Asian/Pacific Islander women.

Limitations

The presented analysis should be interpreted in the context of several study limitations. First, individual-level information was limited. While we had data on many tumor characteristics from SEER, we did not have information on other tumor markers, genetic factors, family history, adjuvant chemotherapy and lifestyle characteristics that would also potentially influence risk of second primary cancers. In particular, information on socioeconomic status and utilization of health care such as screening mammography was not available. Second, there is a possibility that the second cancers documented in SEER, particularly second

primary BC, were actually recurrences or metastases rather than true second primary cancers. However, along with the established rules for documenting multiple primary tumors in SEER, we used a 6-month latency period to exclude synchronous tumors and further misclassification would likely be non-differential. Finally, determination of our variable of interest, race/ethnicity, was based on information documented in SEER only.

Conclusions

With the current treatment options for BC, many women will be cured of their disease, making secondary cancers a real concern for the growing population of BC survivors. The results presented here demonstrate increased risks of second primary cancers following BC relative to the general population,, and suggest that some of these risks differ by race/ethnicity. The exact mechanisms that underlie these racial/ethnic differences in risk remain unclear, and our findings support further investigation into the possible mechanisms. These findings also suggest that future treatment options and cancer surveillance may need to be individualized with consideration given to race/ethnicity in order to reduce secondary malignancies.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Figure 1.

Race/ethnicity-specific risk estimates for second primary acute myeloid leukemia by index breast cancer AJCC stage in the Surveillance, Epidemiology and End Results 13 registries, 2001–2010

Descriptive characteristics of women ages 20 years with stages I–III breast cancer in the Surveillance, Epidemiology and End Results 13 registries by race/ethnicity, 2001–2010

	Non-Hispanic White (n=134,868)		Black (n=17,484)		Hispanic (n=18,034)		Asian/ Pacific Islander (n=19,802)	
	n	%	n	%	n	%	n	%
Age at index BC								
Mean (SD)	60.8	(13.4)	56.7	(13.3)	55.7	(13.3)	56.6	(13.1)
Median (IQR)	60	(51–71)	56	(47–66)	54	(46–65)	55	(47–66)
20–49 years	30,329	(22.5)	5,688	(32.5)	6,531	(36.2)	6,544	(33.0)
50–64 years	51,560	(38.2)	6,835	(39.1)	6,716	(37.2)	7,687	(38.8)
65–74 years	27,214	(20.2)	2,910	(16.6)	2,944	(16.3)	3,354	(16.9)
75–85 years	19,975	(14.8)	1,669	(9.5)	1,536	(8.5)	1,845	(9.3)
85+ years	5,790	(4.3)	382	(2.2)	307	(1.7)	372	(1.9)
SEER registry								
San Francisco–Oakland	14,107	(10.5)	1,796	(10.3)	2,072	(11.5)	4,265	(21.5)
Connecticut	17,136	(12.7)	1,276	(7.3)	1,054	(5.8)	257	(1.3)
Detroit	15,521	(11.5)	4,359	(24.9)	326	(1.8)	300	(1.5)
Hawaii	1,699	(1.3)	46	(0.3)	169	(0.9)	4,940	(24.9)
Iowa	15,431	(11.4)	191	(1.1)	156	(0.9)	76	(0.4)
New Mexico	5,102	(3.8)	92	(0.5)	2,302	(12.8)	63	(0.3)
Seattle–Puget Sound	20,705	(15.4)	650	(3.7)	557	(3.1)	1,499	(7.6)
Utah	7,804	(5.8)	43	(0.2)	438	(2.4)	160	(0.8)
Atlanta	8,514	(6.3)	4,386	(25.1)	392	(2.2)	414	(2.1)
San Jose–Monterey	7,461	(5.5)	193	(1.1)	1,586	(8.8)	2,041	(10.3)
Los Angeles	20,936	(15.5)	4,237	(24.2)	8,979	(49.8)	5,786	(29.2)
Rural Georgia	452	(0.3)	215	(1.2)	3	(0.0)	1	(0.0)
AJCC stage								
I	71,335	(52.9)	6,989	(40.0)	7,553	(41.9)	9,757	(49.3)
II	50,223	(37.2)	7,807	(44.7)	7,737	(42.9)	7,978	(40.3)
III	13,310	(9.9)	2,688	(15.4)	2,744	(15.2)	2,067	(10.4)

	Non-Hispanic White (n=134,868)		Black (n=17,484)		Hispanic (n=18,034)		Asian/ Pacific Islander (n=19,802)	
	n	%	n	%	n	%	n	%
Hormone receptor status								
ER(+) / PR (+)	88,554	(65.7)	8,513	(48.7)	10,322	(57.2)	12,674	(64.0)
ER(+) / PR (-)	15,131	(11.2)	2,091	(12.0)	1,929	(10.7)	2,106	(10.6)
ER(-) / PR (+)	1,552	(1.2)	305	(1.7)	260	(1.4)	276	(1.4)
ER(-) / PR (-)	20,853	(15.5)	5,257	(30.1)	3,698	(20.5)	3,392	(17.1)
Missing	8,778		1,318		1,825		1,354	
Tumor size								
<1 cm	23,380	(21.8)	2,618	(15.0)	2,782	(15.4)	3,910	(19.8)
1 cm	103,488	(76.7)	14,512	(83.0)	14,879	(82.5)	15,490	(78.2)
Missing	2,000		354		373		402	
Lymph node status								
Negative	92,036	(68.2)	10,585	(60.5)	10,911	(60.5)	13,373	(67.5)
Positive	42,801	(31.7)	6,892	(39.4)	7,119	(39.5)	6,423	(32.4)
Missing	31		7		4		6	
Surgery								
Radical or total mastectomy	51,762	(38.4)	7,115	(40.7)	7,794	(43.2)	9,096	(45.9)
Breast-conserving surgery	82,802	(61.4)	10,316	(59.0)	10,182	(56.5)	10,647	(53.8)
Unspecified surgery	304	(0.2)	53	(0.3)	58	(0.3)	59	(0.3)
Radiation								
Yes	55,865	(41.4)	7,565	(43.3)	6,682	(37.1)	8,923	(45.1)
No	75,821	(56.2)	9,221	(52.7)	8,741	(48.5)	10,412	(52.6)
Unknown	3,182		698		611		467	
Person-years of follow-up								
Mean (SD)	5.4	(2.9)	4.9	(2.8)	5.0	(2.8)	5.2	(2.9)
Median (IQR)	5.2	(2.9–7.8)	4.5	(2.5–7.2)	4.7	(2.6–7.3)	4.8	(2.8–7.5)
<1 year	1,827	(1.4)	338	(1.9)	420	(2.3)	308	(1.6)
1–3 years	33,183	(24.6)	5,057	(28.9)	4,927	(27.3)	5,231	(26.4)
3–5 years	29,759	(22.1)	4,245	(24.3)	4,205	(23.3)	4,621	(23.3)
5+ years	70,099	(52.0)	7,844	(44.9)	8,482	(47.0)	9,642	(48.7)

	Non-Hispanic White (n=134,868)		Black (n=17,484)		Hispanic (n=18,034)		Asian/ Pacific Islander (n=19,802)	
	n	%	n	%	n	%	n	%
Outcome status								
Second primary breast cancer	7,901	(5.9)	959	(5.5)	822	(4.6)	970	(4.9)
Non-breast second primary cancer	8,467	(6.3)	989	(5.7)	756	(4.2)	933	(4.7)
Died (all causes)	19,921	(14.8)	3,535	(20.2)	2,406	(13.3)	1,944	(9.8)

Risk of site-specific second primary cancers among women with first primary stages I–III breast cancer by race/ethnicity in the Surveillance, Epidemiology and End Results 13 Registries, 2001–2010

Table 2

	Non-Hispanic White			Black			Hispanic			Asian/Pacific Islander		
	SIR	95% CI		SIR	95% CI		SIR	95% CI		SIR	95% CI	
Second primary cancer site												
All Sites ^a	1.08*	1.06–1.10	1.47*	1.38–1.56	1.04	0.97–1.11	1.51*	1.42–1.61				
Breast	1.17*	1.12–1.21	2.16*	1.96–2.36	1.39*	1.24–1.54	1.80*	1.62–2.00				
All Solid Tumors	1.10*	1.07–1.12	1.48*	1.39–1.57	1.05	0.98–1.13	1.51*	1.41–1.62				
Oral Cavity	1.22	1.02–1.45	1.44	0.78–2.41	0.78	0.36–1.48	1.79	1.06–2.84				
Esophageal	1.27	0.94–1.68	1.34	0.54–2.76	1.08	0.29–2.76	0.80	0.10–2.89 ^b				
Stomach	0.99	0.80–1.22	1.50	0.96–2.23	1.70	0.95–2.80	1.64*	1.13–2.29				
Colon and Rectum	1.00	0.93–1.08	1.13	0.93–1.37	0.99	0.78–1.25	1.23	1.00–1.51				
Liver	0.58*	0.40–0.83	0.36	0.07–1.04 ^b	1.61	0.74–3.06	0.86	0.48–1.43				
Pancreatic	1.08	0.95–1.22	1.06	0.72–1.51	0.95	0.58–1.46	1.34	0.90–1.93				
Lung and Bronchus	1.01	0.95–1.07	1.05	0.86–1.26	0.63*	0.49–0.81	1.29	1.04–1.59				
Cervical	0.55*	0.39–0.75	0.59	0.24–1.21	0.32	0.07–0.94	0.63	0.26–1.31				
Uterine	1.22*	1.12–1.33	1.16	0.87–1.53	0.99	0.74–1.31	1.71	1.33–2.16				
Ovarian	1.05	0.92–1.19	1.14	0.70–1.76	1.25	0.85–1.78	1.52	1.02–2.19				
Bladder	1.05	0.91–1.20	0.84	0.43–1.47	0.58	0.29–1.04	1.03	0.49–1.89				
Kidney	1.00	0.85–1.17	1.17	0.75–1.73	0.85	0.48–1.40	1.86*	1.16–2.81				
Thyroid	1.50*	1.32–1.69	2.19*	1.51–3.08	1.39	0.96–1.96	1.78*	1.29–2.38				
Lymphoma	0.87	0.77–0.97	1.08	0.70–1.60	0.80	0.53–1.16	1.26	0.86–1.78				
Hodgkin Lymphoma	0.61	0.30–1.08	0.55	0.01–3.05 ^b	0.92	0.11–3.34 ^b	1.01	0.03–5.65 ^b				
Non-Hodgkin Lymphoma	0.88	0.78–0.99	1.13	0.72–1.68	0.79	0.52–1.16	1.27	0.87–1.81				
Myeloma	0.90	0.71–1.11	1.08	0.68–1.62	0.67	0.24–1.45	1.20	0.55–2.27				
Leukemia	1.33*	1.17–1.51	2.52*	1.74–3.52	1.19	0.74–1.82	3.20*	2.21–4.47				
Acute Lymphocytic Leukemia	1.29	0.59–2.46	1.52	0.04–8.48 ^b	1.22	0.03–6.81 ^b	1.36	0.03–7.59 ^b				
Chronic Lymphocytic Leukemia	0.65*	0.49–0.86	0.83	0.23–2.12 ^b	0.13	0.01–0.73 ^b	0.54	0.01–3.02 ^b				

	Non-Hispanic White			Black			Hispanic			Asian/Pacific Islander		
	SIR	95% CI		SIR	95% CI		SIR	95% CI		SIR	95% CI	
Acute Myeloid Leukemia	2.31 [*]	1.92–2.76		4.86 [*]	3.05–7.36		2.62 [*]	1.43–4.40		5.00 [*]	3.26–7.32	
Chronic Myeloid Leukemia	1.43	0.97–2.03		2.11	0.57–5.39 ^b		1.85	0.50–4.74 ^b		1.46	0.18–5.26	

^a Excludes non-melanoma skin cancer

^b SIR based on <5 second primary cancer cases

^{*} indicates risk estimate is statistically significant at $P<0.001$

Table 3

Absolute excess risk per 10,000 person-years of site-specific second primary cancers among women with stages I-III breast cancer by race/ethnicity in the Surveillance, Epidemiology and End Results 13 registries, 2001–2010

	Non-Hispanic White	Black	Hispanic	Asian/ Pacific Islander
Second primary cancer site				
All Sites ^a	9.28	45.59	3.97	35.54
Breast	5.68	33.26	11.72	17.24
All Solid Tumors	10.02	41.93	4.44	32.51
Oral Cavity	0.39	0.57	−0.32	0.89
Esophagus	0.17	0.24	0.04 ^b	−0.06 ^b
Stomach	−0.01	1.07	0.78	1.47
Colon and Rectum	0.03	1.69	−0.08	2.00
Liver	−0.36	−0.73 ^b	0.43	−0.26
Pancreatic	0.27	0.25	−0.14	0.82
Lung and Bronchus	0.13	0.65	−4.74	2.24
Cervical	−0.51	−0.66	−0.79 ^b	−0.45
Uterine	1.61	0.96	−0.03	3.24
Ovarian	0.18	0.33	0.79	1.11
Bladder	0.16	−0.30	−1.00	0.03
Kidney	0.01	0.46	−0.33	1.13
Thyroid	1.41	2.41	1.17	2.14
Lymphoma	−0.71	0.26	−0.87	0.74
Hodgkin Lymphoma	−0.11	−0.11 ^b	−0.02 ^b	0.01 ^b
Non-Hodgkin Lymphoma	−0.60	0.37	−0.85	0.74
Myeloma	−0.15	0.23	−0.38	0.17
Leukemia	0.95	2.75	0.42	2.60
Acute Lymphocytic Leukemia	0.03	0.05 ^b	0.02 ^b	0.03 ^b
Chronic Lymphocytic Leukemia	−0.44	−0.11 ^b	−0.83 ^b	−0.09 ^b
Acute Myeloid Leukemia	1.11	2.35	1.09	2.31
Chronic Myeloid Leukemia	0.15	0.28 ^b	0.23 ^b	0.07 ^b

^aExcludes non-melanoma skin cancer

^bCalculation based on <5 second primary cancer cases