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Original Article

Incidence trends in triple-negative breast cancer among women in the United States from 2010 to 2019 by race/ethnicity, age and tumor stage

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Abstract: There were substantial ethnic disparities in the incidence rates of triple-negative breast cancer, but few studies were conducted on the incidence trend of triple-negative breast cancer by race/ethnicity. This study aimed to address the longer trends in the incidence of triple-negative breast cancer by race/ethnicity in women from 2010 to 2019, examine the incidence trends by patient age, tumor stage and time periods, and explore the changing proportions of three component receptors over time for triple-negative breast cancer. Our study identified 573,168 women with incident breast cancer at age ≥20 years between 2010 and 2019 in 18 SEER (Surveillance, Epidemiology, and End Results) registries. Of them, 62,623 (10.9%) were incident triple-negative breast cancer and 510,545 were non-triple negative breast cancer cases. The denominator of population included 320,117,009 women aged ≥20 in the same SEER areas. The study found that overall age-adjusted incidence rate of triple-negative breast cancer in women aged ≥20 years was 18.3 cases per 100,000 women. Age-adjusted incidence rate of triple-negative breast cancer was the highest in black women (33.8 cases per 100,000 women), followed by white (17.5), American Indian and Alaska Native (AIAN) (14.7), Hispanic (14.7), and Asian women (12.4). The significantly higher age-adjusted incidence of triple-negative breast cancer in black women as compared to white women appeared to be limited in younger women aged 20-44 only. Annual percentage changes in age-adjusted incidence of triple-negative breast cancer slightly decreased insignificantly in white, black and Asian women aged 20-44 and 45-54 years. There was a statistically significant annual percentage increase in age-adjusted incidence of triple-negative breast cancer in Asian and black women aged ≥55 years. In conclusion, there was a significantly higher incidence of triple-negative breast cancer in black women aged 20-44 years. From 2010 to 2019, there were no significant annual percentage changes in age-adjusted incidence of triple-negative breast cancer in all ethnic groups of women aged <55 years, with the exception of a significant decrease among AIAN women aged 45-54 years. However, there was a statistically significant annual percentage increase in age-adjusted incidence of triple-negative breast cancer in Asian and black women aged ≥55 years.

Keywords: Triple-negative breast cancer, cancer incidence, incidence trend, racial disparities, SEER

Introduction

It has been well documented that breast cancer incidence rates varied significantly by race and ethnicity with a higher risk of breast cancer in non-Hispanic (NH) white and black women and a lower risk in women from Hispanics, Asians and Pacific Islanders, and American Indians and Alaska Natives (AIAN) [1-8]. From 2000 to 2018, there was a slightly increasing trend in overall breast cancer incidence for all ethnic women in the United States, except for NH-white women who experienced a decreasing trend [9]. Over the past decade, there have been an increasing number of investigations on the incidence of an aggressive molecular subtype of breast cancer, i.e., triple-negative breast cancer which refers to the fact that estrogen receptor (ER), progesterone receptor (PR), and human epidermal growth factor receptor-2 (HER2) are all negative [10-19]. Triple-negative breast cancer is more aggressive, tends to grow and spread faster, and currently has fewer options of effective treatment, leading to worse

outcomes and higher mortality [15, 20]. Triple-negative breast cancer accounts for approximately 10%~15% of all breast cancers in women and appears to be more common in black women [10-19]. A number of studies reported racial and ethnic disparities in the incidence rates of triple-negative breast cancer [21-25]. Only one study specifically examined the incidence trends of molecular subtypes of breast cancer by race/ethnicity over multiple years from 2010 to 2016 [25], which concluded that triple-negative breast cancer incidence rates decreased among midlife non-Hispanic white and black women. This current study aims to 1) address the longer trends in the incidence of triple-negative breast cancer by race/ethnicity in women in the SEER areas from 2010 to 2019, 2) examine the incidence trends stratified by patient age, tumor stage and time periods, and 3) explore the changing proportions of three component receptors over time to see if any factor is the main driver for triple-negative breast cancer incidence trend.

Methods

Data sources

The National Cancer Institute's Surveillance, Epidemiology, and End Results (SEER) Public Use Datasets released in November 2021 were used for this study. Both breast cancer cases (numerator) and population (denominator) from SEER areas from 2010 to 2019 are available for cancer incidence calculation [26]. The year 2010 is the earliest year for triple-negative breast cancer data available in SEER data and the year 2019 is the latest dataset. The SEER program supports 18 population-based tumor registries in 9 areas (San Francisco/Oakland, San Jose-Monterey, Los Angeles, Greater California, Detroit, Seattle, Atlanta, Rural Georgia, and Greater Georgia) and 9 states (Alaska, Connecticut, Iowa, New Mexico, Utah, Hawaii, Louisiana, Kentucky, and New Jersey), accounting for 28% of the U.S. population. The SEER registries ascertain all newly diagnosed (incident) cancer cases from multiple reporting sources. The estimated completeness of cancer case reporting in SEER areas was 97.7% [26]. Cancer-related variables collected in SEER registries include tumor location and size; histologic type and grade of tumor; demographic characteristics such as age, gender, race/ethnicity, and marital status; and type of treatments provided in the first course of therapy after diagnosis. This study was considered exempt for Institutional Review Board (IRB) review because it did not involve any patient contact, only had the analysis of de-identified existing SEER Public Use Data, and had no any health risk to study subjects.

Study population

Our study identified 573,168 women who were diagnosed with incident breast cancer at age ≥20 years between 2010 and 2019 in 18 SEER registries. Of them, 62,623 (10.9%) were incident triple-negative breast cancer and 510,545 (89.1%) were non-triple negative breast cancer cases. Because this study focused on the incidence trend of triple-negative breast cancer [hormone receptor (HR) negative: HR-/HER2-], other three groups of breast cancer (HR+/HER2+, HR+/HER2-, and HR-/HER2+) were considered as non-triple negative breast cancers. The denominator of population data included all 320,117,009 women aged ≥20 years in the same SEER areas that were provided in the SEER*Stat package.

Study variables

Race/ethnicity variable was classified into non-Hispanic white (white), non-Hispanic black (black), non-Hispanic Asians/Pacific Islanders (Asian), Hispanic women, and American Indians and Alaska Natives (AIAN), and others or unknown race. Patients with unknown or missing information on race/ethnicity were included for the incidence calculation for overall population and some sup-total stratified groups, but were not presented as a separate race/ethnicity group because the SEER*Stat software did not provide this incidence information for this group. Patient age was divided into 3 broad groups as young (20-44 years), middle-age (45-54) who were recommended to start for regular screening, and older age (≥55) in order to avoid small number of cases in stratified analyses by race/ethnicity, tumor stage, age group, and year of diagnosis. The other covariates included year of diagnosis (2010 to 2019) and geographic areas (18 SEER registries). Tumor factors included triple-negative vs non-triple negative breast cancer, estrogen receptor status, progesterone receptor status, HER2 receptor

status, and tumor stage (in-situ or local, regional, distant stage, or unknown/missing).

Statistical analysis

We utilized the SEER*Stat software (version 8.4.0.1) that was provided by the National Cancer Institute together with the SEER data for analyses in cancer incidence rates and trends. Incidence of breast cancer in women is defined as a ratio of the number of women with a new breast cancer at age ≥20 years over the number of total female population at age ≥20 years in the same SEER areas by year, which is presented as the number of breast cancer cases per 100,000 persons. Because age is a significant risk factor for cancer incidence, the incidence rates of breast cancer in all comparison groups by race/ethnicity or time periods that may consist of different age compositions are standardized by age. The incidence rates in this study are adjusted to the year 2000 U.S. population by age available from the SEER* Stat. The age-adjusted incidence rates, 95% confidence intervals for incidence rates, incidence rate ratios (IRR) and their 95% confidence intervals, and annual percentage change (APC) of incidence rates are calculated from the SEER*Stat software. A p value <0.05 is considered statistically significant.

Results

Table 1 presents the number of total female population, number of incident triple-negative breast cancer cases, number of incident non-triple-negative breast cancer cases, unadjusted and age-adjusted breast cancer incidence rates, and incidence rate ratio by race/ethnicity. The overall age-adjusted incidence rate of triple-negative breast cancer in women aged ≥20 years was 18.3 cases per 100,000 women. The age-adjusted incidence rate of triple-negative breast cancer was the highest in black women (33.8 cases per 100,000 women), followed by white (17.5), AIAN (14.7), Hispanic (14.7), and Asian women (12.4). When compared to white women, the incidence rate ratio was statistically significantly higher in black women (incidence rate ratio: 1.93, 95% CI: 1.88-1.97) and significantly lower in AIAN (0.84, 0.75-0.93), Hispanic (0.84, 0.82-0.86), and Asian women (0.71, 0.68-0.73). However, the patterns of age-adjusted incidence rates of non-triple-negative breast cancer cases by race/ethnicity were different. The age-adjusted non-triple-negative breast cancer incidence rate ratio was statistically significantly lower in black women (0.83, 0.83-0.84) and in all other ethnic women as compared to white women (**Table 1**).

Figure 1 presents the age-adjusted incidence trends over time from 2010 to 2019 for both triple-negative breast cancer (**Figure 1A**) and non-triple-negative breast cancer cases (**Figure 1B**) by race/ethnicity. The age-adjusted incidence rate of triple-negative breast cancer was much higher in black women than other ethnic women and increased slightly over time from 2010 to 2019, whereas the age-adjusted incidence rate of non-triple-negative breast cancer was much higher in white women than other ethnic women and increased more sharply over time.

Annual percentage change (APC) in age-adjusted incidence of triple-negative breast cancer in the total population aged ≥20 years from 2010 to 2019 slightly increased in Hispanic, black, and Asian women, and slightly decreased in white and AIAN women, but none of these trends was statistically significant (**Table 2**). In the stratified analyses by the 3 age groups (20-44, 45-54, and ≥55), annual percentage changes in age-adjusted incidence of triple-negative breast cancer slightly decreased but not significantly in white, black and Asian women aged 20-44 and 45-54 years. In AIAN and Hispanic women, there were no significant annual percentage changes in age-adjusted incidence of triple-negative breast cancer except a significant decrease in AIAN women aged 45-54 years. Interestingly, there was a statistically significant annual percentage increase in age-adjusted incidence of triple-negative breast cancer in Asian and black women aged 55 years or older. However, annual percentage change in age-adjusted incidence of non-triple-negative breast cancer from 2010 to 2019 increased significantly in all ethnic women except in AIAN and black women aged 45-54 years.

Table 3 presents the age-adjusted incidence of triple-negative breast cancer and non-triple-negative breast cancer by 3 time periods (2010-2013, 2014-2016, and 2017-2019) and race/ethnicity. The age-adjusted incidence of triple-negative breast cancer marginally

Table 1. Number of population, number of triple-negative breast cancer cases and non-triple negative breast cancer, and incidence rates of breast cancer in all SEER areas, 2010-2019, by race/ethnicity

Race/Ethnicity	Number of population	Number of breast cancer cases	Unadjusted Incidence rates (N of cases per 100,000) (95% CI)	Age-adjusted* incidence rates (N of cases per 100,000) (95% CI)	Rate ratio (between age-adjusted incidence rates) (95% CI)
Triple-negative breast cancer					
Non-Hispanic white	178,531,435	36,695	20.6 (20.3-20.8)	17.5 (17.4-17.7)	1.00 (reference)
Non-Hispanic Asians and Pacific Islanders	37,051,694	4,727	12.8 (12.4-13.1)	12.4 (12.0-12.7)	0.71* (0.68-0.73)
Non-Hispanic black	2,608,851	12,102	33.9 (33.3-34.5)	33.8 (33.2-34.4)	1.93* (1.88-1.97)
American Indians and Alaska Natives	2,608,851	371	14.2 (12.8-15.7)	14.7 (13.2-16.3)	0.84* (0.75-0.93)
Hispanics	66,191,520	8,494	12.8 (12.6-13.1)	14.7 (14.4-15.1)	0.84* (0.82-0.86)
Sub-Total	320,117,009	62,623	19.6 (19.4-19.7)	18.3 (18.1-18.4)	1.04* (1.03-1.06)
Non-Triple-negative breast cancer					
Non-Hispanic white	178,531,435	349,087	195.5 (194.9-196.2)	159.4 (158.9-160.0)	1.00 (reference)
Non-Hispanic Asians and Pacific Islanders	37,051,694	48,061	129.7 (128.6-130.9)	125.8 (124.7-127.0)	0.79* (0.78-0.80)
Non-Hispanic black	2,608,851	47,156	132.0 (130.8-133.2)	133.0 (131.7-134.2)	0.83* (0.83-0.84)
American Indians and Alaska Natives	2,608,851	3,057	117.2 (113.1-121.4)	116.7 (112.5-121.0)	0.73* (0.71-0.76)
Hispanics	66,191,520	60,528	91.4 (90.7-92.2)	109.4 (108.5-110.3)	0.69* (0.68-0.69)
Sub-Total	320,117,009	510,545	159.5 (159-159.9)	145.8 (145.4-146.2)	0.91* (0.91-0.92)

*Incidence rates were adjusted to the 2000 US population by age. Breast cancer cases with unknown or missing information on race/ethnicity were included in the total or sub-total incidence calculation.

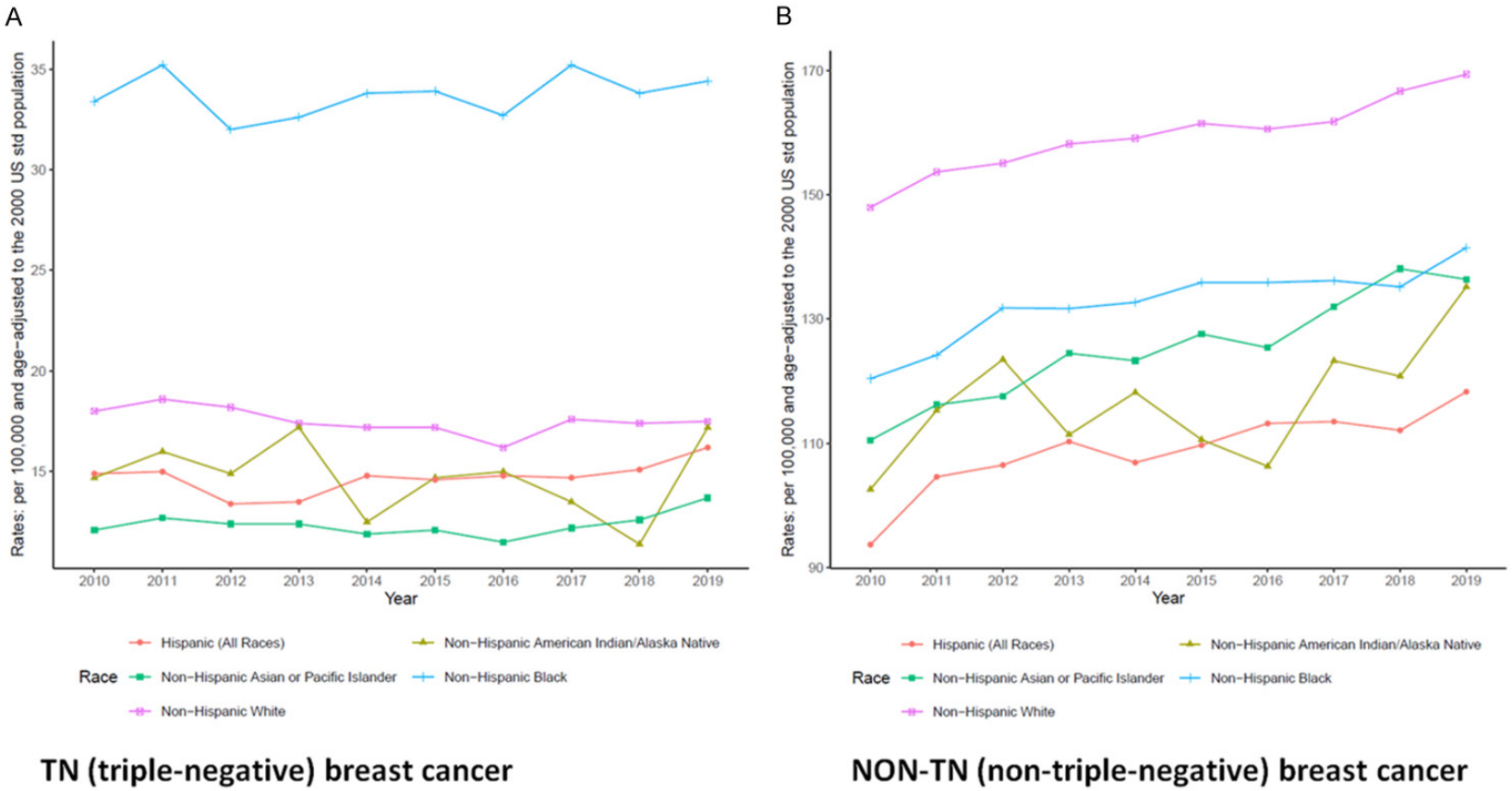

Figure 1. Trends in age-adjusted incidence rates of triple-negative (TN) breast cancer versus incidence trends in age-adjusted non-triple-negative (Non-TN) breast cancer (number of breast cancer cases per 100,000 population) among women in SEER areas from 2010 to 2019, by race/ethnicity.

Table 2. Annual percentage change (APC) in age-adjusted incidence rates (number of breast cancer cases per 100,000 population) in women in 2010-2019 by triple-negative breast cancer status, race/ethnicity and age groups

Race/Ethnicity	Triple-negative breast cancer				Non-Triple-negative breast cancer				Total breast cancer (triple-negative and non-triple-negative breast cancer)			
	N. Cases	Incidence rate (95% CI)	APC (95% CI) from 2010 to 2019	*P* value	N. Cases	Incidence rate (95% CI)	APC (95% CI) from 2010 to 2019	*P* value	N. Cases	Incidence rate (95% CI)	APC (95% CI) from 2010 to 2019	*P* value
All breast cancer cases aged 20 or older												
Non-Hispanic white	36,695	17.5 (17.4-17.7)	-0.7 (-1.5-0.1)	0.1	349,087	159.4 (158.9-160.0)	1.2 (1.0-1.5)	<0.001	385,782	176.9 (176.4-177.5)	1.1 (0.8-1.3)	<0.001
Non-Hispanic Asians and Pacific Islanders	4,727	12.4 (12.0-12.7)	0.6 (-0.6-1.9)	0.3	48,061	125.8 (124.7-127.0)	2.3 (1.8-2.8)	<0.001	52,788	138.2 (137.0-139.4)	2.1 (1.6-2.6)	<0.001
Non-Hispanic black	12,102	33.8 (33.2-34.4)	0.3 (-0.5-1.1)	0.4	47,156	133.0 (131.7-134.2)	1.4 (0.8-1.9)	<0.001	59,258	166.7 (165.4-168.1)	1.2 (0.8-1.5)	<0.001
American Indians and Alaska Natives	371	14.7 (13.2-16.3)	-0.7 (-4-2.7)	0.7	3,057	116.7 (112.5-121.0)	1.7 (-0.1-3.5)	0.1	3,428	131.4 (126.9-136.0)	1.4 (-0.3-3.1)	0.1
Hispanics	8,494	14.7 (14.4-15.1)	1.0 (-0.2-2.2)	0.1	60,528	109.4 (108.5-110.3)	1.7 (0.9-2.5)	<0.001	69,022	124.2 (123.2-125.1)	1.7 (1.0-2.3)	<0.001
Total	62,623	18.3 (18.1-18.4)	-0.2 (-1-0.6)	0.5	510,545	145.8 (145.4-146.2)	1.3 (1.0-1.6)	<0.001	573,168	164.1 (163.7-164.5)	1.1 (0.8-1.4)	<0.001
Breast cancer cases aged 20-44 years												
Non-Hispanic white	4,590	7.3 (7.1-7.5)	-0.7 (-3.0-1.7)	0.2	26,465	42.5 (42.0-43.0)	1.7 (0.7-2.7)	<0.001	31,055	49.8 (49.2-50.3)	1.3 (0.2-2.5)	<0.001
Non-Hispanic Asians and Pacific Islanders	855	4.9 (4.6-5.2)	-1.3 (-7.5-5.3)	0.3	7,214	42.1 (41.2-43.1)	2.4 (0.2-4.7)	<0.001	8,069	47.0 (46.0-48.1)	2.0 (-0.2-4.3)	<0.001
Non-Hispanic black	1,904	12.3 (11.8-12.9)	-0.7 (-6.0-4.9)	0.5	6,045	39.3 (38.3-40.3)	1.5 (-0.3-3.4)	<0.001	7,949	51.7 (50.5-52.8)	1.0 (-0.6-2.6)	<0.001
American Indians and Alaska Natives	80	7.4 (5.9-9.3)	1.7 (-14.4-20.8)	0.6	373	35.7 (32.1-39.5)	4.5 (-4.1-13.8)	<0.001	453	43.1 (39.2-47.3)	4.1 (-3.5-12.3)	<0.001
Hispanics	2,239	6.6 (6.3-6.9)	1.1 (-1.9-4.1)	0.1	10,110	30.4 (29.8-31.0)	2.9 (0.1-5.8)	<0.001	12,349	37.0 (36.3-37.7)	2.6 (0.3-4.9)	<0.001
Sub-Total	9,710	7.4 (7.3-7.6)	-0.4 (-2.1-1.4)	0.3	50,548	39.2 (38.8-39.5)	2.0 (1.1-2.9)	<0.001	60,258	46.6 (46.2-47.0)	1.6 (0.7-2.6)	<0.001
Breast cancer cases aged 45-54 years												
Non-Hispanic white	7,060	21.7 (21.2-22.2)	-0.7 (-2.4-1.1)	0.1	61,500	189.2 (187.7-190.7)	1.7 (0.7-2.7)	<0.001	68,560	210.9 (209.3-212.5)	1.4 (0.5-2.4)	<0.001
Non-Hispanic Asians and Pacific Islanders	1,033	15.3 (14.4-16.3)	-0.4 (-8.0-7.7)	0.8	12,143	180.4 (177.2-183.6)	2.7 (1.4-4.0)	<0.001	13,176	195.7 (192.4-199.1)	2.5 (0.8-4.1)	<0.001
Non-Hispanic black	3,100	45.5 (43.9-47.1)	-0.2 (-4.0-3.8)	0.8	10,175	149.8 (146.9-152.8)	1.2 (-1.6-4.1)	0.1	13,275	195.4 (192-198.7)	0.9 (-1.4-3.2)	0.1
American Indians and Alaska Natives	89	18.1 (14.5-22.3)	-6.0 (-16.7-6.0)	<0.001	642	130.6 (120.6-141.2)	2.7 (-6.8-13.2)	0.2	731	148.7 (138-159.9)	1.5 (-6.4-10.1)	0.4
Hispanics	2,338	19.8 (19.0-20.6)	-0.5 (-5.7-5.0)	0.7	15,762	133.5 (131.4-135.6)	1.8 (-0.6-4.2)	<0.001	18,100	153.3 (151.1-155.6)	1.5 (-0.6-3.6)	<0.001
Sub-Total	13,688	23.4 (23.0-23.8)	-0.6 (-3.1-2.0)	0.3	100,804	172.7 (171.7-173.8)	1.6 (0.6-2.6)	<0.001	114,492	196.2 (195-197.3)	1.3 (0.4-2.3)	<0.001
Breast cancer cases aged 55 years or older												
Non-Hispanic white	25,045	32.4 (32.0-32.9)	-0.7 (-2.8-1.6)	0.2	261,122	340.2 (338.9-341.5)	1.0 (0.4-1.6)	<0.001	286,167	372.6 (371.3-374)	0.9 (0.3-1.4)	<0.001
Non-Hispanic Asians and Pacific Islanders	2,839	23.3 (22.4-24.1)	1.7 (-1.7-5.2)	<0.001	28,704	234.3 (231.6-237.1)	2.0 (0.5-3.5)	<0.001	31,543	257.6 (254.7-260.5)	2.0 (0.7-3.3)	<0.001
Non-Hispanic black	7,098	62.9 (61.4-64.5)	0.8 (-0.1-1.8)	<0.001	30,936	282.1 (278.9-285.4)	1.4 (0.1-2.7)	<0.001	38,034	345.1 (341.5-348.7)	1.3 (0.3-2.3)	<0.001
American Indians and Alaska Natives	202	25.0 (21.6-28.9)	0.6 (-8.8-10.9)	0.8	2,042	246.2 (235.2-257.5)	0.6 (-5.3-6.7)	0.7	2,244	271.2 (259.7-283.1)	0.6 (-5.2-6.7)	0.6
Hispanics	3,917	25.5 (24.7-26.3)	1.7 (-2.2-5.8)	0.1	34,656	229.1 (226.6-231.6)	1.5 (-0.1-3.1)	<0.001	38,573	254.6 (252-257.2)	1.5 (0.2-2.8)	<0.001
Sub-Total	39,225	33.6 (33.3-34.0)	0.0 (-1.7-1.8)	0.9	359,193	310.8 (309.8-311.9)	1.0 (0.4-1.6)	<0.001	398,418	344.5 (343.4-345.5)	0.9 (0.4-1.5)	<0.001

Table 3. Annual percentage change (APC) in age-adjusted incidence rates* of triple-negative breast cancer (number of breast cancer cases per 100,000 population) in women by time period and race/ethnicity

Race/Ethnicity	2010-2013			2014-2016			2017-2019			APC (95% CI)	*P* value
	N. Population	N. Cases	Incidence rate (95% CI)	N. Population	N. Cases	Incidence rate (95% CI)	N. Population	N. Cases	Incidence rate (95% CI)		
Triple-negative breast cancer											
NH-white	71,255,586	14,871	18.1 (17.8-18.4)	53,725,401	10,615	16.9 (16.5-17.2)	53,550,448	11,209	17.5 (17.2-17.9)	-0.7 (-1.5-0.1)	0.1
NH-Asians and P. Islanders	13,667,498	1,696	12.4 (11.8-13.0)	11,287,880	1,387	11.8 (11.2-12.4)	12,096,316	1,644	12.8 (12.2-13.5)	0.6 (-0.6-1.9)	0.3
NH-black	13,649,493	4,502	33.3 (32.3-34.3)	10,818,753	3,637	33.5 (32.4-34.6)	11,265,263	3,963	34.5 (33.4-35.6)	0.3 (-0.5-1.1)	0.4
American Indians and AN	1,008,653	149	15.7 (13.2-18.5)	789,737	108	14.1 (11.5-17.1)	810,461	114	14.0 (11.5-17.0)	-0.7 (-4-2.7)	0.7
Hispanics	24,791,947	2,997	14.2 (13.7-14.7)	20,108,413	2,574	14.7 (14.1-15.3)	21,291,160	2,923	15.3 (14.8-15.9)	1.0 (-0.2-2.2)	0.1
Total	124,373,177	24,283	18.5 (18.3-18.8)	96,730,184	18,387	17.7 (17.5-18.0)	99,013,648	19,953	18.5 (18.2-18.8)	-0.2 (-1-0.6)	0.5
Non-Triple-negative breast cancer											
NH-white	71,255,586	131,546	153.8 (152.9-154.6)	53,725,401	106,100	160.4 (159.4-161.4)	53,550,448	111,441	165.9 (164.9-167.0)	1.2 (1-1.5)	<0.001
NH-Asians and P. Islanders	13,667,498	16,194	117.4 (115.6-119.2)	11,287,880	14,640	125.5 (123.4-127.5)	12,096,316	17,227	135.5 (133.4-137.5)	2.3 (1.8-2.8)	<0.001
NH-black	13,649,493	16,773	127.2 (125.2-129.1)	10,818,753	14,531	134.9 (132.6-137.1)	11,265,263	15,852	137.7 (135.5-139.9)	1.4 (0.8-1.9)	<0.001
American Indians and AN	1,008,653	1,108	113.5 (106.7-120.6)	789,737	892	111.6 (104.2-119.4)	810,461	1,057	126.6 (118.8-134.8)	1.7 (-0.1-3.5)	0.1
Hispanics	24,791,947	20,567	104.0 (102.6-105.5)	20,108,413	18,607	110.0 (108.4-111.7)	21,291,160	21,354	114.7 (113.1-116.3)	1.7 (0.9-2.5)	<0.001
Total	124,373,177	186,874	140.4 (139.8-141.1)	96,730,184	155,540	146.6 (145.8-147.3)	99,013,648	168,131	151.7 (151.0-152.5)	1.3 (1.0-1.6)	<0.001

*Incidence rates were age adjusted to the 2000 US population.

increased during these time periods among Hispanic, black and Asian women. For example, the age-adjusted incidence of triple-negative breast cancer in black women was 33.3 cases per 100,000 women for 2010-2013, 33.5 cases for 2014-2016, and 34.5 cases for 2017-2019. The age-adjusted incidence of non-triple-negative breast cancer increased in white, black, Asian and Hispanic women by these 3 time periods, while the age-adjusted incidence of non-triple-negative breast cancer among AIAN women was lower in 2014-2016 than in 2010-2013 but was higher in 2017-2019.

Table 4 presents the age-adjusted incidence of triple-negative breast cancer and incidence rate ratio by age groups (20-44, 45-54, and ≥55), 3 time periods (2010-2013, 2014-2016, and 2017-2019) and race/ethnicity. The significantly higher age-adjusted incidence of triple-negative breast cancer in black women as compared to white women appeared to be limited in younger women aged 20-44 only (incidence rate ratio: 1.04, 95% CI: 1.00-1.08 for 2010-2013; 1.03, 1.00-1.09 for 2014-2016, and 1.03, 0.98-1.07 for 2017-2019). There were significantly lower age-adjusted incidence rates of triple-negative breast cancer in black women than in white women in other 2 age groups (44-54 and 55 or older). The age-adjusted incidence rates of triple-negative breast cancer were generally lower in the 3 age groups among Asian, AIAN and Hispanic women than white women.

Table 5 presents the annual percentage change in age-adjusted incidence of triple-negative breast cancer and non-triple-negative breast cancer by tumor stage (in-situ/local, regional, distant stage, or unknown stage) and race/ethnicity. Among patients with local stage breast cancer, annual percentage change in age-adjusted incidence of triple-negative breast cancer from 2010 to 2019 slightly decreased in white women but increased in Hispanic, black, Asian, and AIAN women ($P>0.05$). Among patients with regional stage breast cancer, annual percentage change in age-adjusted incidence of triple-negative breast cancer from 2010 to 2019 decreased in all ethnic women but only statistically significantly decreased in white women. In contrast, annual percentage change in age-adjusted incidence of triple-negative breast cancer from 2010 to 2019 increased significantly in white and Hispanic women with distant stage and in white women with unknown stage breast cancer, but not significantly increased in black and Asian women. Annual percentage change in age-adjusted incidence of non-triple-negative breast cancer from 2010 to 2019 increased significantly in almost all ethnic women with local or distant stage breast cancer and slightly increased in those with regional stage breast cancer. In those with unknown stage breast cancer, annual percentage change in age-adjusted incidence of non-triple-negative breast cancer from 2010 to 2019 increased for white, Asian and Hispanic women, but decreased for black and AIAN women.

Table 6 presents the changes in the proportion of estrogen receptor, progesterone receptor and HER2 receptor status from 2010 to 2019 to determine if the changing trends in the incidence of triple-negative breast cancer was affected more or less by the changing proportions of the 3 individual receptors over time. Of all incident (triple-negative and non-triple-negative) breast cancer cases in 2010-2019, the proportion of patients with estrogen receptor negative slightly decreased from 17.7% in 2010 to 15.3% in 2019; the proportion of patients with progesterone receptor negative also slightly decreased from 29.2% in 2010 to 26.0% in 2019; and the proportion of patients with HER2 receptor negative slightly increased from 85.1% to 86.7%.

Discussion

This study examined the age-adjusted incidence rates and trends by race/ethnicity for both triple-negative breast cancer and non-triple-negative breast cancer. The age-adjusted incidence rate of triple-negative breast cancer was the highest in black women, followed by white, AIAN, Hispanic, and Asian women. The incidence rate ratio was statistically significantly higher in black women and significantly lower in AIAN, Hispanic, and Asian women as compared to white women. The significantly higher age-adjusted incidence of triple-negative breast cancer in black women as compared to white women appeared to be limited in younger women aged 20-44 only. There was no significant difference in age-adjusted incidence of triple-negative breast cancer among women

Table 4. Age-adjusted incidence rates of triple-negative breast cancer (number of breast cancer cases per 100,000 women) by age groups, race/ethnicity, and time period

Race/ Ethnicity	Age 20-44 yrs				Age 45-54 yrs				Age ≥55 yrs			
	N. Population	N. Cases	Incidence rate* (95% CI)	Rate ratio (95% CI)	N. Population	N. Cases	Incidence rate* (95% CI)	Rate ratio (95% CI)	N. Population	N. Cases	Incidence rate* (95% CI)	Rate ratio (95% CI)
2010-2013												
NH-white	27,673,809	12,411	47.9 (47.1-48.8)	1.00 (ref)	13,849,991	28,442	203.6 (201.2-205.9)	1.00 (ref)	29,731,786	105,564	363.3 (361.1-365.6)	1.00 (ref)
NH-Asians and P. Islanders	6,822,173	2,875	44.3 (42.7-46.0)	0.92 (0.89-0.96)	2,550,269	4,667	182.4 (177.2-187.7)	0.90 (0.87-0.92)	4,295,056	10,348	242.4 (237.7-247.2)	0.67 (0.65-0.68)
NH-black	6,865,584	3,040	49.9 (48.2-51.7)	1.04 (1.00-1.08)	2,736,798	5,212	189.5 (184.3-194.7)	0.93 (0.90-0.96)	4,047,111	13,023	330.9 (325.1-336.8)	0.91 (0.89-0.93)
American Indians and AN	501,604	163	38.6 (32.9-45.0)	0.81 (0.69-0.94)	206,716	290	139.1 (123.5-156.1)	0.68 (0.61-0.77)	300,333	804	277.6 (257.9-298.4)	0.76 (0.71-0.82)
Hispanics	15,051,841	4,442	34.3 (33.3-35.3)	0.72 (0.69-0.74)	4,408,238	6,460	146.7 (143.1-150.3)	0.72 (0.70-0.74)	5,331,868	12,662	243.5 (239.1-247.9)	0.67 (0.66-0.68)
Sub-Total (2010-2013)	56,915,011	23,044	44.5 (43.9-45.1)		23,752,012	45,266	189.3 (187.6-191.1)		43,706,154	142,847	335.2 (333.4-336.9)	
2014-2016												
NH-white	20,443,406	9,217	50.1 (49.0-51.1)	1.00 (ref)	9,587,313	20,423	210.5 (207.6-213.4)	1.00 (ref)	23,694,682	87,075	373.4 (370.9-376)	1.00 (ref)
NH-Asians and P. Islanders	5,491,452	2,452	46.9 (45.0-48.8)	0.94 (0.9-0.98)	2,027,709	3,953	194.5 (188.5-200.7)	0.92 (0.89-0.96)	3,768,719	9,622	255.4 (250.3-260.7)	0.68 (0.67-0.70)
NH-black	5,333,868	2,387	52.2 (50.1-54.3)	1.04 (1.00-1.09)	2,025,818	4,084	199.3 (193.2-205.5)	0.95 (0.92-0.98)	3,459,067	11,697	347.1 (340.6-353.6)	0.93 (0.91-0.95)
American Indians and AN	384,892	130	41.3 (34.4-49.0)	0.83 (0.69-0.98)	145,382	218	149.1 (129.8-170.5)	0.71 (0.62-0.81)	259,463	652	254.9 (235-276.1)	0.68 (0.63-0.74)
Hispanics	11,764,741	3,811	37.7 (36.5-38.9)	0.75 (0.73-0.78)	3,596,453	5,541	154.0 (149.9-158.1)	0.73 (0.71-0.75)	4,747,219	11,829	254.9 (250.2-259.7)	0.68 (0.67-0.70)
Sub-Total (2014-2016)	43,418,359	18,108	46.9 (46.2-47.6)		17,382,675	34,411	196.2 (194.1-198.3)		35,929,150	121,408	344.6 (342.7-346.6)	
2017-2019												
NH-white	20,200,529	9,427	52.1 (51.0-53.2)	1.00 (ref)	8,766,150	19,695	222.9 (219.7-226)	1.00 (ref)	24,583,769	93,528	382.7 (380.3-385.2)	1.00 (ref)
NH-Asians and P. Islanders	5,732,601	2,742	50.5 (48.6-52.4)	0.97 (0.93-1.01)	2,144,483	4,556	212.4 (206.3-218.7)	0.95 (0.92-0.98)	4,219,232	11,573	274.9 (269.9-280.1)	0.72 (0.70-0.73)
NH-black	5,470,780	2,522	53.5 (51.4-55.6)	1.03 (0.98-1.07)	1,980,094	3,979	199.4 (193.2-205.7)	0.89 (0.86-0.93)	3,814,389	13,314	357.7 (351.5-364)	0.93 (0.92-0.95)
American Indians and AN	389,128	160	51.2 (43.5-59.8)	0.98 (0.83-1.15)	134,852	223	163.1 (142.3-186.1)	0.73 (0.64-0.84)	286,481	788	279.1 (259.4-299.9)	0.73 (0.68-0.78)
Hispanics	12,067,250	4,096	39.7 (38.5-40.9)	0.76 (0.73-0.79)	3,801,546	6,099	160.4 (156.4-164.4)	0.72 (0.70-0.74)	5,422,364	14,082	265.1 (260.6-269.6)	0.69 (0.68-0.71)
Sub-Total (2017-2019)	43,860,288	19,106	49.2 (48.5-49.9)		16,827,125	34,815	205.7 (203.6-207.9)		38,326,235	134,163	354.5 (352.6-356.4)	
Total (2010-2019)	144,193,65	60,258	46.6 (46.2-47.0)		57,961,812	114,492	196.2 (195.0-197.3)		117,961,539	398,418	344.5 (343.4-345.5)	

*Incidence rates were age adjusted to the 2000 US population in each of the 3 age groups.

Table 5. Annual percentage change (APC) in age-adjusted incidence rates (number of breast cancer cases per 100,000 population) in women in 2010-2019 by tumor stage, triple-negative breast cancer status and race/ethnicity

Race/Ethnicity	Triple-negative breast cancer			Non-Triple-negative breast cancer			Total breast cancer (triple-negative and non-triple-negative breast cancer)		
	N. Cases	Incidence rate (95% CI)	APC (95% CI) from 2010 to 2019	N. Cases	Incidence rate (95% CI)	APC (95% CI) from 2010 to 2019	N. Cases	Incidence rate (95% CI)	APC (95% CI) from 2010 to 2019
Local stage Breast Cancer									
Non-Hispanic white		11.0 (10.9-11.2)	-0.5 (-2.5-1.5)	238,689	107 (106.6-107.4)	1.8*** (1.0-2.5)	262,038	118.0 (117.6-118.5)	1.5*** (0.8-2.3)
Non-Hispanic Asians and Pacific Islanders	2,893	7.5 (7.3-7.8)	1.1 (-2.4-4.7)	31,778	83.0 (82-83.9)	2.4*** (1.3-3.5)	34,671	90.5 (89.5-91.5)	2.3*** (1.2-3.3)
Non-Hispanic black	6,689	18.6 (18.1-19.1)	0.4 (-1.7-2.6)	27,340	77.2 (76.3-78.2)	2.1*** (0.4-3.8)	34,029	95.8 (94.8-96.9)	1.7*** (0.3-3.2)
American Indians and Alaska Natives	215	8.4 (7.3-9.6)	0.5 (-10.8-13.3)	1,909	72.4 (69.1-75.8)	1.9 (-3.4-7.4)	2,124	80.8 (77.3-84.4)	1.7 (-3.7-7.5)
Hispanics	4,739	8.3 (8.1-8.5)	1 (-3-5.1)	36,253	66.8 (66.1-67.5)	2.4*** (0.6-4.3)	40,992	75.1 (74.4-75.9)	2.3*** (0.8-3.8)
Sub-Total	38,016	11.0 (10.9-11.1)	-0.2 (-2.1-1.8)	337,626	95.4 (95.1-95.8)	1.7*** (1.0-2.5)	375,642	106.5 (106.1-106.8)	1.5*** (0.8-2.3)
Regional Stage Breast Cancer									
Non-Hispanic white	10,616	5.2 (5.1-5.4)	-1.8** (-4.3-0.7)	91,171	43.7 (43.4-44.0)	-0.2 (-0.9-0.6)	101,787	48.9 (48.6-49.3)	-0.4 (-1.0-0.2)
Non-Hispanic Asians and Pacific Islanders	1,504	4.0 (3.8-4.2)	-0.7 (-6.0-5.0)	13,706	36.2 (35.6-36.8)	1.7* (-0.5-3.9)	15,210	40.1 (39.5-40.8)	1.5* (-0.8-3.8)
Non-Hispanic black	4,310	12.1 (11.7-12.5)	-0.1 (-3.1-3.0)	15,763	44.4 (43.7-45.1)	0.4 (-1.2-2.1)	20,073	56.5 (55.7-57.3)	0.3 (-1.2-1.8)
American Indians and Alaska Natives	119	4.9 (4.1-5.9)	-2.1 (-18.9-18)	944	36.2 (33.9-38.7)	0.0 (-5.9-6.2)	1,063	41.1 (38.6-43.8)	-0.3 (-5.5-5.1)
Hispanics	3,058	5.2 (5-5.4)	0.0 (-2.8-3.0)	20,575	35.9 (35.4-36.4)	0.3 (-1.6-2.3)	23,633	41.1 (40.6-41.7)	0.3 (-1.2-1.8)
Sub-Total	19,678	5.9 (5.8-5.9)	-1.0* (-2.8-0.8)	142,801	41.8 (41.6-42)	0.1 (-0.7-1.0)	162,479	47.6 (47.4-47.9)	0.0 (-0.8-0.8)
Distant Stage Breast Cancer									
Non-Hispanic white	2,458	1.1 (1.1-1.2)	2.0** (-0.8-5)	17,047	7.8 (7.7-7.9)	1.9** (0.0-3.8)	19,505	8.9 (8.8-9.0)	1.9*** (0.3-3.5)
Non-Hispanic Asians and Pacific Islanders	277	0.7 (0.6-0.8)	1.7 (-10.7-15.8)	2,224	5.8 (5.6-6.0)	3.6** (-0.4-7.8)	2,501	6.5 (6.3-6.8)	3.4*** (0.3-6.7)
Non-Hispanic black	1,004	2.8 (2.6-3.0)	0.8 (-3.2-4.9)	3,677	10.3 (10.0-10.6)	0.7 (-1.9-3.4)	4,681	13.1 (12.7-13.5)	0.7 (-1.5-3.1)
American Indians and Alaska Natives	32	1.2 (0.8-1.7)	-8.5 (-29.9-19.4)	179	7.0 (5.9-8.1)	8.1*** (1.5-15.2)	211	8.2 (7.1-9.4)	5.4 (-3.8-15.4)
Hispanics	593	1.1 (1.0-1.2)	5.4** (0.1-11.0)	3,205	5.7 (5.5-5.9)	2.1* (-1.1-5.3)	3,798	6.8 (6.0.6-7)	2.6** (-0.1-5.3)
Sub-Total	4,371	1.3 (1.2-1.3)	2.1 (-1.4-5.7)	26,421	7.6 (7.5-7.6)	1.8*** (0.4-3.1)	30,792	8.8 (8.7-8.9)	1.8*** (0.7-2.9)
Unknown stage or missing/not coded									
Non-Hispanic white	272	0.1 (0.1-0.1)	10.0* (-5.3-27.7)	2,180	0.9 (0.9-1.0)	4.9* (-5.0-15.9)	2,452	1.1 (1.0-1.1)	5.5* (-4.7-16.8)
Non-Hispanic Asians and Pacific Islanders	53	0.1 (0.1-0.2)	3.3 (-19.2-32.1)	353	0.9 (0.0.8-1.0)	3.8 (-11.1-21.3)	406	1.1 (1-1.2)	4.1 (-10.6-21.2)
Non-Hispanic black	99	0.3 (0.2-0.3)	1.9 (-16.6-24.6)	376	1.1 (1.0-1.2)	-0.4 (-8.0-7.8)	475	1.4 (1.2-1.5)	0.2 (-8.0-9.0)
American Indians and Alaska Natives	104	0.2 (0.1-0.5)	~ (~-~)$	25	1.1 (0.7-1.7)	-0.1 (-25.4-33.9)	30	1.3 (0.9-1.9)	1.9 (-19.3-28.6)
Hispanics	5	0.2 (0.1-0.2)	7.7 (-22.2-48.9)	495	0.9 (0.8-1.0)	6.1 (-16.0-34.1)	599	1.1 (1.0-1.2)	6.2 (-16.5-35.1)
Sub-Total	558	0.2 (0.1-0.2)	7.7* (-7.2-25.1)	3,697	1.0 (1.0-1.1)	4.9 (-6.5-17.7)	4,255	1.2 (1.2-1.2)	5.3 (-6.4-18.5)

*P<0.05, **P<0.01, and ***P<0.001, indicating the incidence rate other ethnic groups is significantly different than the rate for Non-Hispanic White. $ APC was not obtainable from the SEER*Stat.

Table 6. Proportion of breast cancer cases having hormone-receptor negative and HER2-negative tumors by year

Year	Total N	Number by estrogen receptor status negative	Row % by estrogen receptor status negative	Number by progesterone receptor status negative	Row % by progesterone receptor negative	Number by HER2-receptor status negative	Row % by HER2-receptor negative
2010	49,404	8,740	17.70%	14,410	29.20%	42,036	85.10%
2011	52,452	9,131	17.40%	14,845	28.30%	44,894	85.60%
2012	53,808	9,099	16.90%	14,919	27.70%	45,877	85.30%
2013	55,493	9,001	16.20%	14,785	26.60%	47,335	85.30%
2014	56,482	9,342	16.50%	15,084	26.70%	47,538	84.20%
2015	58,491	9,583	16.40%	15,714	26.90%	49,071	83.90%
2016	58,954	9,241	15.70%	15,704	26.60%	49,594	84.10%
2017	60,770	9,810	16.10%	16,077	26.50%	51,379	84.50%
2018	62,709	9,731	15.50%	16,517	26.30%	53,865	85.90%
2019	64,605	9,870	15.30%	16,769	26.00%	55,999	86.70%
Total	573,168	93,548	16.30%	154,824	27.00%	487,588	85.10%

aged 44-54 and ≥55 years. The study found that there were no significant annual percentage changes in age-adjusted incidence of triple-negative breast cancer from 2010 to 2019 in all ethnic groups of women aged 20-44 and 45-54 years, with the exception of a significant decrease in AIAN women aged 45-54 years. However, there was a statistically significant annual percentage increase in age-adjusted incidence of triple-negative breast cancer in Asian and black women aged ≥55 years. All ethnic women, with the exception of AIAN women, experienced a significant annual percentage increase in age-adjusted incidence of non-triple-negative breast cancer from 2010 to 2019. The trends in age-adjusted incidences of triple-negative breast cancer were not affected by dramatical changes in proportions in any of the 3 receptors.

Several previous studies examined the incidence rates of triple-negative breast cancer by race/ethnicity [21-25], of which only one study examined the incidence trends of triple-negative breast cancer among various racial and ethnic women [25]. Clarke and colleagues examined a large cohort of women with invasive breast cancer in California in 2006-2009 and found that black women had statistically significantly higher incidence rates of triple-negative breast cancer than white women at all ages [21]. Howlader and colleagues examined the incidence of triple-negative breast cancer in 2010, which was the first year for HER2-receptor status to be available in the complete SEER data [22]. They found that non-Hispanic black women had the highest incidence rates of triple-negative breast cancer across all age groups and non-Hispanic black women were much more likely to be diagnosed with this subtype of breast cancer than were the three other racial/ethnic groups [22]. Kohler and colleagues specifically examined the incidence of triple-negative breast cancer in 2011 by race/ethnicity in SEER areas and found that the incidence rate of triple-negative breast cancer was highest among non-Hispanic black women with an aged-adjusted rate of 27.2 cases per 100,000 women, as compared with all other racial/ethnic women [23]. Acheampong and colleagues reported the trends in triple-negative breast cancer incidence rates from 2010 to 2016 in SEER areas and found that triple-negative breast cancer incidence decreased in non-Hispanic white women aged 40-54 and 55-69 years as well as in non-Hispanic Black women aged 55-69 years [25]. Our study examined the incidence trends in more recent years from 2010 to 2019 and also addressed the incidence rates and trends among various racial/ethnic women, stratified by age groups and tumor stage. Our study found that there were no significant annual percentage changes in age-adjusted incidence of triple-negative breast cancer in all ethnic women aged 20-44 and 45-54 years except a significant decrease in AIAN women aged 45-54 years. However, there was a statistically significant annual per-

centage increase in age-adjusted incidence of triple-negative breast cancer from 2010 to 2019 in Asian and black women aged ≥55 years. Some of these findings appeared to differ from a previous study reporting breast cancer cases in 2010-2016 [25]. These differences in age-adjusted incidence rates of triple-negative breast cancer for some older ethnic women may have been resulted from more breast cancer cases in recent years (2017-2019).

Because triple-negative breast cancer is a more aggressive subtype of cancer, spreads much faster than other subtypes of cancer, and has limited effective treatment options, patients with triple-negative breast cancer often have much poorer clinical outcomes and lower survival [10-20]. A higher risk of developing triple-negative breast cancer in black women with limited treatment choices may be one of the reasons why black women with breast cancer were reported to have a significantly higher risk of mortality [10-20]. Apparent racial and ethnic disparities in triple-negative breast cancer incidence and outcomes could be explained by a number of factors according to previous studies [10-20]. These include both biologic factors (such as genetic factors, early menarche, high parity, lack of breastfeeding, and obesity in promoting this subtype of disease biology) and non-biologic factors (such as unsafe neighborhoods, poverty, unmarried household, social stress, and toxic-waste dumping) [12-17, 27-34]. Once triple-negative breast cancer can be detectable clinically, it would be critical to have access to medical care in order to improve outcomes. Health insurance, transportation, timely treatment, compliance, and regular follow-up care are some of the factors that have been shown to have an impact on racial/ethnic disparities in breast cancer outcomes [35-40].

There are several limitations in this study. First, because triple-negative breast cancer was based on the coding of estrogen receptor, progesterone receptor, and HER2 receptor status, there were some concerns about completeness and accuracy of information on these receptors and about the number of breast cancer cases with missing or unknown status on these receptors, which could significantly affect the estimates of incidence of triple-negative breast cancer. Second, women aged ≥20 years in SEER areas as dynamic populations and denominators for the incidence rates may change over time due to migration, hence affecting the incidence rates. Third, women were grouped into broader categories of non-Hispanic whites, blacks, Asians, and Hispanics. Variations by sub-Saharan African women, subgroups of Hispanic population (Cuban or Mexico), and subgroups of Asian and Pacific Islanders were not considered in the analyses. Therefore, it should require a caution at interpreting and generalizing the study findings to sub-groups of various racial/ethnic populations.

In conclusion, age-adjusted incidence rates of triple-negative breast cancer was statistically significantly higher in black women and significantly lower in AIAN, Hispanic, and Asian women as compared to white women. The significantly higher age-adjusted incidence of triple-negative breast cancer in black women than white women were observed only in younger women aged 20-44. There were no significant annual percentage changes in age-adjusted incidence of triple-negative breast cancer from 2010 to 2019 in all ethnic women age 20-44 and 45-54 years except a significant decrease in AIAN aged 45-54 years. However, there was a statistically significant annual percentage increase in age-adjusted incidence of triple-negative breast cancer in Asian and black women aged ≥55 years. More research may be needed to explore why there is a significantly higher incidence of triple-negative breast cancer only in younger women aged 20-44 years and why there is significant annual percentage increase in age-adjusted incidence of triple-negative breast cancer in Asian and black women aged ≥55 years.

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Disclosure of conflict of interest

None.

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References

[1] Bray F, McCarron P and Parkin DM. The changing global patterns of female breast cancer incidence and mortality. Breast Cancer Res 2004; 6: 229-239.

[2] Ravdin PM, Cronin KA, Howlader N, Berg CD, Chlebowski RT, Feuer EJ, Edwards BK and Berry DA. The decrease in breast cancer incidence in 2003 in the United States. N Engl J Med 2007; 356: 1670-1674.

[3] Porter P. "Westernizing" women's risks? Breast cancer in lower-income countries. N Engl J Med 2008; 358: 213-216.

[4] Shin HR, Joubert C, Boniol M, Hery C, Ahn SH, Won YJ, Nishino Y, Sobue T, Chen CJ, You SL, Mirasol-Lumague MR, Law SC, Mang O, Xiang YB, Chia KS, Rattanamongkolgul S, Chen JG, Curado MP and Autier P. Recent trends and patterns in breast cancer incidence among Eastern and Southeastern Asian women. Cancer Causes Control 2010; 21: 1777-1785.

[5] Zbuk K and Anand SS. Declining incidence of breast cancer after decreased use of hormone-replacement therapy: magnitude and time lags in different countries. J Epidemiol Community Health 2012; 66: 1-7.

[6] DeSantis CE, Bray F, Ferlay J, Lortet-Tieulent J, Anderson BO and Jemal A. International variation in female breast cancer incidence and mortality rates. Cancer Epidemiol Biomarkers Prev 2015; 24: 1495-1506.

[7] DeSantis CE, Fedewa SA, Goding Sauer A, Kramer JL, Smith RA and Jemal A. Breast cancer statistics, 2015: convergence of incidence rates between black and white women. CA Cancer J Clin 2016; 66: 31-42.

[8] DeSantis CE, Ma J, Gaudet MM, Newman LA, Miller KD, Goding Sauer A, Jemal A and Siegel RL. Breast cancer statistics, 2019. CA Cancer J Clin 2019; 69: 438-451.

[9] Du XL and Song L. Breast cancer incidence trends in Asian women aged 20 or older as compared to other ethnic women in the United States from 2000 to 2018 by time period, age and tumor stage. Cancer Epidemiol 2022; 76: 102076.

[10] Foulkes WD, Smith IE and Reis-Filho JS. Triple-negative breast cancer. N Engl J Med 2010; 363: 1938-1948.

[11] Kurian AW, Fish K, Shema SJ and Clarke CA. Lifetime risks of specific breast cancer subtypes among women in four racial/ethnic groups. Breast Cancer Res 2010; 12: R99.

[12] Newman LA and Kaljee LM. Health disparities and triple-negative breast cancer in African American women: a review. JAMA Surg 2017; 152: 485-493.

[13] Siddharth S and Sharma D. Racial disparity and triple-negative breast cancer in African-American women: a multifaceted affair between obesity, biology, and socioeconomic determinants. Cancers (Basel) 2018; 10: 514.

[14] Garlapati C, Joshi S, Sahoo B, Kapoor S and Aneja R. The persisting puzzle of racial disparity in triple-negative breast cancer: looking through a new lens. Front Biosci (Schol Ed) 2019; 11: 75-88.

[15] Tao L, Gomez SL, Keegan TH, Kurian AW and Clarke CA. Breast cancer mortality in African-American and non-Hispanic white women by molecular subtype and stage at diagnosis: a population-based study. Cancer Epidemiol Biomarkers Prev 2015; 24: 1039-1045.

[16] Brinton LA, Figueroa JD, Awuah B, Yarney J, Wiafe S, Wood SN, Ansong D, Nyarko K, Wiafe-Addai B and Clegg-Lamptey JN. Breast cancer in Sub-Saharan Africa: opportunities for prevention. Breast Cancer Res Treat 2014; 144: 467-478.

[17] Dietze EC, Sistrunk C, Miranda-Carboni G, O'Regan R and Seewaldt VL. Triple-negative breast cancer in African-American women: disparities versus biology. Nat Rev Cancer 2015; 15: 248-254.

[18] Zahnd WE, Sherman RL, Klonoff-Cohen H, McLafferty SL, Farner S and Rosenblatt KA. Disparities in breast cancer subtypes among women in the lower Mississippi Delta Region states. Cancer Causes Control 2019; 30: 591-601.

[19] Scott LC, Mobley LR, Kuo TM and Il'yasova D. Update on triple-negative breast cancer disparities for the United States: a population-based study from the United States Cancer Statistics database, 2010 through 2014. Cancer 2019; 125: 3412-3417.

[20] Du X. Racial disparities in health insurance, triple-negative breast cancer diagnosis, tumor stage, treatment and survival in a large nationwide SEER cohort in the United States. Mol Clin Oncol 2022; 16: 95.

[21] Clarke CA, Keegan TH, Yang J, Press DJ, Kurian AW, Patel AH and Lacey JV Jr. Age-specific incidence of breast cancer subtypes: understanding the black-white crossover. J Natl Cancer Inst 2012; 104: 1094-1101.

[22] Howlader N, Altekruse SF, Li CI, Chen VW, Clarke CA, Ries LA and Cronin KA. US incidence

of breast cancer subtypes defined by joint hormone receptor and HER2 status. J Natl Cancer Inst 2014; 106: dju055.

[23] Kohler BA, Sherman RL, Howlader N, Jemal A, Ryerson AB, Henry KA, Boscoe FP, Cronin KA, Lake A, Noone AM, Henley SJ, Eheman CR, Anderson RN and Penberthy L. Annual report to the nation on the status of cancer, 1975-2011, featuring incidence of breast cancer subtypes by race/ethnicity, poverty, and state. J Natl Cancer Inst 2015; 107: djv048.

[24] Kong X, Liu Z, Cheng R, Sun L, Huang S, Fang Y and Wang J. Variation in breast cancer subtype incidence and distribution by race/ethnicity in the United States from 2010 to 2015. JAMA Netw Open 2020; 3: e2020303.

[25] Acheampong T, Kehm RD, Terry MB, Argov EL and Tehranifar P. Incidence trends of breast cancer molecular subtypes by age and race/ethnicity in the US from 2010 to 2016. JAMA Netw Open 2020; 3: e2013226.

[26] Surveillance, Epidemiology, and End Results (SEER) Program (www.seer.cancer.gov) SEER* Stat Database: Incidence - SEER Research Data, 18 Registries, Nov 2020 Sub (2000-2019) - National Cancer Institute, DCCPS, Surveillance Research Program, released April 2022, based on the November 2021 submission.

[27] Sørlie T, Perou CM, Tibshirani R, Aas T, Geisler S, Johnsen H, Hastie T, Eisen MB, van de Rijn M, Jeffrey SS, Thorsen T, Quist H, Matese JC, Brown PO, Botstein D, Lønning PE and Børresen-Dale AL. Gene expression patterns of breast carcinomas distinguish tumor subclasses with clinical implications. Proc Natl Acad Sci U S A 2001; 98: 10869-10874.

[28] Pierobon M and Frankenfeld CL. Obesity as a risk factor for triple-negative breast cancers: a systematic review and meta-analysis. Breast Cancer Res Treat 2013; 137: 307-314.

[29] Jiralerspong S and Goodwin PJ. Obesity and breast cancer prognosis: evidence, challenges, and opportunities. J Clin Oncol 2016; 34: 4203-4216.

[30] Plasilova ML, Hayse B, Killelea BK, Horowitz NR, Chagpar AB and Lannin DR. Features of triple-negative breast cancer: analysis of 38,813 cases from the national cancer database. Medicine (Baltimore) 2016; 95: e4614.

[31] Gershuni V, Li YR, Williams AD, So A, Steel L, Carrigan E and Tchou J. Breast cancer subtype distribution is different in normal weight, overweight, and obese women. Breast Cancer Res Treat 2017; 163: 375-81.

[32] Prakash O, Hossain F, Danos D, Lassak A, Scribner R and Miele L. Racial disparities in triple-negative breast cancer: a review of the role of biologic and non-biologic factors. Front Public Health 2020; 8: 576964.

[33] Moss JL, Tatalovich Z, Zhu L, Morgan C and Cronin KA. Triple-negative breast cancer incidence in the United States: ecological correlations with area-level sociodemographics, healthcare, and health behaviors. Breast Cancer 2021; 28: 82-91.

[34] Siegel SD, Brooks MM, Lynch SM, Sims-Mourtada J, Schug ZT and Curriero FC. Racial disparities in triple negative breast cancer: toward a causal architecture approach. Breast Cancer Res 2022; 24: 37.

[35] McCarthy AM, Friebel-Klingner T, Ehsan S, He W, Welch M, Chen J, Kontos D, Domchek SM, Conant EF, Semine A, Hughes K, Bardia A, Lehman C and Armstrong K. Relationship of established risk factors with breast cancer subtypes. Cancer Med 2021; 10: 6456-6467.

[36] Aoki RF, Uong SP, Gomez SL, Alexeeff SE, Caan BJ, Kushi LH, Torres JM, Guan A, Canchola AJ, Morey BN, Lin K and Kroenke CH. Individual- and neighborhood-level socioeconomic status and risk of aggressive breast cancer subtypes in a pooled cohort of women from Kaiser Permanente Northern California. Cancer 2021; 127: 4602-4612.

[37] Luo J, Kroenke CH, Hendryx M, Shadyab AH, Liu N, Chen X, Wang F, Thomas F, Saquib N, Qi L, Cheng TD, Arthur R and Wactawski-Wende J. Mediation analysis of racial disparities in triple-negative breast cancer incidence among postmenopausal women. Breast Cancer Res Treat 2021; 188: 283-293.

[38] Michaels EK, Canchola AJ, Beyer KMM, Zhou Y, Shariff-Marco S and Gomez SL. Home mortgage discrimination and incidence of triple-negative and Luminal A breast cancer among non-Hispanic Black and non-Hispanic White females in California, 2006-2015. Cancer Causes Control 2022; 33: 727-735.

[39] Sinha S, Bhatia R, Narasimamurthy M, Rayne S and Grover S. Epidemiology of breast cancer presentation in Botswana, South Africa, and the United States. J Surg Res 2022; 279: 533-539.

[40] Siegel SD, Brooks MM, Sims-Mourtada J, Schug ZT, Leonard DJ, Petrelli N and Curriero FC. A population health assessment in a community cancer center catchment area: triple-negative breast cancer, alcohol use, and obesity in New Castle County, Delaware. Cancer Epidemiol Biomarkers Prev 2022; 31: 108-116.