Breast Cancer Mortality Among American Indian and Alaska Native Women, 1990–2009

Arica White, PhD, MPH, Lisa C. Richardson, MD, MPH, Chunyu Li, MD, PhD, Donatus U. Ekwueme, PhD, and Judith S. Kaur, MD

Objectives. We compared breast cancer death rates and mortality trends among American Indian/Alaska Native (AI/AN) and White women using data for which racial misclassification was minimized.

Methods. We used breast cancer deaths and cases linked to Indian Health Service (IHS) data to calculate age-adjusted rates and 95% confidence intervals (CIs) by IHS-designated regions from 1990 to 2009 for AI/AN and White women; Hispanics were excluded. Mortality-to-incidence ratios (MIR) were calculated for 1999 to 2009 as a proxy for prognosis after diagnosis.

Results. Overall, the breast cancer death rate was lower in AI/AN women (21.6 per 100 000) than in White women (26.5). However, rates in AI/ANs were higher than rates in Whites for ages 40 to 49 years in the Alaska region, and ages 65 years and older in the Southern Plains region. White death rates significantly decreased (annual percent change [APC] = –2.1; 95% CI = –2.3, –2.0), but regional and overall AI/AN rates were unchanged (APC = 0.9; 95% CI = 0.1, 1.7). AI/AN women had higher MIRs than White women.

Conclusions. There has been no improvement in death rates among AI/AN women. Targeted screening and timely, high-quality treatment are needed to reduce mortality from breast cancer in AI/AN women. (*Am J Public Health.* 2014;104: S432–S438. doi:10.2105/AJPH.2013.301720)

Breast cancer is the most frequently diagnosed cancer and a leading cause of cancer mortality among American Indian/Alaska Native (AI/AN) women.[1,2] Despite having a lower incidence of breast cancer than White women, AI/AN women are more likely to be diagnosed at younger ages and later stages.[3,4] Furthermore, breast cancer incidence rates vary considerably across the Indian Health Service (IHS) Contract Health Service Delivery Areas (CHSDAs). Incidence rates in the Alaska region are similar to those of White women, but other regions have lower incidence rates than White women.[4]

Breast cancer death rates among AI/AN women show patterns similar to incidence rates and are lower than rates in the general US population.[5,6] Furthermore, among AI/AN women, mortality trends exhibit similar patterns in regional variation. Espey et al.[5] found that 1996 to 2001 breast cancer death rates for AI/AN women were lower in the East, Pacific Coast, and Southwest, but similar for Alaska and the Southern Plains, compared with the rate for the general US population. Although all races experienced decreases in death rates from 1990 to 1995 to 1996 to 2001, the rates for AI/AN women were stable during these 2 time periods,[5] with no noted improvements.

It is uncertain whether there has been any progress in reducing breast cancer mortality among AI/AN women since 2001. To date, the study by Espey et al.[5] is the only one that has examined 1990 to 2001 breast cancer mortality trends among AI/AN women compared with the general population, while also controlling for racial misclassification of AI/AN women. In addition, no studies have used mortality-to-incidence ratios (MIRs) to assess the burden of breast cancer among AI/AN women. The MIR measures prognosis after diagnosis, and therefore, can serve as an indicator of survival.[7] Furthermore, the MIR differential between AI/AN and White women serves as a proxy for excess mortality among AI/AN women, controlling for incidence.[7]

To better understand the burden of breast cancer among AI/AN women, we examined breast cancer mortality trends in 1990 to 2009 data and fatality after breast cancer diagnosis in 1999 to 2009 data among AI/AN and White women. We used an incidence and mortality data set for which racial misclassification was minimized. Furthermore, we described geographic variations and trends over time of mortality caused by breast cancer among AI/AN women during this same time period. These mortality estimates provided a baseline for measuring the impact of breast cancer control programs in decreasing the burden of breast cancer among this population and identifying geographic areas where additional outreach is needed.

METHODS

We used denominators to calculate incidence and death rates included in the bridged single-race population estimates developed by the US Census Bureau and the Centers for Disease Control and Prevention (CDC) National Center for Health Statistics (NCHS).[8] The bridged single-race data allowed for comparability between the pre- and post-2000 racial/ethnic population estimates.[8] We adjusted these denominator data for the population shifts caused by Hurricanes Katrina and Rita in 2005. During preliminary analyses, we discovered that the updated bridged intercensal populations estimates significantly overestimated AI/AN persons of Hispanic origin.[9] Therefore, to avoid underestimating mortality and incidence in AI/AN persons, we limited analyses to non-Hispanic AI/AN individuals. Non-Hispanic Whites were chosen as the most homogeneous referent group. Henceforth, the term "non-Hispanic" was omitted when discussing both groups.

Death Data

Death data were obtained from death certificates compiled by each state and sent to the NCHS. NCHS then edits these data for consistency, strips them of personal identifiers, and makes this information available for research as part of the National Vital Statistics System

(NVSS).[10] Data from this system include underlying and multiple causes of death fields, state and county of residence, age, gender, race, and ethnicity.[10] NCHS applies a bridging algorithm similar to the one used by the Census Bureau to assign a single race to decedents with multiple races reported on the death certificate.[10]

To identify AI/AN deaths misclassified as non-Native and to determine vital status and cause of death of decedents who received health care in IHS or tribal facilities, the Indian Health Service (IHS) patient registration database was linked to death certificate data in the National Death Index (NDI). This linkage process, a collaborative effort by the IHS Division of Epidemiology and Disease Prevention and the NCHS, is described in detail elsewhere in this supplement.[11] This file, which included an indicator of whether there was a positive link to IHS, was combined with population estimates to create an analytical file in SEER*Stat (version 8.0.2; National Cancer Institute, Bethesda, Maryland; AI/AN-US Mortality Database [AMD]). This final data set included all deaths for all races reported to NCHS from 1990 to 2009.

Assignment of race for AI/AN deaths was based on a combination of race classification by NCHS for death certificates and information derived from data linkages between the IHS patient registration database and the NDI. Details of race assignment are reported elsewhere in this supplement.[11]

We originally coded cancer deaths according to the *International Classification of Disease, Ninth Revision* (*ICD-9*)[12] for 1990 to 1998 and the *10th Revision* (*ICD-10*) for 1999 to 2009.[13] To account for the change in the *ICD* system and ease comparisons across the 2 periods, we converted breast cancer deaths with *ICD-9* codes to standard cause of death codes 39, 113, and 130. For deaths caused by breast cancer, we used *ICD-10* code C50.

Incidence Data

Data on invasive breast cancers diagnosed from 1999 to 2009 were obtained from population-based cancer registries affiliated with the CDC National Program of Cancer Registries (NPCR) and the National Cancer Institute's Surveillance, Epidemiology, and End Results (SEER) Program.[1] These data met the data quality criteria for publication in the United States Cancer Statistics. Cancer cases were originally coded according to the *International Classification of Diseases for Oncology, Third Edition* (*ICD-O-3*).[14] Codes C50.0 to C50.9 were used for breast cancer.

Geographic Coverage

We restricted all analyses in this study to women residing in IHS CHSDA counties, which contain federally recognized tribal reservations or off-reservation trust lands, or are adjacent to them. The IHS uses CHSDA residence to determine eligibility for services not available within the IHS,[15] and linkage studies indicated less misclassification of race for AI/AN persons in these counties.[11,15] These 637 counties, which represent 20% of the 3141 counties in the United States, have a higher proportion of the AI/AN population (64%) than do non-CHSDA counties, and thus, less race misclassification for AI/AN individuals.[15]

Although less geographically representative, restricting analyses to these regions offered improved accuracy in interpreting mortality statistics for AI/AN persons. We completed analyses for all regions combined and by individual IHS regions, including the Alaska, East, Northern Plains, Pacific Coast, Southern Plains, and Southwest regions. Additional details about CHSDA counties and IHS regions, including population coverage, are provided elsewhere.[11,15]

Statistical Analysis

We used SEER*Stat statistical software (version 8.0.2) to extract age- and race-specific breast cancer mortality, incidence, and associated population data for 1990 to 2009. Rates were expressed per 100 000 population and were directly age-adjusted to the 2000 US standard population using 11 age groups.[16] We also calculated standardized rate ratios (RRs) using the age-adjusted mortality and incidence rates for AI/AN women compared with White women, a population that is homogeneous across regions.

To measure prognosis after diagnosis, we calculated the MIR as the age-adjusted death rate divided by the age-adjusted incidence rate

TABLE 1—Death Rates for Breast Cancer by Indian Health Service Region for American Indian/Alaska Native Compared With White Women, All Ages: Contract Health Service Delivery Areas, United States, 1990–2009

IHS Region	AI/AN Count	AI/AN Rate	White Rate	AI/AN:White Rate Ratio (95% CI)
Northern Plains	376	26.6	25.6	1.04 (0.93, 1.16)
Alaska	178	27.9	24.9	1.12 (0.94, 1.33)
Southern Plains	475	29.3	25.2	1.16* (1.06, 1.28)
Southwest	410	13.9	25.6	0.54* (0.49, 0.60)
Pacific Coast	407	22.5	27.2	0.83* (0.75, 0.92)
East	124	17.6	26.9	0.65* (0.54, 0.78)
Total	1970	21.6	26.5	0.82* (0.78, 0.85)

Note. AI/AN = American Indian/Alaska Native; CHSDA = Contract Health Service Delivery Areas; CI = confidence interval; IHS = Indian Health Service. IHS regions are defined as follows: AK[a]; Northern Plains (IL, IN,[a] IA,[a] MI,[a] MN,[a] MT,[a] NE,[a] ND,[a] SD,[a] WI,[a] WY[a]); Southern Plains (OK,[a] KS,[a] TX[a]); Southwest (AZ,[a] CO,[a] NV,[a] NM,[a] UT[a]); Pacific Coast (CA,[a] ID,[a] OR,[a] WA,[a] HI); East (AL,[a] AR, CT,[a] DE, FL,[a] GA, KY, LA,[a] ME,[a] MD, MA,[a] MS,[a] MO, NH, NJ, NY,[a] NC,[a] OH, PA,[a] RI,[a] SC,[a] TN, VT, VA, WV, DC). Percent regional coverage of AI/AN persons in CHSDA counties to AI/AN persons in all counties: Northern Plains = 64.8%; Alaska = 100%; Southern Plains = 76.3%; Southwest = 91.3%; Pacific Coast = 71.3%; East = 18.2%; total US = 64.2%. Cancer causes of death were created using the Surveillance Epidemiology and End Results (SEER) Cause of Death recode. Analyses are limited to persons of non-Hispanic origin. The following states and years of data are excluded because Hispanic origin was not collected on the death certificate: LA: 1990; NH: 1990–1992; OK: 1990–1996. AI/AN race is reported from death certificates or through linkage with the IHS patient registration database. Rates are per 100 000 persons and are age-adjusted to the 2000 US standard population (11 age groups; Census P25-1130)[19]; CIs (Tiwari modification) are 95% for ratios. Rate ratios (RR) are calculated in SEER*Stat before rounding of rates and may not equal RR calculated from rates presented in the table.
Source. AI/AN-US Mortality Database (AMD 1990–2009).
[a]Identifies states with at least 1 county designated as CHSDA.
*$P < .05$.

within each group.[7] The MIR represents the number of breast cancer deaths per 100 breast cancers diagnosed. We calculated 95% confidence intervals (CIs) for age-adjusted rates, and standardized RRs were calculated based on methods described by Tiwari et al.[17]

We used Joinpoint regression software (National Cancer Institute, Bethesda, MD) to examine the annual percentage change (APC) in breast cancer death rates among AI/AN and White women overall and by IHS region. This software uses a Monte Carlo permutation test to identify points where the direction or magnitude of the trend changes and then fits the model containing the fewest number of trend segments.[18] We then graphed these trends by race/ethnicity and geographic regions.

RESULTS

Table 1 presents the death rates for breast cancer in CHSDA counties by IHS region and race for all ages. From 1990 to 2009, 1970 AI/AN women died of breast cancer, compared with 146 357 White women. Overall, AI/AN women had a lower death rate (21.6 deaths per 100 000) compared with White women (26.5 per 100 000).

Table 2 shows that there was significant variation in race- and age-specific breast cancer death rates from 1990 to 2009 by IHS region. Among women aged 39 years and younger, breast cancer mortality was lower for AI/ANs than Whites in the Pacific Coast region (RR = 0.5; 95% CI = 0.29, 0.92). For women aged 40 to 49 years, AI/ANs were nearly twice as likely as Whites to die of breast cancer (RR = 1.9; 95% CI = 1.2, 2.7) in the Alaska region. Death rates were lower for AI/ANs compared with Whites in the Southwest (RR = 0.7; 95% CI = 0.58, 0.91), Pacific Coast (RR = 0.7; 95% CI = 0.55, 0.93), and East (RR = 0.5; 95%

TABLE 2—Breast Cancer Death Rates by Indian Health Service Region and Age for American Indian/Alaska Native and White Women: Contract Health Service Delivery Area Counties, United States, 1990–2009

	Aged 0–39 Years		Aged 40–49 Years		Aged 50–64 Years		Aged ≥ 65 Years	
IHS Region/Race	Rate (95% CI)	RR (95% CI)	Rate (95% CI)	RR (95% CI)	Rate (95% CI)	RR (95% CI)	Rate (95% CI)	RR (95% CI)
Northern Plains								
White	1.7 (1.5, 1.8)		18.8 (18.1, 19.6)		47.1 (46.0, 48.3)		115.6 (113.7, 117.4)	
AI/AN	1.8 (1.2, 2.7)	1.1 (0.67, 1.60)	19.0 (14.5, 24.6)	1.0 (0.77, 1.30)	47.6 (39.8, 56.6)	1.0 (0.84, 1.20)	124.5 (105.9, 145.5)	1.1 (0.92, 1.30)
Alaska								
White	1.5 (1.0, 2.0)		14.8 (12.2, 17.8)		44.7 (39.5, 50.3)		120.4 (107.4, 134.5)	
AI/AN	2.8 (1.6, 4.6)	1.9 (0.98, 3.50)	27.3 (19.0, 38.0)	1.9* (1.20, 2.70)	58.1 (44.9, 73.9)	1.3 (0.98, 1.70)	106.4 (81.1, 137.0)	0.9 (0.66, 1.20)
Southern Plains								
White	1.8 (1.5, 2.1)		19.0 (17.5, 20.6)		48.2 (46.0, 50.5)		110.3 (106.9, 113.7)	
AI/AN	1.8 (1.1, 2.8)	1.0 (0.62, 1.60)	23.5 (18.2, 29.8)	1.2 (0.95, 1.60)	55.2 (47.0, 64.5)	1.2 (0.97, 1.30)	130.5 (114.0, 148.8)	1.2* (1.00, 1.40)
Southwest								
White	1.6 (1.4, 1.7)		19.7 (18.8, 20.6)		48.5 (47.2, 49.9)		113.5 (111.5, 115.6)	
AI/AN	1.4 (1.0, 2.0)	0.9 (0.62, 1.30)	14.3 (11.4, 17.8)	0.7* (0.58, 0.91)	28.0 (23.6, 32.9)	0.6* (0.48, 0.68)	52.7 (44.6, 61.9)	0.5* (0.39, 0.55)
Pacific Coast								
White	1.6 (1.6, 1.7)		20.8 (20.2, 21.5)		51.1 (50.2, 52.0)		121.3 (119.8, 122.7)	
AI/AN	0.9 (0.5, 1.5)	0.5* (0.29, 0.92)	15.1 (11.5, 19.5)	0.7* (0.55, 0.93)	42.2 (35.7, 49.4)	0.8* (0.70, 0.97)	105.6 (90.5, 122.5)	0.9 (0.75, 1.00)
East								
White	1.7 (1.6, 1.8)		20.5 (19.9, 21.2)		50.8 (49.9, 51.7)		119.2 (117.9, 120.5)	
AI/AN	. . .	. . .	10.1 (5.5, 16.9)	0.5* (0.27, 0.83)	41.0 (30.7, 53.6)	0.8 (0.60, 1.06)	71.5 (52.7, 94.9)	0.6* (0.44, 0.80)
Total								
White	1.7 (1.6, 1.7)		20.1 (19.7, 20.4)		49.7 (49.2, 50.3)		118.0 (117.2, 118.8)	
AI/AN	1.6 (1.3, 1.9)	0.9 (0.77, 1.10)	17.4 (15.5, 19.4)	0.9* (0.77, 0.97)	42.0 (39.0, 45.2)	0.8* (0.78, 0.91)	93.5 (87.2, 100.1)	0.8* (0.74, 0.85)

Note. AI/AN = American Indian/Alaska Native; CHSDA = Contract Health Service Delivery Areas; CI = confidence interval; IHS = Indian Health Service; RR = rate ratio. Dashes indicate that counts less than 10 were suppressed; as a result, rates and RRs could not be calculated. IHS regions are defined as follows: AK[a]; Northern Plains (IL, IN,[a] IA,[a] MI,[a] MN,[a] MT,[a] NE,[a] ND,[a] SD,[a] WI,[a] WY[a]); Southern Plains (OK,[a] KS,[a] TX[a]); Southwest (AZ,[a] CO,[a] NV,[a] NM,[a] UT[a]); Pacific Coast (CA,[a] ID,[a] OR,[a] WA,[a] HI); East (AL,[a] AR, CT,[a] DE, FL,[a] GA, KY, LA,[a] ME,[a] MD, MA,[a] MS,[a] MO, NH, NJ, NY,[a] NC,[a] OH, PA,[a] RI,[a] SC,[a] TN, VT, VA, WV, DC). Percent regional coverage of AI/AN persons in CHSDA counties to AI/AN persons in all counties: Northern Plains = 64.8%; Alaska = 100%; Southern Plains = 76.3%; Southwest = 91.3%; Pacific Coast = 71.3%; East = 18.2%; total US = 64.2%. Cancer causes of death were created using the Surveillance Epidemiology and End Results (SEER) Cause of Death recode. Analyses are limited to persons of non-Hispanic origin. The following states and years of data are excluded because Hispanic origin was not collected on the death certificate: LA: 1990; NH: 1990–1992; OK: 1990–1996. AI/AN race is reported from death certificates or through linkage with the IHS patient registration database. Rates are per 100 000 persons and age-adjusted to the 2000 US Standard Population (19 age groups; Census P25-1130[19]). CIs (Tiwari modification) are 95% for rates and ratios. RRs are calculated in SEER*Stat before rounding of rates and may not equal RRs calculated from rates presented in the table.
Source. AI/AN-US Mortality Database (AMD 1990–2009).
[a]Identifies states with at least 1 county designated as CHSDA.
*Indicates RR is statistically significant ($P < .05$).

CI = 0.27, 0.83) regions. Among women aged 50 to 64 years, AI/ANs were less likely than Whites to die of breast cancer in the Pacific Coast (RR = 0.8; 95% CI = 0.70, 0.97) and Southwest (RR = 0.6; 95% CI = 0.48, 0.68) regions. For women aged 65 years and older, the death rate was higher for AI/ANs than Whites (RR = 1.2; 95% CI = 1.0, 1.4) in the Southern Plains. Death rates by regions for AI/AN women were lower than rates for Whites in the East (RR = 0.6; 95% CI = 0.44, 0.80) and Southwest (RR = 0.5; 95% CI = 0.39, 0.55).

Overall breast cancer mortality from 1990 to 2009 for AI/AN women was essentially unchanged (APC = 0.9; 95% CI = 0.1, 1.7; Figure 1). By contrast, White women experienced an overall statistically significant decrease in mortality (APC = –2.1; 95% CI = –2.3, –2.0). Region trends followed a similar pattern for AI/AN and White women.

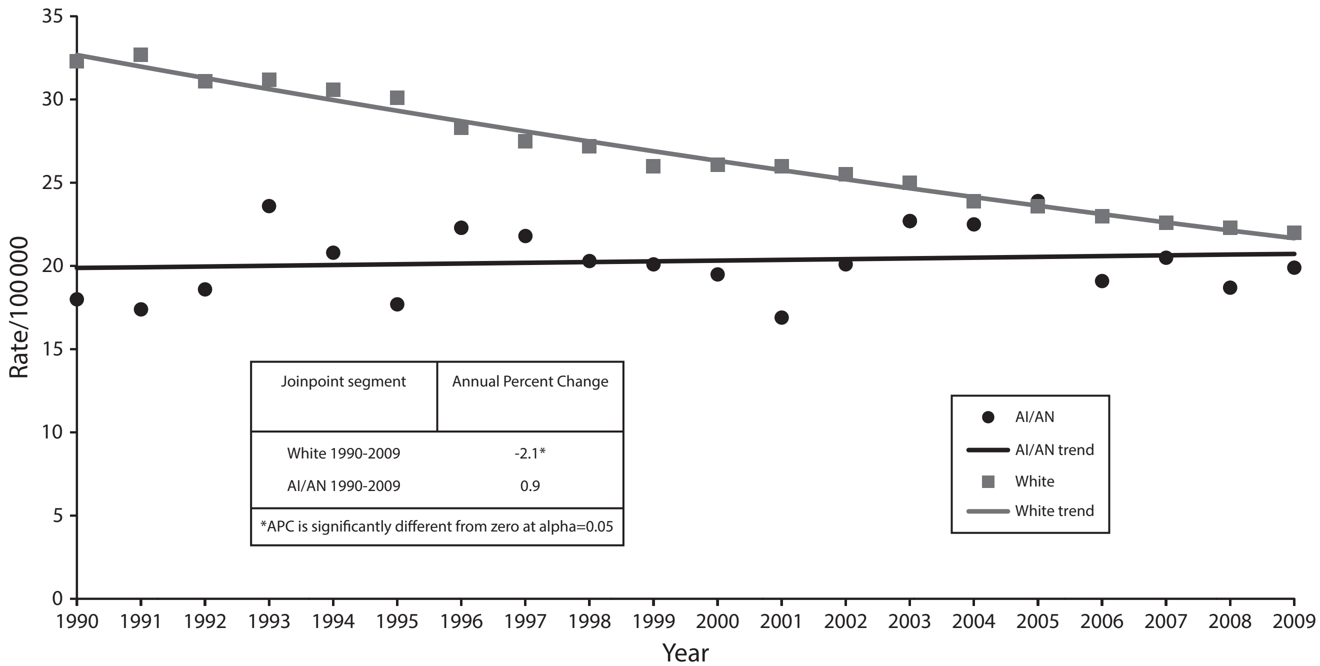
Table 3 shows incidence, mortality, and MIRs for each IHS region for AI/AN and White women by age. Compared with White women, death rates were higher for AI/AN women in the Northern Plains (26.2 vs 22.8), Alaska (29.1 vs 23.1), and the Southern Plains (29.4 vs 24.6). Furthermore, incidence was higher for AI/AN women compared with White women in Alaska (141.3 vs 135.5) and in the Southern Plains (136.1 vs 127.7). Overall, from 1999 to 2009, AI/AN women had higher MIRs than White women (MIR for AI/AN women = 0.22; 95% CI = 0.21, 0.24; MIR for White women = 0.18; 95% CI = 0.18, 0.19). This pattern was consistent, regardless of age group or region.

DISCUSSION

In this study, AI/AN women experienced lower breast cancer mortality than White women in most IHS geographic regions. However, breast cancer death rates among AI/AN women were higher than the rates for White women for those aged 40 to 49 years in the Alaska region, and those aged 65 years and older in the Southern Plains region. Although the death rates for White women declined from 1990 to 2009, death rates for AI/AN women did not change. In addition, MIRs were higher for AI/AN than for White women, indicating that AI/AN women had worse survival rates after a breast cancer diagnosis than White women.

Our results support previous literature that reported death rates among AI/AN women were lower relative to White women in 3 regions: Pacific Coast, Southwest, and East.[5] However, our study was the first to show significant variation by age within these regions. Furthermore, our study and previous studies were consistent in that breast cancer survival, measured as MIRs in our study, among AI/AN women was worse than among White women.[20,21]

There were several possible explanations for the observed mortality patterns and trends among AI/AN women compared with White women. First, overall and age-specific geographic patterns of breast cancer mortality mirrored those of breast cancer incidence. Previous CDC reports on AI/AN breast cancer



Note. AI/AN = American Indian/Alaska Native. Joinpoint analyses with up to 3 joinpoints are based on rates per 100 000 persons and were age-adjusted to the 2000 US standard population (19 age groups, Census P25-1130[19]); Joinpoint (JP) Regression Program, Version 4.0.1. January 2013; Statistical Research and Applications Branch, National Cancer Institute.
Source. AI/AN-US Mortality Database (AMD 1990–2009).

FIGURE 1—Trends in age-adjusted breast cancer death rates using Joinpoint: Contract Health Service Delivery Area counties, all Indian Health Service regions combined, United States, 1990–2009.

TABLE 3—Indian Health Service Region-Specific Breast Cancer Mortality and Incidence Rates and Mortality-to-Incidence Ratios Among American Indian/Alaska Native and White Women: Contract Health Service Delivery Area Counties, United States, 1999–2009

	Mortality Rate (95% CI)		Incidence Rate (95% CI)		MIR (95% CI)	
	AI/AN	White	AI/AN	White	AI/AN	White
Northern Plains	26.2 (22.6, 30.1)	22.8 (22.4, 23.2)	112.6 (105.7, 119.8)	125.5 (124.5, 126.5)	0.23 (0.20, 0.27)	0.18 (0.18, 0.19)
Alaska	29.1 (23.8, 35.1)	23.1 (20.9, 25.5)	141.3 (130.2, 153.2)	135.5 (130.3, 140.8)	0.21 (0.17, 0.25)	0.17 (0.15, 0.19)
Southern Plains	29.4 (26.6, 32.5)	24.6 (23.9, 25.3)	136.1 (130.1, 142.4)	127.7 (126.1, 129.3)	0.22 (0.19, 0.24)	0.19 (0.19, 0.20)
Pacific Coast	21.9 (19.0, 25.0)	24.9 (24.6, 25.2)	106.6 (100.6, 112.8)	138.7 (137.9, 139.4)	0.21 (0.18, 0.24)	0.18 (0.18, 0.18)
East	17.0 (13.2, 21.6)	24.0 (23.7, 24.3)	72.9 (65.1, 81.4)	132.9 (132.2, 133.6)	0.23 (0.18, 0.30)	0.18 (0.18, 0.18)
Southwest	15.2 (13.5, 17.1)	23.8 (23.3, 24.2)	59.6 (56.2, 63.2)	121.0 (120.0, 122.0)	0.26 (0.22, 0.29)	0.20 (0.19, 0.20)
Total	22.3 (21.1, 23.6)	24.1 (23.9, 24.2)	100.0 (97.5, 102.5)	131.3 (130.9, 131.7)	0.22 (0.21, 0.24)	0.18 (0.18, 0.19)

Note. AI/AN = American Indian/Alaska Native; CHSDA = Contract Health Service Delivery Areas; CI = confidence interval; IHS = Indian Health Service; MIR = mortality-to-incidence ratio; SEER = Surveillance Epidemiology and End Results. IHS regions are defined as follows: AK[a]; Northern Plains (IL, IN,[a] IA,[a] MI,[a] MN,[a] MT,[a] NE,[a] ND,[a] SD,[a] WI,[a] WY[a]); Southern Plains (OK,[a] KS,[a] TX[a]); Southwest (AZ,[a] CO,[a] NV,[a] NM,[a] UT[a]); Pacific Coast (CA,[a] ID,[a] OR,[a] WA,[a] HI); East (AL,[a] AR, CT,[a] DE, FL,[a] GA, KY, LA,[a] ME,[a] MD, MA,[a] MS,[a] MO, NH, NJ, NY,[a] NC,[a] OH, PA,[a] RI,[a] SC,[a] TN, VT, VA, WV, DC). Percent regional coverage of AI/AN persons in CHSDA counties to AI/AN persons in all counties: Northern Plains = 64.8%; Alaska = 100%; Southern Plains = 76.3%; Southwest = 91.3%; Pacific Coast = 71.3%; East = 18.2%; total US = 64.2%. Cancer causes of death were created using the SEER Cause of Death recode. Analyses are limited to persons of non-Hispanic origin. AI/AN race is reported from death certificates or through linkage with the IHS patient registration database. Rates are per 100 000 and age-adjusted to the 2000 US Standard Population (19 age groups; Census P25–1130[19]). CIs (Tiwari modification) are 95% for rates and ratios.
Source. Mortality data: AI/AN-US Mortality Database (AMD 1990–2009). Incidence data: population-based cancer registries that participate in the National Program of Cancer Registries or the SEER Program, and meet criteria for high data quality. Years of data and registries used: 1999–2009 (43 states): AK, AL, AZ, CA, CO, CT, DE, FL, GA, HI, IA, ID, IL, IN, KS, KY, LA, MA, MD, ME, MI, MN, MO, MT, ND, NE, NH, NJ, NM, NV, NY, OH, OK, OR, PA, RI, SC, TX, UT, VT, WA, WV, WY; 1999–2008: WI; 1999–2001 and 2003–2009: DC; 2001–2009: AR, NC, SD; 2002–2009: VA; 2003–2009: MS, TN.
[a]Identifies states with at least 1 county designated as CHSDA.

were the first solid data to note a 3-fold difference in incidence between the Alaska and Southwest regions.[4,21] The highest incidence rates were observed for Alaska, Northern Plains, and Southern Plains regions from 1999 to 2004.[4] Furthermore, AI/AN women were diagnosed with breast cancer at an earlier age, relative to White women, with more than twice as many AI/AN women diagnosed with breast cancer at younger than 40 years than Whites (8.5% vs 3.9%).[4] Similarly, in this study, overall death rates were also highest in these areas and lowest in the Southwest. In the Alaska region, the death rate from breast cancer in women aged 40 to 49 years was higher for AI/ANs than Whites.

These age and regional differences suggest a need to better understand the biology of cancer in these populations. Thus far, no prospective studies have identified whether the estrogen receptor (ER), the progesterone receptor (PR), or human epidermal growth factor receptor 2 (HER2) status are part of a higher aggressiveness of cancer in young AI/AN women. In a small retrospective pathology review of 100 breast cancer cases from the Alaska and Southwest regions, there were no molecular patterns that explained excess mortality (J. S. K., unpublished data). As previously mentioned, there was higher mortality in AI/AN women than among White women at younger ages (i.e., 40–49 years) in the Alaska region. These patterns might be influenced by many factors, including familial cancers with mutations, such as breast cancer 1 or 2, or Lynch syndrome. However, no genetic studies have been completed in a large AI/AN population. This could be the result of concerns for confidentiality in a smaller population, lack of genetic counselors within the IHS, or limited access to specialists and resources outside of IHS.

The decline in breast cancer mortality among Whites in every IHS region—but not among AI/ANs—partially reflected a decline in incidence, which might be associated with decreases in hormone replacement therapy (HRT) use.[22] Breast cancer incidence mirrored the social patterning of hormone use in which affluent White women were more likely to use HRT than other racial/ethnic and socioeconomic groups before the 2002 Women's Health Initiative Study.[22] After the findings of that study suggested that HRT was linked to an increased risk of breast cancer, use of HRT decreased among White women. Fewer AI/ANs and other racial/ethnic groups of women used HRT and had not experienced the same net harms of treatment as had White women. Therefore, AI/ANs and other racial/ethnic groups of women could not experience as much benefit from stopping those treatments.

Breast cancer screening can lead to detection of breast cancer at an early stage when it is amenable to treatment.[23] Racial differences in mammography use might contribute to the racial differences in breast cancer mortality observed in this study. Estimates from the 2000 to 2010 Behavioral Risk Factor Surveillance System data revealed that mammography use was higher among White women (76.7%) compared with AI/AN women (71.6%).[24] Also, mammography use varied considerably by region, with rates being lowest in the Southwest region (61.1%) and highest in the Southern Plains region (73.6%).[24] These lower screening rates might contribute to a later stage at diagnosis.

Stage at diagnosis is a key predictor of breast cancer mortality and survival.[25] Diagnosis at a later (regional or distant) stage relative to an early stage is more likely to lead to higher mortality. AI/AN women had less favorable socioeconomic status and more limited access to health care compared with White women,[26] and this contributed to persistent lower rates of screening and a higher percentage of late-stage diagnosis.[21,27] Data for 1999 to 2003 showed that 31.8% of invasive breast cancer cases among AI/AN women were diagnosed at a regional or distant stage compared with 27.0% of White women.[4] AI/AN women tended to be younger at the time of breast cancer diagnosis, with an average age at diagnosis of 57.5 years versus 63.4 years among White women.[4] Additionally, more than 30% of AI/AN women were diagnosed before age 50 years, compared with 19% of White women.[4]

The CDC National Breast and Cervical Cancer Early Detection Program (NBCCEDP) has provided screening for the underserved and uninsured population since 1991 and allows state programs some flexibility in screening for breast cancer in AI/AN women between the ages of 40 and 50 years. AI/AN women represented the highest percentage (9.7%) of US women screened through this program.[28] In addition, 49.2% of AI/AN women who were eligible for breast cancer screening through the NBCCEDP were actually screened; by contrast, only 11.2% of eligible White women were screened.[28] Further study is warranted to determine the extent to which the NBCCEDP has had an impact on stage at diagnosis for AI/AN women.

Advances in treatment accounted for about half of the decrease in breast cancer deaths from 1975 to 2000, but not all women benefited equally.[29] For AI/AN women, the ability to access health care varied geographically and tribally.[30] If available, access to health care services might be limited by travel distances to facilities or lack of transportation.[30,31] AI/AN women were more likely to experience delays in treatment after a mammogram with abnormal findings.[31] Wilson et al.[31] found that among Medicare beneficiaries, the interval from diagnosis to surgery was greater among AI/AN women than that for White women, and as a result, AI/AN women experienced a 5.6-fold higher breast cancer mortality than White women. Obtaining referrals to a cancer specialist might further delay treatments[31] and adversely affect survival of AI/AN women. Furthermore, for many reasons—ranging from the presence of comorbidities to transportation and sociocultural barriers—few AI/AN persons participated in clinical trials, which mainly represent state-of-the-art cancer care.[32]

Strengths and Limitations

Our study's key strength was that great effort was made to minimize misclassification of AI/AN race.[4,11,15] Race coding for AI/AN decedents included a combination of NCHS race classification on the death certificate and information derived from data linkages between the IHS patient registration database and the NDI.

Our findings were subject to some limitations. First, our study was restricted to AI/AN and White women living in CHSDA counties; therefore, the findings could not be generalized beyond women residing in these areas. In addition, racial misclassification of AI/ANs varied across the United States. Although effort was made to minimize these biases, there might still be some underestimation of breast cancer among AI/AN women. Furthermore, although the exclusion of Hispanic AI/AN women from the analyses reduced the overall count of deaths among AI/AN women by less than 5%, it might disproportionately affect some states. Another limitation was the use of death certificates to examine breast cancer mortality by race. A study by German et al.,[33] however, found that deaths from breast cancer were reported with high accuracy. Finally, the MIR might underestimate survival for breast cancer in cases where causes of death were not accurate and incidence and survival were not stable.[34]

Conclusions

The decline in breast cancer mortality among White women, but not among AI/AN women, suggested that there is a need for more targeted screening of AI/ANs and improved access to cancer care to ensure that breast cancers are detected at an early stage and followed by timely, high-quality treatment. These efforts are particularly important for AI/AN women who experience higher mortality from breast cancer than White women, such as young women (40–49 years) in the Alaska region and older women (≥ 65 years) in the Southern Plains region. Furthermore, these findings identified regions where survival from breast cancer was poor and where additional outreach is needed. They also provided a benchmark to measure the impact of breast cancer prevention and control interventions and programs in these areas. ■

About the Authors

Arica White, Lisa C. Richardson, Chunyu Li, and Donatus U. Ekwueme are with the Division of Cancer Prevention and Control, National Center for Chronic Disease and Health Promotion, Centers for Disease Control and Prevention (CDC), Atlanta, GA. Judith S. Kaur is with the Mayo Clinic, Rochester, MN.

Correspondence should be sent to Arica White, Centers for Disease Control and Prevention, Division of Cancer Prevention and Control, Epidemiology and Applied Research Branch, 4770 Buford Hwy NE, Mailstop F76, Atlanta, GA 30341-3717 (e-mail: awhite5@cdc.gov). Reprints can be ordered at http://www.ajph.org by clicking the "Reprints" link.

This article was accepted October 1, 2013.

***Note.** The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the CDC.*

Contributors

A. White designed and provided oversight for the study, acquired the data, conducted analysis and drafted the article. L. C. Richardson, C. Li, and D. U. Ekwueme contributed to the study design. All authors participated in the interpretation of the findings, reviewed and revised drafts, and approved the final draft of the article.

Acknowledgments

We would like to acknowledge David Espey, Donald Haverkamp, Melissa Jim, and William Helsel for their contributions to the data acquisition and analyses in this article.

Human Participant Protection

CDC and the Indian Health Service determined this project constituted public health practice and not research; therefore, no formal institutional review board approvals were required.

References

1. US Cancer Statistics Working Group. *United States Cancer Statistics: 1999–2009 Incidence and Mortality Web-based Report.* Atlanta, GA: US Department of Health and Human Services, Centers for Disease Control and Prevention and National Cancer Institute; 2013.

2. Jemal A, Simard EP, Dorell C, et al. Annual report to the nation on the status of cancer, 1975–2009, featuring the burden and trends in human papillomavirus (HPV)-associated cancers and HPV vaccination coverage levels. *J Natl Cancer Inst.* 2013;105(3):175–201.

3. Roubidoux MA. Breast cancer and screening in American Indian and Alaska Native women. *J Cancer Educ.* 2012;27(suppl 1):S66–S72.

4. Wingo PA, King J, Swan J, et al. Breast cancer incidence among American Indian and Alaska Native women: US, 1999–2004. *Cancer.* 2008;113(5 suppl):1191–1202.

5. Espey D, Paisano R, Cobb N. Regional patterns and trends in cancer mortality among American Indians and Alaska Natives, 1990–2001. *Cancer.* 2005;103(5):1045–1053.

6. Cobb N, Paisano RE. Patterns of cancer mortality among Native Americans. *Cancer*. 1998;83(11):2377–2383.

7. Hébert JR, Daguise VG, Hurley DM, et al. Mapping cancer mortality-to-incidence ratios to illustrate racial and sex disparities in a high-risk population. *Cancer*. 2009;115(11):2539–2552.

8. National Center for Health Statistics. US census populations with bridge race categories. 2012. Available at: http://www.cdc.gov/nchs/nvss/bridged_race.htm. Accessed August 15, 2012.

9. Edwards BK, Noone AM, Mariotto AB, et al. Annual report to the nation on the status of cancer, 1975–2010, featuring prevalence of comorbidity and impact on survival among persons with lung, colorectal, breast, or prostate cancer. *Cancer*. 2013;Epub ahead of print.

10. National Center for Health Statistics Division of Vital Statistics. National Vital Statistics System. 2012. Available at: http://www.cdc.gov/nchs/nvss.htm. Accessed August 15, 2012.

11. Espey DK, Jim MA, Richards T, Begay C, Haverkamp D, Roberts D. Methods for improving the quality and completeness of mortality data for American Indians and Alaska Natives. *Am J Public Health*. 2014;104(6 suppl 3):S286–S294.

12. *International Classification of Diseases, Ninth Revision*. Geneva, Switzerland: World Health Organization; 1980.

13. *International Classification of Diseases, 10th Revision*. Geneva, Switzerland: World Health Organization; 1992.

14. *International Classification of Diseases for Oncology, Third Edition*. Geneva, Switzerland: World Health Organization; 2000.

15. Jim MA, Arias E, Seneca DS, et al. Racial misclassification of American Indians and Alaska Natives by Indian Health Service Contract Health Service Delivery Area. *Am J Public Health*. 2014;104(6 suppl 3):S295–S302.

16. Anderson RN, Rosenberg HM. Age standardization of death rates: implementation of the year 2000 standard. *Natl Vital Stat Rep*. 1998;47(3):1–16, 20.

17. Tiwari RC, Clegg LX, Zou Z. Efficient interval estimation for age-adjusted cancer rates. *Stat Methods Med Res*. 2006;15(6):547–569.

18. Kim H-J, Fay MP, Feuer EJ, Midthune DN. Permutation tests for Joinpoint regression with applications to cancer rates. *Stat Med*. 2000;19:335–351.

19. Day JC. *Population Projections of the United States by Age, Sex, Race, and Hispanic Origin: 1995 to 2050*. US Bureau of the Census, Current Population Reports, P25-1130. Washington, DC: US Government Printing Office; 1996.

20. Wampler NS, Lash TL, Silliman RA, Heeren TC. Breast cancer survival of American Indian/Alaska Native women, 1973-1996. *Soz Praventivmed*. 2005;50(4):230–237.

21. Espey DK, Wu XC, Swan J, et al. Annual report to the nation on the status of cancer, 1975–2004, featuring cancer in American Indians and Alaska Natives. *Cancer*. 2007;110(10):2119–2152.

22. Krieger N, Chen JT, Waterman PD. Decline in US breast cancer rates after the Women's Health Initiative: socioeconomic and racial/ethnic differentials. *Am J Public Health*. 2010;100(suppl 1):S132–S139.

23. Hofvind S, Ursin G, Tretli S, Sebuodegard S, Moller B. Breast cancer mortality in participants of the Norwegian Breast Cancer Screening Program. *Cancer*. 2013;119(17):3106–3112.

24. Cobb N, Espey D, King J. Health behaviors and risk factors among American Indians and Alaska Natives, 2000–2010. *Am J Public Health*. 2014;104(6 suppl 3):S481–S489.

25. Howlader NNA, Krapcho M, Neyman N, et al. SEER cancer statistics review, 1975–2009 (vintage 2009 populations). Available at: http://seer.cancer.gov/csr/1975_2009_pops09. Accessed August 15, 2012.

26. Kaiser Family Foundation. *Putting Women's Health Care Disparities on the Map: Examining Racial and Ethnic Disparities at the State Level*. Menlo Park, CA: Henry J. Kaiser Foundation; 2009.

27. Li CI, Malone KE, Daling JR. Differences in breast cancer stage, treatment, and survival by race and ethnicity. *Arch Intern Med*. 2003;163(1):49–56.

28. Tangka FK, Dalaker J, Chattopadhyay SK, et al. Meeting the mammography screening needs of underserved women: the performance of the National Breast and Cervical Cancer Early Detection Program in 2002–2003 (United States). *Cancer Causes Control*. 2006;17(9):1145–1154.

29. Berry DA, Cronin KA, Plevritis SK, et al. Effect of screening and adjuvant therapy on mortality from breast cancer. *N Engl J Med*. 2005;353(17):1784–1792.

30. Cunningham PJ, Cornelius LJ. Access to ambulatory care for American Indians and Alaska Natives; the relative importance of personal and community resources. *Soc Sci Med*. 1995;40(3):393–407.

31. Wilson RT, Adams-Cameron M, Burhansstipanov L, et al. Disparities in breast cancer treatment among American Indian, Hispanic and non-Hispanic White women enrolled in Medicare. *J Health Care Poor Underserved*. 2007;18(3):648–664.

32. Hodge FS, Weinmann S, Roubideaux Y. Recruitment of American Indians and Alaska Natives into clinical trials. *Ann Epidemiol*. 2000;10(8 suppl 1):S41–S48.

33. German RR, Fink AK, Heron M, et al. The accuracy of cancer mortality statistics based on death certificates in the United States. *Cancer Epidemiol*. 2011;35(2):126–131.

34. Asadzadeh Vostakolaei F, Karim-Kos HE, Janssen-Heijnen ML, Visser O, Verbeek AL, Kiemeney LA. The validity of the mortality to incidence ratio as a proxy for site-specific cancer survival. *Eur J Public Health*. 2011;21(5):573–577.

This article has been cited by:

1. Mary C. White, David K. Espey, Judith Swan, Charles L. Wiggins, Christie Eheman, Judith S. Kaur. 2014. Disparities in Cancer Mortality and Incidence Among American Indians and Alaska Natives in the United States. *American Journal of Public Health* **104**:S3, S377-S387. [Abstract] [Full Text] [PDF] [PDF Plus]