Ovarian and Uterine Cancer Incidence and Mortality in American Indian and Alaska Native Women, United States, 1999–2009

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Objectives. We examined geographic differences and trends in incidence and mortality of ovarian and uterine cancer in American Indian/Alaska Native (AI/AN) women.

Methods. We linked mortality data (1990–2009) and incidence data (1999–2009) to Indian Health Service (IHS) records. Death (and incidence) rates for ovarian and uterine cancer were examined for AI/AN and White women; Hispanics were excluded. Analyses focused on Contract Health Service Delivery Area (CHSDA) counties.

Results. AI/AN and White women had similar ovarian and uterine cancer death rates. Ovarian and uterine cancer incidence and death rates were higher for AI/ANs residing in CHSDA counties than for all US counties. We also observed geographic differences, regardless of CHSDA residence, in ovarian and uterine cancer incidence and death rates in AI/AN women by IHS region; Pacific Coast and Southern Plains women had higher ovarian cancer death rates and Northern Plains women had higher uterine cancer death rates.

Conclusions. Regional differences in the incidence and mortality of ovarian and uterine cancers among AI/AN women in the United States were significant. More research among correctly classified AI/AN women is needed to understand these differences. (*Am J Public Health.* 2014;104:S423–S431. doi:10.2105/AJPH.2013.301781)

Ovarian and uterine cancers are among the top 10 leading causes of cancer deaths and incidence among US women. In 2009, 14 436 deaths resulted from ovarian cancer and 7713 deaths resulted from cancer of the uterine corpus. Additionally, 20 460 new cases of ovarian cancer and 44 192 cases of cancer of the uterine corpus occurred in the United States, accounting for 3% and 6% of all cancer among women, respectively.[1] Incidence rates (IRs) for ovarian cancer decreased from 2005 to 2009, and although ovarian cancer still causes more deaths than any other cancer of the female reproductive system, the average death rate for ovarian cancer also decreased by 2.0% per year during this time period.[1] Alternatively, both death rates and IRs increased for uterine cancer among all women from 2005 to 2009.[2]

Cancer, including ovarian and uterine cancer, is a major public health concern in American Indian/Alaska Native (AI/AN) communities.[3] Studies examining cancer incidence patterns among AI/AN populations have generally been limited to restricted time intervals or selected geographic regions.[4–12] Additionally, misclassification of AI/AN race in central cancer registry data and on death certificates has led to underestimation of cancer burden in these populations.[13,14] Previous studies have documented misclassification of AI/AN persons as another race in central cancer registry data and that the extent of variation varies by registry.[15–17] Arias et al.[14] reported that approximately 42% of AI/AN decedents were misclassified as White on death certificates. Cancer information for AI/AN populations is known to be incomplete because the racial/ethnic status of many of these individuals is not correctly identified in medical and death records.[18] Although linkages between central cancer registries and Indian Health Service (IHS) records have improved incidence estimates for AI/AN populations,[17,19] most estimates of cancer mortality currently available likely underestimate death rates in this population.

According to a study of data from the Alaska Tumor Registry, Alaska Native women have exhibited some of the highest IRs of cancer overall and different patterns of site-specific incidence compared with other US populations.[20] Reportedly, trends in cancer IRs among AI/AN people have been stable or decreasing, whereas cancer death rates have increased.[20] Although differences in overall cancer rates have been observed,[21] little is known about the rates of cancer of the uterine corpus and ovary in AI/AN populations.

This article provides a detailed overview of the burden of cancer of the ovaries and uterine corpus among AI/AN populations. The main objective of this study was to improve our understanding of uterine and ovarian cancer incidence, stage at diagnosis, and mortality in AI/AN women relative to White women by minimizing the effect of racial misclassification in the cancer data. The secondary objective is to examine geographic differences and trends in incidence and mortality of ovarian and uterine cancer in AI/AN populations.

METHODS

Newly diagnosed cancers of the uterus and ovary from 1999 through 2009 were identified from the population-based central cancer registries participating in the Centers for Disease Control and Prevention's National Program of Cancer Registries and the National Cancer Institute's Surveillance, Epidemiology, and End Results program. For data to be included for a given year, registries had to meet data quality and completeness standards developed for US Cancer Statistics.[1] Participating registries classified tumor histology, tumor behavior, and primary cancer site according to the 3rd edition of the *International Classification of Diseases for Oncology* (*ICD-O-3*).[22] We included only invasive cancers of the uterus (*ICD-O-3* codes C540–C549 and C559), and ovaries (*ICD-O-3* code C569) in our analysis. More detailed description about data sources and methodology can be found elsewhere in this supplement.[13]

To identify AI/AN cancer cases misclassified as other races, central cancer registries regularly link their cancer records with IHS patient registration files.[17] AI/AN individuals must provide proof of enrollment in a federally recognized tribe to receive health care from the IHS. The access to health care by IHS is greatest in Contract Health Service Delivery Area (CHSDA) counties, which, in general, contain, or are adjacent to, a federally recognized tribal reservation, tribal lands, or both.[19]

Standards for coding of stage of disease at diagnosis changed during the period of this study; therefore, we restricted the analysis of stage at diagnosis to incident cases diagnosed during the most recent years (2004–2009). We examined stage at diagnosis using the Collaborative Stage Derived Surveillance, Epidemiology, and End Results Summary Stage 2000 variable.[23]

Mortality Data

We obtained mortality data from the Centers for Disease Control and Prevention's National Center for Health Statistics (NCHS). NCHS combined vital record death files obtained from each state to create the National Death Index and then linked it with the IHS patient registration database to determine vital status and cause of death of decedents who had received health care in IHS or tribal facilities.[24] After this linkage, a flag indicating a positive link to IHS was added to the National Vital Statistics System's mortality file as an additional indicator of AI/AN ancestry. This death information is combined with corresponding annual bridged race intercensal population estimates to create an AI/AN–US Mortality Database within SEER*Stat version 8.0.4 (National Cancer Institute, Bethesda, MD).[25] This database combines race classification by NCHS on the basis of the death certificate and information derived from data linkages between the IHS patient registration database and the National Death Index. It includes every death for all races reported to NCHS from 1990 through 2009.[26] NCHS and the Census Bureau use nearly identical bridging algorithms to assign a single race to decedents with multiple races reported on the death certificate.

The underlying causes of death were coded according to the *International Classification of Diseases, Ninth Revision*[27] (*ICD-9*) and *International Classification of Diseases, 10th Revision*[28] (*ICD-10*) for 1990 to 1998 and 1999 to 2009, respectively. We converted *ICD-9* death codes (182, 172, 183.0) from 1990 to 1998 to standard *ICD-10* death codes (C54, C55, C56) to ease comparisons across the 2 periods.[29]

Population Estimates

Bridged single-race population estimates developed by the US Census Bureau and NCHS and adjusted for population shifts resulting from Hurricanes Katrina and Rita in 2005 were included as denominators in the calculations of cancer incidence and death rates.[30] Postcensal population denominators were race-specific, ethnicity-specific, and sex-specific county population estimates from the 2000 US Census, as modified by the Surveillance, Epidemiology, and End Results program and aggregated to the state and national levels.[17,19] Bridged single-race data allowed for comparability between the pre- and post-2000 race/ethnicity population estimates during this study period.

Geographic Coverage

To create most of the tabulations in this article, we restricted the analyses to IHS Contract Health Service Delivery Area or Tribal Service Delivery Area (abbreviated henceforth as "CHSDA" although TSDA are also implied) counties that, in general, contain federally recognized tribal or off-reservation trust land or are adjacent to tribal lands.[19] The IHS uses CHSDA residence to determine eligibility for services not directly available within the IHS. Linkage studies have indicated less misclassification of race for AI/AN population in these counties.[14,19] The CHSDA counties also have higher proportions of AI/AN individuals in relation to the total population than do non-CHSDA counties, with 64% of the US AI/AN population residing in the 634 counties designated as CHSDA (these counties represent 20% of the 3141 counties in the United States). For this reason, we conducted analyses for residents of all US counties, for residents of CHSDA counties, and for each of the 6 IHS regions separately (Alaska, Pacific Coast, Northern Plains, Southern Plains, Southwest, and East). Similar regional analyses have been used for other health-related studies focusing on AI/AN populations.[21,31,32] Although less geographically representative, analyses restricted to CHSDA counties are presented for death rates in this article for the purpose of offering improved accuracy in interpreting mortality statistics for AI/AN populations.

Analysis

We analyzed incidence data from registries that met high quality criteria for publication in the annual US Cancer Statistics Web-based report.[1] The states that met quality criteria and were thus included in the analysis are listed in the footnotes of the tables. We excluded mortality data from Louisiana (1990), New Hampshire (1990–1992), and Oklahoma (1990–1996) because Hispanic origin was not collected on death certificates in those states for those years. We conducted all analyses using SEER*Stat version 8.0.4 (National Cancer Institute, Bethesda, MD). Age-adjusted death rates, IRs, standardized rate ratios (RRs), and 95% confidence intervals (CIs) were calculated for AI/AN women overall and by age group (<50, 50–59, 60–69, ≥ 70 years) for all US counties and CHSDA counties and compared with those for White women.[33] During preliminary analyses, it was discovered that the updated bridged intercensal population estimates significantly overestimated AI/ANs of Hispanic origin.[34] Therefore, to avoid underestimating mortality and incidence in AI/ANs, we limited analyses to non-Hispanic AI/ANs. Non-Hispanic Whites were chosen as the most homogeneous referent group. For conciseness, the term "non-Hispanic" is omitted henceforth when discussing both groups.

All rates are expressed per 100 000 and were age adjusted by the direct method to the 2000 US standard population (Census P25-1130). The 95% CIs were estimated using the Tiwari method.[35] We assessed temporal changes in annual age-adjusted incidence and death rates, including the annual percentage change (APC) for each interval, using Joinpoint regression techniques developed by the National Cancer Institute and available within the SEER*Stat software.[36] Statistical significance was set at a *P* level of less than .05.

RESULTS

Age-adjusted ovarian and uterine cancer death rates, RRs, and 95% CIs by IHS region for CHSDA counties and all US counties for AI/AN women compared with White women are presented in Table 1. There were 135 549 ovarian cancer deaths (death rate = 9.1) and 59 540 uterine cancer deaths (death rate = 3.9) among AI/AN and White women from 1999 through 2009. Of these, 705 ovarian and 314 uterine cancer deaths were among AI/AN women. In CHSDA counties, AI/AN women accounted 1.7% of ovarian and 1.8%

TABLE 1—Age-Adjusted Death Rates and Counts for Ovarian Cancer and Uterine Cancer, by IHS Region, for AI/AN Compared With White Females, All Ages: United States, 1999–2009

	CHSDA Counties					All US Counties				
Variable	AI/AN Count	AI/AN Rate	White Count	White Rate	AI/AN: White RR (95% CI)	AI/AN Count	AI/AN Rate	White Count	White Rate	AI/AN: White RR (95% CI)
Ovary										
IHS region										
Northern Plains	74	8.3	5015	9.0	0.92 (0.71, 1.16)	98	6.9	24 488	9.2	0.75* (0.60, 0.93)
Alaska	27	7.0	122	6.5	1.08 (0.68, 1.67)	27	7.0	122	6.5	1.08 (0.68, 1.67)
Southern Plains	126	9.7	1839	8.4	1.15 (0.95, 1.38)	148	8.7	9837	8.6	1.02 (0.86, 1.20)
Southwest	168	9.5	4065	8.6	1.10 (0.93, 1.29)	175	9.1	6636	8.7	1.05 (0.89, 1.22)
Pacific Coast	105	10.2	10 143	10.1	1.01 (0.81, 1.23)	141	9.2	18 940	10.1	0.91 (0.76, 1.08)
East	22	5.4	9640	8.9	0.61* (0.37, 0.92)	116	4.7	74 821	9.1	0.52* (0.43, 0.63)
Age, y										
All ages	522	9.0	30 824	9.2	0.98 (0.90, 1.08)	705	7.5	134 844	9.2	0.82* (0.76, 0.89)
< 50	53	0.9	1977	1.1	0.84 (0.63, 1.10)	75	0.8	9453	1.2	0.66* (0.52, 0.83)
50–59	116	13.1	4578	12.9	1.01 (0.82, 1.20)	148	9.8	20 465	13.3	0.74* (0.62, 0.87)
60–69	133	26.9	6909	28.8	0.93 (0.90, 1.28)	188	23.6	29 821	28.5	0.83* (0.71, 0.96)
≥ 70	220	54.1	17 360	52.3	1.04 (0.85, 1.11)	294	45.6	75 105	51.1	0.89 (0.79, 1.00)
Corpus uteri										
IHS region										
Northern Plains	40	5.4	2497	4.4	1.22 (0.85, 1.67)	56	4.5	11 941	4.4	1.03 (0.76, 1.34)
Alaska	. . .	1.9	39	2.2	0.88 (0.34, 1.93)	–	1.9	39	2.2	0.88 (0.34, 1.93)
Southern Plains	62	4.5	819	3.7	1.22 (0.92, 1.59)	72	4.1	4024	3.4	1.18 (0.91, 1.49)
Southwest	59	3.3	1490	3.1	1.06 (0.80, 1.38)	63	3.3	2451	3.2	1.03 (0.78, 1.33)
Pacific Coast	50	4.7	4044	4.0	1.19 (0.86, 1.58)	61	3.9	7867	4.1	0.96 (0.72, 1.24)
East	15	3.6	3944	3.6	1.00 (0.55, 1.66)	54	2.4	32 904	3.9	0.62* (0.46, 0.81)
Age, y										
All ages	234	4.0	12 883	3.8	1.07 (0.94, 1.23)	314	3.4	59 226	3.9	0.87* (0.77, 0.97)
< 50	30	0.5	593	0.3	1.61 (1.08, 2.32)	40	0.4	2734	0.3	1.23 (0.88, 1.68)
50–59	42	4.8	1604	4.5	1.06 (0.76, 1.43)	51	3.4	7546	4.9	0.69 (0.51, 0.91)
60–69	65	13.0	2767	11.5	1.13 (0.87, 1.45)	80	10.0	12 886	12.3	0.81 (0.64, 1.01)
≥ 70	97	23.9	7919	23.5	1.02 (0.82, 1.24)	143	22.1	36 060	24.2	10.91 (0.77, 1.08)

Note. AI/AN = American Indians/Alaska Natives; CHSDA = Contract Health Service Delivery Areas; CI = confidence interval; IHS = Indian Health Service; NPCR = National Program of Cancer Registries; RR = rate ratio; SEER = Surveillance, Epidemiology, and End Results program. Dashes indicate that counts < 6 are suppressed; if no cases reported, then rates and RRs could not be calculated. RRs were calculated in SEER*Stat before rounding of rates and may not equal RRs calculated from rates presented in table. Analyses are limited to persons of non-Hispanic origin. Rates are per 100 000 persons and were age adjusted to the 2000 US standard population (11 age groups; Census P25-1130). AI/AN race is reported by NPCR and SEER registries or through linkage with the IHS patient registration database. 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%. 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). Cancer causes of death were created using the SEER cause of death recode.
Source. AI/AN–US Mortality Database (1990–2009).
[a]State with ≥ 1 county designated as CHSDA.
**P* < .05.

of uterine cancer deaths. The death rate for ovarian cancer among AI/AN women residing in CHSDA counties was 9.0 per 100 000 women, whereas for uterine cancer it was 4.0. We observed that AI/AN and White women in CHSDA counties had similar death rates from ovarian cancer (9.0 vs 9.2) and uterine cancer (4.0 vs 3.8). The observed death rates varied by region. From 1999 to 2009, among AI/AN women residing in CHSDA counties, ovarian cancer death rates ranged from 5.4 in the East to 10.2 in the Pacific Coast; uterine cancer death rates ranged from 1.9 in Alaska to 5.4 in the Northern Plains. When examined by age, death rates for both uterine and ovarian cancer increased with age regardless of geography.

Cancer Incidence Rates

Ovarian and uterine cancer case counts and age-adjusted IRs, RRs, and 95% CIs by IHS region, CHSDA county, and age group for AI/AN

TABLE 2—Age-Adjusted Incidence Rates and Counts for Ovarian Cancer and Uterine Cancer, by IHS Region, for AI/AN Compared With White Females: United States, 1999–2009

	CHSDA Counties					All US Counties				
Variable	AI/AN Count	AI/AN Rate	White Count	White Rate	AI/AN: White RR (95% CI)	AI/AN Count	AI/AN Rate	White Count	White Rate	AI/AN: White RR (95% CI)
Ovary										
IHS region										
Northern Plains	112	11.2	6976	13.7	0.82* (0.67, 0.99)	165	10.3	34 674	13.9	0.74* (0.62, 0.87)
Alaska	52	12.5	266	12.1	1.04 (0.74, 1.41)	52	12.5	266	12.1	1.04 (0.74, 1.41)
Southern Plains	239	16.8	2719	13.2	1.28* (1.11, 1.46)	280	14.7	14 477	13.2	1.12 (0.99, 1.26)
Southwest	268	13.5	5886	13.0	1.04 (0.91, 1.18)	282	13.1	9767	13.3	0.99 (0.87, 1.11)
Pacific Coast	144	12.4	13 793	14.4	0.86 (0.72, 1.03)	182	10.5	25 823	14.4	0.73* (0.62, 0.85)
East	36	7.9	13 829	13.9	0.57* (0.39, 0.79)	142	5.4	102 188	13.8	0.39* (0.33, 0.46)
Age, y										
All ages	851	13.3	43 469	13.8	0.96 (0.89, 1.03)	1103	10.6	187 195	13.8	0.77* (0.72, 0.82)
< 50	234	4.0	6957	4.0	1.0 (0.87, 1.14)	301	3.2	31 979	4.2	0.75* (0.67, 0.84)
50–59	210	24.0	8981	25.8	0.93 (0.81, 1.07)	275	18.5	38 980	26.1	0.71* (0.63, 0.80)
60–69	194	39.1	9790	41.1	0.95 (0.82, 1.1)	259	32.7	41 539	40.8	0.8* (0.71, 0.91)
≥ 70	213	52.6	17 741	55.0	0.96 (0.83, 1.1)	268	42.1	74 697	53.1	0.79* (0.70, 0.90)
Corpus uteri										
IHS region										
Northern Plains	224	22.9	13 474	26.4	0.86* (0.75, 0.99)	308	19.0	67 703	27.2	0.70* (0.62, 0.79)
Alaska	74	17.1	507	23.1	0.74* (0.56, 0.95)	74	17.1	507	23.1	0.74* (0.56, 0.95)
Southern Plains	392	27.0	4128	20.0	1.35* (1.21, 1.50)	435	22.4	21 883	19.8	1.13* (1.02, 1.25)
Southwest	451	21.5	9034	19.6	1.09 (0.99, 1.20)	475	20.7	15 131	20.2	1.03 (0.93, 1.13)
Pacific Coast	296	23.6	23 046	23.9	0.99 (0.87, 1.11)	378	20.2	44 239	24.4	0.83* (0.74, 0.92)
East	67	14.8	25 029	25.2	0.59* (0.45, 0.75)	258	9.9	190 045	25.5	0.39* (0.34, 0.44)
Age, y										
All ages	1504	22.6	75 218	23.8	0.95* (0.90, 1.00)	1928	17.9	339 508	24.9	0.72* (0.69, 0.75)
< 50	465	8.3	8997	5.1	1.62* (1.47, 1.78)	584	6.3	41 753	5.4	1.17* (1.08, 1.27)
50–59	422	48.2	19 917	56.8	0.85* (0.77, 0.93)	535	36.0	90 628	60.4	0.6* (0.55, 0.65)
60–69	334	66.8	20 722	86.9	0.77* (0.69, 0.86)	441	55.1	93 669	91.8	0.6* (0.54, 0.66)
≥ 70	283	68.8	25 582	80.7	0.85* (0.76, 0.96)	368	57.3	113 458	82.3	0.7* (0.63, 0.77)

Note. AI/AN = American Indians/Alaska Natives; CHSDA = Contract Health Service Delivery Areas; CI = confidence interval; IHS = Indian Health Service; NPCR = National Program of Cancer Registries; RR = rate ratios; SEER = Surveillance, Epidemiology, and End Results program. Dashes indicate that counts < 6 are suppressed; if no cases reported, then rates and RRs could not be calculated. RRs were calculated in SEER*Stat before rounding of rates and may not equal RRs calculated from rates presented in table. Analyses are limited to persons of non-Hispanic origin. Rates are per 100 000 persons and were age adjusted to the 2000 US standard population (19 age groups; Census P25-1130). AI/AN race is reported by NPCR and SEER registries or through linkage with the IHS patient registration database. 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%. 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).

Source. Cancer registries in the Centers for Disease Control and Prevention's NPCR; the National Cancer Institute's SEER program. Years of data and registries used: 1999–2008: WI[a]; 1999–2009 (43 states): AK,[a] AL,[a] AZ,[a] CA,[a] CO,[a] CT,[a] DE, FL,[a] GA, HI, IA,[a] ID,[a] IL, IN,[a] KS,[a] KY, LA,[a] MA,[a] MD, ME,[a] MI,[a] MN,[a] MO, MT,[a] ND,[a] NE,[a] NH, NJ, NM,[a] NV,[a] NY,[a] OH, OK,[a] OR,[a] PA,[a] RI,[a] SC,[a] TX,[a] UT,[a] VT, WA,[a] WV, WY[a]; 1999–2001 and 2003–2009: DC; 2001–2009: AR, NC,[a] SD[a]; 2002–2009: VA; 2003–2009: MS,[a] TN.

[a]State with ≥ 1 county designated as CHSDA.

*$P < .05$.

women are presented and compared with those for White women in Table 2. In all US counties, there were a total of 188 298 ovarian and 341 436 uterine cancer cases, of which 1103 (0.6%) ovarian and 1928 (0.6%) uterine were diagnosed in AI/AN women. In CHSDA counties, there were 44 320 ovarian and 76 722 uterine cancer cases. Of these, 851 (1.9%) ovarian and 1504 (2.0%) uterine cancer cases were reported in AI/AN women. In CHSDA counties, the IRs for ovarian and uterine cancer cases were, respectively, 13.3 and 22.6 per 100 000 in AI/AN women. When compared with Whites, uterine cancer IRs for AI/AN women were marginally but significantly lower for women residing in CHSDA counties, whereas we found no significant differences for ovarian cancer IRs. IRs for ovarian and uterine cancers showed regional variations in AI/AN women. From 1999 to 2009, among AI/AN women residing in CHSDA counties, ovarian cancer incidence ranged from 7.9 in the East to 16.8 in the Southern Plains, and uterine cancer incidence ranged from 14.8 in the East to 27.0 in the Southern Plains. When examined by age, IRs for both uterine and ovarian cancer increased with age regardless of race/ethnicity. Although overall ovarian cancer IRs in CHSDA counties for AI/AN women were similar to those in Whites, rates for women living in the Southern Plains were significantly higher in AI/AN women. When examined by age and region, ovarian cancer rates were either significantly lower or similar to White women in all age groups, with the exception of the 60 to 69 years age group (53.2 vs 40.0) and 70 years and older age group (70.5 vs 53.8) in the Southern Plains, for which rates in AI/AN women residing in CHSDA counties were significantly higher than those in White women (data not shown). Similarly, uterine cancer IRs were significantly higher in AI/AN women than in White women in all age groups in the Southern Plains region, and the younger than 50 years age group in the Southwest (IRs 10.7 vs 4.5) and Pacific Coast (IRs 6.8 vs 4.7) regions (data not shown). Overall in the United States, uterine cancer IRs were significantly higher in AI/AN women than in White women in the younger than 50 years age group (8.3 vs 5.1).

Stage at Diagnosis

We compared invasive ovarian and uterine cancer IRs and percentage distribution by stage at diagnosis for AI/AN women residing in CHSDA counties and diagnosed in 2004 to 2009 with those for White women (Table 3). From 2004 to 2009, 495 ovarian and 934 uterine cancers were diagnosed among AI/AN women residing in CHSDA counties and 23 304 ovarian and 42 683 uterine cancers were diagnosed among White women. About 11.3% of ovarian and 9.1% of uterine cancer cases were not staged in AI/AN women and about 10.6% of ovarian and 6.5% of uterine cancer cases were not staged in White women. When compared with White women, a slightly higher percentage of ovarian cancer cases were diagnosed at a local stage and a slightly higher percentage of uterine cancer cases were diagnosed at a distant stage among AI/AN women. Among AI/AN women, we observed a higher rate and proportion of ovarian cancer cases diagnosed at a distant stage regardless of region (Tables A and B, available as a supplement to the online version of this article at http://www.ajph.org). Conversely, the majority of uterine cancers were diagnosed at a localized stage, regardless of region (Tables C and D, available as a supplement to the online version of this article at http://www.ajph.org).

Cancer Incidence and Death Trends

Overall, 1023 ovarian and 453 uterine cancer deaths were reported from 1990 to 2009 in AI/AN women in all US counties. Ovarian and uterine cancer IRs by year for CHSDA counties are shown in Figure 1, and death rates are shown in Figure 2. The death rates for both cancers among AI/AN women

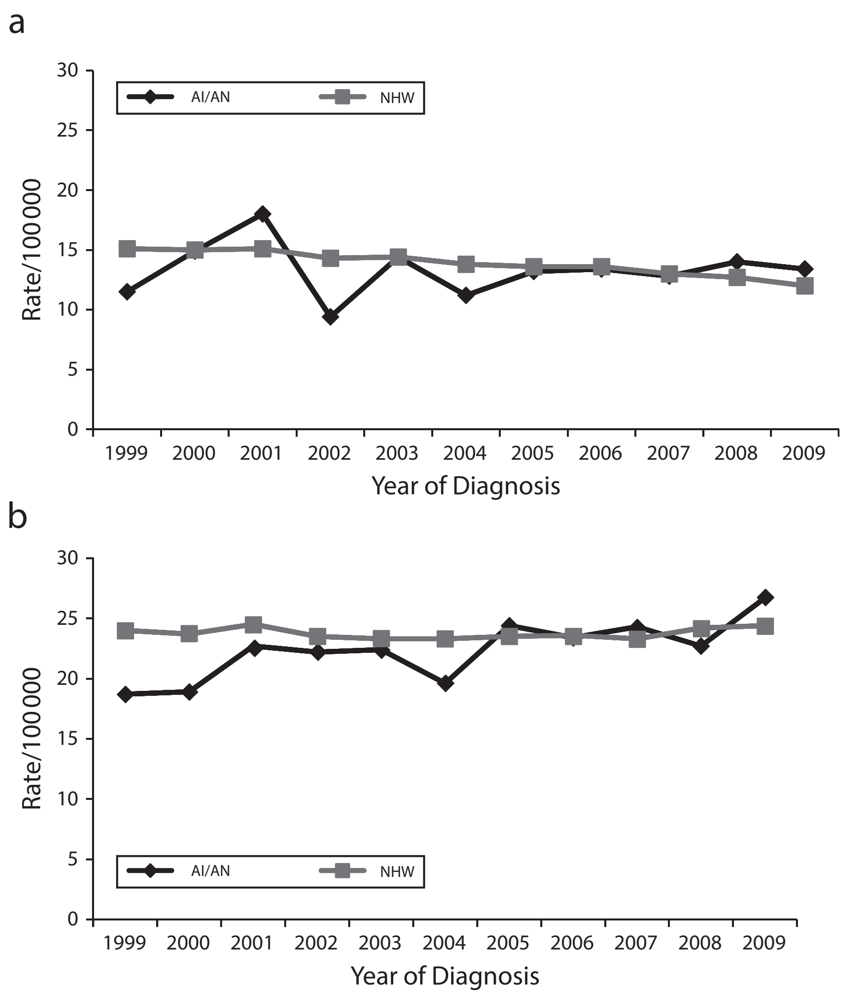
TABLE 3—Invasive Ovarian and Uterine Cancer Incidence Rates and Percentage Distribution by Stage for AI/AN Compared With White Females: CHSDA Counties, United States, 2004–2009

	Localized		Regional		Distant		Unstaged		All	
Site and Race/Ethnicity	Count (%)	Rate (95% CI)	Count (%)	Rate (95% CI)	Count (%)	Rate (95% CI)	Count (%)	Rate (95% CI)	Count (%)	Rate (95% CI)
Ovary										
AI/AN	77 (15.55)	1.8 (1.4, 2.2)	78 (15.75)	2.0 (1.6, 2.5)	284 (57.37)	7.5 (6.6, 8.5)	56 (11.31)	1.8 (1.3, 2.3)	495 (100)	13.0 (11.9, 14.3)
White	3004 (12.89)	1.9 (1.8, 1.9)	3941 (16.91)	2.3 (2.2, 2.4)	13 884 (59.57)	7.7 (7.5, 7.8)	2475 (10.62)	1.3 (1.2, 1.3)	23 304 (100)	13.1 (12.9, 13.3)
Corpus uteri										
AI/AN	600 (64.23)	14.8 (13.6, 16.0)	175 (18.73)	4.4 (3.8, 5.2)	74 (7.92)	2.0 (1.6, 2.6)	85 (9.10)	2.4 (1.9, 2.9)	934 (100)	23.6 (22.0, 25.2)
White	28 750 (67.35)	16.1 (15.9, 16.3)	8279 (19.39)	4.6 (4.5, 4.7)	2882 (6.75)	1.6 (1.5, 1.6)	2772 (6.49)	1.5 (1.4, 1.5)	42 683 (100)	23.7 (23.5, 24.0)

Note. AI/AN = American Indians/Alaska Natives; CHSDA = Contract Health Service Delivery Areas; CI = confidence interval; IHS = Indian Health Service; NPCR = National Program of Cancer Registries; SEER = Surveillance, Epidemiology, and End Results program. Analyses are limited to persons of non-Hispanic origin. Rates are per 100 000 persons and were age adjusted to the 2000 US standard population (19 age groups; Census P25-1130). AI/AN race is reported by NPCR and SEER registries or through linkage with the IHS patient registration database. 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%. 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).

Source. Cancer registries in the Centers for Disease Control and Prevention's NPCR; the National Cancer Institute's SEER program. Years of data and registries used: 1999–2008: WI[a]; 1999–2009 (43 states): AK,[a] AL,[a] AZ,[a] CA,[a] CO,[a] CT,[a] DE, FL,[a] GA, HI, IA,[a] ID,[a] IL, IN,[a] KS,[a] KY, LA,[a] MA,[a] MD, ME,[a] MI,[a] MN,[a] MO, MT,[a] ND,[a] NE,[a] NH, NJ, NM,[a] NV,[a] NY,[a] OH, OK,[a] OR,[a] PA,[a] RI,[a] SC,[a] TX,[a] UT,[a] VT, WA,[a] WV, WY[a]; 1999–2001 and 2003–2009: DC; 2001–2009: AR, NC,[a] SD[a]; 2002–2009: VA; 2003–2009: MS,[a] TN.

[a]State with ≥ 1 county designated as CHSDA.



Note. AI/AN = American Indians/Alaska Natives; CHSDA = Contract Health Service Delivery Areas; CI = confidence interval; IHS = Indian Health Service; NHW = non-Hispanic White; NPCR = National Program of Cancer Registries; SEER = Surveillance, Epidemiology, and End Results Program. Rates per 100 000 persons and were age adjusted to the 2000 US standard population (11 age groups; Census P25-1130). AI/AN race is reported by NPCR and SEER registries or through linkage with the IHS patient registration database. Includes only AI/AN of non-Hispanic origin.

Source. Cancer registries in the Centers for Disease Control and Prevention's NPCR or the National Cancer Institute's SEER program. Years of data and registries used are as follows: 1999–2008: WI[a]; 1999–2009 (43 states): AK,[a] AL,[a] AZ,[a] CA,[a] CO,[a] CT,[a] DE, FL,[a] GA, HI, IA,[a] ID,[a] IL, IN,[a] KS,[a] KY, LA,[a] MA,[a] MD, ME,[a] MI,[a] MN,[a] MO, MT,[a] ND[a] NE,[a] NH, NJ, NM,[a] NV,[a] NY,[a] OH, OK,[a] OR,[a] PA,[a] RI,[a] SC,[a] TX,[a] UT,[a] VT, WA,[a] WV, WY[a]; 1999–2001 and 2003–2009: DC; 2001–2009: AR, NC,[a] SD[a]; 2002–2009: VA; and 2003–2009: MS,[a] TN.

[a]State with ≥ 1 county designated as CHSDA.

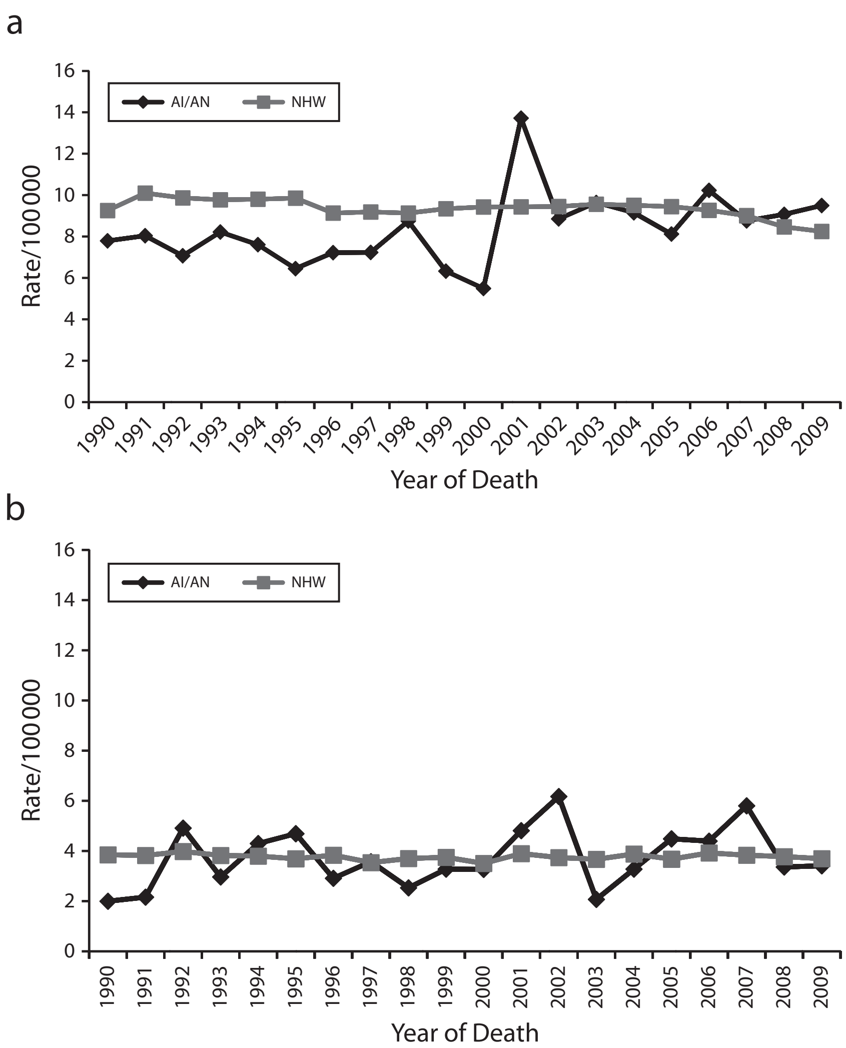
FIGURE 1—Incidence rates by year for (a) ovarian cancer and (b) uterine cancer: CHSDA counties; United States; 1999–2009.

fluctuated over the past 2 decades. Among White women, ovarian cancer death rates showed a nonsignificant increase from 1990 to 1992 (APC = 3.3%), followed by a significant decrease from 1992 to 1997 (APC = –1.8%). Ovarian cancer rates remained level from 1997 to 2005 (APC = 0.5%) followed by a significant decrease from 2005 to 2009 (APC = 3.7%). Uterine cancer death rates remained level from 1990 to 2009 for both AI/AN and White women. Ovarian cancer incidence showed a decreasing trend for White women (APC = –6.0 for 1999–2002, APC = –2.3 for 2002–2009). Uterine cancer IRs remained level for AI/AN and White women (Joinpoint trend data tables are not shown).

DISCUSSION

Our results demonstrated that, overall, ovarian and uterine cancer death rates in AI/AN women in CHSDA areas were similar to those in White women. We observed differences in IRs and death rates for ovarian and uterine cancer in AI/AN women by IHS region, with women in the Pacific Coast and Southern Plains having a higher ovarian cancer death rate and women in the Northern Plains having a higher uterine cancer death rate. Furthermore, comparing AI/AN women with White women, ovarian cancer death rates were higher in the Alaska, Southern Plains, and Southwest regions. Uterine cancer death rates, when comparing AI/AN women with White women, were higher in the Northern Plains, Southern Plains, Southwest, and Pacific Coast regions. Although overall uterine cancer IRs were marginally lower in AI/AN women in the Southern Plains, they were 35% higher than those of White women. Ovarian cancer IRs were also higher in AI/AN women than in White women in the Southern Plains. For AI/AN women aged 50 years or younger, uterine cancer IRs were higher than for White women. We observed, in comparison with White women, AI/AN women had a higher rate and proportion of ovarian cancer cases diagnosed at a distant stage and the majority of uterine cancers diagnosed at a localized stage.

To our knowledge, this study is the first focused on both ovarian and uterine cancers in AI/AN women using cancer incidence and mortality data that have been linked to improve race misclassification. Our ovarian cancer findings for all US counties were similar to a national study by Howe et al.,[37] who also observed lower ovarian cancer death rates in American Indian women in comparison with White women, though this observation did not hold when looking only at CHSDA counties. As in our analysis, they also observed similar geographic variation in ovarian cancer rates, with AI/AN women in the Northeast region having the lowest rates. However, these data are from the 1990s, relied solely on vital statistics data, and did not consider



Source: AI/AN-US Mortality Database (1990–2009).
Note. AI/AN = American Indian/Alaska Native; CHSDA = contract health service delivery areas; IHS indicates Indian Health Service; NHW = non-Hispanic White;. Analyses are limited to persons of non-Hispanic origin. Cancer causes of death was created using the Surveillance, Epidemiology and End Results (SEER) Cause of Death recode. AI/AN race is created using death certificate race and IHS Link. Rates are per 100 000 persons and are age-adjusted to the 2000 US standard population (11 age groups - Census P25-1130). States and years of data excluded because Hispanic Origin was not collected on the death certificate: LA: 1990; NH: 1990–1992; OK: 1990–1996. Percentage of regional coverage of AI/AN in CHSDA counties to AI/AN 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%.

FIGURE 2—Death rates by year for (a) ovarian cancer and (b) uterine cancer: CHSDA counties; United States; 1990–2009.

misclassification of race on death certificates. Other studies describing ovarian and uterine cancer incidence and mortality have been limited to a particular geographic region or state.[6,38–41]

In addition to potential misclassification of race, the incidence and mortality variations we observed among IHS regions may, in part, reflect geographic variations in environmental, social, and personal determinants of health. These geographic variations in IRs may highlight differences in the prevalence of risk factors such as obesity and physical activity known to be associated with both ovarian and uterine cancers.[42–44] According to Behavioral Risk Factor Surveillance System survey data, AI/AN women have a higher prevalence of obesity (35.4%) than White women (21.5) regardless of geographic region.[45] Also, AI/AN women are physically less active than White women (30.6% vs 22%),[45] and AI/AN women have a higher prevalence of cigarette smoking, especially in the Alaska, East, and Northern Plains regions.[45] In addition, hypertension and adult onset of diabetes mellitus are associated with increased risk of uterine cancer.[46,47] AI/AN women have a higher prevalence of diabetes than White women (13.9% vs 6.9%),[45] and AI/AN women have been reported to have a higher rate of mortality as a result of diabetes than the general population.[48]

Regional variations may also be caused by differences in other risk factors influencing ovarian and uterine cancer, such as pregnancy, long-term use of oral contraceptives, hormone replacement therapy, tubal ligation, or hysterectomy (with retention of the ovaries).[49] How many AI/AN women were exposed to postmenopausal hormone therapy is unknown. Observational epidemiologic evidence has strongly supported that tubal ligation and hysterectomy are associated with a decrease in the risk of ovarian cancer by approximately 26% to 30%.[50] AI/AN women had a higher prevalence of hysterectomy (23.1%) compared with White women (20.9%), and higher hysterectomy rates in AI/AN women decrease risk for uterine cancer.[51] In addition, trends in hysterectomy and oophorectomy may influence observed trends in ovarian and uterine cancer mortality. Tubal sterilization rates, which may influence rates of ovarian cancer, also vary by race.[52] To our knowledge, accurate counts of those who have intact ovaries and uteri are not available.

Genetic variations may also partially explain observed geographic differences in IRs, though no large study has been done in AI/AN populations for genetic testing for familial cancers. Sporadic cases of breast and ovarian cancer suggestive of BRCA1/2 carriers as well as documentation of families diagnosed with Lynch syndrome have been found in Utah, Oklahoma, and Navajo Nation.[53]

Observed variations in stage at diagnosis and death rates for ovarian and uterine cancer for

AI/AN populations may be attributable to differences in diagnostic and treatment patterns. No screening tests are recommended for either ovarian or uterine cancer[54]; however, differences in time of diagnosis may have resulted from differences in clinical presentation of both cancer types. Most uterine cancer presents with symptoms such as postmenopausal bleeding, and ovarian cancer presents with minimal or nonspecific symptoms such as bloating.[55] The lack of screening tests and the nonspecificity of symptoms result in later stage at diagnosis for both ovarian and uterine cancer. Public education and provider education may be important to affect stage at time of diagnosis, referral for appropriate and timely treatment, and ultimately survival. A molecular screening test, particularly for ovarian cancer, may change patterns of disease for a small segment of the population for whom genetic screening may be warranted. Prophylactic total hysterectomy has been shown to reduce risk of uterine and ovarian cancer in families with BRCA mutations or Lynch syndrome.[56]

Finally, differences in mortality by geographic region may be reflective of geographic differences in the biological variation of the disease and access to state-of-the-art cancer care. The IHS has no gynecologic oncology surgeons, and therefore referral patterns may lead to delay in diagnosis and treatment that may affect death rates, but not IRs.[57] Although public service announcements such as the Centers for Disease Control and Prevention's *Inside Knowledge* campaign have been aimed at the general public, no concerted educational efforts have been made in AI/AN communities alerting women to the symptoms that require assessment by a clinician.

Limitations

Several limitations should be considered when interpreting results presented in this study. Even though the dataset used for this study was linked to the IHS patient registration dataset to improve misclassification of race for AI/AN cases, AI/AN persons who are not members of the federally recognized tribes, live in counties other than CHSDA counties, reside in urban areas, or are not eligible for IHS services are likely underrepresented.[17,19] Of note is the last census showing that two thirds of AI/AN persons reside in urban areas and migrate back and forth to their tribal lands. AI/AN residents of urban areas differ from all AI/AN individuals in poverty level, health care access, and other factors that may influence incidence and mortality trends.[44,58] Also, some eligible decedents may never have used IHS services and are therefore not included in the IHS database. Our findings suggest less variation for Whites than for AI/AN persons in regional analyses using data from CHSDA counties only. Perhaps an alternate aggregation of states or counties would reveal a different level of variation. Furthermore, bridged intercensal population estimates significantly overestimated AI/AN individuals of Hispanic origin,[34] limiting our ability to include all the AI/AN women in our analysis.[13,19] Exclusion of Hispanic AI/AN individuals from the analysis reduced overall AI/AN deaths by less than 5% and may also have disproportionately excluded some tribal members residing in states along the US–Mexico border who have Hispanic surnames and may be coded as Hispanic at death.

Conclusions

This is the first comprehensive review of both incidence and mortality patterns for uterine and ovarian cancer in AI/AN women compared with White women in the same regions. Significant regional differences were found in these trends as for other cancers included in this supplement. More research is needed to identify and better understand the environmental, genetic, and clinical factors that may contribute to geographic differences in incidence and mortality among AI/AN populations.

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***Note.** The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.*

Contributors

S. D. Singh accessed and analyzed the cancer surveillance data and drafted the article, with multiple iterations of editing and critical review by A. B. Ryerson, M. Wu, and J. S. Kaur. All authors were responsible for study concept, design, and interpretation of the data analysis.

Human Participant Protection

The Centers for Disease Control and Prevention and the Indian Health Service determined this project to constitute public practice and not research; therefore, no formal institutional review board approvals were required.

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