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Regional Differences in Colorectal Cancer Incidence, Stage, and Subsite Among American Indians and Alaska Natives, 1999–2004

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An Update on Cancer in American Indians and Alaska Natives, 1999-2004

Supplement to ***Cancer***

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BACKGROUND. Colorectal cancer (CRC) is a leading cause of cancer morbidity and mortality for American Indians and Alaska Natives (AI/ANs), but misclassification of race causes underestimates of disease burden.

METHODS. The authors compared regional differences in CRC incidence, stage at diagnosis, and anatomic distribution between AI/ANs and non-Hispanic whites (NHWs). To reduce misclassification, data from the National Program of Cancer Registries; the Surveillance, Epidemiology, and End Results Program; and the Indian Health Service (IHS) were linked. The analysis was limited to the 56% of AI/AN who live in IHS Contract Health Service Delivery Areas.

RESULTS. From 1999 to 2004, the overall incidence rate (per 100,000 persons per year) of CRC was 9% lower in the AI/AN population (46.3) than in the NHW population (50.8). However, AI/AN CRC incidence rates varied nearly 5-fold regionally, from 21 in the Southwest to 102.6 in Alaska. Compared with NHW rates, AI/AN rates were significantly higher in Alaska (rate ratio [RR], 2.03), the Northern Plains (RR, 1.39), and the Southern Plains (RR, 1.16) but were lower in the Pacific Coast (RR, 0.80), the East (RR, 0.65), and the Southwest (RR, 0.45). AI/ANs were diagnosed more often with advanced CRC than with localized CRC (RR, 1.92) compared with NHWs (RR, 1.48). Females more often had proximal CRC among both the AI/AN population (females, 40.1%; males, 33.5%) and the NHW population (females, 50.1%; males, 40.3%), although AI/ANs had a higher proportion of distal cancers overall.

CONCLUSIONS. CRC incidence rates in AI/AN populations varied dramatically between regions. Efforts are needed to make CRC screening a priority, overcome barriers to endoscopic screening, and to engage AI/AN communities in culturally appropriate ways to participate in prevention and early detection programs. ***Cancer*** **2008;113(5 suppl):1179–90.** *Published 2008 by the American Cancer Society.**

KEYWORDS: colorectal cancer, epidemiology, incidence, Indians of North America, health disparities, screening, colonic subsite, cancer stage.

Colorectal cancer (CRC) is a leading cause of cancer morbidity and mortality for American Indian and Alaska Native (AI/AN) males and females.[1-3] Although CRC mortality rates fell for most US

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populations from 1995 to 2004, there was no significant change in AI/AN rates.[2] It has been demonstrated that CRC mortality varies significantly between AI/AN populations living in different regions of the US, with a >3-fold difference between the Southwest and Alaska.[1] AI/AN males and females, as a group, reportedly have CRC incidence rates that are lower than the US average; however, summary measures may miss important rate heterogeneity between AI/AN populations.[4]

Accurate determination of cancer burden is a critical first step for addressing health disparities. Race misclassification in medical records and on death certificates makes determining cancer rates for AI/AN populations difficult.[5,6] Forthcoming data from the National Longitudinal Mortality Survey correlating self-identified race from Current Population Surveys with information on death certificates indicate that AI/ANs are classified as another race 44.8% of the time.[7] Such misclassification results in underestimates of both cancer incidence and mortality.[8-11]

The objective of the current analysis was to compare regional CRC incidence rates by age, stage at diagnosis, and the colonic location of CRC tumors between AI/AN and non-Hispanic white (NHW) populations living in the same counties. This study is part of a larger effort linking the Centers for Disease Control and Prevention (CDC) National Program of Cancer Registries (NPCR) database; the National Cancer Institute (NCI) Surveillance, Epidemiology, and End Result (SEER) database; and the Indian Health Service (IHS) database to minimize the effects of race misclassification on estimates of cancer incidence.

MATERIALS AND METHODS

Data Sources

A more comprehensive description of the analytical methods used for this and other articles in this supplement of *Cancer* is published separately.[12] We analyzed population-based cancer incidence data from the NPCR and from the SEER Program.[13,14] If data from central cancer registries that provided permission for their use met quality criteria, then they were included in the analysis (see footnote to Table 1 for a list of registries). Population estimates from the US Bureau of the Census, modified by the CDC and the NCI, were used as denominators in the rate calculations.[15,16] We included incident cases of invasive CRC as detailed elsewhere.[17] Data on disease stage spanned changes in SEER Summary Stage coding. Stage was coded according to the SEER Summary Stage 1977 rules for diagnosis years 1999 through 2000 and SEER Summary Stage 2000 rules for diagnosis years 2001 through 2003; collaborative stage data, which were reported first for 2004, were not available for analysis. CRC stage data for 1999 through 2003 were combined for this analysis, because the differences observed in comparative studies of the 2 systems were minimal.[18,19] Tumor histology was categorized as proposed by Berg[20] and modified by Stewart et al.[21]

To reduce the misclassification of AI/AN cases as other races, all cancer case records from NPCR and SEER registries were linked with IHS patient registration databases using a probabilistic linkage software developed by the CDC.[14] The IHS database identifies all individuals who have ever accessed IHS services. In addition, we focused on those AI/AN and NHW populations that were living in counties where individuals were eligible for IHS contract care services, called Contract Health Service Delivery Areas (CHSDAs).

The 6 IHS regions used in this analysis (Alaska, Pacific Coast, Northern Plains, Southern Plains, Southwest, and East) and their constituent CHSDA counties are shown in Figure 1. CHSDA counties, in general, contain federally recognized tribal lands or are adjacent to tribal lands. AI/AN males and females must live within CHSDA boundaries and be members of a federally recognized tribe to be eligible for health services that are not available at IHS or tribal health facilities. The proportions of the population that are AI/AN relative to the total population are higher in CHSDA counties than in non-CHSDA counties, and there is inherently less misclassification of race in medical and death records.[7] Overall, 56% of AI/ANs live in CHSDA counties; however, this varies by region (Alaska, 100%; East, 13.1%; Northern Plains, 59%; Southern Plains, 64.1%; Pacific Coast, 55.6%; and Southwest, 87.5%).

Statistical Analyses

Two sets of statistics are provided for AI/AN and NHW cancer cases: 1) data from all counties in the respective regions (referred to as 'All Counties'), and 2) data from all counties designated as CHSDA (referred to as 'CHSDA counties'). The results described below refer to individuals who reside in CHSDA counties unless otherwise noted.

The age groups for analysis (<40 years, 40-49 years, 50-64 years, and ≥65 years) were selected with consideration of recommendations that average-risk individuals begin CRC screening at age 50 years and that screening colonoscopy coverage by Medicare, which is available to most US citizens, begin at age 65 years.[22,23] Anatomic subsites of incident cancers

TABLE 1
Colorectal Cancer Incidence by Sex and Indian Health Service Region for American Indians/Alaska Natives and Non-Hispanic Whites: US, 1999-2004[a]

		CHSDA Counties						All Counties					
IHS Region	Sex	AI/AN Count	AI/AN Rate[b]	95% CI for AI/AN Rate	NHW Rate[b]	RR (AI/AN:NHW)	95% CI for RR	AI/AN Count	AI/AN Rate[b]	95% CI for AI/AN Rate	NHW Rate[b]	RR (AI/AN:NHW)	95% CI for RR
Northern Plains	Both sexes	513	72.5	65.9-79.5	52.3	1.39[c]	1.26-1.52	660	54.9	50.4-59.6	54.7	1.00	0.92-1.09
	Males	281	88.9	77.5-101.3	61.3	1.45[c]	1.26-1.66	355	66.9	59.0-75.3	65.0	1.03	0.91-1.16
	Females	232	59.8	52.0-68.4	45.1	1.33[c]	1.15-1.52	305	46.1	40.7-51.8	46.7	0.99	0.87-1.11
Alaska[d]	Both sexes	370	102.6	91.9-114.2	50.6	2.03[c]	1.78-2.31	370	102.6	91.9-114.2	50.6	2.03[c]	1.78-2.31
	Males	163	98.5	82.6-116.4	61.4	1.60[c]	1.31-1.95	163	98.5	82.6-116.4	61.4	1.60[c]	1.31-1.95
	Females	207	106.2	91.8-122.1	40.6	2.62[c]	2.18-3.14	207	106.2	91.8-122.1	40.6	2.62[c]	2.18-3.14
Southern Plains	Both sexes	772	60.2	55.9-64.7	51.8	1.16[c]	1.08-1.25	861	49.1	45.8-52.7	50.1	0.98	0.91-1.05
	Males	378	70.3	62.9-78.2	63.2	1.11	0.99-1.24	421	56.2	50.5-62.3	60.7	0.93	0.83-1.03
	Females	394	53.8	48.5-59.4	43.2	1.25[c]	1.12-1.38	440	44.5	40.3-48.9	41.9	1.06	0.96-1.17
Pacific Coast	Both sexes	464	38.7	35.0-42.7	48.5	0.80[c]	0.72-0.88	574	26.4	24.2-28.8	49.0	0.54[c]	0.49-0.59
	Males	231	44.0	37.8-50.7	56.5	0.78[c]	0.67-0.90	291	30.1	26.4-34.2	57.2	0.53[c]	0.46-0.60
	Females	233	35.0	30.4-40.0	42.1	0.83[c]	0.72-0.95	283	23.7	20.9-26.8	42.4	0.56[c]	0.49-0.63
East	Both sexes	112	36.0	29.4-43.6	55.2	0.65[c]	0.53-0.79	432	19.1	17.2-21.1	55.1	0.35[c]	0.31-0.38
	Males	44	31.1	21.9-42.5	65.8	0.47[c]	0.33-0.65	218	21.9	18.7-25.3	65.4	0.33[c]	0.29-0.39
	Females	68	39.7	30.6-50.4	47.1	0.84	0.65-1.07	214	17.1	14.8-19.7	47.1	0.36[c]	0.31-0.42
Southwest	Both sexes	390	21.0	18.9-23.3	46.8	0.45[c]	0.40-0.50	419	20.0	18.0-22.1	45.9	0.44[c]	0.39-0.48
	Males	211	25.7	22.1-29.7	55.1	0.47[c]	0.40-0.54	224	24.0	20.8-27.7	53.9	0.45[c]	0.39-0.51
	Females	179	17.3	14.8-20.1	39.7	0.44[c]	0.37-0.51	195	16.9	14.5-19.5	39.3	0.43[c]	0.37-0.50
Total	Both sexes	2621	46.3	44.4-48.2	50.8	0.91[c]	0.87-0.95	3316	33.9	32.6-35.1	53.2	0.64[c]	0.61-0.66
	Males	1308	52.6	49.5-55.8	59.8	0.88[c]	0.83-0.93	1672	38.7	36.7-40.8	63.1	0.61[c]	0.58-0.65
	Females	1313	41.6	39.3-44.0	43.6	0.95	0.90-1.01	1644	30.3	28.8-31.9	45.6	0.66[c]	0.63-0.70

Source: Cancer registries in the Centers for Disease Control and Prevention's National Program of Cancer Registries (NPCR) and/or the National Cancer Institute's Surveillance, Epidemiology, and End Results (SEER) Program.

CHSDA indicates Contract Health Service Delivery Area; IHS, Indian Health Service; AI/AN, American Indians/Alaska Natives; 95% CI, 95% confidence interval; NHW, non-Hispanic whites; RR, rate ratio.

[a] AI/AN race is reported by NPCR and/or SEER registries or through linkage with the IHS patient registration database. AI/AN persons of Hispanic origin are included.

[b] Rates are per 100,000 persons and are age-adjusted to the 2000 US standard population (19 age groups; Census P25-1130).

[c] The RR is statistically significant ($P < .05$).

[d] Rates and RRs for Alaska in the CHSDA Counties section are the same as those in the All Counties section, because all counties in Alaska are CHSDA counties.

Years of data and registries used: 1999-2004 (41 states and the District of Columbia): Alaska,* Alabama,* Arkansas, Arizona,* California,* Colorado,* Connecticut,* the District of Columbia, Delaware, Florida,* Georgia, Hawaii, Iowa,* Idaho,* Illinois, Indiana,* Kentucky, Louisiana,* Massachusetts,* Maine,* Michigan,* Minnesota,* Missouri, Montana,* North Carolina,* Nebraska,* New Hampshire, New Jersey, New Mexico,* Nevada,* New York,* Ohio, Oklahoma,* Oregon,* Pennsylvania,* Rhode Island,* Texas,* Utah,* Washington,* Wisconsin,* West Virginia, and Wyoming*; 1999 and 2002-2004: North Dakota*; 2001-2004: South Dakota*; 2003-2004: Mississippi* and Virginia; 2004: Tennessee (asterisks indicate states with at least 1 county designated as a CHSDA).

Percent regional coverage of AI/AN in CHSDA counties to AI/AN in all counties: Alaska, 100%; East, 13.1%; Northern Plains, 59%; Southern Plains, 64.1%; Pacific Coast, 55.6%; Southwest, 87.5%.

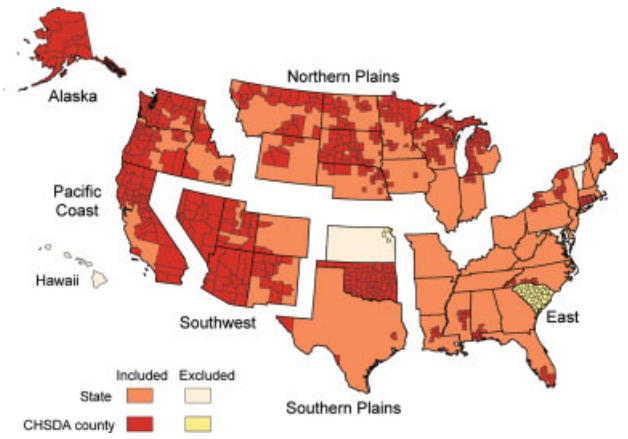

FIGURE 1. States and Contract Health Service Delivery Areas (CHSDA) counties by Indian Health Service region.

was divided into proximal (from the cecum to the splenic flexure) and distal colon and rectum based on International Classification of Diseases for Oncology, Ninth Revision codes. Proximal includes the cecum (C18.0), ascending colon (C18.2), hepatic flexure (C 18.3), transverse colon (C18.4), and splenic flexure (18.5); distal includes the descending colon (C18.6) and sigmoid colon (C18.7); and rectum includes the rectosigmoid junction (C19.9) and rectum (C20.9). This convention was chosen because flexible sigmoidoscopy is capable of observing the distal 60 cm of the colon to approximately the splenic flexure.

For all AI/AN and NHW populations, cancer incidence rates were expressed per 100,000 persons per year and were age-adjusted by 19 age groups (<1 year, 1-4 years, 5-9 years, . . . , 80-84 years, ≥85 years) to the 2000 US standard population using the direct method.[13] Percent distributions for histology, stage, and anatomic subsite also were age-adjusted to the 2000 population. Ninety-five percent confidence intervals (CIs) for age-adjusted rates were calculated using the modification of Tiwari et al.[24] Rate ratios (RRs) were calculated as the age-adjusted incidence rate for the AI/AN population of interest divided by the age-adjusted incidence rate for the same-area NHW population. The cancer incidence data were analyzed using SEER*Stat software, version 6.3.6.[25]

RESULTS

Over the 6-year study period (1999 to 2004), there were 3316 cases of invasive CRC diagnosed in the All-Counties AI/AN population and 681,801 cases diagnosed in the NHW population. Of these, 95.3% of AI/AN cases and 96.5% of NHW cases were confirmed microscopically. Microscopically confirmed cancers among AI/AN cases were 94.7% adenocarcinomas, 3% other specified carcinomas, 0.9% carcinomas not otherwise specified (NOS), 0.3% epidermoid carcinomas, and 1.1% other histologic types. The corresponding percentages among NHW cases were 95.7%, 2%, 1.2%, 0.4%, and 0.7%, respectively. Signet ring cell carcinomas accounted for 0.9% of microscopically confirmed CRC cases among AI/ANs and 1.1% among NHWs.

Among AI/ANs with CRC, 79% (2621 individuals) were residents of CHSDA counties compared with 21% (143,160) of NHWs (Table 1). The age-adjusted CRC incidence rate among AI/ANs was 46.3 in CHSDA counties and 33.9 in All Counties. CHSDA AI/ANs had a 9% lower overall incidence rate of CRC compared with the rate among CHSDA NHWs (RR, 0.91; 95% CI, 0.87-0.95). In contrast, the All-County AI/AN incidence rate was 36% lower than the All County NHW incidence rate. The remaining results presented below are limited to residents of CHSDA counties, because All-County data are likely underestimates because of misclassification of race not corrected by our IHS linkage strategy.

Regional CHSDA incidence rates were significantly higher in AI/ANs than NHWs in Alaska, the Northern Plains, and the Southern Plains, whereas the rates were significantly lower in the Pacific Coast, East, and Southwest (Table 1). There was a nearly 5-fold regional variation in incidence among AI/AN populations (from 21.0 in the Southwest to 102.6 in Alaska) compared with modest geographic variation among NHW populations (from 46.8 in the Southwest to 55.2 in the East). The pattern of regional variation in incidence was apparent for both AI/AN males and females. CRC incidence rates were consistently higher among males with the exception of Alaska and the East region. In Alaska, the AI/AN female incidence rate of 106.2 was 2.6 times higher than that of NHW Alaskan females and the highest of any group in the analysis.

Stratifying by age (Tables 2 and 3) and among those living in CHSDA counties, AI/AN populations had comparable or slightly higher rates of CRC than NHW populations (<40 years: RR, 1.25; 40-49 years: RR, 1.05; 50-64 years: RR, 1.05). One exception was that the overall CRC rate was significantly lower in AI/ANs aged ≥65 years (RR, 0.84). Important regional differences also were observed within and between age strata: 9.5% of CRC cases occurred among AI/AN males and females aged <50 years (the age for initiating CRC screening among average-risk individuals) compared with 7.9% of CRC cases among NHW individuals. Dramatically higher rates of CRC were

TABLE 2
Colorectal Cancer Invasive Incidence Rates and Percent Distribution by Age and Indian Health Service Region for American Indians/ Alaska Natives and Non-Hispanic Whites in Contract Health Service Delivery Area Counties: US, 1999-2004

	<40 Years				40-49 Years				50-64 Years				≥65 Years			
IHS Region	Count	% of Cases[a]	Rate[b]	95% CI	Count	% of Cases[a]	Rate[b]	95% CI	Count	% of Cases[a]	Rate[b]	95% CI	Count	% of Cases[a]	Rate[b]	95% CI
AI/AN																
Northern Plains	19	2.0	2.5	1.5-3.9	61	7.1	33.5[c]	25.7-43.1	175	24.5	118.3[c]	101.4-137.2	258	66.4	380.7[c]	334.3-431.7
Alaska	8	1.3	2.3	1.0-4.5	40	6.9	46.1[c]	32.9-62.8	128	26.9	183.8[c]	153.2-218.5	194	64.9	527.2[c]	453.6-609.5
Southern Plains	40	3.7	3.9	2.8-5.3	61	6.1	24.0	18.3-30.8	241	25.1	100.7[c]	88.3-114.2	430	65.1	309.9	281.1-340.9
Pacific Coast	16	1.8	1.2	0.7-2.0	42	5.1	12.9	9.3-17.5	161	23.5	60.8	51.7-70.9	245	69.5	212.9[d]	186.4-242.0
East	4	2.2	1.4	0.4-3.4	11	6.3	14.7	7.4-26.4	33	21.4	51.5[d]	35.4-72.4	64	70.1	199.7[d]	153.3-255.8
Southwest	38	6.0	2.2	1.6-3.0	48	9.0	12.2[d]	9.0-16.2	150	32.7	45.7[d]	38.7-53.7	154	52.3	86.9[d]	73.5-102.0
Total	125	2.8	2.3	1.9-2.7	263	6.7	20.0	17.7-22.6	888	25.8	79.6	74.5-85.1	1345	64.7	236.8[d]	224.1-250.0
NHW																
Northern Plains	425	2.0	1.8	1.6-2.0	1361	5.4	18.3	17.4-19.3	5863	21.8	76.1	74.1-78.1	19,508	70.8	292.8	288.7-296.9
Alaska	36	2.7	2.3	1.6-3.2	73	4.3	14.0	11.0-17.7	276	18.9	63.8	56.4-71.9	483	74.2	296.9	270.4-325.2
Southern Plains	197	2.6	2.3	2.0-2.7	561	6.4	21.5	19.8-23.4	2452	23.6	81.4	78.2-84.7	7201	67.5	276.5	270.1-282.9
Pacific Coast	718	2.0	1.7	1.5-1.8	2477	5.7	18.1	17.4-18.8	10,319	22.1	71.4	70.0-72.8	32,816	70.2	269.9	267.0-272.8
East	587	2.2	2.1	1.9-2.3	1863	6.0	21.5	20.5-22.5	8167	23.1	85.2	83.4-87.1	27,404	68.7	300.1	296.5-303.7
Southwest	289	2.0	1.6	1.4-1.8	970	5.8	17.7	16.6-18.9	4674	22.7	70.8	68.8-72.9	14,440	69.5	257.2	253.0-261.5
Total	2252	2.1	1.8	1.8-1.9	7305	5.8	19.0	18.6-19.5	31,751	22.4	76.0	75.1-76.8	101,852	69.8	280.3	278.6-282.0

Source: Cancer registries in the Centers for Disease Control and Prevention's National Program of Cancer Registries and/or the National Cancer Institute's Surveillance, Epidemiology, and End Results Program.
IHS indicates Indian Health Service; 95% CI, 95% confidence interval; AI/AN, American Indians/Alaska Natives; NHW, non-Hispanic whites.
[a] Percents may not add to 100% due to rounding.
[b] Rates are per 100,000 persons and are age-adjusted to the 2000 US standard population (19 age groups; Census P25-1130).
[c] The AI/AN rate is statistically significantly higher than the NHW rate ($P < .05$).
[d] The AI/AN rate is statistically significantly lower than the NHW rate ($P < .05$).
Years of data and registries used: 1999-2004 (41 states and the District of Columbia): Alaska,* Alabama,* Arkansas, Arizona,* California,* Colorado,* Connecticut,* the District of Columbia, Delaware, Florida,* Georgia, Hawaii, Iowa,* Idaho,* Illinois, Indiana,* Kentucky, Louisiana,* Massachusetts,* Maine,* Michigan,* Minnesota,* Missouri, Montana,* North Carolina,* Nebraska,* New Hampshire, New Jersey, New Mexico,* Nevada,* New York,* Ohio, Oklahoma,* Oregon,* Pennsylvania,* Rhode Island,* Texas,* Utah,* Washington,* Wisconsin,* West Virginia, and Wyoming*; 1999 and 2002-2004: North Dakota*; 2001-2004: South Dakota*; 2003-2004: Mississippi* and Virginia; 2004: Tennessee (asterisks indicate states with at least 1 county designated as a Contract Health Service Delivery Area).

TABLE 3
Colorectal Cancer Invasive Incidence Rates and Rate Ratios by Age and Indian Health Service Region for American Indians/ Alaska Natives and Non-Hispanic Whites in Contract Health Service Delivery Area Counties: US, 1999-2004

	<40 Years				40-49 Years				50-64 Years				≥65 Years			
IHS Region	AI/AN Rate[a]	NHW Rate[a]	RR	95% CI	AI/AN Rate[a]	NHW Rate[a]	RR	95% CI	AI/AN Rate[a]	NHW Rate[a]	RR	95% CI	AI/AN Rate[a]	NHW Rate[a]	RR	95% CI
Northern Plains	2.5	1.8	1.42	0.84-2.22	33.5	18.3	1.83[b]	1.39-2.37	118.3	76.1	1.55[b]	1.33-1.81	380.7	292.8	1.30[b]	1.14-1.48
Alaska	2.3	2.3	1.00	0.40-2.13	46.1	14.0	3.28[b]	2.17-4.89	183.8	63.8	2.88[b]	2.31-3.57	527.2	296.9	1.78[b]	1.49-2.11
Southern Plains	3.9	2.3	1.66[b]	1.15-2.34	24.0	21.5	1.11	0.84-1.45	100.7	81.4	1.24[b]	1.08-1.41	309.9	276.5	1.12[b]	1.01-1.24
Pacific Coast	1.2	1.7	0.73	0.42-1.20	12.9	18.1	0.72[b]	0.52-0.97	60.8	71.4	0.85[b]	0.72-1.00	212.9	269.9	0.79[b]	0.69-0.90
East	1.4	2.1	0.65	0.18-1.63	14.7	21.5	0.69	0.34-1.23	51.5	85.2	0.60[b]	0.42-0.85	199.7	300.1	0.67[b]	0.51-0.85
Southwest	2.2	1.6	1.39	0.96-1.94	12.2	17.7	0.69[b]	0.50-0.92	45.7	70.8	0.65[b]	0.55-0.76	86.9	257.2	0.34[b]	0.29-0.40
Total	2.3	1.8	1.25[b]	1.04-1.50	20.0	19.0	1.05	0.93-1.19	79.6	76.0	1.05	0.98-1.12	236.8	280.3	0.84[b]	0.80-0.89

Source: Cancer registries in the Centers for Disease Control and Prevention's National Program of Cancer Registries and/or the National Cancer Institute's Surveillance, Epidemiology, and End Results Program.
IHS indicates Indian Health Service; AI/AN, American Indians/Alaska Natives; NHW, non-Hispanic whites; RR, rate ratio; 95% CI, 95% confidence interval.
[a] Rates are per 100,000 persons and are age-adjusted to the 2000 US standard population (19 age groups; Census P25-1130).
[b] The RR is statistically significant ($P < .05$).
Years of data and registries used: 1999-2004 (41 states and the District of Columbia): Alaska,* Alabama,* Arkansas, Arizona,* California,* Colorado,* Connecticut,* the District of Columbia, Delaware, Florida,* Georgia, Hawaii, Iowa,* Idaho,* Illinois, Indiana,* Kentucky, Louisiana,* Massachusetts,* Maine,* Michigan,* Minnesota,* Missouri, Montana,* North Carolina,* Nebraska,* New Hampshire, New Jersey, New Mexico,* Nevada,* New York,* Ohio, Oklahoma,* Oregon,* Pennsylvania,* Rhode Island,* Texas,* Utah,* Washington,* Wisconsin,* West Virginia, and Wyoming*; 1999 and 2002-2004: North Dakota*; 2001-2004: South Dakota*; 2003-2004: Mississippi* and Virginia; 2004: Tennessee (asterisks indicate states with at least 1 county designated as a Contract Health Service Delivery Area).

TABLE 4
Invasive Colorectal Cancer Incidence Counts, Rates, and Rate Ratios by Stage, Indian Health Service Region, and Sex for American Indians Alaska Natives and Non-Hispanic Whites in Contract Health Service Delivery Area Counties: US, 1999-2003

		American Indians/Alaska Natives						Non-Hispanic White					
		Early Stage[a]		Late Stage[a]		Late/Early Stage[a]		Early Stage[a]		Late Stage[a]		Late/Early Stage[a]	
IHS Region	Sex	Count	Rate[b]	Count	Rate[b]	RR[c]	95% CI for RR	Count	Rate[b]	Count	Rate[b]	RR[c]	95% CI for RR
Northern Plains	Both sexes	130	22.4	261	45.4	2.02	1.61-2.56	8226	19.2	12,472	29.2	1.52	1.48-1.56
	Males	72	28.5	140	54.3	1.91	1.37-2.68	4186	22.5	6353	34.1	1.52	1.46-1.58
	Females	58	18.3	121	38.4	2.11	1.51-2.97	4040	16.6	6119	25.3	1.52	1.46-1.58
Alaska	Both sexes	112	38.7	176	60.0	1.55	1.20-2.01	270	19.4	396	28.2	1.46	1.23-1.73
	Males	49	34.7	80	60.9	1.75	1.18-2.64	154	21.6	240	34.6	1.60	1.26-2.03
	Females	63	41.2	96	60.0	1.46	1.04-2.05	116	17.0	156	22.3	1.32	1.02-1.71
Southern Plains	Both sexes	195	18.9	371	34.8	1.85	1.54-2.22	3262	19.5	4861	29.2	1.50	1.43-1.56
	Males	104	24.1	178	38.7	1.61	1.24-2.10	1750	24.4	2554	35.4	1.45	1.36-1.54
	Females	91	15.2	193	32.2	2.11	1.64-2.75	1512	15.9	2307	24.4	1.54	1.44-1.64
Pacific Coast	Both sexes	119	12.6	250	25.5	2.02	1.60-2.58	14,339	18.2	22,116	28.1	1.55	1.51-1.58
	Males	57	14.3	126	28.7	2.00	1.41-2.90	7523	21.7	11,204	32.2	1.49	1.44-1.53
	Females	62	11.5	124	23.3	2.02	1.46-2.83	6816	15.4	10,912	24.7	1.60	1.56-1.65
East	Both sexes	25	10.4	62	25.0	2.41	1.48-4.10	12,049	21.2	16,338	28.8	1.36	1.33-1.39
	Males	7	7.0	25	23.9	3.42	1.39-10.74	6281	26.0	8066	33.4	1.29	1.24-1.33
	Females	18	13.0	37	26.2	2.01	1.12-3.80	5768	17.5	8272	25.2	1.44	1.39-1.49
Southwest	Both sexes	84	5.7	198	12.5	2.19	1.68-2.90	5969	16.6	8979	25.1	1.51	1.47-1.57
	Males	42	6.6	118	16.9	2.57	1.76-3.84	3295	20.1	4821	29.3	1.46	1.39-1.52
	Females	42	5.1	80	9.1	1.79	1.21-2.70	2674	13.7	4158	21.4	1.57	1.49-1.65
Total	Both sexes	665	14.7	1318	28.2	1.92	1.74-2.12	44,115	18.9	65,162	28.1	1.48	1.46-1.50
	Males	331	16.8	667	32.1	1.91	1.65-2.21	23,189	22.8	33,238	32.6	1.43	1.41-1.46
	Females	334	13.2	651	25.2	1.91	1.67-2.20	20,926	15.9	31,924	24.4	1.53	1.51-1.56

Source: Cancer registries in the Centers for Disease Control and Prevention's National Program of Cancer Registries and/or the National Cancer Institute's Surveillance, Epidemiology, and End Results (SEER) Program.

IHS indicates Indian Health Service; RR, rate ratio; 95% CI, 95% confidence interval.

[a] For 1999-2000, SEER Summary Stage 1977 was used; for 2001-2003, SEER Summary Stage 2000 was used. Data for the 2 staging systems are combined because the differences observed in comparative analyses were minimal (see Howe 2005[18] and Phillips 2003[19]). Early stage includes local disease; late stage includes regional and distant stage disease.

[b] Rates are per 100,000 persons and are age-adjusted to the 2000 US standard population (19 age groups; Census P25-1130). In situ cancers are excluded.

[c] All RRs are statistically significant ($P < .05$).

Years of data and registries used: 1999-2004 (41 states and the District of Columbia): Alaska,* Alabama,* Arkansas, Arizona,* California,* Colorado,* Connecticut,* the District of Columbia, Delaware, Florida,* Georgia, Hawaii, Iowa,* Idaho,* Illinois, Indiana,* Kentucky, Louisiana,* Massachusetts,* Maine,* Michigan,* Minnesota,* Missouri, Montana,* North Carolina,* Nebraska,* New Hampshire, New Jersey, New Mexico,* Nevada,* New York,* Ohio, Oklahoma,* Oregon,* Pennsylvania,* Rhode Island,* Texas,* Utah,* Washington,* Wisconsin,* West Virginia, and Wyoming*; 1999 and 2002-2004: North Dakota*; 2001-2004: South Dakota*; 2003-2004: Mississippi* and Virginia; 2004: Tennessee (asterisks indicate states with at least 1 county designated as a Contract Health Service Delivery Area).

observed among AI/AN populations ages 40 to 49 years in Alaska (RR, 3.28) and the Northern Plains (RR, 1.83). Although AI/ANs aged <50 years from the Southwest had lower CRC rates relative to most other regions, they accounted for 15% of Southwest AI/AN cases. Similarly, AI/ANs aged <40 years in the Southern Plains accounted for 3.7% of cases and had a significantly higher incidence of CRC than NHWs of similar age (RR, 1.66).

In CHSDA counties, the overall rate of CRC among AI/ANs ages 50 to 64 years was not significantly different from that among NHWs (RR, 1.05), although the RR ranged from 2.88 in Alaska to 0.60 in the East. The cohort aged ≥65 years accounted for 64.7% of CRC cases that occurred in the AI/AN population and 69.8% of CRC cases that occurred in the NHW population. Nationally, AI/ANs in this age group had a lower rate of CRC (RR, 0.84;), although the RR varied from 0.34 in the Southwest to 1.78 in Alaska.

Data on disease stage at diagnosis were available for the years 1999 through 2003. Eight percent were unstaged among AI/ANs and 9.4% were unstaged among NHWs. Among staged cancers, 66.5% of AI/ANs were diagnosed at late-stage disease compared with 59.6% of NHWs: AI/AN males and females were more likely to have late-stage disease at diagnosis in each region (Table 4). Overall, the RR for late-stage versus early-stage CRC at diagnosis was 1.92 for AI/ANs and 1.48 for NHWs. AI/AN males and females

TABLE 5
Invasive Colorectal Cancer Incidence Counts, Rates, and Rate Ratios by Tumor Location, Indian Health Service Region, and Sex for American Indians/Alaska Natives and Non-Hispanic Whites in Contract Health Service Delivery Area Counties: US, 1999-2004[a]

		American Indians/Alaska Natives						Non-Hispanic Whites					
		Proximal		Distal and Rectum		Proximal/Distal and Rectum		Proximal		Distal and Rectum		Proximal/Distal and Rectum	
IHS Region	Sex	Count	Rate[b]	Count	Rate[b]	RR	95% CI for RR	Count	Rate[b]	Count	Rate[b]	RR	95% CI for RR
Northern Plains	Both sexes	156	22.5	324	44.1	0.51[c]	0.41-0.63	11,755	22.4	13,431	26.1	0.86[c]	0.84-0.88
	Males	77	25.7	181	53.7	0.48[c]	0.35-0.65	5251	23.7	7618	33.3	0.71[c]	0.69-0.74
	Females	79	20.3	143	36.2	0.56[c]	0.42-0.75	6504	21.5	5813	20.2	1.06[c]	1.02-1.10
Alaska	Both sexes	141	42.0	211	56.2	0.75[c]	0.59-0.94	326	21.1	485	26.3	0.80[c]	0.69-0.93
	Males	52	33.9	105	61.3	0.55[c]	0.38-0.80	177	23.5	307	33.8	0.70[c]	0.56-0.86
	Females	89	49.0	106	51.7	0.95	0.70-1.27	149	18.9	178	19.3	0.98	0.77-1.24
Southern Plains	Both sexes	237	19.4	429	32.1	0.60[c]	0.51-0.71	3947	19.5	5292	26.5	0.74[c]	0.71-0.77
	Males	109	22.0	215	37.4	0.59[c]	0.46-0.75	1840	21.6	3041	34.6	0.62[c]	0.59-0.66
	Females	128	17.9	214	28.6	0.63[c]	0.50-0.79	2107	17.9	2251	20.3	0.89[c]	0.83-0.94
Pacific Coast	Both sexes	166	15.3	281	21.5	0.71[c]	0.58-0.88	20,161	21.0	23,515	24.9	0.84[c]	0.83-0.86
	Males	69	15.2	153	26.2	0.58[c]	0.42-0.79	9174	22.2	13,315	31.3	0.71[c]	0.69-0.73
	Females	97	15.8	128	17.7	0.89	0.67-1.18	10,987	20.0	10,200	19.6	1.02	1.00-1.05
East	Both sexes	45	15.7	64	19.5	0.80	0.53-1.20	15,890	22.5	19,726	29.2	0.77[c]	0.76-0.79
	Males	16	12.2	28	18.9	0.64	0.31-1.28	7236	25.0	10,762	36.7	0.68[c]	0.66-0.70
	Females	29	18.0	36	20.2	0.89	0.52-1.50	8654	20.8	8964	23.4	0.89[c]	0.86-0.92
Southwest	Both sexes	123	7.0	237	12.1	0.58[c]	0.46-0.73	8289	18.9	10,341	23.8	0.80[c]	0.77-0.82
	Males	52	7.0	142	16.4	0.43[c]	0.30-0.60	4076	20.8	5973	29.6	0.70[c]	0.68-0.73
	Females	71	7.1	95	8.7	0.81	0.58-1.12	4213	17.4	4368	18.8	0.92[c]	0.89-0.97
Total	Both sexes	868	16.3	1546	25.9	0.63[c]	0.58-0.69	60,368	21.2	72,790	26.1	0.81[c]	0.80-0.82
	Males	375	16.6	824	31.0	0.53[c]	0.47-0.61	27,754	22.9	41,016	32.9	0.69[c]	0.68-0.71
	Females	493	16.3	722	22.0	0.74[c]	0.66-0.84	32,614	19.9	31,774	20.5	0.97[c]	0.95-0.98

Source: Cancer registries in the Center for Disease Control and Prevention's National Program of Cancer Registries and/or the National Cancer Institute's Surveillance, Epidemiology, and End Results (SEER) Program.

IHS indicates Indian Health Service; RR, rate ratio; 95% CI, 95% confidence interval.

[a] Rates are per 100,000 persons and are age-adjusted to the 2000 US standard population (19 age groups; Census P25-1130). Excludes in situ cancers.

[b] The RR is statistically significant ($P < .05$).

Years of data and registries used: 1999-2004 (41 states and the District of Columbia): Alaska,* Alabama,* Arkansas, Arizona,* California,* Colorado,* Connecticut,* the District of Columbia, Delaware, Florida,* Georgia, Hawaii, Iowa,* Idaho,* Illinois, Indiana,* Kentucky, Louisiana,* Massachusetts,* Maine,* Michigan,* Minnesota,* Missouri, Montana,* North Carolina,* Nebraska,* New Hampshire, New Jersey, New Mexico,* Nevada,* New York,* Ohio, Oklahoma,* Oregon,* Pennsylvania,* Rhode Island,* Texas,* Utah,* Washington,* Wisconsin,* West Virginia, and Wyoming*; 1999 and 2002-2004: North Dakota*; 2001-2004: South Dakota*; 2003-2004: Mississippi* and Virginia; 2004: Tennessee (asterisks indicate states with at least 1 county designated as a Contract Health Service Delivery Area).

from Alaska were the least likely to have late-stage CRC at diagnosis, whereas Eastern males and Northern and Southern Plains females were the most likely.

Excluding the appendix, NOS subsites, and overlapping lesions, 36% of CRCs among AI/ANs were located in the proximal portion (cecum to splenic flexure) of the colon compared with 45.3% of CRCs among NHW males and females from 1999 through 2004. The overall RR of proximal to distal (splenic flexure through rectum) disease was lower among AI/ANs than among NHWs, indicating a lower propensity toward proximal disease; the exceptions were for both sexes in the East and among females in Alaska, the Pacific Coast, and the Southwest, where AI/AN rates of proximal and distal CRC were not statistically different (Table 5). Females were more likely than males to be diagnosed with proximal disease among both AI/ANs and NHWs (40.6% and 50.7% among AI/AN and NHW females, respectively, compared with 31.3% and 40.4% among AI/AN and NHW males).

DISCUSSION

The objective of this study was to describe more accurately the incidence of CRC in AI/AN populations by linking NPCR and SEER cancer registry data with IHS records and then focusing on CHSDA counties where the misclassification of race was less pre-

valent. During the study period, CRC was the third most commonly diagnosed cancer among CHSDA AI/AN males and females, accounting for 11.8% of all cancers.[26] Our most dramatic finding was the regional variation in CRC incidence, with an almost 5-fold difference observed between AI/AN populations in Alaska and the Southwest. Also important were differences in incidence, stage of diagnosis, and colonic subsite distribution between AI/AN and NHW populations. Because only 56% of AI/ANs live in CHSDA counties (15% in the East Region), caution should be exercised not to generalize our results to the entire AI/AN population.

Geographic, racial, and gender differences in both CRC incidence and the distribution of incident cancers by colonic subsite may provide insights into etiologic risk factors and are important for guiding CRC screening recommendations. Regional differences in CRC incidence are likely a function of the heterogeneity of AI/AN populations, which vary greatly in culture, diet, resources, environment, and, theoretically, even genetic risk. Regional data from the Behavioral Risk Factor Surveillance System (BRFSS) suggest that AI/AN males and females have a higher prevalence of known CRC risk factors, including diabetes, obesity, smoking, and binge alcohol consumption.[27] Except for smoking, however, regional variations of these risk factors do not appear to mirror regional differences in CRC incidence rates. Smoking rates during 1999 through 2003 for Southwest AI/ANs (20.4%) were less than 50% of those reported in the Northern Plains and Alaska (both 43.9%).

Regional differences in diet and environmental micronutrients also may modify CRC risk.[28,29] For example, previous studies have suggested that solar irradiance and its role in vitamin D production may explain in part the North-South CRC incidence gradient observed in the general population.[30,31] It also is believed that calcium intake decreases CRC risk, and calcium is plentiful in the ground water of the Navajo reservation.[32,33] Other population differences that also may alter the risk of CRC include the dietary intake of animal fats, folate, and the consumption patterns of fresh produce.[34-37]

In several areas, AI/ANs appeared to be susceptible to CRC at younger ages than NHWs. During the study period, there were 40 cases of CRC in the Southern Plains that occurred in AI/ANs aged $<$40 years, a rate 66% higher than that for NHWs in this age group. Significantly higher rates of CRC also were observed among AI/ANs ages 40 to 49 years in Alaska and the Northern Plains. The onset of CRC in young populations should raise suspicion for the presence of hereditary CRC syndromes. Indeed, Navajo kindreds with hereditary nonpolyposis CRC syndrome have been followed for decades.[38] Further work is needed in these populations to elucidate CRC risk factors and to assess whether CRC screening recommendations should be modified to include younger individuals.

Regional differences in CRC screening also may affect incidence. It is believed that screening primarily is responsible for the declining rate of CRC in the general population while it also contributes to a shift toward earlier stages of disease at diagnosis.[22,39] Flexible sigmoidoscopy screening also has been implicated in a temporal shift of incident CRCs from the distal colon and rectum to more proximal sites.[40-43] Although BRFSS data suggest that AI/ANs have lower CRC fecal occult blood testing (FOBT) and endoscopic screening rates than NHWs (overall, 44.0% and 53.8%, respectively),[27] the true screening disparity may be far greater. Participation in the BRFSS requires individuals have a telephone and be willing to be interviewed.[44] For AI/ANs, this tends to select those with more income, higher levels of education, and less traditional ways of life, all of which have been associated with higher rates of screening participation.[8,45,46] In addition, cultural factors, including a reluctance to trust outsiders, modesty, and hesitancy to discuss one's health, may bias BRFSS prevalence estimates further for AI/ANs.

Data from other sources suggest significant variation in screening rates between AI/ANs and NHWs. For example, a 2007 review of CRC screening compliance among patients who visited Alaska tribal health centers reported that 34.8% of individuals aged $\geq$50 years were current with U.S. Preventive Services Task Force CRC screening recommendations, although rates from individual tribal health facilities ranged from 5.5% to 60.8%.[47] This compares with a reported Alaska AI/AN BRFSS rate of 49.5%.[27] Although financial, institutional, geographic, and cultural barriers to CRC screening vary widely between communities, AI/ANs in the Southwest and Northern Plains are significantly less likely than the general population to have undergone CRC screening.[48,49] Poverty, low education attainment, and insufficient health coverage are major challenges for AI/AN communities and also most likely contribute to lower screening rates.[50-52]

The colonic subsite distribution of CRC has major relevance for the choice of methods used for screening. For example, prior reports have demonstrated that females in the US have a higher prevalence of adenomatous polyps and CRCs in the

proximal colon than men, leading to conclusions that colonoscopy is a preferable CRC screening option for females.[42,53] Our work also indicated that females had a greater propensity toward proximal CRC. NHW females had a near equal prevalence of proximal to distal cancers, whereas NHW males had proportionally fewer proximal cancers. Similarly, AI/AN females had a higher proportion of proximal cancers than AI/AN men. However, as a population, AI/ANs had proportionately more distal cancers (64%) than NHWs (55%). Factors other than gender that are believed to influence subsite distribution include smoking, physical activity, alcohol abuse, diabetes, nonsteroidal anti-inflammatory drug use, and dietary factors.[40,54-63] A better understanding of the relative risks of these variables and CRC in AI/AN populations is needed.

Our analysis revealed that AI/ANs were diagnosed more commonly with later stage CRC than NHWs. Many factors influence the stage at which CRC is diagnosed. AI/AN communities face substantial barriers to the early detection and prevention of CRC. Limited availability of endoscopic services, provider time pressures, health systems that are geared and used primarily for acute and subacute care, and an underfunded health system are institutional barriers to screening for many AI/AN healthcare systems. In addition, cultural hesitance to access Western medicine for nonacute health problems, infrequent provider recommendations to get screened, insufficient health coverage, inability to afford Medicare or insurance copays, and transportation difficulties are factors commonly cited as cancer screening barriers by AI/AN individuals.[46,64-66]

Alaska, although it has the highest AI/AN population CRC rates, had the highest proportion of cases detected in early stages. Among IHS regions, Alaska has been the most proactive toward CRC screening. Since 2000, Alaska has increased its CRC screening rate by >50%.[47] Vanguard efforts have included the training and employment of a nurse practitioner who conducts screening colonoscopies in Anchorage and programs to train mid-level providers to conduct flexible sigmoidoscopies at regional health facilities.[67,68] Innovation has been spurred by the CRC burden as well as by the necessary abandonment of guaiac-based FOBT because of a high prevalence of *Helicobacter pylori*-associated hemorrhagic gastritis.[69] The commitment of the Alaska Native Tribal Health Consortium to increasing endoscopic capacity, overcome cost and transportation barriers, and the implementation of screening promotion programs are having a positive impact on disease stage at diagnosis.

In our study, CRC incidence rates appeared to be much higher among AI/AN males and females living in CHSDA counties than in all counties. This difference is most likely because of higher rates of race misclassification in non-CHSDA areas that are not corrected by our linkage rather than true differences in incidence. In 2000, 64.1% of the AI/AN population lived outside of Census Bureau-defined 'American Indian areas,' and >31% were not considered part of the IHS population.[70,71] Data on the health status of these mostly urban AI/AN populations are scarce and resources are fleeting, with only 1% of the annual IHS appropriation available to support 34 urban AI/AN clinics across the nation. More work to define and address the health of urban AI/AN populations clearly is needed.

For this study, linkages and geographic analyses were used to reduce the misclassification of race in AI/AN populations to more accurately describe CRC incidence. Clearly, there are significant regional differences in CRC rates among AI/AN males and females. Work to understand the reasons behind this 5-fold variation holds great promise for elucidating CRC risk factors, not only for AI/AN populations but for all populations. Our findings that AI/AN tend to be diagnosed with more advanced disease, coupled with the apparent success of Alaskan endoscopic screening programs in capturing earlier stage diagnoses, call for resources and diligence in approaching this disparity. Currently, approximately 1 in 18 Americans will be diagnosed with CRC in their lifetime.[72] The lifetime risk for AI/AN males and females in Alaska and the Northern and Southern Plains is higher. Although efforts aimed at modifying CRC risk factors are important, they are often a generational objective. Meanwhile, up to 90% of CRC can be prevented by screening and surveillance because of the efficacy of removing adenomatous polyps before they become cancers.[43,73] Disparities in CRC incidence and stage at diagnosis are likely to persist until screening is made a priority for tribal health systems, the many barriers to screening are overcome, and AI/AN communities are engaged in culturally appropriate ways to participate.

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