

# Geographic Variation in Colorectal Cancer Incidence and Mortality, Age of Onset, and Stage at Diagnosis Among American Indian and Alaska Native People, 1990–2009

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Colorectal cancer (CRC) is the second leading cause of cancer death for cancers that affect both men and women in the United States, following lung cancer.<sup>1</sup> At current rates, approximately 1 in 17 men and women in the United States will be diagnosed with this disease in their lifetime.<sup>2</sup> Understanding the epidemiology of CRC in minority populations is critical to inform cancer prevention and control programs. However, high rates of racial misclassification in medical records and death certificates of American Indian and Alaska Native (AI/AN) people have led to underestimates of their CRC burden.<sup>3</sup> As a result, cancer disparities in AI/AN populations have been underappreciated and underserved.

Because Indian Health Service (IHS) and tribal health facilities predominately serve AI/AN individuals, linking IHS and tribal user data to national cancer registry data affords a more accurate determination of CRC epidemiology for the AI/AN population.<sup>4</sup> Previously, we applied this approach to cancer incidence data from 1999 to 2004 and found that AI/AN persons were more often diagnosed with CRC at younger ages, and had more advanced stages of disease compared with non-Hispanic White persons.<sup>5</sup> The linkage also unveiled significant regional variation in AI/AN colorectal cancer incidence.

Screening can lower CRC incidence and mortality.<sup>6</sup> Removing premalignant polyps can prevent the disease, and diagnosing CRC at an earlier stage offers significant survival benefit.<sup>7,8</sup> AI/AN screening lags significantly behind that of Whites.<sup>9</sup> Although this would portend higher CRC death rates among AI/AN persons than in Whites, more accurate data on CRC mortality differences are needed.

We applied a linkage methodology to both incidence and mortality data to more

**Objectives.** We characterized estimates of colorectal cancer (CRC) in American Indians/Alaska Natives (AI/ANs) compared with Whites using a linkage methodology to improve AI/AN classification in incidence and mortality data.

**Methods.** We linked incidence and mortality data to Indian Health Service enrollment records. Our analyses were restricted to Contract Health Services Delivery Area counties. We analyzed death and incidence rates of CRC for AI/AN persons and Whites by 6 regions from 1999 to 2009. Trends were described using linear modeling.

**Results.** The AI/AN colorectal cancer incidence was 21% higher and mortality 39% higher than in Whites. Although incidence and mortality significantly declined among Whites, AI/AN incidence did not change significantly, and mortality declined only in the Northern Plains. AI/AN persons had a higher incidence of CRC than Whites in all ages and were more often diagnosed with late stage CRC than Whites.

**Conclusions.** Compared with Whites, AI/AN individuals in many regions had a higher burden of CRC and stable or increasing CRC mortality. An understanding of the factors driving these regional disparities could offer critical insights for prevention and control programs. (*Am J Public Health*. 2014;104:S404–S414. doi: 10.2105/AJPH.2013.301654)

accurately characterize CRC incidence and mortality for AI/AN persons by region.

## METHODS

Detailed methods for generating the analytical mortality files are described elsewhere in this supplement.<sup>10</sup> Detailed methods describing incidence data and analysis are available in a previous publication.<sup>4</sup> An abbreviated description of our methods follows.

### Data Sources

**Population estimates.** 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), which were adjusted for population shifts because of Hurricanes Katrina and Rita in 2005, are included as denominators in the calculations of death

rates.<sup>11,12</sup> Bridged single-race data allow for comparability between the pre- and post-2000 race/ethnicity population estimates.

During preliminary analyses, we discovered that the updated bridged intercensal populations estimates significantly overestimated AI/AN persons of Hispanic origin.<sup>13</sup> Therefore, to avoid underestimating incidence and mortality in AI/AN populations, our analyses were limited to non-Hispanic AI/AN individuals. We chose Non-Hispanic Whites as the most homogeneous referent group. Henceforth, the qualifying term “non-Hispanic” is omitted when discussing both groups.

**Death records.** Death certificate data are compiled by each state and sent to the NCHS, where they are edited for consistency and stripped of personal identifiers. NCHS publishes this information as part of the National Vital Statistics System (NVSS) and includes underlying and multiple cause of death fields,

state of residence, age, gender, race, and ethnicity.<sup>14</sup> NCHS applies a bridging algorithm nearly identical to that used by the Census Bureau to assign a single race to decedents with multiple races on their death certificates.<sup>15a</sup>

The IHS patient registration database was linked to death certificate data in the National Death Index to identify AI/AN deaths misclassified as non-Native.<sup>10</sup> Following this linkage, a flag indicating a positive link to IHS was added as an indicator of AI/AN ancestry to the NVSS mortality file. This file was combined with the population estimates to create an analytical file in SEER\*Stat version 8.0.4 (National Cancer Institute [NCI], Bethesda, Maryland; AI/AN-US Mortality Database [AMD]), which includes all deaths for all races reported to the NCHS from 1990 to 2009. Race for AI/AN deaths in this report were based on criteria described elsewhere in this supplement, combining race classification by NCHS based on the death certificate and information from data linkages between the IHS patient registration database and the National Death Index.<sup>10</sup> For deaths between 1990 and 1998, the underlying cause of death was coded according to the *International Classification of Diseases, Ninth Revision (ICD-9)*.<sup>15b</sup> For 1999 to 2009, the *ICD-10* was used.<sup>15c</sup>

**Incidence data.** We identified incidence of CRC cases between 1999 and 2009 from population-based central cancer registries in the CDC National Program of Cancer Registries (NPCR)<sup>16</sup> and the NCI Surveillance, Epidemiology, and End Results (SEER) program.<sup>17</sup> For data to be included for a given year, registries had to meet data standards developed for the US Cancer Statistics report.<sup>16</sup> Participating registries classified tumor histology, tumor behavior, and primary cancer site according to the *International Classification of Diseases for Oncology, Third Edition (ICD-O-3)*.<sup>18</sup> To identify CRC cases among AI/ANs misclassified as other races, we linked central cancer registries to cancer registry records with IHS patient registration files as previously described.<sup>4,16,19</sup> Stage at diagnosis was based on the SEER summary staging system: localized (confined to colon or rectum); regional (direct extension of the cancer to adjacent organs or tissues, or to regional lymph nodes); distant (metastasis to other areas of the body); and unstaged.<sup>20</sup> Stage was then grouped into early

(localized) and late (regional or distant) categories.

**Geographic coverage.** Final analyses were restricted to Contract Health Service Delivery Area (CHSDA) counties that contained federally recognized tribal lands or are adjacent to tribal lands (Figure 1).<sup>10</sup> CHSDA residence is used by the IHS to determine eligibility for services not directly available within the IHS. Linkage studies indicate less racial misclassification for AI/AN persons in these counties.<sup>10,21</sup> CHSDA counties also have higher proportions of AI/AN persons than do non-CHSDA counties, with 64% of AI/AN individuals residing in the 637 CHSDA counties (representing 20% of the 3141 counties in the United States). Although less geographically representative, we used analyses restricted to CHSDA counties for incidence and death rates to improve accuracy in interpreting AI/AN colorectal cancer statistics.

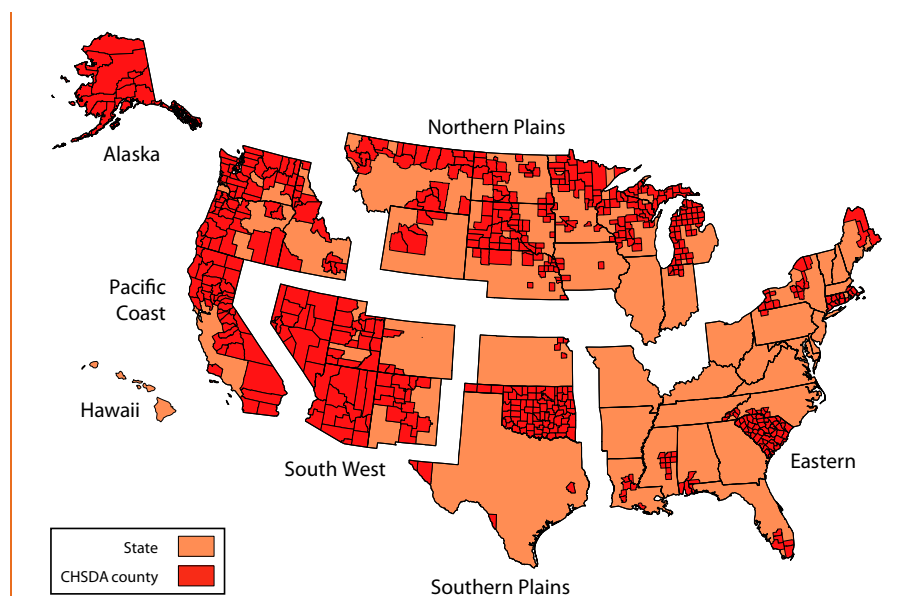
We completed analyses for all regions combined and by individual IHS regions: Northern Plains, Alaska, Southern Plains, Southwest, Pacific Coast, and East (Figure 1).<sup>10</sup> We used identical or similar regional analyses for other health-related publications focusing on AI/AN persons.<sup>22-24</sup> We found regional strata to be

preferable to using smaller jurisdictions, such as the administrative areas defined by IHS,<sup>25</sup> which yielded less stable estimates. Additional details about CHSDA counties and IHS regions are provided elsewhere (Table 1).<sup>10</sup>

### Statistical Methods

All rates, expressed per 100 000 population, were directly age-adjusted, using SEER\*Stat software, to the 2000 US standard population and should not be compared with published incidence and death rates adjusted using a different standard.

Using age-adjusted incidence and death rates, we calculated standardized rate ratios (RRs) for AI/AN persons compared with Whites. We calculated RRs by SEER\*Stat to the fourth decimal place and rounded the RRs for presentation. We calculated confidence intervals (CIs) for age-adjusted rates and RRs using SEER\*Stat 8.0.2 based on the methods described by Tiwari et al.<sup>26</sup> Temporal changes in annual age-adjusted incidence and death rates, including the annual percent change (APC) for each interval, were assessed with joinpoint regression techniques using statistical software developed by the NCI.<sup>27</sup> Statistical significance was set at a *P* value of less than .05.



**FIGURE 1—States and Contract Health Service Delivery Area (CHSDA) Counties by Indian Health Service Region: Colorectal Cancer Mortality and Incidence in American Indian/Alaska Native Persons, 1999–2009.**

**TABLE 1—Colorectal Cancer Incidence Rates, Death Rates, and Mortality/Incidence Rate Ratios by Indian Health Service Region and Contract Health Service Delivery Area and Gender for American Indian/Alaska Native and White Persons: United States, 2005–2009**

IHS Region/ Gender	Incidence				Mortality				Mortality/Incidence				
	AI/AN Cases, No.	AI/AN Rate	White Cases, No.	White Rate	AI/AN/White RR (95% CI)	AI/AN Deaths, No.	AI/AN Rate	White Deaths, No.	White Rate	AI/AN/White RR (95% CI)	AI/AN 1-(M/I)	White RR (95% CI)	White 1-(M/I)
<b>CHSDA counties</b>													
Northern Plains													
Both genders	510	67.3	19 949	44.0	1.53* (1.39, 1.68)	196	26.9	7784	16.1	1.65* (1.43, 1.96)	0.41 (0.34, 0.49)	0.59	0.37 (0.36, 0.38)
Men	275	78.5	10 124	49.8	1.58* (1.37, 1.81)	110	34.5	3869	18.6	1.83* (1.46, 2.31)	0.45 (0.34, 0.58)	0.55	0.38 (0.36, 0.39)
Women	235	57.9	9825	39.2	1.48* (1.28, 1.69)	86	21.5	3915	13.9	1.49* (1.21, 1.93)	0.38 (0.29, 0.50)	0.62	0.36 (0.34, 0.37)
Alaska													
Both genders	325	92.7	809	43.2	2.15* (1.86, 2.47)	106	33.0	228	14.2	2.32* (1.80, 2.98)	0.36 (0.28, 0.45)	0.64	0.33 (0.28, 0.39)
Men	168	105.4	455	47.2	2.23* (1.81, 2.73)	55	35.4	132	16.7	2.12* (1.46, 3.03)	0.34 (0.24, 0.48)	0.66	0.36 (0.29, 0.45)
Women	157	83.9	354	39.1	2.14* (1.75, 2.61)	51	30.4	96	11.8	2.58* (1.77, 3.69)	0.36 (0.26, 0.50)	0.64	0.30 (0.24, 0.38)
Southern Plains													
Both genders	833	69.0	8312	45.8	1.51* (1.40, 1.62)	350	30.4	3180	17.4	1.75* (1.55, 1.96)	0.44 (0.39, 0.50)	0.56	0.38 (0.36, 0.40)
Men	410	75.7	4340	53.5	1.42* (1.26, 1.58)	180	35.1	1715	21.6	1.62* (1.36, 1.92)	0.47 (0.38, 0.57)	0.53	0.40 (0.38, 0.43)
Women	423	63.8	3972	39.5	1.61* (1.45, 1.79)	170	26.8	1465	14.0	1.91* (1.61, 2.24)	0.42 (0.35, 0.51)	0.58	0.35 (0.33, 0.38)
Pacific Coast													
Both genders	482	48.6	36 949	42.8	1.14* (1.03, 1.25)	193	21.9	13 718	15.6	1.40* (1.19, 1.63)	0.45 (0.37, 0.54)	0.55	0.37 (0.36, 0.37)
Men	252	53.5	19 028	48.6	1.10 (0.95, 1.27)	100	26.9	6985	18.1	1.48* (1.16, 1.85)	0.50 (0.38, 0.66)	0.50	0.37 (0.36, 0.38)
Women	230	44.3	17 921	37.7	1.17* (1.02, 1.35)	93	18.7	6733	13.6	1.38* (1.10, 1.71)	0.43 (0.33, 0.55)	0.57	0.36 (0.35, 0.37)
East													
Both genders	149	36.4	40 734	45.4	0.80* (0.67, 0.95)	62	17.7	14 322	15.6	1.13 (0.85, 1.47)	0.48 (0.35, 0.67)	0.52	0.34 (0.34, 0.35)
Men	75	38.5	20 713	52.8	0.73* (0.56, 0.93)	27	16.9	7173	18.6	0.90 (0.56, 1.36)	0.45 (0.26, 0.73)	0.55	0.35 (0.34, 0.36)
Women	74	33.7	20 021	39.5	0.85 (0.66, 1.08)	35	18.0	7149	13.3	1.35 (0.93, 1.90)	0.52 (0.33, 0.80)	0.48	0.33 (0.32, 0.34)
Southwest													
Both genders	520	31.0	16 879	39.1	0.79* (0.72, 0.87)	184	12.1	6676	15.5	0.78* (0.67, 0.91)	0.39 (0.33, 0.47)	0.61	0.40 (0.38, 0.41)
Men	266	34.9	8979	44.5	0.78* (0.68, 0.89)	88	12.9	3550	18.1	0.71* (0.56, 0.89)	0.37 (0.28, 0.48)	0.63	0.41 (0.39, 0.42)
Women	254	27.8	7900	34.3	0.81* (0.71, 0.92)	96	11.5	3126	13.2	0.87 (0.69, 1.06)	0.42 (0.32, 0.53)	0.58	0.39 (0.37, 0.40)
All regions													
Both genders	2819	52.5	123 632	43.4	1.21* (1.16, 1.26)	1091	22.0	45 908	15.8	1.39* (1.31, 1.49)	0.42 (0.39, 0.58)	0.58	0.36 (0.36, 0.37)
Men	1446	58.8	63 639	49.7	1.18* (1.12, 1.25)	560	25.3	23 424	18.6	1.37* (1.24, 1.50)	0.43 (0.39, 0.48)	0.57	0.37 (0.37, 0.38)
Women	1373	47.2	59 993	38.1	1.24* (1.17, 1.31)	531	19.4	22 484	13.5	1.44* (1.31, 1.57)	0.41 (0.37, 0.46)	0.59	0.35 (0.35, 0.36)
<b>All counties</b>													
Northern Plains													
Both genders	661	54.4	103 728	47.5	1.15* (1.05, 1.25)	266	22.7	38 424	16.8	1.35* (1.17, 1.54)			
Men	358	64.3	52 385	54.7	1.18* (1.03, 1.33)	143	28.1	19 177	20.0	1.40* (1.14, 1.70)			
Women	303	46.6	51 343	41.6	1.12 (0.99, 1.26)	123	18.9	19 247	14.3	1.32* (1.08, 1.59)			

Continued



We evaluated CRC mortality trends for 1990 to 2009 and reported them as the APC of the age-adjusted rates. If a joinpoint (change in trend) was identified during this period, the average annual percent change (AAPC) for the 10-year period 2000 to 2009 was reported. If no joinpoint was identified, the 20-year APC and the 10-year AAPC would be the same. Subtracting the mortality/incidence ratio from 1 approximated the probability of 5-year survival, and was shown to be reliable for use with CRC rates.<sup>28</sup>

## RESULTS

From 2005 to 2009, 3604 AI/AN persons were diagnosed with CRC; of these, 2819 (78.2%) resided in CHSDA counties (Table 1). During the same period, 1494 AI/AN persons died from CRC; 1091 (73.0%) were CHSDA residents.

The all-counties CRC incidence rate was 10% lower ( $P < .05$ ) among AI/AN individuals compared with Whites; the death rate was 11% higher ( $P < .05$ ). For CHSDA counties only, the CRC incidence rate was 21% higher ( $P < .05$ ) among AI/AN individuals, and the death rate 39% higher, with similar elevations for both men and women. The remainder of the results referred to CHSDA counties only.

AI/AN colorectal cancer incidence varied regionally (Table 1). The rate among AI/AN populations was significantly higher ( $P < .05$ ) than for Whites in 4 regions (Northern Plains, Alaska, Southern Plains, and Pacific Coast), and significantly lower ( $P < .05$ ) in 2 regions (East and Southwest). This pattern was seen among both men and women, although it was not always statistically significant. Regional CRC incidence rates for both genders combined varied by 199% among AI/AN populations (31.0 in the Southwest to 92.7 in Alaska), but only by 17% among Whites.

CRC death rates also showed significant regional differences. The risk of dying from CRC was elevated ( $P < .05$ ) among AI/AN persons in the same 4 regions with elevated incidence (Northern Plains, Alaska, Southern Plains, and Pacific Coast; Table 1). In the other 2 regions AI/AN death RRs were either not statistically significant (East) or lower by a similar magnitude as for incidence (Southwest). Regional CRC death rates for both genders

combined varied by 173% among AI/AN persons (12.1 in the Southwest to 33.0 in Alaska) and by only 23% among White CHSDA residents.

The mortality/incidence RR for CHSDA residents as a whole was 0.42 (95% = CI 0.39, 0.58) for AI/AN individuals compared with 0.36 (95% CI = 0.36, 0.37) for Whites; this difference was similar for men and women. The mortality/incidence RR was higher for AI/AN individuals than Whites in each region, except the Southwest. The East, which had a significantly lower CRC incidence rate for AI/AN persons, had the highest mortality/incidence RR among AI/AN persons, and showed the most within region difference from Whites.

### Age at Diagnosis

When data from all regions were combined, AI/AN individuals had an increased risk of CRC diagnosis compared with Whites in all age strata. This risk was 45% higher for men and women younger than 50 years, 32% higher among those aged 50 to 64 years, and 13% higher among those aged 65 years or older (all  $P < 0.05$ ) (Table 2).

By region, AI/AN persons in the Northern Plains, Alaska, and the Southern Plains had increased incidence of CRC among all age groups. In the Pacific Coast, there was a significant increased risk among AI/AN persons aged 65 years and older, and nonsignificant increases in other age groups. In the East, there was significantly lower incidence among AI/AN persons aged 65 years and older compared with Whites and a nonsignificant decreased risk in the other age groups, the largest difference being for persons younger than 50 years. In the Southwest, there was a 37% lower incidence of CRC among AI/AN persons aged 65 years and older, whereas AI/AN persons younger than 50 years had a 34% higher incidence compared with Whites.

### Stage at Diagnosis

The age-adjusted rate of early stage CRC was 9% higher among AI/AN individuals compared with Whites for both genders combined, whereas the rate of late-stage CRC was 25% higher (Table 3). In the Northern Plains, Alaska, and Southern Plains, the rate of both early- and late-stage CRC were consistently elevated among AI/AN individuals, although

the increase in risk was larger for late-stage disease. This was reflected in higher late-to early stage RRs among AI/AN individuals compared with Whites in these regions.

### Colorectal Cancer Incidence Trends

CRC incidence trends were evaluated for 1999 to 2009 and reported as the APC in the age-adjusted rate (Table 4). The age-adjusted CRC incidence rate among Whites in CHSDA counties significantly decreased ( $P < .05$ ) in every region from 1999 to 2009, falling 2.1% per year between 1999 and 2003, and accelerating to 3.7% per year between 2003 and 2009 for all regions combined.

When all CHSDA counties were combined, there was no significant change in CRC incidence rate among AI/AN populations between 1999 and 2009. Only Alaska (3.1% per year) and the Pacific Coast (1.9% per year) had a significant decrease in AI/AN colorectal cancer incidence rate during this period. In the Southwest, CRC incidence rates among AI/AN populations significantly increased at 7.7% per year from 1999 to 2005, but had no significant change from 2005 to 2009.

### Mortality Trends

The age-adjusted CRC death rate among Whites significantly ( $P < .05$ ) decreased in every region from 1990 to 2009 (Table 4). In most regions, the decrease in death rates accelerated in the latest decade, with a combined decline of 3.1% per year between 2000 and 2009.

Conversely, CRC death rates among AI/AN persons showed no statistically significant change when regional data were combined. Only the Northern Plains region experienced a decline in death rate among AI/AN persons, falling 1.6% per year between 1990 and 2009, whereas the rate among White persons in this region fell at a rate of 2.0% per year between 1999 and 2000 and 2.9% between 2000 and 2009. The AI/AN colorectal cancer death rate increased in the Pacific Coast at a rate of 1.5% per year between 1990 and 2009. No significant death rate change was seen in the other regions during the analysis period.

## DISCUSSION

The purpose of our study was to characterize estimates of CRC incidence and mortality in

**TABLE 2—Colorectal Cancer Incidence by Indian Health Service Region and Age at Diagnosis for American Indian/Alaska Native and White Persons: CHSDA Counties, United States, 2005–2009**

IHS Region/Age at Diagnosis	AI/AN		White		AI/AN:White RR (95% CI)
	Cases, No. (%)	Rate	Cases, No. (%)	Rate	
<b>Northern Plains</b>					
< 50 y	79 (15.49)	9.6	1514 (7.59)	5.9	1.64* (1.29, 2.05)
50–64 y	192 (37.65)	113.2	5007 (25.10)	65.9	1.72* (1.48, 1.98)
≥ 65 y	239 (46.86)	343	13 428 (67.31)	236.2	1.45* (1.26, 1.66)
All ages	510 (100.00)	67.3	19 949 (100.00)	44.0	1.53* (1.39, 1.68)
<b>Alaska</b>					
< 50 y	54 (16.62)	15.4	109 (13.47)	6.1	2.53* (1.79, 3.54)
50–64 y	118 (36.31)	159.2	309 (38.20)	63.2	2.52* (2.02, 3.13)
≥ 65 y	153 (47.08)	456.5	391 (48.33)	232.0	1.97* (1.61, 2.39)
All ages	325 (100.00)	92.7	809 (100.00)	43.2	2.15* (1.86, 2.47)
<b>Southern Plains</b>					
< 50 y	137 (16.45)	12.8	713 (8.58)	7.3	1.74* (1.44, 2.10)
50–64 y	274 (32.89)	110.9	2229 (26.82)	74.3	1.49* (1.31, 1.69)
≥ 65 y	422 (50.66)	341.4	5370 (64.61)	232.3	1.47* (1.32, 1.63)
All ages	833 (100.00)	69.0	8312 (100.00)	45.8	1.51* (1.40, 1.62)
<b>Pacific Coast</b>					
< 50 y	66 (13.69)	6.9	2942 (7.96)	6.1	1.13 (0.87, 1.44)
50–64 y	166 (34.44)	70.9	9737 (26.35)	64.5	1.10 (0.94, 1.28)
≥ 65 y	250 (51.87)	261.2	24 270 (65.69)	226.8	1.15* (1.01, 1.31)
All ages	482 (100.00)	48.6	36 949 (100.00)	42.8	1.14* (1.03, 1.25)
<b>East</b>					
< 50 y	20 (13.42)	5.4	3431 (8.42)	7.0	0.76 (0.46, 1.18)
50–64 y	56 (37.58)	64.2	10 469 (25.70)	72.3	0.89 (0.67, 1.15)
≥ 65 y	73 (48.99)	181.5	26 834 (65.88)	233.5	0.78* (0.60, 0.99)
All ages	149 (100.00)	36.4	40 734 (100.00)	45.4	0.80* (0.67, 0.95)
<b>Southwest</b>					
< 50 y	121 (23.27)	7.6	1275 (7.55)	5.7	1.34* (1.10, 1.61)
50–64 y	194 (37.31)	60.9	4346 (25.75)	59.9	1.02 (0.88, 1.17)
≥ 65 y	205 (39.42)	129.8	11 258 (66.70)	205.5	0.63* (0.55, 0.73)
All ages	520 (100.00)	31.0	16 879 (100.00)	39.1	0.79* (0.72, 0.87)
<b>All regions</b>					
< 50 y	477 (16.92)	9.3	9984 (8.08)	6.4	1.45* (1.32, 1.59)
50–64 y	1000 (35.47)	88.4	32 097 (25.96)	67.0	1.32* (1.24, 1.41)
≥ 65 y	1342 (47.61)	257.8	81 551 (65.96)	227.5	1.13* (1.07, 1.20)
All ages	2819 (100.00)	52.5	123 632 (100.00)	43.4	1.21* (1.16, 1.26)

Note. AI/AN = American Indian/Alaska Native; CHSDA = Contract Health Service Delivery Area; CI = confidence interval; IHS = Indian Health Service; RR = rate ratio. Analyses are limited to persons of non-Hispanic origin. AI/AN race is reported by National Program of Cancer Registries and Surveillance, Epidemiology, and End Results Registries 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 (19 age groups; Census P25-1130). Rate ratios are calculated in SEER\*Stat before rounding of rates and may not equal RRs calculated from rates presented in table. IHS regions are defined as follows: Alaska<sup>a</sup>; Northern Plains (IL, IN, IA, MI, MN, MT, NE, ND, SD, WI, WY<sup>a</sup>); Southern Plains (OK, KS, TX<sup>a</sup>); Southwest (AZ, CO, NV, NM, UT<sup>a</sup>); Pacific Coast (CA, ID, OR, WA, HI); East (AL, AR, CT, DE, FL, GA, KY, LA, ME, MD, MA, MS, MO, NH, NJ, NY, NC, OH, PA, RI, SC, TN, VT, VA, WV, DC). Percentage 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%.

Source: Incidence data are from population-based cancer registries that participate in the National Program of Cancer Registries or the Surveillance, Epidemiology, and End Results Registries (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.

<sup>a</sup>Identifies states with at least 1 county designated as CHSDA.

\*P < .05.

**TABLE 3—Colorectal Cancer Incidence by Indian Health Service Region, Stage at Diagnosis, and Gender for American Indian/Alaska Native and White Persons: CHSDA Counties, United States, 2005–2009**

IHS Region/Gender	Stage	AI/AN			White			AI/AN:White RR <sup>a</sup>
		Cases, No. (%)	Rate	Late/Early Stage RR (95% CI)	Cases, No. (%)	Rate	Late/Early Stage RR (95% CI)	
<b>Northern Plains</b>								
Both genders	Early	175 (37.80)	23.9		7638 (44.66)	16.9		1.41
	Late	288 (62.20)	36.4	1.52* (1.23, 1.88)	9465 (55.34)	21.0	1.25* (1.21, 1.28)	1.73
Men	Early	91 (36.11)	27.3		3954 (45.40)	19.4		1.41
	Late	161 (63.89)	43.3	1.59* (1.18, 2.15)	4755 (54.60)	23.2	1.20* (1.15, 1.25)	1.87
Women	Early	84 (39.81)	21.1		3684 (43.89)	14.7		1.44
	Late	127 (60.19)	30.3	1.44* (1.06, 1.95)	4710 (56.11)	19.1	1.30* (1.24, 1.36)	1.59
<b>Alaska</b>								
Both genders	Early	115 (37.10)	32.3		329 (45.63)	18.0		1.79
	Late	195 (62.90)	55.8	1.73* (1.35, 2.23)	392 (54.37)	20.0	1.11 (0.95, 1.31)	2.79
Men	Early	64 (40.25)	39.4		173 (42.30)	18.0		2.19
	Late	95 (59.75)	61.0	1.55* (1.08, 2.24)	236 (57.70)	23.8	1.32* (1.05, 1.67)	2.56
Women	Early	51 (33.77)	26.5		156 (50.00)	18.0		1.47
	Late	100 (66.23)	53.5	2.02* (1.41, 2.92)	156 (50.00)	16.3	0.91 (0.71, 1.15)	3.28
<b>Southern Plains</b>								
Both genders	Early	289 (40.36)	24.4		3259 (43.95)	17.9		1.36
	Late	427 (59.64)	34.7	1.42* (1.21, 1.67)	4157 (56.05)	23.0	1.28* (1.22, 1.34)	1.51
Men	Early	129 (37.61)	24.7		1704 (43.96)	20.9		1.18
	Late	214 (62.39)	38.3	1.55* (1.22, 1.99)	2172 (56.04)	26.6	1.27* (1.19, 1.36)	1.44
Women	Early	160 (42.90)	24.1		1555 (43.93)	15.4		1.56
	Late	213 (57.10)	32.0	1.33* (1.07, 1.65)	1985 (56.07)	20.0	1.29* (1.21, 1.38)	1.60
<b>Pacific Coast</b>								
Both Genders	Early	162 (35.37)	16.7		14 411 (41.38)	16.7		1.00
	Late	296 (64.63)	28.7	1.72* (1.39, 2.13)	20 415 (58.62)	23.7	1.42* (1.39, 1.45)	1.21
Men	Early	88 (36.67)	18.9		7562 (41.95)	19.3		0.98
	Late	152 (63.33)	30.0	1.58* (1.17, 2.15)	10 464 (58.05)	26.6	1.38* (1.34, 1.43)	1.13
Women	Early	74 (33.94)	14.6		6849 (40.77)	14.5		1.01
	Late	144 (66.06)	27.3	1.87* (1.39, 2.55)	9951 (59.23)	21.1	1.46* (1.41, 1.51)	1.29
<b>East</b>								
Both genders	Early	63 (45.32)	14.3		17 039 (45.14)	19.0		0.75
	Late	76 (54.68)	18.9	1.31 (0.91, 1.91)	20 707 (54.86)	23.2	1.22* (1.20, 1.25)	0.81
Men	Early	39 (57.35)	18.0		8848 (45.83)	22.4		0.80
	Late	29 (42.65)	15.2	0.84 (0.47, 1.45)	10 459 (54.17)	26.6	1.19* (1.16, 1.22)	0.57
Women	Early	24 (33.80)	10.5		8191 (44.42)	16.3		0.64
	Late	47 (66.20)	21.6	2.06* (1.21, 3.62)	10 248 (55.58)	20.4	1.26* (1.22, 1.30)	1.06
<b>Southwest</b>								
Both genders	Early	194 (42.73)	11.8		6546 (43.96)	15.1		0.78
	Late	260 (57.27)	15.1	1.28* (1.05, 1.56)	8346 (56.04)	19.4	1.29* (1.24, 1.33)	0.78
Men	Early	107 (45.15)	14.8		3510 (44.48)	17.2		0.86
	Late	130 (54.85)	16.0	1.08 (0.82, 1.44)	4382 (55.52)	21.7	1.26* (1.20, 1.32)	0.74
Women	Early	87 (40.09)	9.5		3036 (43.37)	13.1		0.73
	Late	130 (59.91)	14.1	1.49* (1.12, 1.99)	3964 (56.63)	17.3	1.32* (1.26, 1.38)	0.82

Continued

TABLE 3—Continued

All regions								
Both genders	Early	998 (39.29)	18.8		49 222 (43.67)	17.3		1.09
	Late	1542 (60.71)	28.1	1.49* (1.37, 1.62)	63 482 (56.33)	22.4	1.30* (1.28, 1.31)	1.25
Men	Early	518 (39.88)	21.6		25 751 (44.23)	20.0		1.08
	Late	781 (60.12)	30.5	1.41* (1.25, 1.60)	32 468 (55.77)	25.3	1.26* (1.24, 1.28)	1.21
Women	Early	480 (38.68)	16.5		23 471 (43.08)	15.0		1.10
	Late	761 (61.32)	25.9	1.57* (1.39, 1.77)	31 014 (56.92)	19.9	1.33* (1.31, 1.35)	1.30

Note. AI/AN = American Indian/Alaska Native; CHSDA = Contract Health Service Delivery Area; CI = confidence interval; IHS = Indian Health Service; RR = rate ratio. Analyses are limited to persons of non-Hispanic origin. AI/AN race is reported by National Program of Cancer Registries and Surveillance, Epidemiology, and End Results registries 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 (19 age groups; Census P25-1130). Rate ratios are calculated in SEER\*Stat before rounding of rates and may not equal RRs calculated from rates presented in table. IHS regions are defined as follows: Alaska<sup>b</sup>; Northern Plains (IL, IN, IA, MI, MN, MT, NE, ND, SD, WI, WY<sup>a</sup>); Southern Plains (OK, KS, TX<sup>b</sup>); Southwest (AZ, CO, NV, NM, UT<sup>b</sup>); Pacific Coast (CA, ID, OR, WA, HI); East (AL, AR, CT, DE, FL, GA, KY, LA, ME, MD, MA, MS, MO, NH, NJ, NY, NC, OH, PA, RI, SC, TN, VT, VA, WV, DC). Percentage 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%.

Source. Incidence data are from population-based cancer registries that participate in the National Program of Cancer Registries or the Surveillance, Epidemiology, and End Results Registries (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; 1999–2001 and 2003–2009: DC; 2001–2009: AR, NC, SD; 2002–2009: VA; 2003–2009: MS, TN.

<sup>a</sup>RRs between rate for AI/AN persons and rate for White persons by stage.

<sup>b</sup>Identifies states with at least 1 county designated as CHSDA.

\* $P < .05$ .

AI/AN persons by region compared with Whites using a linkage methodology to improve AI/AN classification in the incidence and mortality data. Restricting the study population to CHSDA counties unveiled significantly higher incidence and death rates among AI/AN persons compared with those for all US counties. The difference between the CHSDA and all counties rates was likely driven by higher rates of misclassification in the cancer registries and death records for AI/AN persons living in urban and other non-CHSDA areas.<sup>3</sup>

Our previous application of this method examined incidence from 1999 to 2004.<sup>5</sup> In that analysis, the overall CHSDA CRC incidence was 9% lower among all AI/AN populations than Whites; however, the AI/AN rate varied approximately 5-fold regionally, from 21.0 in the Southwest to 102.6 in Alaska. Over the subsequent 5 years covered in this report, CRC incidence among AI/AN persons increased from 46.3 to 52.5, whereas it decreased among Whites from 50.8 to 43.4. Hence, although rates decreased steadily in Whites across regions, the incidence in AI/AN individuals fell in only Alaska and the Pacific Coast, albeit at a slower rate. Meanwhile, incidence did not significantly change in the other regions from 2005 to 2009.

Others reported a steady decline in the US CRC incidence rate, driven primarily by

downward trends among Whites.<sup>29</sup> The accelerated decline in recent years was primarily attributed to the efficacy of removing precancerous polyps during screening colonoscopy.<sup>30</sup> Significant disparities existed between Whites and AI/ANs in the use of CRC screening, especially with endoscopic screening.<sup>31</sup> Reasons for these disparities were multifactorial, but included a lack of endoscopic services at most IHS and tribal facilities, underfunded referral systems, and fecal occult blood testing (with either guaiac or fecal immunochemical methods) as the primary CRC screening modality employed by the majority of IHS and tribal facilities. Although effective at finding CRC before symptoms arise, fecal testing does not remove precancerous polyps, which can be removed during endoscopic screening.<sup>6</sup> Data from the 2010 National Health Interview Survey reported 59.8% of Whites to be current with screening guidelines compared with 49.5% of AI/AN persons.<sup>9</sup> The Government Performance Results Act requires IHS-funded facilities to submit CRC screening data. In 2010, 37% of AI/AN men and women served by the IHS were current with screening guidelines, although rates ranged from 24% in the IHS Phoenix area to 55% in the IHS Alaska area.<sup>32</sup> Because screening rates significantly rose over the last decade, as has the use of endoscopic screening, more time might be

needed to see an effect on incidence and mortality.<sup>32</sup>

Between 2005 and 2009, AI/AN persons in Alaska had a 115% greater CRC incidence rate and a 132% greater death rate than Whites. The Alaska Area program has been responding to this disparity with innovative programs designed to increase screening, including the deployment of itinerant colonoscopy teams who travel to regional health centers.<sup>33</sup> The Northern Plains had the second highest CRC incidence and death rate, but was distinguished by being the only region with a significantly declining death rate. Innovative community-based programs such as Minnesota's Intertribal Colorectal Cancer Council, which brings together tribal health champions to improve screening, and the Wisdom Steps program, which rewards elders for meeting preventative health measures, might be affecting this change.<sup>34,35</sup>

By comparison, between 2005 and 2009, the incidence of CRC among Southwest AI/AN persons was more than 21% lower than Whites. Despite lower CRC burden, the incidence of CRC among Southwest AI/AN persons increased at an alarming rate of 7.7% per year between 1999 and 2005, whereas mortality increased at 1.3% per year. Work is needed to identify the factors behind these concerning trends.



**TABLE 4—Incidence Rate (1999–2009) and Death Rate (1990–2009) Trends for Colorectal Cancer With Joinpoint Analyses for American Indian/Alaska Native Persons Compared With Whites: CHSDA Counties, United States**

IHS Region/Race	Trend 1		Trend 2		Trend 3		Trend 4	
	Years	APC <sup>a</sup>	Years	APC <sup>a</sup>	Years	APC <sup>a</sup>	Years	APC <sup>a</sup>
<b>Incidence rate joinpoint analysis<sup>b</sup></b>								
Northern Plains								
White <sup>c</sup>	1999-2003	-1.8	2003-2009	-4.4*				
AI/AN <sup>c,d</sup>	1999-2009	-1.8						
Alaska								
White	1999-2009	-3.4*						
AI/AN	1999-2009	-3.1*						
Southern Plains								
White	1999-2001	0.2	2001-2009	-2.6*				
AI/AN	1999-2009	0.3						
Pacific Coast								
White	1999-2009	-2.4*						
AI/AN	1999-2009	-1.9*						
East								
White	1999-2003	-2.2*	2003-2009	-4.6*				
AI/AN	1999-2009	-1.6						
Southwest								
White	1999-2002	-0.9	2002-2009	-3.6*				
AI/AN	1999-2005	7.7*	2005-2009	-3.2				
All regions								
White	1999-2003	-2.1*	2003-2009	-3.7*				
AI/AN	1999-2009	-0.7						
<b>Death rate joinpoint analyses</b>								
Northern Plains								
White	1990-2000	-2.0*	2000-2009	-2.9*				
AI/AN	1990-2009	-1.6*						
Alaska								
White	1990-2009	-3.0*						
AI/AN	1990-2009	-1.6						
Southern Plains <sup>c</sup>								
White	1997-2009	-1.6*						
AI/AN	1997-2009	1.8						
Pacific Coast								
White	1990-2001	-1.5*	2001-2009	-2.6*				
AI/AN	1990-2009	1.5*						
East								
White	1990-2000	-1.8*	2000-2009	-3.8*				
AI/AN	1990-2009	1.7						
Southwest								
White	1990-2003	-1.0*	2003-2009	-3.5*				
AI/AN	1990-2009	1.3						

Continued

The reasons for the substantial interregional variation in AI/AN colorectal cancer incidence and mortality were unclear, but were likely multifactorial. Genetic differentiation might play a role in these diverse, often isolated communities.<sup>36</sup> AI/AN populations also vary widely in their diets, environments, and access to care. Many Alaskan AI/AN persons maintain subsistence diets high in animal fats and low in fresh fruits and vegetables.<sup>37</sup> The high cigarette smoking rate and high prevalence of vitamin D deficiency because of low dietary intake and low ultraviolet B exposure could also play a role.<sup>38,39</sup> By comparison, AI/AN persons in the Southwest have lower cigarette smoking use,<sup>40</sup> whereas year-round ultraviolet B exposure results in lower rates of vitamin D deficiency.<sup>38</sup> Given the dramatic regional CRC differences among AI/AN populations, these populations might be ideally suited for further research into the influence of risk factors, such as diet, environment, genetics, and screening on CRC mortality. Such findings might have important implications for all populations.

Understanding the relationship between CRC incidence and age at diagnosis is critical for informing screening guidelines. The rationale for when to begin screening is based on the benefit of early stage diagnoses in terms of added life-years, attenuated by the risk of screening.<sup>6</sup> In this study, the incidence rate of CRC cases occurring in AI/AN individuals younger than age 50 years ranged from 5.4 in the East to 15.4 in Alaska. By comparison, the rate among Whites ranged from 5.7 in the Southwest to 7.3 in the Southern Plains. Although the American College of Gastroenterology recommends CRC screening beginning at age 50 years in average-risk persons, it recommends that African Americans begin screening at age 45 years because they were shown to acquire a survival benefit from screening at a younger age.<sup>41</sup> Given our data, modeling the risks and benefits of earlier age CRC screening in AI/AN individuals might be warranted.

Based on the mortality/incidence ratio, AI/ANs diagnosed with CRC had a lower 5-year survival probability than Whites in all IHS regions, with exception of the Southwest, where it was the same. A major predictor of CRC mortality odds was stage at diagnosis. Five-year survival was more than 90% for CRC

TABLE 4—Continued

All regions								
White	1990-1994	-1.1*	1994-1997	-2.9*	1997-2000	-0.6	2000-2009	-3.1*
AI/AN	1990-2009	0.8						

Note. AI/AN = American Indian/Alaska Native; APC = annual percent change; CHSDA = Contract Health Service Delivery Area; IHS = Indian Health Service. Analyses are limited to persons of non-Hispanic origin. AI/AN race for incidence data are reported by National Program of Cancer Registries and Surveillance, Epidemiology, and End Results registries or through linkage with the IHS patient registration database. AI/AN race for deaths is reported from death certificates or through linkage with the IHS patient registration database. IHS regions are defined as follows: Alaska<sup>d</sup>; Northern Plains (IL, IN, IA, MI, MN, MT, NE, ND, SD, WI, WY<sup>b</sup>); Southern Plains (OK, KS, TX<sup>c</sup>); Southwest (AZ, CO, NV, NM, UT<sup>d</sup>); Pacific Coast (CA, ID, OR, WA, HI); East (AL, AR, CT, DE, FL, GA, KY, LA, ME, MD, MA, MS, MO, NH, NJ, NY, NC, OH, PA, RI, SC, TN, VT, VA, WV, DC). Percentage 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%.

Source. Incidence data are from population-based cancer registries that participate in the National Program of Cancer Registries or the Surveillance, Epidemiology, and End Results Registries (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.

<sup>a</sup>APC is based on rates that were age-adjusted to the 2000 US standard population (11 age groups; Census P25-1130).

<sup>b</sup>Jointpoint analyses with up to 3 jointpoints that are based on rates per 100 000 persons and are age-adjusted to the 2000 US standard population (11 age groups; Census P25-1130).

<sup>c</sup>Mortality trend is calculated only for 1997-2009.

<sup>d</sup>Identifies states with at least 1 county designated as CHSDA.

\* $P < .05$ .

diagnosed at an early, localized stage, but decreased precipitously to 70% with localized spread or lymph node involvement, and to 12% with metastatic disease.<sup>42</sup> In our analysis, 61% of incident cases occurring in AI/AN persons were late stage versus 56% in Whites. Pacific Coast, East, and Alaska women had the highest proportion of late-stage CRC diagnosis (66% of cases in each region), whereas men in the Northern Plains were diagnosed at advanced stages 64% of the time. These proportions were from 7% to 11% higher than those seen in Whites, and likely represented inequities in CRC screening. Continued efforts to improve screening uptake among AI/AN populations are therefore needed.

Additional factors likely played a role in survival disparities. Proximity to a cancer center, the availability of resources to pay for care, patient comorbidities, and patient acceptance of treatment could all affect cancer outcomes.<sup>43,44</sup> A better understanding of how these factors affected AI/AN colorectal cancer survival disparities is needed.

Our results must be considered in light of several limitations. Although we approximated survival probability, making inferences about the relationship between incidence and mortality based on 5 years of data was problematic. Incident cases might die from CRC after

the catchment period, whereas mortality cases might have been diagnosed before catchment. Linking incidence and mortality so case-fatality ratios might be discerned would better characterize survival disparities.

It was also probable that our reported incidence and death rates for CRC in AI/AN populations were still underestimates. The IHS provides care to 2.2 million of the estimated 3.4 million AI/AN persons in the United States.<sup>45</sup> Individuals who self-identified as AI/AN persons on census records, but did not have direct tribal ties, were from non-federally recognized tribes, lived long distances from IHS and tribal health facilities, were multiracial, were less likely to access the IHS.<sup>46</sup> AI/AN residents of urban areas might also differ from all AI/AN persons in poverty level, health care access, and other factors that might influence mortality.<sup>47,48</sup> Our approach could not correct racial misclassification in these cases. Furthermore, there was substantial variation between federally recognized tribes in the proportion of Native ancestry required for tribal membership, and therefore, for eligibility for IHS services. Whether and how this discrepancy in tribal membership requirements might influence some of our findings was unclear, although our findings were consistent with previous reports. Finally, although the exclusion of Hispanic

AI/AN persons from the analyses reduced the overall count of deaths in AI/AN persons by less than 5%, it might disproportionately exclude some tribal members in some states.

This study found dramatic geographic variations in AI/AN colorectal cancer incidence and mortality compared with Whites. Future presentations of AI/AN cancer data should consider the effects of racial misclassification and regional variations might have on summary statistics. The higher prevalence of advanced disease at diagnosis and corresponding mortality disparities among AI/AN populations call for more attention to improve access to and utilization of CRC screening programs. An understanding of the factors driving these regional disparities could offer critical insights for prevention and control programs. ■

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#### Contributors

D. G. Perdue was the lead writer of the article. D. Haverkamp analyzed the data and populated the tables. C. Perkins interpreted the data for the results section. C. M. Daley and E. Provost contributed in the editing of the article drafts.

#### Human Participant Protection

Human participant protection was not required because no human participants were involved.

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