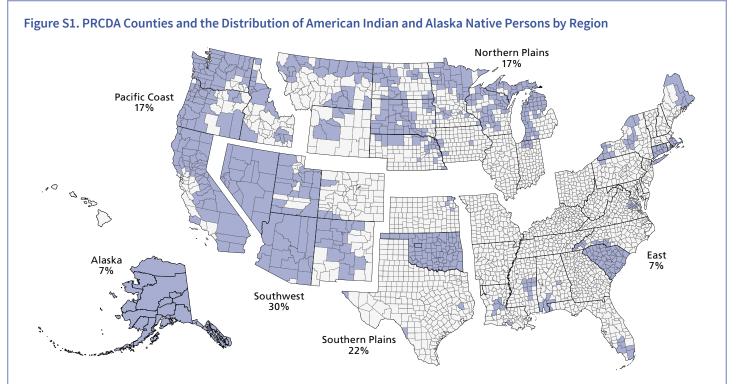
Special Section: Cancer in the American Indian and Alaska Native Population

Introduction

In 2020, an estimated 9.7 million people identified as American Indian or Alaska Native (AIAN), representing about 3% of the US population.¹ According to the US Office of Management and Budget, the term AIAN refers to a person "having origins in any of the original peoples of North and South America (including Central America) and who maintains tribal affiliation or community attachment."² The AIAN population is incredibly diverse, with 574 federally recognized tribes and more than 200 that remain unrecognized, encompassing many distinct customs, languages, and history.³⁻⁶

At least in part because of genocide, forced displacement, and relocation perpetrated by US citizens and the military (e.g., the Indian Removal Act of 1830),⁷⁻⁹ approximately two-thirds of AIANs live in tribal areas or surrounding counties, referred to as Purchased/Referred Care Delivery Area (PRCDA) counties. These counties are concentrated in the Western US and are more rural than non-PRCDA counties.^{10, 11} There are 6 PRCDA regions: Alaska, East, Northern Plains, Pacific Coast, Southern Plains, and Southwest (Figure S1).

Continued systemic racism has resulted in limited access to health care, high-quality education, and economic opportunity for AIANs.^{12,13} For example, people who are AIAN are twice as likely to live in poverty as those who are White, regardless of where they live (Table S1). In addition, although AIANs in PRCDA regions are served by the Indian Health Service (IHS), which was established in 1955 as part of ongoing payment for the coerced cession of tribal lands, they have the lowest health care



PCRDA: Purchased/Referred Care Delivery Area. Percentages represent the proportion of the non-Hispanic American Indian/Alaska Native PRCDA population that lives in each region (shown in blue). **Source:** US Census Bureau, 2019.

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Table S1. Sociodemographic Characteristics and Health Care Access by Race and Census Region, US, 2019

Sociodemographic characteristics*

		American Indian/Alaska Native White									
	All	Northeast	Midwest	South	West	Alaska	All				
Median age, years	32.9	34.8	32.0	34.1	32.0	28.5	40.1				
Average household size (# of persons)	2.7	2.4	2.5	2.6	2.9	3.0	2.5				
Poverty (%) [†]	20.3	18.2	23.9	19.1	20.2	19.7	10.5				
Per capita income (\$) [‡]	24,497	28,529	21,842	25,325	24,090	21,822	38,198				
Educational attainment, ages ≥25 yrs (%)											
Less than high school graduate	15.6	16.4	13.6	15.5	16.3	11.6	9.6				
High school graduate	28.3	26.3	30.3	27.7	28.3	40.7	26.9				
Some college or associate's degree	35.3	30.6	67.3	34.3	36.4	33.8	29.1				
Bachelor's degree or higher	20.8	26.7	18.8	22.5	19.0	13.9	34.4				

Health care access (%)*

			Tot	al US	Region§							
	All		N	1ale	Female		Midwest		South		W	est
	AIAN	White	AIAN	White	AIAN	White	AIAN	White	AIAN	White	AIAN	White
Uninsured, ages 18-64 yrs	27	10	38	11	18	10	25	9	29	15	25	9
No regular source of medical care	12	12	18	15	-	8	-	11	17	14	-	12
	All	All AIAN		an Indian	Alaskan Native							
Insurance status by IHS usage, ages ≥18 yrs	IHS	non-IHS	IHS	non-IHS	IHS	non-IHS						
Uninsured	32	13	32	13	31	_						
Private insurance	37	56	36	57	36	49						
Public insurance	32	32	32	30	33	39						

AIAN: American Indian and Alaska Native; IHS: Indian Health Service. Data are not restricted to Purchased/Referred Care Delivery Area counties. *Persons of Hispanic ethnicity are included in sociodemographic data due to data limitations but are excluded from health care access data. †Excludes persons in institutions, military group quarters, or college dormitories, and unrelated individuals under age 15 years. ‡Mean income computed for every man, woman, and child, including those living in group quarters. §Information by region is limited due to sparse data for AIANs. – Statistic not shown due to sparse data.

Sources: Sociodemographic characteristics – American Community Survey 1-year estimates, Selected Population Profiles 2019. Health care access – National Health Interview Survey, 2019. Insurance status by IHS usage – US Census Microdata, 2019.

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coverage and health status of any population. This is in part because the IHS is chronically underfunded and understaffed.¹⁴⁻¹⁶ Of the \$48 billion per year required to fully fund the IHS, only \$6.23 billion was budgeted for FY 2021.^{17, 18} As a result, the IHS is unable to fully provide for the health care needs of those it serves, many of whom lack health insurance. Compared to their White counterparts, AIANs are more than twice as likely to be uninsured (Table S1), leaving many without access to care. Consequently, AIANs have a higher prevalence of many chronic health conditions than any other racial or ethnic group.¹⁰ Further, AIANs are nearly 4 times more likely to be hospitalized with coronavirus disease 2019 (COVID-19) and twice as likely to die from the illness compared to White people.¹⁹⁻²¹

Despite these challenges, native communities demonstrate remarkable resiliency and tirelessly advocate for improved

health care, self-governance, and fair and equitable treatment.^{17, 22-24} This special section presents information on cancer among AIANs, including this population's unique challenges in accessing health care. Although cancer data by tribal affiliation are unavailable, differences between PRCDA regions are described when possible to shed light on the substantial heterogeneity of the cancer burden within this population. Cancer statistics are presented for non-Hispanic AIAN individuals residing in PRCDA counties to minimize racial misclassification (see sidebar on page 32).

Cancer Occurrence among AIANs

Incidence

Nationally, cancer incidence among AIANs is higher than among Whites for lung, colorectal, and kidney cancers, as well as cancers associated with infectious agents (liver,

Improving the Accuracy of Cancer Statistics for American Indians and Alaska Natives

American Indians and Alaska Natives (AIANs) have the highest racial misclassification in health data of any group,²⁵⁻²⁷ which results in an underestimation of disease burden when left unaddressed. One method of improving accuracy is data linkage with the Indian Health Service (IHS), which provides health care to approximately 2.6 million AIANs in 25 states.²⁸ IHS linkage has been shown to increase cancer incidence and mortality rates by 30% or more.²⁹⁻³¹ Although IHS-linked cancer incidence data are publicly available, IHS-linked cancer mortality data are housed at the Centers for Disease Control and Prevention (CDC) and unavailable to external researchers. Thus, because of the high percentage of misclassification on death certificates, we were unable to include high-quality mortality data in this special section. The lack of broad availability of IHS-linked mortality data hinders the much-needed promotion of cancer prevention and control for this underserved population.

Misclassification is additionally reduced by restricting analyses to non-Hispanic individuals residing in Purchased/Referred Care Delivery Area (PRCDA) counties, where receipt of care through the IHS is most common.^{31, 32} Hispanic ethnicity exclusion improves precision because bridged race intercensal population estimates used to calculate disease rates have overestimated the number of Hispanic AIANs since 2010.^{33, 34} All cancer incidence data presented in this report are confined to non-Hispanic AIANs residing in PRCDA counties and have gone through linkage with IHS enrollment files. The Urban Indian Health Institute and American Indian Cancer Foundation are working to further reduce misclassification in health data, which will especially improve representation of AIANs living in urban settings.³⁵

stomach, cervix; Table S2). These racial disparities are similar regardless of whether the comparison is with Whites overall or those residing in PRCDA counties. However, cancer risk and disparities vary substantially by PRCDA region. For example, incidence of lung cancer, the most commonly diagnosed cancer among AIANs, ranges from 16.8 cases per 100,000 in the Southwest (Figure S2), where it is 64% lower than in Whites (Table S3), to 109.3 in the Northern Plains, where it is 80% higher than in Whites. For all cancers combined, rates among AIANs range from 323.2 cases per 100,000 persons in the Southwest (23% lower than in Whites) to 666.7 in the Southern Plains (49% higher than in Whites). However, incidence in AIANs is most favorable compared to Whites in the East region (29% lower), partly because rates among Whites there are the highest of any PRCDA region.

Stage Distribution and Survival

Cancer is generally diagnosed at a later stage in AIANs than in Whites, with some of the largest disparities for breast and stomach cancers (Figure S3). Consequently, 5-year relative survival rates are lower among AIANs than Whites for most cancer types (Figure S4). The largest difference is for stomach cancer, for which 5-year survival is 19% among AIANs versus 32% among Whites. Importantly, these disparities are likely underestimated because of racial misclassification and other biases that undermine accurate cancer statistics for indigenous and other non-White populations.³⁶

Later-stage diagnosis and lower survival among AIANs likely reflect less access to high-quality health care and other obstacles to early detection and treatment.³⁷⁻³⁹ Although the IHS is a health care option for many, it is not health insurance and thus, not governed by legislative protections like the Affordable Care Act. As a result, the IHS has limited "specialty services," such as cancer screening.^{40,41} A 2005 report of 13 IHS facilities found that more than half did not have recommended colonoscopy services.⁴² (See Cancer Screening in AIANs, page 41.)

In addition, more than half (54%) of AIANs live in rural areas or small towns,⁴³ where access to health care professionals, hospital services, and specialty care is limited.^{44, 45} Increased distance to providers is an even greater challenge for rural residents who are poor.⁴⁶

Selected Cancers

Breast (female)

Incidence: Breast cancer is the most commonly diagnosed cancer in AIAN women, as it is in the general population (Table S2).^{47, 48} Disparities in incidence between AIAN and White women vary regionally, ranging from 45% lower than Whites in the Southwest (69.9 versus 126.7 per 100,000) to 35% higher in the Southern Plains (166.8 versus 123.6 per 100,000, Table S3). These differences likely reflect regional variation in obesity prevalence (Table S4) and reproductive factors that influence breast cancer risk, such as age at first birth⁴⁹ and use of oral contraceptives and menopausal hormone therapy.^{16, 50-52} (See page 11 for information about how these factors influence breast cancer risk.) Differences in the prevalence and quality of breast cancer screening also likely contribute (see Cancer Screening in AIANs, page 41). Breast cancer incidence rates have been increasing slowly for over a decade among women overall, but appear to have stabilized in recent years among AIAN women (Figure S6).

Stage at diagnosis and survival: The 5-year relative survival rate for breast cancer is 90% among AIAN women (Figure S4). AIAN women are less likely than White women to be diagnosed with localized-stage disease (59% versus 67%, Figure S3) and have a higher prevalence of triple-negative tumors (estrogen- and progesteronereceptor negative and human epidermal growth factor receptor 2-negative), which have the lowest survival rate of all major breast cancer subtypes.⁵³⁻⁵⁴ Biennial mammography rates are lower among AIAN than White women nationally (62% versus 72%, Table S5), and are lower still in AIAN women receiving care at IHS facilities (55% in women ages 52-64 years, Table S6).⁵⁵

Colon and Rectum

Incidence: Colorectal cancer (CRC) is the third most commonly diagnosed cancer among all AIAN men and women (Table S2) but is the second most commonly diagnosed cancer among Alaska Native men and women, who have the highest incidence globally.⁵⁶⁻⁵⁸ Incidence rates among AIANs regionally range from similar to those in Whites in the East to more than 2.5-fold higher in Alaska (91.3 versus 35.5 cases per 100,000, Table S3). Elevated rates among AIANs may reflect higher prevalence of cigarette smoking and obesity (Table S4) and lower receipt of CRC screening (Table S5),⁵⁹ which allows for detection and removal of precancerous lesions. Additional factors specific to Alaska Natives may include vitamin D deficiency due to less sun exposure and a diet low in dietary fiber, fruits, and vegetables.⁶⁰ In contrast to rapid declines in CRC incidence among Whites in recent decades, rates among AIANs have decreased very slowly, by about 0.5% per year from 1998 through 2018 (Figure S6).³⁰

Stage at diagnosis and survival: Five-year relative survival for CRC is similar in AIANs and Whites when diagnosed at the same stage (Figure S4). However, AIANs are less likely to be diagnosed with localized-stage disease (32% versus 35%, respectively, Figure S3). Later-stage diagnosis likely relates in part to lack of colonoscopy services at many IHS and other health care facilities that serve AIAN patients (see Cancer Screening in AIANs, page 41).⁶¹ Only 41% of persons ages 50-75 years who used IHS services (Table S6)⁵⁵ and 56% of AIANs overall are up-to-date for CRC screening versus 69% of Whites (Table S5).

Kidney and Renal Pelvis

Incidence: Kidney cancer incidence rates are about 80% higher in AIANs than in Whites (31.6 versus 17.7 cases per 100,000, Table S2), and are likewise elevated in all regions except the East.⁶² This pattern likely reflects the higher prevalence among AIANs of obesity (Table S4), which accounts for one-third of cases in the general population.⁶³ Additional factors that may contribute include a higher prevalence of cigarette smoking, type 2 diabetes, kidney disease, and hypertension.^{64, 65} In particular, AIANs have

IHS Areas

The IHS has 12 service areas named for the location of their headquarters: Alaska, Albuquerque, Bemidji, Billings, California, Great Plains, Nashville, Navajo, Oklahoma, Phoenix, Portland, and Tucson. Each catchment area provides health care to a unique group of tribes with different geographic challenges. For more information, including a map of IHS facilities, visit https://www.ihs.gov/locations/. the highest rates of type 2 diabetes of any major racial/ ethnic group in the US,^{66,67} which increases kidney cancer risk independent of excess body weight.⁶⁸ Kidney cancer incidence has been increasing rapidly since 1998 among AIANs (Figure S7); from 2009-2018, the rate increased by 2.8% per year, compared to 1.1% per year among Whites.³⁰

Stage at diagnosis and survival: AIAN individuals have similar kidney cancer stage distribution to Whites (Figure S3), despite lower overall 5-year relative survival rates (Figure S4). This may reflect less access to high-quality treatment among AIANs and/or differences in cancer subtype distribution.

Liver and Intrahepatic Bile Duct

Incidence: AIANs have the highest liver cancer incidence of any major racial/ethnic group in the US,^{69, 70} with rates 2.5 times higher than those in Whites overall (19.1 versus 7.4 cases per 100,000, Table S2) and more than 3 times higher in the Northern Plains and in the Southwest among women.⁶² Rates are elevated among AIANs in nearly every region, likely reflecting a high prevalence of risk factors, including obesity, diabetes, cigarette smoking, and chronic hepatitis C virus (HCV) infection, the strongest risk factor for liver cancer.⁷¹ Improving access to health care and antiviral medications is needed to reduce liver cancer incidence among AIANs.⁷² An estimated 7 in 10 cases among the general population are due to modifiable risk factors, and thus potentially preventable.⁶³

Liver cancer incidence has been increasing for decades in the US, largely because of the HCV epidemic associated with the use of contaminated needles for intravenous drug use among baby boomers (see additional information on liver cancer in the general population on page 17). However, rates appear to be stabilizing in recent years among AIAN individuals, especially men, similar to the pattern overall.³⁰

Stage at diagnosis and survival: Liver cancer is one of the most fatal cancer types, with a 5-year relative survival rate of 17% among AIANs and 19% among Whites. AIANs and Whites have similar stages of diagnosis (Figure S3).

Table S2. Comparison of Cancer Incidence Rates in American Indians and Alaska Natives (AIAN) in PRCDA counties with Whites Nationally, US, 2014-2018

-					
		AIAN	White	RR	
-	Total	488.3	477.9	1.02*	
All sites	Male	515.0	514.2	1.00	
	Female	473.3	454.0	1.04*	
Breast	Female	119.1	134.7	0.88*	
	Total	52.4	36.7	1.43*	
Colon & rectum [†]	Male	59.4	42.2	1.41*	
	Female	46.7	31.8	1.47*	
	Total	5.5	5.1	1.09	
Esophagus	Male	9.5	8.8	1.09	
	Female	2.3	1.9	1.22	
	Total	31.6	17.7	1.79*	
Kidney & renal pelvis	Male	41.7	24.0	1.73*	
Terial pervis	Female	23.4	12.1	1.93*	
	Total	19.1	7.4	2.59*	
Liver & intrahepatic bile duct	Male	27.9	11.2	2.49*	
bile ddet	Female	11.8	4.0	2.93*	
	Total	66.4	62.5	1.06*	
Lung & bronchus	Male	73.0	70.0	1.04*	
	Female	61.5	56.8	1.08*	
	Total	12.8	13.5	0.95	
Oral cavity & pharynx	Male	19.6	20.5	0.96	
priaryinx	Female	7.0	7.2	0.98	
	Total	14.4	13.2	1.09*	
Pancreas	Male	16.7	15.3	1.09	
	Female	12.6	11.4	1.10	
Prostate	Male	89.1	104.9	0.85*	
	Total	10.3	5.3	1.92*	
Stomach	Male	13.4	7.5	1.78*	
	Female	7.9	3.5	2.24*	
Uterine cervix	Female	11.5	7.4	1.56*	

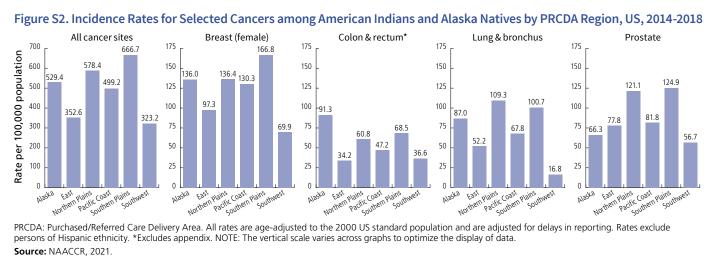
PRCDA: Purchased/Referred Care Delivery Area; RR: incidence rate ratio. All rates are per 100,000 non-Hispanic persons, age-adjusted to the 2000 US standard population, and adjusted for delays in reporting. Rate ratios represent the unrounded incidence rate in AIANs living in PRCDA counties divided by the unrounded incidence rates in Whites nationally. *The rate in AIANs is statistically significantly different from that in Whites (p<0.05). †Excludes appendix.

Source: NAACCR, 2021.

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Lung and Bronchus

Incidence: Lung cancer is the second most commonly diagnosed cancer in AIAN men and women (Table S2). As mentioned previously, incidence rates vary dramatically by region, from less than 20 per 100,000 in the Southwest to greater than 100 per 100,000 in the Northern and Southern Plains (Figure S2). Rates are also high in Alaska (87 per 100,000), where they are 59% higher than those in Whites. In contrast to higher incidence in men than in



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women among other racial and ethnic groups (Table 9), rates among AIAN women are comparable to those in men in the East and Pacific Coast and higher than those among men in the Northern Plains (111.5 versus 106.2 per 100,000).

This wide variation reflects historical differences in smoking prevalence.⁷³ Although smoking has typically been more common in men than in women, the reverse is true among AIANs, with current prevalence 27% in women versus 24% in men (Table S4). Both historically

and contemporarily, AIANs have the highest smoking prevalence and the fewest quit attempts of any major racial/ethnic group in the US.⁷⁴⁻⁷⁷ The relative gap in smoking prevalence between AIANs and Whites has widened from 30% in the early 1990s to 56% in 2019 (Figure S7). Reasons for the higher rates of smoking in AIANs are complex and include lower socioeconomic status (SES),⁷⁸ targeted advertising,^{79,80} deceptive tobacco product marketing,⁸¹ and the cultural importance of tobacco in some regions.⁸² (See Tobacco Use on page 52 for more information.)

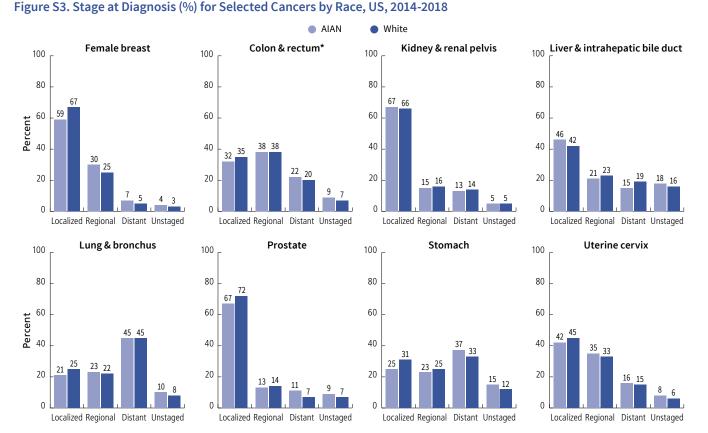
Table S3. Incidence Rates for the Four Most Common Cancers by PRCDA Region and Sex among American Indians and Alaska Natives versus Whites, 2014-2018

		Alaska			Alaska East			Nort	Northern Plains			Pacific Coast			Southern Plains			Southwest		
		AIAN	White	RR	AIAN	White	RR	AIAN	White	RR	AIAN	White	RR	AIAN	White	RR	AIAN	White	RR	
	Total	529.4	437.6	1.21*	352.6	495.7	0.71*	587.4	464.6	1.26*	499.2	457.6	1.09*	666.7	447.9	1.49*	323.2	422.0	0.77*	
All sites	Male	543.3	459.8	1.18*	354.4	537.6	0.66*	618.7	500.3	1.24*	509.4	485.2	1.05*	720.6	486.5	1.48*	341.1	447.6	0.76*	
	Female	529.2	420.7	1.26*	354.5	467.1	0.76*	566.9	439.6	1.29*	496.4	439.9	1.13*	632.8	421.3	1.50*	315.1	403.4	0.78*	
Breast	Female	136.0	129.2	1.05	97.3	139.9	0.70*	136.4	130.2	1.05	130.3	134.9	0.97	166.8	123.6	1.35*	69.9	126.7	0.55*	
	Total	91.3	35.5	2.57*	34.2	35.6	0.96	60.8	36.0	1.69*	47.2	34.0	1.39*	68.5	38.0	1.81*	36.6	31.6	1.16*	
Colon & rectum†	Male	89.4	40.1	2.23*	32.9	40.8	0.81	74.5	41.0	1.82*	49.8	38.3	1.30*	80.6	44.3	1.82*	43.3	36.1	1.20*	
rectum	Female	91.8	30.7	2.99*	35.6	30.9	1.15	50.3	31.5	1.60*	45.5	30.0	1.52*	58.5	32.4	1.81*	31.2	27.4	1.14	
	Total	87.0	54.6	1.59*	52.2	65.2	0.80*	109.3	60.6	1.80*	67.8	53.1	1.28*	100.7	66.7	1.51*	16.8	46.4	0.36*	
Lung & bronchus	Male	97.8	61.7	1.59*	51.7	71.4	0.72*	106.2	67.8	1.56*	67.8	56.4	1.20*	120.8	78.2	1.55*	21.6	50.1	0.43*	
STOREIUS	Female	79.3	47.7	1.66*	52.7	60.6	0.87	111.5	55.1	2.02*	68.0	50.6	1.34*	85.5	57.7	1.48*	13.6	43.3	0.31*	
Prostate	Male	66.3	99.6	0.67*	77.8	113.1	0.69*	121.1	107.9	1.12*	81.8	98.7	0.83*	124.9	93.4	1.34*	56.7	92.7	0.61*	

AIAN: American Indian and Alaska Native; PRCDA: Purchased/Referred Care Delivery Area; RR: incidence rate ratio. All rates are per 100,000 non-Hispanic persons diagnosed in PRCDA counties (including for Whites); age-adjusted to the 2000 US standard population; and adjusted for delays in reporting. Rate ratios represent the unrounded incidence rate in American Indians and Alaska Natives divided by that in Whites. *The rate in American Indians and Alaska Natives is statistically significantly different from that in Whites ($p \le 0.05$). †Excludes appendix.

Source: NAACCR, 2021.

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AIAN: American Indian and Alaska Native. Data for AIANs are restricted to patients diagnosed in Purchased/Referred Care Delivery Area counties. Data for Whites and AIANs exclude persons of Hispanic ethnicity. Percentages may not total 100% due to rounding. *Excludes appendix. **Source:** NAACCR, 2021.

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Lung cancer incidence in the general population has been declining since the early 1990s among men and the mid-2000s among women.³⁰ In contrast, rates in AIANs since the late 1990s remained generally stable in women and only began to decline recently in men (by 5.4% per year during 2014 through 2018, Figure S5).

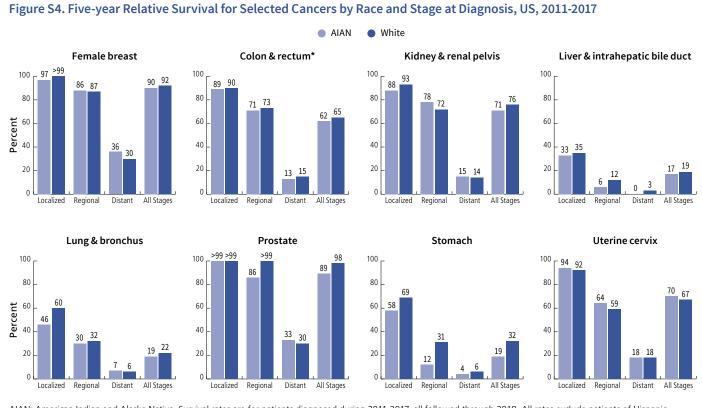
Stage at diagnosis and survival: Five-year relative survival for lung cancer is 19% among AIANs compared to 22% among Whites (Figure S4). Localized-stage disease is diagnosed less often in AIANs compared to Whites (21% versus 25%, Figure S3), and also has the largest racial gap in 5-year relative survival, 46% versus 60%.

Prostate

Incidence: Prostate cancer is the most commonly diagnosed cancer in AIAN men (Table S2). Incidence rates range from 56.7 per 100,000 in the Southwest to 124.9 in

the Southern Plains and are lower than those in White men in most regions (Table S3). Regional incidence patterns likely reflect differences in screening with the prostate specific antigen (PSA) test, which detects asymptomatic, often indolent, cancers. The only established risk factors for prostate cancer are older age, a family history of the disease, and African ancestry (see information on prostate cancer in the general population on page 23). PSA screening rates are lower among AIAN men than other racial/ethnic groups, suggesting that overdiagnosis contributes to higher rates among White men.⁸³

Fluctuations in prostate cancer incidence reflect changes in uptake of routine PSA testing, coinciding with changes in the USPSTF screening recommendations. Rates declined from 2008-2014 in the wake of recommendations against routine PSA testing, but have stabilized in recent years.³⁰



AIAN: American Indian and Alaska Native. Survival rates are for patients diagnosed during 2011-2017, all followed through 2018. All rates exclude patients of Hispanic ethnicity. Rates for American Indians and Alaska Natives are confined to patients diagnosed in Purchased/Referred Care Delivery Area counties. *Excludes appendix. **Source:** SEER 18 registries, 2021.

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Stage at diagnosis and survival: The 5-year relative survival rate for prostate cancer is lower in AIAN than White men (89% versus 98%, Figure S4), likely in part reflecting the lower proportion of localized disease diagnosed in AIAN men (67% versus 72%, Figure S3). Notably, 5-year survival rates for men diagnosed with regional-stage disease are 86% among AIANs while approaching 100% in Whites.

Stomach

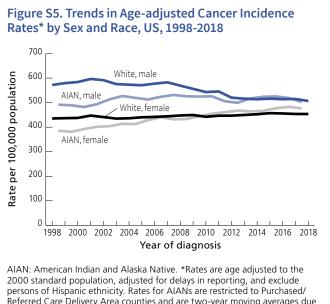
Incidence: Stomach cancer incidence in AIANs is double that in Whites (10.3 versus 5.3 cases per 100,000, Table S2) nationally and is particularly elevated in Alaska, where rates are more than 4 times higher.⁶⁵ *Helicobacter pylori* infection, the principal risk factor for stomach cancer, ^{63, 84} is most common in persons with lower SES and is especially prevalent in Alaska Natives.^{85, 86} Cigarette smoking and obesity also likely contribute to excess risk among AIANs (Table S4).^{87, 88} From 2009 to 2018, incidence

rates were stable among AIAN women, but decreased by 1.4% per year among AIAN men. $^{\rm 30}$

Stage at diagnosis and survival: The 5-year relative survival rate for stomach cancer is lower among AIANs than Whites overall and for every stage of diagnosis, with the largest gap for regional-stage disease (12% versus 31%, Figure S4). AIANs are also less likely than Whites to be diagnosed with localized-stage disease (25% versus 31%, Figure S3).

Uterine Cervix

Incidence: Cervical cancer incidence rates are 56% higher among AIAN women (11.5 cases per 100,000, Table S2) than White women (7.4), reflecting higher underlying prevalence of persistent infection with human papillomavirus (HPV) and less access to screening, which can prevent cancer.⁸⁹ Rates among AIAN women are elevated in all PRCDA regions except for the East and Southwest,⁶⁵ likely reflecting



Referred Care Delivery Area counties and are two-year moving averages due to data sparseness. Source: NAACCR, 2021.

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regional variation in HPV rates and screening. Vaccination against HPV infections that cause the majority of cervical cancers has been available since 2006; data from 2019 show that HPV vaccination is suboptimal among both AIAN and White adolescents (see more information on HPV on page 41).⁹⁰ Although screening with the Pap test has led to historical declines in incidence among all women, trends have leveled off in recent years. From 2009 to 2018, cervical cancer incidence rates were stable in both AIAN and White women.³⁰

Stage at diagnosis and survival: Five-year relative survival is 70% among AIAN women, similar to that in White women (Figure S4) despite a lower likelihood of localized-stage disease (42% versus 45%, Figure S3) and cervical cancer screening (Table S5). Screening is particularly low among women utilizing IHS services, with only 55% of women ages 24-64 years up to date on screening in 2017 (Table S6, see Cancer Screening in AIANs, page 41).⁵⁵ Persistently low screening prevalence may help explain the survival paradox in AIAN women because populations that are less screened have a higher proportion of squamous cell carcinoma, which has better survival, and a lower proportion of adenocarcinoma, which has worse outcomes.91-93

Prevalence of Major Cancer Risk Factors

More than 40% of all cancers in the general population are attributable to potentially modifiable risk factors such as tobacco use, excess body weight, excess alcohol consumption, and infectious agents.⁶³ Prevalence of these risk factors and their associated cancer burden varies substantially by region and could help inform priorities for local cancer control programs. Unfortunately, however, risk factor data are not available for PRCDA counties specifically and are herein presented by census region to approximate PRCDA regions. If national health surveys targeted residents of PRCDA counties and oversampled AIANs, the accuracy of AIAN health behavior data would improve and cancer control and prevention in this population would be facilitated.

Tobacco

Cigarette smoking is the single largest contributing risk factor to cancer in the United States.⁶³ One-quarter of AIAN adults were current smokers in 2019, more than any other major racial/ethnic group,75 with rates 1.5 times higher than in White adults (Table S4). Notably, smoking prevalence is higher among AIAN women than men (27% versus 24%), whereas it is currently the same among White men and women (16%). Smoking prevalence is lower among people who live in the West census region than in the Midwest or South and among those with higher educational attainment. For example, among AIANs, prevalence in 2010-2015 was more than twice as high in persons with less than a high school diploma (45.1%) as in those with at least a college degree (13.1%).⁷⁹ Tobacco use has cultural importance in social relationships and spiritual and medicinal ceremonies among some AIAN tribes.82

Tobacco Control and Cessation

Cigarettes are less expensive on tribal lands because they are not subject to state excise tax.⁸¹ Additionally, the tobacco industry directly targets AIAN communities through the use of culturally specific names, symbols, and icons in their marketing.^{79, 80} Most importantly, improving the social determinants of health, such as

Table S4. Prevalence of Cancer Risk Factors (%) among Ages ≥18 Years by Race, Sex, and Region, US, 2016-2019

	Total US							Region*							
	Both	sexes	М	Male		Female		west	South		West				
	AIAN	White	AIAN	White	AIAN	White	AIAN	White	AIAN	White	AIAN	White			
Smoking (NHIS 2019)															
Current	25	16	24	16	27	16	27	17	27	18	21	13			
Former	22	25	29	29	17	22	28	25	23	26	20	24			
Never	52	59	47	55	56	62	46	58	50	56	59	63			
Alcohol use (NHIS 2016 & 2018)															
Binge drinking [†]	23	31	32	37	16	27	29	36	26	27	21	31			
Heavy drinking‡	6	6	8	6	-	7	-	6	10	6	5	8			
Excess body weight (NHIS 2019)															
Overweight/obese (BMI ≥25.0 kg/m²)	73	64	76	71	70	57	62	67	71	65	77	59			
Overweight (BMI = 25.0-29.9)	33	33	38	39	28	27	29	33	30	32	34	32			
Obese (BMI ≥30.0)	40	31	38	33	41	30	32	35	42	32	43	27			
Physical activity (NHIS 2018)															
No leisure time physical activity	23	22	24	20	23	23	35	22	30	26	13	16			
Met recommended levels of aerobic activity	52	58	59	61	46	55	45	55	43	54	66	65			

BMI: body mass index; AIAN: American Indian and Alaska Native. All estimates are age adjusted. Data exclude persons of Hispanic ethnicity and are not restricted to Purchased/ Referred Care Delivery Area counties. *Information by region is limited due to sparse data for AIANs. †Includes men who have had \geq 5 drinks/women who have had \geq 4 drinks in one day at least once during the past year (among current drinkers). ‡Men who consume >14 drinks per week and women who consume >7 drinks per week. – Estimate not provided due to sparse data.

Source: National Health Interview Survey (NHIS), 2016, 2018, and 2019.

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economic stability and access to high-quality education, are critical for reducing cigarette smoking in AIAN populations because low SES and income are closely associated with tobacco use.

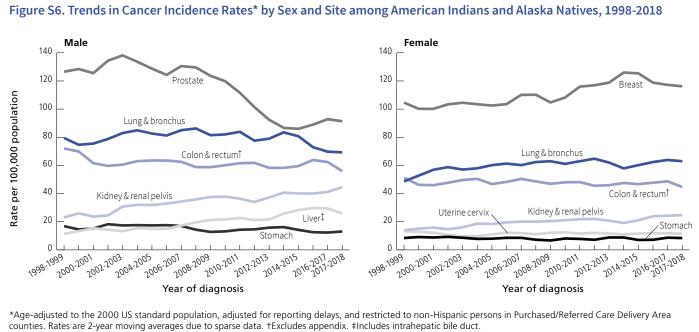
Excess Body Weight

Excess body weight increases the risk of several cancers and contributes to the development of other cancer risk factors, such as nonalcoholic fatty liver disease and type 2 diabetes. Normal weight is defined as body mass index (BMI, kg/m²) of 18.5-24.9, while overweight is 25-29.9 and obese is \geq 30. AIAN persons are more likely to be obese than Whites (40% compared to 31% overall, Table S4), except for those in the Midwest census region (32% versus 35%).

Many factors contribute to high obesity in the AIAN population, but a primary cause is low access to healthy food because of disproportionate poverty and rural residence. The Food Distribution Program on Indian Reservations was implemented as a solution to limited grocery store access, but contributes to increased obesity by supplying highly processed, high-calorie shelf-stable foods.³ Food insecurity is also a major factor in excess body weight among urban AIANs.¹¹ Ironically, the traditional native American diet of high fruit and vegetable consumption¹⁶ and low intake of simple carbohydrates and fats is associated with reduced risk of obesity and chronic disease,⁹⁴⁻⁹⁶ but is largely unavailable because of barriers related to historical injustice and continued racism as previously described.³ Improving food sovereignty and expanding access to locally grown food could significantly improve overall nutrition and reduce obesity in the AIAN population.

Diabetes

Type 2 diabetes increases the risk of several cancers, including colorectal and kidney.⁹⁷ The prevalence of type 2 diabetes is twice as high in AIAN adults than in White adults.¹⁶ Promisingly, among AIANs utilizing IHS services, rates of diabetes declined from 2013-2017 after increasing in previous years.⁹⁸ However, rates among AIAN youth increased significantly from 2003-2012, with the rate in 2012 more than 10 times higher than in White youth.⁹⁹ Excess body weight contributes to the high rates and earlier onset of diabetes in the AIAN population.^{100, 101} Low SES and food insecurity, both of which are elevated among AIANs (Table S1),^{11, 102} are associated with type 2



Source: NAACCR, 2021.

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diabetes,¹⁰³ and are of particular concern for urban AIAN households due to the high prevalence of food deserts in high-poverty neighborhoods.³

Alcohol

Alcohol consumption is associated with an increased risk of several cancers.¹⁰⁴ Overall binge drinking (>4 drinks in one day for men or >3 drinks in one day for women) is lower among AIANs than in Whites, whereas the prevalence of heavy drinking (>14 drinks per week for men or >7 for women) is similar (Table S4). Despite generally lower alcohol consumption among AIANs,¹⁰⁵ alcohol-attributable mortality is significantly higher than Whites,¹⁰⁶ in part reflecting less access to care.¹⁰⁷ In addition, binge and heavy drinking varies substantially by PRCDA region and is more common among AIANs in the Northern Plains, Pacific Coast, and East.¹⁶

Physical Activity

AIANs engage in similar levels of leisure-time physical activity as Whites (23% versus 22% no leisure-time physical activity, respectively), but are less likely to meet recommended levels of physical activity (52% versus 58%, respectively, Table S4). However, studies have shown that among Alaska Natives in particular, sedentary activity, such as hours spent watching TV, is lower than the general population.^{108, 109} These studies have also shown that Alaska Natives spend more time engaging in low-intensity outdoor work, such as wild-food gathering,¹¹⁰ which is protective against cancer and other chronic disease.

Infectious Agents

Helicobacter pylori

Chronic infection with *Helicobacter pylori (H. pylori)* is the primary cause of non-cardia gastric cancer.⁸⁴ Although the exact route of transmission is unknown, the bacteria probably spreads from person to person through bodily fluids or contaminated water or food.¹¹¹ In the US, infection is more likely among individuals with lower SES.¹¹² The majority of available research on *H. pylori* prevalence among AIANs has focused on Alaska Natives due to their especially elevated burden of gastric cancer.^{85, 113} Household crowding, rurality, and use of non-municipal water sources, which are associated with *H. pylori*,¹¹⁴ are more common in AIANs. Although national *H. pylori* prevalence is not available for the AIAN population, a study based on more than 500 Alaska Natives found a prevalence of about 75%,¹¹⁴ in contrast to Table S5. Cancer Screening Test Use (%), Vaccination Coverage (%), and Hepatitis Testing (%) by Race, US, 2017-2019

	AIAN	White
Cervical cancer screening, women* 25-65 years (NHIS 2015 & 2018)		
Pap test within past 3 years	77	84
Up-to-date†	84	86
Breast cancer screening (NHIS 2015 & 2018)		
Women 50 to 74 years		
Mammogram within past 2 years (USPSTF)	62	72
Mammogram within past year	46	56
Women ≥45 years		
Up-to-date [‡]	57	63
Colorectal cancer screening§ (NHIS 2015 & 2018)		
Ages ≥45 years		
Total	48	57
Men	52	58
Women	44	57
Ages ≥50 years		
Total	57	67
Men	60	68
Women	54	66
Ages 50-75 years (USPSTF)		
Total	56	69
Men	60	69
Women	55	68
HPV vaccine utilization, boys and girls 13-17 years (2019)		
≥1 dose	71	68
Up-to-date¶	58	52
Hepatitis B testing, ages ≥18 years (NHIS 2017)		
Has received hepatitis B test	32	30
Hepatitis C testing, ages 48-68 years (NHIS 2017)		
Has received hepatitis C test	21	18

AIAN: American Indian and Alaska Native; HPV: human papillomavirus; USPSTF: United States Preventive Services Task Force. All estimates are age adjusted. Data exclude persons of Hispanic ethnicity and are not confined to Purchased/Referred Care Delivery Area counties. *Among women with an intact uterus. †Pap test in the past 3 years among women 25-65 years OR Pap test and HPV test within the past 5 years among women 30-65 years. \$Mammogram within the past year (ages 45-54 years) or past two years (ages ≥55 years). §For ages ≥45 and ≥50 years: fecal occult blood test (FOBT)/ fecal immunochemical test (FIT), sigmoidoscopy, colonoscopy, computed tomography (CT) colonography, OR sDNA test in the past 1, 5, 10, 5, and 3 years, respectively. For ages 50-75 years: FOBT/FIT, sigmoidoscopy, colonoscopy, CT colonography, OR sDNA test in the past 1, 5, 10, 5, and 3 years, respectively, OR sigmoidoscopy in past 10 years with FOBT/FIT in past 1 year. ¶Includes those with ≥3 doses, and those with 2 doses when the first HPV vaccine dose was initiated before age 15 years and there were at least five months minus four days between the first and second dose.

Sources: National Health Interview Survey (NHIS), 2015, 2017 and 2018. HPV: Elam-Evans LD, et al. *MMWR Morb Mortal Wkly Rep* 2020;69:1109-1116. ©2022 American Cancer Society, Inc., Surveillance and Health Equity Science

reported national prevalence of 27% for all races/ ethnicities combined.¹¹⁵ Despite evidence of a high prevalence of infection in Alaska Natives, communitywide treatment is not recommended because reinfection rates and risk of antimicrobial resistance are high.¹¹⁶⁻¹¹⁸ More research is needed to ascertain the costs and benefits of expanded treatment for gastric cancer prevention in high-risk populations.

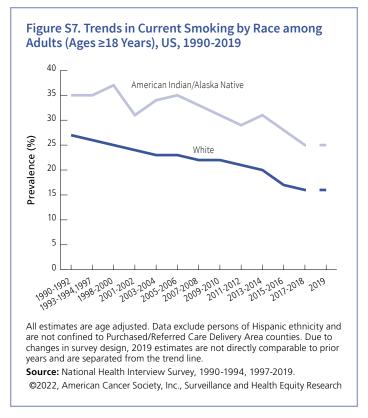
Hepatitis B Virus and Hepatitis C Virus Chronic infection with hepatitis B virus (HBV) or hepatitis C virus (HCV) increases risk of several cancers, most notably liver cancer.¹¹⁹ AIANs have HBV infection prevalence similar to that in the general population, but the highest rates of HCV infection in the US, nearly triple that of any other racial group.¹²⁰ The US Department of Health and Human Services has designated AIANs as a priority population in its viral hepatitis action plan.¹²¹ Antiviral therapy regimens can often clear established HCV infection and are associated with significantly improved outcomes,122 including reduced liver cancer risk.⁷² However, these drugs are expensive and unaffordable for many in the AIAN community). Further, many state Medicaid programs have restrictive requirements for HCV treatment, exacerbating disparities in liver cancer and other viral hepatitisrelated liver disease.¹²³

HPV

Nearly all cervical cancers are caused by persistent human papillomavirus (HPV) infection, as well as 90% of anal cancers, about 70% of oropharyngeal cancers, and 60%-70% of vaginal, vulvar, and penile cancers.^{124, 125} Vaccines to prevent the most common oncogenic types of HPV have been available since 2006 and are recommended for boys and girls between 9 and 12 years of age, and for those ages 13 through 26 years as catch-up strategies. Receipt of the vaccination before the age of 17 in girls has been shown to lower the risk of invasive cervical cancer by 90%.¹²⁶ AIAN vaccination utilization among ages 13-17 years is higher than that of Whites (58% versus 52% in boys and girls combined, Table S5), but lower than the Healthy People 2020 goal of 80%.¹²⁷

Cancer Screening in AIANs

In national survey data, AIANs are less likely than Whites to be up-to-date for breast (62% versus 72%, respectively), colorectal (56% versus 69%), and cervical cancer screening (84% versus 86%; Table S5). Screening rates are



even lower for the 2.6 million AIANs who utilize the IHS, in part because these facilities often do not offer cancer screening.⁴² For example, up-to-date cervical cancer screening in AIANs utilizing IHS facilities was 55% in 2017 (Table S6) versus 77% among AIAN women overall (Table S5). Further, the Purchased/Referred Care (PRC) program that covers health care services received at non-IHS facilities designates cancer screening as medical priority level II, meaning that these services can be denied when PRC funding is low.⁵⁵

IHS screening rates vary considerably by region, ranging from a high of 70% for mammography in Oklahoma down to 30% for colorectal cancer in Phoenix (Table S6). Screening prevalence is generally lowest on the Pacific Coast (<50% for all cancers) and highest in Oklahoma and Alaska.

Access to colonoscopy for CRC screening is of particular importance for Alaska Natives due to their high risk for the disease and for *H. pylori*-associated hemorrhagic gastritis (see *H. pylori* section, page 40),^{113, 128} which can cause false-positive fecal occult blood tests.¹²⁹ However, Alaska Natives face many challenges in obtaining colonoscopy services, most notably transportation barriers given that half of the population lives in areas that lack road networks. Since the late 1990s, the Alaska Native Tribal Health Consortium (ANTHC) has worked to improve access to endoscopy services by supporting colonoscopy field clinics in remote areas.¹²⁹ These efforts likely contribute in large part to Alaska achieving the highest screening rate (59%) of any IHS area (Table S6).

Improving screening access for rural AIAN populations is a crucial component of reducing cancer disparities. Overall, IHS facilities are located primarily in rural and isolated settings with little access to specialty services.⁴⁰ Innovative programs designed to improve screening in the Northern Plains, such as Minnesota's Intertribal Colorectal Cancer Council and the Wisdom Steps program, appear to have driven positive change and could be used as models in other tribal regions with a high colorectal cancer burden.⁵⁹ In addition, mobile mammography was used by the Great Plains IHS from 2005-2017 to reduce long travel times to screening mammography among American Indian women.¹³⁰⁻¹³¹ At the federal level, the CDC's National Breast and Cervical Cancer Early Detection Program partners with tribal groups to increase access to screening and diagnostic services for native women.

Summary and Opportunities to Alleviate AIAN Cancer Burden

AIAN men and women are vulnerable to cancer disparities due to long-standing inequalities in SES, education, and access to care. This population not only has a higher burden of major cancer risk factors (e.g., cigarette smoking, obesity, and cancer-causing infections) compared to Whites, but are also more likely to be diagnosed at a later stage and receive substandard treatment. Many of these disparities could be reduced by increasing access to high-quality cancer prevention, early detection, and treatment.

The IHS, the primary health care service for many AIANs, is underfunded and understaffed. IHS funding must be increased to an adequate level as a cornerstone of eliminating AIAN cancer disparities. However, as of fall 2021, the FY 2022 budget appropriations bill provides \$7.61 billion for the IHS,¹⁸ significantly less than the \$12.8

Table S6. Cancer Screening Test Use (%) among American Indians and Alaska Natives by PRCDA Region and IHS Area, 2017

	PRCDA	Alaska	East	Nor	thern Pl	ains	Southern Plains		So	uthwest		Pacific	Coast
		Alaska	Nashville	Billings	Great Plains	Bemidji	Oklahoma	Navajo	Phoenix	Tucson	Albuquerque	California	Portland
Cervical cancer screening, women 24-64 years*	55	65	60	46	46	53	63	58	49	52	65	49	49
Breast cancer screening, women 52-64 yearst	55	59	63	50	50	55	70	55	45	49	60	49	46
Colorectal cancer screening, ages 50-75‡	41	59	50	34	33	48	52	41	30	34	43	38	42

PRCDA: Purchased/Referred Care Delivery Area; IHS: Indian Health Service. *Ages 24-64 with Pap test in the past 3 years or ages 30-64 years with Pap test and human papillomavirus DNA test within 5 years. †Mammography in previous 2 years. ‡Patients who have received appropriate colorectal cancer screening. **Source:** Indian Health Service Data: FY 2017 GPRA/GPRAMA National and Area Results, Indian Health Service (IHS) GPRA Performance Results. https://www.ihs.gov/sites/crs/themes/responsive2017/display_objects/documents/gpra/FY_2017_GPRA_GPRAMA_NationalandAreaResults.pdf.

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billion requested by tribal leaders and a mere 16% of the \$48 billion that would be required to fully fund the organization.¹⁷ In addition, the IHS falls outside the jurisdiction of the Affordable Care Act (ACA), which expanded access to care for low-income persons. However, Medicaid expansion through the ACA has the potential to increase insurance access for AIANs who would not otherwise qualify and are too poor to gain coverage through the ACA marketplace. As of September 2021, 25 of the 36 states with PRCDA counties had expanded Medicaid.¹³²

Finally, AIANs are the only major racial/ethnic group for which high-quality cancer mortality data are not readily available to researchers through the National Center for Health Statistics (NCHS). As mortality data are the gold standard for measuring progress against cancer, linkage to IHS data should be standard practice in the creation of mortality databases for surveillance research. In particular, these data should be included in standard national reports that monitor progress against cancer by race and ethnicity, such as the Annual Report to the Nation on the Status of Cancer.

Additional Resources

The American Indian Cancer Foundation (AICAF) https://www.americanindiancancer.org/

The American Indian Cancer Foundation (AICAF) is a national nonprofit organization that strives to reduce the burden of cancer in AIANs through community-based

programs like Screen Our Circle, which aims to increase cancer screening and early detection rates in urban, native-serving clinics across the nation by raising awareness, promoting health system improvements, and facilitating education and outreach. The AICAF also provides culturally specific cancer survivorship resources to native communities.

Keep it Sacred National Native Network https://keepitsacred.itcmi.org/

Keep it Sacred is a national network of tribes, tribal organizations, and tribal health programs that works to reduce tobacco use and cancer disparities among AIANs across the United States. The network disseminates informative resources to organizations that serve AIAN populations that are tailored to the unique cultural needs of AIANs. Keep it Sacred also provides assistance in implementing culturally competent interventions, policies, and cancer control systems for native populations.

Partnership for Native American Cancer Prevention (NACP)

https://nartc.fcm.arizona.edu/partnership-native-americancancer-prevention-nacp

The Partnership for Native American Cancer Prevention is a collaboration between Northern Arizona University and the University of Arizona Cancer Center. Through research, education, and community outreach, the NACP seeks to reduce the cancer burden of AIANs living in the Southwestern US.

New Mexico Cancer Council (NMCC) https://www.nmcancercouncil.org/

The New Mexico Cancer Council is a public/private collaboration that combats cancer in AIANs living in New Mexico through their New Mexico Cancer Plan, which includes measures such as increasing healthy behaviors, decreasing environmental exposures, and increasing recommended cancer screening test use.

Tribal Comprehensive Cancer Control (CCC) programs

https://www.cdc.gov/cancer/ncccp/ccc_plans.htm

Funded through the CDC, the Comprehensive Cancer Control programs address the cancer burden for a specific tribal group and provide culturally appropriate education, resources, and support to assist tribal health providers in preventing and treating cancer. Five-year plans are implemented utilizing strategies that have been successful for that specific tribe or in a similar area and are later evaluated at the end of the five years.

National Breast and Cervical Cancer Early Detection Program (NBCCEDP)

https://www.cdc.gov/cancer/nbccedp/index.htm

The National Breast and Cervical Cancer Early Detection Program is a CDC program that provides access to screening and diagnostic services for low-income, uninsured, and underserved women. The NBCCEDP has partnerships with 13 AIAN organizations and tribes, including the AICAF, Navajo, Hopi, and Cheyenne River Sioux. The list of available partnerships can be found here: https://www.cdc.gov/cancer/nbccedp/data/summaries/.

Colorectal Cancer Control Program (CRCCP) https://www.cdc.gov/cancer/crccp/

The Colorectal Cancer Control Program awards health systems serving high-need populations with funding to improve access to evidence-based interventions that increase colorectal cancer screening. The program partners with the Alaska Native Tribal Health Consortium and the Inter-Tribal Council of Michigan.

Tribal Tobacco Control Programs

These programs seek to improve the health of AIANs through education on the importance of commercial tobacco use prevention, providing access to cessation tools, and promoting prevention policies while respecting the use of ceremonial tobacco.

Alaska Native Tribal Health Consortium (ANTHC) – Tobacco Prevention & Control https://anthc.org/what-we-do/wellness/tobacco/

Black Hills Center for American Indian Health – Southwest Navajo Tobacco Education Prevention Project https://www.bhcaih.org/sntepp

Northern Plains Tribal Tobacco Technical Assistance Center (NPTTTAC) https://health.gptchb.org/nptttac/

Southeast Alaska Regional Health Consortium (SEARHC) – Freedom from Smoking – Smoking Cessation Program https://searhc.org/freedom-smoking-smoking-cessation-program-2/

Nez Perce Tribe – Students for Success

https://www.nezperce.org//wp-content/uploads/2019/02/ sfsprofile.pdf

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