

HHS Public Access

Author manuscript *Am J Gastroenterol.* Author manuscript; available in PMC 2021 December 01.

Published in final edited form as:

Am J Gastroenterol. 2020 December; 115(12): 1989–1997. doi:10.14309/ajg.00000000000748.

Gastric Cancer Among American Indian and Alaska Native Populations in the United States, 2005–2016

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Abstract

Objectives: American Indian and Alaska Native (AI/AN) populations have higher gastric cancer rates than the general U.S. population. This study provides a comprehensive overview of incidence rates among AI/AN persons during 2005–2016 compared with non-Hispanic whites (whites).

Methods: Population-based cancer registry data for 2005–2016 were linked with the Indian Health Service (IHS) patient registration databases to address racial misclassification. Age-adjusted gastric cancer incidence rates were expressed per 100,000 per year. Incidence and trend analyses were restricted to purchased/referred care delivery area (PRCDA) counties in 6 geographic regions, comparing gastric cancer incidence rates for AI/AN versus white populations in the U.S.

Results: Gastric cancer rates were higher in the AI/AN compared to white populations in nearly every U.S. region. Incidence rates for central/distal portions of the stomach were higher in AI/AN individuals compared to whites. Rates of later stage gastric cancer were higher in AI/AN populations overall and in every region except the Pacific Coast and East. Incidence rates decreased significantly over time in both populations. Declining rates in the AI/AN populations were driven by changes in the Pacific Coast and Northern Plains regions.

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No conflicts of interest to disclose.

Conclusions: AI/AN populations have a disproportionately high incidence of gastric cancer, especially in Alaska. High incidence in the central/distal portions of the stomach among AI/AN populations likely reflects a high prevalence of *Helicobacter pylori* infection in these populations. These data can be used to develop interventions to reduce risk factors and improve access to health services among AI/AN popules at high risk for gastric cancer.

Keywords

gastric cancer; disparity; American Indian; Alaska Native; cancer incidence

INTRODUCTION

Despite the decline in incidence rates of gastric cancer in the general U.S. population over the past 10 years [1, 2], survival remains relatively low [3]. Gastric cancer patients are generally diagnosed with late stage disease, which is difficult to treat and often results in poorer prognosis [4–6]. In the United States, the American Indian and Alaska Native (AI/AN) populations have some of the highest rates of gastric cancer incidence and death [2, 7–9]. The prevalence of *Helicobactor pylori* (*H. pylori*), which is a known risk factor for gastric cancer, is particularly high among Alaska Native people [10–13]. Because of these high rates, much of the current gastric cancer research in AI/AN people focuses specifically on the Alaska Native population [14–17]. The prevalence and effect of other gastric cancer risk factors for AI/AN populations have remained largely uncharacterized.

The study of *H. pylori* as a risk factor for gastric cancer has enhanced researchers' understanding of gastric cancer etiology [18]. Changes and variations in gastric cancer incidence can also be associated with variations in other factors linked to gastric cancer incidence, including consumption of fruits and vegetables, intake of foods preserved with salt or by smoking, availability of refrigeration, and reduced or varied prevalence of *H. pylori* infection [1, 5, 19, 20]. The prevalence of these factors varies by racial and ethnic subgroup, which suggests possible reasons for the disparities in gastric cancer incidence by race and ethnicity in the United States.

The purpose of this study is to provide an updated, comprehensive overview of the burden of gastric cancer, by region, in AI/AN populations in the United States using the non-Hispanic white (white) population for comparison. Racial misclassification is addressed using previously described methodologies for linking cancer registry data with Indian Health Service (IHS) patient registration databases [21]. Understanding regional variations in gastric cancer incidence in AI/AN populations may provide additional opportunities to prevent gastric cancer in this population.

MATERIALS AND METHODS

Gastric cancer cases diagnosed during 2005–2016 were identified from population-based registries that participate in the National Program of Cancer Registries of the Centers for Disease Control and Prevention (CDC) or the Surveillance, Epidemiology, and End Results (SEER) program of the National Cancer Institute or both programs [22, 23]. During the time covered by this study, tumor histology, tumor behavior, and primary cancer site (topography)

were classified according to the *International Classification of Diseases for Oncology, Third Edition* (ICD-O-3) [24].

For this study, eligible cases included all malignant neoplasms of the stomach (ICD-O-3 topography cases C16.0–C16.9 and ICD-O-3 behavior code 3) except lymphomas and Kaposi sarcomas. Benign and in situ tumors (ICD-O-3 behavior codes 0 and 2, respectively) and tumors of uncertain or unknown behaviors (ICD-O-3 behavior code 1) were excluded.

Results from previous studies have shown that AI/AN patients are often misclassified as non-Native in central cancer registries that rely solely on medical records for identification [25, 26]. For the current analysis, cancer registry records were linked with IHS patient services files to identify AI/AN individuals with proof of membership in a federally recognized tribe receiving health care from the IHS. These linkages were conducted using LinkPlus, a probabilistic software program developed by CDC that uses key patient identifiers (e.g., social security number, first name, last name, middle initial, date of birth).

These methods for addressing racial misclassification for AI/AN cases are most effective in geographic areas that are well-served by IHS [27]. Therefore, we restricted our analyses to purchased/referred care delivery area (PRCDA) counties, as defined by IHS. These counties (previously called contract health service delivery area counties) contain or are located adjacent to federally recognized tribal lands and have higher proportions of AI/AN residents than non-PRCDA counties. This use of PRCDA counties, as well as a description of the regions, was described in a previous publication and are shown in Supplemental Figure 1 [2].

Our analysis also examined the anatomic site of primary tumor growth for gastric cancer cases [4]. Generally, cancers that arise in the central/distal regions of the stomach are associated more closely with *H. pylori* infection than cancers in the proximal stomach. To characterize the distribution of primary site, cases were grouped as follows: proximal (cardia and fundus) distal (gastric body, lesser curvature, greater curvature, antrum, and pylorus), and overlapping/unknown (overlapping sites or unknown primary site). Consistent with other studies of gastric cancer etiology, our analysis of cases by anatomic subsite was restricted to patients with adenocarcinoma [28].

Cancer cases diagnosed during 2005–2016 were staged using the following *Seer Summary Stage 2000* [29] categories: *localized* for disease restricted to the stomach, *regional* for disease extended directly into organs and adjacent areas, *distant* for disease metastasized to parts of the body not directly adjacent to the stomach, and *unstaged* for instances where stage was undocumented in the medical record or when there was insufficient documentation in the medical record to determine the stage at diagnosis.

Previous analyses have found that updated bridged intercensal population estimates significantly overestimate AI/AN populations of Hispanic origin [27, 30]. Therefore, we limited all analyses to non-Hispanic populations. Non-Hispanic white was chosen as the referent group. Because all analyses reported here were limited to non-Hispanic populations, we omitted the term "non-Hispanic" from the present study when discussing both groups.

Statistical analysis

Average annual age-adjusted incidence rate were calculated using the direct method [31]. Rates were expressed per 100,000 and adjusted by 19 age groups to the 2000 U.S. standard population [32]. Rate ratios (RR) with 95% confidence intervals (CI) were calculated for comparison of incidence rates between AI/AN and white populations, overall and by sex, region, age group (<40, 40–59, 60–74 and 75), stage, and primary site according to methods described by Tiwari et al using SEER*Stat software 8.3.2 [33]. Denominators for rate calculations were derived from population estimates from the U.S. Bureau of the Census.

Time trends (1999–2016) were estimated by joinpoint regression using Joinpoint Regression Program 4.3.10 (National Cancer Institute, Bethesda, MD) [34, 35]. Average annual percent change (AAPC) was used to describe fixed interval trends during 1999–2016 [33].

RESULTS

Gastric cancer incidence rates varied by geographic region, sex and race (Table 1). During 2005–2016, a total of 1,505 gastric cancer cases were diagnosed in AI/AN populations residing in PRCDA counties (compared to 41,319 in the U.S. white population, not shown). For all regions combined, rates for AI/AN populations were about double those of the white population for both sexes. Rates varied substantially by region, ranging from 9.0 in the Pacific Coast to 27.0 in Alaska among AI/AN males and from 6.3 in the Pacific Coast to 15.7 in Alaska among AI/AN females. Rate ratios were the highest in Alaska, with gastric cancer rates nearly 4 times higher in AI/AN males than white males and over 5 times higher in AI/AN females.

Gastric cancer incidence rates increased with age for both populations across all regions and for the total U.S. population for males and females combined (Table 2). In AI/AN males, incidence rates were higher in all age groups in Alaska and the Southwest, with the highest rates occurring in the oldest age group in Alaska (111.5). In AI/AN males aged 60–74 and 75 years, rates were higher compared to the white population for all regions, except in the East and Pacific Coast. The largest rate ratio (comparing AI/AN to white incidence rates) was observed in the youngest age group for AI/AN males in Alaska (RR = 14.39). In females, rates in Alaska and the Southwest were significantly higher in the AI/AN compared to white populations for all age groups. In the Northern Plains, Southern Plains, Pacific Coast, and Southwest, rates were higher in AI/ANs than in whites for females aged 40 years. In females, the highest rates were in AI/ANs aged >75 in Alaska (75.3) and the Southwest (57.6). Similar to AI/AN males in Alaska, AI/AN women in Alaska had the largest rate ratio in the youngest age group (21.7).

Distribution and incidence rates of gastric cancer cases by stage of diagnosis are shown in Figure 1 and Supplemental Table 1. For both sexes, between 25.4% (Southwest) to 42.2% (Alaska) of gastric cancers in AI/AN people (compared to 23%–35.5% in the white population) were diagnosed at distant disease (Supplemental Table 1). In AI/AN males, rates of distant disease were significantly higher in the AI/AN compared to white population in the Northern Plains (RR=2.67), Alaska (RR=4.22), Southern Plains (RR=1.77) and

Southwest (RR=2.50). In AI/AN females, rates of distant diseases were higher in the AI/AN versus white population in the Northern Plains (RR = 1.93), Alaska (RR = 2.58), Southern Plains (RR = 2.61), and Southwest (RR = 2.02), with the highest rate occurring in Alaska (3.0/100,000).

Incidence rates of gastric adenocarcinoma by anatomic subsite are shown in Figure 2 and Supplemental Table 2. For all regions combined, incidence rates of adenocarcinoma of the proximal stomach were similar in the AI/AN and white populations for both sexes combined, as well as for males (Supplemental Table 2). Rates in AI/AN females were higher than rates in white females. Rates of adenocarcinoma of the central/distal stomach were significantly higher in AI/AN males than in whites for each region individually, with rate ratios ranging from 2 in the East to over 11 in Alaska, and for all regions combined (overall RR = 3.74, 95% CI 3.30-4.22). Similarly, rates of central/distal cancer were higher in AI/AN females compared to white females, for each region individually, except in the East, and for all regions combined (overall RR = 3.30, 95% CI 2.86-3.79). The highest rate ratio was in Alaska (RR = 8.58).

Overall gastric cancer incidence trends during 1995–2016 for males and females separately are shown in Figure 3; average annual percent change (AAPC) by region and sex is shown in Supplemental Table 3. Overall in the United States, rates for both sexes combined have decreased significantly in the AI/AN (AAPC -1.4) and white (AAPC -1.5) populations. Overall, decreases in rates in AI/AN males (AAPC -1.7) were similar, largely driven by the significant decrease in incidence rates in the Pacific Coast (AAPC -4.0) (Supplemental Table 3). Decreases in rates in AI/AN males in other regions, including Alaska, were not significant, while rates in white males decreased significantly in the East, Southwest, and Pacific Coast. In AI/AN females, significant decreases in rates were observed only in the Northern Plains (AAPC -4.3, Supplemental Table 3), while a significant increase was observed in the East (AAPC 4.4). No significant decreases in rates were observed for the remaining regions or overall (Figure 3, Supplemental Table 3) in AI/AN females. In white females, significant decreases in gastric cancer incidence rates were observed overall (AAPC -1.2) in the Pacific Coast (AAPC -1.2) and Southwest (AAPC -0.8). Gastric cancer incidence rates in Alaska did not decrease by either race or sex.

DISCUSSION

The results of this study indicate significant differences between gastric cancer incidence rates in AI/AN populations compared to the white population in the United States. Rates also varied by region in AI/AN populations, with the highest rates occurring in Alaska for both males and females. Rates of central/distal gastric cancer were 3.5 times higher in AI/AN people compared to whites overall and significantly higher in Alaska Native populations compared with all other IHS sites. The high rates of gastric cancer in AI/AN people, particularly of central/distal gastric cancer, could indicate a disproportionate prevalence of important gastric cancer risk factors, including prevalence of *H. pylori* infection [1, 5]. These data also showed that a higher percentage of gastric cancers in AI/AN populations were diagnosed at a later stage, with rates 5 times higher than the general U.S. population.

Previous evidence has established an association between *H. pylori* infection and gastric cancer that has provided an important understanding of variation in gastric cancer incidence rates worldwide [12, 18]. *H. pylori* is a common gram-negative bacteria that is typically acquired early in life through person-to-person contact and known to cause chronic gastritis and peptic ulcer disease [12]. Chronic infection with *H. pylori* has been characterized by the International Agency for Research on Cancer as a Class 1 carcinogen in humans [36]. *H. pylori* infection results in a chronic, active immune response that, when left untreated, persists for the life of the host [37].

In the United States, the prevalence and incidence of *H. pylori* infection varies by age, geographic location, and race [38]. Most research on *H. pylori* prevalence in AI/AN populations focuses on Alaska Native populations, where the burden of *H. pylori* infection is particularly high (ranging from 64% to 81%) [15, 39]. Similar data regarding H. pylori prevalence is not currently available for the other regions examined in the present study. Although socioeconomic factors are strongly linked with *H. pylori* prevalence in studies of Alaska Native people and gastric cancers in other populations [15, 40–42], little data are available on *H. pylori* prevalence and associated risk factors in American Indian populations in other regions. Further research in this area is needed to understand the variation in gastric cancer incidence in AI/AN populations.

H. pylori infection has been associated with living in a more crowded or multifamily household because *H. pylori* transmission is mainly intrafamilial [17]. Water source and lack of in-home water have also been identified as risk factors [17]. In addition to the high rates of seroprevalence of *H. pylori* infection, a recent study conducted in three regions of Alaska found a cumulative reinfection rate of 16.1% within the first 2 years of *H. pylori* treatment [16], which is much higher than the rate in the general U.S. population. Disparities in rates of *H. pylori* infection, as well as factors associated with transmission and reinfection, could be driving the higher rates of gastric cancers (specifically central/distal gastric cancer) in the Alaska Native population [11, 13]. Further research is needed to characterize the prevalence of *H. pylori* infection in American Indian populations outside of Alaska.

Although *H. pylori* is a known risk factor, gastric cancer is a multifactorial disease [1, 43], and some of the observed variation in incidence rates could be due to differences in the prevalence of risk factors other than *H. pylori* that may also contribute to gastric cancer incidence. To date, little research has been done to assess these risk factors specifically in AI/AN populations. Previous research suggests that environmental and behavioral factors play an important role in the development of gastric cancer. Dietary factors, such as the high consumption of fresh fruits and vegetables, have been associated with lowered risk of gastric cancer [20, 44]. Conversely, high intake of salt, nitrites, and nitrates have been associated with higher risk [35, 45, 46]. Refrigeration may have played a role in reducing gastric cancer rates over the last 60 years by decreasing reliance on food preservation methods, such as salt curing, pickling, and meat smoking, which have been shown to be sources of carcinogenic compounds associated with gastric cancer [19, 47, 48]. Although these dietary factors have been associated with gastric cancer in studies of other populations, none of these studies have specifically assessed the effect of dietary patterns in AI/AN populations on gastric cancer incidence.

Although many studies are unable to take into account the role of potential confounders (such as *H. pylori* infection and dietary intake), substantial evidence exists that smoking is associated with gastric cancer [4, 5, 48–50]. Recent studies have shown that this association persists across gender and race [49]. Further work is needed to understand how this association might be affected by other gastric cancer risk factors.

Family history may also play a role in gastric cancer risk [51]. Case control studies of gastric cancer have reported that the odds ratios associated with family history varied from 2 to 10, depending on the country [52], and 10%–30% of gastric cancer patients had a family history of the disease [51, 53, 54]. Since early detection and diagnosis of gastric cancer play an important role in cancer-related outcomes [1], future studies of family history of gastric cancer in AI/AN populations could help focus screening and intervention programs.

Obesity has also been associated with gastric cancer incidence, particularly gastric cancers of the stomach cardia or proximal site [55–58]. Previous data from the Behavioral Risk Factor Surveillance System suggest that prevalence of obesity is higher in AI/AN populations compared to whites [14] and that prevalence varies by region [59]. Risk factors associated with higher rates of certain subtypes of gastric cancer may be the same risk factors associated with the increasing rates of esophageal adenocarcinoma in the United States, including obesity and gastroesophageal reflux disease [51, 53, 54].

Although this study used the most accurate and current data for cancer incidence in AI/AN populations, it has limitations. Because racial misclassification was addressed by linking with the IHS patient registration database, this correction applied only to people who had ever accessed services through IHS and were members of federally recognized tribes. People who lived in urban, non-PRCDA areas, who were members of a non-federally recognized tribe, or who had not accessed services through IHS were underrepresented. Therefore, our results may not be generalizable to all AI/AN people in the United States or in individual geographic regions. Additionally, information regarding prevalence of important gastric cancer risk factors, including *H. pylori* infection, was not available. Finally, the exclusion of non-Hispanic AI/AN people may affect rates for certain regions.

This study highlights higher incidence of gastric cancer in AI/AN populations, with particularly high rates in Alaska and the Southwest. These disparities call for new, comprehensive prevention and treatment strategies to reduce disease and death related to gastric cancer, including strategies to identify and address risk factors associated with gastric cancer. Screening and early detection are critical to improving outcomes because later stage disease is difficult to treat and often results in poorer prognosis. While screening high-risk populations for gastric cancer is appropriate in countries with a relatively high incidence rate, screening is generally thought to be costly and unwarranted in countries with low rates of gastric cancer, such as the United States[1]. However, recent studies have shown that gastric cancer screening in high-risk populations can be both cost effective and effective at reducing mortality[60, 61]. Future research is needed to identify people at high risk by considering all potential risk factors and to support, for example, development of a risk prediction or risk stratification model for targeted interventions for this population [62]. Monitoring regional variations in gastric cancer incidence may help identify important

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgements

CDC coauthors participated as a part of their official duties. Additional support was provided by Contract HHSN261201800014I, Task Order HHSN26100001 from the National Cancer Institute (*C. Wiggins*) and grant number T32CA09168 National Cancer Institute (NCI) (*D.Pete*).

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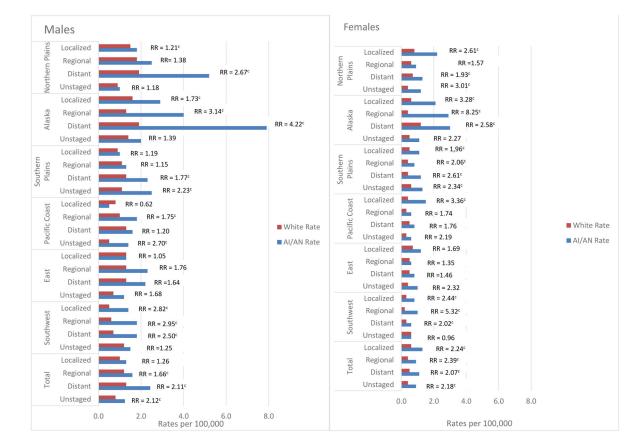


Figure 1:

Gastric cancer incidence rates^a and rate ratios by stage of diagnosis, sex, and Indian Health Service region for American Indian/Alaska Native^b and white populations in PRCDA counties, 2005–2016.

Figure 1 contains two bar separate bar graphs, one for male and one for females. Each show gastric cancer incidence rates for AI/AN compared to white populations by stage of disease and Indian Health service region for those regions that are Purchased/Referred Care Delivery Area (PRCDA) counties. The figures also show the AI/AN versus white rate ratio. ^aRates are per 100,000 and age-adjusted to the 2000 US Std Population (19 age groups-Census P25–1130) standard; Confidence Intervals (Tiwari model) are 95% for rates and ratios

^b AI/AN race is reported by NPCR and SEER registries or through linkage with the IHS patient registration database. The updated bridged intercensal population estimates significantly overestimate AI/AN populations of Hispanic origin. All analyses are limited to non-Hispanic AI/AN populations. Non-Hispanic White was chosen as the reference population. The term "non-Hispanic" is omitted when discussing both groups

^c The rate ratio indicates that the AI/AN rate is significantly different than the rate for whites (P<0.05). Rates are per 100,000 and age-adjusted to the 2000 US Std Population (19 age groups-Census P25–1130) standard; Confidence Intervals (Tiwari model) are 95% for rates and ratios

Localized: Disease restricted to the stomach

Regional: Disease extended into organ and areas adjacent to the stomach.

Distant: Disease metastasized to portions of the body not adjacent to the stomach Unstaged: Diagnosis could not be determined

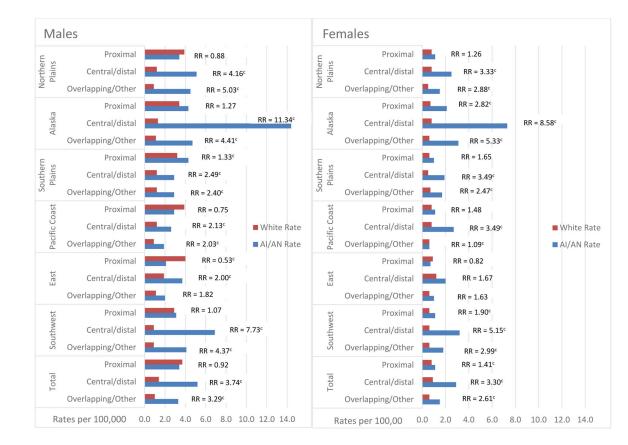


Figure 2:

Gastric adenocarcinoma incidence rates^a and rate ratios by anatomic subsite, sex, and Indian Health Service region for American Indian/Alaska Native^b and white populations in PRCDA counties, 2005–2016.

Figure 2 contains two bar separate bar graphs, one for male and one for females. Each show gastric cancer incidence rates for AI/AN compared to white populations by anatomic subsite and Indian Health service region for those regions that are Purchased/Referred Care Delivery Area (PRCDA) counties. The figures also show the AI/AN versus white rate ratio. ^aRates are per 100,000 and age-adjusted to the 2000 US Std Population (19 age groups-Census P25–1130) standard; Confidence Intervals (Tiwari model) are 95% for rates and ratios

^b AI/AN race is reported by NPCR and SEER registries or through linkage with the IHS patient registration database. The updated bridged intercensal population estimates significantly overestimate AI/AN populations of Hispanic origin. All analyses are limited to non-Hispanic AI/AN populations. Non-Hispanic White was chosen as the reference population. The term "non-Hispanic" is omitted when discussing both groups
 ^c The rate ratio indicates that the AI/AN rate is significantly different than the rate for whites (P<0.05). Rates are per 100,000 and age-adjusted to the 2000 US Std Population (19 age groups-Census P25–1130) standard; Confidence Intervals (Tiwari model) are 95% for rates and ratios

^d Includes primary Sites C16.0-C16.1 (topography codes from the International Classification of Diseases for Oncology)

^e Includes primary sites C16.2-C16.6 ^f Includes primary sites C16.8-C16.9

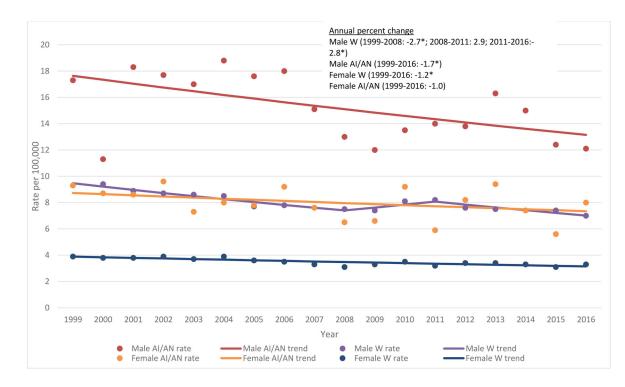


Figure 3.

Trends in gastric cancer incidence for American Indian/Alaska Native and white males and females, all regions, PRCDA counties, 1999–2016

Figure 3 contains four lines describing the gastric cancer incidence rates and trends between 1999—2016 for AI/AN males, AI/AN females, white males and white females. It also contains the average annual percent change in incidence rates for these groups.

Source: Cancer Registries in the National Program of Cancer Registries (NPCR) of the Centers for Disease Control and Prevention and the Surveillance, Epidemiology, and End Results (SEER) program of the National Cancer Institute

PRCDA Purchased/Referred Care Delivery Areas; *IHS* Indian Health Service; AI/AN; American Indian/Alaska Native; W; non-Hispanic white

^a APC (Annual Percent Change) is based on rates that were age-adjusted to the 2000 US standard population (11 age groups, Census P25–1130). * 2-sided P < 0.05 Author Manuscript

Gastric cancer incidence by region and sex for American Indian/Alaska Native^a and white populations in PRCDA counties, 2005–2016.

Region	Sex	AI/AN Count AI/AN Rate	AI/AN Rate ^b	95% CI for AI/AN Rate White Rate	White Rate ^b	RR ^c (AI/AN:W)	95% CI for RR
Northern Plains	Both sexes	225	10.4	9.0–12.0	5.1	2.04 ^d	1.75–2.35
	Males	137	14.6	11.9–17.6	7.5	1.94^{d}	1.59 - 2.35
	Females	88	7.2	5.79.0	3.1	2.33 ^d	1.84–2.91
Alaska	Both sexes	211	20.9	18.124.1	4.9	4.23 ^d	3.47-5.17
	Males	130	27.0	22.2–32.6	6.9	3.93^{d}	3.04-5.07
	Females	81	15.7	12.3–19.6	2.9	5.39 ^d	3.83-7.59
Southern Plains	Both sexes	282	8.8	6.6–7.7	4.7	1.85 ^d	1.62 - 2.10
	Males	166	12.1	10.2–14.2	7.0	1.73^{d}	1.44–2.06
	Females	116	6.4	5.2-7.7	2.9	2.20 ^d	1.78-2.69
Pacific Coast	Both sexes	212	7.4	6.4–8.6	5.1	1.46^{d}	1.25-1.68
	Males	117	9.0	7.2–11.0	7.4	1.20	0.97 - 1.47
	Females	95	6.3	5.0-7.7	3.1	2.02 ^d	1.61 - 2.50
East	Both sexes	92	8.1	6.4–10.0	6.0	1.34^{d}	1.07-1.66
	Males	53	10.0	7.3–13.4	8.6	1.17	0.85-1.56
	Females	39	6.4	4.58.9	4.0	1.63^{d}	1.14-2.24
Southwest	Both sexes	483	11.9	10.813.1	4.3	2.78 ^d	2.51-3.06
	Males	295	17.4	15.3–19.6	6.0	2.89 ^d	2.53-3.27
	Females	188	8.1	6.99.3	2.7	2.93^{d}	2.50–3.42
Total	Both sexes	1,505	10.4	9.9–11.0	5.3	1.98^{d}	1.87 - 2.09
	Males	898	14.2	13.2–15.2	7.6	1.87^{d}	1.74–2.01
	Females	607	7.6	7.08.2	3.3	2.27^{d}	2.09–2.47

Source: Cancer Registries in the National Program of Cancer Registries (NPCR) of the Centers for Disease Control and Prevention and the Surveillance, Epidemiology, and End Results (SEER) program of the National Cancer Institute

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PRCDA purchased/referred care delivery areas, IHS Indian Health Service; AI/AN American Indian/Alaska Native; CI confidence interval; W non-Hispanic white

^aAI/AN race is reported by NPCR and SEER registries or through linkage with the IHS patient registration database. Updated bridged intercensal population estimates significantly overestimate AI/AN populations of Hispanic origin. All analyses are limited to non-Hispanic AI/AN populations. Non-Hispanic white was chosen as the reference population. The term "non-Hispanic" is omitted when discussing both groups

b Rates are per 100,000 and age-adjusted to the 2000 US Standard Population (19 age groups-Census P25–1130) Confidence Intervals (Tiwari model) are 95% for rates and ratios

^C Rate ratios are AI/AN versus white and calculated in SEER*Stat software before rounding of rates and may not equal the RR calculated from rates presented in table

 $d_{\rm Indicates}$ that the AVAN rate is significantly different than the rate for whites (p < 0.05).

Coast (CA,* ID,* OR,* WA,* HI), and East (AL,* AR, CT,* DE, FL,* GA, KY, LA,* ME,* MD, MA,* MS,* NH, NJ, NY,* NC,* OH, PA,* RI,* SC,* TN, VT, VA, WV, DC). The * identifies states with at Regions defined as follows: AK*, Northern Plains (IL, IN,* IA,* MO,* MN,* NT,* NE,* ND,* SD,* W1,* WY*), Southern Plains (OK,* KS,* TX*), Southwest (AZ,* CO,* NV,* NM,* UT*), Pacific least 1 country designated as PRCDA

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Table 2.

Gastric cancer incidence rates and rate ratios by age, sex, and region for American Indian/Alaska Native^a and white populations in PRCDA counties, 2005-2016

		Both Sexes				Males				Females			
Region	Stage	AI/AN Rate ^b	$rac{W}{Rate}^{b}$	RR ^C (AI/ AN:W)	95% CI	AI/AN Rate ^b	W Rate ^b	RR ^C (AI/ AN:W)	95% CI	AI/AN Rate ^b	${ m W} { m Rate}^b$	RR ^c (AI/ AN:W)	95% CI
Northern Plains	<40 Years	$p^{9.0}$	0.3	2.49	(1.16-4.63)	0.8	0.3	2.76	(0.97–6.10)	0.5	0.2	2.19	(0.58–5.65)
	40–59 Years	11.1 ^d	4.1	2.72	(2.17–3.38)	13.9 ^d	5.4	2.59	(1.93–3.42)	8.5 ^d	2.8	3.1	(2.10-4.37)
	60–74 Years	29.5 ^d	17.7	1.67	(1.30–2.11)	$_{38.4}^{d}$	26.7	1.44	(1.03–1.95)	22.1 ^d	9.2	2.41	(1.61–3.48)
	75 Years	66.2 ^d	33.5	1.98	(1.46–2.62)	106.2^{d}	51.5	2.06	(1.39–2.95)	39.5 ^d	21.2	1.86	(1.10–2.96)
Alaska	<40 Years	3.1 ^d	0.2	17.59	(6.37– 59.74)	2.7^d	0.2	14.39	(3.54– 81.20)	3.4 ^d	0.2	21.7	(4.78-197.70)
	40–59 Years	27.4 ^d	4.3	6.38	(4.67–8.72)	36.5 ^d	5.1	7.14	(4.84-10.56)	18.4^{d}	3.3	5.49	(3.18–9.48)
	60–74 Years	62.5 ^d	17.6	3.56	(2.56-4.90)	86.4 ^d	26	3.32	(2.23–4.88)	40.9 ^d	7.9	5.21	(2.78–9.79)
	75 Years	89.1 ^d	30.9	2.88	(1.80-4.54)	111.5 ^d	44.3	2.51	(1.28-4.68)	75.3 ^d	18.3	4.11	(1.98 - 8.48)
Southern Plains	<40 Years	0.5	0.3	1.97	(0.91–3.81)	0.6	0.3	1.79	(0.60-4.26)	0.5	0.2	2.29	(0.65–6.31)
	40–59 Years	8.3 ^d	4.3	1.94	(1.52–2.44)	$p^{0.6}$	6.1	1.48	(1.06–2.03)	$p^{L:L}$	2.5	3.01	(2.08-4.30)
	60–74 Years	30.4 ^d	17	1.78	(1.45–2.17)	40.6^{d}	25.2	1.61	(1.24–2.07)	21.5 ^d	9.7	2.21	(1.56–3.06)
	75 Years	51.0^{d}	27.6	1.85	(1.41 - 2.38)	84.3 ^d	41.8	2.01	(1.42–2.78)	30.4^{d}	18.2	1.67	(1.05–2.54)
Pacific Coast	<40 Years	$^{0.6}d$	0.3	2.19	(1.07–3.97)	0.7	0.3	2.23	(0.86-4.71)	0.5	0.2	2.12	(0.56–5.44)
	40–59 Years	6.3 ^d	4.2	1.51	(1.15–1.94)	6.4	5.6	1.13	(0.77–1.61)	6.2^d	2.7	2.29	(1.54–3.28)
	60–74 Years	22.1	17.7	1.25	(0.98-1.56)	29.3	26.6	1.1	(0.81–1.46)	15.7^{d}	9.5	1.65	(1.10–2.38)
	75 Years	51.2 ^d	32.8	1.56	(1.18-2.04)	62.7	49.4	1.27	(0.83 - 1.86)	45.1 ^d	20.9	2.16	(1.45–3.11)
East	<40 Years	0.4	0.3	1.37	(0.27 - 3.90)	0.3	0.3	1.04	(0.03 - 5.18)	0.6	0.3	1.68	(0.20 - 6.02)

		Both Sexes				Males				Females			
Region	Stage	AI/AN Rate ^b	\mathbf{W} Rate ^b	RR ^C (AI/ AN:W)	95% CI	AI/AN Rate ^b	\mathbf{W} Rate b	RR ^C (AI/ AN:W)	95% CI	AI/AN Rate ^b	\mathbf{W} Rate ^b	RR ^C (AI/ AN:W)	95% CI
	40–59 Years	$^{8.4}$	4.9	1.71	(1.17–2.42)	11.6 ^d	6.7	1.73	(1.06–2.66)	5.5	3.2	1.73	(0.88–3.07)
	60–74 Years	25.4	20.5	1.24	(0.85–1.74)	34	30.1	1.13	(0.70–1.72)	17.6	11.9	1.47	(0.75–2.59)
	75 Years	48.9	39.7	1.23	(0.77 - 1.87)	53	57.6	0.92	(0.42 - 1.75)	46.9	27.9	1.68	(0.89 - 2.88)
Southwest	<40 Years	1.0^d	0.2	4.34	(2.75–6.62)	$p^{6.0}$	0.2	3.76	(1.85–7.02)	1.1^d	0.2	4.97	(2.63–8.89)
	40–59 Years	$^{2.8}d$	3.6	2.16	(1.76–2.63)	$_{9.2}^d$	4.8	1.92	(1.45–2.49)	9.9	2.4	2.73	(1.98–3.69)
	60–74 Years	36.8 ^d	14.1	2.6	(2.21–3.04)	56.8 ^d	20.9	2.72	(2.23–3.29)	21.3 ^d	7.8	2.73	(2.03–3.59)
	75+ Years	90.1^{d}	28.6	3.15	(2.67–3.71)	$^{140.8}d$	40.3	3.5	(2.81–4.31)	57.6 ^d	19.3	2.9	(2.26–3.86)
Total	<40 Years	$p^{6.0}$	0.3	3.06	(2.40–3.84)	$p^{6.0}$	0.3	2.83	(2.00–3.89)	p80	0.3	3.34	(2.36–4.60)
	40–59 Years	_{9.5} d	4.3	2.18	(1.99–2.40)	11.4^{d}	5.9	1.95	(1.72–2.20)	$p^{L:L}$	2.8	2.72	(2.35–3.15)
	60–74 Years	$_{31.9}^{d}$	18	1.77	(1.62–1.93)	44.6 ^d	26.8	1.66	(1.49–1.86)	21.2 ^d	10	2.12	(1.83–2.45)
	75+ Years	67.5 ^d	34.3	1.96	(1.77–2.17)	99.3 ^d	50.6	1.96	(1.71–2.24)	47.0^{d}	23.1	2.04	(1.73–2.38)

PRCDA purchased/referred care delivery areas, IHS Indian Health Service; AI/AN American Indian/Alaska Native; CI confidence interval; W non-Hispanic white

Am J Gastroenterol. Author manuscript; available in PMC 2021 December 01.

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b bates are per 100,000 and age-adjusted to the 2000 US standard population (19 age groups-Census P25–1130). Confidence intervals (Tiwari model) are 95% for rates and ratios

 $c_{\rm r}$

 d_{The} rate ratio indicates that the Al/AN rate is significantly different than the rate for whites (P<0.05).

Regions defined as follows: AK*; Northern Plains (IL, IN,* IA,* MO,* MN,* MT,* NE,* ND,* SD,* WI,* WY*); Southern Plains (OK,* KS,* TX*); Southwest (AZ,* CO,* NV,* NM,* UT*); Pacific Coast (CA,* ID,* OR,* WA,* HI); East (AL,* AR, CT,* DE, FL,* GA, KY, LA,* ME,* MD, MA,* MS,* NH, NI, NY,* NC,* OH, PA,* RI,* SC,* TN, VT, VA, WV, DC)

 $\overset{*}{\operatorname{Model}}$ Identifies states with at least 1 country designated as PRCDA