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Cancer Mortality in a Population-Based Cohort of American Indians - The Strong Heart Study

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Abstract

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Data Sharing Statement

The data underlying this article cannot be shared publicly in an unrestricted manner due to limitations in the consent forms and in the agreements between the Strong Heart Study tribal communities and the Strong Heart Study investigators. The data can be shared to external investigators following the procedures established by the Strong Heart Study, available at https://strongheartstudy.org/.

Background.—Cancer mortality among American Indian (AI) people varies widely, but factors associated with cancer mortality are infrequently assessed.

Methods.—Cancer deaths were identified from death certificate data for 3516 participants of the Strong Heart Study, a population-based cohort study of AI adults ages 45–74 years in Arizona, Oklahoma, and North and South Dakota. Cancer mortality was calculated by age, sex and region. Cox proportional hazards model was used to assess independent associations between baseline factors in 1989 and cancer death by 2010.

Results.—After a median follow-up of 15.3 years, the cancer death rate per 1000 person-years was 6.33 (95% CI 5.67–7.04). Cancer mortality was highest among men in North/South Dakota (8.18; 95% CI 6.46–10.23) and lowest among women in Arizona (4.57; 95% CI 2.87–6.92). Factors independently associated with increased cancer mortality included age, current or former smoking, waist circumference, albuminuria, urinary cadmium, and prior cancer history. Factors associated with decreased cancer mortality included Oklahoma compared to Dakota residence, higher body mass index and total cholesterol. Sex was not associated with cancer mortality. Lung cancer was the leading cause of cancer mortality overall (1.56/1000 person-years), but no lung cancer deaths occurred among Arizona participants. Mortality from unspecified cancer was relatively high (0.48/100 person-years; 95% CI 0.32–0.71).

Conclusions.—Regional variation in AI cancer mortality persisted despite adjustment for individual risk factors. Mortality from unspecified cancer was high. Better understanding of regional differences in cancer mortality, and better classification of cancer deaths, will help healthcare programs address cancer in AI communities.

Keywords

American Indian; Native American; Cancer Mortality; Risk Factors; Epidemiology

1. Introduction

American Indian (AI) people experience reduced longevity [1] and higher chronic disease mortality [2] compared with non-Hispanic Whites (NHW) in the US. While nationwide data in the past suggested lower cancer incidence and mortality for AI people, such data were compromised by racial misclassification [1,3–8]. Studies that focus on areas served by indigenous or Indian Health Service (IHS) areas reduce misclassification error [9]. For example, overall cancer mortality in a study of AI and Alaska Natives (AI/AN) in 2013–2017 was 166/100000, higher than the All Races rate of 158/100,000 [10]. AI/AN in another study had the highest relative risk of cancer death (1.51, 95% CI 1.46–1.56) compared to NHW from 2006–2012 [11]. Cancer mortality among AI/AN persons worsened or remained unchanged before 2010, in contrast to improved NHW rates [2,13,12]. Although cancer mortality among AI/AN began to fall 0.8% annually from 2010–2014, it fell faster among NHW persons (1.4% annually) [11].

Premature cancer mortality among AI/AN populations also worsened from 1999 to 2014–2016 [14, 15]. IHS data reported that cancer, not heart disease, was the leading cause of death from 2007–2009 among AI persons aged 55–64 years [16]. Premature cancer mortality was worse among AI/AN than NHW persons in other studies [15,17]. For example, cancer mortality among AI persons in South Dakota aged 40–49 was 77/100000 from 2000–2010, compared to 54/100000 among NHW [17]. For ages 50–59, AI cancer mortality was 221/100000 versus 176/100000 for NHW [17]. AI/AN cancer survival is also relatively low [11,18]. From 2006–2012, the five-year cancer survival (60.5%) among AI/AN was lower than for other racial/ethnic groups, including NHW (68%) [11].

Aggregate statistics mask marked regional variations in cancer mortality. From 1999–2009, cancer mortality among AI men and women in the Northern Plains was 338.1/100,000 and 246.9/100,000, respectively compared to 163.8/100,000 and 125.9/100,000 in the Southwest [12]. While these differences were thought largely due to smoking [12], few studies directly accounted for factors in assessing regional differences.

The Strong Heart Study (SHS) was designed to study cardiovascular disease (CVD) among middle- to older-aged AI participants in three geographic regions [19]. Since 1989, SHS systematically collected data on factors common to both CVD and cancer. Previous SHS studies examined specific risk factors for cancer mortality [20–22] but did not focus on regional differences. This study describes regional differences in cancer mortality in the SHS cohort, and explores whether differences persist after controlling for potential explanatory factors.

2. Methods

2.1 Study population

The SHS is a population-based cohort study of AI adults ages 45–74 years at baseline recruited from three centers in Arizona, Oklahoma, and North and South Dakota [19].Detailed methods are described elsewhere [19]. Recruitment was based on tribal rolls. Baseline participation was 72% in Arizona, 62% in Oklahoma, and 55% in South/North Dakota [23]. of the original 13 tribes, one subsequently withdrew participation. The current study summarizes the cancer mortality experience from baseline through 2010 for 3,516 participants from the remaining 12 tribes.

2.2 Baseline data collection

Baseline data collection occurred from 1989–1991. Study visits included a questionnaire, physical examination, and bio-specimen collection, using standardized study procedures by certified examiners [19]. In addition to study center (Arizona, Oklahoma, or North/South Dakota), several variables for this study were chosen because they were established risk factors in other populations. Others were included to explore less well-established associations with cancer mortality that may prove important in this population. Baseline variables included age, sex, education (completion of high school/equivalent or more), smoking status (current [past 30 day], former, never), alcohol use in previous year, and prior history of cancer. Baseline measured variables included waist circumference and body mass index (BMI), defined as weight (kg) divided by height (m) squared. Obesity was defined as BMI ≥ 30 kg/m^2 [24]. Fasting triglyceride and total cholesterol were included, as was albuminuria, defined as urinary albumin-to-creatinine ratio ≥ 30 mg/g. Spot urinary cadmium, expressed as micrograms per gram (mcg/g) of creatinine, was measured as previously described [21]. Because arsenic was not associated with total cancer mortality in a previous SHS study, [22] it was not included.

Type 2 diabetes mellitus criteria included 12-hour fasting plasma glucose ≥ 126 mg/dl, 1-hour post-load plasma glucose ≥200 mg/dl, glycated hemoglobin ≥ 6.5%, or use of glucose-lowering medication. Persons who received renal dialysis or kidney transplant and had ever been told by a medical person that they had diabetes were also included. For hypertension, the average of the final two of three blood pressure measurements was recorded. Hypertension was defined as mean systolic blood pressure ≥ 140 mm Hg, mean diastolic blood pressure ≥ 90 mm Hg, or antihypertensive medication use.

2.3 Cancer Mortality

SHS staff regularly ascertained the vital status of participants. When decedents were identified, death certificates were obtained from the state departments of health. Autopsy reports were obtained if the death certificate indicated one was performed. Mortality case ascertainment was complete for 99.8%. For the remainder, at least one death occurred in a foreign country, and others occurred in other states. Causes of death were recorded according to the International Classification of Diseases 9th Revision by a trained nosologist (Appendix A). Unspecified, or ill-defined, cancels were those “not otherwise specified” or only noted as “metastatic”.

2.4 Statistical, Analysis

Baseline characteristics are presented with descriptive statistics. Cancer mortality is expressed per 1000 person-years with 95% confidence intervals. Time to follow-up was defined as the duration from the date of baseline examination to the date of cancer death, death from any other cause, last follow-up, or December 31st, 2010, whichever occurred first. Cox proportional hazards model was used to assess associations of region with cancer mortality adjusting for other factors. For cancer mortality, time to date of death from other causes, to the date of last follow up, or to December 31st, 2010 were treated as censored. In the final exploratory Cox model, factors were selected by backward selection method [25] with a two-sided alpha = 0.05 stay significance level. Sensitivity analyses included stepwise selection models with an inclusion p-value of 0.05, treating persons who died from cancer within two years as having prior cancer at baseline, and removing persons with prior history of cancer.

3 Results

3.1 Baseline characteristics.

Table 1 shows baseline characteristics of the 3,516 participants. Arizona participants comprised 13.3%, and Oklahoma and North/South Dakota each comprised about 43% of the sample. Mean age was 56.4 years. Women comprised 58.5%. Overall, 58.0% completed at high school/equivalent or further, 71% were current or former smokers, and 42% used alcohol in the past year. Nearly one-half were obese. Mean waist circumference was 104 cm. Mean total cholesterol was nearly 200 mg/dl and median triglyceride was 119 mg/dl.

Twenty-four percent had albuminuria, 43.6% diabetes, 37.7% hypertension, and nearly 6% prior history of cancer.

3.2 Cancer mortality

Table 2 shows unadjusted cancer mortality overall and by age group, sex, and center. Median follow-up time was 15.3 years (inter-quartile range 10.5, 20.2). The number of cancer deaths was 340. Cancer mortality was highest among North/South Dakota participants and lowest among Arizona participants. Cancer mortality was lower among the younger age groups, and somewhat lower among women than men.

Table 3 shows associations between baseline characteristics and overall cancer mortality for the full model and the final model. Hazard ratio estimates changed minimally between the full and final model, although the association for Oklahoma vs. Dakota center was marginally significant. Age was associated with cancer mortality, but sex was not. Current and former smoking conferred increased risk compared to never smoking. Obesity carried a reduced risk, in contrast to waist circumference, which carried an increased risk. Total cholesterol was inversely associated with cancer mortality. Albuminuria, urinary cadmium, and prior cancer history all carried increased risks of cancer mortality. Repeating analyses using stepwise selection did not alter the results (data not shown). Treating persons who died from cancer within the first two years as having history of cancer at baseline did not alter the results (Appendix B). Excluding 207 persons with baseline history of cancer did not alter results from the full cohort (Appendix C).

Table 4 shows the leading causes of cancer deaths overall, and rates of these cancers by center and by sex. Lung cancer was the leading cause of cancer mortality, for both men and women, but no cases were reported for Arizona participants. Colorectal cancer was the second leading cause of death overall, but the rate was very low among Arizona participants. Rates for women were nearly twice those for men. Unspecified or ill-defined cancer accounted for nearly 8% of all cancer deaths. Kidney cancer was the fourth most common cause of cancer death, and was a leading cause of death for each center and sex. Pancreatic cancer was fifth overall and for all centers. Among men, prostate cancer was the second leading cause of cancer death, but no such deaths occurred among the Arizona participants (data not shown). Among women, breast cancer was the third leading cause of cancer death. Liver cancer, stomach cancer, and lymphoma completed the remaining leading causes of death overall, but no deaths due to lymphoma were identified among the Arizona participants.

4 Discussion

4.1 Cancer mortality, and risk and protective factors

This study is among the very few to describe cancer mortality and risk/protective factors longitudinally among a population-based cohort of older AI adults. For comparison, the Atherosclerosis Risk in Communities study followed a cohort of 12792 Black and White adults ages 45–64 at baseline in 1990. After 15 years, cancer mortality was 4.89/1000 person-years [26], slightly lower than the 5.23/1000 person-years for same-aged participants in the SHS (data not shown). In the Cardiovascular Health Study of 5888 White and Black participants aged 65 and older in 1989–1992, cancer mortality after 16 years of follow-up was 12.1/1000 person-years [27], similar to 12.9/1000 person-years for this age group in the SHS cohort.

Although Arizona participants had the lowest cancer mortality, the small sample limited the power to detect significant differences between other centers. A 25% lower cancer mortality risk occurred in Oklahoma vs. Dakota center after adjustment for smoking and other potential confounders, but significance was marginal. Again, our study may have limited power to detect residual differences by center. Regional differences in cancer mortality in other AI studies [12,28] are often attributed to differences in smoking [12,29,30]. We could not assess investigate other factors such as access to care that may contribute to regional differences [31,32].

Male sex was not associated with cancer mortality. The relatively high prevalence of smoking among AI men and women in the Oklahoma and Dakota sites may explain the relative lack of sex differences in cancer mortality in the SHS.

Current and former smoking were associated with increased cancer mortality. Smoking is implicated in a wide variety of cancers, including the leading causes of cancer death in this cohort. A previous study demonstrated that smoking carries a high proportion of attributable mortality risk in the SHS [33]. Effective strategies to prevent smoking initiation and promote cessation would have a major impact in reducing cancer deaths.

Waist circumference was associated with increased cancer mortality but obesity was associated with reduced cancer mortality. Waist circumference may increase the risk of several cancers [34–40]. In contrast, high BMI, while associated with some incident cancers [41–43], is also associated with a reduced risk of lung cancer [35,44,45] and improved lung cancer survival [46].

Triglyceride and cholesterol levels were inversely associated with cancer mortality in other studies [47–49], but the association is controversial. Possible explanations include reverse causation due to subclinical cancer or effect of lipid-lowering medication [50, 51].

Albuminuria was associated with increased cancer mortality, as has been found in other populations [52,53], particularly among men [54]. Larger studies are needed to assess whether this association is related to renal cancer, or a marker of comorbidities affecting a person’s ability to receive or survive treatment.

Urinary cadmium was associated with increased cancer mortality, even after adjustment for smoking, as previously described [21]. Although smoking is a major source of cadmium exposure, other environmental sources may contribute [12].

Significant associations with cancer mortality did not occur for education, alcohol use, diabetes, or hypertension, unlike other studies. For example, educational attainment was strongly and inversely associated with cancer mortality for both Black and White men and for White women [55]. Alcohol use, diabetes, and hypertension have been associated with increased mortality from selected cancers [20,56,57], but such analyses were beyond the scope of this study.

4.2 Cancer-Specific Mortality

Lung cancer was the leading cause of cancer death but no such deaths were reported for Arizona participants. Lung cancer was the most common incident cancer in the US AI population [58],with markedly lower rates also occurring among Southwest AI [12,28,29], largely due to the lower prevalence of smoking [59].

Colorectal cancer mortality was higher among AI/AN compared to NHW persons in a large study [60]. Colorectal cancer mortality increased among AI/AN persons from 1990–2017, in contrast to a decrease in other racial groups [61]. Possible explanations include the higher prevalence of obesity and smoking among AI/AN as well as lower screening [62]. However, lower colorectal cancer mortality is reported for Southwest AI persons [28,60], despite lower rates of screening [63]. Colorectal cancer mortality was higher among women than men, unlike a larger study [12]. More research is needed to elucidate effects of gender, BMI, smoking, physical activity and screening on colorectal cancer mortality among AI/AN [64].

Unspecified, or ill-defined, cancer mortality is an indicator of deficiencies in cancer reporting or health systems [65]. Mortality from unspecified cancer was high, accounting for 7.6% of all cancer deaths. While cancer as cause of death is generally accurate on death certificates [66,67], type of cancer is subject to further error. A study found significant differences by type of certifier in the accuracy of cancer mortality on death certificates [68], a factor beyond the scope of our study. Higher mortality from unspecified, or ill-defined, cancer has been reported for African American persons [65], but has not been reported for AI. Geographic remoteness was associated with more advanced stages of cancer in Australia [69], where indigenous communities had the highest rates of cancers of unknown primary [70]. Unknown primary cancers in tumor registries vary by clinical setting, disease severity, and socioeconomic status [71,72], all of which may affect cancer ascertainment among AI people.

Kidney cancer incidence rates among AI/AN are among the highest in the US [13] and the racial disparity widened from 1990–2009 [73]. Although the disparity may be related to smoking [74], high BMI is also associated with renal cancer [75–77] and is more prevalent among the Arizona SHS participants [59]. Another study showed increased renal cell carcinoma mortality among AI/AN in Arizona, but not nationwide [81]. Whether diabetes is associated with renal cell carcinoma is controversial [78], and diabetes was not associated with renal cancer mortality in a prior SHS study [20]. The prevalence and incidence of diabetes among AI in the Southwest is also higher than for AI than other areas [79,80] whereas smoking prevalence is much lower [59]. Larger studies of kidney cancer risk and protective factors are needed.

Pancreatic cancer was a leading cause of cancer death in this cohort. Potential explanations include the high prevalence of smoking and obesity, but cadmium exposures may contribute as well. In one study, pancreatic cancer mortality among AI/AN women was higher than among NHW women in the Southern Plains, but not in the Northern Plains or Southwest US [12], for unclear reasons.

Liver cancer was a leading cause of cancer death, consistent with findings in the general AI population [12]. A marked disparity in liver cancer mortality exists for AI/AN compared to NHW persons [12,82]. While the present study cannot ascertain etiology, hepatitis B and C infections may be implicated [12], as may obesity and physcial inactivity [83]. Cirrhosis due to alcohol or non-alcoholic steatohepatitis may contribute [84]. Hepatic steatosis is projected to become the leading cause of liver cancer in the US due to the epidemic of obesity [85], which disproportionately affects AI people.

Reasons for the marked regional difference in prostate cancer mortality are unclear, but have been noted previously [86]. Disproportionate mortality from high-risk prostate cancer has been linked to low income and race in other studies, possibly due to less receipt of definitive therapy [87,88]. Notably, Northern and Southern Plains AI men have significantly higher prostate cancer mortality than their regional NHW male counterparts [86], a finding in need of further study.

Breast cancer was a leading cause of cancer death among women and in all regions (data not shown). Regional differences in other studies show higher breast cancer death rates among southwest AI women compared to AI women in the Plains states [89] but reasons for this need further study as well.

4.3. Limitations

Risk and protective factors for cancer mortality cannot be assumed to be factors for cancer incidence. This study could not adequately account for latency of cancer or risk factors. Although type of cancer was missing for many cancer deaths, cancer as the cause of death was coded by an independent nosologist. The limited sample size decreased the ability to detect factors or interactions modestly associated with cancer mortality. Finally, the analyses of risk factors for cancer mortality are exploratory, as the SHS was designed to study CVD, not cancer. Because no longitudinal cohort studies of cancer risk factors and outcomes for AI communities currently exist, these data therefore provide support for future efforts to improve cancer research in AI populations.

5 Conclusions

Regional variation in cancer mortality in this AI cohort persisted despite adjustment for individual factors. Other factors independently associated with increased cancer mortality included age, current and former smoking, waist circumference, albuminuria, urinary cadmium, and prior cancer history. Factors associated with reduced cancer mortality included obesity and total cholesterol. Causes of cancer deaths differed widely between study centers. Unspecified, or ill-defined, cancer was a major cause of cancer mortality, indicating an important gap that needs improvement. Larger, systematic studies are needed to improve our understanding of cancer among AI people.

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Appendix

APPENDIX A

International Classification of Diseases Version 9 (ICD-9) CODES USED FOR CANCER CLASSIFICATIONS

Site-specific cancer mortality	ICD-9 Code
Lip, oral cavity and pharynx	140.0–149.9
Digestive organs and peritoneum	150.0–159.9
Colon or rectal (colorectal)	153.0–154.9
Esophagus	150.0–150.9
Gallbladder	156.0–156.9
Liver	155.0–155.9
Pancreas	157.0–157.9
Small intestine	152.0–152.9
Stomach	151.0–151.9
Other GI	158.0–159.9
Respiratory and intrathoracic organs	160.0–165.9
Larynx	161.0–161.9
Lung	162.0–162.9
Nasal cavity	160.0–160.9
Pleura	163.0–163.9
Bone, connective tissue, skin and breast	170.0–175.9
Breast	174.0–174.9
Genitourinary organs	179.0–189.9
Bladder	188.0–188.9
Kidney	189.0–189.9
Prostate	185.0–185.9
Testis	186.0–186.9

Site-specific cancer mortality	ICD-9 Code
Ovary	183.0–183.9
Uterus	179.0–179.9, 182.0–182.9
Cervix	180.0–180.9
Unspecified (Ill-Defined)	
Solid Tumor, NOS	195.0–195.9
Metastatic cancer	196.0–199.9
Lymphatic and hematopoietic tissue	200.0–208.9
Lymphoma	202.8
Myeloma	203.0
Other lymphohematopoietic tissue	204.0–208.9

Appendix

Appendix B.

Associations between baseline characteristics and cancer mortality among American Indian adults, with persons who died due to cancer within the first two years treated as having prior cancer - the Strong Heart Study, 1989–2010*, (n = 3516)

Variable	HR[1]	95% CI	
AZ vs. N/SD	0.84	0.58	1.25
OK vs. N/SD	0.83	0.62	1.05
Male vs. Female	1.26	0.97	1.60
Age (years)	**1.07**	1.06	1.10
>=12 years education vs. <	0.84	0.65	1.07
Current smoking vs. Never	**2.60**	1.92	3.45
Former smoking vs. Never	**1.41**	1.03	1.99
Current alcohol user (Yes vs. No)	0.88	0.68	1.13
Obese (BMI>=30 kg/m^2) vs. others	**0.70**	0.51	0.95
Waist circumference (cm)[(1)]	**1.07**	1.00	1.12
Total cholesterol (mg/dl)[(1)]	**0.96**	0.92	0.98
Log triglyceride (mg/dL)	0.93	0.73	1.18
Albuminuria (Yes vs. No)	**1.40**	1.11	1.92
Urinary cadmium (mcg/g of creatinine)	**1.02**	1.01	1.05
Diabetes (Yes vs. No)	1.08	0.85	1.45
Hypertension (Yes vs. No)	0.92	0.70	1.17
Cancer history* (Yes vs. No)	**3.08**	2.26	4.17

AZ, Arizona center; CI, Confidence Interval; HR, Hazards Ratio; mcg/g, microgram per gram; N/SD, North and South Dakota center; OK, Oklahoma center; SHS, Strong Heart Study.

*Cox model includes all listed variables. Person who died due to cancer within the first two years were treated as having cancer history at baseline.

(1)Hazards ratio for waist was given per 5-unit change and for total cholesterol per 10-unit change.

Appendix

Appendix C.

Associations of baseline characteristics with cancer mortality among American Indian adults without a previous history of cancer - the Strong Heart Study, 1989–2010 (n = 3309)

Characteristic	HR*	95% CI	
AZ vs. N/SD	0.72	0.49	1.17
OK vs. N/SD	**0.75**	0.57	0.97
Age (years)	**1.08**	1.07	1.10
Current smoking vs. Never	**2.95**	2.01	4.08
Former smoking vs. Never	**1.94**	1.41	2.53
Obese (BMI>=30 kg/m^2) vs. other	**0.67**	0.45	0.92
Waist circumference (cm)(1)	**1.06** (1)	1.00	1.14
Total cholesterol (mg/dl)(1)	**0.95**	0.91	0.98
Albuminuria	**1.43**	1.14	2.06
Urinary cadmium (mcg/g of creatinine)	**1.03**	1.00	1.05

AZ, Arizona center; BMI, Body Mass Index; CI, Confidence Interval; HR, Hazards Ratio; N/SD, North and South Dakota center; OK, Oklahoma center; SE, standard error; SHS, Strong Heart Study.

*Estimated from a Cox Proportional Hazards model in which characteristics were selected among center, age, sex, education, smoking status, alcohol use, BMI, waist circumference, total cholesterol, triglyceride, albuminuria, urinary cadmium, diabetes mellitus, and hypertension, by backward selection method with 0.05 stay significance level.

(1)Hazards ratio for waist was given per 5-unit change and for total cholesterol per 10-unit changes.

Abbreviations:

AI	American Indian
AI/AN	American Indian and Alaska Native
IHS	Indian Health Service
NHW	Non-Hispanic White
SHS	Strong Heart Study

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Highlights

- Cohort studies of cancer mortality among American Indian (AI) adults are rare
- We explored regional differences in cancer mortality in a cohort of older AI adults
- Differences by region occurred after adjustment for potential confounders
- Leading causes of cancer mortality also differed markedly by region
- Mortality from unspecified cancel was relatively common in all regions

Table 1.

Baseline characteristics of Strong Heart Study participants (n=3516), 1989–1991

Center	
Arizona, %	13.3%
Oklahoma, %	43.4%
North and South Dakota, %	43.3%
Age (years), mean (SD)	56.4 (8.1)
Sex	
Women, %	58.5%
Men, %	41.5%
Highest education completed, %	
11^{th} grade or less	42.0%
High school graduate/GED or more	58.0%
Smoking history	
Current cigarette smoker, %	38.2%
Former cigarette smoker, %	32.8%
Current alcohol user, %	42.0%
Weight status	
Not obese (BMI < 30 kg/m^2)	51.4%
Obese (BMI ≥ 30 kg/$m^{2)}$, %	48.6%
Waist circumference (cm), mean (SD)	104.0 (14.2)
Total cholesterol (mg/dL), mean (SD)	195.5 (39.5)
Triglyceride (mg/dL), median (Q1, Q3)	119.0 (82,171)
Albuminuria, %	24.3%
Urinary cadmium (mcg/g of creatinine), mean (SD)	1.30 (2.04)
Diabetes mellitus, %	43.6%
Hypertension, %	37.7%
Cancer history, %	5.9%

Abbreviations: BMI, Body Mass Index; GED, General Equivalency Degree; mcg/g, microgram per gram; SD, standard deviation

Table 2.

Unadjusted total cancer mortality by age group, sex, and center – the Strong Heart Study, 1989–2010

Characteristic	Center	No. of participants	No. of cancer deaths	Person-years of follow-up	Cancer Mortality*	95% Confidence Interval	
Total	All	3516	340	53739.7	6.33	5.67	7.04
Age (years)							
45–54	All	1710	104	28733.1	3.62	2.96	4.39
55–64	All	1167	137	17332.2	7.90	6.64	9.34
65–74	All	639	99	7674.5	12.90	10.48	15.71
Sex							
Male	All	1460	146	21064.3	6.93	5.85	8.15
Female	All	2056	194	32675.4	5.94	5.13	6.83
Center							
AZ		467	33	6868.9	4.80	3.31	6.75
OK		1527	138	24203.1	5.70	4.79	6.74
N/SD		1522	169	22667.8	7.46	6.37	8.67
Sex and Center							
Female	AZ	307	22	4810.9	4.57	2.87	6.92
Female	OK	885	80	14605.4	5.48	4.34	6.82
Female	N/SD	864	92	13259.1	6.94	5.59	8.51
Male	AZ	160	11	2058.0	5.35	2.67	9.56
Male	OK	642	58	9597.7	6.04	4.59	7.81
Male	N/SD	658	77	9408.7	8.18	6.46	10.23

Abbreviations: AZ, Arizona Center; N/SD, North and South Dakota Center; OK, Oklahoma Center.

*Mortality is expressed cancer deaths per 1000 person-years.

Table 3.

Associations between baseline characteristics and cancer mortality among American Indian adults - the Strong Heart Study, 1989–2010 (n = 3516)

Characteristic	Full Model HR	95% CI		Final Model HR*	95% CI	
AZ vs. N/SD	0.75	0.49	1.16	0.78	0.51	1.19
OK vs. N/SD	0.79	0.61	1.03	**0.78**	0.60	0.99
Age (years)	**1.08**	1.06	1.09	**1.07**	1.06	1.09
Male vs. Female	1.23	0.96	1.59	---	---	---
Education ≥ 12 yr vs. < 12 yr	0.98	0.74	1.29	---	---	---
Current smoking vs. Never	**2.47**	1.77	3.44	**2.53**	1.84	3.48
Former smoking vs. Never	**1.82**	1.37	2.42	**1.79**	1.36	2.34
Current alcohol (Yes vs. No)	0.89	0.68	1.16	---	---	---
Obese (BMI ≥ 30 kg/m^2) vs. other	**0.68**	0.48	0.94	**0.66**	0.47	0.92
Waist circumference (cm)[(1)]	**1.07** [(1)]	1.01	1.13	**1.07** [(1)]	1.01	1.13
Total cholesterol (mg/dl)[(1)]	**0.95** [(1)]	0.92	0.99	**0.94** [(1)]	0.91	0.98
Log triglyceride (mg/dl)	1.02	0.80	1.30	---	---	---
Albuminuria (Yes vs. No)	**1.55**	1.14	2.10	**1.56**	1.18	2.06
Urinary cadmium (mcg/g creatinine)	**1.03**	1.01	1.05	**1.03**	1.01	1.05
Diabetes (Yes vs. No)	1.15	0.88	1.51	---	---	---
Hypertension (Yes vs. No)	0.85	0.65	1.11	---	---	---
Cancer history (Yes vs. No)	**2.16**	1.50	3.11	**2.15**	1.51	3.07

Abbreviations: AZ, Arizona center; BMI, Body Mass Index; CI, Confidence Interval; N/SD, North and South Dakota center; OK, Oklahoma center; SHS, Strong Heart Study.

*Estimated from a Cox Proportional Hazards model by backward selection method with 0.05 stay significance level.

(1)Hazards ratio for waist was given per 5-unit change and for total cholesterol per 10-unit change.

Table 4.

Leading causes of cancer mortality overall, by center, and by sex among American Indian adults - the Strong Heart Study, 1989–2010 (n = 3516)

Rank	Cancer*	No. of Cancer Deaths	Cancer Mortality per 1000 person-years	95% Confidence Interval	
Overall**					
1	Lung	84	1.56	1.25	1.94
2	Colorectal	32	0.60	0.41	0.84
3	Unspecified	26	0.48	0.32	0.71
4	Kidney	22	0.41	0.26	0.62
5	Pancreas	21	0.39	0.24	0.60
6	Liver	15	0.28	0.16	0.46
7	Stomach	13	0.24	0.13	0.41
8	Lymphoma	12	0.22	0.12	0.39
Arizona**					
1	Kidney	4	0.58	0.16	1.49
2	Unspecified	4	0.58	0.16	1.49
3	Pancreas	2	0.29	0.04	1.05
4	Liver	2	0.29	0.04	1.05
5	Colon***	1	0.15	0.00	0.81
6	Stomach	1	0.15	0.00	0.81
7	Lung	0	0.00	0.00	0.00
8	Lymphoma	0	0.00	0.00	0.00
Oklahoma**					
1	Lung	28	1.16	0.77	1.67
2	Colorectal	15	0.62	0.35	1.02
3	Kidney	10	0.41	0.20	0.76
4	Pancreas	10	0.41	0.20	0.76
5	Lymphoma	9	0.37	0.17	0.71
6	Unspecified	8	0.33	0.14	0.65
7	Liver	7	0.29	0.17	0.60
8	Stomach	7	0.29	0.17	0.60
Dakotas**					
1	Lung	56	2.47	1.87	3.21
2	Colorectal	16	0.71	0.40	1.15
3	Unspecified	14	0.62	0.34	1.04
4	Pancreas	9	0.40	0.18	0.75
5	Kidney	8	0.35	0.15	0.70
6	Liver	6	0.27	0.10	0.58
7	Stomach	5	0.22	0.07	0.52
8	Lymphoma	3	0.13	0.0	0.39
Male					

Rank	Cancer*	No. of Cancer Deaths	Cancer Mortality per 1000 person-years	95% Confidence Interval	
1	Lung	45	2.14	1.56	2.86
2	Prostate	16	0.76	0.43	1.23
3	Kidney	11	0.52	0.26	0.93
4	Pancreas	11	0.52	0.26	0.93
5	Colon***	8	0.38	0.16	0.75
6	Unspecified	8	0.38	0.16	0.758
7	Liver	6	0.29	0.11	0.62
8	Stomach	4	0.19	0.05	0.49
Female					
1	Lung	39	1.19	0.85	1.63
2	Colorectal	24	0.73	0.47	1.09
3	Breast	22	0.67	0.42	1.02
4	Unspecified	18	0.55	0.33	0.87
5	Kidney	11	0.34	0.17	0.60
6	Pancreas	10	0.31	0.15	0.56
7	Liver	9	0.28	0.13	0.52
8	Lymphoma	9	0.28	0.13	0.52
9	Stomach	9	0.28	0.13	0.52

*Cancers with the identical mortality rates are presented in alphabetical order

**Overall and statewide rankings exclude breast and prostate cancer mortality.

***No deaths from rectal cancer were reported for men or for AZ participants