ORIGINAL ARTICLE

Diabetes and Impaired Glucose Tolerance in Three American Indian Populations Aged 45–74 Years

The Strong Heart Study

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OBJECTIVE — To estimate prevalence rates of diabetes and impaired glucose tolerance (IGT) in three American Indian populations, using standardized diagnostic criteria, and to assess the association of diabetes with the following selected possible risk factors: age, obesity, family history of diabetes, and amount of Indian ancestry.

RESEARCH DESIGN AND METHODS — This cross-sectional study involved enrolled members, men and women aged 45–74 years, of 13 American Indian tribes or communities in Arizona, Oklahoma, and South and North Dakota. Eligible participants were invited to the clinic for a personal interview and a physical examination. Diabetes and IGT status were defined by the World Health Organization criteria and were based on fasting plasma glucose and oral glucose tolerance test results. Data on age, family history of diabetes, and amount of Indian ancestry were obtained from the personal interview, and measures of obesity included body mass index, percentage body fat, and waist-to-hip ratio.

RESULTS — A total of 4,549 eligible participants were examined, and diabetes status was determined for 4,304 (1,446 in Arizona, 1,449 in Oklahoma, and 1,409 in the Dakotas). In all three centers, diabetes was more prevalent in women than in men. Arizona had the highest age-adjusted rates of diabetes: 65% in men and 72% in women. Diabetes rates in Oklahoma (38% in men and 42% in women) and South and North Dakota (33% in men and 40% in women), although considerably lower than in Arizona, were several times higher than those reported for the U.S. population. Rates of IGT among the three populations (14–17%) were similar to those in the U.S. population. Diabetes rates were positively associated with age, level of obesity, amount of Indian ancestry, and parental diabetes status.

CONCLUSIONS — Diabetes is found in epidemic proportions in Native American populations. Prevention programs and periodic screening should be implemented among American Indians. Standards of care and intervention have been developed by the Indian Health Service for individuals in whom diabetes is diagnosed. These programs should be expanded to include those with IGT to improve glycemic control or to reduce the risk of development of diabetes as well as to reduce the risk of diabetic complications.

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BMI, body mass index; CVD, cardiovascular disease; IGT, impaired glucose tolerance; NGT, normal glucose tolerance; NHANES II, National Health and Nutrition Examination and Survey II; NIDDK, National Institute of Diabetes and Digestive and Kidney Diseases; NIDDM, non-insulin-dependent diabetes mellitus; OGTT, oral glucose tolerance test; WHO, World Health Organization; WHR, waist-to-hip ratio.

In the U.S., ~1.5 million American Indians, Eskimos, and Aleuts reside on reservations or live among the general population. Diabetes was rarely diagnosed among the American Indians until the 1930s. However, in the last 60 years, it has become more common in most American Indian tribes/communities (1,2). In most tribes, diabetes has become a major cause of morbidity and mortality and the prevalence of diabetes has been steadily rising (2–6). The type of diabetes suffered by this group is believed to be almost exclusively non-insulin-dependent diabetes mellitus (NIDDM) (8).

Information on the prevalence of diabetes among American Indians is far from complete. It is also difficult to compare prevalence rates of diabetes among American Indians obtained in different studies. Different definitions of being Indian, non-uniform diagnostic criteria for diabetes, varying methodologies used to estimate the population at risk, and various sampling procedures contribute to the variations in the reported rates of diabetes.

The Strong Heart Study (9), a three-center study funded by the National Heart, Lung, and Blood Institute, was initiated in 1988 to estimate cardiovascular disease (CVD) mortality and morbidity rates using standardized methodology and to compare CVD risk factors among American Indians living in three geographic areas: central Arizona, southwestern Oklahoma, and North and South Dakota. Because of the high prevalence of diabetes expected among American Indians and because diabetes is a recognized risk factor for CVD, standard glucose tolerance tests were administered to ascertain diabetic status. To our knowledge, the Strong Heart Study is the first study of CVD and its risk factors, including diabetes, in American Indians using a standardized protocol in several geographic areas. It provides an opportunity to obtain data on the prevalence of diabetes in three major Indian communities. This study re-

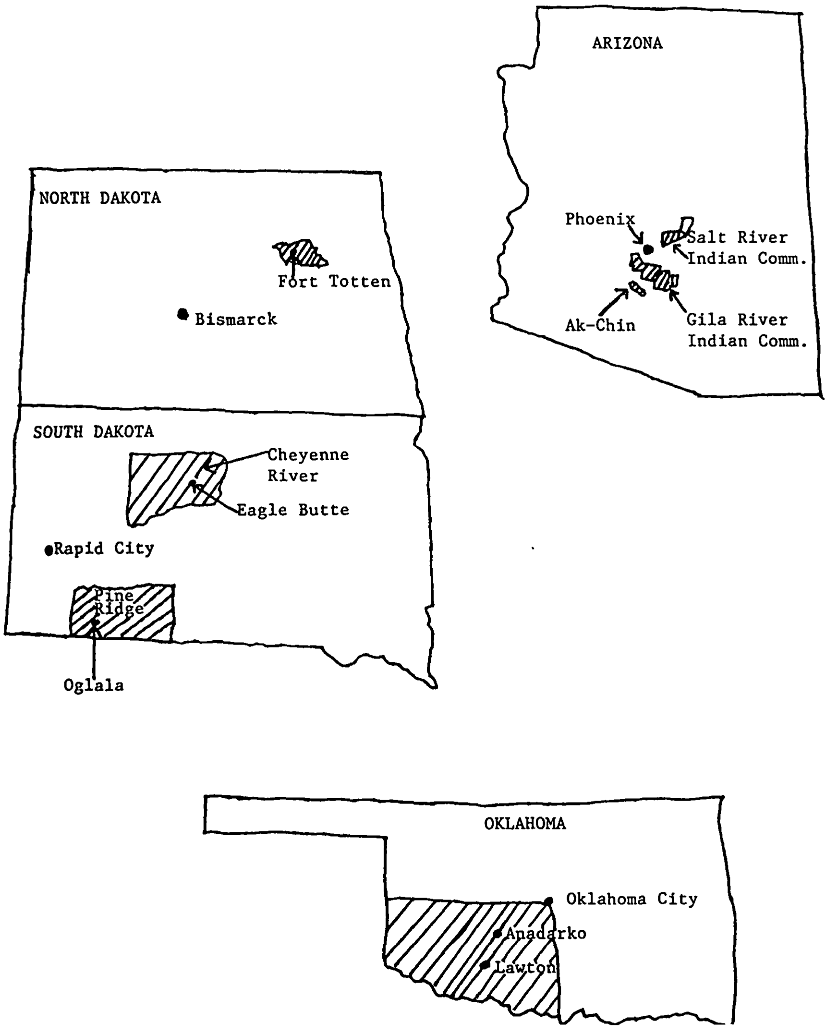

Figure 1—*Locations of Strong Heart Study communities.*

ports the prevalence rates of diabetes, impaired glucose tolerance (IGT), and normal glucose tolerance (NGT) in the Strong Heart Study communities and their association with the following selected possible risk factors of diabetes: age, family history of diabetes, amount of Indian ancestry, and levels of obesity. We recognized that obesity may have been modified in many diabetic patients and thus, etiological interpretations of association would be inappropriate based solely on these cross-sectional data. However, association with family history of diabetes and degree of Indian blood may reflect some etiological role.

RESEARCH DESIGN AND METHODS

RESEARCH DESIGN AND METHODS— The primary objective of the Strong Heart Study was to estimate the prevalence of CVD and relate it to a number of potential risk factors by examining 1,500 men and women, aged 45–74 years, at each of the three centers. Participants were enrolled members of one of the 13 Indian tribes or communities living in the survey areas: the Pima/Maricopa/Papago of the Gila River, Salt River, and Ak-Chin Indian Communities near Phoenix, AZ; the Apache, Caddo, Comanche, Delaware, Fort Sill Apache, Kiowa, and Wichita in southwestern Oklahoma; and the Oglala Sioux and Cheyenne River Sioux in South Dakota and the Devils Lake Sioux in the Fort Totten area of North Dakota. The map in Fig. 1 identifies the study communities and their locations. In Arizona and Oklahoma, every eligible person was invited to participate. In North and South Dakota, a cluster sampling technique was used to obtain the 1,500 subjects needed: 900 from Pine Ridge, 400 from Eagle Butte area, and 200 from Fort Totten area. Participants were all volunteers.

The clinical examination consisted of a personal interview and a physical examination. Details of the examination have been described previously (9). Briefly, the personal interview assessed demographic information, family health history, personal medical history, and lifestyle factors, such as smoking and alcohol consumption, and physical activity. The physical examination included anthropometric measurements, blood pressure measurements, examination of the heart, lungs, pulses, and vessels for bruits, a 12-lead electrocardiogram, fasting glucose and 2-h glucose tolerance tests, fasting blood samples for measurements of lipids, lipoproteins, insulin, glycated hemoglobin, apolipoproteins, and fibrinogen, and a morning urine collection for measurements of albumin and creatinine.

Medical records were reviewed for previous glucose values, history of diabetes, and evidence of treatment for diabetes. A 2-h oral glucose tolerance test (OGTT) was performed after ingestion of a 75-g glucose load (Glutol, Paddock, Minneapolis, MN) on all participants except the following: *1*) diabetic patients being treated with insulin, 2) diabetic patients who were taking oral hypoglycemic agents and whose medical records indicated at least two previous random glucose values ≥250 mg/dl, and 3) participants with a fasting glucose values of ≥225 mg/dl as determined by Accu-Chek II (Baxter Healthcare, Grand Prairie, TX). The participants were classified into five diabetes status groups based on their OGTT results and whether they were receiving hypoglycemia therapy. Criteria used for diabetes mellitus and IGT followed the World Health Organization (WHO) recommendations (10,11):

- Known diabetes. If the participant *1*) was receiving insulin treatment, 2) was receiving a hypoglycemic agent and had two prior measurements of elevated blood glucose (≥250 mg/dl) recorded, 3) was on renal dialysis or had kidney transplantation and a history of diabetes by questionnaire, or 4) had a fasting blood glucose value ≥140 mg/dl or a 2-h blood glucose value ≥200 mg/dl and a history of diabetes by questionnaire.
- New diabetes. If the participant had either a fasting blood glucose value ≥140 mg/dl or a 2-h blood glucose value ≥200 mg/dl and no mention of a history of diabetes by questionnaire.
- IGT. If the participant had either a fasting blood glucose value <140 mg/dl or a 2-h blood glucose value between 140 and 199 mg/dl.
- NGT. If the participant had fasting blood glucose and 2-h blood glucose values <140 mg/dl and no history of diabetes by questionnaire.
- Diabetic status undetermined. *1*) If the participant was on renal dialysis or had a kidney transplant without mention of diabetes in the medical history by questionnaire, 2) if the result of the OGTT was missing, or 3) if the participant refused an OGTT and, in some cases, if the fasting blood specimen was not sufficient to determine the diabetic status.

Indexes of obesity included body mass index (BMI) and percentage body fat, and fat distribution was measured by waist-to-hip ratio (WHR). BMI was calculated as weight in kilograms divided by the square of height in meters. Overweight was defined as a BMI of 27.8–31.09 for men and 27.3–32.29 for women. Obesity was defined as a BMI ≥31.1 for men and ≥32.3 for women. These criteria were approximately the 85th and 95th percentiles for men and women aged 20–29 from The National Health and Nutrition Examination and Survey II (NHANES II) (12). Of the study sample, these cutoff points corresponded to the 28th and 59th percentiles for women and the 39th and 64th percentiles for men. In comparing diabetes rates, subjects were also divided into two groups according to percentage body fat and WHR. Percentage body fat was estimated by bioelectrical impedance using a RJL impedance meter (model B14101, RJL Equipment, Detroit, MI) and an equation based on total body water. The lean body mass was computed by multiplying the total body water by 0.732 (personal communication, M. Singer, RJL). Obesity was defined for men as having >34% body fat and for women >45% body fat. Waist girth was measured at the level of the umbilicus with the participant supine. The hip girth was measured at the level of maximal protrusion of the gluteal muscles. WHRs >0.98 for men and >0.96 for women were used as cutoff points. These values were approximately the 65th percentiles of the percentage body fat and WHR distributions of the study sample.

Statistical analysis

Statistical methods used include the direct method for standardizing prevalence rates (13) for age using 1980 U.S. census data, χ^2 test for comparing rates, analysis of variance technique, and Student's *t* tests for comparing continuous variables among different diabetic status groups and the three study centers.

RESULTS — A total of 4,549 eligible participants were examined, 1,500 in Arizona, 1,522 in South and North Dakota, and 1,527 in Oklahoma. These numbers represent a participation rate of 71% in Arizona, 53% in South and North Dakota, and 62% in Oklahoma (14). To determine how representative the participants were, a random sample of 311 (100 each in Arizona and Oklahoma and 111 total in the Dakotas) nonparticipants was interviewed to obtain information about diabetes and some major CVD risk factors. Results of the comparison are reported in a separate study (14) that focuses on recruitment of the study participants. Briefly, there is a higher participation rate among women, and the participants are slightly younger than the nonparticipants (mean ages 56 and 58 years, respectively). Overall, the rate of self-reported diabetes was similar in the participants (40%) and nonparticipants (38%).

Approximately 4% of the eligible participants, more men than women, refused the OGTT (84 men and 56 women), and a small number of blood samples (*n* = 65) were lost during shipping to the core laboratory in Washington, DC. Thus, of the 4,549 participants examined, diabetes status was determined for 4,304 (95%; 1,446 in Arizona, 1,449 in Oklahoma, and 1,409 in the Dakotas). Among them, 831 had known diabetes (499 taking insulin and 332 taking oral agents) and 61 were on dialysis or had kidney transplants (45 in Arizona, 11 in the Dakotas, and 5 in Oklahoma). A total of 1,512 participants were classified as having NGT, including 44 participants who indicated that they were told by a health professional that they had diabetes at one time but were not taking insulin or hypoglycemic agents and had no abnormal blood glucose values or evidence of therapy seen in medical records.

Table 1 shows the age- and sex-specific and standardized prevalence rates and the total number of participants with IGT and diabetes by center. In all three centers, diabetes was more prevalent in women than in men. Arizona had the highest age-adjusted rates of diabetes, 65% in men and 72% in women. While Arizona had the highest rate of diabetes in both men and women and in every age category, IGT rates were comparable in men among the three centers. In women, the rates of IGT were lower in Arizona than in the other two centers. No substantial differences were found in the rate of diabetes between Districts 1–5 of the Gila River Indian Community (65% in men and 73% in women) and other districts of the Gila River Indian Community and the Salt River Indian Community combined

Table 1—*Age- and sex-specific and standardized prevalence of IGT and diabetes in three American Indian populations*

	Arizona			Oklahoma			South and North Dakota			Total		
	n	IGT (%)	Diabetes (%)	*n*	IGT (%)	Diabetes (%)	*n*	IGT (%)	Diabetes (%)	*n*	IGT (%)	Diabetes (%)
Men												
Age (years)												
45–54	301	14	63	311	14	30	303	12	30	915	13	41
55–65	152	13	72	189	13	40	208	15	34	549	14	47
65–74	68	22	57	118	19	47	94	15	35	280	18	45
All ages	521	15	65	618	15	36	605	13	32	1,744	14	43
Age-standardized prevalence (%)		15	65		15	38		14	33		15	44
95% CI		12.0–18.8	60.3–69.1		12.0–17.8	33.9–41.8		10.7–16.4	29.0–36.8		12.8–16.3	41.7–46.5
Women												
Age (years)												
45–54	471	14	65	363	23	32	389	22	33	1,223	19	45
55–65	306	12	78	296	14	47	271	17	51	873	14	59
65–74	148	16	74	172	21	49	144	19	56	464	19	59
All ages	925	14	71	831	19	41	804	20	43	2,560	17	52
Age-standardized prevalence (%)		14	72		19	42		19	46		17	54
95% CI		11.6–16.4	69.3–75.3		16.4–21.8	38.6–45.4		16.4–22.1	42.1–49.1		15.8–18.8	51.9–55.9
Total age-standardized prevalence (%)		14	70		17.3	40		17	40		16	50
95% CI		12.5–16.5	67.2–72.2		15.3–19.2	37.7–42.8		14.8–18.9	37.5–42.8		15.1–17.3	48.5–51.6

CI, confidence interval.

(63% in men and 69% in women). Districts 1–5 of the Gila River Indian Community have been the site of the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) longitudinal diabetes study for the last 25 years. Diabetes rates in Oklahoma (38% in men and 42% in women) and the Dakotas (33% in men and 40% in women) were similar to each other and considerably lower than those in Arizona. In Oklahoma and the Dakotas, prevalence rates were higher in each successive age-group. In Arizona, the rate was lower in both men and women after age 65. The IGT rate in Arizona was slightly higher in the 65- to 74-year-old than in the younger age-groups, while this was not observed in Oklahoma or the Dakotas.

Table 2 shows the prevalence of known cases and newly diagnosed cases by center. Among the three centers, Arizona had the lowest new:known ratios. For every 10 known cases of diabetes, there were ~1–2 patients with newly diagnosed diabetes. A close examination of the two Arizona Indian Communities (Gila River and Salt River) revealed that Gila River Districts 1–5 had a lower new: known ratio than the other districts (0.15 vs. 0.17 in men and 0.13 vs. 0.14 in women). In Oklahoma and the Dakotas, for every 10 known cases, there were 3 to 7 new cases. The overall ratio in men was higher in the Dakotas than in Oklahoma, but the reverse was observed in women. The highest ratio occurred in the 65- to 74-year-old men in the Dakotas (0.67), indicating a considerable reservoir of undiagnosed cases of diabetes in this group. In Oklahoma, the highest ratio occurred in women aged 45–54 (0.41).

In the participants known to be diabetic, the mean duration of diagnosed diabetes was the longest in Arizona (14.37 years) compared with that in Oklahoma (7.8 years) and the Dakotas (6.9 years). Of the diabetic patients in Arizona, diabetes had been diagnosed for >10 years in 58% and for >20 years in 31%. The duration distribution of the Oklahoma patients was similar to that of South and North Dakota, in that diabetes was diagnosed for >5 years before the Strong Heart Study examination in 45% of the patients in the Dakotas and 50% of those in Oklahoma.

Parental diabetes status

Of those participants whose diabetes status was determined (n = 4,304), 26% of the women and 29% of the men did not know whether diabetes had been diagnosed in one or both of their parents. Table 3 gives the percentage of diabetic subjects and mean age at diagnosis by sex, center, and diabetic status of parents (among those with known parental status only). Diabetes rates were not different

Table 2—Prevalence of newly diagnosed and known cases of diabetes in three American Indian populations

	Arizona			Oklahoma			South and North Dakota			Total		
	New	Known	Ratio	New	Known	Ratio	New	Known	Ratio	New	Known	Ratio
Men												
Age (years)												
45–54	7	55	0.13	8	23	0.35	9	21	0.43	8	33	0.24
55–65	12	60	0.20	11	30	0.37	11	24	0.46	11	36	0.31
65–74	9	49	0.18	10	36	0.28	14	21	0.67	11	34	0.32
All ages	9	56	0.16	9	27	0.33	10	22	0.45	9	34	0.26
Women												
Age (years)												
45–54	9	56	0.16	9	22	0.41	10	24	0.42	9	36	0.25
55–65	9	69	0.13	12	35	0.34	10	41	0.24	10	49	0.20
65–74	6	68	0.09	13	36	0.36	13	42	0.31	11	48	0.23
All ages	8	62	0.13	11	30	0.37	10	33	0.30	10	43	0.23

Data are %.

between participants who had only a diabetic father or only a diabetic mother, and thus, they were combined. Parental diabetes was significantly associated ($P < 0.01$) with diabetes; the prevalence of diabetes increased with the number of diabetic parents. The rates of diabetes in offspring of two diabetic parents were almost twice those in offspring with no diabetic parents among the women in Oklahoma and the Dakotas. Overall, the prevalence odds ratios were 1.84 and 1.80 in men and women, respectively, for individuals with one or two diabetic parents relative to those without any diabetic parents. No clear patterns were found between the rate of IGT and parental diabetes status (data not shown).

Age at diagnosis

Table 3 also shows that parental diabetes status was related to age at diagnosis. Diabetes was diagnosed at a younger age in participants with one or both parents having diabetes than in those with neither parent having diabetes. In each parental diabetes status group, the average age at diagnosis was significantly lower for Arizona diabetic participants ($P < 0.05$) than for those from Oklahoma and from South and North Dakota.

Figure 2 (Arizona, Oklahoma, and North and South Dakota) shows the distributions of reported age at diagnosis for all diabetic participants by centers. Age at diagnosis peaked during the 4th decade of life for both men and women in Arizona. The average age at diagnosis in Districts 1–5 of the Gila River Indian Community was approximately the same as that in the other districts. In Oklahoma, diabetes was diagnosed in men at a younger age (peaked in 40–49 years) than in women (peaked in 50–59 years). In South and North Dakota, the distributions for men and women are similar, but an almost equal percentage of participants has diabetes diagnosed in the 4th

Table 3—*Prevalence of diabetes and age at diagnosis by parental diabetes status, sex, and center*

Parental diabetes status	Arizona		Oklahoma		South and North Dakota	
	Prevalence (%)	Age (years)	Prevalence (%)	Age (years)	Prevalence (%)	Age (years)
Men						
Neither	57.1	46.6	29.1	51.8	30.6	53.0
Either	69.6	42.4	41.8	49.7	37.5	47.9
Both	71.9	38.3	47.1	45.4	48.2	45.7
Women						
Neither	63.9	46.4	31.7	53.3	33.3	52.2
Either	73.3	41.8	48.0	48.4	44.7	49.6
Both	76.6	39.6	61.5	50.3	63.8	46.9

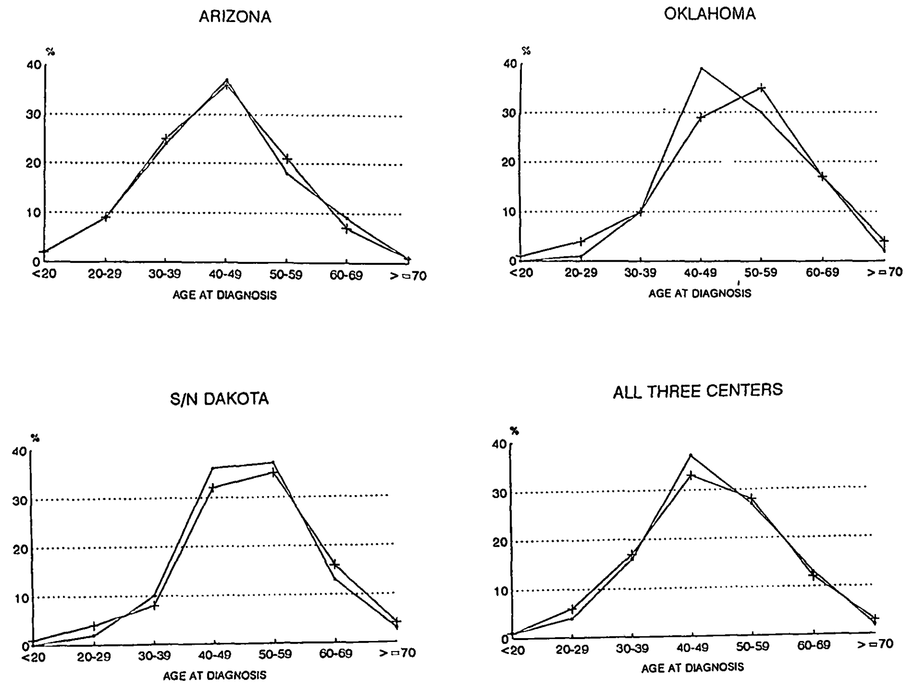

Figure 2—*Distribution of age at diagnosis.* ■, *men;* +, *women.*

decade as in the 5th decade. When all three centers are combined, a single peak during the fourth decade was observed because of the dominating effect of the large number of diabetic patients in Arizona.

Obesity

Obesity is prevalent in all three centers. Among them, Arizona had the highest prevalence of obesity (75%; BMI ≥27.8 for men and ≥27.3 for women), followed by Oklahoma (70%) and the Dakotas (62%). The average BMIs in men (women) were 31.1 (33.1), 30.2 (31.3), and 28.5 (30.1), respectively, in Arizona, Oklahoma, and South and North Dakota. For the men of all three centers and the women in Arizona, the average BMI was highest in the 45- to 54-year-old group and lowest in the 65- to 74-year-old group. Figure 3 shows the overall prevalence of diabetes by BMI in men and women in the three centers combined. The rate of diabetes increased steadily with increasing BMI in both sexes, except that it declined slightly in women in the highest BMI group.

In Oklahoma and in North and South Dakota, there was a consistent pattern of significantly increased prevalence rates of diabetes across the normal, overweight, and obese groups ($P < 0.001$; Table 4). Similar results were obtained using percentage body fat. In the Arizona men, diabetes rates were slightly lower in the most obese (based on BMI), although the differences were not statistically significant. Similar results were observed in the Arizona women when percentage body

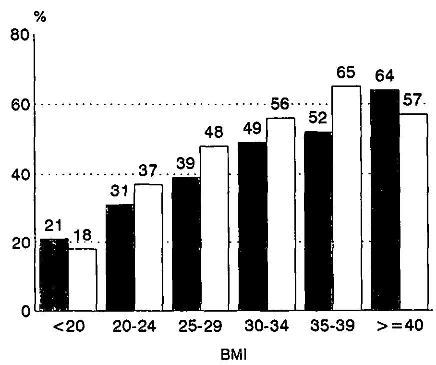

Figure 3—Prevalence of diabetes by age, sex, and BMI. ■, men; □, women.

fat was used. Women in all three centers with a WHR ≥0.96 had a significantly ($P < 0.001$) higher rate of diabetes than those with a WHR <0.96. We also examined the association of obesity using BMI and percentage body fat and diabetes prevalence, taking age into consideration. Overall, the rate of diabetes increased significantly ($P < 0.05$) in the obese group after adjustment for age (data not shown). However, the association between the prevalence of IGT and degree of obesity was not so consistent across centers or sex. Only in Arizona were IGT rates slightly higher in the obese group than the overweight and normal weight groups, in both men and women. Participants with ≥34% body fat had slightly higher IGT rates than those with less body fat except for the Oklahoma women. Men with a WHR ≥0.98 had slightly higher IGT rates than those with lower WHR. However, none of the differences was statistically significant.

Table 5 compares the diabetes and IGT rates of the Strong Heart Study populations to NHANES II data (15) by parental diabetes status and level of obesity. In Oklahoma and South and North Dakota, the presence of either obesity or diabetic parents increased the total diabetes rate, and both factors together increased the rate almost threefold. Also, obesity was more closely associated with diabetes prevalence than parental diabetic status in these two centers. However, in Arizona, where both obesity and diabetes were most prevalent, parental diabetes appeared to be a more dominating factor than obesity. The rates of new diabetes were, in general, higher in the obese group than in the nonobese group. In the nonobese group, the rate of new diabetes in those with parents having diabetes was equal to or smaller than that in those without parents having diabetes. The reverse was observed in the obese group. Thus, there appeared to be a considerable reservoir of undiagnosed cases of diabetes in the obese group and in the nonobese group with no parents having diabetes.

Table 4—*Prevalence of diabetes and IGT by sex, obesity, percentage body fat, WHR, and center*

	Arizona			Oklahoma			South and North Dakota		
	%	Diabetes	IGT	%	Diabetes	IGT	%	Diabetes	IGT
Men									
Obesity									
Normal weight	33.1	63.9	13.9	35.4	28.6*	11.1	46.4	19.4*	8.4
Overweight	26.0	68.7	10.5	24.5	26.3	17.8	27.1	38.6	13.9
Obese	40.9	62.0	18.3	40.1	49.6	15.7	26.5	47.3	20.6
Body fat (%)									
≥34	40.4	63.0†	19.2	38.5	45.8*	19.1	31.0	45.4*	22.2
<34	59.6	64.9	11.9	61.5	30.0	11.9	69.0	26.3	9.6
WHR									
≥0.98	39.7	64.1	17.5	37.7	45.2*	14.8	51.5	14.0*	17.0
<0.98	60.3	65.6	12.2	62.3	31.2	14.7	48.5	23.4	9.8
Women									
Obesity									
Normal weight	19.9	72.5	10.1	29.2	20.6*	21.9	34.2	31.6*	18.2
Overweight	29.9	73.9	11.2	30.9	38.0	21.3	33.5	43.4	21.5
Obese	50.3	68.4	16.8	40.0	57.3	15.8	32.4	54.2	19.5
Body fat (%)									
≥45	43.4	67.3†	18.2	37.3	50.3*	18.1	29.4	52.2*	20.0
<45	56.6	73.5	10.4	62.7	34.8	20.0	70.6	38.6	19.8
WHR									
≥0.96	50.6	77.7*	11.5	26.6	51.8*	15.3	38.2	52.8*	19.6
<0.96	49.4	63.9	16.4	73.4	36.8	20.7	61.8	36.2	19.6

Normal weight: BMI <27.8 for men and <27.3 for women; overweight: BMI 27.8–31.09 for men and 27.3–32.29 for women; obese: BMI ≥31.1 for men and ≥32.3 for women. $*P < 0.001$; $\dagger P < 0.05$.

Amount of Indian ancestry

Self-reported amount of Indian ancestry (as a percentage) was available from 95% of the participants. The Arizona participants have the highest reported quantum of Indian ancestry (average 98%, 93.6% full-blood), followed by the Oklahoma participants (average 88%, 74.3% full-blood) and the Dakota participants (average 79%, 48.7% full-blood). None of the participants in Arizona had <50% Indian ancestry and all the Oklahoma participants had at least 25% Indian ancestry. Figure 4 shows that the prevalence of diabetes increased with degree of Indian ancestry in both the overweight or obese (BMI ≥27.3 for women, ≥27.8 for men) and nonobese subgroups. Table 6 gives

Table 5—*Diabetes and IGT rates (weighted to U.S. population) according to parental diabetes status and level of obesity as compared with NHANES II data*

	Nonobese								Obese							
	No diabetic parent				Diabetic parent				No diabetic parent				Diabetic parent			
Diagnostic catetory	AZ	OK	SD/ ND	NHANES	AZ	OK	SD/ ND	NHANES	AZ	OK	SD/ ND	NHANES	AZ	OK	SD/ ND	NHANES
Known diabetes	56.0	12.6	11.9	3.5	67.0	20.7	17.8	10.6	52.1	26.1	29.6	6.2	65.1	39.7	36.9	13.9
New diabetes	7.0	6.8	5.3	3.9	7.0	3.7	2.0	3.5	11.5	10.7	11.9	8.6	7.4	11.9	12.7	14.3
Total diabetes	63.0	19.4	17.2	7.4	74.0	24.4	19.8	14.1	63.6	36.8	41.5	14.8	72.5	51.6	49.6	28.2
IGT (WHO criteria)	9.0	15.3	11.5	12.8	11.0	14.6	5.9	19.7	17.6	19.8	18.8	21.5	13.2	15.2	20.2	31.1

Data are %.

Table 6—*Diabetes rates of participants by sex, center, and amount of Indian ancestry*

Amount of Indian ancestry (%)	Men			Women		
	AZ	OK	SD/ND	AZ	OK	SD/ND
<25	—	0 (1)	8.3 (24)	—	0 (1)	5.6 (36)
25–49	—	13.8 (29)	20.2 (89)	0 (1)	11.5 (26)	13.9 (79)
50–74	58.8 (17)	25.9 (108)	24.2 (95)	66.7 (24)	29.6 (125)	44.4 (108)
75–99	60.0 (20)	27.3 (33)	38.8 (121)	64.5 (31)	46.9 (49)	43.9 (171)
100	65.1 (484)	41.2 (447)	38.4 (276)	71.4 (869)	43.8 (630)	51.2 (410)

Data are % (*n*).

diabetes rates by sex, center, and amount of Indian ancestry. The rate of diabetes increased consistently in all three centers with amount of Indian ancestry. The prevalence in individuals with 50% or more Indian ancestry was significantly ($P < 0.0001$) higher than that in those with <50% Indian ancestry. In South and North Dakota, diabetes rates in the full-blood Indians were more than four and nine times higher in men and women, respectively, than in the Indians with <25% Indian ancestry. The full-blood Indians in Oklahoma had more than three times higher diabetes rates than those reporting 25–49% Indian ancestry. The differences in diabetes rates among the groups defined by degrees of Indian ancestry (Table 6) are highly significant ($P < 0.01$) in both the Dakotas and Oklahoma, even after controlling for the effect of obesity.

Figure 5 shows the prevalence of diabetes of participants stratified by number of diabetic parents, obesity status, and amount of Indian ancestry. For participants with at least 50% Indian ancestry, the rates are also stratified by center. Clearly, individuals with <50% Indian ancestry had much lower diabetes rates than those with at least 50% Indian ancestry. The obese group had higher rates than the nonobese group, and participants with parents having diabetes had higher rates than those with no parents having diabetes. In participants with at least 50% Indian ancestry, the rates increased with obesity and the number of diabetic parents. Similar results were obtained when the number of diabetic parents was replaced by age (data not shown).

CONCLUSIONS—

The Strong Heart Study is the first study in which standardized criteria were used to diagnose diabetes and IGT in multiple American Indian populations. Diabetes rates in the three Indian populations have all reached epidemic proportions. The Pima/Maricopa/Papago Indian communities have the highest diabetes rates (65% in men and 72% in women) among the three centers. These rates may also be the highest among all populations in the world (16). The prevalence of diabetes in Oklahoma (38% in men and 42% in women) and the Dakotas (33% in men and 40% in women), although lower than those in Arizona, are much higher than those reported for other U.S. populations. The comparison between participants and nonparticipants shows that participants are younger (an average of 2–4 years younger among the men and women in the three centers). The estimated rates may be lower than the true rates in the communities. On the other hand, women had a higher participation rate, and diabetes rates are higher in women, which may lead to an overestimate. We believe that the estimation biases are very small.

The 1976–1980 NHANES II (15) reported that in the U.S. population, a history of diabetes was reported for 4.3, 6.6, and 9.3% of the 45- to 54-, 55- to

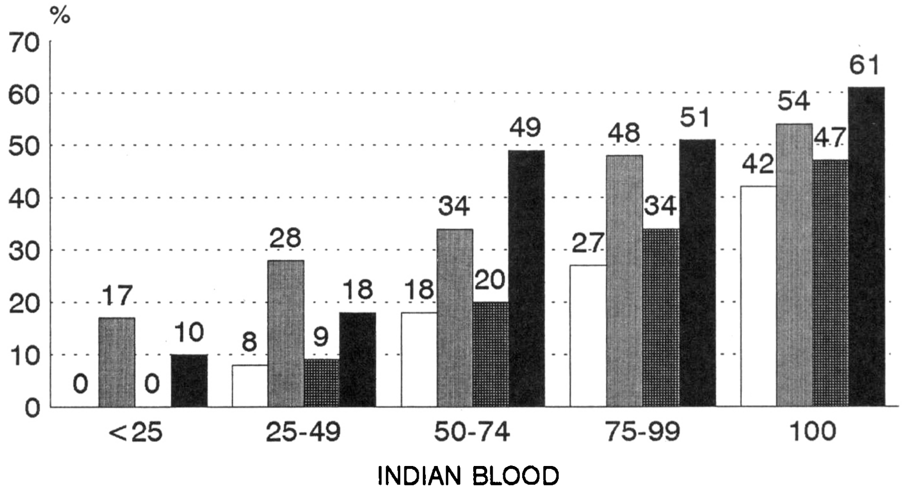

Figure 4—Prevalence of diabetes by Indian ancestry, sex, and obesity. □, nonobese men; □, obese men; ■, nonobese women; ■, obese women.

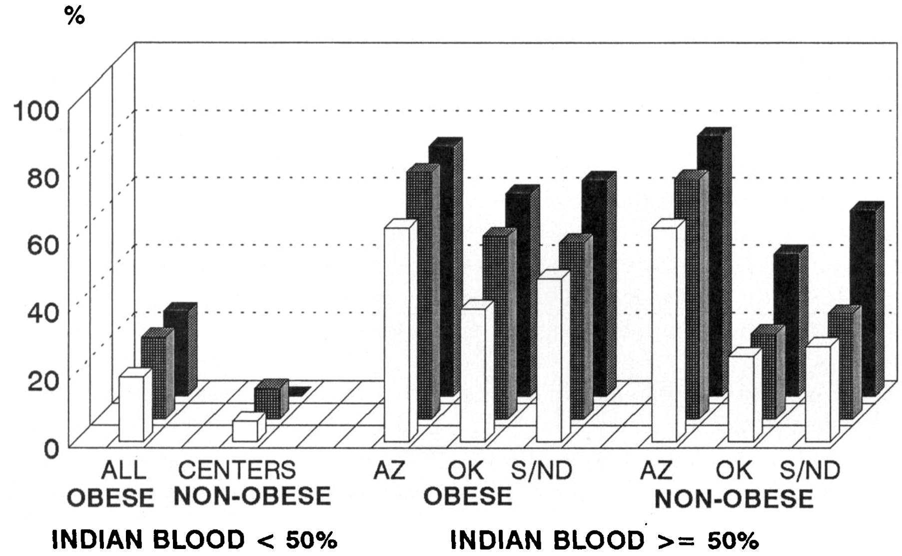

Figure 5—*Prevalence of diabetes by Indian ancestry, obesity, center, and parental diabetes.* □, *0;* ■, *1;* ■, 2.

64-, and 65- to 74-year-old age-groups, respectively. The prevalence was higher in men than in women and in blacks than in whites. Rates of undiagnosed diabetes in NHANES II were similar to the rates for known diabetes. Rates of IGT using WHO criteria (10,11) were 14.8, 15.1, and 22.8%, respectively, in the three above-listed age-groups. More recently, the Centers for Disease Control (17) reported that based on their Behavioral Risk Factor Surveillance System, the prevalence of self-reported diabetes ranged from 4.0% among individuals aged 35–54 years to 12.5% among individuals aged 65–74 years. A population-based study in Minnesota (18) showed similar rates of NIDDM (93.2 per 1,000 in individuals aged 40–59 years and 206.8 per 1,000 in those older than 60) and IGT (183.3 per 1,000 in individuals aged 40–59 years and 294.8 per 1,000 in those over 60). The rates of NIDDM and IGT were 11.9% and 27.8%, respectively, in a California community of adults aged 40–79 years (19).

While the rates of IGT obtained by the Strong Heart Study were comparable with or slightly lower than those reported from these studies, which included largely white populations, the rates of diabetes in the Strong Heart Study populations were four to eight times higher. Although different ascertainment methods were used, it is unlikely that variation in study design and methods alone could account for the large differences in the rate of diabetes between white and American Indian populations.

In addition to blacks, Hispanic men and women have a higher prevalence of NIDDM than non-Hispanic whites (20). The age-adjusted prevalences of NIDDM were 9.9 and 10.7%, respectively, in Hispanic men and women aged 30–69 years, compared with 4.5 and 3.5% in the non-Hispanic whites. The San Antonio Heart Study (21) had similar results, with prevalence rates in Hispanic men ranging from 5.5 to 13.4% and in Hispanic women ranging from 3.7 to 13.7%. The lowest prevalence rates were seen in those living in suburban San Antonio. The Hispanic Health and Nutrition Examination Survey in 1982–1984 (22) found that among the 45- to 74-year-old Mexican-Americans, 13.4% of the men and 15.2% of the women had diabetes. These rates, although higher than those reported by the NHANES II for the white population, were still much lower than those obtained by the Strong Heart Study.

There have been several previous epidemiological studies to determine the prevalence of NIDDM in different Indian tribes. However, methods used to ascertain NIDDM varied; some studies used OGTT tests and others were based on self-reported data or other patient information data bases. The 1987 Survey of American Indians and Alaska Natives showed that based on self-reported data, the age-/sex-adjusted prevalence rate of diabetes was 12.2%, which was 2.35 times higher than that in the general U.S. population (23). In the Pima tribe of Arizona, a tribe that has participated in an NIDDK-sponsored longitudinal study of diabetes for over 25 years (Districts 1–5 of the Gila River Indian Community), the prevalence rates of NIDDM increased from 3.2% (all ages) in the early 1950s to 19% (age ≥5 years) in the 1960s (24). There was a 42% increase in age-adjusted diabetes prevalence rates between 1967 and 1977 (26). By the early 1980s, 50% of Pima Indians older than age 35 had diabetes (25). Between 1982 and 1990, the prevalence of diabetes in those older than 35 years of age ranged from 46% (women between 35 and 44 years) to 74% (women over 65 years) (27). In this study, fasting glucose levels and OGTTs were used at the biennial examination to classify diabetes according to WHO criteria (10,11), and the reported diabetes rates were very similar to those obtained by the Strong Heart Study. This ongoing study of NIDDK may have promoted early detection and thereby produced a slightly lower new:known diabetes ratio than in other areas of the Arizona center (0.15 vs. 0.17 in men and 0.13 vs. 0.14 in women). In fact, the overall prevalence rate of newly diagnosed cases in the Strong Heart Study was <10%, much lower than the nearly 50% found in the NHANES II (15). The lower proportion of newly diagnosed cases may have resulted from the high suspicion level of the health care providers at the Indian Health Service facilities and their efforts in increasing the awareness of diabetes and promoting early detection.

Although no other tribes have been studied as extensively as the Pima, scattered reports have shown varying rates of diabetes in other tribes. The overall age-adjusted prevalence of diabetes, 15.7 per 1,000, in the Alaskan Eskimos, Indians, and Aleuts was lower than the overall U.S. rate of 24.7 per 1,000 (5). Among these three populations, prevalence rates ranged from 8.8 per 1,000 for the Eskimos to 22.0 per 1,000 for the Indians and 27.2 per 1,000 for the Aleuts. Diabetes cases were ascertained from the Patient Care Information System established by the Indian Health Service in Alaska and verified by chart review. The Navajo Indians, the largest Indian tribe in the U.S., were classified as having a low prevalence of diabetes in the 1970s (1). However, a recent report (4) showed that estimated age-adjusted prevalence rates for the Navajo between 20 and 74 years of age were 13.9 and 18.4% for men and women, respectively, which were 2.5 times the U.S. rates. In this study, diabetes was ascertained according to the criteria of WHO (11) for the OGTT. In a study of 29,000 American Indians living on or near 10 reservations in the Pacific Northwest (Washington, Oregon, and Idaho), the Indian Health Service facilities' records showed an age- and sex-adjusted prevalence rate of 7.1%, which was three times higher than the comparable U.S. rate in 1980 (6). The age-adjusted prevalence of diabetes among all Bands of Sioux in the Dakotas in 1987 was 236.1 per 1,000 for those aged 45–64 years and 267.9 per 1,000 for those aged 65 or over (28). The 1987 age-adjusted prevalence of diabetes for all ages among the three Sioux tribes included in the Strong Heart Study, based on ambulatory care data, ranged from 2.8 to 4.5 times the U.S. rate (29).

Some Indian reservations had prevalence rates of diabetes close to those found in the Strong Heart Study. For example, in the Warm Springs reservation community, women aged 55–64 years had a prevalence rate of 46.7% (6). In addition, the prevalence rates of diabetes among the Navajos approach those in the Strong Heart Study in some older age-groups (4); rates ranged from 26.7% in men aged 45–54 to 45.7% in women aged 55–64 years. It appears that, besides the Pima, only the Naurus of the Pacific Ocean had a reported diabetes prevalence (~41.5% in the age range 30–64 years) close to those found in the Strong Heart Study (30).

Age, obesity, parental diabetes, and degree of Indian ancestry have been consistently and strongly associated with diabetes (1,5,25,27,31). The prevalence of diabetes was higher in older age-groups in all three centers of the Strong Heart Study except Arizona, where the rate was lower in those older than 65 years. This may be due to a possible cohort effect or excess mortality rates in this population (33,34). In the Pima Indians, several risk factors have been reported to predict the development of diabetes. These include age, diet, obesity, genetic markers, and parental diabetes (25,27). Similar results were observed in the Strong Heart Study. In addition, we found that the rates of diabetes were significantly higher in persons with greater amounts of Indian ancestry, similar to results obtained in other Northern Plains Tribes in North Dakota (35).

The reason for the high prevalence of diabetes in the Indian population remains unclear. However, the increasing diabetes rates in persons with higher amounts of Indian ancestry provide strong evidence that Indian race is highly associated with the disease. Our observation is that obesity has increased over the last few decades, and it has occurred in young individuals, even children. Diabetes has also been diagnosed in young American Indians. All this supports the "thrifty" genotype hypothesis. More genetic studies are needed.

Interestingly, the prevalence of IGT in our study cohorts was similar to that of the general U.S. population, but the prevalence of diabetes was much higher. Does this imply that the glucose values of many Native Americans increase rapidly from normal to diabetic levels without going through an IGT period? Our ongoing follow-up study will be able to shed some light on this issue.

Standards of care have been developed and implemented by the Indian Health Service for those American Indians in whom diabetes has been diagnosed, emphasizing therapy, diet, and exercise to improve glycemic control or reduce the risk of development of diabetic complications. The extent of implementation is being monitored periodically. Further study is needed to define the most effective intervention for patients with IGT and newly diagnosed diabetes. However, the best strategy would be the prevention of IGT and diabetes. Currently, screening for diabetes is not included in national recommendations for preventive care. Because of the epidemic of diabetes in American Indians, regular screening with a OGTT (75-g) should be considered for American Indians older than 40 years of age, particularly those who are overweight and those who have diabetic parents or a high amount of Indian ancestry. In addition, much more needs to be done in developing effective programs for preventing diabetes.

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