



Relation of generalized and central obesity to cardiovascular risk factors and prevalent coronary heart disease in a sample of American Indians: the Strong Heart Study

RS Gray¹, RR Fabsitz², LD Cowan³, ET Lee³, TK Welty⁴, KA Jablonski¹ and BV Howard^{1*}

¹MedStar Research Institute, Washington, DC, USA; ²National Heart, Lung and Blood Institute, Bethesda, MD, USA; ³Department of Biostatistics and Epidemiology, University of Oklahoma, Oklahoma City, OK, USA; and ⁴Aberdeen Tribal Chairmen's Health Board, Rapid City, SD, USA

OBJECTIVE: To examine the hypothesis linking measures of obesity including body mass index (BMI), waist circumference (waist) and percentage body fat to coronary heart disease (CHD) prevalence and its risk factors in American Indians.

DESIGN: The Strong Heart Study assesses the prevalence of CHD and its risk factors in American Indians in Arizona, Oklahoma and South/North Dakota. Participants underwent a physical examination and an electrocardiogram; anthropometric and blood pressure measurements were taken, as were measurements of glucose, lipoproteins, fibrinogen, insulin, hemoglobin A_{1c} and urinary albumin.

PARTICIPANTS: Data were available for 4549 men and women between 45 and 74 y of age.

MEASUREMENTS: Obesity, measured using body mass index, waist circumference and percentage body fat, was correlated with prevalent CHD and its risk factors.

RESULTS: More than 75% of participants were overweight (BMI > 25 kg/m²). Measures of obesity were greater in women than in men, in younger than in older participants, and in participants with diabetes than in nondiabetic participants. CHD risk factors were associated with measures of obesity but, except for insulin concentration, changes in metabolic variables with increasing obesity were small. Associations were not stronger with waist than with BMI. The prevalence of CHD in those whose BMI and/or waist measurements lay in the lowest and highest quintiles, by gender and diabetic status, was similar.

CONCLUSIONS: Although CHD risk factors are associated with obesity in American Indians, distribution of obesity (ie waist) is no more closely related to risk factors than is generalized obesity (ie BMI), and changes in CHD risk factors with obesity were small. Thus, the relations among obesity, body fat distribution and CHD risk may differ in this population.

International Journal of Obesity (2000) 24, 849–860

Keywords: Indian; North American; coronary heart disease; obesity

Introduction

Obesity is a risk factor for coronary heart disease (CHD).^{1–4} Rates of CHD clearly increase with extreme obesity, but very underweight individuals also appear to have increased rates of CHD.⁵ This U-shaped relationship may, however, partly be due to the confounding influence of smoking on body weight.⁶ Body mass index (BMI) provides a measure of weight in relation to height⁷ and is recognized to be associated with altered lipids, hypertension and diabetes, which are themselves regarded as risk factors for emergent CHD.^{8–10} Large-scale prospective stu-

dies of cardiovascular disease and its risk factors have described a significant, independent relationship between BMI and CHD.^{9,11,12} Recently, the distribution of obesity has been proposed as a more reliable predictor of CHD than BMI.^{12–18} Waist/hip ratio, as an index of central obesity, has been shown to correlate more strongly than BMI with a cluster of metabolic risk factors for CHD.^{19–22} Central body fat distribution may,²³ or may not,²⁴ be the most telling index of insulin resistance, which is believed to determine an individual's metabolic risk factor profile and likelihood of developing CHD.²⁵

The above relationships have been derived mainly from studies of White individuals of European origin. It is necessary to challenge the epidemiological endorsement of the hypothesis linking body fat distribution, metabolic risk factors and CHD by examining a wide range of ethnic subgroups. When African American populations have been considered, initial studies suggested that the relationship between CHD risk and

*Correspondence: BV Howard, MedStar Research Institute, 108 Irving Street NW, Washington, DC 20010-2933, USA.
E-mail: bvh1@mhg.edu
Received 16 July 1999; revised 10 January 2000; accepted 27 January 2000

BMI was evident in men²⁶ but not in women.^{26,27} More recently, a prospective review of a large population of White and African American men and women has indicated a U-shaped relationship between mortality and BMI that was remarkably similar for both races in men and women.²⁸ African Americans may be more insulin resistant than Hispanics and non-Hispanic Whites.²⁹ The relationship between waist/hip ratio and insulin resistance is found in African American as in other ethnic subgroups,²⁹ although the relationship between waist circumference and fasting insulin may be weaker.³⁰ Central obesity also has been reported to correlate with cardiovascular risk factors in Japanese³¹ and Chinese^{32,33} cohorts.

American Indians represent an ethnic group of particular interest in this regard because they are characterized by high rates of obesity, insulin resistance and diabetes. However, a large population study of Pima Indians showed little relation between obesity and mortality.³⁴ We therefore examine a large and geographically diverse population of American Indians in the Strong Heart Study, whose cardiovascular disease prevalence and metabolic risk profiles have already been well characterized. Our aims were to explore (a) the relation of BMI to those metabolic parameters thought to be CHD risk factors, (b) whether body fat distribution is more closely related than BMI to CHD risk factors, and (c) whether body fat distribution is more closely related than BMI to prevalent CHD.

Research design and methods

Study design

The study design, survey methods and laboratory techniques of the Strong Heart Study have been reported previously.^{35,36} Briefly, the study population included resident tribal members aged 45–74 y examined between July 1989 and January 1992 at three study centers: Arizona, Oklahoma and North/South Dakota. Participants were members of the following tribes: Pima/Maricopa/Papago of central Arizona in the Gila River, Salt River and Ak Chin Indian communities; the seven tribes of southwestern Oklahoma (Apache, Caddo, Comanche, Delaware, Fort Sill Apache, Kiowa and Wichita); the Oglala and Cheyenne River Sioux in South Dakota; and the Spirit Lake Tribe in the Fort Totten area of North Dakota. Geographically diverse tribes were included to represent the wide variation in predisposition to CHD that occurs among American Indian groups.³⁵

Approximately 1500 individuals from each of the three centers were included. Participation rates were 71% in the Arizona center, 61% in the Oklahoma center and 53% in the Dakota center.³⁷ Non-respondents did not differ significantly from respondents in age, BMI or self-reported frequency of diabetes.

Respondents were more often female and nonsmokers, and had slightly higher self-reported frequencies of hypertension and obesity than did non-respondents.³⁷ For the prevalence rates of CHD and risk factors, the denominators are all tribal members aged 45–74 y who attended the clinical examination.

Clinical examination

The clinical examination consisted of a personal interview and a physical examination. Participants reported in the morning after at least a 12 h overnight fast. After informed consent was obtained, fasting blood samples were drawn for measurements of glucose, insulin, fibrinogen, glycated hemoglobin (HbA_{1c}), lipids and lipoproteins. A urine specimen was obtained on arrival to the clinic (usually between 08:00 and 09:00 h) for measurement of creatinine and albumin content. A 75 g oral glucose tolerance test was performed on all participants, except for diabetic persons treated with insulin or oral hypoglycemic agents or participants with a fasting glucose ≥ 12.5 mmol/l (225 mg/dl) as determined by an Accu Check II (Baxter Healthcare Corporation, Grand Prairie, TX). Cholesterol, triglyceride and glucose levels were determined by enzymatic methods using a Hitachi chemistry analyzer. High-density lipoprotein (HDL) cholesterol was determined in the supernatant following precipitation of apolipoprotein B (apoB)-containing lipoproteins by heparin manganese. Low-density lipoprotein (LDL) size was determined on plasma samples using the method of Krauss and Burke³⁸ in the laboratory of Medstar Research Institute (Washington, DC). Insulin was measured by a modification of the method of Morgan and Lazarow;³⁹ it could not be measured in 65 patients with diabetes who showed evidence of anti-insulin antibodies. Fibrinogen was determined by the method of von Clauss⁴⁰ and HbA_{1c} by high-pressure liquid chromatography.⁴¹ Urinary albumin was measured by a nephelometric immunochemical procedure⁴² and creatinine by the alkaline picrate method.⁴³

Anthropometric measurements included weight, height and waist circumference measured with participants wearing light clothing and without shoes. Waist was measured at the level of the umbilicus while the participant was supine. BMI was defined as weight (kg)/height (m²). Percentage of body fat was estimated with an RJL impedance meter (Model B14101; RJL Equipment Company, Detroit, MI) using an equation based on total body water (M Singer, RJL Equipment Company, personal communication, 1992). Three consecutive measurements of blood pressure, using the first and fifth Korotkoff sounds, were performed with the participants seated, after 5 min rest, on the right arm using the appropriate size cuff with a Baum mercury sphygmomanometer (WA Baum Company, Copiague, NY). The mean of the last two measurements was used to estimate the blood pressure. American Indian heritage was

expressed as percentage Indian blood and based on self-reported data obtained during the interview.

A 12-lead electrocardiogram (ECG) was taken using a Marquette system (MAC-PC or MAC-12, Marquette Electronics, Milwaukee, WI). All electrocardiograms were read clinically by three staff cardiologists at the Fitzsimons Medical Center and were forwarded to the University of Minnesota electrocardiogram center for application of Minnesota codes.⁴⁴

Urinary albumin excretion was expressed by the ratio of albumin (mg) to creatinine (g); this ratio is highly correlated with the albumin excretion rate in a 24 h urine collection.⁴⁵

Definitions of terms

The participants' medical histories included the Rose Questionnaire for angina pectoris.⁴⁶ Criteria used to define prevalent CHD have been previously described.³⁵ Definite myocardial infarction (MI) was determined by Minnesota-coded Q wave changes on ECG or by history of MI verified as definite by medical record review and confirmed by a Strong Heart Study cardiologist.³⁵ Possible MI included ECGs with a broader range of Minnesota codes or a history of MI verified as possible by medical record review and confirmed by a Strong Heart Study cardiologist.³⁵ Criteria for definite CHD included definite MI, evidence in the medical record of coronary angioplasty or bypass surgery, thrombolytic therapy, a positive angiogram, or angina pectoris by Rose Questionnaire when accompanied by Minnesota Code 4.1 or 5.1 or a verified history of possible MI. Possible CHD included an ECG with a broad range of Minnesota codes, angina pectoris by Rose Questionnaire, or a history of MI by interview.

Participants were classified as diabetic according to World Health Organization criteria⁴⁷ if they were taking insulin or oral anti-diabetic medication, or if they had fasting glucose concentrations ≥ 7.8 mmol/l (≥ 140 mg/dl) or 2 h glucose ≥ 11.0 mmol/l (≥ 200 mg/dl) after a 75 g oral glucose tolerance test. In this analysis, participants with normal glucose tolerance (NGT) had fasting and 2 h glucose values < 7.8 mmol/l (< 140 mg/dl), whereas those with impaired glucose tolerance (IGT) had fasting glucose levels < 7.8 mmol/l (< 140 mg/dl) but 2 h glucose levels between 7.8 and 11.0 mmol/l (140–199 mg/dl).

Obesity was defined as BMI > 30 kg/m² and overweight was defined as BMI > 25 kg/m², as recommended by the National Heart, Lung, and Blood Institute.⁴⁸

Data analysis

Summary analyses were done by gender and diabetic status. Where diabetic status was considered, only

participants with NGT or diabetes (being extremes in carbohydrate metabolism) were included in the analysis. Those with IGT ($n = 693$, 16%) were eliminated from further consideration because it remains questionable as to whether they should be classified with NGT or diabetes. Correlation analysis, either Pearson's or Spearman's, adjusting for age and center, was used to compute the correlation between each obesity-related (BMI, percentage body fat and waist) and metabolic variable. Center was coded as an indicator variable using Oklahoma as the reference center. Reciprocal and logarithmic transformations were done as necessary to ensure normality. No adjustments were made to the *P* values to control for multiple comparisons. To partially account for multiple tests of significance, correlations and associations were considered significant only at the 1% level. *P* values < 0.05 were considered to be significant for comparisons of means and prevalences.

The prevalence of CHD and odds ratios were compared in the upper and lower quintiles of obesity-related variables by gender and diabetes status, adjusting by age and center. Those participants with possible CHD ($n = 182$) were excluded from this analysis because of concern that obesity-related *T*-wave changes on ECG might be spuriously accepted as evidence of CHD.

To demonstrate the impact of increasing obesity (BMI and waist) on each CHD risk factor measurement, a regression model was computed by gender, adjusting for age and center in nondiabetic patients. The CHD risk factors included triglycerides, total cholesterol, HDL cholesterol, ratio of urinary albumin to creatinine, fasting insulin, HbA_{1c}, fibrinogen, LDL size, and systolic (SBP) and diastolic blood pressures (DBP). Only statistically significant regression models with an $R^2 > 0.10$ with normally distributed residuals were used to compute 95% confidence intervals of predicted CHD risk measurements.

For the following CHD risk factors, the normal range was defined as follows: < 200 mg/dl for triglycerides, < 200 mg/dl for total cholesterol, ≥ 35 mg/dl for HDL cholesterol, ≤ 140 mmHg for SBP, ≤ 90 mmHg for DBP (and not on anti-hypertension medication), and < 30 mg/g for the ratio of urinary albumin to creatinine. For fasting insulin, HbA_{1c}, and fibrinogen, the highest quartile was considered beyond the normal range, whereas for LDL size, the lowest quartile was considered beyond the normal range. A value outside the normal range was counted as a risk. Current smokers were considered as having an additional risk factor.

For each participant, the number of CHD risk factors was computed. The median test was then used to check for a difference in the distribution of risk factor counts between the first and fifth quintile of each obesity-related variable by gender. Box and whisker plots by quintile were used to visually display the differences in the distribution of total risk factor counts.

Results

The Strong Heart Study cohort included 4549 men and women aged 45–74 y. Table 1 shows measures of obesity, including weight, BMI, waist circumference, and percentage body fat, together with the prevalence of overweight and obesity in participants by center and gender. Measures of weight, waist, BMI and prevalence of overweight and obesity, respectively, were similar when comparing men from Arizona and Oklahoma, whose measures were greater than those of men from South/North Dakota. For men, percentage body fat was highest in Arizona and lowest in South/North Dakota. For women, each measure of obesity was highest in Arizona and lowest in South/North Dakota. Measures of obesity other than weight were greater in women than in men.

When participants were divided into two groups according to diabetic status, nondiabetic (NGT) and diabetic (DM) women both demonstrated consistently greater mean values of BMI, prevalence of obesity, waist and percentage body fat compared to men. Diabetic participants of each gender showed statistically significant larger values for each measure of obesity than did nondiabetic participants.

Table 2 shows comparative measures of weight, including prevalence of overweight and obesity, by decade of age, according to gender and diabetic status. These tables show that with increasing age each measure of obesity declines in men and in diabetic women. No statistically significant age-related trends in measures of obesity were evident in nondiabetic women. In view of these observations, the analysis of measures of obesity is hereafter described by gender and diabetic status and is corrected for age and center.

Table 1 Obesity-related characteristics of study participants, by gender and center

	Arizona		Oklahoma		South/North Dakota		Total	
	Men	Women	Men	Women	Men	Women	Men	Women
<i>n</i>	546	954	642	885	658	864	1846	2703
Age (y)	55±8	56±8	56±8	57±8	56±8	57±8	56±8	57±8
Percentage with diabetes	65	71	36	41	32	43	43	52
Weight (kg)	91±21	83±18	92±17	80±18	88±17	78±15	90±19	80±17
BMI (kg/m ²)	30.9±6.7	33.1±7.0	30.2±5.3	31.3±6.4	28.5±4.9	30.1±5.7	30±6	32±6
Percentage overweight	87	89	85	85	77	81	83	85
Percentage obese	48	64	48	54	36	47	44	55
Waist (cm)	104±14	112±15	104±12	105±15	101±13	103±14	103±13	107±15
Percentage body fat	30.4±6.7	42.7±7.1	28.9±5.5	41.0±7.1	27.6±5.8	39.8±6.9	29±6	41±7

Data are presented as mean±s.d. Overweight is defined as BMI > 25 kg/m² and obese is defined as BMI > 30 kg/m². Statistically significant differences ($P < 0.0002$) are found in men between Oklahoma/Arizona vs South//North Dakota for all measurements except percentage body fat. Statistically significant differences ($P = 0.0001$) between centers in percentage body fat are found in men. Statistically significant differences ($P = 0.0001$) in all measurements are found between centers in women. Gender differences ($P < 0.0003$) are found in all within-center measurements except in Oklahoma for waist ($P = 0.108$) and percentage overweight ($P = 0.907$), and in Arizona in percentage overweight ($P = 0.177$).

Table 2 Obesity-related variables by diabetic status and age group

	NGT			DM		
	45–54 y	55–64 y	65–74 y	45–54 y	55–64 y	65–74 y
<i>Men</i>						
<i>n</i>	413	218	99	370	256	127
Weight (kg)	89±18	83±14 ^a	78±14 ^a	96±19	91±18	86±14 ^a
BMI (kg/m ²)	29.1±5.6	27.4±4.4 ^a	26.3±4.4 ^a	31.8±5.8	30.7±5.9	29.5±4.4 ^a
Percentage overweight	80	72	63 ^a	88	88	83
Percentage obese	37	29	19 ^a	60	46	41 ^a
Waist (cm)	100±13	98±11 ^a	96±11 ^a	107±13	105±13	103±11 ^a
Percentage body fat	27.8±5.7	26.5±5.6 ^a	26.4±5.7	30.2±6.0	30.0±5.7	28.1±6.1 ^a
Percentage current smoker	78	81	84	80	77	68 ^a
<i>Women</i>						
<i>n</i>	431	234	100	550	513	271
Weight (kg)	77±17	75±15	73±16	86±17	83±16 ^a	76±15 ^a
BMI (kg/m ²)	29.7±6.5	29.8±5.7	29.3±6.3	33.3±6.5	32.7±6.0	30.8±5.9 ^a
Percentage overweight	75	79	76	92	89	87
Percentage obese	43	43	42	66	64	52 ^a
Waist (cm)	100±16	102±14	103±16	111±14	111±14	108±13 ^a
Percentage body fat	39.9±7.4	40.0±6.8	40.1±7.2	42.8±6.7	42.1±6.6	39.6±6.9 ^a
Percentage current smoker	65	57 ^a	52 ^a	58	47 ^a	42 ^a

^a $P < 0.05$ for comparison with age 45–54 y. Overweight is defined as BMI > 25 kg/m² and obese is defined as BMI > 30 kg/m². For each measure of obesity, a significantly ($P < 0.05$) lower value was observed for nondiabetic men than for men with diabetes. For each measure of obesity, and for each age group, a significantly ($P < 0.05$) lower value was observed for nondiabetic women than for women with diabetes (except age 65–74 for percentage BMI > 30 kg/m² and percentage body fat where no significant difference was observed).

Table 3 Partial correlations between obesity-related variables and CVD risk factors (all coefficients adjusted for center and age)

	DM																		
	NGT						DM												
	Waist			Log BMI			Waist			Log BMI			Log BMI (adjusted for waist)			Waist (adjusted for log BMI)			
	r	P	r	P	r	P	r	P	r	P	r	P	r	P	r	P	r	P	
Men																			
Triglycerides ^a	0.28	< 0.01	0.30	< 0.01	0.13	< 0.01	0.00	0.93	-0.02	0.52	0.03	0.45	0.12	< 0.01	-0.12	< 0.01	0.01	< 0.01	
Total cholesterol	-0.05	0.19	0.03	0.51	0.17	< 0.01	-0.18	< 0.01	-0.14	< 0.01	-0.11	< 0.01	0.05	0.24	-0.10	0.05	0.01	0.01	
HDL cholesterol	-0.32	< 0.01	-0.34	< 0.01	-0.10	< 0.01	-0.05	0.21	-0.13	< 0.01	-0.16	< 0.01	-0.11	< 0.01	0.04	0.04	0.29	0.28	
Insulin ^a	0.61	< 0.01	0.61	< 0.01	0.16	< 0.01	0.17	< 0.01	0.40	< 0.01	0.42	< 0.01	0.16	< 0.01	0.04	0.04	0.28	0.28	
HbA _{1c} ^a	0.14	< 0.01	0.15	< 0.01	0.04	0.31	0.03	0.40	-0.10	0.01	-0.09	0.02	-0.01	0.71	-0.02	0.60	0.60	0.60	
SBP	0.16	< 0.01	0.18	< 0.01	0.05	0.20	0.00	0.99	0.03	0.44	0.05	0.16	0.08	0.05	-0.06	0.15	0.15	0.15	
DBP	0.21	< 0.01	0.19	< 0.01	0.01	0.71	0.06	0.14	0.04	0.33	0.06	0.10	0.06	0.11	-0.05	0.23	0.23	0.23	
Urinary albumin/ creatinine ^a	-0.05	0.18	-0.07	0.08	-0.05	0.19	0.02	0.53	-0.15	< 0.01	-0.13	< 0.01	0.03	0.50	-0.09	0.02	0.02	0.02	
Fibrinogen ^a	-0.02	0.65	-0.06	0.11	-0.11	< 0.01	0.09	0.02	0.05	0.21	0.01	0.79	-0.08	0.05	0.09	0.02	0.02	0.02	
LDL size ^a	-0.11	< 0.01	-0.11	< 0.01	-0.02	0.53	-0.03	0.50	-0.03	0.43	-0.02	0.66	0.02	0.53	-0.04	0.37	0.37	0.37	
Percentage Indian blood	-0.03	0.44	-0.10	< 0.01	-0.16	< 0.01	0.13	< 0.01	0.00	0.96	-0.01	0.77	-0.03	0.45	0.03	0.48	0.48	0.48	
Current smoker	-0.04	0.32	-0.07	0.05	-0.08	0.02	0.06	0.12	0.03	0.44	0.02	0.59	0.00	0.79	0.02	0.55	0.55	0.55	
Women																			
Triglycerides ^a	0.12	< 0.01	0.07	0.06	-0.04	0.25	0.10	0.01	-0.07	0.01	-0.05	0.06	0.02	0.54	-0.05	0.08	0.08	0.08	
Total cholesterol	-0.17	< 0.01	-0.16	< 0.01	-0.02	0.63	-0.07	0.07	-0.13	< 0.01	-0.14	< 0.01	-0.06	0.06	-0.02	0.61	0.61	0.61	
HDL cholesterol	-0.24	< 0.01	-0.25	< 0.01	-0.07	0.07	-0.06	0.10	-0.03	0.23	-0.04	0.14	-0.03	0.29	0.01	0.71	0.71	0.71	
Insulin ^a	0.55	< 0.01	0.55	< 0.01	0.19	< 0.01	0.15	< 0.01	0.29	< 0.01	0.34	< 0.01	0.19	< 0.01	-0.02	0.48	0.48	0.48	
HbA _{1c} ^a	0.15	< 0.01	0.16	< 0.01	0.06	0.12	0.02	0.53	-0.01	0.70	-0.04	0.13	-0.07	0.02	0.06	0.05	0.05	0.05	
SBP	0.21	< 0.01	0.17	< 0.01	0.00	0.93	0.09	0.02	0.00	0.97	0.01	0.85	0.05	0.09	-0.05	0.12	0.12	0.12	
DBP	0.18	< 0.01	0.16	< 0.01	0.02	0.60	0.07	0.08	0.08	< 0.01	0.10	< 0.01	0.08	< 0.01	-0.04	0.13	0.13	0.13	
Urinary albumin/ creatinine ^a	-0.04	0.31	-0.05	0.19	-0.04	0.24	0.02	0.57	-0.07	0.02	-0.12	< 0.01	-0.11	< 0.01	-0.06	0.04	0.04	0.04	
Fibrinogen ^a	0.20	< 0.01	0.17	< 0.01	0.00	0.89	0.10	0.01	0.10	< 0.01	0.06	0.04	-0.06	0.05	0.10	< 0.01	< 0.01	< 0.01	
LDL size ^a	-0.12	< 0.01	-0.12	< 0.01	-0.04	0.33	-0.03	0.50	-0.01	0.82	-0.01	0.66	-0.01	0.62	0.01	0.75	0.75	0.75	
Percentage Indian blood	0.04	0.24	0.02	0.59	-0.04	0.26	0.06	0.11	0.04	0.12	0.00	0.91	-0.06	0.02	0.08	0.01	0.01	0.01	
Current smoker	-0.02	0.55	0.00	0.90	0.03	0.36	-0.04	0.27	0.02	0.56	0.00	0.89	-0.04	0.19	0.04	0.15	0.15	0.15	

^a Log values. P values < 0.01 are considered statistically significant. Correlations with a coefficient of determination (r²) > 0.05 are in bold, indicating that > 5% of the variability is accounted for by these variables.

Table 3 shows the correlations (adjusted for age and center) between measures of obesity and risk factor variables for diabetic and nondiabetic men and women, as well as the partial correlations (adjusted for age and center) between BMI adjusted for waist and waist adjusted for BMI. BMI and waist are highly correlated ($r=0.90$, $P<0.0001$ for men; $r=0.87$, $P<0.0001$ for women). Among nondiabetic men, statistically significant positive correlations were observed between each measure of obesity and log triglycerides, log insulin, HbA_{1c}, and SBP and DBP, whereas statistically significant inverse correlations were observed between each measure of obesity and HDL cholesterol. Among nondiabetic women, statistically significant positive correlations were observed between each measure of obesity and log insulin, HbA_{1c}, SBP, DBP and log fibrinogen, whereas significant inverse correlations were observed between each measure of obesity and total cholesterol and HDL cholesterol. A significant inverse relationship was observed between BMI and waist with log LDL size for nondiabetic men and women. The only correlations representing more than 5% of the variance were with insulin and HDL cholesterol in men and women, and triglycerides in men. For diabetic participants, there were fewer and weaker associations with risk factors. Among diabetic men, both measures of obesity had significant, positive correlations with log insulin and significant inverse correlations with HDL cholesterol and log urinary albumin/creatinine. Among diabetic women, both measures of obesity had

significant positive correlations with log insulin and diastolic blood pressure and significant inverse correlations with total cholesterol. Of these, only the correlations with insulin represented more than 5% of the variance.

Table 4 gives 95% confidence intervals for the predicted value of a CHD risk measurement computed at increments of BMI and waist representing a range of overweight to obesity; only significant regressions are shown. Because the range of BMI was greater than that of waist, four categories of BMI were used, compared with three categories of waist. Although triglycerides, HDL cholesterol and LDL size in men, and total cholesterol, HDL cholesterol, fibrinogen and LDL size in women were all statistically associated with obesity, changes with increasing BMI or waist were relatively small. On the other hand, insulin varied by as much as 100% over the range of BMI and waist in men and women.

The number of CHD risk factors is shown to increase with obesity (Table 5). For nondiabetic men and women, those in the highest quintile of each measure of obesity had a higher median number of risk factors than did those in the lowest quintile. No single measure of obesity was more closely associated with risk factors than the others. For diabetic participants, the number of CHD risk factors was unrelated to measures of obesity, except in BMI in men ($P<0.015$). Risk factor scores were similar for each measure of obesity in men and women, whether diabetic or nondiabetic. Diabetic men and women

Table 4 Predicted mean values of risk factor measurements in nondiabetic men and women by category of BMI and waist measurement^a

	Men				Women			
	BMI	Mean (95% CI)	Waist	Mean (95% CI)	BMI	Mean (95% CI)	Waist	Mean (95% CI)
Triglycerides (mg/dl)	25	110 (51–236)	92	123 (90–169)	25		90	83 (67–104)
	28	123 (56–272)	99	135 (96–190)	29		99	86 (67–109)
	30	132 (59–296)	106	148 (103–213)	33		110	88 (68–114)
	35	154 (66–359)			35			
Total cholesterol (mg/dl)	25		92		25	165 (123–207)	90	159 (142–175)
	28		99		29	161 (116–205)	99	156 (138–173)
	30		106		33	157 (111–203)	110	153 (134–172)
	35				35	155 (108–202)		
HDL cholesterol (mg/dl)	25	46 (33–77)	92	44 (38–52)	25	46 (36–67)	90	44 (40–49)
	28	43 (31–71)	99	41 (36–49)	29	44 (35–62)	99	43 (39–48)
	30	42 (30–68)	106	39 (34–47)	33	43 (33–60)	110	42 (38–47)
	35	39 (28–61)			35	42 (33–60)		
LDL size (Å)	25	257 (244–271)	92	257 (251–262)	25	258 (247–270)	90	257 (253–262)
	28	257 (243–271)	99	256 (250–262)	29	258 (246–270)	99	257 (252–261)
	30	256 (243–271)	106	256 (249–262)	33	257 (246–270)	110	256 (251–261)
	35	255 (241–270)			35	257 (244–269)		
Insulin (mU/l)	25	6.21 (2.80–13.78)	92	7.86 (5.67–10.89)	25	5.74 (3.07–10.73)	90	8.40 (6.58–10.67)
	28	8.30 (3.64–18.94)	99	10.14 (7.13–14.41)	29	7.48 (3.89–14.41)	99	9.88 (7.62–12.82)
	30	9.91 (4.27–22.98)	106	13.07 (8.97–19.05)	33	9.43 (4.78–18.62)	110	11.66 (8.82–15.41)
	35	14.70 (6.10–35.42)			35	10.48 (5.25–20.93)		
Fibrinogen (mg/dl)	25		92		25	223 (174–287)	90	232 (211–256)
	28		99		29	229 (176–298)	99	237 (214–263)
	30		106		33	234 (177–308)	110	242 (217–270)
	35				35	237 (179–313)		

^a Only significant regressions are shown.

Mean (95% CI) values of CHD risk factors are provided according to BMI (across a range of overweight to obesity) and according to waist (across a range observed in this population).

Table 5 Median number of risk factors by quintile of measures of obesity, by gender and diabetic status

	Men				Women			
	NGT	P	DM	P	NGT	P	DM	P
<i>BMI</i>								
5th quintile	3 (0–10)	< 0.00	4 (0–8)	0.02	3 (0–7)	< 0.00	3 (0–8)	0.80
1st quintile	2 (0–9)		3 (0–9)		2 (0–6)		3 (0–8)	
<i>Percentage body fat</i>								
5th quintile	3 (0–10)	< 0.00	3 (0–8)	0.52	3 (0–7)	< 0.00	3 (0–8)	0.98
1st quintile	2 (0–7)		3 (0–9)		2 (0–6)		3 (0–8)	
<i>Waist</i>								
5th quintile	3 (0–10)	< 0.00	4 (0–8)	0.08	3 (0–7)	< 0.00	3 (0–8)	0.30
1st quintile	2 (0–9)		3 (0–9)		2 (0–5)		3 (0–8)	

Data are presented as median (min–max). (Note: no adjustments were made to control the type I error rate.) The normal range was defined as < 200 mg/dl for triglycerides, < 200 mg/dl for total cholesterol, ≥ 35 mg/dl for HDL cholesterol, ≤ 140 mmHg for SBP, ≤ 90 mmHg for DBP (and not on anti-hypertension medication) and < 30 mg/g for the ratio of urinary albumin to creatinine. For fasting insulin, HbA_{1c} and fibrinogen, the highest quartile was considered beyond the normal range. A value outside the normal range was counted as a risk. Current smokers were considered as having an additional risk factor.

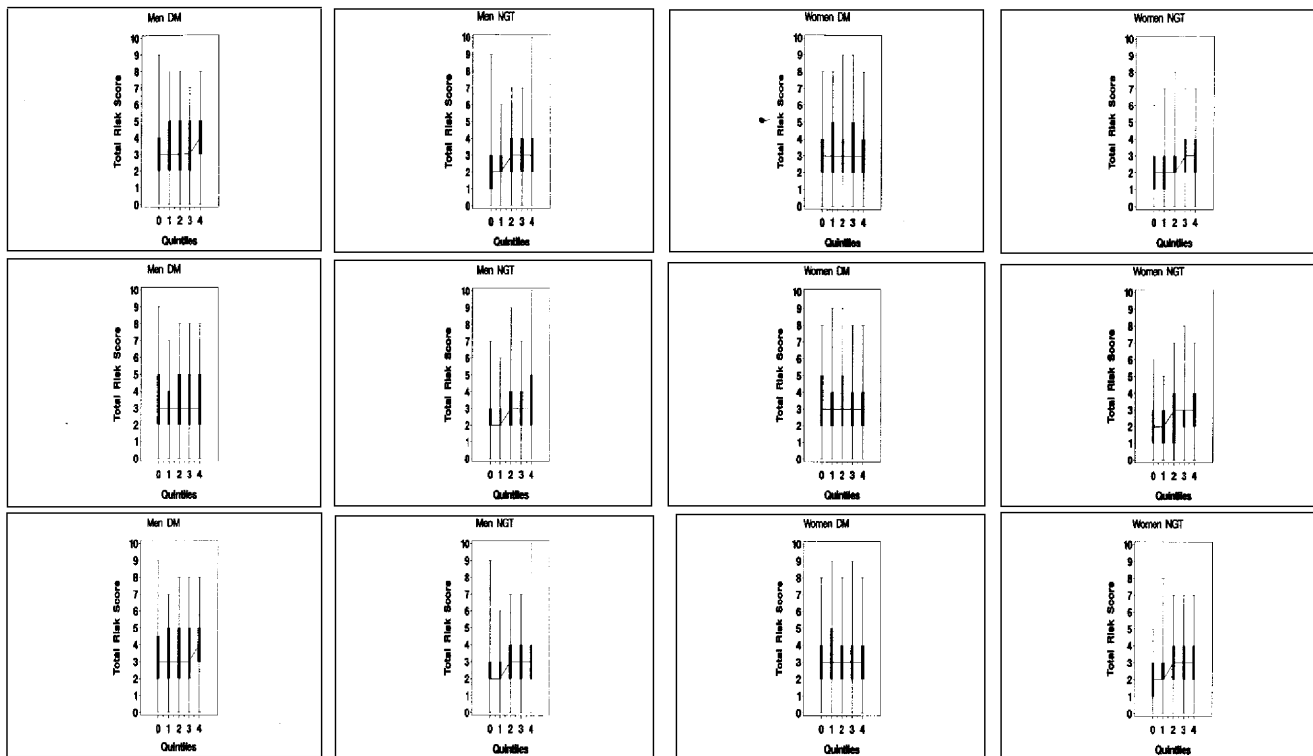


Figure 1 Distribution of the number of risk factors for each quintile of measures of obesity, by gender and diabetic status. The tops and bottoms of the boxes represent the 25th and 75th percentiles of the distribution. The whiskers extend to the most extreme point within the 1.5 interquartile range. An interquartile range is the distance between the 25th and 75th percentiles. The lines connect the medians of the distributions. These lines appear at the bottoms of the boxes in cases in which the 25th and 75th percentiles are the same.

had a significantly higher median risk factor score ($P < 0.001$) than did nondiabetic men and women (data not shown).

The distribution of the median number of risk factors for each quintile of measures of obesity, by gender and diabetic status, is shown in Figure 1. Although significant differences are apparent owing to the large population size, they are modest in biological terms.

Table 6 compares the prevalence rates per 100 of definite CHD in participants whose measures of obe-

sity lay in the lowest and highest quintiles, by gender and diabetic status, and shows them to be similar.

Discussion

Obesity, however it is defined, is extremely common among American Indians and has contributed greatly to the epidemic of diabetes that is currently afflicting

Table 6 Comparison of prevalence per 100 of CHD in upper and lower quintiles of obesity-related variables by gender and diabetes status, adjusted by age and center

	Men						Women					
	NGT			DM			NGT			DM		
	Cases n	%	Odds ratio (95% CI)	Cases n	%	Odds ratio (95% CI)	Cases n	%	Odds ratio (95% CI)	Cases n	%	Odds ratio (95% CI)
<i>BMI</i>												
1st quintile	4	3.01	1.01 (0.28–3.71)	11	7.91	1.61 (0.57–4.54)	0	0.00	0.28 (0.06–1.39)	3	1.20	0.67 (0.20–2.23)
5th quintile	5	3.57		6	4.20		6	4.17		7	2.85	
<i>Percentage body fat</i>												
1st quintile	4	3.03	0.87 (0.25–3.09)	8	5.97	1.86 (0.62–5.64)	2	1.41	0.70 (0.16–3.15)	2	0.81	0.60 (0.15–2.48)
5th quintile	6	4.23		5	3.57		5	3.42		7	2.81	
<i>Waist</i>												
1st quintile	3	2.31	0.80 (0.22–2.92)	7	5.34	1.91 (0.57–6.42)	0	0.00	0.27 (0.05–1.36)	4	1.65	0.81 (0.26–2.50)
5th quintile	6	3.85		4	2.58		6	4.03		10	3.69	

this population.^{49,50} The present study shows that more than 75% of middle-aged and older American Indian men and women from each Strong Heart Study center are overweight, with the majority of participants exhibiting central obesity (mean waist circumference > 100 cm). Percentage body fat, arguably the most relevant measure of the extent to which an individual is overweight,⁵¹ is extremely high among these American Indian groups.

To a large extent, degree of obesity is dictated by socioeconomic and environmental factors, of which diet is most probably the most telling determinant. As illustrated by Ravussin *et al*,⁵² when comparing American Indians of similar genetic stock living in different environments in the Americas, American Indians exhibit a marked disparity in prevalence of obesity. Similarly, the present study shows that Arizona Indians have significantly higher BMI when compared with Oklahoma and South/North Dakota Indians, which may be partially due to their more sedentary lifestyles.⁵³ As described in African Americans, although not in Whites,²⁸ American Indian women have higher BMI values than American Indian men and percentage body fat is higher for a given BMI in women than in men.

The risk of developing type 2 (non-insulin-dependent) diabetes is closely associated with obesity in White populations,^{54,55} as in other ethnic groups including Mexican Americans,⁵⁶ African Americans,⁵⁷ Aborigines,⁵⁸ and Mauritians.⁵⁹ A similar relationship between diabetes and obesity has been described previously in American Indians.⁶⁰ The findings of the present study, based on cross-sectional data, support the view that diabetes and obesity are intimately linked in this ethnic subgroup. It has been suggested that fat distribution, rather than obesity, is more closely allied to the development of diabetes,¹⁷ although this has been contested.⁵⁴ The present study shows that measures of BMI, waist and percentage body fat are greater in diabetic than in nondiabetic participants, regardless of gender.

We have also demonstrated, on a cross-sectional basis, that each measure of obesity tends to decline with increasing age in men and in diabetic women. This may be related to the cohort of participants whose older age may correspond with a more traditional lifestyle, ie one that is more conducive, in terms of diet and energy expenditure, to avoidance of obesity.

In light of these and previous findings, further relationships between measures of obesity and CHD risk factors and prevalence of CHD were explored after adjustment for center and age. Similarly, men and women with and without diabetes were considered independently.

Central obesity is intimately associated with insulin resistance and has been suggested to induce insulin resistance and hyperinsulinemia, owing to the influence of free fatty acids, derived from visceral fat, on the liver.⁶¹ The association between visceral adiposity and those risk factors thought to constitute the metabolic syndrome, ie carbohydrate intolerance, hypertriglyceridemia, reduced LDL size and reduced HDL, is considered to be a function of inherent insulin resistance.^{19–22} Validation of this hypothesis has come largely from studies of White populations. When other ethnic subgroups have been considered, the pivotal role of central obesity, as compared with general obesity, is less persuasive.^{30,62–64} Obesity, regardless of its distribution, is acknowledged to be related to insulin resistance syndrome-associated dyslipidemia, hyperinsulinemia, diabetes, hypertension and fibrinogen excess^{65,66} and to be inversely related to smoking.⁶⁷

Among nondiabetic populations, our data support the associations of obesity with other risk factors, including HDL, insulin, HbA_{1c}, blood pressure and LDL size. Thus, those variables recognized to be associated with insulin resistance in nondiabetic White populations demonstrated similar relationships among nondiabetic American Indians. However, central distribution of obesity (as illustrated by waist

measurement) was not more closely correlated with these variables than were BMI or percentage body fat in this population of American Indians. Waist measurement cannot distinguish between visceral and abdominal subcutaneous fat mass, of which visceral adiposity is arguably the predominant determinant of CHD-associated risk factors. To this extent, waist measurement may not be a sufficiently precise measure of body fat distribution to reflect the hazard of visceral adiposity. Alternatively, insulin resistance may be related to body fat at any site in American Indians. Ethnicity may, itself, bear upon the relationship between visceral fat distribution and waist measurement. American Indians, however, have yet to be characterized in this regard. The very high prevalence of central obesity among American Indians may have obscured the potential for distribution of obesity rather than BMI to reflect the distribution of insulin resistance-related risk variables, and yet the range of waist circumference was sufficiently great to have revealed such discrimination if it had existed. The 'thrifty gene' hypothesis holds that a protective gene causes the body to store energy as fat instead of glycogen so as to better withstand periods of food deprivation. If this hypothesis is to be believed, then obesity might be more prevalent among American Indians of pure blood now that food deprivation no longer occurs. No such relationship was evident in this study. Indeed, an inverse correlation between log BMI and percentage Indian blood was observed in nondiabetic men. These findings are in contrast to those reported in the San Antonio Heart Study, in which the prevalence of obesity was higher among women with a higher degree of Amerindian admixture.⁶⁷ Smoking might be expected to show an inverse correlation with measures of obesity,⁶⁸ but no such relationship was observed in this study.

Among diabetic participants, fasting insulin concentration fails to provide a reliable index of insulin resistance with increasing hyperglycemia owing to Starling's Law of the Pancreas.⁶⁹ However, increasing lack of insulin and consequent deterioration in glycemic control leads to worsening glycosuria, such that diabetic participants usually lose weight, thereby preserving the relationship between measures of obesity and fasting insulin concentration. Accordingly, our data demonstrate a strong positive correlation between each measure of obesity and fasting insulin concentration in diabetic men and women. An inverse correlation between waist and HbA_{1c} was evident in diabetic men. The confounding influence of deteriorating glycemic control on the pattern of dyslipidemia and on measures of obesity, along with the divergence of fasting insulin concentration and the prevailing degree of insulin resistance, may help explain the paucity of correlations between measures of obesity and other variables within the diabetic participants. Nevertheless, an important inverse relationship was evident when measures of obesity were correlated with degree of albuminuria, perhaps again attesting

to the part played by deteriorating glycemic control to induce both weight loss and nephropathy. The sporadic inverse correlations between triglyceride concentration and measures of obesity in certain subgroups also may be explained by poor glycemic control, ie triglyceride concentrations may be controlled to a greater extent by the hyperglycemia. Waist circumference failed to demonstrate any closer relationship with CHD risk factors than did BMI or percentage body fat, with the exception of fibrinogen concentration in diabetic women.

Among nondiabetic men and women, for each measure of obesity, those in the fifth quintile showed a significantly greater number of CHD risk factors than did those in the first quintile. This pattern was consistent whichever measure of obesity was considered, there being no greater tendency for waist, as compared to BMI or percentage body fat, to show the stronger relationship with CHD risk factors. It should be emphasized that, although the relationship between measures of obesity and CHD risk factor score is highly significant, there was only a modest increase in risk factor score with increasing obesity. Among diabetic women, measures of obesity were not related to an allied risk factor score whereas, for diabetic men, those with a BMI within the fifth quintile showed a higher risk factor score than did those in the first quintile. These findings suggest that, for American Indians, increasing obesity has only a modest influence on CHD risk factors and waist circumference may not be any more influential than BMI in determining the CHD risk status of any given individual. Diabetes, on the other hand, is clearly associated with an increased number of CHD risk factors in American Indian men and women, as previously described, and obesity is the most important modifiable risk factor for the development of diabetes.⁶⁵

Our data suggest that the association between measures of obesity and CHD-related risk factors is stronger in nondiabetic than in diabetic participants. Our study fails to demonstrate an obesity-related predisposition to prevalent, definite CHD in men or women when diabetic status is considered, although the number of patients with CHD may be insufficient to illustrate such a relationship. We have previously indicated that when nondiabetic and diabetic participants are considered together, the prevalence of CHD was greater in obese than in non-obese participants.⁷⁰ It is necessary to acknowledge that both the present and the previous⁷⁰ studies of associations with CHD are subject to potential distortion as with any cross-sectional analysis. It could be argued that we have only been able to study survivors, and that a proportion of individuals, characterized by extreme central obesity, already may have died from CHD or become diabetic, thereby obscuring such a relationship within the American Indian community as has been described in other ethnic groups. This shortcoming can only be addressed by prospective review of

incident CHD. Nevertheless, on the basis of this cross-sectional analysis of the data, waist circumference does not appear to be more closely associated with concomitant CHD risk factors, nor prevalent CHD itself, than does BMI. To this extent, the relationship of obesity and insulin resistance to CHD risk factors may be unique to the American Indian population and distinct from that described in White Caucasians of European descent. Alternatively, such a relationship may prove to be a feature of any population characterized by extreme adiposity, regardless of ethnic derivation.

In conclusion, we found that more than 75% of middle aged and elderly American Indians in our study were overweight and that participants in the heaviest quintile had significantly more CHD risk factors than those in the lowest quintile. However, except for insulin, the changes in risk factors with increasing obesity were not large. The distribution of obesity was no more closely related to CHD risk factors than was generalized obesity and we were unable to demonstrate the prevalence of definite CHD to be related to any measure of obesity. Because obesity is a potent risk factor for diabetes, diabetes might be the major mechanism by which obesity increases CHD risk in this population. The high rates of obesity in this population emphasize the need for further obesity-prevention research to combat the epidemic of diabetes and chronic disease that has emerged over the past few generations as American Indians shift from their traditional subsistence lifestyle and low-fat, high-fiber diet to a sedentary lifestyle and a Western diet that is high in fat and low in fiber.

Acknowledgements

The authors acknowledge the assistance and cooperation of the AkChin Tohono O'odham (Papago)/Pima, Apache, Caddo, Cheyenne River Sioux, Comanche, Delaware, Spirit Lake Community, Fort Sill Apache, Gila River, Pima/Maricopa, Kiowa, Oglala Sioux, Salt River Pima/Maricopa and Wichita Indian communities, without whose support this study would not have been possible. The authors also wish to thank the Indian Health Service hospitals and clinics at each center, and Betty Jarvis, Martha Stoddart and Beverly Blake, Directors of the Strong Heart Study clinics and their staffs, and acknowledge the editorial assistance of Ellen Shair. This study was conducted by cooperative agreement grants (nos U01-HL41642, U01HL41652 and UL01HL41654) from the National Heart, Lung and Blood Institute. The views expressed in this paper are those of the authors and do not necessarily reflect those of the Indian Health Service.

References

1 Lew EA, Garfinkel L. Variations in mortality by weight among 750,000 men and women. *J Chronic Dis* 1979; **32**: 563–576.

2 Feinleib M. Epidemiology of obesity in relation to health hazards. *Ann Intern Med* 1985; **103**: 1019–1024.

3 Barrett-Connor E. Obesity, atherosclerosis, and coronary artery disease. *Ann Intern Med* 1985; **103**: 1010–1019.

4 Manson JE, Stampfer MJ, Hennekens CH, Willett WC. Body weight and longevity. *JAMA* 1987; **257**: 353–358.

5 Jarret RJ, Shipley MJ, Rose G. Weight and mortality in the Whitehall Study. *BMJ Clin Res Ed* 1982; **285**: 535–537.

6 Garrison RJ, Feinleib M, Castelli WP, McNamara PM. Cigarette smoking as a confounder of the relationship between relative weight and long-term mortality: the Framingham Heart Study. *JAMA* 1983; **249**: 2199–2203.

7 Keys A, Fidanza F, Karvonen MJ, Kimura N, Taylor HL. Indices of relative weight and obesity. *J Chronic Dis* 1972; **25**: 329–343.

8 Chapman JM, Coulson AH, Clark VA, Borun ER. The differential effect of serum cholesterol, blood pressure, and weight on the incidence of myocardial infarction and angina pectoris. *J Chronic Dis* 1971; **23**: 631–645.

9 Rabkin SW, Mathewson FAL, Ping-Hwa H. Relation of body weight to development of ischaemic heart disease in a cohort of young North American men after a 26-year observation period. The Manitoba Study. *Am J Cardiol* 1977; **39**: 452–458.

10 Pooling Project Research Group. Relationship of blood pressure, serum cholesterol, smoking habit, relative weight, and ECG abnormalities to incidence of major coronary events: final report of the pooling project. *J Chronic Dis* 1978; **31**: 201–306.

11 Stokes J III, Garrison RJ, Kannel WB. The independent contributions of various indices of obesity to the 22-year incidence of coronary heart disease: the Framingham Heart Study. In Vague J et al (eds). *Metabolic complications of human obesities*. Elsevier: Amsterdam, 1985, p 49.

12 Tuomilehto J, Salonen JT, Marti B, Jalkanen L, Puska P, Nissinen A, Wolf E. Body weight and risk of myocardial infarction and death in the adult population of eastern Finland. *BMJ Clin Res Edn* 1987; **295**: 623–627.

13 Larsson B, Svardsudd K, Welin L, Wilhelmsen L, Bjorntorp P, Tibblin G. Abdominal adipose tissue distribution, obesity, and risk of cardiovascular disease and death: a 13-year follow up of participants in the study of men born in 1913. *BMJ Clin Res Ed* 1984; **288**: 1401–1404.

14 Lapidus L, Bengtsson C, Larsson B, Pennert K, Rybo E, Sjoström L. Distribution of adipose tissue and risk of cardiovascular disease and death: a 12-year follow-up of participants in the population study of women in Gothenburg, Sweden. *BMJ Clin Res Ed* 1984; **289**: 1257–1261.

15 Ducimetiere P, Richard J, Cambien F. The pattern of subcutaneous fat distribution in middle-aged men and the risk of coronary heart disease: the Paris Prospective Study. *Int J Obes* 1986; **10**: 229–240.

16 Donahue RP, Abbott RD, Bloom E, Reed DM, Yano K. Central obesity and coronary heart disease in men. *Lancet* 1987; **1**: 821–824.

17 Despres JP, Moorjani S, Lupien PJ, Tremblay A, Nadeau A, Bouchard C. Regional distribution of body fat, plasma lipoproteins, and cardiovascular disease. *Arteriosclerosis* 1990; **10**: 497–511.

18 Filipovsky J, Ducimetiere P, Darne B, Richard JL. Abdominal body mass distribution and elevated blood pressure are associated with increased risk of death from cardiovascular diseases and cancer in middle-aged men. The results of a 15- to 20-year follow-up in the Paris Prospective Study 1. *Int J Obes* 1993; **17**: 197–203.

19 Kissebah AH, Vydellingum N, Murray R, Evans DJ, Hartz AJ, Kalkhoff RK, Adams PW. Relation of body fat distribution to metabolic complications of obesity. *J Clin Endocrinol Metab* 1982; **54**: 254–260.

20 Kalkhoff RK, Hartz AH, Rupley D, Kissebah AH, Kelber S. Relationship of body fat distribution to blood pressure, carbohydrate tolerance, and plasma lipids in healthy obese women. *J Lab Clin Med* 1983; **102**: 621–627.

- 21 Evans DJ, Hoffman RG, Kalkhoff RK, Kissebah AH. Relationship of body fat topography to insulin sensitivity and metabolic profiles in premenopausal women. *Metab Clin Exp* 1984; **33**: 68–75.
- 22 Gillum RF. The association of body-fat distribution with hypertension, hypertensive heart disease, coronary heart disease, diabetes and cardiovascular risk factors in men and women aged 18–79 years. *J Chronic Dis* 1987; **40**: 421–428.
- 23 Peiris AN, Struve MF, Mueller RA, Lee MB, Kissebah AH. Glucose metabolism in obesity: influence of body fat distribution. *J Clin Endocrinol Metab* 1988; **67**: 760–767.
- 24 Abate N, Garg A, Peshock RM, Stray-Gundersen J, Grundy SM. Relationships of generalized and regional adiposity to insulin sensitivity in men. *J Clin Invest* 1995; **96**: 88–98.
- 25 Di Fronzo RA, Ferrannini MD. Insulin resistance. A multifaceted syndrome responsible for NIDDM, obesity, hypertension, dyslipidemia, and atherosclerotic cardiovascular disease. *Diabetes Care* 1991; **14**: 173–194.
- 26 Wienpahl J, Ragland DR, Sidney S. Body mass index and 15-year mortality in a cohort of black men and women. *J Clin Epidemiol* 1990; **43**: 949–960.
- 27 Stevens J, Keil JE, Rust PF, Tyroler HA, Davis CE, Gazes PC. Body mass index and body girths as predictors of mortality in black and white women. *Arch Intern Med* 1992; **152**: 1257–1262.
- 28 Durazo-Arvizu R, Cooper RS, Luke A, Prewitt TE, Liao Y, McGee DL. Relative weight and mortality in US blacks and whites: findings from representative national population samples. *Ann Epidemiol* 1997; **7**: 383–395.
- 29 Haffner SM, D'Agostino R, Saad MF, Revers M, Mykhanen L, Selby J, Howard G, Savage PJ, Hamman RF, Wagenknecht LE, Bergman RN. Increased insulin resistance and insulin secretion in non-diabetic African Americans and Hispanics compared with non-Hispanic Whites. *Diabetes* 1996; **45**: 742–748.
- 30 Karter AJ, Mayer-Davis EJ, Selby JV, D'Agostino RB Jr, Haffner SM, Sholinsky P, Bergman R, Saad MF, Hamman RF. Insulin sensitivity and abdominal obesity in African American, Hispanic, and non-Hispanic white men and women. The Insulin Resistance and Atherosclerosis Study. *Diabetes* 1996; **45**: 1547–1555.
- 31 Masuda T, Imai K, Komiya S. Relationship of anthropometric indices of body fat to cardiovascular risk in Japanese women. *Ann Physiol Anthropol* 1993; **12**: 135–144.
- 32 Woo J, Ho SC, Chan SG, Sham A, Yuen YK, Masarei JL. Lipid profile in the Chinese elderly: comparison with younger age groups and relationship with some cardiovascular risk factors and presence of diseases. *Cardiology* 1993; **83**: 407–414.
- 33 Ko GT, Chan JC, Woo J, Lau E, Yeung VT, Chow CC, Wai HP, So WY, Cockram CS. Simple anthropometric indices and cardiovascular risk factors in Chinese. *Int J Obes* 1997; **21**: 995–1001.
- 34 Pettitt DJ, Lisse JR, Knowler WC, Bennett PH. Mortality as a function of obesity and diabetes mellitus. *Am J Epidemiol* 1982; **115**: 359–366.
- 35 Lee ET, Welty TK, Fabsitz RR, Cowan LD, Le NA, Oopik AJ, Cucchiara AJ, Savage PJ, Howard BV. The Strong Heart Study—a study of cardiovascular disease in American Indians: design and methods. *Am J Epidemiol* 1990; **132**: 1141–1155.
- 36 Howard BV, Welty TK, Fabsitz RR, Cowan LD, Oopik AJ, Le NA, Yeh J, Savage PJ, Lee ET. Risk factors for coronary heart disease in diabetic and nondiabetic Native Americans: the Strong Heart Study. *Diabetes* 1992; **41**: 4–11.
- 37 Stoddart M, Jarvis B, Blake B, Fabsitz RR, Howard BV, Lee ET, Welty TK. Recruitment of American Indians in epidemiologic research—the Strong Heart Study. *Proceedings of the 121st Annual Meeting of the American Public Health Association*, San Francisco, CA, October 1993.
- 38 Krauss RM, Burke DJ. Identification of multiple subclasses of plasma low density lipoproteins in normal humans. *J Lipid Res* 1982; **23**: 97–104.
- 39 Morgan C, Lazarow A. Immunoassay of insulin: two antibody system. Plasma insulin levels in normal, subdiabetic and diabetic rats. *Diabetes* 1963; **12**: 115–126.
- 40 von Clauss A. Gerinnungsphysiologische schnellmethode zur Bestimmung des Fibrinogens. *Acta Haematol* 1957; **27**: 237–246.
- 41 Little RR, England JD, Wiedmeyer HM, McKenzie EM, Mitra R, Erhart PM, Durham JB, Goldstein DE. Interlaboratory standardization of glycated hemoglobin determinations. *Clin Chem* 1986; **32**: 358–360.
- 42 Vasquez B, Flock EV, Savage PJ, Nagulesparan M, Bennion LJ, Baird HR, Bennett PH. Sustained reduction of proteinuria in type 2 (non-insulin-dependent) diabetes following diet-induced reduction of hyperglycaemia. *Diabetologia* 1984; **26**: 127–133.
- 43 Chasson AL, Grady HJ, Standley MA. Determination of creatinine by means of automatic chemical analysis. *Tech Bull Regist Met Technol* 1960; **30**: 207–312.
- 44 Prineas RJ, Crow RS, Blackburn H. *The Minnesota code manual of electrocardiographic findings* John Wright PSC: Littleton, MA 1982.
- 45 Bennett PH, Nelson RG, Knowler WC et al. Urine albumin/creatinine ratio estimates albumin excretion and predicts nephropathy in type II (non-insulin-dependent) diabetes. (Abstract). *Diabetologia* 1990; **33**: A147.
- 46 Rose GA, Blackburn H. *Cardiovascular survey methods*, 2nd edn. (monograph series no. 56 G). World Health Organization: Geneva, 1982.
- 47 *WHO Expert Committee on Diabetes Mellitus, second report* (Technical Report Series no. 646). World Health Organization: Geneva, 1980.
- 48 National Institutes of Health, National Heart, Lung and Blood Institute. *Clinical Guidelines on the Identification, Evaluation, and Treatment of Overweight and Obesity in Adults: The Evidence Report*. US Department of Health and Human Services, Public Health Service, NIH, NHLBI, June 1998.
- 49 Knowler WC, Pettit DJ, Savage PJ, Bennett PH. Diabetes incidence in Pima Indians: contributions of obesity and parental diabetes. *Am J Epidemiol* 1981; **113**: 144–156.
- 50 Welty TK. Health implications of obesity in American Indians and Alaska Natives. *Am J Clin Nutr* 1991; **53** (Suppl): 1616S–1620S.
- 51 Smalley KJ, Knerr AN, Kendrick ZV, Collier JA, Owen OE. Reassessment of body mass indices. *Am J Clin Nutr* 1990; **52**: 405–408.
- 52 Ravussin R, Valencia ME, Esparza J, Bennett PH, Schultz LO. Effects of a traditional lifestyle on obesity in Pima Indians. *Diabetes Care* 1994; **17**: 1067–1074.
- 53 Welty TK, Lee ET, Yeh J, Cowan LD, Go O, Fabsitz RR, Le NA, Oopik AJ, Robbins DC, Howard BV. Cardiovascular disease risk factors among American Indians. The Strong Heart Study. *Am J Epidemiol* 1995; **142**: 269–287.
- 54 Colditz GA, Willett WC, Stampfer MJ, Manson JE, Hennekens CH, Arky RA, Speizer FE. Weight as a risk factor for clinical diabetes in women. *Am J Epidemiol* 1990; **132**: 501–513.
- 55 Chan JM, Stampfer MJ, Rimm EB, Willett WC, Colditz GA. Obesity, fat distribution, and weight gain as risk factors for clinical diabetes in men. *Diabetes Care* 1994; **17**: 961–969.
- 56 Haffner SM, Mitchell BD, Stern MP, Hazuda HP, Patterson JK. Public health significance of upper body adiposity for non-insulin-dependent diabetes mellitus in Mexican Americans. *Int J Obes* 1992; **16**: 177–184.
- 57 Lipton RB, Liao Y, Cao G, Cooper RS, McGee D. Determinants of incident non-insulin-dependent diabetes mellitus among blacks and whites in a national sample. The NHANES I Epidemiologic Follow-up Study. *Am J Epidemiol* 1993; **138**: 826–839.

- 58 O'Dea K, White NG, Sinclair AJ. An investigation of nutrition-related risk factors in an isolated Aboriginal community in Northern Australia: advantages of a traditional orientated life-style. *Med J Austral* 1988; **148**: 177–180.
- 59 Dowse GK, Zimmet PZ, Gareeboo H, Alberti K, Tuomilehto J, Finch CF, Chitson P, Tulsidas H. Abdominal obesity and physical inactivity as risk factors for NIDDM and impaired glucose tolerance in Indian, Creole, and Chinese Mauritians. *Diabetes Care* 1991; **14**: 271–272.
- 60 Knowler WC, Pettit DJ, Saad MF, Charles MA, Nelson RG, Howard BV, Bogardus C, Bennett PH. Obesity in the Pima Indians: its magnitude and relationship with diabetes. *Am J Clin Nutr* 1991; **53**: 1543S–1551S.
- 61 Kissebah AH, Peiris AN, Evans DJ. Biology of regional body fat distribution: relationship to non-insulin-dependent diabetes mellitus. *Diabetes Metab Rev* 1989; **5**: 83–109.
- 62 Haffner SM, Stern MP, Hazuda H, Rosenthal M, Knapp A. The role of behavioral variables and fat patterning in explaining ethnic differences in serum lipids and lipoproteins. *Am J Epidemiol* 1986; **123**: 830–839.
- 63 Dowling HJ, Pi-Sunyer X. Race-dependent health risks of upper body obesity. *Diabetes* 1993; **42**: 537–543.
- 64 Chan JCN, Cheung JCK, Lau EMC, Wooa J, Chan AYW, Swaminathan RS, Cockrama CS. The metabolic syndrome in Hong Kong Chinese. The interrelationships among its components analyzed by structural equation modelling. *Diabetes Care* 1996; **19**: 953–959.
- 65 Schmidt MI, Watson RL, Duncan BB, Metcalf P, Brancati FFL, Sharrett AR, Davis CE, Heiss G. Clustering of dyslipidemia, hyperuricemia, diabetes, and hypertension and its association with fasting insulin and central and overall obesity in a general population. Atherosclerosis Risk and Communities Study Investigators. *Metabolism* 1996; **45**: 699–706.
- 66 Avellone G, Di Garbo V, Cordova R, Raneli G, De Simone R, Bompiani G. Coagulation, fibrinolysis and haemorheology in premenopausal obese women with different body fat distribution. *Thromb Res* 1994; **75**: 223–231.
- 67 Mitchell BD, Williams-Blangero S, Chakraborty R, Valdez R, Hazuda HP, Haffner SM, Stern MP. A comparison of three methods for assessing Amerindian admixture in Mexican Americans. *Ethn Dis* 1993; **3**: 22–31.
- 68 Williamson DF, Madans J, Anda RF, Kleinman JC, Giovino GA, Byers T. Smoking cessation and severity of weight gain in a national cohort. *N Engl J Med* 1991; **324**: 739–745.
- 69 De Fronzo RA, Bonadonna RC, Ferrannini E. Pathogenesis of NIDDM: a balanced overview. *Diabetes Care* 1992; **15**: 318–368.
- 70 Howard BV, Lee ET, Cowan LD, Fabsitz RR, Howard WJ, Oopik AJ, Robbins DC, Savage PJ, Yeh JL, Welty TK. Coronary heart disease prevalence and its relation to risk factors in American Indians: the Strong Heart Study. *Am J Epidemiol* 1995; **142**: 254–268.