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The metabolic syndrome and the impact of diabetes on coronary heart disease mortality in women and men: The San Antonio Heart Study

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Abstract

Purpose—An explanation for the differential impact of diabetes on coronary heart disease (CHD) mortality in men and women is that diabetes and cardiovascular disease (CVD) share a common antecedent that differentially affects men and women. In the San Antonio Heart Study we examined the relationship between gender, the metabolic syndrome defined by the National Cholesterol Education Program (NCEP-MetS) and diabetes and their ability to predict CHD mortality.

Methods—Over 15.5 years, 4996 men and women 25-64 years experienced 254 cardiovascular deaths including 121 from CHD (ICD-9 codes 410-414).

Results—At baseline, NCEP-MetS occurred more often in men than women among those with normal glucose levels (12.3% versus 9.7%, $p < 0.05$), but less often in men than women among those with diabetes (65.7% versus 74.4%, $p<0.05$). Adjusted for age, ethnic group and a history of CVD, relative to women with neither diabetes nor NCEP-MetS, women with both had a 14-fold [hazard ratio (HR)=14.3 (95% confidence interval: 6.62, 30.7)] increased risk of CHD mortality, while men had only a 4-fold [HR=4.21 (95% confidence interval: 2.32, 7.65)] increased risk, respectively.

Conclusion—When diabetes occurred with NCEP-MetS, gender was a strong modifier of the joint effect of diabetes and NCEP-MetS on CHD mortality.

MeSH Keywords

Coronary Disease; Mortality; Diabetes Mellitus; Type 2; Metabolic Syndrome X; Gender; Epidemiology; Risk Factors

At least three meta-analyses have examined whether diabetes reduces the gender differential in coronary heart disease (CHD) mortality(1-3). Two of the three meta-analyses report that the impact of diabetes on the risk of CHD death is greater in women than in men and that standard cardiovascular risk factors do not fully account for this gender difference(1,3), while the third

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meta-analysis reports that elevated levels of the standard cardiovascular risk factors (i.e., age, hypertension, total cholesterol, and smoking) are responsible for the excess relative risk of CHD mortality in women versus men with diabetes(2). If cardiovascular risk factor levels account for all or part of the attenuation of the CHD mortality gender differential in individuals with diabetes, then relative to men, women with diabetes must have higher levels of cardiovascular risk factors. This could be explained if diabetes either had a more adverse effect on cardiovascular risk factors in women than in men, or diabetes and CHD shared a common antecedent that differentially affected men and women.

An atherogenic state prior to the onset of clinical diabetes that is consistent with a common etiology underlying diabetes and cardiovascular disease (CVD) is suggested by elevated cardiovascular risk factors in pre-diabetic individuals (4-8), elevated cardiovascular risk prior to a clinical diagnosis of diabetes in the Nurses' Health Study(9) and increased carotid artery intima-media thickness in pre-diabetic individuals in our Mexico City study(10). The metabolic syndrome is a strong predictor of type 2 diabetes and its component parts are elevated in pre-diabetic individuals. Therefore, the metabolic syndrome, recognized as a cluster of cardiovascular risk factors that frequently coincides with insulin resistance and hyperglycemia (11,12), may be an early manifestation of the common etiology underlying diabetes and CHD.

Recently, we reported that there was evidence from the San Antonio Heart Study (SAHS) that sex modified the ability of the metabolic syndrome to predict cardiovascular mortality. Furthermore, when both the metabolic syndrome and diabetes were used to classify individuals and absence of both disorders was used as the referent category, the attenuation of the sex difference in cardiovascular mortality was statistically significant only in individuals with both disorders(13). However, because waist circumference was measured at baseline on only 57 percent of participants enrolled in phase two of the SAHS we did not have sufficient power to examine which components of the metabolic syndrome in combination with diabetes were driving the relationship, or examine whether sex modified the ability of the metabolic syndrome and diabetes to predict CHD mortality. In order to have sufficient statistical power we impute ‘high waist circumference’ as a dichotomous trait in phase one SAHS participants based on weight, height and gender. We use this additional power to examine the relationship between gender, the metabolic syndrome as defined by the National Cholesterol Education Program (14,15) (NCEP-MetS) and diabetes and their ability to predict CHD mortality as well as to examine which components of the metabolic syndrome in combination with diabetes are driving the relationship.

Materials and Methods

The SAHS design and population

The SAHS cohort consists of 5158 participants, recruited at baseline in two phases: phase one between 1979 and 1982, and phase two between 1984 and 1988. Details of the study design have been previously published(16-18). The Institutional Review Board of the University of Texas Health Science Center at San Antonio approved the study, and all subjects gave informed consent.

Baseline SAHS cohort examination

The baseline SAHS cohort examination was standardized and included interviews, blood pressure measurements, anthropometry, a fasting venipuncture (12-hour overnight), and an oral glucose tolerance test(18,19). Ethnic group was defined by a validated algorithm(16). A history of CVD was defined as having had a self-reported physician-diagnosed heart attack or stroke.

The metabolic syndrome was defined according to the NCEP ATP III criteria. The waist criterion for phase 1 participants (43 percent; n=2217) was imputed using logistic regression from weight and height within gender subgroups. NCEP-MetS was defined(14) as having at least three of the following NCEP metabolic abnormalities: fasting glucose ≥ 100 mg/dL or taking medication for diabetes)(15), abdominal obesity (waist circumference > 102 cm in men, or > 88 cm in women), high blood pressure (HBP, ≥ 130/ ≥ 85 mm Hg) or taking medication for hypertension, triglycerides ≥ 150 mg/dL, or low HDL cholesterol (< 40 mg/dL in men, < 50 mg/dL in women).

Diabetes was defined as fasting plasma glucose ≥ 126 mg/dL, 2-hour postload glucose ≥ 200 mg/dL and/or self-reported physician diagnosed diabetes requiring medication (either oral or insulin) (20). In non-diabetic individuals, impaired glucose tolerance (IGT) was defined as a 2-hour glucose level ≥ 140 mg/dL(20), impaired fasting glucose (IFG) was defined as fasting plasma glucose ≥ 100 mg/dL and impaired glucose regulation (IGR) was defined as having IFG and/or IGT.

Study population, follow-up and events

Of the 5,158 SAHS participants eligible for inclusion, 162 individuals were excluded because the information required to define NCEP-MetS and/or diabetes was missing (n=126), they were lost to follow-up since their baseline examination (n=32), or their death certificate was missing (n=4). Vital status was determined by annual mailed questionnaires, completed by a participant or their next of kin. In cases of non-response, we used telephone interviews, home visits, voting records, driver registration, the National Death Index, and addresses from the San Antonio Retail Merchants' Association. Among the 4,996 participants in this study, 61 people had incomplete vital status ascertainment through January 1st 2000 (ascertainment rate=98.8 percent).

Information on cause of death was abstracted from death certificates (with names and ethnic identifiers suppressed) and sent to a certified nosologist (Medical Coding and Consultation Services, Rolesville, North Carolina) for coding according to the *International Classification of Diseases, Ninth Revision* (ICD-9). CHD mortality was not limited to the underlying cause of death, but was defined as death with the mention anywhere on the death certificate of ICD-9 codes 410-414 (ischaemic).

Statistical analyses

Prospective analyses were carried out in which NCEP-MetS and diabetes determined a person's exposure status and CHD mortality was the outcomes of interest.

Participants were grouped into one of four categories: individuals with neither NCEP-MetS nor diabetes; individuals with NCEP-MetS only; individuals with diabetes only; and individuals with both disorders. Age- and ethnic group-adjusted means and proportions were determined for participant characteristics stratified by sex and the four NCEP-MetS/diabetes categories. Age- and ethnic group-adjusted prevalence of each of the NCEP-MetS criterion were determined stratified by normal glucose regulation, IGR and diabetes status.

Poisson regression was used to determine age- and ethnic group- adjusted CHD mortality rates stratified by sex and the four NCEP-MetS/diabetes categories. Cox proportional hazard models adjusted for age, ethnic group and a history of CVD were used to calculate hazard ratios (HRs) for CHD mortality in relation to the four NCEP-MetS/diabetes categories stratified by sex. Models with the appropriate interaction terms were used to model interactions between sex and the four NCEP-MetS/diabetes categories in relation to CHD mortality. For all analyses the

assumption of proportional hazards was evaluated by testing for interaction with a continuous time variable.

For each of the four NCEP-MetS criterion other than high fasting glucose, four NCEP-MetS criterion/diabetes categories were created and analyses were completed as stated for the four NCEP-MetS/diabetes categories.

Results

Of the 4,996 study participants 3,701 (74.1 percent) had neither NCEP-MetS nor diabetes, 771 (15.4 percent) had NCEP-MetS only, 138 (2.8 percent) had diabetes only, and 386 (7.7 percent) had both disorders. Across these four categories 57.7 percent, 51.2 percent, 50.0 percent and 61.1 percent respectively were female.

Fasting glucose, BMI and LDL cholesterol levels were significantly higher in men than women in individuals without either disorder, while in the other categories levels were similar in both sexes (Table 1). Two-hour glucose levels were lower in men than women in all categories except in individuals with diabetes without the metabolic syndrome, while HDL cholesterol levels were lower in men across all four categories. Among individuals who did not have diabetes, fasting insulin levels were higher in men than women among persons without NCEP-MetS, but similar in men and women among persons with NCEP-Mets; while 2-hour insulin levels were lower in men than women regardless of their NCEP-MetS status. Among individuals with diabetes, the duration of diabetes and reported age of onset were similar in men and women regardless of their NCEP-MetS status.

NCEP-MetS occurred less often in women than men among those with normal glucose levels (9.7 percent versus 12.3 percent, $p < 0.05$), but more often in women than men among those with diabetes (74.4 percent versus 65.7 percent, $p < 0.01$) (Table 2). The prevalence of NCEP-high waist circumference and NCEP-low HDL cholesterol was higher in women than men across all three categories of glucose regulation; moreover, the largest difference between men and women was in individuals with diabetes. The prevalence of NCEP-high triglycerides and NCEP-high blood pressure was similar in men and women only when diabetes was present, while in individuals with normal and IGR the prevalence was higher in men. Finally, men with IGR or diabetes were more likely than women to have NCEP-high fasting glucose with the gender difference being smaller in individuals with diabetes.

Over an average of 15.5 years (range 11.2 to 20.2) 254 CVD deaths occurred, including 121 from CHD. In individuals with neither diabetes nor NCEP-MetS the CHD mortality rate was higher in men than women, while in individuals with both disorders the CHD mortality rate was similar in men and women (Table 3). Interestingly, the male excess in CHD mortality was somewhat preserved in diabetic individuals without NCEP-MetS.

Relative to women with neither diabetes nor NCEP-MetS, women with both disorders had a 14-fold [HR=14.3 (95 percent confidence interval: 6.62, 30.7)] increased risk of CHD mortality, while men had only a 4.2-fold increased risk (Table 3). Results were similar when either the 194 individuals who reported a prior physician-diagnosed heart attack or stroke were excluded from the analysis, or when the individual component parts of NCEP-MetS as well as smoking status and LDL cholesterol levels were adjusted for as covariates. When the 194 individuals with a prior history of cardiovascular disease were excluded from the analysis relative to women with neither diabetes nor NCEP-MetS, women with both disorders had a 18-fold [HR=18.1 (95 percent confidence interval: 8.03, 41.0)] increased risk of CHD mortality, while men had only a 6.6-fold increased risk (Table 3). Similarly, when the additional covariates were adjusted for relative to women with neither diabetes nor NCEP-MetS, women

with both disorders had a 10-fold increased risk of CHD mortality, while men had only a 2.9-fold increased risk.

Due to the limited number of CHD events and limited statistical power we used cardiovascular mortality as the outcome to test for interaction between the four NCEP-MetS/diabetes categories, sex and ethnic group. Although none of the *p* values for 3-way interaction were statistically significant there was the suggestion that the gender difference in the HRs for individuals with both disorders relative to individuals with neither disorder was stronger in Mexican Americans than non-Hispanic whites. In Mexican Americans, women had an 11-fold [HR=11.2 (95 percent confidence interval: 6.01, 21.0)] and men had a 3.7-fold [HR=3.66 (95 percent confidence interval: 2.23, 5.98)] increased risk of cardiovascular mortality comparing individuals with diabetes and NCEP-MetS to those without either disorder, while in non-Hispanic whites corresponding HRs were 3.22 and 2.76 in women and men, respectively (Table 4).

Among individuals with diabetes without a history of CVD (n = 405) we examined whether either the duration of diabetes or 2-hour glucose levels explained the gender differential in increased risk associated with NCEP-MetS for CHD mortality. The CHD mortality HR associated with NCEP-MetS among diabetic individuals was 7.22 (95 percent confidence interval: 0.96, 54.5) in women and 0.66 (95 percent confidence interval: 0.26, 1.65) in men (male versus female *p* value=0.034) adjusted for age and ethnic group. After additional adjustment for duration of diabetes as well as 2-hour glucose levels HRs were 5.53 (95 percent confidence interval: 0.73, 41.8) and 0.58 (95 percent confidence interval: 0.23, 1.44) in women and men, respectively (male versus female *p* value=0.046).

For each of the NCEP-defined components of the metabolic syndrome, we examined the rates and HRs for CHD mortality in the absence and presence of diabetes (Table 3). Comparing individuals with both low HDL cholesterol and diabetes relative to those with neither condition, the HR for CHD mortality in women was statistically significantly higher than in men. For high triglycerides, the HRs for CHD mortality were statistically significantly higher for women than for men across all three comparisons. Comparing individuals with diabetes with and without high waist circumference to individuals with neither disorder, there was the suggestion that the HR for CHD mortality in women was higher than the HR in men. CHD mortality HRs for high blood pressure were similar for women and men across all three comparisons.

Discussion

Gender was a strong modifier of the joint effect of diabetes and the metabolic syndrome on CHD mortality, and the predictive ability of the metabolic syndrome when coupled with diabetes was stronger in women than in men. Not only is the majority of the SAHS population Mexican American, but the prevalence of NCEP-MetS and diabetes is higher in Mexican Americans than non-Hispanic whites. When we tested for interaction between the NCEP-MetS/diabetes categories, sex and ethnic group relative to cardiovascular mortality, none of the *p* values for the 3-way interaction were statistically significant. However, there was a suggestion that the gender difference in HRs for men and women with both NCEP-MetS and diabetes relative to men and women with neither disorder was stronger in Mexican Americans than in non-Hispanic whites. These results suggest that the reduced gender differential in CHD mortality among diabetic individuals observed in many, but not all populations(1-3), is more pronounced in populations such as the Mexican American population in which the metabolic syndrome and diabetes are more likely to co-occur.

Among individuals with neither the metabolic syndrome nor diabetes, cardiovascular risk factor levels (including fasting glucose, BMI, LDL and HDL cholesterol) indicate a higher

cardiovascular mortality risk in men relative to women. In contrast, among individuals with the metabolic syndrome regardless of whether or not they have diabetes, cardiovascular risk factor levels, with the exception of HDL cholesterol, indicate a similar or lower cardiovascular morality risk in men relative to women. Similarly, for each component part of the metabolic syndrome that has a higher prevalence in women than in men the *greatest* sex difference is among individuals with diabetes. In contrast, for each component part of the metabolic syndrome that has a higher prevalence in men than in women, the *smallest* sex difference is among individuals with diabetes. As a result, the metabolic syndrome is present less often in women than in men among individuals with normal or IGR, but more often in women than in men among individuals with diabetes.

A publication from the Atherosclerosis Risk in Communities (ARIC) study limited to non-diabetic individuals reports that men and women with NCEP-MetS were 1.5 and 2 times more likely, respectively, to develop CHD than were control subjects and that there was a significant MetS-sex interaction(21). Hence, in contrast to our findings they report a significant MetS-sex interaction in individuals without diabetes(21). The ARIC finding may be explained by a failure to exclude all individuals with diabetes because an oral glucose tolerance test (OGTT) was not available, the inclusion of non-fatal cardiovascular events, or the increased statistical power available in ARIC versus the SAHS.

The current manuscript not only expands our earlier findings that gender modified the joint effect of diabetes and NCEP-MetS on cardiovascular mortality to include CHD mortality, but examines the contribution of each component part of the metabolic syndrome. None of the component parts of the metabolic syndrome clearly drove the observed relationship between gender, diabetes and CHD mortality. While HDL-cholesterol and triglyceride levels appear to be of particular interest, it is pertinent to bear in mind that temporal relationships between the component parts of the metabolic syndrome may be important. For instance, because diabetes often causes weight loss, a diabetic individual's current weight and waist circumference may not accurately reflect their pre-diabetic weight and waist circumference. In addition, despite our attempts to increase the available statistical power through imputation, the power available to determine whether a particular component of the metabolic syndrome was driving the relationship of interest remained somewhat limited. In total there were only 121 CHD deaths with particularly few events occurring in some of the exposure categories created based on gender, diabetes status and each NCEP-MetS component part in turn.

One possible explanation for increased cardiovascular risk in women with both NCEP-MetS and diabetes could be a longer duration of diabetes, or more severe diabetes. However, in our study among individuals with diabetes, age of diabetes onset and duration of diabetes were similar in men and women regardless of whether or not they also had NCEP-MetS. Moreover, among individuals with diabetes and no history of CVD, the difference in HRs for NCEP-MetS in relation to CHD mortality between men and women was only slightly attenuated by adjustment for duration of diabetes or 2-hour glucose levels. A second possible explanation for the increased cardiovascular risk in women with both NCEP-MetS and diabetes could be more aggressive treatment of the component parts of the metabolic syndrome in men than women because of greater perceived risk among men. Moreover, differential treatment of the component parts of the metabolic syndrome in men and women is likely to be exacerbated by the major developments in treatment which occurred during the study. Unfortunately we do not have information available on treatment throughout the follow-up period to test this hypothesis. Finally, it is important to bear in mind that the greater impact of diabetes and the metabolic syndrome on cardiovascular risk in women is largely a result of lower baseline risk in women than men in individuals without NCEP-MetS or diabetes.

Obesity, specifically increased central adiposity, is an underlying component of the metabolic syndrome that differentially affects men and women. In general men tend to have a lower percentage of total fat, but higher amounts of central or visceral adiposity(22-24). The Strong Heart Study examined sex-specific differences between diabetic and non-diabetic individuals and similar to our findings reported that differences in waist circumference between diabetic and non-diabetic individuals were greater in women than men(25). Adverse lipoprotein changes between diabetic and non-diabetic individuals differentially affect women and men, are associated with obesity and represent two components of the metabolic syndrome (18, 25-32). In the SAHS diabetes was associated with a greater increase in LDL and a greater decrease in HDL cholesterol levels in Mexican American women than in Mexican American men(18,33). Adverse lipoprotein changes reported in other studies include greater decreases in HDL-cholesterol, apoAI and LDL size and greater increases in LDL-cholesterol and apoB in diabetic women than diabetic men(25-34).

In summary, when diabetes occurred with the metabolic syndrome, CHD mortality rates were similar in men and women; while in individuals with neither disorder, CHD mortality rates were significantly lower in women than in men. Thus, gender was a strong modifier of the joint effect of diabetes and NCEP-MetS on CHD mortality, suggesting that the metabolic syndrome when coupled with diabetes may affect men and women differentially relative to CHD mortality.

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Abbreviations

ARIC
: Atherosclerosis Risk in Communities

CHD
: Coronary Heart Disease

CVD
: Cardiovascular Disease

HR
: Hazard Ratio

ICD-9
: International Classification of Diseases, Ninth Revision

IFG
: Impaired fasting glucose

IGR
: Impaired glucose regulation

IGT
: Impaired glucose tolerance

NCEP-MetS
: National Cholesterol Education Program – Metabolic Syndrome

SAHS

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Table 1

Characteristics [mean (standard error) or percent)] of individuals in the study population stratified by NCEP-MetS and Diabetes status adjusted for age and ethnic group.

	NCEP-MetS (no)/ Diabetes (no)			NCEP-MetS (yes)/ Diabetes (no)		
	Women (n=2137)	**Men (n=1564)**	**Difference* (95% CI)**	**Women (n=395)**	**Men (n=376)**	**Difference* (95% CI)**
Cardiovascular deaths† (n)	32	62	----	20	27	----
CHD deaths† (n)	9	26	----	11	13	----
History of CVD† (n)	35	60	----	19	22	----
Age† (years)	41.8 (0.2)	42.1 (0.3)	-0.3 (-1.0, 0.4)	47.5 (0.5)	45.5 (0.6)	2.1 (0.6, 3.6)
Mexican American† (%)	61.0 (1.0)	60.4 (1.2)	0.6 (2.6, 3.7)	72.7 (2.4)	63.0 (2.5)	9.6 (2.9, 16.4)
Fasting Insulin (IU/mL)	10.8 (0.3)	11.9 (0.4)	-1.1 (-2.1, -0.1)	23.4 (0.8)	21.5 (0.8)	1.8 (-0.3, 4.0)
2-Hour Insulin (IU/mL)	79 (3)	65 (3)	14 (6, 21)	159 (5)	129 (5)	30 (15, 45)
Fasting Glucose (md/dL)	86 (0.5)	89 (1)	-3 (-5, -2)	94 (1)	95 (1)	-2 (-5, 1)
2-Hour Glucose (mg/dL)	107 (1)	100 (1)	7 (5, 10)	127 (2)	118 (2	9 (3, 15)
BMI (kg/m^2)	25.7 (0.1)	26.6 (0.1)	-0.6 (-1.0, -0.2)	32.9 (0.2)	31.1 (0.2)	2.1 (1.3, 2.9)
Waist Circumference‡ (mm)	818 (3)	926 (4)	-108 (-118, -98)	991 (7)	1037 (7)	-46 (-66, -26)
LDL-cholesterol (mg/dL)	119 (1)	129 (1)	-10 (-12, -8)	128 (2)	122 (2)	-5 (-10, 0)
HDL-cholesterol (mg/dL)	58 (0.3)	49 (0.3)	9 (8, 10)	43 (1)	38 (1)	5 (4, 7)
Hypertension (%)	9.1 (0.7)	10.6 (0.8)	-1.5 (-3.7, 0.6)	37.5 (1.7)	39.5 (1.7)	-2.0 (-6.7, 2.6)
	NCEP-MetS (no)/ Diabetes (yes)			**NCEP-MetS (yes)/ Diabetes (yes)**		
	Women (n=69)	Men (n=69)	Difference* (95% CI)	Women (n=236)	Men (n=150)	Difference* (95% CI)
Cardiovascular deaths† (n)	9	14	----	51	39	----
CHD deaths† (n)	3	9	----	29	21	----
History of CVD† (n)	3	7	----	23	25	----
Age† (years)	52.6 (1.3)	52.6 (1.3)	0 (-3.6, 3.6)	52.1 (0.7)	52.5 (0.9)	-0.4 (-2.6, 1.8)
Mexican American† (%)	72.5 (5.7)	72.5 (5.7)	0 (-15.9, 15.9)	84.3 (3.1)	77.3 (3.9)	6.0 (-2.8, 6.7)
Diabetes onset (age, years)	48.8 (0.9)	47.9 (0.9)	0.9 (-1.7, 3.4)	47.4 (0.5)	47.5 (0.6)	-0.1 (-1.6, 1.5)
Diabetes duration (years)	3.6 (0.9)	4.5 (0.9)	-0.9 (-3.4, 1.7)	4.9 (0.5)	4.9 (0.6)	0.1 (-1.5, 1.6)
Fasting glucose (md/dL)	140 (3)	139 (3)	0 (-7, 8)	171 (1)	167 (2)	5 (0, 9)
2-hour glucose (mg/dL)	270 (5)	272 (5)	-2 (-16, 13)	306 (3)	293 (4)	13 (4, 22)

	NCEP-MetS (no)/ Diabetes (no)			NCEP-MetS (yes)/ Diabetes (no)		
	Women (n=2137)	**Men (n=1564)**	**Difference[*] (95% CI)**	**Women (n=395)**	**Men (n=376)**	**Difference[*] (95% CI)**
BMI (kg/m^2)	26.5 (0.6)	25.8 (0.6)	1.3 (-1.3, 4.0)	32.7 (0.3)	30.9 (0.4)	2.6 (1.3, 3.8)
Waist Circumference[‡] (mm)	842 (21)	895 (23)	-53 (-114, 9)	1005 (9)	1022 (12)	-17 (-48, 12)
LDL-cholesterol (mg/dL)	119 (4)	120 (4)	-1 (-13, 11)	128 (2)	125 (3)	2 (-5, 10)
HDL-cholesterol (mg/dL)	60 (2)	53 (2)	6 (2, 11)	44 (1)	38 (1)	6 (3, 8)
Hypertension (%)	11.6 (4.0)	21.8 (4.0)	-10.2 (-21.2, 0.9)	34.5 (2.2)	33.6 (2.7)	0.9 (-5.9, 7.6)

NCEP-MetS, the metabolic syndrome as defined by the National Cholesterol Education Program; CI, confidence interval;

[*] Difference between women and men;

[†] Unadjusted;

[‡] Limited to participants who had waist circumference measured

Table 2

Prevalence (%) of the metabolic syndrome and its individual components stratified by glucose regulation, diabetes and gender and adjusted for age and ethnic group.

	Normal GR		Impaired GR		Diabetic Individuals	
	Women	**Men**	**Women**	**Men**	**Women**	**Men**
N	2021	1507	511	433	305	219
NCEP-IFG	----	----	45.8	67.6*	90.6	96.9*
NCEP-High Waist Circumference	26.8	20.6*	55.9	35.1*	66.5	36.3*
NCEP-High Triglycerides	19.2	37.0*	40.3	53.1*	57.6	62.4
NCEP-Low HDL Cholesterol	36.1	31.5*	46.8	35.3*	62.8	47.4*
NCEP-HBP	17.4	27.6*	28.0	37.7*	40.9	43.1
NCEP- components (n)	0.99	1.16*	2.17	2.28	3.17	2.84*
NCEP-MetS	9.7	12.3*	40.7	45.6*	74.4	65.7*

* *p* value < 0.05 for difference between women and men; GR, glucose regulation

Table 3

Adjusted[*†] CHD mortality rates per 1,000 person-years and Cox proportional hazard ratios predicting CHD mortality stratified by the metabolic syndrome and each component part of the metabolic syndrome in turn and diabetes.

	Rate/1,000 person-years (95% CI)		Hazard Ratios (95% CI)		
	Women	**Men**	**Women**	**Men**	**p[‡]**
NCEP-MetS: General Population[*]					
DM, no; MetS, no	0.47 (0.23, 0.97)	1.70 (1.03, 2.80)	1.00	1.00	
DM, no; MetS, yes	1.84 (0.92, 3.67)	2.74 (1.46, 5.15)	4.17 (1.72, 10.1)	1.77 (0.91, 3.45)	0.130
DM, yes; MetS, no	2.24 (0.67, 7.50)	5.82 (2.65, 12.8)	4.94 (1.33, 18.4)	3.38 (1.56, 7.31)	0.623
DM, yes; MetS, yes	6.11 (3.55, 10.5)	6.56 (3.60, 11.9)	14.3 (6.62, 30.7)	4.21 (2.32, 7.65)	0.011
NCEP-MetS: Individuals without a History of CVD[†]					
DM, no; MetS, no	0.39 (0.18, 0.83)	0.97 (0.52, 1.81)	1.00	1.00	
DM, no; MetS, yes	1.36 (0.61, 3.05)	2.18 (1.05, 4.51)	3.70 (1.38, 9.95)	2.46 (1.09, 5.56)	0.531
DM, yes; MetS, no	1.31 (0.30, 5.69)	6.47 (2.83, 14.8)	3.44 (0.72, 16.3)	7.01 (2.91, 16.9)	0.432
DM, yes; MetS, yes	6.38 (3.52, 11.5)	6.17 (3.07, 12.4)	18.1 (8.03, 41.0)	6.63 (3.10, 14.1)	0.070
NCEP-High WC: General Population[*]					
DM, no; WC, no	0.5 (0.2, 1.1)	1.7 (1.0, 2.8)	1.00	1.00	
DM, no; WC, yes	1.2 (0.6, 2.3)	2.5 (1.4, 4.7)	2.22 (0.91, 5.45)	1.58 (0.81, 3.09)	0.555
DM, yes; WC, no	4.7 (2.2, 10.3)	6.0 (3.2, 11.2)	9.26 (3.53, 24.3)	3.70 (2.02, 6.77)	0.108
DM, yes; WC, yes	5.2 (2.9, 9.2)	6.0 (2.8, 12.5)	10.7 (4.69, 24.3)	3.72 (1.78, 7.78)	0.058
NCEP-Low HDL: General Population[*]					
DM, no; HDL, no	0.7 (0.4, 1.4)	1.3 (0.7, 2.2)	1.00	1.00	
DM, no; HDL, yes	1.1 (0.6, 2.3)	3.2 (1.8, 5.4)	2.36 (0.98, 5.73)	3.15 (1.67, 5.94)	0.604
DM, yes; HDL, no	2.2 (0.9, 5.4)	6.3 (3.3, 12.0)	4.08 (1.47, 11.3)	5.44 (2.77, 10.7)	0.641
DM, yes; HDL, yes	6.1 (3.5, 10.9)	4.8 (2.4, 9.8)	13.4 (6.20, 28.8)	4.32 (2.07, 8.99)	0.031
NCEP-High TG: General Population[*]					
DM, no; TG, no	0.6 (0.3, 1.2)	2.1 (1.3, 3.6)	1.00	1.00	
DM, no; TG, yes	1.3 (0.6, 2.5)	1.6 (0.9, 2.9)	2.45 (1.01, 5.92)	0.71 (0.37, 1.35)	0.026
DM, yes; TG, no	3.4 (1.5, 7.6)	3.4 (1.3, 8.4)	6.90 (2.64, 18.0)	1.58 (0.64, 3.95)	0.028
DM, yes; TG, yes	5.6 (3.2, 10.0)	7.3 (4.1, 13.0)	11.7 (5.31, 25.7)	3.48 (1.93, 6.27)	0.013
NCEP-High BP: General Population[*]					
DM, no; BP, no	0.6 (0.3, 1.2)	1.4 (0.8, 2.5)	1.00	1.00	

	Rate/1,000 person-years (95% CI)		Hazard Ratios (95% CI)		
	Women	**Men**	**Women**	**Men**	**p‡**
DM, no; BP, yes	1.2 (0.6, 2.5)	2.9 (1.7, 4.9)	2.26 (0.92, 5.53)	2.22 (1.16, 4.23)	0.972
DM, yes; BP, no	5.9 (3.1, 11.1)	7.5 (3.9, 14.5)	11.5 (4.95, 26.6)	5.46 (2.64, 11.3)	0.180
DM, yes; BP, yes	5.0 (2.7, 9.5)	5.7 (2.9, 11.0)	9.25 (4.02, 21.3)	4.54 (2.18, 9.46)	0.194

CI, confidence interval; WC, waist circumference; TG, triglycerides; BP, blood pressure;

*p value for men versus women.

*Total study population (n=4,996) adjusted for age, ethnic group and a history of CVD;

†Limited to individuals without a history of CVD (n=4,802) adjusted for age and ethnic group;

‡p-value for men versus women.

Table 4

Cox proportional hazard ratios (and 95% confidence intervals) for NCEP-MetS/diabetes categories predicting CVD mortality stratified by sex and ethnic group.

	Women	*P**	Men	*P†*	*P‡*
Non-Hispanic White					
DM, no; MetS, no	1.00		1.00		
DM, no; MetS, yes	1.31 (0.49, 3.50)	----	1.60 (0.81, 3.15)	----	0.740
DM, yes; MetS, no	3.47 (1.18, 10.2)	----	0.98 (0.23, 4.12)	----	0.166
DM, yes; MetS, yes	3.22 (1.29, 8.09)	----	2.76 (1.20, 6.34)	----	0.805
Mexican American					
DM, no; MetS, no	1.00		1.00		
DM, no; MetS, yes	3.27 (1.56, 6.88)	0.145	1.52 (0.83, 2.79)	0.913	0.118
DM, yes; MetS, no	5.19 (1.84, 14.6)	0.598	2.98 (1.53, 5.80)	0.166	0.375
DM, yes; MetS, yes	11.2 (6.01, 21.0)	0.027	3.66 (2.23, 5.98)	0.566	0.005

*P** *p* values for ethnic group interaction in women;

P† *p* values for ethnic-group interaction in men;

P‡ *p* values for sex interaction in non-Hispanic whites and Mexican Americans.