The National Cholesterol Education Program–Adult Treatment Panel III, International Diabetes Federation, and World Health Organization Definitions of the Metabolic Syndrome as Predictors of Incident Cardiovascular Disease and Diabetes

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OBJECTIVE — The clinical value of metabolic syndrome is uncertain. Thus, we examined cardiovascular disease (CVD) and diabetes risk prediction by the National Cholesterol Education Program (NCEP)-Adult Treatment Panel III (ATPIII), International Diabetes Federation, and World Health Organization definitions of the metabolic syndrome.

RESEARCH DESIGN AND METHODS — We analyzed the risks associated with metabolic syndrome, the NCEP multiple risk factor categories, and 2-h glucose values in the San Antonio Heart Study (n = 2,559; age range 25–64 years; 7.4 years of follow-up).

RESULTS — Both ATPIII metabolic syndrome plus age ≥45 years (odds ratio 9.25 [95% CI 4.85–17.7]) and multiple (two or more) risk factors plus a 10-year coronary heart disease (CHD) risk of 10–20% (11.9 [6.00–23.6]) had similar CVD risk in men without CHD, as well as CHD risk equivalents. In women counterparts, multiple (two or more) risk factors plus a 10-year CHD risk of 10–20% was infrequent (10 of 1,254). However, either a 10-year CHD risk of 5–20% (7.72 [3.42–17.4]) or ATPIII metabolic syndrome plus age ≥55 years (4.98 [2.08–12.0]) predicted CVD. ATPIII metabolic syndrome increased the area under the receiver operating characteristic curve of a model containing age, sex, ethnic origin, family history of diabetes, and 2-h and fasting glucose values (0.857 vs. 0.842, P = 0.013). All three metabolic syndrome definitions imparted similar CVD and diabetes risks.

CONCLUSIONS — Metabolic syndrome is associated with a significant CVD risk, particularly in men aged ≥45 years and women aged ≥55 years. The metabolic syndrome predicts diabetes beyond glucose intolerance alone.

Diabetes Care 30:8–13, 2007

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Received for publication 5 July 2006 and accepted in revised form 6 October 2006.

Abbreviations: ATPIII, Adult Treatment Panel III; CHD, coronary heart disease; CVD, cardiovascular disease; FPR, false-positive rate; IDF, International Diabetes Federation; IFG, impaired fasting glucose; IGT, impaired glucose tolerance; NCEP, National Cholesterol Education Program; ROC, receiver operating characteristic; SAHS, San Antonio Heart Study; WHO, World Health Organization.

A table elsewhere in this issue shows conventional and Système International (SI) units and conversion factors for many substances.

DOI: 10.2337/dc06-1414

Sixty-four of 201 million U.S. individuals aged ≥20 years have the metabolic syndrome (1). The metabolic syndrome increases the risk for future cardiovascular disease (CVD), as well as diabetes (2). However, its clinical value has been questioned in a recent joint statement from the American Diabetes Association and the European Association for the Study of Diabetes (3). First, this statement points out that the metabolic syndrome is an ill-characterized entity with no proven value as a risk assessment tool for future CVD. Second, it brings up a concern: the possibility of misleading practitioners in the treatment of individuals who had one or two CVD risk factors. Finally, it acknowledges that this syndrome is effective in predicting future diabetes but questions its predictive value beyond that of glucose intolerance.

To shed some light to these questions, we examined the predictive discrimination of the metabolic syndrome in the context of other readily available risk factors (such as age, sex, ethnic origin, and family, as well as past medical history of diabetes and CVD). Particularly, we took into account the higher CVD risk of men aged ≥45 years and women aged ≥55 years (4) and hypothesized that metabolic syndrome plus age ≥45/55 years in men/women would be a good CVD marker. We also considered the high diabetes risk associated with impaired fasting glucose (IFG) and postulated that the combination of IFG and/or metabolic syndrome would be a better predictor of diabetes than either of them alone.

We tested these hypotheses in the San Antonio Heart Study (SAHS) by comparing the metabolic syndrome with current standards for predicting coronary heart disease (CHD) (National Cholesterol Education Program [NCEP] risk factor cate-

gories) (4) and diabetes (2-h glucose value) (5). We performed these analyses using the NCEP-Adult Treatment Panel III (ATPIII) (6), International Diabetes Federation (IDF) (7), and World Health Organization (WHO) (8) definitions of the metabolic syndrome.

RESEARCH DESIGN AND METHODS

— SAHS was designed as a population-based study with approved protocols by the institutional review board of the University of Texas Health Science Center at San Antonio. All subjects gave written informed consent. Detailed descriptions have already been published (9,10). Briefly, all Mexican Americans and non-Hispanic whites (men and nonpregnant women) aged 25–64 years that resided in randomly selected households from low-, middle-, and high-income census tracts were invited to participate in two phases (response rate 65.3%). Phase 1 participants were not eligible for analysis because waist circumference was not measured. Phase 2 participants were enrolled between January 1984 and December 1988 ($n = 2,941$) and reexamined between October 1991 and October 1996 ($n = 2,646$). The median for the follow-up period was 7.4 years. Incident CVD was assessed in 2,559 of 2,941 (87.0%) participants and incident diabetes in 1,709 of 2,459 (69.5%) nondiabetic participants who were alive at follow-up.

Definitions of variables and outcomes

Interview questionnaires were administered to assess CVD, current cigarette smoking, treatment for diabetes and hypertension, and family history of diabetes and heart attack in any first-degree relative. Waist circumference was measured at the level of the umbilicus. Blood pressure was recorded with the participant in the sitting position and reported as the mean of the second and third readings. Blood specimens were obtained after a 12- to 14-h fast and 2 h after a 75-g oral glucose load (Orangedex; Custom Laboratories, Baltimore, MD). Plasma glucose and serum lipids were measured with an Abbott Bichromatic Analyzer (South Pasadena, CA) (9).

We defined CVD as self-reported heart attack, stroke, coronary revascularization procedure, or angina (by the Rose Angina questionnaire) (11) at baseline; incident CVD was defined as self-reported heart attack, stroke, or coronary revascularization procedure during follow-up or any mention of cardiovascular death on the death certificate (ICD-9 codes 390–459) (10).

We used the 2003 American Diabetes Association definitions of diabetes (fasting glucose level ≥7.0 mmol/l, 2-h glucose ≥11.1 mmol/l, or pharmacological treatment), impaired glucose tolerance (IGT) (2-h glucose ≥7.8 and <11.1 mmol/l), and IFG (fasting glucose ≥5.6 and <7.0 mmol/l) (5).

We calculated the 10-year risk for developing CHD using Framingham risk scoring tables (4). We counted the number of NCEP major risk factors: current cigarette smoking, hypertension (systolic blood pressure ≥140 mmHg and/or diastolic blood pressure ≥90 mmHg and/or pharmacological treatment), low HDL cholesterol level (<1.04 mmol/l), heart attack in any first-degree relative (family history of premature CHD was unavailable), and age (≥45 years in men and ≥55 years in women). We removed one risk factor from the total count in individuals with HDL cholesterol level ≥1.55 mmol/l. We examined CVD risk associated with CHD and/or CHD risk equivalents (CVD, diabetes, or multiple risk factors plus a 10-year CHD risk >20%) and multiple risk factors (two or more), plus a 10-year CHD risk of 10–20% and a 10-year CHD risk of 5–20%.

The ATPIII definition (6) of the metabolic syndrome required three or more of the following five disorders: elevated waist circumference (≥102 cm in men and ≥88 cm in women), hypertriglyceridemia (≥1.7 mmol/l), low HDL cholesterol level (<1.03 mmol/l in men and <1.3 mmol/l in women), high blood pressure (systolic blood pressure ≥130 mmHg and/or diastolic blood pressure ≥85 mmHg and/or pharmacological treatment), and elevated fasting glucose (≥5.6 mmol/l and/or pharmacological treatment). The IDF definition (7) used those same components and cut points, except for waist circumference cut points (≥94 cm in non-Hispanic white men or ≥90 cm in Mexican-American men and ≥80 cm in women). The IDF definition required elevated waist circumference plus two of the other four components.

The WHO definition (8) required hyperinsulinemia (fasting insulin level ≥75th percentile), IGT, fasting glucose ≥6.1 mmol/l, and/or diabetes plus two of the following three disorders: obesity (BMI ≥30 kg/m^2 and/or waist-to-hip ratio >0.9 in men or >0.85 in women), dyslipidemia (triglyceride level ≥1.7 mmol/l and/or HDL cholesterol level <0.9 mmol/l in men or <1.0 mmol/l in women), and high blood pressure (systolic blood pressure ≥140 mmHg and/or diastolic blood pressure ≥90 mmHg and/or pharmacological treatment). The SAHS lacked information regarding microalbuminuria, as well as specific treatment for hypertriglyceridemia and low HDL cholesterol level.

Data analysis

Statistical analyses were performed with the SAS statistical software (SAS Institute, Cary, NC). Logistic regression analysis was used to calculate odds ratio (OR) for developing a 7.4-year incident CVD (or diabetes) for potential risk factors. The ability of the 2-h glucose value (alone or in combination with other variables) to predict incident diabetes was examined by receiver operating characteristic (ROC) curves. ROC curves were constructed by plotting the sensitivity against the corresponding false-positive rate (FPR), which equals 1-specificity. Areas under the ROC curves were compared by the algorithm developed by DeLong et al. (12). McNemar's test was used to compare sensitivities and FPRs between markers. All probability values were two sided.

RESULTS

— Baseline characteristics of the participants are presented in Table 1. The prevalence of the metabolic syndrome was definition dependent: highest with the IDF definition and lowest with the WHO definition.

CVD risk

Ninety-three of 1,088 (8.5%) men and 63 of 1,471 (4.3%) women developed new CVD events. ATPIII (OR 2.00 [95% CI 1.33–3.01]), IDF (1.69 [1.13–2.54]), and WHO (1.73 [1.12–2.67]) definitions of the metabolic syndrome predicted incident CVD risk independently of age, sex, ethnic origin, history of CVD and type 2 diabetes, non-HDL cholesterol, smoking status, and family history of heart attack.

All three metabolic syndrome definitions had similar ORs but different sensitivity and FPR (Table 2). The IDF definition had a higher sensitivity (except for the comparison with the ATPIII definition in men) than the other two definitions but also had a higher FPR. The metabolic syndrome imparted a lower risk than CHD and/or CHD risk equivalents because of the lower FPR of the latter. The metabolic syndrome did not predict new CVD events in subjects with

Table 1—*Baseline characteristics of study participants*

	Men		Women	
	Non-Hispanic whites	Mexican Americans	Non-Hispanic whites	Mexican Americans
n	422	842	506	1,171
Age (years)	44 ± 11	43 ± 12	44 ± 11	43 ± 11
BMI (kg/m^2)	27.1 ± 4.3	28.3 ± 4.6	25.5 ± 5.4	29.2 ± 6.5
Waist circumference (cm)	96.2 ± 11.2	95.0 ± 11.5	81.9 ± 13.3	88.7 ± 15.5
Systolic blood pressure (mmHg)	121.7 ± 13.5	123.9 ± 14.2	113.7 ± 15.5	118.0 ± 16.5
Diastolic blood pressure (mmHg)	73.9 ± 8.3	74.5 ± 9.2	69.0 ± 9.4	71.2 ± 8.9
Fasting glucose level (mmol/l)	5.00 ± 1.14	5.37 ± 1.92	4.73 ± 0.93	5.40 ± 2.25
2-h glucose level (mmol/l)	5.58 ± 2.62	6.96 ± 4.5	5.83 ± 2.52	7.82 ± 4.59
Total cholesterol level (mmol/l)	5.08 ± 1.01	5.22 ± 1.19	5.04 ± 1.05	5.07 ± 1.04
HDL cholesterol level (mmol/l)	1.09 ± 0.30	1.08 ± 0.31	1.38 ± 0.39	1.24 ± 0.33
Triglyceride level (mmol/l)	1.42 ± 0.02	1.63 ± 0.02	1.08 ± 0.02	1.36 ± 0.02
Insulin level (mmol/l)	8.84 ± 2.36	11.2 ± 2.32	7.07 ± 2.52	11.3 ± 2.35
IFG (≥5.6 and <7.0 mmol/l) (%)	9.8 (7.2–13.1)	11.5 (9.4–14.1)	4.6 (3.0–6.9)	7.4 (5.9–9.2)
Type 2 diabetes (%)	5.0 (3.3–7.5)	11.5 (9.5–13.9)	4.0 (2.6–6.1)	14.7 (12.8–16.9)
History of CVD (%)	6.2 (4.2–8.9)	9.7 (7.9–11.9)	5.1 (3.5–7.4)	7.4 (6.1–9.1)
ATPIII metabolic syndrome (%)	24.0 (20.2–28.4)	29.6 (26.6–32.8)	16.8 (13.8–20.4)	30.9 (28.3–33.6)
IDF metabolic syndrome (%)	28.4 (24.2–32.9)	40.4 (37.1–43.9)	24.7 (21.1–28.7)	38.5 (35.7–41.4)
WHO metabolic syndrome (%)	18.8 (15.3–23.0)	28.3 (25.2–31.7)	12.1 (9.5–15.5)	27.3 (24.7–30.1)
Cigarette smoking (%)	29.6 (25.5–34.2)	34.6 (31.4–37.8)	23.7 (20.2–27.6)	20.6 (18.4–23.0)
First-degree relative with diabetes (%)	19.4 (15.8–23.5)	36.5 (33.3–39.8)	20.6 (17.3–24.4)	43.4 (40.6–46.3)
First-degree relative with heart attack (%)	35.0 (30.6–39.7)	23.9 (21.2–26.9)	35.3 (31.3–39.6)	30.5 (27.9–33.2)

Data are *n*, means ± SD, or percent (95% CI).

CHD and/or CHD risk equivalents (Table 2). In subjects who were free of CHD and/or CHD risk equivalents, ATPIII, IDF, and WHO definitions had similar ORs, but the IDF definition had a higher sensitivity and FPR than the other two (Table 2).

Age ≥45/55 years in men/women increased the ability of the metabolic syndrome to predict CVD because of the decrease in FPR. In men, CVD risk of metabolic syndrome plus age ≥45 years was comparable with the risk of multiple (two or more) risk factors plus a 10-year CHD risk of 10–20%. In women, multiple (two or more) risk factors plus a 10-year CHD risk of 10–20% was uncommon (10 of 1,254 women) and associated with wide CIs. However, a 10-year CVD risk of 5–20% had a significant risk, as did metabolic syndrome plus age ≥55 years.

Diabetes risk

Incident diabetes developed in 195 subjects (11.4%). The predictive discrimination of the metabolic syndrome was similar to that of the 2-h glucose value at a comparable level of prevalence of the former (Fig. 1). All three definitions had similar diabetes risk, but the IDF definition had both a higher sensitivity and FPR than the other two. ATPIII (OR 6.90 [95% CI 4.97–9.58]), IDF (5.76 [4.11–9.07]), and WHO (6.67 [4.75–9.35]) definitions predicted incident diabetes independently of age, sex, ethnic origin, and family history of diabetes.

A very high risk was present in subjects with both IFG and metabolic syndrome (Table 3). Increased risk was also present in subjects who had normal fasting glucose levels and metabolic syndrome and those who had IFG without metabolic syndrome.

We generated modified definitions of the metabolic syndrome to assess the ability of this syndrome to predict diabetes beyond that of glucose intolerance. Fasting glucose was excluded, and subjects were defined as having ATPIII metabolic syndrome if they had three of the four remaining components (IDF metabolic syndrome if they had elevated waist circumference plus two of the other three components). The area under the curve of a model containing age, sex, ethnic origin, family history of diabetes, and 2-h and fasting glucose values increased by adding either modified ATPIII (0.842 vs. 0.857, $P = 0.013$) or IDF metabolic syndrome (0.858, $P = 0.004$).

CONCLUSIONS — The metabolic syndrome is associated with a significant CVD risk, particularly in men aged ≥45 years and women aged ≥55 years. This is not surprising since individual components are major CVD risk factors (3). However, increased risk associated with a marker is not equivalent to adequate marker performance for identifying high-risk subjects (13), and performance is at the center (3,14).

Several studies (15–18), but not all (19), have reported similar risk for total and CVD mortality associated with ATPIII, IDF, or WHO definitions of the metabolic syndrome. In our study, these definitions are also associated with similar risk for new CVD events, even though they have different sensitivity and FPR.

CVD risk prediction by metabolic syndrome is inferior to the Framingham score (16,20), but whether the metabolic syndrome conveys an additional risk remains unresolved (21). In some studies (22–24), but not in all (25), the metabolic syndrome is associated with an increased CVD risk in subjects with CHD or diabetes. In our study, this effect is not statistically significant. Nevertheless, the metabolic syndrome may be a less relevant concept in individuals with CHD or CHD risk equivalents because all modifiable risk factors require aggressive treatment.

The metabolic syndrome increases CVD risk in subjects who are free of either CVD or diabetes (26). In this heteroge-

Table 2—*ORs with 95% CIs for developing CVD over 7.4 years using NCEP risk factor categories or metabolic syndrome*

	Men			Women		
	Sensitivity	FPR	OR (95% CI)	Sensitivity	FPR	OR (95% CI)
In all subjects (93 events in 1,088 men; 63 events in 1,471 women)						
CHD and/or CHD risk equivalents	52.7	9.9*	10.1 (6.38–15.9)	49.2†	13.2	6.36 (3.79–10.7)
IDF definition‡	64.5	32.1	3.85 (2.47–6.01)	63.5	32.2*	3.65 (2.16–6.18)
ATPIII definition	60.2	23.6*	4.89 (3.15–7.60)	57.1†	24.5*	4.11 (2.46–6.87)
WHO definition	49.4†	22.1*	3.43 (2.19–5.40)	48.1†	21.0*	3.50 (2.02–6.06)
In subjects who had CHD or CHD risk equivalents (49 events in 148 men; 31 events in 217 women)						
IDF definition‡	69.4	75.8	0.72 (0.34–1.55)	87.1	75.3	2.22 (0.74–6.67)
ATPIII definition	73.5	68.7	1.26 (0.59–2.71)	80.6	67.7	1.98 (0.77–5.09)
WHO definition	63.4	58.4	1.23 (0.57–2.64)	72.0	61.7	1.60 (0.63–4.04)
In subjects who were free of CHD or CHD risk equivalents (44 events in 940 men; 32 events in 1,254 women)						
Multiple (two or more) risk factors plus a 10-year CHD risk of 10–20%	72.7	18.6*	11.9 (6.00–23.6)	3.1§	0.7*	4.35 (0.53–35.4)
10-year CHD risk of 5–20%	84.1§	37.6*	8.77 (3.86–19.9)	28.1	4.8*	7.72 (3.42–17.4)
IDF definition‡	59.1	27.2	3.86 (2.08–7.17)	40.6	25.7	1.98 (0.97–4.05)
IDF definition plus age ≥45/55 years in men/women	54.5	11.2*	9.55 (5.09–17.9)	25.0†	7.0*	4.40 (1.92–10.1)
ATPIII definition	45.4†	18.6*	3.64 (1.96–6.74)	34.4	17.9*	2.40 (1.14–5.05)
ATPIII definition plus age ≥45/55 years in men/women	43.2†	7.6*	9.25 (4.85–17.7)	21.9†	5.3*	4.98 (2.08–12.0)
WHO definition	36.4§	18.3*	2.54 (1.34–4.82)	27.6	15.1*	2.15 (0.94–4.92)
WHO definition plus age ≥45/55 years in men/women	34.1§	7.4*	6.47 (3.30–12.7)	20.7	4.3*	5.85 (2.28–15.0)

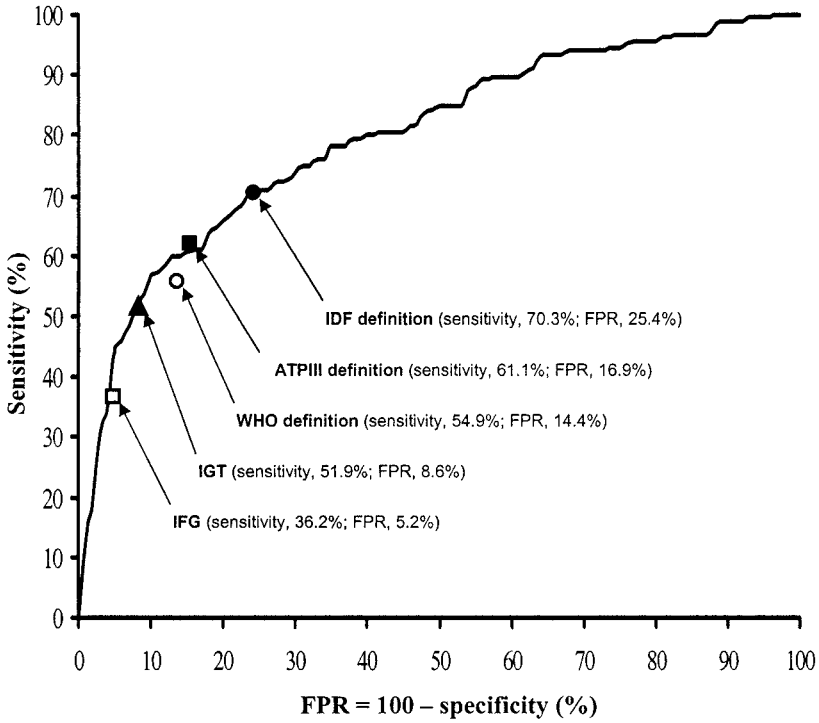
‡The sensitivity (or FPR) of the IDF definition was compared with that of the other categories by McNemar's test; *$P < 0.001$; †$P < 0.05$; §$P < 0.01$.

neous group of individuals, the number of risk factors is counted and an estimation of the 10-year CHD risk is required for individuals with multiple (two or more) risk factors (4). Those with a 10-year CHD risk of 10–20% are eligible for treatment, including lifestyle therapies and a LDL cholesterol goal of <3.4 mmol/l (<130 mg/dl) (6). Men with metabolic syndrome are also at increased risk, particularly those aged ≥45 years, since metabolic syndrome or metabolic syndrome plus ≥45 years have practically equal sensitivity. Risk prediction by the metabolic syndrome plus age ≥45 years is similar to multiple (two or more) risk factors plus a 10-year CHD risk of 10–20%. Therefore, men with metabolic syndrome plus ≥45 years may be eligible for the same therapeutic recommendations. Nevertheless, multiple (two or more) risk factors plus a 10-year CHD risk of 10–20% may be considered a better maker because of its greater sensitivity. Even so, metabolic syndrome plus age ≥45 years may be a useful marker on account of its simplicity.

In the absence of CHD and CHD risk equivalents, a large proportion of men (72.7%) who develop new CVD events have multiple (two or more) risk factors plus a 10-year CHD risk of 10–20%. This is not so in women (3.1%) because few middle-aged women can be included in this risk category (27). In women, the 10-year CHD risk of 5–20% is associated with a more significant risk, even though this category only identifies a relatively small proportion of women who develop CVD (28.1%). The metabolic syndrome does not detect a larger proportion of these women (the number of events are small and the difference not statistically relevant). Nevertheless, the predictive ability of the metabolic syndrome is enhanced by age ≥55 years.

Diabetes risk associated with either IGT or IFG is higher than the risk associated with any of the other metabolic disorders (28). The American Diabetes Association favors using IFG to avoid the costs and inconveniences of an oral glucose tolerance test (5). Both the metabolic syndrome and the 2-h glucose value have the same predictive discrimination when comparisons are performed at the same level of prevalence as the former. The metabolic syndrome increases the risk associated with IGT (29) or IFG. Additionally, a significant diabetes risk is imparted by both a metabolic syndrome definition that excludes IFG and IFG in the absence of metabolic syndrome. Likewise, Wilson et al. (30) have already described that combinations of metabolic components that do not include IFG confer an increased risk, but IFG deserves special attention even if no other metabolic abnormality is present. Therefore, risk assessment may be better accomplished by considering all subjects with glucose intolerance and/or metabolic syndrome present at high risk for diabetes.

This study has several limitations. First, some of our results have wide CIs, particularly in the assessment of CVD risk among women. Nonetheless, results are similar in both sexes and consistent in all NCEP risk factor categories. Second, data on CVD outcomes derive from questionnaires and death certificates. Therefore,



McNemar's test comparing sensitivities and FPR's between the 2-hour glucose value and metabolic syndrome at the same prevalence of the latter:

2-hour glucose value vs. ATPIII definition (prevalence of 21.8%)
- Sensitivity: 61.1% vs. 61.1%, $p = 1.000$
- FPR: 16.8% vs. 16.9%, $p = 0.957$

2-hour glucose value vs. the IDF definition (prevalence of 30.4%)
- Sensitivity: 70.8% vs. 70.3%, $p = 0.895$
- FPR: 25.3% vs. 25.4%, $p = 0.962$

2-hour glucose value vs. the WHO definition (prevalence of 19.0%)
- Sensitivity: 59.8% vs. 54.9%, $p = 0.216$
- FPR: 13.8% vs. 14.4%, $p = 0.559$

Figure 1—*ROC curve for predicting diabetes for the 2-h glucose value and sensitivity and FPR of IGT, IFG, and metabolic syndrome. The ATPIII definition was less sensitive* ($P < 0.001$) *and more specific* ($P < 0.001$) *than the IDF definition. The difference in sensitivity between ATPIII and WHO definitions was close to significant* ($P = 0.058$), *but the WHO definition was more specific* ($P = 0.014$).

our study may have misclassification and could underestimate the risk of CVD (bias toward the null hypothesis). Even so, our results are consistent with expected CVD risks for each one of the NCEP risk factor categories.

In summary, ATPIII, IDF, and WHO definitions of the metabolic syndrome have a similar ability to predict incident CVD and diabetes, even though they have different sensitivity and FPR. The metabolic syndrome is a simple method that can be used to identify individuals who are free of CHD and/or CHD risk equivalents but who are at increased risk for future CVD risk. This might be a step forward over routine Framingham risk scoring in some subjects. It is not that Framingham scoring is not as robust in risk prediction (it is definitively better in men). However, the metabolic syndrome may complement Framingham scoring for men aged ≥45 years and women aged ≥55 years. Finally, the metabolic syndrome is particularly useful for predicting diabetes; its ability is not fully explained by glucose intolerance.

Table 3—*Diabetes risk stratified by IFG and metabolic syndrome (7.4 years incident diabetes)*

Fasting glucose level	ATPIII metabolic syndrome	OR (95% CI)
Normal	No	Ref.
Normal	Yes	5.03 (3.39–7.48)
IFG	No	7.07 (3.32–15.1)
IFG	Yes	21.0 (13.1–33.8)
Fasting glucose level	**IDF metabolic syndrome**	**OR (95% CI)**
Normal	No	Ref.
Normal	Yes	4.51 (3.05–6.68)
IFG	No	10.5 (5.50–24.3)
IFG	Yes	21.5 (13.3–34.8)

Results adjusted for age, sex, ethnic origin, and family history of diabetes.

Acknowledgments— This work was supported by grants from the National Heart, Lung, and Blood Institute (RO1-HL24799 and RO1-HL36820).

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