

Design and Validation of a Population-Based Definition of the Metabolic Syndrome

CARLOS A. AGUILAR-SALINAS, MD¹
ROSALBA ROJAS, MD²
CLICERIO GONZALEZ-VILLALPANDO, MD³
FRANCISCO J. GÓMEZ-PÉREZ, MD¹

ROOPA MEHTA, MD¹
GUSTAVO OLAIZ, MD, PHD²
JUAN A. RULL, MD¹
DAVID R. COX, MD, PHD⁴

OBJECTIVE — The National Cholesterol Education Program (NCEP) definition of the metabolic syndrome was modified to be described as a continuous variable and adapted to the characteristics of a Hispanic population.

RESEARCH DESIGN AND METHODS — Age/sex population percentiles for every component of the NCEP criteria were included in this approach using population-based data from a Mexican nationwide survey (2,158 subjects). One point was given per decile for every component. The total number of points accumulated was used to classify subjects. The predictive power for incident diabetes was evaluated using the 7-year follow-up results of the Mexico City Diabetes Study.

RESULTS — Our population-based method had a significantly better prognostic power compared with the original and the updated NCEP definitions (area under the receiver operating characteristic curve 0.746 vs. 0.697 and 0.723, respectively, $P < 0.05$). Using individuals with ≤ 1 component of the NCEP definition as reference, the odds ratio was greater in the upper quartile of the points scale (≥ 39 points) (12.71 [95% CI 5.67–28.49]) compared with that calculated for the original (9.52 [4.69–19.31]) and the updated (11.14 [5.33–23.30]) NCEP criteria. The major advantage of our approach is the detection of subjects at the extremes of the range of diabetes risk and the ability to estimate this risk as a continuum.

CONCLUSIONS — Our method adapts the NCEP criteria to the characteristics of a Hispanic population. It improves the predictive power of the NCEP criteria for future diabetes.

Diabetes Care 29:2420–2426, 2006

The concept of the metabolic syndrome integrates, in a single diagnosis, the abnormalities associated with insulin resistance and/or abdominal obesity that precede type 2 diabetes and lead to increased cardiovascular morbidity (1–3). The definition of this disorder is an area fueled by controversy (4). Primarily, significant conceptual differences exist between the currently available definitions (5,6). Furthermore, the thresholds for defining abnormality of the

individual components vary. The National Cholesterol Education Program (NCEP) criteria (6) have been criticized because identification of those affected is strongly influenced by ethnicity (7). The NCEP thresholds were selected based on evidence from studies in Caucasian populations; variability among ethnic groups was not taken into account. For example, the thresholds for BMI, waist circumference and HDL cholesterol are probably different in Asian and Hispanic popula-

tions (8–11). If the definition is modified to acknowledge this fact, a twofold difference in prevalence is found.

Ford (12) evaluated the prognostic ability of the original NCEP definition in various prospective studies and determined an odds ratio (OR) of 1.65 (95% CI 1.38–1.99) for cardiovascular disease and 2.99 (1.96–4.57) for diabetes. However, variability existed between reports depending on the ethnicity and the confounding variables included in the analysis. Although alterations to the NCEP criteria have been suggested (e.g., the International Diabetes Federation definition), agreement between the NCEP and such adjusted definitions is poor (13,14). Regrettably, such alterations were proposed without evaluating the effect on the predictive power of the resulting definition. Hence, the prognostic ability of these adapted definitions tends to vary (14).

The risk for incident diabetes or a cardiovascular event is a progressive function of the variables included in the metabolic syndrome definition. The presence or absence of the condition should not be based on arbitrarily selected threshold values. We propose a new method for defining the metabolic syndrome derived from the distribution of this disorder in a Mexican population-based survey. The majority of the components of the NCEP definition have been included (BMI was used instead of waist circumference) in this new approach. The age/sex distribution curve for each variable in the population-based survey was divided into deciles. An increasing number of points were given per decile of each curve. The total number of points accumulated is used to define the metabolic risk for each case. This population-based definition has been validated using the prospective data from the Mexico City Diabetes Study.

RESEARCH DESIGN AND METHODS

Construction of the population-based definition of the metabolic syndrome

The variables of the NCEP criteria were used because they are easily measurable.

From the ¹Departamento de Endocrinología y Metabolismo del Instituto Nacional de Ciencias Médicas y Nutrición “Salvador Zubirán,” Mexico City, Mexico; the ²Instituto Nacional de Salud Pública, Cuernavaca, Morelos, Mexico; the ³Centro de Estudios en Diabetes, American British Coudray Hospital, Mexico City, Mexico; and ⁴Perlegen Sciences, Mountain View, California.

Address correspondence and reprint requests to Dr. Rosalba Rojas, National Institute of Public Health, Av. Universidad 655, Col Sta Maria Ahuacatitlan, Cuernavaca, Morelos, C.P. 62508, Mexico. E-mail: rojas@insp.mx.

Received for publication 20 March 2006 and accepted in revised form 10 August 2006.

Abbreviations: NCEP, National Cholesterol Education Program; ROC, receiver operating characteristic.

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

DOI: 10.2337/dc06-0611

© 2006 by the American Diabetes Association.

The costs of publication of this article were defrayed in part by the payment of page charges. This article must therefore be hereby marked “advertisement” in accordance with 18 U.S.C. Section 1734 solely to indicate this fact.

BMI was used instead of waist circumference because only the distribution of the former was available (National Survey of Chronic Diseases 1992–1993) (15–18). Our definition is based on the decile distribution of the variables: 1 point is given per decile. The sum of the points (or total number of points) is considered a new variable with the maximum number being 60 (Table 1). Subjects with previously diagnosed hypertension received the maximal points in the diastolic and systolic blood pressure scales. For hyperlipidemic subjects under medical treatment, maximal points were also allocated in the triglycerides and HDL scales. Individuals with diabetes were excluded.

National Survey of Chronic Diseases 1992–1993

This is a cross-sectional, population-based, nationwide study including 15,607 subjects designed to describe the prevalence of the most common cardiovascular risk factors and metabolic disorders. The methodology is described in detail in a previous article (16). The sample was representative of the Mexican urban population. Only the results of nondiabetic subjects sampled after a 9- to 12-h fast were analyzed for this article ($n = 2,099$). A standardized questionnaire was used to obtain demographic and socioeconomic information. Body weight and blood pressure measurements were also taken. Blood samples were drawn from each subject and analyzed in the Instituto Nacional de Ciencias Médicas y Nutrición “Salvador Zubirán.” These data were used to construct our population-based approach as discussed above.

The Mexico City Study

This is a population-based study designed to characterize the prevalence and natural history of type 2 diabetes in a low-income urban population located in Mexico City. The methodology has been described in detail elsewhere (19–22) and was similar to that used in the National Survey of Chronic Diseases. A total of 3,326 study-eligible subjects were identified. Of these, 2,813 completed a home interview, and 2,282 (68.6%) completed a baseline medical examination. At follow-up, 7 years later, 1,764 (77.3%) were interviewed; of these, 1,584 were nondiabetic at baseline. We analyzed these subjects. Blood samples were drawn for the measurement of serum lipids, fasting plasma glucose, and 2-h postchallenge glucose. Laboratory analyses were conducted in the University

of Texas Health Science Center (19). Data from this study was used to validate our population-based approach.

Definitions

Diabetes was considered present in subjects with a fasting glucose value ≥ 7 mmol/l or a 2-h postchallenge glucose value ≥ 11.1 mmol/l or in those receiving glucose-lowering medication. Hyperinsulinemia was defined as a fasting insulin concentration ≥ 21 μ U/ml; this value corresponds to the 75th percentile in Mexican adults (17). The original (6) and the updated NCEP III criteria (23) were applied for the diagnosis of the metabolic syndrome. BMI ≥ 30 kg/m² was used instead of the increased waist circumference criterion, because these data were not available in National Survey of Chronic Diseases.

Statistical analysis

Significance of the differences between the subgroups of the population was tested by one-way ANOVA using Scheffé's multiple comparison method. Multiple logistic regression models were carried out to calculate the odds ratio for incident diabetes. We constructed receiver operating characteristic (ROC) curves and computed the areas under the curve for the population-based method and for the original and updated versions of the NCEP criteria (subjects were stratified by the number of components: ≤ 1 , 2, and ≥ 3). All statistical analyses were conducted using SAS statistical package 9.0 (SAS Institute, Cary, NC).

RESULTS— Our population-based approach is constructed from the distribution of the NCEP III criteria variables reported in the National Survey of Chronic Diseases 1992–1993. The distribution of these variables is expressed as deciles (Table 1) with 1 point being given per decile. The sum of these points is used for estimating risk of diabetes. This example clarifies the method: a 28-year-old man with a BMI of 27.7 kg/m², HDL cholesterol of 0.63 mmol/l, triglycerides of 3.37 mmol/l, fasting glycemia of 5.38 mmol/l, and blood pressure of 120/80 mmHg collects 43 points. This subject falls within the 80th and 90th percentile when classified according to the total number of points accumulated; he would not be considered to be affected by the NCEP definition.

In the National Survey of Chronic Diseases, 542 individuals fulfilled the

original NCEP criteria. The updated NCEP version detected a further 88 patients ($n = 630$). Table 2 shows how all subjects are distributed into percentiles as illustrated above; data are stratified according to the presence of the metabolic syndrome. More than 60% of the patients identified with the original NCEP criteria (379 of 542, 69.9%) had a total number of points in the upper quintile of the scale; this percentage was smaller than with the updated NCEP definition (412 of 630, 65.3%). The majority of the remaining patients identified with the NCEP definitions fell within the 50th–79th percentile; very few were < 50 th percentile. On further analysis, 147 of the 559 individuals who fell in the upper quintile were not identified as affected by either of the NCEP definitions; they had an adverse metabolic profile, but all of them fulfilled only two NCEP criteria. Therefore, the population-based method provides complementary information for individuals with ≤ 2 NCEP components.

We evaluated the ability of the population-based definition to detect individuals with hyperinsulinemia (fasting insulin > 75 th percentile). The prevalence of hyperinsulinemia grew as the total number of points increased (Table 2); 234 of the 533 (43.9%) individuals with hyperinsulinemia had a total number of points in the upper quintile. Similar proportions were identified by both the original NCEP definition ($n = 231$ individuals, 43.4%) and the updated version ($n = 265$, 49.7%). The sensitivity (0.43 and 0.49 vs. 0.44), specificity (0.80 and 0.76 vs. 0.79), and positive predictive value (0.42 and 0.42 vs. 0.41) were almost the same for all three methods. To compare the predictive power for incident diabetes of the NCEP and the population-based method, results from the Mexico City Diabetes Study were evaluated (Table 3). Of the 1,584 subjects who completed this study, 451 (28.5%) fulfilled the original NCEP criteria for the metabolic syndrome at baseline; using the updated NCEP definition, 47 additional subjects were considered affected ($n = 498$, 31.4%). On follow-up, incident diabetes was diagnosed in 7.6% of the participants. Of these 117 subjects with incident cases of diabetes, 68 had the metabolic syndrome according to the original NCEP criteria syndrome at baseline (OR 3.92 [95% CI 2.67–5.77]). Hence, for the prediction of incident diabetes, the sensitivity, specificity, and positive predictive value of the NCEP criteria were 0.58,

Definition of metabolic syndrome

Table 1—Percentile distribution of the variables included in the NCEP definition of the metabolic syndrome found in a population-based, nationwide Mexican survey

	Decile									
	10 (1)	20 (2)	30 (3)	40 (4)	50 (5)	60 (6)	70 (7)	80 (8)	90 (9)	>90 (10)
BMI (kg/m ²) points										
Men										
20–29 years	20.04	21.36	22.12	23.05	23.81	24.91	26.17	27.73	30.47	>30.47
30–39 years	21.45	22.77	23.62	24.43	25.09	26.33	27.45	28.66	30.47	>30.47
40–49 years	22.15	23.61	24.76	25.83	26.55	27.84	29.03	30.87	32.98	>32.98
50–59 years	20.83	23.14	24.77	25.95	26.70	27.17	29.06	30.09	32.11	>32.11
60–69 years	20.74	22.36	23.00	25.31	26.51	26.94	28.75	29.70	33.98	>33.98
Women										
20–29 years	19.71	20.94	22.07	22.99	23.93	25.09	26.68	28.21	30.84	>30.84
30–39 years	21.51	23.12	24.13	25.72	26.48	27.56	28.95	30.70	33.78	>33.78
40–49 years	23.33	24.77	25.94	26.91	28.10	29.48	30.80	32.46	36.51	>36.51
50–59 years	22.93	24.41	25.86	27.59	29.21	30.86	32.67	34.43	37.89	>37.89
60–69 years	21.77	23.13	24.49	25.55	26.15	28.53	29.55	30.91	33.67	>33.67
Fasting glucose (mmol/l) points										
Men										
20–29 years	4.27	4.55	4.66	4.83	4.94	5.11	5.27	5.44	5.72	>5.72
30–39 years	4.38	4.55	4.66	4.88	5.00	5.22	5.33	5.50	5.83	>5.83
40–49 years	4.44	4.66	4.88	4.94	5.11	5.22	5.44	5.61	6.00	>6.00
50–59 years	4.27	4.61	4.83	5.05	5.11	5.38	5.66	5.88	6.05	>6.05
60–69 years	4.55	4.72	4.94	5.22	5.27	5.38	5.61	5.77	6.05	>6.05
Women										
20–29 years	4.05	4.27	4.44	4.61	4.72	4.83	4.94	5.11	5.38	>5.38
30–39 years	4.11	4.38	4.55	4.72	4.83	5.00	5.16	5.38	5.66	>5.66
40–49 years	4.44	4.66	4.77	5.00	5.11	5.27	5.38	5.61	5.88	>5.88
50–59 years	4.61	4.77	4.88	5.11	5.22	5.55	5.83	6.11	6.44	>6.44
60–69 years	4.55	4.72	4.88	5.00	5.22	5.44	5.61	5.77	6.50	>6.50
Systolic blood pressure (mmHg) points										
Men										
20–29 years	112	118	120	122	126	128	132	134	143	>143
30–39 years	112	116	120	124	128	130	132	134	144	>144
40–49 years	112	122	124	128	130	132	136	142	150	>150
50–59 years	118	122	126	128	132	132	136	142	156	>156
60–69 years	128	132	134	137	140	142	152	161	166	>166
Women										
20–29 years	104	110	112	116	118	122	124	128	132	>132
30–39 years	108	112	114	118	122	124	128	132	141	>141
40–49 years	112	116	120	122	128	132	136	142	152	>152
50–59 years	111	117	122	128	132	137	142	148	159	>159
60–69 years	118	130	136	138	142	144	150	160	172	>172
Diastolic blood pressure (mmHg) points										
Men										
20–29 years	68	74	78	80	82	84	84	90	98	>98
30–39 years	72	78	80	82	83	84	88	92	98	>98
40–49 years	74	80	82	83	84	86	92	98	106	>106
50–59 years	76	82	84	85	86	88	92	96	100	>100
60–69 years	77	81	82	88	91	97	98	99	107	>107
Women										
20–29 years	64	68	72	74	76	78	82	82	88	>88
30–39 years	68	72	76	78	80	82	84	86	94	>94
40–49 years	72	76	78	80	82	84	88	92	102	>102
50–59 years	72	76	78	84	86	90	94	98	102	>102
60–69 years	72	80	82	84	88	94	98	100	110	>110

Continued on following page

Table 1—Continued

	Decile									
	10 (1)	20 (2)	30 (3)	40 (4)	50 (5)	60 (6)	70 (7)	80 (8)	90 (9)	>90 (10)
Triglyceride (mmol/l) points										
Men										
20–29 years	0.68	0.85	0.96	1.12	1.29	1.48	1.71	2.12	3.03	>3.03
30–39 years	0.93	1.15	1.41	1.67	1.88	2.21	2.52	2.94	4.48	>4.48
40–49 years	1.11	1.29	1.48	1.68	1.93	2.08	2.51	3.12	4.07	>4.07
50–59 years	1.24	1.42	1.57	1.69	1.97	2.22	2.48	2.96	3.75	>3.75
60–69 years	0.89	1.13	1.39	1.48	1.69	2.22	2.25	2.82	3.14	>3.14
Women										
20–29 years	0.61	0.74	0.84	0.94	1.12	1.25	1.42	1.71	2.17	>2.17
30–39 years	0.77	0.92	1.05	1.26	1.44	1.59	1.77	2.10	2.58	>2.58
40–49 years	0.81	1.03	1.21	1.41	1.60	1.83	2.08	2.37	3.02	>3.02
50–59 years	0.97	1.15	1.33	1.53	1.67	1.86	2.14	2.56	2.95	>2.95
60–69 years	0.98	1.10	1.25	1.47	1.64	1.73	1.89	2.47	3.62	>3.62
HDL cholesterol (mmol/l) (expressed in inverse order) points										
Men										
20–29 years	1.28	1.19	1.10	1.01	0.92	0.88	0.82	0.73	0.64	<0.64
30–39 years	1.28	1.10	1.01	0.92	0.88	0.82	0.73	0.71	0.64	<0.64
40–49 years	1.19	1.10	1.01	0.92	0.83	0.82	0.73	0.64	0.64	<0.64
50–59 years	1.10	1.01	0.92	0.86	0.82	0.78	0.73	0.68	0.64	<0.64
60–69 years	1.28	1.26	1.15	1.10	1.01	0.92	0.84	0.73	0.64	<0.73
Women										
20–29 years	1.47	1.28	1.19	1.10	1.05	1.01	0.92	0.82	0.73	<0.73
30–39 years	1.38	1.28	1.19	1.10	1.01	0.92	0.86	0.82	0.73	<0.73
40–49 years	1.38	1.28	1.19	1.01	0.96	0.92	0.86	0.82	0.73	<0.73
50–59 years	1.47	1.38	1.19	1.10	1.02	0.92	0.86	0.82	0.73	<0.73
60–69 years	1.56	1.38	1.28	1.19	1.10	1.01	0.92	0.82	0.73	<0.73
Sum of points	6–18	19–22	23–26	27–29	30–32	33–35	36–38	39–42	43–47	48–60

The upper limits of each decile are shown. The lower limits correspond to the value immediately above the previous decile.

0.73, and 0.15, respectively. With the updated NCEP definition, 80 of the 117 subjects with incident cases of diabetes would be considered affected at baseline (5.42 [3.61–8.14]). The sensitivity, specificity, and positive predictive value for the updated definition were 0.68, 0.71, and 0.16, respectively.

Next, we evaluated the population-based method using these follow-up data. The incidence of diabetes was directly proportional to the total number of points

accumulated; the ORs for several strata of the sum of points are shown in Table 3. The risk became significant at >40th percentile (≥ 30 points) compared with the reference group (6–26 points). To have a reasonable comparison between methods, we selected the subjects with ≤ 1 component of the updated version ($n = 457$) as the reference group for all methods. The areas under the ROC curve and OR (Table 3) were calculated. The population-based definition had a significantly

better prognostic power compared with the original and the updated NCEP criteria, based on a greater area under the ROC curve (0.746 vs. 0.697 and 0.723, respectively, $P < 0.05$). Also, the OR was greater in the upper quartile of the sum of points (≥ 39 points; OR 12.71 [95% CI 5.67–28.49]) compared with that found for the original (9.52 [4.69–19.31]) and the updated (11.14 [5.33–23.30]) NCEP definitions.

The population-based definition pro-

Table 2—Agreement between the NCEP definition of the metabolic syndrome and the population-based strategy

Points at baseline stratified by percentiles	Original NCEP definition of the metabolic syndrome		Updated NCEP definition of the metabolic syndrome		Insulin resistance		Total
	Yes	No	Yes	No	Yes	No	
≤ 20	0 (0)	338 (100)	0 (0)	338 (100)	37 (10.9)	301 (89.1)	338
21–50	17 (2.8)	591 (97.2)	32 (5.3)	576 (94.7)	105 (17.3)	503 (82.7)	608
50–79	146 (24.6)	448 (75.4)	186 (31.3)	408 (68.7)	157 (26.4)	437 (73.6)	594
≥ 80	379 (67.8)	180 (32.2)	412 (73.7)	147 (26.3)	234 (41.8)	325 (58.1)	559
Total	542 (25.8)	1,557 (74.2)	630 (30.0)	1,469 (70.0)	533 (25.4)	1,566 (74.6)	2,099

Data are n (%). Percentages are expressed within rows.

Table 3—Population-based strategy as applied to the NCEP definition of the metabolic syndrome and the incidence of type 2 diabetes during the 7-year follow-up of the Mexico City Study

Points at baseline stratified by percentiles (range of points)	n	Incident diabetes	OR (95% CI)	Prevalence at baseline		OR (95% CI) considering subjects with ≤1 component of the updated NCEP definition as reference group
				Original NCEP	Updated NCEP definition	
≤29 (0–26)	800	21 (2.6)	Reference group	47 (5.8)	55 (6.8)	2.26 (0.94–5.39)
30–59 (27–35)	531	50 (9.4)	3.90 (2.34–6.49)	196 (36.9)	221 (41.6)	6.64 (3.12–14.15)
60–79 (36–42)	191	29 (15.2)	6.34 (3.55–11.3)	151 (79.0)	163 (85.3)	10.0 (4.50–22.42)
≥80 (43–60)	62	17 (27.4)	14.1 (7.1–28.3)	57 (91.9)	59 (95.1)	22.4 (9.24–54.51)
Total	1,584	117 (7.6)		451 (29.2)	498 (32.2)	

Data are n (%) unless otherwise indicated. Percentages are expressed within rows. ORs were estimated using logistic regression models.

vides complementary information to the NCEP definitions. It allows us to identify individuals with metabolic syndrome with various rates of incident diabetes. This is demonstrated in Table 4, in which subjects with a 7-year incidence of diabetes as low as 8.5% (original NCEP with <26 points) can be differentiated from others with rates >25% (original NCEP with ≥43 points). All subjects with incident diabetes who had a total number of points in the upper quintile were identified by both NCEP versions. In contrast, subjects with incident diabetes who had a total number of points at baseline in the middle of the range were frequently missed by both NCEP definitions. Logistic regression models were built to estimate the odds ratio for incident diabetes associated with each stratum of the points scale after controlling for the presence of the metabolic syndrome as defined by the original NCEP criteria (Table 4). When this result is compared with the crude OR, the risk estimate was decreased, but remained significant for those with ≥30 points. Similar results were found with the updated NCEP definition (data not shown). In sum, our points system allows us to categorize individuals with meta-

bolic syndrome with various metabolic risk. Furthermore, individuals missed by the current NCEP criteria who are still at significant risk for incident diabetes can also be identified.

CONCLUSIONS— The usefulness of the NCEP metabolic syndrome definition is under debate. The arbitrary selection of its components (including their thresholds) and the categorical nature of the definition are its major weaknesses. Here, we describe a strategy to avoid these drawbacks of the NCEP definition. Instead of interpreting each variable in a dichotomous fashion, each is analyzed as a continuous variable. Individual results are compared against the distribution of the variables encountered in population-based data, with points given per decile for each variable (Table 1). The ability of this approach to detect hyperinsulinemia and for predicting future diabetes was validated with cross-sectional and prospective data. The population-based approach had a better prognostic power for incident diabetes compared with previous versions of the NCEP definition.

The predictive power of the original NCEP criteria for incident diabetes has

been assessed in several epidemiological studies (24–28). In these studies, the OR for incident diabetes at follow-up ranged from 1.95 to 8.8. Hanley et al. (27) compared the ability of various metabolic syndrome definitions for predicting type 2 diabetes in the Insulin Resistance Atherosclerosis Study. They reported that modifications (e.g., including indirect markers of insulin sensitivity) did not significantly improve the predictive power of the original NCEP criteria (OR changing from 4.14 to 5.58). However, the different versions had a 300% disparity in their prevalence results. Thus, the clinical proficiency of the NCEP definition is unlikely to be improved by including additional categorical elements or by changing diagnostic thresholds. Furthermore, Wilson et al. (26) showed that the risk for incident diabetes is already present in individuals fulfilling one or two components of the NCEP criteria; these individuals are not considered to be affected by the currently accepted definition.

The characteristics of a population are best described using information obtained from an unbiased sample (i.e., population-based, nationwide surveys).

Table 4—Population-based strategy provides complementary information to the original and updated versions of the NCEP definitions

Points at baseline stratified by percentiles (range of points)	Incident diabetes among subjects identified by the original NCEP definition		Incident diabetes among subjects identified by the updated NCEP definition		OR (95% CI) considering for the presence of the original NCEP definition*
	Without incident diabetes	Incident diabetes	Without incident diabetes	Incident diabetes	
≤ 29 (0–26)	43 (91.5)	4 (8.5)	50 (90.9)	5 (9.1)	0.87 (0.35–2.09)
30–59 (27–35)	170 (86.7)	26 (13.3)	190 (86.0)	31 (14.0)	4.19 (1.97–8.92)
60–79 (36–42)	130 (86.1)	21 (13.9)	136 (83.4)	27 (16.6)	7.17 (3.23–16.07)
≥80 (43–60)	40 (70.2)	17 (29.8)	42 (71.2)	17 (28.8)	19.12 (7.89–46.57)
Total	383 (84.9)	68 (15.1)	418 (83.9)	80 (16.1)	

Data are n (%). Percentages are expressed within rows. *Subjects with ≤1 component of the updated NCEP definition is the reference group.

In the National Survey of Chronic Diseases, the distributions of the majority of the NCEP criteria variables were measured, stratifying for age (by decades) and sex. Instead of using arbitrary thresholds, we analyze every component as a continuous variable. For practical reasons, the distribution curves were divided into deciles; the result is a total number of points rendered by the number of deciles accumulated by every case. The strategy adjusts for the differences in the distribution of the NCEP variables due to ethnicity, taking into account confounders (i.e., age and sex), and provides a longitudinal estimate of risk. The prevalence of hyperinsulinemia and the OR for incident diabetes are directly proportional to the total number of points. The range of OR is wider and more informative than the single estimate provided by the NCEP definition.

The clinical application of our method may be limited by the necessity for a decile distribution of the variables. The main value of this report may be in research studies. The population-based strategy provides an epidemiological basis for identifying individuals with an extremely low risk for developing diabetes. Such individuals could be used as a valid control group. In addition, the proposed method may be useful for individuals with one or two components of the NCEP definition or for better stratification of risk among patients with metabolic syndrome patients. Subjects who do not fulfill the NCEP definition constitute a heterogeneous group that may have a wide range of risk for incident diabetes (28).

Strengths and limitations should be acknowledged. The cross-sectional survey from which the decile distribution of the variables was obtained and the prospective study in which the method was validated were both carried out in the early 1990s. The populations were comparable and had a similar prevalence of the metabolic syndrome identified by NCEP criteria. The main outcome in the prospective study (i.e., incident diabetes) was assessed using the gold standard test (i.e., a 2-h postchallenge glucose value). Limitations include the applicability of the results to other ethnic groups. However, the conceptual basis of the approach results in improved risk estimation. We could not measure the ability of our method to predict cardiovascular outcomes because of the small number of coronary events in the Mexico City Study.

However, the NCEP definition is a stronger predictor for incident diabetes than for future cardiovascular complications (26). In our analysis, the Mexico City Study data are different from those reported by Stern et al. (29); this is because subjects with incomplete information were excluded.

References

1. Groop L, Orho-Melander M: The dysmetabolic syndrome. *J Intern Med* 250: 105–120, 2001
2. Ford E, Giles W, Dietz W: Prevalence of the metabolic syndrome among US adults. *JAMA* 287:356–359, 2002
3. Meigs J: The metabolic syndrome: may be a guidepost or detour to preventing type 2 diabetes and cardiovascular disease. *BMJ* 327:61–62, 2003
4. Reaven GM: Insulin resistance, cardiovascular disease and the metabolic syndrome: how well do the emperor's clothes fit? *Diabetes Care* 27:1011–1012, 2004
5. Alberti FGMM, Zimmet PZ, the WHO Consultation: Definition, diagnosis and classification of diabetes mellitus and its complications. Part 1: Diagnosis and classification of diabetes mellitus, provisional report of a WHO consultation. *Diabet Med* 15:539–553, 1998
6. Expert Panel on Detection, Evaluation and Treatment of High Blood Cholesterol in Adults: Executive summary of the third report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation and Treatment of High Cholesterol. *JAMA* 285:2486–2497, 2001
7. The International Diabetes Federation: The IDF consensus worldwide definition of metabolic syndrome[article online]. 2005. Available from http://www.idf.org/webdata/docs/MetSyndrome_FINAL.pdf. Accessed 3 May 2005
8. Sanchez-Castillo C, Velázquez-Monroy O, Berber A, Lara A, Tapia Conyer R, James P, the Encuesta Nacional de Salud 2000 Working Group: Anthropometric cutoff points for predicting chronic diseases in the Mexican National Health Survey 2000. *Obes Res* 11:442–451, 2003
9. WHO Expert Consultation: Appropriate body mass index for Asian populations and its implications for policy and intervention strategies. *Lancet* 363:157–163, 2004
10. Liao Y, Kwon S, Shaughnessy S, Wallace P, Hutto A, Jenkins A, Klein R, Garvey WT: Critical evaluation of the Adult Treatment Panel III criteria in identifying insulin resistance with dyslipidemia. *Diabetes Care* 27:978–983, 2004
11. Deurenberg P, Yap M, van Staveren WA: Body mass index and percent body fat: a meta analysis among different ethnic

groups. *Int J Obes Relat Metab Disord* 22: 1164–1171, 1998

12. Ford ES: Risk for all-cause mortality, cardiovascular disease, and diabetes associated with the metabolic syndrome. *Diabetes Care* 28:1769–1778, 2005
13. Tan CE, Ma S, Wai D, Chew SK, Tai ES: Can we apply the National Cholesterol Education Program Adult Treatment Panel definition of the metabolic syndrome to Asians? *Diabetes Care* 27:1182–1186, 2004
14. Ford ES: Prevalence of the metabolic syndrome defined by the International Diabetes Federation among adults in the U.S. *Diabetes Care* 28:2745–2749, 2005
15. Aguilar-Salinas CA, Rojas R, Gómez-Pérez FJ, Valles V, Rios-Torres JM, Franco A, Olaiz G, Rull JA, Sepúlveda J: High prevalence of the metabolic syndrome in México. *Arch Med Res* 35:76–81, 2004
16. Aguilar-Salinas CA, Olaiz G, Valles V, Rios-Torres JM, Gomez-Perez FJ, Rull JA, Rojas R, Franco A, Sepúlveda J: High prevalence of low HDL cholesterol concentrations and mixed hyperlipidemia in a Mexican nationwide survey. *J Lipid Res* 42:1298–307, 2001
17. Aguilar-Salinas CA, Rojas R, Gómez-Pérez FJ, Garcia E, Valles V, Rios-Torres JM, Franco A, Olaiz G, Sepúlveda J, Rull JA: Prevalence and characteristics of early-onset type 2 diabetes in Mexico. *Am J Med* 113:569–574, 2002
18. Valles V, Aguilar-Salinas CA, Gómez-Pérez FJ, Rios-Torres JM, Gomez-Perez FJ, Rull JA, Rojas R, Franco A, Sepúlveda J: Apolipoprotein B and A-I distribution in the Mexican urban adults: results of a nationwide survey. *Metabolism* 51:560–568, 2002
19. Meigs J, Williams K, Sullivan L, Hunt K, Haffner SM, Stern M, Gonzalez Villalpando C, Perhanidis J, Nathan D, D'Agostino R, D'Agostino R, Wilson P: Using metabolic syndrome traits for efficient detection of impaired glucose tolerance. *Diabetes Care* 27:1417–1426, 2004
20. Gonzalez-Villalpando C, Rivera-Martinez D, Cisneros-Castolo M, Gonzalez-Villalpando ME, Simon J, Williams K, Haffner S, Stern M: Seven-year incidence and progression of obesity: characterization of body fat pattern evolution in low-income Mexico City urban population. *Arch Med Res* 34:348–353, 2003
21. Hunt KJ, William K, Rivera D, O'Leary DH, Haffner SM, Stern MP, Gonzalez Villalpando C: Elevated carotid artery intima-media thickness levels in individual who subsequently develop type 2 diabetes. *Arterioscler Thromb Vasc Biol* 23: 1845–1850, 2003
22. Han TS, Sattar N, William K, Gonzalez Villalpando C, Lean ME, Haffner SM: Prospective study of C-reactive protein in relation to the development of diabetes and metabolic syndrome in the Mexico City

Definition of metabolic syndrome

- Diabetes Study. *Diabetes Care* 25:2016–2021, 2002
23. Grundy SM, Hansen B, Smith S, Cleeman JI, Kahn RA: Clinical management of metabolic syndrome. Report of the American Heart Association/National Heart, Lung, and Blood Institute/American Diabetes Association conference on scientific issues related to management. *Circulation* 109:551–556, 2004
 24. Sattar N, Gaw A, Scherbakova O, Ford I, O'Reilly DS, Haffner SM, Isles C, Macfarlane PW, Packard CJ, Cobbe SM, Shepherd J: Metabolic syndrome with and without C-reactive protein as a predictor of coronary heart disease and diabetes in the West of Scotland Coronary Prevention Study. *Circulation* 108:414–419, 2003
 25. Wannamethee SG, Shaper G, Lennon L, Morris R: Metabolic syndrome vs Framingham risk score for prediction of coronary heart disease, stroke and type 2 diabetes. *Arch Intern Med* 165:2644–2650, 2005
 26. Wilson P, D'Agostino R, Parise H, Sullivan L, Meigs J: Metabolic syndrome as a precursor of cardiovascular disease and type 2 diabetes mellitus. *Circulation* 112:3066–3072, 2005
 27. Hanley A, Karter A, Williams K, Festa A, D'Agostino R, Wagenknecht L, Haffner SM: Prediction of type 2 diabetes mellitus with alternative definitions of the metabolic syndrome. *Circulation* 112:3713–3721, 2005
 28. Malik S, Wong N, Franklin S, Kamath T, L'Italien G, Pio J, Rhys William G: Impact of the metabolic syndrome on mortality from coronary heart disease, cardiovascular disease and all causes in United States adults. *Circulation* 110:1245–1250, 2004
 29. Stern MP, Williams K, Gonzalez-Villalpando C, Hunt KJ, Haffner SM: Does the metabolic syndrome improve identification of individuals at risk of type 2 diabetes and/or cardiovascular disease? *Diabetes Care* 27:2676–2681, 2004