Factor Analysis of Metabolic Syndrome Using Directly Measured Insulin Sensitivity

The Insulin Resistance Atherosclerosis Study

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Factor analysis, a multivariate correlation technique, has been used to provide insight into the underlying structure of metabolic syndrome, which is characterized by physiological complexity and strong statistical intercorrelation among its key variables. The majority of previous factor analyses, however, have used only surrogate measures of insulin sensitivity. In addition, few have included members of multiple ethnic groups, and only one has presented results separately for subjects with impaired glucose tolerance. The objective of this study was to investigate, using factor analysis, the clustering of physiologic variables using data from 1,087 nondiabetic participants in the Insulin Resistance Atherosclerosis Study (IRAS). This study includes information on the directly measured insulin sensitivity index (S_I) from intravenous glucose tolerance testing among African-American, Hispanic, and non-Hispanic white subjects aged 40–69 years at various stages of glucose tolerance. Principal factor analysis identified two factors that explained 28 and 9% of the variance in the dataset, respectively. These factors were interpreted as *1*) a "metabolic" factor, with positive loadings of BMI, waist, fasting and 2-h glucose, and triglyceride and inverse loadings of log(S_I+1) and HDL; and *2*) a "blood pressure" factor, with positive loadings of systolic and diastolic blood pressure. The results were unchanged when surrogate measures of insulin resistance were used in place of log(S_I+1). In addition, the results were similar within strata of sex, glucose tolerance status, and ethnicity. In conclusion, factor analysis identified two underlying factors among a group of metabolic syndrome variables in this dataset. Analyses using surrogate measures of insulin resistance suggested that these variables provide adequate information to explore the underlying intercorrelational structure of metabolic syndrome. Additional clarification of the physiologic characteristics of metabolic syndrome is required as individuals with this condition are increasingly being considered candidates for behavioral and pharmacologic intervention. *Diabetes* 51:2642–2647, 2002

The relationships among type 2 diabetes, insulin resistance, and associated metabolic abnormalities are both physiologically and statistically complex (1,2). Regarding physiology, the multiple feedback mechanisms involved in the maintenance of glucose and lipid homeostasis make it difficult to establish primary events that lead to the subsequent cascade of disorders that characterize metabolic disease (1). Regarding statistics, strong intercorrelation among the variables that are considered to be central features of metabolic syndrome raises complexities in the interpretation of independent associations in multivariate statistical models (2).

Factor analysis has been proposed as an approach that might address some of these challenges (2,3). This multivariate statistical technique reduces a large number of intercorrelated variables to a smaller set of latent or underlying independent factors (2,4). Over the past 7 years, there have been several publications reporting factor analyses of the metabolic syndrome in various populations (2,3,5–19). As reviewed by Meigs (2), a number of common findings have emerged from these studies, including *1*) the identification of between two and four factors; *2*) the loading of insulin on more than one factor, including those that have been interpreted as "glycemia," "obesity," and "dyslipidemia;" and *3*) a separate factor for blood pressure. In addition, studies conducted in the Framingham Offspring and Bogalusa cohorts have reported that factor patterns appear to be relatively stable

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FSIGTT, frequently sampled intravenous glucose tolerance test; HOMA-IR, homeostasis model assessment index of insulin resistance; IGT, impaired glucose tolerance; IRAS, Insulin Resistance Atherosclerosis Study; NGT, normal glucose tolerance; S_I, insulin sensitivity index.

TABLE 1
Baseline anthropometric and metabolic characteristics of nondiabetic subjects in the IRAS (n = 1087)

Variable	
Age (years)	54.8 ± 8.4 (40–69)
BMI (kg/m^2)	28.5 ± 5.7 (14.2–63.3)
Waist circumference (cm)	90.6 ± 12.9 (58.9–167.0)
Fasting glucose (mg/dl)	98.8 ± 11.4 (74.0–139.0)
2-h glucose (mg/dl)	125.2 ± 34.3 (33.0–199.0)
Fasting insulin (μU/ml)	15.8 ± 14.6 (1.0–255.0)
2-h insulin (μU/ml)	100.0 ± 93.3 (2.0–900.0)
HOMA-IR	4.0 ± 4.0 (0.2–73.7)
$S_I \times 10^{-4}$ ($min^{-1} \cdot UU^{-1} \cdot ml^{-1}$)	2.2 ± 2.0 (0.0–19.4)
Triglyceride (mg/dl)	134.8 ± 86.9 (16.0–712.0)
LDL cholesterol (mg/dl)	141.6 ± 34.7 (37.0–299.0)
HDL cholesterol (mg/dl)	47.1 ± 15.3 (11.0–125.0)
Systolic blood pressure (mmHg)	122.4 ± 17.0 (85.0–219.0)
Diastolic blood pressure (mmHg)	77.7 ± 9.3 (41.0–119.0)
Albumin/creatinine ratio (mg/mmol)	14.64 ± 40.6 (1.1–643.1)
Sex (% female)	56.4
Non-Hispanic white/African-American/Hispanic American (%)	40.0/26.5/33.5
IGT (%)	34.0
Hypertensive (%)	32.0
Never/former/current smoker (%)	45.3/38.3/16.5
Premenopausal/perimenopausal/postmenopausal (%)	20.1/26.5/33.5

Data are means ± SD (range) or proportions.

across demographic, metabolic, and lifestyle risk factor subgroups (5,9).

There are, however, a number of gaps in the existing literature on factor analysis of metabolic syndrome. First, there have been only two studies conducted to date that have used direct measures of insulin sensitivity (7,17), and the sample sizes of both of these studies were small (n = 50 and 74, respectively). Second, few published studies have included members of multiple ethnic groups, and none, to our knowledge, have included Hispanic Americans, a population at high risk for type 2 diabetes. Finally, little information is available on whether factor patterns differ between subjects with normal glucose tolerance (NGT) and impaired glucose tolerance (IGT) (5).

The objective of the present study was to investigate, using factor analysis, the clustering of anthropometric and metabolic variables using data from the Insulin Resistance Atherosclerosis Study (IRAS). This observational epidemiologic study includes a multiethnic cohort of middle-aged individuals at various stages of glucose tolerance and has used direct measures of insulin sensitivity (insulin sensitivity index [S_I]) from the frequently sampled intravenous glucose tolerance test (FSIGTT).

RESEARCH DESIGN AND METHODS

Study subjects. The IRAS is a multicenter observational epidemiologic study of the relationships among insulin resistance, cardiovascular disease and its known risk factors in different ethnic groups, and varying states of glucose tolerance. The design and methods of this study have been described in detail in previous publications (20,21). Briefly, the study was conducted at four clinical centers. At centers in Oakland and Los Angeles, CA, non-Hispanic white and African-American subjects were recruited from Kaiser Permanente, a nonprofit health maintenance organization. Centers in San Antonio, TX, and San Luis Valley, CO, recruited non-Hispanic white and Hispanic American subjects from two ongoing population-based studies (the San Antonio Heart Study and the San Luis Valley Diabetes Study) (20). A total of 1,625 individuals participated in the baseline IRAS examination (56% women), which occurred between October 1992 and April 1994. The IRAS protocol was approved by local institutional review committees, and all participants provided written informed consent. The present report includes information on 1,087 individuals who were free of diabetes at baseline and for whom information was available on metabolic variables of interest (Table 1).

Clinical measurements and procedures. The IRAS protocol required two visits, 1 week apart, of ~4 h each. Subjects were asked before each visit to fast for 12 h, to abstain from heavy exercise and alcohol for 24 h, and to refrain from smoking the morning of the examination. During the first visit, a 75-g oral glucose tolerance test was administered, with glucose tolerance status determined using World Health Organization criteria (22). During the second visit, insulin sensitivity and insulin secretion were determined using an FSIGTT with two modifications to the original protocol (23). First, an injection of regular insulin, rather than tolbutamide, was used to ensure adequate plasma insulin levels for the accurate computation of insulin sensitivity across a broad range of glucose tolerance (24). Second, a reduced sampling protocol (with 12 rather than 30 samples) was used for efficiency because of the large number of participants (25). Insulin sensitivity, expressed as S_I, was calculated using mathematical modeling methods (MINMOD version 3.0) (26). The repeatability of S_I has been demonstrated in a subsample of the IRAS cohort (27), and the estimate of S_I from this modified protocol has been validated against gold-standard measures of insulin resistance from the hyperinsulinemic-euglycemic clamp technique (r = 0.95) (28).

Height and weight were measured to the nearest 0.5 cm and 0.1 kg, respectively. BMI (kg/m^2) was used as an estimate of overall adiposity. Waist circumference, a validated estimate of visceral adiposity (29), was measured to the nearest 0.5 cm using a steel tape. Duplicate measures were made following a standardized protocol, and averages were used in the analysis. Resting blood pressure (systolic and fifth-phase diastolic) was recorded with a standard mercury sphygmomanometer after a 5-min rest. The average of the second and third measurements was used. Ethnicity was assessed by self-report.

Laboratory procedures. Glucose concentration was determined using standard methods as previously described (20). Insulin levels were measured using the dextran-charcoal radioimmunoassay (30), which has a 19% external coefficient of variation. This assay displays a high degree of cross-reactivity with proinsulin. The homeostasis model assessment index of insulin resistance (HOMA-IR) was calculated as described by Matthews et al. (31). Plasma lipid and lipoprotein concentrations were determined from fasting plasma samples at the central IRAS laboratory (Medlantic Research Institute, Washington, DC) using the Lipid Research Clinics methodology. Urinary albumin and creatinine concentrations were assessed in a random morning spot urine sample using procedures described previously (32).

Statistical analyses. Means, SDs, and ranges, or proportions, were presented for subjects in the study. Associations between baseline anthropometric and metabolic variables were determined using Spearman correlation analysis.

TABLE 2
Spearman correlation analysis of baseline variables among nondiabetic subjects in the IRAS

	Waist	Fasting glucose	2-h glucose	Fasting insulin	2-h insulin	HOMA-IR	S_I	Triglyceride	HDL	Systolic BP	Diastolic BP	ACR
BMI	0.78	0.33	0.31	0.53	0.38	0.55	−0.54	0.21	−0.22	0.25	0.20	0.08
Waist		0.42	0.32	0.52	0.36	0.55	−0.54	0.30	−0.38	0.27	0.24	0.02
Fasting glucose			0.43	0.37	0.26	0.52	−0.34	0.15	−0.18	0.24	0.15	−0.04
2-h glucose				0.32	0.53	0.37	−0.50	0.28	−0.13	0.22	0.07	0.03
Fasting insulin					0.66	0.98	−0.68	0.34	−0.33	0.20	0.19	0.05
2-h insulin						0.65	−0.67	0.32	−0.26	0.22	0.15	0.08
HOMA-IR							−0.68	0.33	−0.33	0.23	0.20	0.04
S_I								−0.30	0.29	−0.25	−0.16	−0.08
Triglyceride									−0.44	0.07	0.06	−0.01
HDL cholesterol										0.06	−0.05	0.06
Systolic BP											0.57	0.18
Diastolic BP												0.04

$P < 0.0001$ for $r > 0.12$; $P > 0.05$ for $r < 0.06$. ACR, albumin/creatinine ratio; BP, blood pressure.

The distributions of continuous variables were assessed, and log transformations of skewed variables were used in subsequent analyses, as appropriate. Given that some subjects had $S_I = 0$, we used $\log(S_I+1)$ as the transformation for the insulin sensitivity variable. Analyses using the rank transformation of S_I yielded identical results (data not shown). Factor analysis was conducted using the FACTOR procedure of SAS. Principle factor analysis was used to identify the initial set of uncorrelated factors. The number of components to be retained was based on Scree plot analysis (factors above the break in the curve were retained) and eigenvalue criteria (0.9), both of which have been described and recommended elsewhere (2,4,5). Varimax (orthogonal) rotation was used to obtain a set of independent interpretable factors. The resulting factor pattern was interpreted using factor loadings of ≥0.4. The analysis was initially conducted with a set of core variables that are considered central features of metabolic syndrome, including adiposity, fasting and postchallenge glucose concentrations $\log(S_I+1)$, blood pressure, lipid concentrations, and microalbuminuria. The $\log(S_I+1)$ variable was then replaced with HOMA-IR (or fasting and 2-h insulin concentrations) to assess the effect of using surrogate measures of insulin resistance on the factor pattern. These analyses were initially carried out with all nondiabetic subjects pooled. We then re-ran the analysis within strata of sex, glucose tolerance (NGT versus IGT), and ethnicity (non-Hispanic white, African-American, and Hispanic American) to assess the role of these potential effect-modifying variables. Coefficients of congruence (2,4) were calculated to evaluate similarities among loadings on the same factor stratified by these variables.

RESULTS

Table 1 presents baseline anthropometric and metabolic characteristics of nondiabetic subjects in the IRAS. The results of Spearman correlation analyses of baseline variables are presented in Table 2. Fasting insulin and HOMA-IR were significantly associated with S_I (both $r = -0.68$, $P < 0.0001$). In addition, fasting insulin, HOMA-IR, and S_I were each moderately to strongly associated with BMI, waist, and insulin and glucose concentrations.

Table 3 displays the results of factor analysis of core metabolic variables among nondiabetic subjects in the IRAS. A two-factor solution, which was supported by the retention criteria described in RESEARCH DESIGN AND METHODS, explained 37% of the total variance (28% factor 1 and 9% factor 2), and 96% of the common variance in the dataset (73% factor 1 and 23% factor 2). These factors were interpreted as a *1*) "metabolic" factor, with positive loadings of BMI, waist, fasting and 2-h glucose, and log triglyceride and inverse loadings of $\log(S_I+1)$ and HDL; and *2*) a "blood pressure" factor, with positive loadings of systolic and diastolic blood pressure. The results were unchanged when HOMA-IR was substituted for $\log(S_I+1)$ (Table 4) or when fasting and 2-h insulin concentrations were substituted for $\log(S_I+1)$ (data not shown). In these analyses, HOMA-IR and fasting and 2-h insulin had positive loadings on factor 1. We also explored the possibility of a three-factor solution; however, this conclusion was rejected because it did not meet any of the evaluation

TABLE 3
Results of factor analysis of anthropometric and metabolic variables, including directly measured insulin sensitivity from the FSIGTT among nondiabetic subjects in the IRAS

	Factor	
Variable	Metabolic	Blood pressure
BMI	**0.71**	0.24
Waist	**0.81**	0.22
Fasting glucose	**0.44**	0.24
2-h glucose	**0.51**	0.18
Log(S_I+1)	**−0.67**	−0.19
Log triglyceride	**0.44**	−0.09
HDL cholesterol	**−0.46**	0.15
Systolic BP	0.12	**0.71**
Diastolic BP	0.09	**0.61**
Log albumin/creatinine ratio	0.01	0.25
% Total variance	28.1	8.8
% Cumulative variance	28.1	36.9

Loadings ≥0.40 in bold type. BP, blood pressure.

TABLE 4
Results of factor analysis of anthropometric and metabolic variables among nondiabetic subjects in IRAS

	Factor	
Variable	Metabolic	Blood pressure
BMI	**0.72**	0.23
Waist	**0.82**	0.21
Fasting glucose	**0.51**	0.23
2-h glucose	**0.46**	0.16
Log HOMA-IR	**0.66**	0.19
Log triglyceride	**0.44**	−0.08
HDL cholesterol	**−0.46**	0.15
Systolic BP	0.12	**0.70**
Diastolic BP	0.11	**0.62**
Log albumin/creatinine ratio	0.01	0.23
% Total variance	28.4	8.6
% Cumulative variance	28.4	37.0

Loadings ≥0.40 in bold type. BP, blood pressure.

TABLE 5
Results of factor analysis of anthropometric and metabolic variables, including directly measured insulin sensitivity from the FSIGTT, among nondiabetic subjects in the IRAS within strata of sex, glucose tolerance, and ethnicity

	Factor													
	Sex				Glucose tolerance				Ethnicity					
	Men		Women		NGT		IGT		NHW		AA		HA	
Variable	M	BP	M	BP	M	BP	M	BP	M	BP	M	BP	M	BP
BMI	**0.78**	0.23	**0.79**	0.25	**0.70**	0.25	**0.71**	0.37	**0.72**	0.20	**0.71**	0.28	**0.78**	0.05
Waist	**0.84**	0.22	**0.84**	0.25	**0.82**	0.27	**0.79**	0.31	**0.84**	0.18	**0.79**	0.27	**0.85**	0.10
Fasting glucose	0.32	0.25	**0.48**	0.24	0.28	0.29	0.31	0.17	**0.53**	0.07	**0.40**	0.30	**0.44**	0.30
2-h glucose	**0.41**	0.23	**0.58**	0.15	0.31	0.27	0.22	0.01	**0.52**	0.06	**0.49**	0.32	**0.50**	0.17
Log (S_I+1)	**−0.63**	−0.18	**−0.68**	−0.27	**−0.57**	−0.28	**−0.59**	−0.13	**−0.69**	−0.10	**−0.59**	−0.26	**−0.70**	−0.20
Log triglyceride	**0.47**	−0.13	0.39	−0.03	**0.43**	−0.05	0.31	−0.13	**0.48**	−0.09	0.39	−0.04	**0.40**	0.10
HDL cholesterol	**−0.42**	0.23	**−0.43**	0.08	**−0.52**	0.12	**−0.44**	0.11	**−0.49**	0.20	**−0.43**	0.05	−0.37	−0.02
Systolic BP	0.04	**0.76**	0.15	**0.68**	0.07	**0.74**	−0.05	**0.66**	0.17	**0.68**	0.05	**0.71**	0.18	**0.74**
Diastolic BP	0.07	**0.64**	0.04	**0.63**	0.08	**0.62**	0.02	**0.60**	0.13	**0.58**	0.03	**0.59**	0.09	**0.72**
Log albumin/creatinine ratio	0.06	0.30	0.03	0.19	0.01	0.26	0.09	0.25	−0.07	0.23	0.13	0.32	0.04	0.26
% Total variance	26.5	11.2	31.1	7.8	25.7	9.3	22.2	8.7	28.8	8.7	27.9	8.1	29.4	10.0
% Cumulative variance	26.5	37.7	31.1	38.9	25.7	35.0	22.2	30.9	28.8	37.5	27.9	36.0	29.4	39.4

Loadings ≥0.40 in bold type. AA, African-American; BP, blood pressure; HA, Hispanic American; M, metabolic factor; NHW, non-Hispanic white.

criteria described in RESEARCH DESIGN AND METHODS (eigenvalue for third factor, 0.50).

The factor patterns were stable in separate analyses among men and women and among subjects with NGT and IGT, although, in the latter case, positive loadings of fasting and 2-h glucose on factor 1 fell below the 0.40 threshold (Table 5). The factor pattern was also remarkably consistent in separate analyses among non-Hispanic whites, African-Americans, and Hispanics (Table 5). Coefficients of congruence for these subgroup analyses are presented in Table 6 and reflect the similar factor loadings by sex, glucose tolerance status, and ethnicity.

DISCUSSION

In the present study, we used factor analysis to investigate the clustering of variables that are thought to be important components of metabolic syndrome. Two factors emerged (metabolic and blood pressure), and these factors were consistent across sex, glucose tolerance, and ethnic subgroups. These findings have made two major contributions to the literature. First, no other large factor analysis study has included information on directly measured S_I. Despite the fact that surrogate measures of insulin resistance (such as HOMA-IR and fasting insulin) correlate only moderately with S_I, our study demonstrates that they yield factor analysis results that are very similar to those using direct measures. This observation is of substantial importance for large epidemiologic and clinical studies in which surrogate measures are the only option. Second, the IRAS included non-Hispanic whites, African-Americans, and Hispanics. These latter two ethnic groups experience high rates of metabolic syndrome and type 2 diabetes; however, less is known about the epidemiology and pathogenesis of the disease in these individuals.

TABLE 6
Similarity of factor loading patterns among subgroups of sex, glucose tolerance, and ethnicity

	Coefficient of congruence	
Subgroups	Metabolic factor	Blood pressure factor
Men vs. women	0.99	0.98
NGT vs. IGT	0.99	0.95
NHW vs. HA	0.99	0.92
NHW vs. AA	0.98	0.93
HA vs. AA	0.99	0.94

Measures are coefficients of congruence (see refs. 2 and 4) that range from 0 to 1 and can be interpreted in a similar fashion as correlation coefficients (1 = perfect agreement among subgroups; 0 = no agreement). AA, African American; HA, Hispanic American; NHW, non-Hispanic white.

Our analyses yielded only two factors, which is unusual but not unprecedented in the literature. The majority of studies of core metabolic variables have reported three to four factors, although three reports have reported two factors (9,17,18). There do not appear to be any design or demographic characteristics that distinguish these two-factor studies from the others, although there is some evidence to suggest a modest positive association between the number of factors and mean age of the study subjects. Our results are highly consistent with the literature in the identification of a separate blood pressure factor (2). Although the microalbuminuria variable did not load clearly on either of the two factors identified in the present analysis, it did have borderline loadings (>0.30) on the blood pressure factor among men and African-Americans in subgroup analyses. Thus, the presence of microalbuminuria in the metabolic syndrome phenotype may differ by sex and ethnicity.

As reviewed by Meigs (2), the identification of only one underlying factor in a factor analysis of metabolic variables might be interpreted as support for the "unity hypothesis," which suggests that a single pathophysiologic process (in this case insulin resistance) accounts for the observed risk variable clustering. Identification of two or more factors would suggest the rejection of this hypothesis. Our results imply that at least two pathophysiologic processes are operating and that reduced insulin sensitivity is an important component of the anthropometric, dysglycemic, and dyslipidemic aspects of metabolic syn-

drome. The loading pattern of our first factor (anthropometry, glucose, insulin sensitivity, and lipids) is similar to some (9,18), but not all, previous studies. Those that reported three or four factors tended to have separate factors for body mass, lipids, and insulin/glucose (3,6,16).

The present study is the largest of only three published to date to have used a direct measure of insulin sensitivity (7,17). S_I loaded strongly on the first factor together with measures of glucose, lipids, and adiposity, all of which are well-established components of the insulin resistance syndrome. We found that factor patterns in our study were similar when either HOMA-IR or fasting and 2-h insulin concentrations were substituted for S_I. Similarly, Donahue et al. (17) reported that the addition of the *M* value from a euglycemic-hyperinsulinemic clamp to their analysis (which included fasting insulin) did not markedly change the resulting factor patterns. These findings lend additional support to evidence from studies examining correlations with direct measures, suggesting that fasting insulin concentration and the HOMA-IR index are reasonable surrogate measures of insulin resistance for use in large epidemiologic studies among nondiabetic subjects (33,34).

Very few previous studies reporting results of factor analysis have included individuals from multiple ethnic groups (9,14,17). To our knowledge, this is the first investigation to have included Hispanic Americans, a population known to be at high risk for type 2 diabetes and associated metabolic disorders (35). We found that the factor patterns among Hispanic Americans were similar to those in non-Hispanic whites and African-Americans. In addition, factor patterns among African-Americans were similar to those in the other two ethnic groups. Two previous factor analysis studies from the Bogalusa Heart Study reported factor patterns that were generally similar among black and white children, adolescents, and young adults (9,14). Minor ethnic differences in these studies included slightly lower loadings of glucose, insulin, and ponderal index on the blood pressure factor among blacks, as well as no loading of renin with the insulin resistance factor in this ethnic group.

Previous studies have reported differences in factor patterns between diabetic and nondiabetic subjects (6,8). However, only one previous study of nondiabetic subjects has presented results separately for those with NGT and IGT (5). An understanding of metabolic clustering among individuals with IGT is of interest given the outcomes of recent clinical trials demonstrating that progression from IGT to diabetes was markedly reduced among subjects in intensive lifestyle or pharmacologic intervention groups (36–38). Factor patterns in the present study were very similar in a separate analysis of subjects with NGT and IGT, suggesting that differences in metabolic clustering (as reflected in the factor loading patterns) do not become apparent until diabetes has fully developed.

In conclusion, factor analysis identified two underlying factors among a group of metabolic syndrome variables, including directly measured S_I, in a multiethnic cohort of nondiabetic middle-aged subjects. These factors appeared to be stable across sex, glucose tolerance, and ethnic subgroups. The findings were very similar using indirect measures of insulin resistance, which suggests that these surrogate measures provide adequate information to explore the underlying intercorrelational structure of metabolic syndrome. These findings suggest that metabolic syndrome is likely comprised of two distinct pathophysiologic factors, the dominant one accounting for 30% of the total variance and the subordinate one ~10% of the variance. The dominant "metabolic" factor is comprised of anthropometric and metabolic variables and the subordinate "blood pressure" factor includes systolic and diastolic blood pressure. Although a correlate of the dominating "metabolic" factor, blood pressure may be only a secondary player that is correlated with the metabolic and anthropometric variables without sharing a common pathology.

Patients with metabolic syndrome who are free of clinical disease are increasingly being considered candidates for behavioral interventions and newer generation therapies targeting insulin resistance. Specifying a robust parsimonious case definition for metabolic syndrome is critical to these evolving interventions and to subsequent measurement of treatment effects on metabolic syndrome.

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