

# Joint Scientific Statement

## Harmonizing the Metabolic Syndrome

### A Joint Interim Statement of the International Diabetes Federation Task Force on Epidemiology and Prevention; National Heart, Lung, and Blood Institute; American Heart Association; World Heart Federation; International Atherosclerosis Society; and International Association for the Study of Obesity

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**Abstract**—A cluster of risk factors for cardiovascular disease and type 2 diabetes mellitus, which occur together more often than by chance alone, have become known as the metabolic syndrome. The risk factors include raised blood pressure, dyslipidemia (raised triglycerides and lowered high-density lipoprotein cholesterol), raised fasting glucose, and central obesity. Various diagnostic criteria have been proposed by different organizations over the past decade. Most recently, these have come from the International Diabetes Federation and the American Heart Association/National Heart, Lung, and Blood Institute. The main difference concerns the measure for central obesity, with this being an obligatory component in the International Diabetes Federation definition, lower than in the American Heart Association/National Heart, Lung, and Blood Institute criteria, and ethnic specific. The present article represents the outcome of a meeting between several major organizations in an attempt to unify criteria. It was agreed that there should not be an obligatory component, but that waist measurement would continue to be a useful preliminary screening tool. Three abnormal findings out of 5 would qualify a person for the metabolic syndrome. A single set of cut points would be used for all components except waist circumference, for which further work is required. In the interim, national or regional cut points for waist circumference can be used. (*Circulation*. 2009;120:1640-1645.)

**Key Words:** AHA Scientific Statements ■ metabolic syndrome ■ risk factors ■ diabetes mellitus

The metabolic syndrome is a complex of interrelated risk factors for cardiovascular disease (CVD) and diabetes. These factors include dysglycemia, raised blood pressure,

elevated triglyceride levels, low high-density lipoprotein cholesterol levels, and obesity (particularly central adiposity). The associations and clustering of these factors have been

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known for decades. Recent interest has focused on the possible involvement of insulin resistance as a linking factor, although the pathogenesis remains unclear, as does the establishment of diagnostic criteria. With these risk factors, it has been demonstrated clearly that the syndrome is common and that it has a rising prevalence worldwide, which relates largely to increasing obesity and sedentary lifestyles. As a result, the metabolic syndrome is now both a public health and a clinical problem. In the public health arena, more attention must be given to modification of lifestyles of the general public of all nations to reduce obesity and to increase physical activity. At a clinical level, individual patients with the metabolic syndrome need to be identified so that their multiple risk factors, including lifestyle risk factors, can be reduced.

Although there is general agreement in the medical community that obesity and its medical complications, including the metabolic syndrome, deserve greater attention, there has been considerable disagreement over the terminology and diagnostic criteria related to the metabolic syndrome. Despite this disagreement, there appears to be a consensus in the medical field that the term *metabolic syndrome* is acceptable for the condition of the presence of multiple metabolic risk factors for CVD and diabetes. On the other hand, several clinical definitions of the metabolic syndrome have been proposed. This has led to some confusion on the part of clinicians regarding how to identify patients with the syndrome. Some controversy also exists about whether the metabolic syndrome is a true syndrome or a mixture of unrelated phenotypes. A syndrome is simply a clustering of factors that occur together more often than by chance alone and for which the cause is often uncertain. The metabolic syndrome fulfills these criteria. The metabolic syndrome is not an absolute risk indicator, because it does not contain many of the factors that determine absolute risk, for example, age, sex, cigarette smoking, and low-density lipoprotein cholesterol levels. Nonetheless, patients with the metabolic syndrome are at twice the risk of developing CVD over the next 5 to 10 years as individuals without the syndrome. The risk over a lifetime undoubtedly is even higher. Furthermore, the metabolic syndrome confers a 5-fold increase in risk for type 2 diabetes mellitus. The most widely recognized of the metabolic risk factors are atherogenic dyslipidemia, elevated blood pressure, and elevated plasma glucose. In addition, persons with these characteristics commonly manifest a prothrombotic state and a proinflammatory state. Atherogenic dyslipidemia consists of an aggregation of lipoprotein abnormalities that includes elevated serum triglyceride and apolipoprotein B, increased small low-density lipoprotein particles, and a reduced level of high-density lipoprotein cholesterol. Most persons with the metabolic syndrome have abdominal obesity and insulin resistance. Both of the latter conditions appear to contribute to the development of metabolic risk factors, although the mechanisms underlying these contributions are not fully understood.

The first formalized definition of the metabolic syndrome was proposed in 1998 by a consultation group on the

definition of diabetes for the World Health Organization (WHO).<sup>1</sup> This group emphasized insulin resistance as the major underlying risk factor and required evidence of insulin resistance for diagnosis. A diagnosis of the syndrome by WHO criteria could thus be made on the basis of several markers of insulin resistance plus 2 additional risk factors, including obesity, hypertension, high triglyceride level, reduced high-density lipoprotein cholesterol level, or microalbuminuria. Patients with type 2 diabetes mellitus were not excluded from diagnosis. The other major criteria came from the National Cholesterol Education Program Adult Treatment Panel III (ATP III)<sup>2</sup> in 2001. ATP III criteria did not require demonstration of insulin resistance per se. Moreover, no single factor was required for diagnosis, but instead, ATP III made the presence of 3 of the following 5 factors the basis for establishing the diagnosis: Abdominal obesity (which is highly correlated with insulin resistance), elevated triglyceride, reduced high-density lipoprotein cholesterol, elevated blood pressure, and elevated fasting glucose (impaired fasting glucose or type 2 diabetes mellitus). In the absence of CVD or diabetes, the metabolic syndrome is a predictor of these conditions. Once CVD or diabetes develops, the metabolic syndrome is often present, and the number of components of the metabolic syndrome contributes to disease progression and risk.

In 2005, both the International Diabetes Federation (IDF)<sup>3</sup> and the American Heart Association/National Heart, Lung, and Blood Institute (AHA/NHLBI)<sup>4</sup> attempted to reconcile the different clinical definitions. In spite of this effort, their separate recommendations contained differences related to waist circumference. The IDF dropped the WHO requirement for insulin resistance but made abdominal obesity necessary as 1 of 5 factors required in the diagnosis, with particular emphasis on waist measurement as a simple screening tool; the remainder of the criteria were essentially identical to those provided by ATP III. The AHA/NHLBI slightly modified the ATP III criteria but did not mandate abdominal obesity as a required risk factor. The remaining 4 risk factors were identical in definition to those of the IDF. Moreover, there was no agreement on the definition of abdominal obesity between the IDF and AHA/NHLBI. The IDF recommended that the threshold for waist circumference to define abdominal obesity in people of European origin (Europids) should be  $\geq 94$  cm for men and  $\geq 80$  cm for women; the AHA/NHLBI, in contrast, recommended cut points of  $\geq 102$  and  $\geq 88$  cm, respectively, for the 2 sexes. The latter values are consistent with the definitions of abdominal obesity found in National Institutes of Health obesity guidelines,<sup>5</sup> which equate to a body mass index of approximately 30 kg/m<sup>2</sup> in males. The IDF values are closer to a body mass index of 25 kg/m<sup>2</sup> in males. The IDF guidelines also stressed the need to adopt different values for waist measurement in different ethnic groups based on the relationship of waist measurement either to the other metabolic syndrome components or to longer-term outcome studies such as those on the risk of type 2 diabetes mellitus and CVD.

Recently, IDF and AHA/NHLBI representatives held discussions to attempt to resolve the remaining differences between definitions of metabolic syndrome. Both sides

**Table 1. Criteria for Clinical Diagnosis of the Metabolic Syndrome**

Measure	Categorical Cut Points
Elevated waist circumference*	Population- and country-specific definitions
Elevated triglycerides (drug treatment for elevated triglycerides is an alternate indicator†)	≥150 mg/dL (1.7 mmol/L)
Reduced HDL-C (drug treatment for reduced HDL-C is an alternate indicator†)	<40 mg/dL (1.0 mmol/L) in males; <50 mg/dL (1.3 mmol/L) in females
Elevated blood pressure (antihypertensive drug treatment in a patient with a history of hypertension is an alternate indicator)	Systolic ≥130 and/or diastolic ≥85 mm Hg
Elevated fasting glucose‡ (drug treatment of elevated glucose is an alternate indicator)	≥100 mg/dL

HDL-C indicates high-density lipoprotein cholesterol.

\*It is recommended that the IDF cut points be used for non-Europeans and either the IDF or AHA/NHLBI cut points used for people of European origin until more data are available.

†The most commonly used drugs for elevated triglycerides and reduced HDL-C are fibrates and nicotinic acid. A patient taking 1 of these drugs can be presumed to have high triglycerides and low HDL-C. High-dose  $\omega$ -3 fatty acids presumes high triglycerides.

‡Most patients with type 2 diabetes mellitus will have the metabolic syndrome by the proposed criteria.

agreed that abdominal obesity should not be a prerequisite for diagnosis but that it is 1 of 5 criteria, so that the presence of any 3 of 5 risk factors constitutes a diagnosis of metabolic syndrome. This would result in the common definition shown in Table 1.

Defining thresholds for abdominal obesity is complicated, in part because of differences in the relation of abdominal obesity to other metabolic risk factors. In

addition, predictive values for various levels of abdominal obesity for CVD and diabetes may differ. There is also the problem of generating cut points for continuous variables, although this is true for all components of the syndrome. However, what is particularly needed is evidence based on both cross-sectional and longitudinal data relating waist circumference to risk for both CVD and type 2 diabetes. It is clear that there are and will continue to be differences between sexes and ethnic groups. In addition, there is the practical consideration of what threshold justifies the expenditure of national medical resources for clinical intervention (eg, nutritional and physical activity counseling) in contrast to public health intervention. Of course, this does not mean that there should not be agreed-upon international criteria based on evidence but rather that a particular health system might adopt different cutoff points locally for pragmatic or economic reasons. Long-term prospective studies are required to reach more reliable waist circumference cut points for different ethnic groups, particularly for women.

Neither ATP III nor IDF criteria excluded hyperglycemia in the diabetes range as 1 of the 5 criteria for diagnosis of the metabolic syndrome. By these criteria, most patients with type 2 diabetes mellitus have the metabolic syndrome. Moreover, those with type 2 diabetes mellitus are at higher long-term risk for developing CVD. The same is true for patients with type 1 diabetes mellitus. Therefore, any patient with diabetes mellitus who has other metabolic risk factors should be treated with lifestyle intervention, followed by drugs if necessary, to favorably modify other components of the syndrome.

Table 2 shows current international recommendations proposed by the IDF for thresholds of abdominal obesity to be used as 1 component of the metabolic syndrome.<sup>3</sup> Table 2 also lists waist circumference thresholds currently being recommended in several different populations and ethnic

**Table 2. Current Recommended Waist Circumference Thresholds for Abdominal Obesity by Organization**

Population	Organization (Reference)	Recommended Waist Circumference Threshold for Abdominal Obesity	
		Men	Women
Europid	IDF (4)	≥94 cm	≥80 cm
Caucasian	WHO (7)	≥94 cm (increased risk)	≥80 cm (increased risk)
		≥102 cm (still higher risk)	≥88 cm (still higher risk)
United States	AHA/NHLBI (ATP III)* (5)	≥102 cm	≥88 cm
Canada	Health Canada (8,9)	≥102 cm	≥88 cm
European	European Cardiovascular Societies (10)	≥102 cm	≥88 cm
Asian (including Japanese)	IDF (4)	≥90 cm	≥80 cm
Asian	WHO (11)	≥90 cm	≥80 cm
Japanese	Japanese Obesity Society (12)	≥85 cm	≥90 cm
China	Cooperative Task Force (13)	≥85 cm	≥80 cm
Middle East, Mediterranean	IDF (4)	≥94 cm	≥80 cm
Sub-Saharan African	IDF (4)	≥94 cm	≥80 cm
Ethnic Central and South American	IDF (4)	≥90 cm	≥80 cm

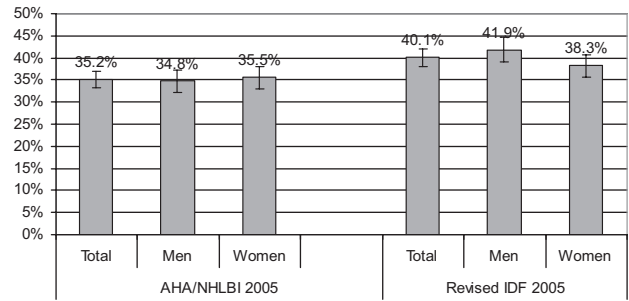
\*Recent AHA/NHLBI guidelines for metabolic syndrome recognize an increased risk for CVD and diabetes at waist-circumference thresholds of ≥94 cm in men and ≥80 cm in women and identify these as optional cut points for individuals or populations with increased insulin resistance.

groups. One key question is whether the same criteria should be applied to someone of a particular ethnic group regardless of their country of residence. This would be logical. IDF waist circumference recommendations for the metabolic syndrome are the same for women everywhere owing in part to the paucity of good data, but they are somewhat higher for men of European origin (Europids) than for those of Asian origin. Levels for Asian populations are based on WHO recommendations.<sup>6</sup> Fewer data are available for other regions, but Europid male recommendations are applied to men of the Middle East, Eastern Mediterranean region, and Sub-Saharan Africa pending the provision of new data.

WHO<sup>7</sup> identifies 2 levels of abdominal obesity in Europids depending on risk for metabolic complications. An increased risk occurs at waist circumferences of  $\geq 94$  cm in men and  $\geq 80$  cm in women, but risk is substantially higher at  $\geq 102$  cm in men and  $\geq 88$  cm in women. Higher thresholds generally are used to define abdominal obesity in the United States,<sup>7</sup> Canada,<sup>8,9</sup> and Europe.<sup>10</sup> These higher thresholds also are used as the waist circumference cut points to identify the metabolic syndrome in the United States. Compared with Europids, an expert consultation for WHO indicated that cut points in the Asian population should be  $\geq 90$  cm for men and  $\geq 80$  cm for women.<sup>6</sup> Several different levels have been suggested in Japan,<sup>11,12</sup> with cutoff points of  $>85$  to  $90$  cm for men and  $>80$  cm for women suggested by the newest studies in contrast with the original cutoff points.<sup>13</sup> In China, cutoff points of  $\geq 85$  cm in men and  $\geq 80$  cm in women have been suggested,<sup>14</sup> and slightly lower values have been suggested in India.

If the higher waist circumference cut points are used to diagnose the metabolic syndrome, fewer individuals should be identified as having the syndrome than if the lower cut point is used. This is true for some countries of the world.<sup>15</sup> However, when the NHLBI/AHA definition is used for the United States with the higher or lower cut points, the difference in metabolic syndrome prevalence is relatively small, both because abdominal obesity is highly correlated with the other 4 components of the syndrome<sup>16</sup> and because the prevalence of obesity is so high (Figure).

We now propose common criteria for the clinical diagnosis of the metabolic syndrome based on the criteria shown in Table 1. This definition recognizes that the risk associated with a particular waist measurement will differ in different populations. Whether it is better at this time to set the level at which risk starts to increase or at which there is already substantially increased risk will be up to local decision-making groups. However, for international comparisons and to facilitate the etiology, it is critical that a commonly agreed-upon set of criteria be used worldwide, with agreed-upon cut points for different ethnic groups and sexes. Obviously, there are many people in the world of mixed ethnicity, and in these cases, pragmatic decisions will have to be made.



**Figure.** Unadjusted prevalence (95% confidence interval) of the metabolic syndrome among US adults  $\geq 20$  years of age, National Health and Nutrition Examination Survey 1999 to 2004. Revised IDF 2005 eliminates elevated waist circumference as a requirement for diagnosis of the metabolic syndrome. In both AHA/NHLBI 2005 and revised IDF 2005 definitions, the presence of any 3 of 5 risk factors constitutes a diagnosis of the metabolic syndrome. Analysis performed by Dr E.S. Ford of the Centers for Disease Control and Prevention.

It is expected that new expert groups will be formed to assess the evidence with regard to waist circumference thresholds and associated risk in the near future. These include WHO and NHLBI. Both organizational bodies are reconsidering the definition of metabolic syndrome, and we hope that the present scientific statement will provide a useful platform for their discussions. We believe that current recommended waist thresholds should be used pro tempore, although it would be helpful if both the lower and higher criteria for Europids were cited for comparative studies. Some new data are available for different ethnic groups, but it is thought advisable to await the outcomes of the deliberations of WHO and NHLBI, when our group will reconvene to produce a further statement with the intention of having a single agreed-upon set of diagnostic criteria. We would stress that the process is evolutionary. In the interim, further studies exploring the relation of waist circumference thresholds to metabolic risk and cardiovascular outcomes in different populations are encouraged, and we continue to recommend the use of waist measurement as a useful screening tool in many primary care situations.

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\*Modest.

†Significant.

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