Metabolic Syndrome Scientific Statement by the American Heart Association and the National Heart, Lung, and Blood Institute

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The metabolic syndrome is a constellation of risk factors that are associated with increased risk for atherosclerotic cardiovascular disease (ASCVD), type 2 diabetes, and their complications. This constellation consists of 5 metabolic risk factors that together increase the risk for ASCVD. These include atherogenic dyslipidemia, elevated blood pressure, elevated glucose, a prothrombotic state, and a proinflammatory state. Atherogenic dyslipidemia consists of elevations of serum total apolipoprotein B (apoB), triglycerides, small particles in low density lipoprotein (LDL), and low levels of high density lipoproteins (HDL). An elevated glucose can be in the range of impaired fasting glucose (IFG), which is called prediabetes, or at the level of diabetes. Available evidence suggests that all of the metabolic risk factors are independently atherogenic. Moreover, individuals with metabolic syndrome, particularly when IFG is present, have a high likelihood of progression to type 2 diabetes.

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The metabolic syndrome has a multifactorial causation. The predominant underlying risk factors are obesity (especially abdominal obesity) and insulin resistance. These often occur together, and their relative contributions to the syndrome have not been fully defined. Nonetheless, there is a general agreement that the increasing prevalence of obesity in the United States and worldwide is mainly responsible for the increasing occurrence of the syndrome. Other factors that can exacerbate the metabolic syndrome are physical inactivity, advancing age, endocrine dysfunction, and genetic susceptibility.

In 2001, the National Cholesterol Education Program Adult Treatment Panel III (ATP III)1,2 proposed that the metabolic syndrome be introduced into clinical practice as a risk companion to elevated LDL cholesterol (LDL-C). The concept of the syndrome presented in ATP III was based on more than 2 decades of research on the clustering of metabolic risk factors. The syndrome was viewed as a clinical condition that is largely elicited by obesity and as one that deserves clinical intervention in practice. The rising prevalence of obesity in the United States was a major stimulus for including the metabolic syndrome as a component of the cholesterol guidelines. For routine practice, simple clinical criteria were proposed for a clinical diagnosis of the syndrome. Diagnosis was based on the identification of at least 3 of 5 risk factors: increased waist circumference (abdominal obesity), increased serum triglyceride, reduced HDL cholesterol (HDL-C), elevated blood pressure, and elevated glucose.

After publication of the ATP III, questions were raised in the cardiovascular and diabetes communities as to whether the diagnostic criteria are reliable and whether clinical intervention to reduce risk for ASCVD and diabetes is warranted. In response, the National Heart, Lung, and Blood Institute (NHLBI) cosponsored a workshop on clinical definition with the American Heart Association (AHA). This was followed by a workshop on clinical management of the metabolic syndrome sponsored by the AHA, NHLBI, and American Diabetes Association (ADA). Summaries of these workshops were published in 2004.3,4 Thereafter the AHA and NHLBI organized a writing group to incorporate the findings of these workshops and to review the emerging information on metabolic syndrome for the purpose of issuing a scientific statement to update the ATP III report.

The AHA/NHLBI update of ATP III metabolic syndrome has recently been published in Circulation.5,6 The executive summary and the full report of this update are available on-line on the Circulation website, on the AHA website under scientific statements, and on the NHLBI website. The full report will be published in print in Circulation. The clinical criteria for diagnosis of metabolic syndrome proposed in the ATP III update are shown in the Table. These criteria represent only minor modifications of the original ATP III report.1,2 Waist circumference thresholds are the same except that it is noted that lower thresholds are appropriate for persons who have clinical evidence of insulin resistance or who are members of ethnic groups in which the prevalence of insulin resistance is high. No changes were made in cutpoints for triglycerides or HDL-C; but when individuals are on lipid-lowering drugs for these risk factors they can be considered to have these risk factors. An elevated blood pressure is defined as a systolic blood pressure ≥130 mm Hg or diastolic blood pressure ≥85 mm Hg or on drug treatment for hypertension. The threshold for increased fasting glucose was reduced from 110 mg/dL to 100 mg/dL in accord with the recent change in the ADA definition of impaired fasting glucose.7

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Appropriate management of the metabolic syndrome offers an opportunity to reduce risk for both ASCVD and type 2 diabetes beyond what can be achieved by therapies directed toward single risk factors.

The AHA/NHLBI update,5,6 the IDF report,8 and a recent article from the ADA9 all point out that more research is needed to better understand the pathogenesis of the metabolic syndrome. It is expected that all of these reports will engender increased interest in the syndrome and will promote research. Because of the complexity of the syndrome, there are many potential areas for research that will enhance our understanding of the metabolism of carbohydrates, fats, proteins, and their regulation and pathogenesis of the syndrome.

### Diagnostic Criteria for Metabolic Syndrome

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<th>Measure (any 3 of the 5 criteria below constitute a diagnosis of metabolic syndrome)</th>
<th>Categorical Cutpoints</th>
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| Elevated waist circumference*† | ≥102 cm (>40 inches) in males  
≥88 cm (>35 inches) in females |
| Elevated triglycerides | ≥150 mg/dL (1.7 mmol/L) or  
On drug treatment for elevated triglyceride‡ |
| Reduced HDL cholesterol | <40 mg/dL (1.0 mmol/L) in males  
<50 mg/dL (1.3 mmol/L) in females or  
On drug treatment for reduced HDL-C‡ |
| Elevated blood pressure | ≥130 mm Hg systolic blood pressure or  
≥85 mm Hg diastolic blood pressure or  
On drug treatment for hypertension |
| Elevated fasting glucose | ≥100 mg/dL or  
On drug treatment for elevated glucose |

*To measure waist circumference, locate top of right iliac crest. Place a measuring tape in a horizontal plane around abdomen at level of iliac crest. Before reading tape measure, ensure that tape is snug but does not compress the skin and is parallel to floor. Measurement is made at the end of a normal expiration.

†In the United States, some adults of non-Asian origin (eg, White, Black, Hispanic) with a marginally increased waist circumference (eg, 94–101 cm [37–39 in] in men and 80–87 cm [31–34 in] in women) may have a strong genetic contribution to insulin resistance; they should benefit from changes in life habits, similarly to men with categorical increases in waist circumference. A lower waist circumference cut point (eg, ≥80 cm [31 in] in men and ≥88 cm [35 in] in women) appears to be appropriate for persons of Asian origin.

‡The most commonly used drugs for elevated TG and reduced HDL-C are fibrates and nicotinic acid. A patient on one of these drugs can be presumed to have high TG and low HDL.

Recently the International Diabetes Federation (IDF) proposed similar criteria for the metabolic syndrome.8 IDF requires that evidence of abdominal obesity be present for a clinical diagnosis of the syndrome. Criteria for abdominal obesity are ethnic-specific. Otherwise, 3 of 5 risk factors, one of which must be abdominal obesity, are needed for diagnosis. The risk factors are identical to those of ATP III, as are the thresholds to define abnormality.

The ATP III update placed primary emphasis on lifestyle therapies for clinical management of metabolic syndrome. These include weight reduction, increased physical activity, and an antiatherogenic diet. Drug therapies for categorical risk factors depend on established guidelines from the AHA, NHLBI, and ADA for treatment of obesity, physical inactivity, lipid disorders, hypertension, a prothrombotic state, and diabetes. The metabolic syndrome is not a risk assessment tool for determining absolute risk to guide clinical management of individual risk factors with drug therapies. Established risk-assessment algorithms should be utilized for this purpose.1,2 But recognition of the syndrome in clinical practice is encouraged for the identification of a multiple-risk-factor condition and to promote lifestyle therapies that will reduce all of the metabolic risk factors simultaneously. Appropriate management of the metabolic syndrome offers an opportunity to reduce risk for both ASCVD and type 2 diabetes beyond what can be achieved by therapies directed toward single risk factors.

### References


