

# The Metabolic Syndrome: Some Second Thoughts?

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The clustering of several cardiovascular disease (CVD) risk factors (i.e., hypertension, dyslipidemia, and type 2 diabetes) and the association of such clustering with insulin resistance led investigators to propose the existence of a distinct entity called “the metabolic syndrome,”<sup>1</sup> which has been defined by reputable organizations<sup>2,3</sup> and assigned its own code (277.7) in the World Health Organization’s ICD-9. Thus, the term metabolic syndrome is now institutionalized and part of the medical vocabulary.

How useful are the existing definitions of the metabolic syndrome for predicting CVD risk? Is there a common underlying pathophysiological process that can explain the syndrome? Does treatment of the metabolic syndrome differ from the treatment of its individual components? Simply put, does a metabolic syndrome exist distinct from its constituent components?

The American Diabetes Association (ADA) and the European Association for the Study of Diabetes (EASD) recently addressed these questions and, after a careful review of literature, have issued a joint statement,<sup>4</sup> which is available in its entirety online at <http://care.diabetesjournals.org/cgi/content/full/28/9/2289>.

Based on currently available evidence, the ADA and the EASD have concluded that:

1. The existing definitions of the metabolic syndrome are based on criteria that are ambiguous or unclear, and the cut points used to define abnormal levels of the individual components seem arbitrary and ignore the continuum in risk associated with

glucose, blood pressure, and lipids levels.

2. A unifying pathophysiology for the existence of a syndrome is unclear, and some doubt as to whether all patients with the metabolic syndrome are indeed insulin resistant. The current definitions include some factors only weakly related to insulin resistance or hyperinsulinemia (e.g., blood pressure) and exclude others that may be closely related (e.g., C-reactive protein, adiponectin).
3. Although individual components in the definitions of the metabolic syndrome are important predictors of CVD risk, it is not clear that the construct of the syndrome adds to CVD prediction beyond the contribution of the component risk factors. In fact, some of the individual components (e.g., glucose intolerance), by themselves, may explain a substantial part of the predictive value of the entire syndrome.

The authors of the ADA/EASD statement advocate the establishment of a research agenda to critically analyze how the syndrome is defined and to determine its usefulness in predicting CVD risk over and above that of its individual components combined. For practicing clinicians, the authors recommend that:

1. Adults with any major CVD risk factor should be evaluated for the presence of other CVD risk factors.
2. Patients with CVD risk variables above the cut point for normal should receive treatment as per established guidelines, and all indi-

vidual CVD risk factors should be treated aggressively.

3. Clinicians should avoid labeling patients with the term metabolic syndrome.

Dr. Gerald Reaven, who originally postulated insulin resistance as the underlying cause of much CVD, wrote recently that “it appears that making the diagnosis of the metabolic syndrome does not bring with it much in the way of pathophysiological understanding or clinical utility, and deciding that individuals do not have it because they fail to satisfy three of five arbitrarily chosen criteria may withhold relevant therapeutic intervention.”<sup>5</sup> Now, the ADA and EASD have also raised important questions about the validity and utility of the metabolic syndrome as a diagnosis.

Half of medical knowledge seems to change every 5 years; the problem is in determining which half. Remaining open to new data and new ideas is thus essential to progress in science and in clinical medicine.

## REFERENCES

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