



Metabolic syndrome—what is the clinical usefulness?

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In today's *Lancet*, Naveed Sattar and co-workers put yet another nail in the coffin of the metabolic syndrome.¹ Their analysis of longitudinal data from two independent population-based cohorts, which document the incidence of cardiovascular events or diabetes in elderly patients, shows that a fasting plasma glucose test is as good as or potentially better than a diagnosis of the metabolic syndrome for predicting diabetes. They also show that a diagnosis of the metabolic syndrome has negligible association with risk of cardiovascular disease; and that the whole is not greater than the sum of the parts. Thus diagnosis of the metabolic syndrome has no apparent clinical value.

In the joint statement from the American Diabetes Association and the European Association for the Study of Diabetes on the metabolic syndrome, eight major concerns were identified (panel).² Since then,

other commentaries support the concept of the metabolic syndrome^{3–5} or, conversely, provide additional perspectives that concerns raised in the statement were justified.^{5,6} Many other studies also affirm the difficulties outlined.^{7–10}

Importantly, critics of the metabolic syndrome do not question or doubt the evidence that many risk factors of cardiovascular disease are found more often in combination than chance would dictate. Thus identification of one risk factor for cardiovascular disease in a patient should prompt the search for others—even those not in the syndrome's construct. Moreover, there is no argument that results from many studies show that metabolic syndrome factors by themselves, or in any combination, portend cardiovascular disease and many other adverse outcomes. It is well known that elevated blood glucose, obesity, increased blood pressure, or dyslipidaemia are serious.

Substantial evidence also shows that insulin resistance plays an important part in risk-factor clustering, and probably contributes in some way to many of the untoward outcomes attributed to the metabolic syndrome. Indeed, nearly everyone agrees that lifestyle modification is a helpful intervention for those who have one or any combination of the syndrome's components and other risk factors for cardiovascular disease or diabetes (eg, raised LDL cholesterol, smoking).

On the other hand, sceptics of the usefulness of the metabolic syndrome's construct would like evidence that diagnosis of an individual with the syndrome somehow focuses attention on the need for lifestyle therapy that would otherwise be ignored or missed. They would also like evidence that such a diagnosis informs clinicians that cardiovascular disease is a multiple risk-factor model of a form they would otherwise not know, or that the diagnosis conveys the seriousness of obesity in a way not currently appreciated. They would also like evidence that the diagnosis inspires patients to take action and be more adherent to therapy than if they were diagnosed with one or more risk factors, but not the metabolic syndrome. And that the diagnosis results in a treatment that would otherwise not be recommended for modifiable risk factors, and that the construct is a valuable risk-assessment method to identify patients at increased risk of cardiovascular disease or diabetes.

Panel: Summary of concerns about the metabolic syndrome²

- Criteria are ambiguous or incomplete; rationale for thresholds is ill-defined
- Value of including diabetes in definition is questionable
- Insulin resistance as unifying cause is uncertain
- No clear basis for including or excluding other cardiovascular risk factors
- Cardiovascular risk value is variable and dependent on specific risk factors present
- Cardiovascular risk associated with the syndrome seems to be no greater than sum of its parts
- Treatment of syndrome is no different from treatment for each of its components
- Medical value of diagnosing the syndrome is unclear

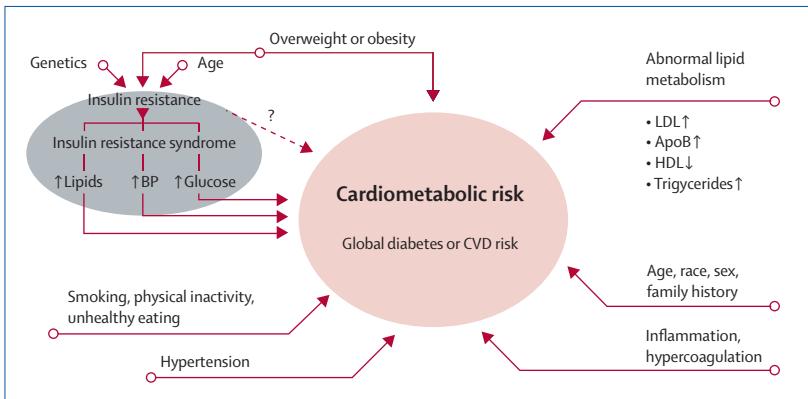


Figure: Factors contributing to cardiometabolic risk¹²

ApoB=apolipoprotein B. BP=blood pressure. CVD=cardiovascular disease.

More than a decade since its formal introduction and thousands of papers later, these six propositions— promulgated by the proponents of the syndrome— remain no more than intriguing thoughts. However, the last argument—ie, metabolic syndrome is valuable for risk assessment and therefore its identification will improve patients' outcomes—is often considered as the syndrome's greatest strength.

That people with metabolic syndrome are at increased risk of cardiovascular disease events or diabetes does not mean that the construct is useful for risk prediction in itself or compared with other approaches. First, as reviewed by Pepe and colleagues,¹¹ odds ratios or relative risks regarded as giving strong associations in observational studies (eg, odds ratios of 1·2–2·5) are inadequate to distinguish between people who do (will) or do not (will not) have the outcome of interest. Much stronger associations are needed (eg, $\geq 4·0$). Second, many reports compare metabolic syndrome with much simpler risk-assessment tests for cardiovascular disease, and those risk-assessment tests are significantly better.^{2,6,7} Additionally, a simple fasting plasma glucose measurement is a much better predictor of future diabetes than the expense and inconvenience necessary to diagnose the syndrome.^{2,10}

What seems to make most sense is for clinicians to focus on global risk assessment that takes into account all the well-established cardiometabolic risk factors (figure),¹³ and then to treat each abnormality appropriately. Also, more research is needed to understand the cause of risk-factor clustering and the pathogenesis of insulin resistance. Both actions would better serve the health of those at risk of diabetes and

cardiovascular disease than seeking a diagnosis of the metabolic syndrome.

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I declare that I have no conflict of interest.

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Neonatal mortality—4 million reasons for progress

By far the most dangerous time to be alive is during the first few days of life—especially if you are one of the 60 million children delivered worldwide without the benefit of a skilled attendant.¹ Most of the 4 million children who die within the first month of life are born into poverty and many remain unnamed and unrecorded.²

This silent toll of neonatal death is in contrast to the decrease in deaths of children aged 2–59 months by a third over the past 25 years.³ Although some progress has been made in improving late neonatal death,

early mortality in the first week of life has remained unchanged.⁴ Any progress towards the Millennium Development Goal target of a decrease in worldwide infant mortality by two-thirds by 2015 will be impossible without substantial decreases in early neonatal mortality. Two conditions—birth asphyxia and sepsis with pneumonia—cause nearly 60% of these deaths worldwide.⁵ However, the biggest issue is restricted access to qualified health-care professionals.

About 30–40% of neonatal deaths are associated with bacterial infection,⁶ which often progresses rapidly and

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