# Obesity and Metabolic Syndrome

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Obesity has become a serious global public health problem. World Health Organization (WHO) estimates that over 1.7 billion people around the world are overweight and 310million are obese.[1] Within the US, two sources of data are available on the prevalence of obesity. One is from the Behavioral Risk Factor Surveillance Survey (BRFSS). These data come from self-reported heights and weights, obtained by telephone interviews. Given the tendency of underestimation of one's weight and overestimation of one's height, the result is likely an underestimate of the actual prevalence of obesity. Nonetheless, according to the BRFSS data, 25% of the population in most states were obese in 2007, and some exceeding 30%. The National Health and Nutrition Examination Surveys data are obtained by direct measurement of heights and weights. According to the most recent data released in November 2007, over 72million American adults are obese, and this represents 33.3% of men and 35.3% of women of the American adult population.

Clinical studies have clearly demonstrated a strong association of obesity with cardiovascular disease (CVD), type 2 diabetes (T2DM), cancers and even death. Why is being obese so detrimental to ones health? Metabolic syndrome has been proposed among many others to be the missing link.

Historically, metabolic syndrome was first proposed by Dr. Reaven in his Banting lecture at Stanford University in 1988.[2] He noticed that a cluster of factors such as impaired glucose intolerance, hypertension and dyslipidemia may be linked to insulin resistance. He named this entity "Syndrome X". He also attempted to show that non-obese people can also have this syndrome. Later research has clearly shown that insulin resistance is frequently associated with increases in abdominal fat. In fact, since the 1988 Banting lecture, abdominal obesity has become the most frequent feature of the metabolic syndrome.[3] Now we know that abdominal fat is an independent risk factor for cardiovascular disease and even mortality.[4] The key features of dyslipidemia associated with obesity include elevated triglycerides, decreased HDL cholesterol, and increased numbers of small, dense LDL particle.[5] Central obesity is a critical determinant of this dyslipidemia, by increasing in fatty acid oxidation and insulin resistance. A number of new candidates have also been recognized for the metabolic syndrome, such as C-reactive protein (CRP), plasminogen activator inhibitor-1 (PAI-1) and fibrinogen.

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There is no consensus on definitions of metabolic syndrome. At least three concepts about the metabolic syndrome exist in the literature, but they are not mutually exclusive. The first concept says that increase in obesity and decrease in physical activity are responsible for the metabolic syndrome epidemic.[6] Behavioral modification to reduce weight and increase physical activity therefore should be the cornerstone of treatment. This is endorsed by the National Cholesterol Education Program (NCEP). The second view is proposed by WHO in that insulin resistance is the underlying cause of the metabolic syndrome.[7] If this is correct, then the treatment strategy of metabolic syndrome should not only include behavioral modification, but also consider insulin sensitizing agent in non-diabetic subjects. A third concept is that inflammation might be the underlying cause of the metabolic syndrome.[8] If this concept is correct, then in addition to behavioral modification and insulin sensitizers, a variety of anti-inflammatory agents would be considered such as statins, ACE inhibitors and ARBs.

The two currently used definitions describe closely overlapping but not identical populations (Table 1). The American Heart Association/National Heart, Lung, and Blood Institute (AHA/NHLBI) definition requests any three out of the five components to define metabolic syndrome, whereas the International Diabetes Foundation (IDF) requires central obesity be present among the 3 components. IDF also has more stringent criteria for central obesity, as defined by waist circumference, in non-Asian population, and a different criterion for the Japanese.

The endocrine society task force recently developed clinical practice guideline for primary prevention of CVD and T2DM in individuals with components of metabolic syndrome who do not yet have the two diseases.[11] The task force recommends use of components in the AHA/NHLBI definition in screening for individuals at high metabolic risks. The principal strategy for the treatment of the metabolic syndrome should be decreased caloric intake, increased physical activity, and behavioral modification to achieve weight and waist circumference reduction. While there are no randomized clinical trials showing the effectiveness of these behavioral therapies for reducing cardiovascular disease, there are several randomized controlled trials showing that modest weight loss (~ 5%) and increased physical activity may reduce the risk of type 2 diabetes by over 50%.[12,13]

The most controversial topic is whether insulin sensitizers should be used in the pharmacological treatment of the metabolic syndrome in non-diabetic individuals. No current clinical studies have evaluated these interventions in subjects with the metabolic syndrome. A more conservative position

perhaps is to perform a 2-hour oral glucose tolerance test (OGTT). About 20-30% of these subjects are likely to have T2DM according to OGTT. These individuals could be treated with insulin sensitizers or other hypoglycemic agents. If they have impaired glucose tolerance (IGT), than a case could be made for pharmacological treatment since there are clinical trials showing delay of the development of T2DM in IGT subjects. In the diabetes prevention program (DPP) study[12] both metformin and a TZD (troglitazone, which was later withdrawn from the market) showed to reduce the conversion of prediabetes to diabetes. This finding was confirmed in two other TZD trials, the TRIPOD study[14] using troglitazone and the DREAM trial using rosiglitazone.[15] However, since there are limited data on the long-term safety of drug therapy for the treatment of prediabetes, and lifestyle therapies appear to be as effective as drug treatment for reducing conversion to diabetes, the guideline suggest that priority be given to reducing risk for diabetes with lifestyle therapies rather than drug therapies.

## References


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**Table 1.** Criteria proposed for clinical diagnosis of the metabolic syndrome

| Clinical measure | AHA/NHLBI (9): any 3 of the following 5 features | IDF (10 ) |
|---|---|---|
| Waist circumference | ≥102 cm in men or ≥88 cm in women (non-Asian origin); ≥90 cm in men or ≥80 cm in women (both East Asians and South Asians) | ≥94 cm in men or ≥80 cm in women (Europids, Sub-Saharan Africans, and Middle Eastern); ≥90 cm in men or ≥ 80 cm in women (both East Asians and South Asians; South and Central Americans); ≥85 cm in men or ≥ 90 cm in women (Japanese), plus any 2 of the following: |
| Triglycerides (fasting) | ≥150 mg/dl or on drug therapy for high triglycerides | ≥150 mg/dl or on drug therapy for high triglycerides |
| HDL-C | <40 mg/dl in men or <50 mg/dl in women or on drug therapy for low HDL-C | <40 mg/dl in men or <50 mg/dl in women or on drug therapy for low HDL-C |
| Blood pressure | ≥ 130 mm Hg systolic or ≥ 85 mm Hg diastolic or on drug therapy for hypertension | ≥130 mm Hg systolic or ≥85 mm Hg diastolic or on drug therapy for hypertension |
| Glucose (fasting) | ≥100 mg/dl or drug therapy for elevated glucose | ≥100 mg/dl (includes diabetes) |

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