Getting Tough With Metabolic Syndrome

As public health epidemics go, metabolic syndrome doesn't seem to pack the punch of more sharply defined health threats, such as lung cancer or heart disease. But statistics expose some harsh realities. According to a 2002 report from the Centers for Disease Control and Prevention, about 22% of US adults have metabolic syndrome. Experts believe that the report, based on data collected between 1988 and 1994, underestimates the current number of persons who have metabolic syndrome.

Primary care physicians, who are already experts at managing patients who have multiple medical conditions, have what it takes to reverse metabolic syndrome trends. Initial prevention and treatment tactics center on diet and exercise interventions. And though physicians aren't generally reimbursed for diet and exercise counseling, the bold step of leveling with at-risk patients about their weight, lack of physical activity, or other risk factors is a known stimulus for lifestyle change.

Mechanisms of metabolic syndrome

Story continues inside the gatefold >>

2004

Watershed events in the history of metabolic syndrome

2000

2001
National Cholesterol Education Program suggests that behavioral interventions promoting weight loss and increased physical activity are basis of treatment for patients who have metabolic syndrome

2001
Adult Treatment Panel III of the National Cholesterol Education Program proposes diagnostic criteria for metabolic syndrome that establish cutoff points for five risk factors: abdominal girth, blood pressure, serum cholesterol, triglycerides, and fasting glucose. Patients with results showing three or more of these risk factors are considered to have metabolic syndrome

1990

1980

1988
Gerald M. Reaven, MD, from Stanford University School of Medicine, first describes syndrome X in a Banting Lecture at annual meeting of American Diabetes Association

1970

1977
German research group also describes a clustering of cardiovascular risk factors

1960

1960
Yalow and Berson establish the concept that obesity, whether associated with diabetes or not, is a cause of insulin resistance

1967
Italian research group first describes a clustering of cardiovascular risk factors (hypertension, diabetes, dyslipidemia, and obesity)

1950

1940

1930

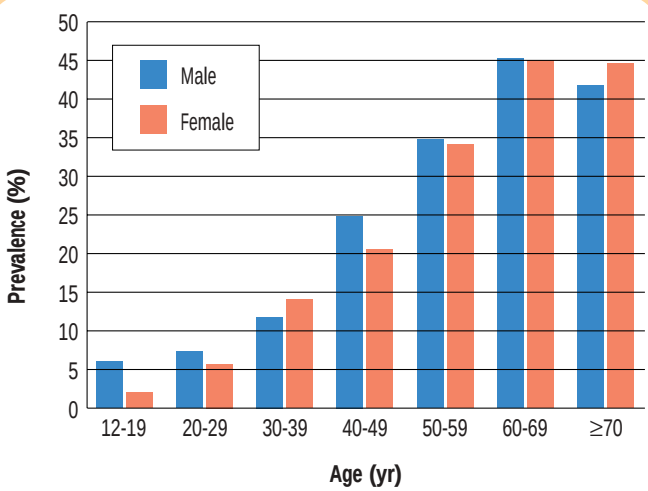
1938
British physician Harold Percival Hinsworth coins the term insulin sensitivity

Definition

Starting in the 1960s and 1970s, researchers began to document a clustering of the elements of cardiovascular risk in certain patients. It wasn't until 1988 that a unifying cause—insulin resistance—was proposed and the term *syndrome X* applied. After several name changes over the past two decades, including the term *diabesity* used in lay publications, the name became *metabolic syndrome*.

Key components of metabolic syndrome are central adiposity, dyslipidemia, hypertension, and glucose intolerance. Chronic inflammation, procoagulation, and impaired fibrinolysis are also thought to play a role.

The coexistence of these conditions in the same patient is related to an increased incidence of cardiovascular disease and its consequences. Risk factors include poor diet, sedentary lifestyle, and genetic predisposition.



Age-specific prevalence of metabolic syndrome in US adolescents and adults, 1988-1994

Adapted from Ford ES, Giles WH, Dietz WH. Prevalence of the metabolic syndrome among US adults: findings from the third National Health and Nutrition Examination Survey. JAMA 2002;287(3):356-9, and Cook S, Weitzman M, Auinger P, et al. Prevalence of a metabolic syndrome phenotype in adolescents: findings from the third National Health and Nutrition Examination Survey, 1988-1994. Arch Pediatr Adolesc Med 2003:157(8):821-7.

Diagnostic criteria for metabolic syndrome

Feature	Criterion*
Abdominal girth	Waist circumference
Men	>102 cm (40 in)
Women	>88 cm (35 in)
Fasting plasma HDL-C	
Men	<40 mg/dL (1.03 mmol/L)
Women	<50 mg/dL (1.29 mmol/L)
Fasting plasma triglycerides	≥150 mg/dL (1.69 mmol/L)
Fasting blood glucose	≥110 mg/dL (6.1 mmol/L)
Blood pressure	≥130/85 mm Hg

HDL-C, high-density lipoprotein cholesterol.
*A diagnosis of metabolic syndrome is made if a patient has three or more of the criteria listed.

Source: *Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults. Executive summary of the third report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III). JAMA 2001;285(3):2486-97.*

Diagnosis

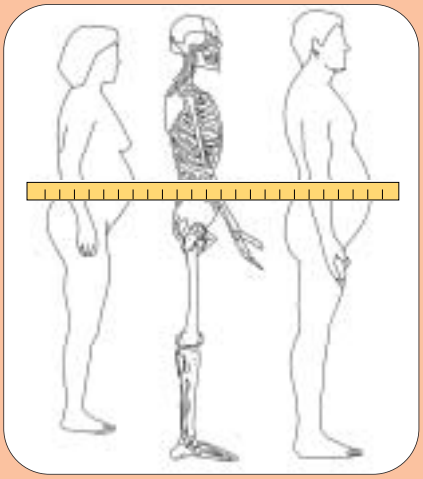
There are no absolutes in diagnosis of metabolic syndrome. The most useful tool is a checklist of five criteria set forth by the Adult Treatment Panel III (ATP III) of the National Cholesterol Education Program. Patients with at least three of the criteria are thought to have metabolic syndrome.

Abdominal fat distribution is a more sensitive indicator of metabolic syndrome than body mass index (BMI). Also, BMI is less useful for assessing body weight in heavily muscled persons, athletes, and certain racial groups. Waist circumference is quick and easy to measure, though physicians sometimes have questions about proper measuring tape placement and procedure.

Experts view the identification of diagnostic criteria for metabolic syndrome as a work in progress. They hope to incorporate a more sensitive test for insulin resistance and measurement of markers for inflammation, such as C-reactive protein.

Waist circumference measurement technique

Place measuring tape, holding it parallel to the floor, around abdomen at the level of the iliac crest. Hold tape snug but do not compress the skin. Measure circumference at end of normal expiration.



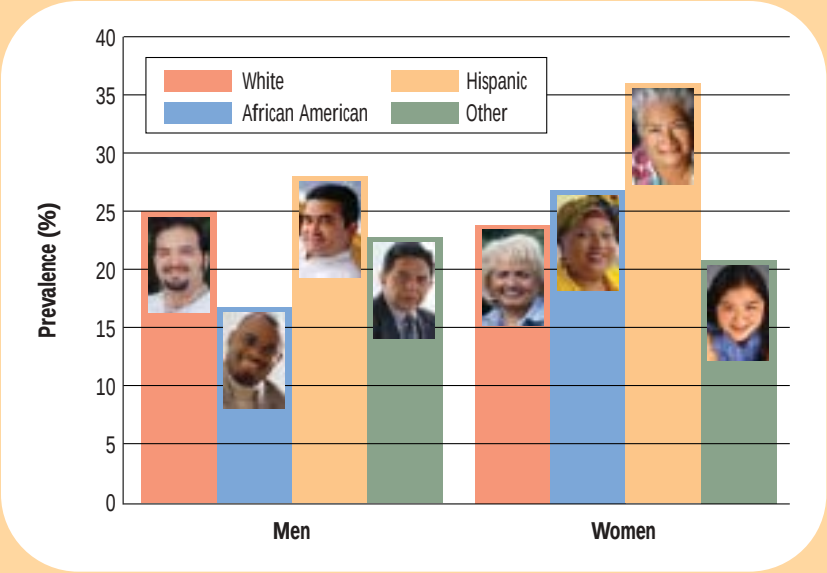
Source: *NHLBI Obesity Education Initiative Expert Panel on the Identification, Evaluation, and Treatment of Overweight and Obesity in Adults. Identification, evaluation, and treatment of overweight and obesity in adults: the practical guide. Bethesda: National Institutes of Health, 2000; NIH publication 00-4084.*

Prevalence

An estimated 47 million US adults have metabolic syndrome. Some experts predict that at least half of persons over age 60 would meet the criteria for this syndrome. A more recent survey analysis found that as many as 4.2% of US adolescents aged 12 to 19 years have the disorder.

Prevalence rates of metabolic syndrome differ across ethnic groups. The highest overall prevalence has been found in Mexican Americans, who make up a rapidly growing segment of the US population.

Obesity and diabetes trends seem to mirror metabolic syndrome trends. From 1999 to 2000, 64% of US adults aged 20 to 74 were overweight or obese, according to data from the Department of Health and Human Services.



Prevalence of metabolic syndrome by sex and ethnicity in US adults, 1988-1994

Adapted, with permission, from Ford ES, Giles WH, Dietz WH. Prevalence of the metabolic syndrome among US adults: findings from the third National Health and Nutrition Examination Survey. JAMA 2002;287(3): 356-9.

Treatment

Debate continues about the best approach for management of metabolic syndrome. Many experts believe that the initial approach is to direct therapy to the syndrome, and if implementing that strategy isn't successful, to target treatment to the individual components.

Therapy should be tailored to a patient's specific risk factors and comorbid conditions, and decisions about what is most appropriate should be made within the context of a close working relationship between patient and physician.

LIFESTYLE CHANGES

The recommended first steps for treatment of metabolic syndrome are weight loss and increased physical activity.

Weight loss: Although some persons with metabolic syndrome are of normal weight, many are overweight or obese, and weight loss through long-term behavior modification and a reduced-calorie diet is the goal. A dietitian can be a valuable resource in designing a diet tailored to the patient.

Trimming even 10 to 15 lb can moderately lower blood pressure, decrease total cholesterol, and reduce the percentage of body weight due to fat. Obesity experts recommend as an initial goal a weight loss of 10% of baseline over a 6-month period. In the Finnish Diabetes Prevention Study, lifestyle changes that yielded modest weight loss produced a 58% reduction in diabetes. The study included 522 middle-aged, overweight participants with impaired glucose tolerance.

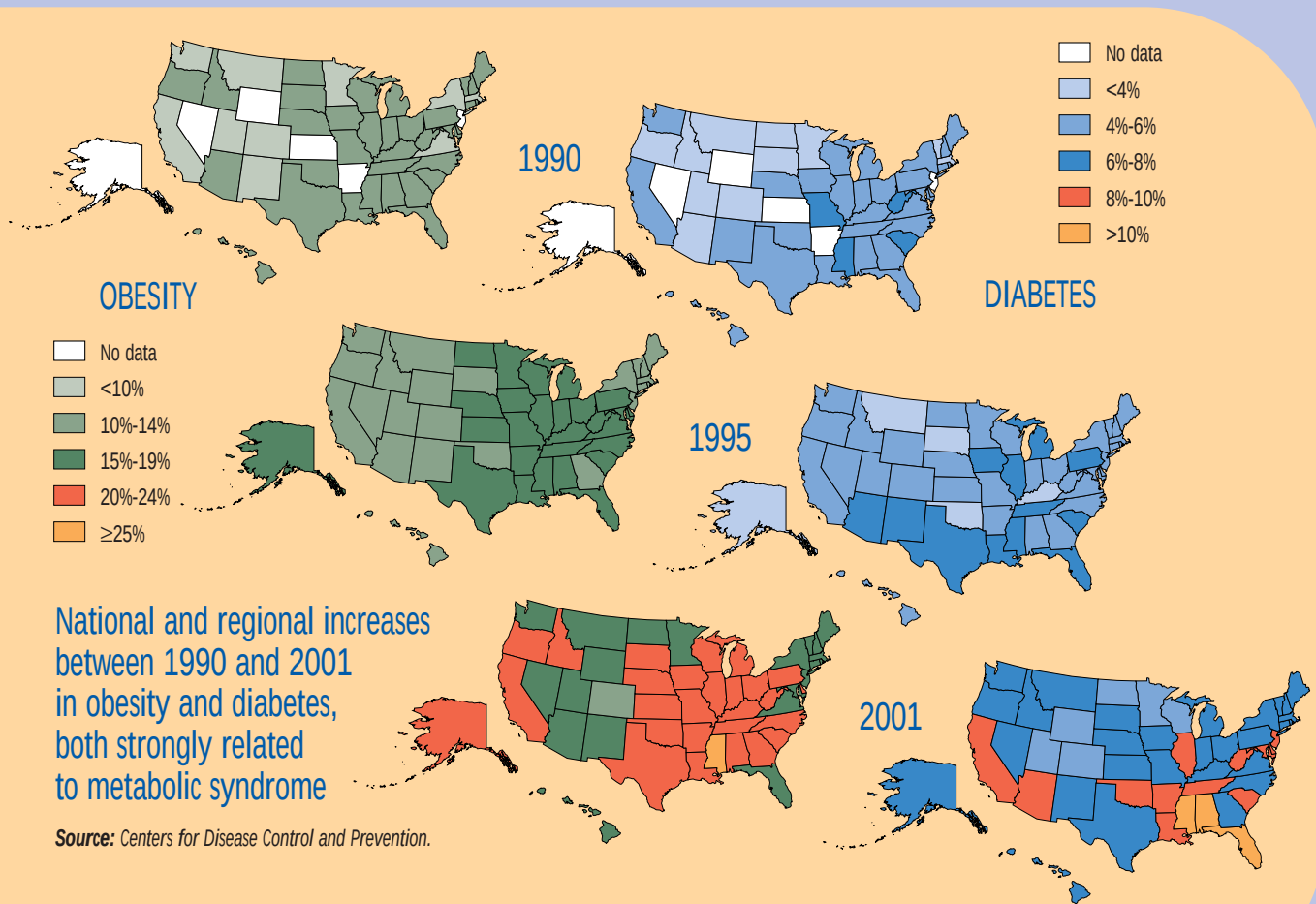
For persons who need to therapeutically lose weight but struggle long and hard to slim down, weight-loss medications can be an adjunct to diet and exercise.

For some obese persons, diet, exercise, and even medication are unsuccessful. If they are extremely obese (BMI, >40 kg/m^2) or have a BMI between 35 and 40 kg/m^2 and one or more serious comorbid conditions, bariatric surgery (eg, gastroplasty, Roux-en-Y gastric bypass) may be appropriate.

Physical activity: The physical activity needed for improved health seems on the surface to be manageable for almost anyone: 30 minutes of moderate exercise 5 days a week. The activity can be broken up during the day as fits the person's schedule.

Exercise generally improves circulation, increases high-density lipoprotein cholesterol (HDL-C) levels, and burns calories. Muscles are the primary disposal and storage site of glucose, and as exercise leads to more muscle and less fat, blood glucose tends to stabilize at a normal level.

Encouragement and advice from their primary care physician can be crucial and can give the support and provide the information and skills that many people need to better manage metabolic syndrome.



National and regional increases between 1990 and 2001 in obesity and diabetes, both strongly related to metabolic syndrome

Source: *Centers for Disease Control and Prevention.*

If efforts at weight control and exercise do not succeed, medications can be effective in reducing risk in metabolic syndrome.

Hypertension: Weight loss, exercise, and a diet low in sodium offer a sound first approach for antihypertensive therapy. However, if these steps do not reduce blood pressure to an acceptable level, medication may be necessary.

"High blood pressure is a very, very important contributor to many complications of metabolic syndrome," says Robert H. Eckel, MD, an atherosclerosis specialist at the University of Colorado School of Medicine. Its control in metabolic syndrome is crucial. The exact blood pressure target for patients with metabolic syndrome is still debated, but Dr Eckel believes that a goal matching that recommended for patients with diabetes—less than 130/80 mm Hg—is appropriate.

Recommendations of the seventh report of the Joint National Committee on the Prevention, Detection, Evaluation, and Treatment of High Blood Pressure also apply to management of metabolic syndrome. As an initial approach, a thiazide diuretic should be used in most cases of uncomplicated hypertension. Diuretic therapy can be used alone or in combination with a drug in the other classes of antihypertensives (eg, angiotensin-converting enzyme inhibitor, angiotensin II receptor blocker, β-blocker, calcium channel blocker).

Findings in the Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial (ALLHAT) showed that therapy using a diuretic and a β-blocker was the best choice to lower blood pressure effectively. Among the patients in ALLHAT, about 25% met the criteria for metabolic syndrome, Dr Eckel notes.

Triglycerides, HDL-C: Strategies to decrease triglycerides and increase HDL-C incorporate (1) increased physical activity, (2) limited fat and alcohol intake, (3) limited dietary sugar and carbohydrates, and (4) smoking cessation. These lifestyle changes may need to be complemented by medications that can better control risk factors. Agents include 3-hydroxy-3-methylglutaryl coenzyme A reductase inhibitors ("statins"), fibric acid derivatives, and niacin.

A conclusion that all patients with metabolic syndrome need a statin is premature, says Dr Eckel. In patients whose Framingham score for heart attack risk is less than 20, the goal for low-density lipoprotein cholesterol (LDL-C) is a concentration less than 130 mg/dL (3.4 mmol/L), and statin use can help achieve that level. For patients whose Framingham score is greater than 20, the LDL-C goal is less than 100 mg/dL (2.6 mmol/L). Adjunctive use of a fibric acid derivative, such as gemfibrozil or fenofibrate, can help reduce triglyceride levels and improve HDL-C levels.

If niacin is used in a patient whose fasting plasma glucose level is 110 to 126 mg/dL (6.1 to 7.0 mmol/L), it may increase production of endogenous glucose and incite diabetes, cautions Dr Eckel. Niacin use requires careful monitoring.

Glucose intolerance: Persons with impaired glucose tolerance (IGT) (fasting blood glucose, 110 to 126 mg/dL) are at risk for diabetes, cardiovascular disease, and metabolic syndrome. Annually, IGT carries a 1% to 10% rate of progression to diabetes. Medication to treat insulin resistance before diabetes occurs is controversial, but it is an area of high interest and active investigation.

The Diabetes Prevention Program showed that metformin hydrochloride reduced diabetes risk by 31% in patients with IGT. Beyond metformin, thiazolidinediones can modify insulin levels as well as other parameters, most specifically triglyceride levels, Dr Eckel says.

Waist circumference: Weight loss and exercise are key to reducing visceral adiposity. However, according to the National Heart, Lung, and Blood Institute, a weight-loss medication may be appropriate for patients with a BMI of 27 to 29.9 kg/m^2 who have comorbid diseases or for those who have a BMI greater than 30 kg/m^2. Such medication should be used only as part of a comprehensive weight-reduction plan.

"High blood pressure is a very, very important contributor to many complications of metabolic syndrome."

The primary classes of weight-loss drugs are appetite suppressants and nutrient absorption inhibitors. Sibutramine and orlistat, typically prescribed as single agents, are approved by the US Food and Drug Administration for long-term use.

Before prescribing weight-loss agents, physicians need to determine the risk-benefit status for the individual and decide if such a drug is appropriate. Once medication is started, the patient should be monitored carefully.

Prothrombotic state: Low-dose aspirin (ie, 81 mg) taken daily is effective in lowering thrombotic risk.

For an online list of suggested resources on metabolic syndrome, visit www.postgradmed.com or www.physsportsmed.com.

☑ Framingham risk scoring

In its cholesterol guidelines, the Adult Treatment Panel III (ATP III) introduced the concept of Framingham risk scoring, a calculation that indicates the probability of having a coronary artery disease event within 10 years. The scoring assigns points, weighted by sex, for several parameters: age, total cholesterol and HDL-C levels, smoking status, systolic blood pressure, and treatment of hypertension. The sum of the scores yields a percentage for 10-year risk.

A guide to Framingham risk scoring can be found in the appendix of the ATP III executive summary, available online at www.nhlbi.nih.gov/guidelines/cholesterol/atp_iii.htm.