Treatment of the Metabolic Syndrome: The Impact of Lifestyle Modification

Allison M. Pritchett, MD, John P. Foreyt, PhD, and Douglas L. Mann, MD*

Address
*Winters Center for Heart Failure Research, Baylor College of Medicine, One Baylor Plaza, MC: 523D, Houston, TX 77030, USA.
E-mail: amp@bcm.tmc.edu

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Along with the increasing prevalence of obesity comes a constellation of metabolic derangements: dyslipidemias, hypertension, insulin resistance, and glucose intolerance, as well as increased prothrombotic and inflammatory markers. The association of these factors has been termed the "metabolic syndrome" and increases the risk of developing cardiovascular disease. Aside from pharmaceutical therapy, lifestyle modification is necessary to aggressively treat this syndrome in its entirety. This involves a holistic approach of behavioral counseling, education, increased physical activity, and dietary modification. Even modest weight loss (7% to 10% of body weight) results in decreased fat mass, blood pressure, glucose, low-density lipoprotein, and triglyceride levels. These benefits can also translate into improved long-term outcome, especially if weight loss and lifestyle alterations are maintained. However, the remaining challenge is how to promote long-term adherence to a healthier, more active lifestyle and avoid reversion to old habits.

Introduction

With the modernization of our society, we have improved transportation, readily available food, and new devices (such as cellular phones, remote controls, riding lawnmowers, garage door openers, and so forth) that allow us to do more while expending less energy and consuming a higher caloric diet. This imbalance between energy intake and energy expenditure has led to the increasing prevalence of obesity. Along with obesity come related diseases of metabolic derangement such as dyslipidemias, hypertension, insulin resistance, and diabetes. Each of these metabolic alterations develops gradually and progressively. They tend to be found in association with each other and all increase the risk of developing cardiovascular disease. Although we have medications to treat each of these diseases individually, we must also implement lifestyle changes to augment energy expenditure while limiting intake. This review summarizes the techniques of lifestyle modification and the impact this therapeutic approach has on each of the components of the metabolic syndrome.

Definition of the Problem: Obesity and the Metabolic Syndrome

The United States is experiencing a dramatic epidemic of obesity. Obesity is classified using categories of body mass index (BMI), which is measured by weight in kilograms divided by height in meters squared. A BMI from 25 to 29.9 kg/m^2 is "overweight," 30 to 35 kg/m^2 is "obese," and greater than 35 kg/m^2 equates to "severe obesity." Data from the National Health and Nutrition Examination Survey demonstrate that the prevalence of obesity increased from 23.3% of adults aged 20 to 74 years from 1988 to 1994 to 30.9% from 1999 to 2000 [1]. The risk of all-cause mortality is increased with increasing BMI [2]. This national rise in obesity is of concern, and it is associated not only with a higher mortality but also a rise in associated health problems and increased healthcare costs.

Cardiovascular risk factors, such as hypertension, insulin resistance, and dyslipidemias, are strongly associated with overweight/obesity. This clustering of risk factors has been classified as "Syndrome X," "the insulin resistance syndrome," or "the metabolic syndrome." Several organizations, including the National Cholesterol Education Program (NCEP) and the World Health Organization (WHO), have delineated criteria for the diagnosis of the metabolic syndrome (Table 1) [3•]. In the United States, 21.8% of adults have the metabolic syndrome according to the NCEP guidelines [4]. The prevalence increases with age and is more common in certain ethnic groups, such as Hispanics and South Asians (*ie*, from the Indian subcontinent) [3•,5••].

The Metabolic Syndrome and Risk for Cardiovascular Disease

The presence of the metabolic syndrome is a predictor of future cardiovascular events. Several studies have demonstrated that in patients referred for coronary angiography,

Table 1. Diagnostic criteria for the metabolic syndrome*

Criteria	NCEP definition (requires at least 3 of the following)	WHO definition (requires insulin resistance + 2 other criteria)
Abdominal obesity	Waist circumference > 102 cm (> 40 in) in men and > 88 cm (> 35 in) in women	Waist-to-hip ratio of > 0.9 in men or > 0.85 in women and/or BMI > 30 kg/m^2
High blood pressure	≥ 130/85 mm Hg or taking antihypertensive medication	≥ 140/90 mm Hg or taking antihypertensive medication
Hypertriglyceridemia	≥ 150 mg/dL	Same as NCEP
Low HDL	< 40 mg/dL in men and < 50 mg/dL in women	< 35 mg/dL in men and <39 mg/dL in women
Insulin resistance	≥ 110 mg/dL or taking hypoglycemic medication	Type 2 diabetes†
		Impaired fasting glucose†
		Impaired glucose tolerance†
		Reduced glucose uptake under hyperinsulinemic conditions†
Microalbuminuria	Not included	Urinary albumin excretion rate ≥ 20 μg/min or albumin-to-creatinine ratio ≥ 30 μg/g

*Other associated components of the metabolic syndrome include prothrombotic and inflammatory states. These parameters are not typically measured clinically and are not included in establishing the diagnosis of metabolic syndrome.
†One measure of insulin resistance is required.
BMI—body mass index; HDL—high-density lipoprotein; LDL—low-density lipoprotein; NCEP—National Cholesterol Education Program; WHO—World Health Organization.
(*Data from* Grundy *et al.* [3•].)

those with the metabolic syndrome had a higher rate of coronary artery disease [6–8]. Overall and cardiovascular mortality are also increased in those with the metabolic syndrome. Men in the Kuopio Ischemic Heart Disease Risk Factor study that met the WHO criteria for the metabolic syndrome had a 16% mortality rate at 13.7 years of follow-up compared with a 10% rate in those without the metabolic syndrome [9]. Similarly, a differential overall mortality rate of 18.0% versus 4.6% between those with and without the metabolic syndrome was seen in the Botnia cohort in Finland and Sweden [10]. A similar difference (12.0% vs 2.2%) was shown for cardiovascular mortality. Recognition that the metabolic syndrome leads to worsened cardiovascular outcomes provides incentive to develop prevention and treatment strategies for this constellation of metabolic derangements.

Treatment of the Metabolic Syndrome

Once identified, aggressive treatment of the metabolic syndrome is crucial to modify the increased cardiovascular risk, events, and mortality associated with the syndrome. The American Heart Association, in collaboration with the National Heart, Lung, and Blood Institute and American Diabetes Association, has recently published recommendations for the clinical management of the metabolic syndrome [5••]. Medications are targeted to individual components such as antihypertensive agents for blood pressure control, and statins, fibrates, and niacin for dyslipidemias. Aspirin may be considered for those with a 10% or greater 10-year risk for developing coronary heart disease. Diabetic patients should maintain glycemic control to achieve a hemoglobin A_{1C} level of less than 7.0%, but there is currently insufficient evidence to recommend initiation of metformin or thiazolidinediones in patients with insulin resistance to prevent the development of cardiovascular disease. However, although medication is often necessary, the cornerstone of treating the metabolic syndrome remains diet and exercise.

Lifestyle Modification

Physical inactivity, an atherogenic diet, and the increasing prevalence of people who are overweight/obese in our society contribute to the development and exacerbation of the components of the metabolic syndrome. Although diet and exercise are proposed as first-line therapy to combat the metabolic syndrome, their implementation, maintenance, and long-term effects have been difficult to achieve. "Lifestyle modification" emphasizes that weight reduction and physical activity must be undertaken in conjunction with behavioral changes. Behavioral modification includes stress management, choice of leisure-time activities (television watching and computer time vs physical activity), planning meals and reducing portion size, reading labels, identifying triggers for eating/inactivity, and self-monitoring and setting achievable goals. The behavioral component is impor-

tant to developing new healthy habits and committing to a long-term lifestyle change.

It is difficult to synthesize the existing data regarding diet and exercise because no uniform approach has been reported in the literature. Diets have used varying percentages of carbohydrate and fat intake as well as total calorie limits. Physical activity programs have promoted different exercise modalities, total daily minutes, exertional level, and frequency. The guidelines for the management of the metabolic syndrome recommend limited intake of saturated fats, cholesterol, and simple sugars, with increased consumption of fruits, vegetables, and whole grains (Table 2) [5••,11••]. In order to achieve long-term modest weight loss (approximately 7% to 10% over 6 to 12 months), reducing total calorie intake by 500 to 1000 calories per day may be more effective than the very low-calorie diets [12••]. The standard physical activity recommendation is 30 minutes of moderate-intensity exercise at least 5 days per week. Initially, it may seem more reasonable to incorporate multiple 10 to 15 minute intervals of activity throughout the day. Finally, diet and exercise must be coupled with behavioral education and counseling. Awareness of habits and stressors, as well as consciously changing lifestyle patterns and setting reasonable goals, are keys to the success of lifestyle modification.

Despite the varied approaches and the challenge of maintaining lifestyle changes, tangible benefits can be seen with even modest weight loss and increased physical activity. Modest weight loss of 5% to 10% total body weight has been demonstrated to improve fasting glucose and hemoglobin A_{1C} levels, lower blood pressure, and improve the lipid profile. In fact, Oster *et al*. [13], through statistical modeling, estimated that a 10% sustained weight loss would lower the lifetime incidence of coronary artery disease by 12 to 38 cases per 1000. This degree of weight loss would also reduce healthcare expenses in treating five chronic, obesity-related diseases (hypertension, hypercholesterolemia, diabetes, coronary heart disease, and stroke) by approximately $3300 to $3800 per person. Also, an increasing level of physical fitness, as measured by VO_2 treadmill testing, is associated with a progressive reduction in overall and cardiovascular mortality in both healthy men and men with the metabolic syndrome [14]. In men with the metabolic syndrome, those in the lowest quintile of fitness had an approximately twofold increase in overall mortality compared with the upper four quintiles. It should be noted that the success of lifestyle modification may be proportional to the intensity with which these dietary and activity changes are implemented [15]. The impact of lifestyle intervention on the individual metabolic syndrome components is discussed in detail in the following text.

Lifestyle Modification and Body Composition

One of the criteria for the metabolic syndrome is the waist circumference or waist-to-hip ratio. These measurements are simple to perform in the clinic and provide an estimation of central obesity. Regional patterns of fat distribution, particularly central/abdominal obesity, are strongly related to the development of diabetes and cardiovascular disease. Dual energy X-ray absorptiometry (DEXA), computed tomography (CT), or magnetic resonance (MRI) imaging have been used to more accurately quantitate the degree and distribution of adiposity for research purposes [16]. Several studies have reported anthropometric measurements using MRI to quantify subcutaneous versus visceral fat both before and after implementation of diet and/or exercise [17,18]. Weight loss by either diet or exercise resulted in significant reductions in both subcutaneous and visceral fat; however, a greater relative reduction in visceral fat was noted. An increasing amount of visceral adipose tissue is positively correlated with the number of metabolic syndrome criteria [19] and inversely related to measures of insulin sensitivity [20]. This suggests that the benefits of moderate weight loss may be partially mediated through reductions in visceral adipose tissue.

Lifestyle Modification and Lipids

There is not uniform agreement in the literature with respect to the effects of diet and exercise on the lipid profile. An increased low-density lipoprotein (LDL) level, although not a criterion for the metabolic syndrome, is a known risk factor for the development of coronary artery disease. Limiting intake of foods with a high content of saturated fat (*ie*, full-fat dairy products and meats), trans unsaturated fatty acids (*ie*, prepared baked goods and oils used at fast-food restaurants), and cholesterol (*ie*, egg yolks and shellfish) can improve LDL levels [11••]. Also, an increased consumption of soy protein (approximately 45 g/d or roughly 3 servings) has been shown to reduce total cholesterol (9.3%), LDL cholesterol (12.9%), and triglycerides (10.5%) [21]. Soy products had the greatest lipid-lowering effects in those with elevated lipid profiles.

Weight loss has been demonstrated to reduce LDL, whereas exercise in isolation has a lesser impact. A study by Beard *et al*. [22] implemented a diet low in fat and cholesterol and high in complex carbohydrates and fiber in conjunction with daily aerobic exercise. In addition to an average weight loss of 4 kg, this program induced a 20% reduction in LDL levels as well as other antiatherogenic qualitative changes in LDL, including an increase in LDL particle size, lower LDL density, and an increased resistance to oxidation.

People with the metabolic syndrome tend to exhibit low high-density lipoprotein (HDL) and elevated triglyceride levels. However, the impact of augmenting the HDL level on future cardiovascular events is unclear. The response of HDL levels to diet and exercise is also variable. In some studies, weight loss results in an increase in

Table 2. Dietary recommendations from the National Cholesterol Education Program expert panel

Nutrient	Recommended intake
Total fat	≥ 25%–35% of total calories
Saturated fat	< 7% of total calories
Monounsaturated fat	≥ 20% of total calories
Polyunsaturated fat	≥ 10% of total calories
Carbohydrate*	≥ 50%–60% of total calories
Fiber	20–30 g/d
Protein	15% of total calories
Cholesterol	< 200 mg/d
Sodium	2400 mg/d or 6 g/d of salt
Alcohol	≥ 2 drinks per day (men) or ≥ 1 drink per day (women)

*Complex carbohydrates from a variety of fruits, vegetables, and whole grains.
(*Data from* Krauss *et al.* [11••].)

HDL levels, whereas in others HDL decreases along with total cholesterol. Diets high in carbohydrates may also induce a reduction in HDL in some individuals.

Elevated triglycerides are strongly associated with insulin resistance and often fluctuate in the opposite direction from HDL levels. There is no recommended goal for triglyceride levels, but increased physical activity, weight loss, and a reduced intake of sugar and simple carbohydrates may not only improve insulin resistance and glycemic control, but lower triglycerides as well. Specific manipulations of dietary composition to include more fiber [23] and a greater intake of omega-3 fatty acids [24,25] (found in fish) may also reduce triglyceride levels.

Lifestyle Modification and Hypertension

In addition to pharmacologic approaches to treating hypertension, nonpharmacologic approaches such as reduction in salt intake, weight loss, and increased physical activity can favorably impact on blood pressure.

Effects of a low-sodium diet

As noted previously, dietary guidelines recommend limiting sodium intake to less than 2400 mg/d or less than 6 g/d of salt. A meta-analysis that summarized the effect of a low-sodium diet on blood pressure demonstrated that dietary sodium restriction had greater efficacy in hypertensive patients than in nonhypertensive patients [26]. Blood pressure was reduced by 4.8/2.5 mm Hg compared with 1.9/1.1 mm Hg in the two groups, respectively. The Dietary Approaches to Stop Hypertension (DASH) diet follows similar dietary guidelines as in Table 2, but promoted even lower salt intake (< 60 mmol/d) and more foods enriched in potassium, calcium, magnesium, fiber, and protein. Sacks *et al.* [27] randomized adults (> 50% black, > 50% women) with a baseline blood pressure of 120 to 159/80 to 95 mm Hg to either a standard American diet or the DASH diet. Meals were provided in each category, and each month the dietary concentration of sodium within the diet was varied from high (150 mmol or 3.5 g/d of sodium) to medium (100 mmol or 2.3 g/d of sodium) to low (50 mmol or 1.2 g/d of sodium). Several conclusions are noted from this study. First, the DASH diet significantly lowered blood pressure at each sodium concentration compared with the control diet. Secondly, decreasing sodium intake alone incrementally decreased blood pressure. The combined effects of the DASH diet and sodium lowering, although not additive, were greater than the effects of either intervention alone and lowered the systolic blood pressure by 11.5 mm Hg, which is comparable to the effect of single-drug antihypertensive therapy. Blacks had a greater response to this dietary intervention than other ethnic groups.

Effects of weight loss

Increasing weight has been shown in several studies to be strongly associated with the development of hypertension, so the effect of weight loss on blood pressure control has been a focus of study [28,29]. Multiple randomized trials have assessed the utility of lifestyle intervention on blood pressure [30–33]. The lifestyle interventions involved regular educational and behavioral sessions, dietary changes, weight loss, and increased physical activity. Specifically, the Trials of Hypertension Prevention, phase II (TOHP-II) [34] randomized overweight adults with high normal blood pressure to one of four treatment groups: weight loss (goal loss of 4.5 kg), sodium reduction (< 80 mmol/d of sodium), weight loss combined with sodium reduction, and usual care. At 6 months, all of the intervention groups had significant reductions in blood pressure, with the combined weight loss and sodium-restriction group having the largest (-4.0/2.8 mm Hg) reduction. As is typical, the changes seen with lifestyle modification tend to drift back to baseline over time. At the end of the study (36 months of follow-up), the degree of blood pressure reduction with the interventions had diminished, although it remained statistically significant. However, those who lost 4.5 kg or more at 6 months and maintained this weight loss over the 36 months of follow-up had a relative risk of progression to hypertension of 0.35 compared with control patients [32]. Those who lost weight initially yet regained it still maintained a slightly lower risk (RR of 0.75) of progression to hypertension. Overall, a meta-analysis of 25 trials (n = 4874 subjects) that used nonpharmacologic methods to attain a mean weight loss of 5.1 kg translated into a 4.44/3.58-mm Hg reduction in systolic/diastolic blood pressure [35]. Put

simply, for every kilogram of weight lost, the blood pressure decreased approximately 1 mm Hg.

Effects of exercise

Currently, greater than 60% of adults in the United States are sedentary [36]. Increasing physical activity can also lower blood pressure. Overall, a meta-analysis of 54 trials implementing a physical activity intervention to treat blood pressure (n = 2419 subjects) demonstrated a pooled effect of -3.84/-2.58 mm Hg [37]. This effect was independent of any change in weight or any type, frequency, or intensity of exercise. Hypertensive participants did have a slightly greater reduction in blood pressure compared with normotensive participants. Although this reported change in blood pressure seems small, a change of as little as 3 mm Hg can have a widespread impact on the population incidence of stroke (15% reduction) and cardiovascular disease (6% reduction) [38].

Lower medication requirement

Most patients would like to take fewer medications, yet physicians are often adding medication to push for tighter risk factor control. One trial has assessed whether antihypertensive medications could be withdrawn if replaced with lifestyle changes. The Trial of Nonpharmacologic Interventions in the Elderly (TONE) study [33] randomized 875 men and women aged 60 to 80 years with a baseline blood pressure of less than 145/85 mm Hg to either usual care, reduced-sodium diet, weight loss (obese participants only), or a combination of low-sodium/weight-loss diet [33]. After 3 months on the assigned regimen, down-titration and eventual withdrawal of antihypertensive medications was attempted. At 30 months in the obese participants, 34% of the reduced-sodium group, 37% of the weight-loss group, 44% of the combined group, and 16% of the usual-care group remained off medication with a blood pressure less than 150/90 mm Hg and free of cardiovascular events. Although this study does not achieve ideal blood pressure control, it does support encouraging patients to make lifestyle changes, as they may significantly reduce the amount or dosages of their medications.

Lifestyle Modification and Glucose Intolerance

Weight loss is currently recommended for all overweight/obese adults with type 2 diabetes as well as those at high risk for developing the disease [39]. This recommendation is based on several randomized studies demonstrating the prevention of or improved outcomes of diabetes with weight reduction [40–42]. These studies have utilized regular counseling sessions on topics such as calorie reduction, change in dietary composition, increased physical activity, and behavioral modification.

Lifestyle modification prevents diabetes

In one such study, the Diabetes Prevention Program Research Group randomized 3234 participants with impaired glucose tolerance to placebo, 850 mg of metformin twice a day, or a lifestyle modification program with a goal of 7% weight loss and 150 minutes of activity per week [40]. Participants had an average BMI greater than 30 kg/m^2 and approximately 50% were from minority ethnic groups. After 2.8 years of follow-up, 38% of lifestyle participants had achieved at least 7% weight loss and 58% met the physical activity goal. The incidence of diabetes was 11%, 7.8%, or 4.8% in the placebo, metformin, and lifestyle groups, respectively. In order to prevent one case of diabetes over a 3-year period, 6.9 people would need to enroll in a lifestyle modification program. Similarly, the Finnish Diabetes Prevention Study Group randomized 552 men and women at risk for developing diabetes to either a lifestyle counseling intervention versus control [42]. The intervention group attained minimal weight loss of 3.5 ± 5.5 kg at 2 years, yet also experienced a 58% reduction in incident diabetes.

Effects of lifestyle modification in diabetic patients

Patients who have already developed diabetes may benefit from implementing lifestyle changes as well. Exercise and moderate weight loss have been shown to decrease fasting glucose levels, decrease the need for hypoglycemic medications, and induce favorable improvements in other cardiovascular risk factors. Although aerobic exercise is typically promoted, resistance training has been shown to improve glycemic control, resulting in a reduced need for medications as well as increased lean body mass with reduced abdominal adiposity [43]. A small study by Collins and Anderson [44] of 40 obese, type 2 diabetic patients on a very low-calorie diet also demonstrated dramatic reductions in the need for diabetic and antihypertensive medications in conjunction with a 14.8% weight loss. Specifically, with aggressive weight loss, some participants no longer required insulin or oral hypoglycemics, and the remaining participants reduced their dosages by about 70%. These results translated into an average pharmaceutical cost savings of approximately $442 per year per person. Thus, in addition to the health benefits of lifestyle modification programs, financial savings may also be achieved.

Weight loss and physical activity also translate into improved long-term outcome. Overweight/obese diabetic patients aged 40 to 64 years enrolled in the Cancer Prevention Study I from 1959 to 1969 who reported intentional weight loss went on to have a 25% lower mortality than those without intentional weight loss [45]. Across the spectrum of intentional weight loss, the largest reduction in total mortality (33%) was noted with a loss of 20 to 29 pounds. Also, the relative reduction in mortality increased with increasing physical activity levels. To assess the impact of lifestyle modification on

cardiovascular events, the ongoing Look-AHEAD (Action for Health in Diabetes) [46] study has randomized more than 5000 diabetic patients to either lifestyle modification or usual care and is following them over a 10-year period. This trial is using meal-replacement beverages, increased physical activity, and individual and group behavioral counseling sessions to achieve a goal of 7% or greater weight loss and 175 minutes per week of exercise.

Lifestyle Modification and Microalbuminuria

Microalbuminuria is associated with hypertension and diabetes, which are diseases that are associated with the metabolic syndrome. An increased BMI is also independently associated with a higher prevalence of microalbuminuria [47,48]. The exact mechanisms leading to obesity-related microalbuminuria are not well defined, although an association with sodium intake has been noted [48]. In diabetic patients, the glomerular filtration rate appears to increase early in the disease, followed by an increased excretion of albumin [49]. This process may also be true for obesity, as food restriction in obese Zucker rats prevented the development of glomerular hyperfiltration and ultimately glomerular sclerosis [50]. These results suggest a potentially preventive effect of diet and weight management on renal function. However, the effects of diet, exercise, and weight loss on microalbuminuria in humans are still not well studied.

Lifestyle Modification and Inflammatory Markers

The metabolic syndrome is associated with elevated markers of inflammation such as interleukin-6 (IL-6), IL-18, tumor necrosis factor-α (TNF-α), and C-reactive protein (CRP). CRP is a sensitive marker of inflammation and increased levels have been associated with the development of diabetes and coronary artery disease [51,52]. Because CRP is an independent risk factor for diseases resulting from metabolic derangements, Tchernof *et al*. [53] assessed correlations of CRP levels with components of the metabolic syndrome and body composition in obese female patients. Plasma CRP levels were positively associated with body weight, fat-free mass, total fat mass, and intra-abdominal adipose tissue area. Intentional weight loss using a reduced calorie diet in a subgroup of this cohort resulted in a significant reduction in CRP levels in proportion to the amount of weight lost. Similar reductions in IL-6, IL-18, and CRP have been described in obese, otherwise healthy women who lost an average of 14 kg with an intensive lifestyle program of increased physical activity, a diet of 1200 to 1500 kcal/d, and dietary composition as seen in Table 1 [54].

Lifestyle Modification and Prothrombotic Markers

A prothrombotic milieu appears to cluster with inflammatory cytokines, increased adiposity, and insulin resistance as part of the metabolic syndrome. In particular, plasminogen activator inhibitor-1 (PAI -1) limits the fibrinolytic process by inhibiting tissue-type plasminogen activator (tPA). The mechanisms underlying how or why PAI-1 is activated or augmented in the metabolic syndrome are currently poorly understood. An increase in PAI-1 predicts cardiovascular events and mortality [55,56]. Measures of obesity, such as the waist-to-hip ratio, BMI, and visceral adipose tissue, are also associated with increased PAI-1 activity and tPA antigen levels [57–59]. Conversely, regular exercise training alone or in combination with weight loss has been shown to improve thrombolysis, as indicated by lower PAI-1 levels and increased tPA activity [60].

Limitations of Lifestyle Modification

Despite strong evidence for the benefits of lifestyle modification, accomplishing and maintaining the changes in diet and physical activity, as well as sustaining weight loss, remains a challenge. Implementation of lifestyle modification programs is labor intensive. For example, in the TOHP-II study, the weight-loss interventions used a combination of individual and group meetings led by health educators or dieticians on a weekly basis for 14 weeks, then bimonthly for several months, followed by monthly meetings thereafter [32]. Participants were required to perform self-monitoring by keeping daily dietary and activity logs. The time and financial constraints of the outpatient healthcare system are not conducive to incorporation of these intensive lifestyle modification programs. Also, despite setting modest goals and enrolling participants who are motivated, many trials are plagued with only partial success in achieving the lifestyle modification goals as well as significant attrition of participants. Better strategies for monitoring patients' efforts, encouraging chronic adherence to the lifestyle regimen, and documenting prevention of secondary diseases may allow more widespread application of these needed measures.

Conclusions

Lifestyle modification incorporating behavioral, dietary, and physical activity changes to induce modest weight loss exerts beneficial effects on the various components of the metabolic syndrome and improves overall survival. This holistic intervention should be the foundation to which pharmaceutical treatment is added as needed. New methods are needed to improve adherence to a healthier

and more active lifestyle. Broader implementation of such changes to combat the alarming increase in obesity may stem the progression to the metabolic syndrome and cardiovascular disease.

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