

## Nutritional Approaches for Prevention and Treatment of Metabolic Syndrome in Adults

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### ABSTRACT

Metabolic syndrome, a clustering of components that reflect overnutrition, sedentary lifestyles, and excess adiposity, has become a major health problem worldwide. The increase in its prevalence could be the result of the increase in obesity and insulin resistance. It is suggested that modification of lifestyle including increasing exercise and improving dietary habits is an effective approach for management of the metabolic syndrome. No single diet is recommended for patients with metabolic syndrome. This paper will review the data and make an evidence-based recommendation for the optimal dietary patterns for reducing cardiometabolic risk.

**Keywords:** Metabolic Syndrome; Diet; Dietary Pattern; Lifestyle; Physical Activity; Weight Loss

### INTRODUCTION

Metabolic Syndrome (MetS), also known as “insulin resistance syndrome” [1], “deadly quartet” [2] or “syndrome X” [3], is a clustering of components that reflect obesity, physical inactivity and consumption of an atherogenic and diabetogenic diet [4]. Individual components that define metabolic syndrome include dysglycemia, raised blood pressure, elevated triglyceride (TG) levels, low high-density lipoprotein cholesterol (HDL-C) levels, obesity, particularly central obesity [4, 5] and recently, a pro-inflammatory and prothrombotic state [6, 7]. The number of studies on MetS in the last two decades indicates the scientific and clinical importance of MetS. The MetS has made its place in the medical literature with more than 32,000 citations now recorded in PubMed. Most studies show 2 fold increase in risk of cardiovascular disease (CVD) and 5 fold increase in risk of type 2 diabetes (T2D) in people with MetS [8, 9]. Recent studies have shown the association of MetS with cancer [10, 11] and chronic kidney disease [12] as well as all cause mortality [13, 14]. Although there is no consensus on the etiology of MetS, it is generally accepted that the prevalence of this syndrome is increasing throughout the world in parallel with the increase in obesity [15] so prevention of this syndrome is necessary to

reduce the associated mortality and morbidity costs[16].

Increasing physical activity and reducing weight is essential for prevention and treatment of MetS but there is no consensus on a single appropriate diet for people with MetS. Thus the aim of this work was to review the current nutritional recommendations for prevention and treatment of MetS. In order to fulfillment of our aim, we reviewed the information from epidemiological and interventional studies on dietary and lifestyle practices proposed for management of MetS. Studies which were published until January 30, 2013 were selected through a computer assisted published data search on PubMed, Scopus, Sciencedirect, Wiley, Springer and Google Scholar databases using keywords related to the aim of the study (i.e., Metabolic syndrome, Syndrome X, Diet, Nutrition, Dietary Pattern, Treatment, Prevention, Lifestyle).

### CLINICAL MANAGEMENT OF METS

According to a report from the National Cholesterol Education Program's Adult Treatment Panel III (NCEP: ATP III) the primary goal of management of MetS is to reduce the risk CVD and T2D. Overall goals of reducing the risk for or preventing CVD and T2D according to MetS components are summarized in table 1 [17].

**Table 1.** Overall goals of reducing the risk for or preventing CVD and T2D according to MetS components

Treatment Targets	Goals and Recommendations
Abdominal obesity	5–10% Weight loss or weight maintenance Lifestyle modification with diet and increased physical activity Pharmacological weight loss therapy Bariatric surgery
Insulin resistance/hyperglycemia	Prevention or delay of progression to type 2 diabetes Lifestyle modification and weight loss as described above Pharmacotherapy Treatment of diabetes Appropriate glycemic control
Metabolic dyslipidemia Primary target: LDL-C Secondary target: non-HDL-C Tertiary target: HDL-C	LDL-C lowering as per NCEP:ATPIII goals If TG $\geq$ 200 mg/dl, lower non-HDL-C to 30 mg/dl plus the LDL-C goal If HDL-C $<$ 40 mg/dl in men or $<$ 50 mg/dl in women, consider therapy for HDL-C raising
Elevated blood pressure	Goal BP is $<$ 140/90 mm Hg ( $<$ 130/80 mm Hg if diabetes or CKD present)

Adapted from [17]

Since the first description of MetS by kylin in 1920 [18], different strategies including lifestyle modification, drug therapy and weight loss surgery have been implied to reduced the risk of the whole syndrome or its individual components. In a recent review, Giugliano [19] has showed that the most effective approach to reduce the risk of MetS is weight loss surgery with a 93% reduction in the risk of MetS in compare with the effect of lifestyle modification (25%) and drug therapy (19%) on reducing the risk of the syndrome. Despite its striking effectiveness, weight reduction surgery can not be a routine treatment of the MetS because many of the people with MetS are not a candidate for weight loss surgery [20].

Lifestyle modifications including weight loss, increased physical activity and dietary modifications have been demonstrated to improve all of the components of MetS simultaneously [21-24]. Among the drugs used to treat MetS, only the weight reduction drugs (i.e. sibutramine and orlistat) may have the same effect. However many adverse side effects of these drugs have limited their use in many patients [25].

Other drugs that are used to correct individual components of MetS do not improve all of them simultaneously [26].

For these reasons lifestyle modifications are considered to have priority over drug treatment and ATP III has proposed lifestyle modifications as the first line intervention in clinical management of MetS [6].

## LIFESTYLE MODIFICATION

Therapeutic lifestyle changes have been demonstrated to improve individual components of MetS as well as the whole syndrome. In a meta-analysis Yamaoka et al. [27] found that lifestyle and dietary education can effectively reduce 2-hour plasma glucose level and the incidence rate of T2D in patients at high risk of T2D. Data from another meta-analysis placed emphasis on the evidence that long-term regular lifestyle modification, including achieving and maintaining a weight reduction through diet and moderate-intensity physical activity is two times more effective at resolving the MetS in compare to control group [21]. It is proposed that the initial therapeutic approach to MetS through lifestyle modification is reversing its key roots including a sedentary lifestyle, overweight or obesity and an atherogenic/diabetogenic diet [19].

### Physical Activity

Increasing physical activity can moderate CVD risk [28], incidence of T2D [29] and protects against development of MetS through its effects on the whole syndrome as well as each of the individual components [29-32]. Physical activity is particularly effective at reducing insulin resistance [33, 34] and hypertension [35] and also improving dyslipidemia, especially increasing HDL-C level [35-37]. Meanwhile regular exercise prevents weight regain in those who have lost weight [38, 39] and play an important role in abdominal fat loss [33, 40]. Both aerobic and resistance exercise seems to be beneficial for patients with MetS. Aerobic exercise is the

cornerstone of preventing Mets because it improves insulin resistance. Resistance exercise also provide additional benefit because it increases the muscle mass, promotes a negative energy balance and leads to weight loss and better metabolic control [41, 42]. The 2008 physical activity guidelines suggest that all individuals have at least 150 minutes per week of moderate-intensity physical activity. All individuals should also have at least 2 days per week of resistance exercise activity. If weight loss is the goal, the combination of physical activity and reduced energy intake has been demonstrated to be more effective than either alone [42].

### **Weight Loss**

Weight loss has profound role in treating all of the components of MetS, including obesity, dyslipidemia, hypertension, insulin resistance, and hyperglycemia [43, 44]. Even modest weight loss can significantly reduce the prevalence of MetS [44]. It is shown that 5–10% reduction of body weight significantly reduces triglycerides and increase HDL-C [45]. Weight loss predicts the reduction in the incidence of diabetes and for every kilogram of weight loss the risk of diabetes development decreases by 16% [46].

In a recent review, Leão et al has shown that low-calorie diets combined with physical activity is the most effective strategy to improve MetS [47]. Low-calorie diet can specifically improve insulin resistance and obesity which are at the core of the pathophysiology of this syndrome.

### **Healthy Diet**

In either a normo-calorie or a low-calorie diet the composition of the whole diet and distribution of macronutrients consumed are also important because they influence the individual components of MetS as well as the overall health of the patient. The first dietary recommendations proposed by ATP III and American Heart Association (AHA) include moderate fat intake (25%-35% of energy), low saturated fat intake (<7% of total energy), avoidance of trans fat, limited cholesterol (<300mg/d) and refined sugar, high intakes of fruits, vegetables and whole grains [5, 48]. These recommendations traditionally emphasize on lowering LDL-C level to reduce the risk of CVD. In management of MetS, triglyceride and

HDL-C level are also important, so more detailed recommendation are required [49].

### **Macronutrient Distribution of Diet**

Recommendations for resolving MetS traditionally focused on lowering fat intake. Although low fat diets effectively reduce LDL-C, they have adverse effect on TG and HDL-C [50, 51] and insulin resistance [52]. Low fat intake may lead to high intake of refined carbohydrates [53, 54]. High carbohydrate intake, especially refined carbohydrates is associated with high blood pressure [55]. Data from NHANES III also shows high intake of carbohydrate (>60% energy intake) in men is associated with MetS [56].

Low carbohydrate diets may be more effective at resolving MetS than low fat diets [57-60]. In low carbohydrate diets, <30% of total energy intake is from carbohydrate [61] or total daily intake of carbohydrate is in the range of 50-150 grams [62]. Low carbohydrate diet is associated with lower TG concentration and higher HDL concentration [63, 64] as well as rapid weight loss and insulin level reduction over short periods of time [65]. However, in such diets uncontrolled intake of high fat meats and products may induce adverse metabolic effects for patients with MetS [66].

Diets high in protein have also been proposed for the treatment of MetS [67]. In addition to rapid weight loss, these diets improve body composition. It has been demonstrated that increasing dietary protein content (30%) and decreasing carbohydrates (40%) reduce fat mass, especially abdominal fat mass [68]. Positive effects of high-protein low-CHO diets on reducing risk factors for MetS have been reported. These effects include reducing serum TG, increasing HDL cholesterol, increasing LDL particle size, and reducing blood pressure [69-71]. Studies show that replacing dietary carbohydrate with either fat or protein reduce triacylglycerides and increase HDL cholesterol even under weight-stable conditions [72, 73]. However, substitution with protein may be more effective for improving lipid profile [72-74] and insulin action [73, 75]. Finally, scientific evidence suggests that reducing dietary carbohydrate is the primary means of prevention or treatment of MetS. Increasing dietary protein as an approach to lowering dietary carbohydrates may be more effective than increasing fat [65, 76, 77].

### **Dietary Pattern**

With increasing evidence on complexity of diets consumed by free-living individuals, it is suggested that studying dietary pattern or all components of diet as a single exposure would be a powerful approach to describe the association between diet and chronic diseases including MetS [78, 79]. Williams et al. in a cross sectional study demonstrated that a healthy balanced diet high in raw and salad vegetables, fruits, fish, pasta, and rice and low in fried foods, sausages, fried fish, and potatoes was negatively associated with central obesity, fasting plasma glucose, and triacylglycerols and also positively associated with HDL-C [80]. Since then several epidemiological studies have demonstrated that diets rich in fruit, vegetables, whole grains, low fat dairy products and monounsaturated and polyunsaturated fats are associated with a lower prevalence of the metabolic syndrome while high intake of processed meat, fried foods, sugar-sweetened

beverages, refined carbohydrates and processed cereals with high glycemic index are associated with high prevalence of Mets in men and women [81-88].

One of the main outcomes of the initial epidemiological evidence was guidelines proposed by ATP III and AHA known as Therapeutic Lifestyle Change diet (TLC) guidelines. Nutrient composition of TLC Diet is summarized in table 2. The efficacy of these recommendations has been evaluated in clinical trial studies. It has been shown that following these guidelines in combination with exercise significantly reduces body weight and waist circumference in women with MetS after 6 month [89]. In another study, 4-month lifestyle modification education based on TLC in Iranian adults using mentioned guidelines improved total cholesterol and LDL-C significantly in Iranian adults with MetS [90].

**Table 2.** Nutrient Composition of the TLC Diet

<b>Nutrients</b>	<b>Recommended Intake</b>
Saturated fat	< 7% of total calories
Trans fat	< 1% of total calories
Polyunsaturated fat	Up to 10% of total calories
Monounsaturated fat	Up to 20% of total calories
Total fat	25% to 35% of total calories
Carbohydrate	50% to 60% of total calories
Fiber	20-30 g/day
Protein	Approximately 15% of total calories
Cholesterol	< 200 mg/day
Total calories	Balance energy intake and expenditure to maintain desirable body

Adapted from (4)

The Dietary Approaches to Stop Hypertension or DASH diet is another dietary approach proposed for management of MetS. DASH Dietary pattern emphasizes on high intake of fruits, vegetables, low-fat dairy foods, whole grains, poultry, fish, and nuts, seeds and legumes. Additionally, it is low in saturated fat, total fat, cholesterol, red meat, sweets, sugared beverages and refined grains. Calcium, potassium and fiber intake in this dietary pattern is high but the amount of sodium intake is low (i.e., 2,400 mg per day) [91, 92]. While DASH was originally developed to manage or prevent high blood pressure [93], it has been found to have many additional advantages and is now recommended for all adults [91]. Azadbakht et

al. in a clinical trial on 116 men and women with MetS demonstrated that 6-month intervention with DASH diet significantly reduced body weight, waist circumference, TG, systolic blood pressure, diastolic blood pressure, and fasting blood sugar and also increased HDL-C [94], thus reduced the risk of the syndrome by 20%. In a randomized crossover clinical trial beneficial effects of DASH diet to reduce cardiometabolic risks among type 2 diabetic patients was also shown [95]. However, a recent review article emphasized the fact that significant improvements in insulin sensitivity are observed only when the DASH diet is implemented as part of a more comprehensive

lifestyle modification program that includes exercise and weight loss [96].

The Mediterranean diet (MD) which was first introduced by Ancel Keys in 1960s [97], is not a specific diet, but rather a collection of eating habits traditionally followed by people in the different countries bordering the Mediterranean Sea including Greece, Spain, southern Italy, Portugal, and Turkey. This dietary pattern is characterized by daily consumption of nonrefined cereals, vegetables (two or three servings per day), fruit (four to six servings per day), different olive oil products and nonfat or low-fat dairy products (one or two servings per day); weekly consumption of potatoes (four to five servings per week), fish (four to five servings per week), olives, pulses and nuts (more than four servings per week), and more rarely poultry, eggs, and sweets (one to three servings per week), and monthly consumption of red meat and meat products (four or five servings per month) as well as a moderate daily consumption of alcohol, normally with meals [98, 99]. MD has been shown to be the optimal diet for preventing non communicable diseases and preserving good health [99, 100]. While MD is a well known cardioprotective diet [101-103] its beneficial roles with regard to all cause mortality and cancer as well as obesity and TDM have also been shown in epidemiological studies and clinical trials [100, 104-111]. The MD also protects against MetS and its individual components and is more effective in resolution of the syndrome compared to the DASH diet [47].

Esposito et al. in a randomized clinical trial on 180 men and women demonstrated that over a course of 24 month intervention with MD, prevalence of MetS reduced by approximately 50%. The reduction in the prevalence of MetS was owed to significant decreases in waist circumference, blood pressure, plasma glucose, total cholesterol, and triglyceride concentrations, and a significant increase in HDL in the intervention group [112].

A recent systematic review and meta-analysis of 50 studies including both observational studies and randomized controlled trials reinforced the benefits of MD on improving the MetS and its individual components and revealed that adherence with MD reduced the risk of developing this syndrome by 31% [113]. Antioxidant and anti-inflammatory properties of the foods included in MD as well as high intake

of vitamins and minerals guarantee the protection against MetS. Recently it is shown that 2 month intervention with MD effectively increases total dietary antioxidant intake and plasma total antioxidant capacity [114].

Olive oil is one of main food items of MD which has been shown to improve cardiovascular risk factors, such as lipid profiles, blood pressure, postprandial hyperlipidemia, endothelial dysfunction, oxidative stress, and antithrombotic profiles [115, 116]. Phenolic compounds in olive oil have also shown antioxidant and anti-inflammatory properties that improve endothelial function [117, 118].

Meanwhile olive oil lowers NF-kB activation, thus leads to decrease in markers of inflammation (CRP, IL-6, IL-8), oxidation, and thrombosis [119]. Nuts are another high-unsaturated fat food commonly consumed in the MD. Epidemiological and clinical trial studies suggests that regular nuts intake might have a positive impact on adiposity [120, 121], insulin resistance [120] and other metabolic disturbances linked to the MetS and CVD [122].

## CONCLUSION

Regarding the increase in the incidence of MetS serious action should be taken to control the whole syndrome and its individual components.

As shown in this review, the most applicable strategy to prevent and treat MetS is improving lifestyle through keeping healthy weight, following a healthy diet and increasing physical activity. Although the ideal diet should be personalized to each patient, dietary factors which are beneficial for effective weight loss and weight maintenance as well as for reducing cardiovascular and diabetes risk should be recommended for all.

Summary of research suggest that high intake of foods rich in antioxidants including fruit and vegetables as well as foods rich in monounsaturated fat such as olive and olive oil, a balanced intake of carbohydrates rich in dietary fiber and low intake of saturated and trans fat, in combination with regular exercise may be beneficial for management of MetS and its components. Further randomized clinical trials are needed in order to establish if it is the best option for the patients with MetS.

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