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IM - REVIEW

Optimizing management of metabolic syndrome to reduce risk: focus on life-style

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Abstract The prevalence of metabolic syndrome (MS) is increasing all over the world and its incidence is expected to rise in the next years. Although genetic predisposition appears to play an important role in the regulation of metabolic parameters and in particular of body weight, the rapid increase in the prevalence of obesity and MS suggests that ecological factors (social, economic, cultural and physical environment) are promoting those conditions in susceptible individuals. People with MS are at increased risk of type 2 diabetes and cardiovascular disease and therefore they represent a priority target for preventive strategies. Life-style modifications based on healthy diet and increased physical activity are an effective preventing and therapeutic approach. Unfortunately, implementation of life-style modification and maintenance of effects is a difficult task both at personal and social level, thus drug therapy can be taken into account.

Keywords Metabolic syndrome · Life-style · Insulin-resistance · Type 2 diabetes · Cardiovascular disease

Introduction

Obesity (especially abdominal adiposity), hyperglycemia, dyslipidemia, and hypertension are common metabolic traits that, concurrently, constitute the distinctive insulin-resistance or metabolic syndrome (MS) [1]. The MS is associated with an increased risk of type 2 diabetes (T2DM) and of cardiovascular (CV) disease [2]. The prevalence of MS is increasing all over the world, though its prevalence may vary a lot, swinging from 8% in India to 24% in USA. The incidence of MS is expected to rise in the years to come [3] driven by lifestyle changes [4] and obesity [5]. Because of the epidemiological spreading of the MS and because of his high associated risk, the MS may be seen as public health problem requiring specific preventative actions.

Changes in environment as causes of metabolic syndrome epidemic

Although genetics appear to play an important role in the regulation of metabolic parameters and in particular of body weight [6], the rapid increase in the prevalence of obesity and MS in the world over the past two decades suggests that ecological factors (social, economic, cultural and physical environment) are determining, or at least favouring those conditions.

Social factors

A major energy imbalance in the population has been triggered by dramatic reduction of physical activity and changes in dietary patterns. Thus, the nature of the food supply has changed; foods are more commonly consumed away from home; food advertising, marketing, and promotion has been exploited and food prices dropped [7]. There are more families in which both parents work, and time limitations have become an important factor in

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determining the types of food consumed. The food industry responds to the family needs by increasing the number of caloric-rich convenience food and pre-cooked meals [8]. Increased consumption of convenience food is associated with reduced eating of fish, fruits, and vegetables. In addition, portion sizes have increased over the past two decades [9], as the per capita availability of added sugar and fat [10]. This food is widely available to children from fast-food restaurants, but also at school and home [11]. Children who regularly eat at fast food have greater calories intake and eat less fruits and vegetables than children not going to fast food restaurants [12, 13]. Surveys curried out in the 1970s, 1980s, and 1990s [14, 15] showed that, in adolescents aged 12–18 years, there is a decrease in the percentage of energy intake from food consumed at home, whereas the proportion of energy intake from restaurant food and fast food has increased over time [13]. The proportion of total daily energy intake of thus adolescents decreased from 74.1% in 1971–1978, to 68.3% in 1989–1991 and to 60.5% in 1994–1996. Concomitantly, fast food consumption increased from 6.5 to 16.7% in the period 1971–1978 to 1989–1991 [14, 15]. Accordingly, money spent on food not consumed at home represented 25% of total food expenditures in 1977–1978, and increased to 40% in 1995 [16]. A similar phenomenon occurs in Italy as well, with an increase of 58.1 billions of euros in 2005, i.e., +2.6% in comparison with the previous year. It has been estimated that in 2008 food consumed away from home will represent 36% of total consumption (http://www.ISTAT.it).

Dietary habits

Eating away from home, including restaurant and fast food consumption, is associated with less macro/micro-nutrient intake, worse diet quality, higher energy density and total energy intake and weight gain [17–19]. In two different studies, women with ‘‘fast food’’ or ‘‘restaurant’’ eating patterns tended to have the greatest intakes of energy, total fat, saturated fat, cholesterol, and sodium [20, 21]. Moreover, among young adult of the CARDIA Study, performed between 1985–1986 and 2000–2001, the frequency of visits to fast-food restaurants was correlated with increase in body-weight and insulin-resistance, the two major risk factors for T2DM [22]. While no weight gain was recorded in subjects with infrequent fast-food restaurant use, those with frequent fast-food restaurant visits gained an extra 4·5 kg body-weight and had a two-fold increase in insulin-resistance [23]. The food consumption patterns in the general Dutch population and their association with CV risk factors has been recently determined [24]. Three patterns were identified: the “cosmopolitan” pattern (greater intake of fried vegetables, salad, rice, chicken, fish, and wine), the “traditional” pattern (greater intake of red meat and potatoes and lesser intakes of low-fat dairy and fruit), and the “refined-foods” pattern (greater intake of French fries, high-sugar beverages, and white bread and less intake of whole-grain bread and boiled vegetables). Traditional and refined-foods pattern were associated with less physical activity and higher body mass index. Independent of other lifestyle factors and body mass index, the cosmopolitan-pattern was associated with lower blood pressure and higher HDL-cholesterol concentrations, while the traditional-pattern was associated with higher blood pressure and higher concentrations of HDL- and total-cholesterol, and glucose. The refined-food-pattern was associated with higher total cholesterol concentrations and lower intake of micronutrients. Similarly, the Malmö Diet and Cancer study [25] demonstrated that dietary patterns dominated by fiber bread (comparatively high in several micronutrients) provide protective effects, while food patterns high in refined bread or cheese, cake, and alcoholic beverages (with lower intakes of several micronutrients) increase the risk for several components of the MS (Table 1).

Exercise and smoking

Life-styles changed dramatically in the past 50 years by modification of urban and suburban space organization, land use, public transportation, free-activity options [52]. The reduction of physical activity in the general population has been attributed to lack of opportunities to walk, as well as to increased access to motorized transport. A review of fourteen studies shows a consistent inverse association between built environment factors (i.e., higher residential density, land mix, and connectivity) and walking or cycling [53]. Walking or bicycling is increasingly uncommon and physical education has been given up in most schools [54]. Special attention may be needed for lower-income and minority communities, which tend to have fewer parks, sport facilities, bike paths, swimming pools, and other places for leisure activity [55]. At the same time, neighbourhoods are increasingly perceived as unsafe for children to play out in, implicitly discouraging active play and forcing children back in front of the television set [56]. The Health Professionals’ Follow-up Study demonstrated that prolonged TV watching is strongly associated with obesity and weight gain, independent of diet and exercise [45], as well as increased risk of T2DM.

Numerous studies showed that the MS and its components are closely associated with lifestyle factors, including low physical activity levels [57, 58]. Data from the National Health and Nutrition Examination Survey 1999–

Table 1 Effects of dietary factors or physical activity on metabolic syndrome components and associated conditions

		Study/ref.
Increased intake		
Daily calories	↑ body fat accumulation	Lichtenstein [26]
	↓ central obesity	Malmo Diet and Cancer cohort [25]
	↑ diabetes risk	DPS [27], DPP [28]
Carbohydrates (mainly refined)	↓ insulin sensitivity	Parillo [29)
	↑ triglycerides, ↓ HDL-cholesterol	Garg [30]
	↑ blood pressure	Obarzanek [31]
Saturated and trans fats	↓ insulin sensitivity	Vessby [32]
	↑ diabetes risk	Howard [132]
	↓ HDL-Cholesterol	Grundy [33]
	↑ inflammation/thrombosis	Lopez-Garcia [34], Esposito [35]
	↑ plasma cholesterol	Lichtenstein [26]
Alcohol	↑ blood pressure	Appel [36]
	↑ triglycerides	Kiechl [37]
Salt	↑ blood pressure	Appel [36]
Reduced intake		
Fibers	↓ insulin sensitivity	Weickert [38]
	↑ plasma insulin levels	Malmo Diet and Cancer cohort [25]
	↑ triglycerides	Brown [39]
Monounstaurated fats	↓ HDL-Cholesterol	Appel [36]
	↓ insulin sensitivity	Prillo [40]
	↑ cardiovascular risk	de Logeril [41]
ω-3 fatty acids	↑ cardiovascular risk	Psota [42]
	↑ triglycerides	Balk [43]
	↑ inflammation/thrombosis	Giugliano [44]
Reduced physical activity		
	↑ body fat accumulation	Hu [45]
	↓ insulin sensitivity	Henriksen [46]
	↑ blood pressure	Whelton [47]
	↑ triglycerides	Thompson [48]
	↓ HDL-cholesterol	Huttunen [49]
	↑ cardiovascular risk	Hu [50], Hu [51]
	↑ diabetes risk	DPS [27], DPP [28], Da Qing Study [102]

2000 show that MS prevalence was higher among subjects with sedentary habits such as TV watching or computer use [59]. Among French adults, the frequency of many MS components increased as a function of the time spent in front of a screen and decreased with increasing physical activity levels [60]. The likelihood to have MS, decreased by one-third with moderate physical activity and by two-thirds with vigorous physical activity even after adjustment for age, education, and smoking, [odds ratio (95% CI), 0.34 (0.17–0.66) in women, 0.44 (0.28–0.68) in men] compared with subjects with insufficient physical activity. In women, independently of physical exercise, time spent in front of a screen was positively associated with the likelihood to have the MS [odds ratio (95% CI), 3.30 (2.04–5.34)].

Another important environmental factor for MS is cigarette smoking. Though the trend of cigarette smoking is declining in adults [61], smoking rate among high school students has recently started to increase [62]. Several studies have demonstrated a clear association between smoking habits and educational level [63, 64]. Smoking is known to be independently associated with CV risk, and seems to have an adverse effect on several components of MS [65–67]. Smoking acutely impairs glucose tolerance and insulin sensitivity, reduces HDL-cholesterol and increases triglyceride levels, and raises blood pressure and heart rate [68]. Moreover, a dose-dependent effect exists between prevalence of the MS and the number of cigarettes smoked [69].

Metabolic syndrome as risk factor for type 2 diabetes and cardiovascular disease

Several studies have shown that MS is a strong predictor of incident T2DM. Both WHO and ATP III definitions for MS can predict incident T2DM in the general population [70, 71]. The prevalence of MS increases along with deterioration of glucose regulation going from 22% in subjects with normal glucose tolerance (NGT) to 75% in those with combined impaired fasting glucose (IFG) and impaired glucose tolerance (IGT) [72] (Fig. 1). Recently, Ford reviewed prospective studies from 1998 through 2004 on MS and reported that the relative risk for T2DM in individuals with MS, as defined by NCEP ATP III, was 2.99 (1.96–4.57) [73]. The same analysis indicated that the relative risk for CV disease and all-cause mortality in subjects with MS was 1.65 (95% CI, 1.38–1.99) and 1.27 (0.90–1.78), respectively. MS comprises a cluster of abnormalities that occur as a result of perturbations in multiple metabolic pathways, leading to hyperinsulinemia, insulin-resistance, hyperglycemia, atherogenic dyslipidemia, and hypertension. Recent findings suggest that obesity and MS are pro-inflammatory conditions, characterized by elevations of serum high-sensitivity C-reactive protein [74, 75]. Atherothrombotic factors also are increased in MS: these include increased levels of plasminogen activator inhibitor-1, serum fibrinogen, von Willebrand factor, factor VII, and thrombin, as well as increased platelet activation and aggregation [76]. Several studies demonstrated that MS is associated with significant increase in the risk of CV morbidity and mortality [77–79]. Data from the Third National Health and Nutrition Examination Survey indicated that MS is associated with increased risk of myocardial infarction and stroke [77]. This finding is in agreement with a study from Finland that examined the relationship between MS and CV disease and overall mortality rate in middle-aged men participating in the population-based Kuopio Ischemic Heart Disease Risk Factor Study [78]. In the Botnia Study, the risk for coronary heart disease and stroke was increased threefold and CV mortality was markedly increased in subjects with MS (12.0 vs. 2.2%; $P < 0.001$) [80]. In another population-based study the risk of incident CV disease, over a 5-year observational period, increased with the number of components of MS being more than 5-fold greater in subjects with four or more MS components compared with those with only one component [79]. In the ARIC Study, after adjustment for age, smoking, LDL cholesterol and ethnicity, subjects with MS were 1.5 and 2 times more likely to develop coronary heart disease and ischemic stroke than control subjects. Furthermore, in patients with a history of myocardial infarction, the presence of the MS is associated with increased risk of death and major CV events [81]. In addition, a high prevalence of the MS (46%) was recently reported in patients with atherosclerotic disease (coronary heart disease, cerebrovascular disease, peripheral artery disease, or abdominal aortic aneurysm) [82]. Even in patients with overt T2DM, the presence of the MS is associated with an almost fivefold increase in CV risk [83–85].

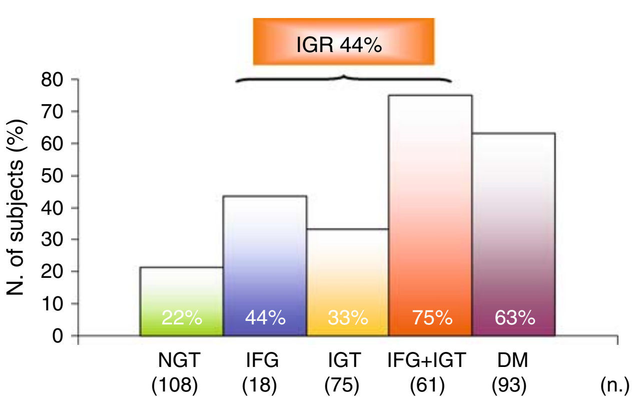


Fig. 1 Prevalence of metabolic syndrome by glucose tolerance categories. *IGR* impaired glucose regulation, *NGT* normal glucose tolerance, *IFG* impaired fasting glucose, *IGT* impaired glucose tolerance, *DM* diabetes mellitus

On the light of these data, MS may provide a simple but useful tool to recognize subjects at high risk for T2DM and CV disease. However, as recently proposed by Després [86] and by the ADA/EASD joint document [87], the presence of the MS should not be a reason for not assessing global CV risk. Rather, in defining the risk, traditional risk factors, as well as potential additional contribution of abdominal obesity and/or insulin resistance and of related metabolic abnormalities, should be promptly considered for an intensive and appropriate treatment.

Benefits of life-style modifications

Since MS can be considered as a T2DM and CV risk factor, the obvious consequence is that people with the syndrome should be identified earlier in order to put at work appropriate preventative strategies (Fig. 2). To this purpose periodical physical examination (including waist circumference measurement) and routine laboratory parameters should be implemented [88].

Given the main effect changes in life-style exerts on the growing incidence of MS, it is obvious that the main goal of preventative actions should promote a modest weight reduction and regular physical activity (Fig. 3).

Modest weight loss can indeed significantly improve all aspects of the MS such as lipid profile, glucose tolerance, blood pressure, and insulin sensitivity [89]. A realistic goal for weight reduction is a 7–10% body weight loss over 6–12 months period. Long-term maintenance of weight loss is best achieved when regular exercise is included in the

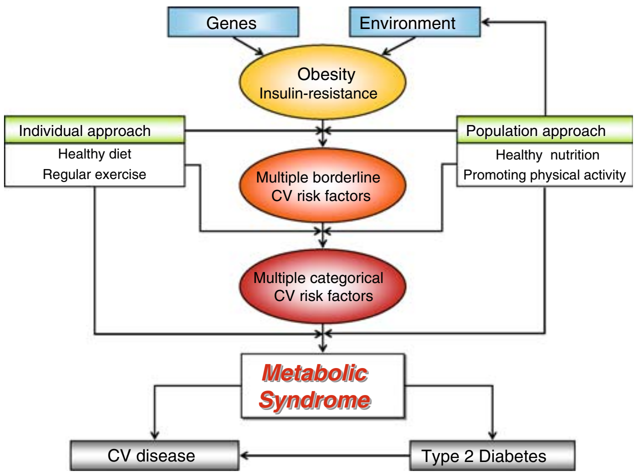


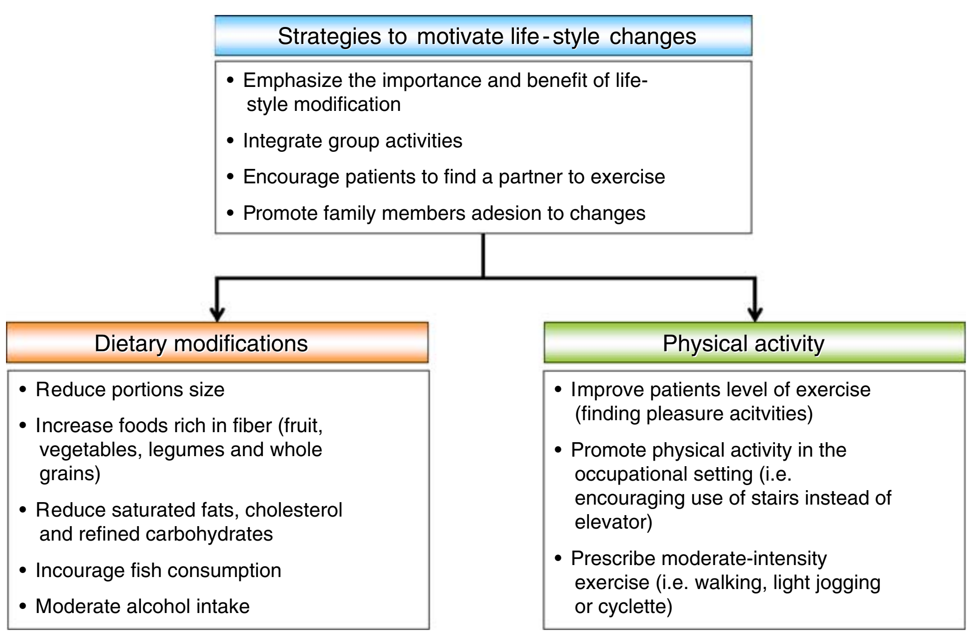
Fig. 2 Strategies for changes of life-style in subjects with metabolic syndrome

weight-reduction regimen. Physical activity can exert its protective effects on the MS through improvements in plasma lipid concentrations, particularly increasing HDL cholesterol [90, 91] and decreasing triglycerides [92, 93]. In addition, physical exercise lowers blood pressure [94], improves glucose tolerance [95, 96] and insulin sensitivity [97, 98], and reduces the risk of developing T2DM [99, 100].

The aim of the HERITAGE Family Study [101] was to determine the efficacy of exercise training in treating the MS. The study population included 621 sedentary and apparently healthy individuals. In this group of people the MS prevalence was 16.9%. After exercise training, 30.5% of the subjects with MS at baseline did no longer meet the diagnostic criteria for MS, suggesting that aerobic exercise can be a useful treatment strategy.

Three studies, the Finnish Diabetes Prevention Study (DPS) [27], the Diabetes Prevention Program (DPP) [28] and the Da Qing Trial [102], have documented the benefits of therapeutic lifestyle change in individuals with impaired glucose tolerance (IGT). These studies have shown that as little as a 10% body weight reduction and regular physical activity can reduce the risk of developing T2DM by more than 50%. Moreover, after 3.2 years of lifestyle intervention, the incidence of MS was much lower than the one observed in the placebo group ($P < 0.001$) [103]. Furthermore, among participants who did not have MS at baseline (47%), the incidence of the MS during follow-up was reduced by 41% with lifestyle intervention ($P < 0.001$) compared to placebo [104]. In agreement with these data are the results of the Oslo Diet and Exercise Study that evaluated the single and combined effects of diet and exercise intervention on MS. After 1 year, as compared with control group, fasting glucose decreased significantly in the diet alone group as well as in the diet plus exercise group. Moreover, in a subgroup analysis of good responders, favourable changes have been observed with respect to total and HDL cholesterol, triglycerides, systolic and diastolic blood pressure [104]. Both dietary and exercise intervention had significant effects on the reduction of cases with MS (MS prevalence −35.3 and −23.5%, respectively; $P < 0.005$ vs. control group) in a group of 137 middle-aged males [105]. Finally, combination of diet and exercise was more effective than diet or exercise alone in the treatment of the MS (−67.4%) (Table 2).

Fig. 3 Individual and population approaches to prevent and treat metabolic syndrome by life-style changes



Healthy diet and promotion of physical activity

Diet in industrialized countries is rich in calories, saturated fat, dietary cholesterol and refined grains. Specific dietary changes are needed for people with MS. This must include reduction of saturated fat intake to lower insulin-resistance, reduction of sodium intake to lower blood pressure, and reduction of high-glycemic index carbohydrate intake to lower triglyceride levels. Such a diet should include more fruits, vegetables, whole grains, monounsaturated fats, and low-fat dairy products.

Recently, evidence-based nutritional recommendations for treatment and prevention of MS have been proposed [125]. According to these recommendations, protein should contribute for 10–20% of total daily energy; saturated fatty acids and *trans* unsaturated fatty acids should be lower than 10% of total energy and further lowered to <8% if serum LDL-cholesterol level is increased; cholesterol intake should be 300 mg or less per day; carbohydrate should range between 45–60% of total energy expenditure. However, in the scientific community the proportion of macronutrients (i.e., protein, fat, and carbohydrates) is still a matter of debate so that it may be advisable to focus on each patient's specific metabolic alterations when offering dietary advice [126].

Bravata et al. published a meta-analysis on the effects of low-carbohydrate diets in obese patients showing that weight loss was associated with longer diet duration and decreased caloric intake, but not with reduced carbohydrate content [127]. In morbidly obese patients with high prevalence of T2DM or MS, a low-carbohydrate diet seems associated to a greater weight loss but also to a higher rate of drop-out in comparison to a low-fat diet [128–130]. Even if low-fat diet may be less tasting, reduction of saturated fats may be useful to improve insulin sensitivity since increased level of free fatty acid, and the saturated to unsaturated fatty acids proportion plays an important role in the development and maintenance of insulin-resistance [131]. The KANWU multicenter study [32] has shown that shifting from a diet rich in saturated fatty acids to one rich in monounsaturated fat improves insulin sensitivity in healthy people, an effect that is not exerted by moderate ω-3 fatty acid supplementation. Finally, diets higher in saturated fat have been claimed to increase T2DM risk as compared to those higher in unsaturated fat [132].

Food rich in dietary fiber is strongly recommended, with a total dietary fibre intake $\geq$40 g/d (or 20 g/1,000 kcal/die), and about half of them in their soluble form. Vegetables, legumes, fruits, and whole-grain cereals represent the most appropriate sources of carbohydrates. Several studies have shown that high intake of dietary fiber is associated with enhanced insulin sensitivity, while diets high in rapidly absorbed carbohydrates and low in cereal fiber are associated with increased risk of T2DM [133, 134]. In a cross-sectional study among participants of the Framingham Offspring Study [115], whole grain and cereal fiber intakes were associated with reduced risk of MS, with cereal fiber accounting for most of the whole grain effect. Higher glycemic index was associated with higher risk of MS, while no association was observed for glycemic load, total carbohydrate intake, refined grain intake, or other sources of dietary fiber.

Diets rich in fruits, vegetables and including low-fat dairy products, whole grains, poultry, fish and nuts, with decreased amounts of red meat, sweets, sugar, cholesterol, total and saturated fat, i.e., a diet very similar to DASH diet, has been associated with lower blood pressure values [135]. Sodium restriction can reduce systolic blood pressure and enhance blood pressure-lowering effect of other dietary manipulations or pharmacologic treatment. In the low-sodium DASH trial [136] reduction of sodium intake from high to intermediate level significantly lowered systolic blood pressure, while reducing sodium intake from intermediate to low level was accompanied by additional reduction. Hence, salt intake should not exceed 6 g/day, with the possibility of further restriction for patients with elevated blood pressure. Studies such as DASH [135] and PREMIER [137] have shown that moderate alcohol consumption can reduce systolic blood pressure. Moreover, moderate alcohol intake has been associated with lower prevalence of MS, favourable influence on lipids, waist circumference, and fasting insulin [138]. Still, alcoholic beverages should be limited to no more than 2 drinks per day for men and 1 drink per day for women usually taken during meals [26]. Greater alcohol consumption has been associated with high risk of overweight and obesity [139].

The DASH diet resulted in a significant improvement of all components of MS [119]. The DASH diet is very similar to the Mediterranean diet, and the results are in agreement with previous findings obtained over a longer period of time (24 months) by Esposito et al. [35]. In this study, participants on Mediterranean diet showed a reduction in the number of the components of the syndrome and a drop in the MS prevalence approximately by half [35]. Consumption of the Mediterranean diet by patients with MS was associated with improvement of endothelial function and reduction of markers of systemic vascular inflammation [35]. Of relevance the observation that the Mediterranean diet has been related with low mortality [140], low prevalence of metabolic disorders (like obesity, and high blood pressure), as well as low incidence of coronary heart disease [141] is of relevance.

Exercise is a key component of effective treatment in patients with MS. individuals should be encouraged to improve their level of physical activity. The greatest health benefits occur when sedentary persons incorporate

Table 2 Effects of dietary habits and physical activity in prevention and treatment of metabolic syndrome and its components

	Study/ref.	Design	Sample	Outcome
Central obesity				
Low energy diet + exercise	Lofgren 106]	Intervention Follow up: 10 weeks	70 premenopausal women	↓ BMI, ↓ waist, ↓ insulin, ↓ leptin
Mediteranean diet	ATTICA Study [107]	Cross sectional	2,282 Greek adults	↓ risk of MS
High fiber intake	IRAS Study [108]	Cross sectional	980 middle-age adults	↓ waist
High complex carbohydrate intake	Halkjaer J [109]	Prospective follow-up: 6 years	2,300 adults	↓ waist
Increased trans fats intake	Koh-Banerjee [110]	Prospective; follow-up: 9 years	16,587 US men	↑ waist
Blood pressure				
DASH diet	Lopes [111]	Intervention follow-up: 8 weeks	12 obese hypertensive 12 lean normotensive	↓ blood pressure
Sodium intake reduction	He [112]	Intervention, cross-over, double-blind follow-up: 1 month	112 hypertensive adults	↓ blood pressure
High potassium intake	NHANES III [113]	Cross sectional	17,030 US adults	↓ blood pressure
Moderate alcohol intake	Zilkens [114]	Intervention, cross-over follow-up: 4 weeks	28 men	↑ blood pressure
Insulin resistance and diabetes				
High whole grain intake	Framingham [115]	Cross sectional	2,834 adults	↓ HOMA-IR, ↓ MS
High fiber intake	IRAS Study [116]	Cross sectional	979 adults	↑ insulin sensitivity
Replacing saturated fats with MUFA	KANWU Study [32]	Intervention; follow-up: 3 months	162 healthy subjects	↑ insulin sensitivity
Increased dairy intake	HPFS [117]	Prospective; follow-up: 12 years	41,254 men	↑ risk of diabetes
Healthier diet + physical activity	DPS [27]	Intervention; follow-up: 3 years	522 IGT subjects	↓ risk of diabetes
	DPP [28]	Intervention	3,234 IFG/IGT subjects	↓ risk of diabetes
	DPP [103]	Follow-up: 3 years		↓ MS
Exercise	Da Qing Study [102]	Intervention; follow-up: 2 years	577 IGT subjects	↓ risk of diabetes
Dyslipidemia				
Low carbohydrate diet	Stern [118]	Intervention; follow-up: 1 year	132 obese	↓ triglycerides, ↑ HDL-C
DASH diet	Azadbaht [119]	Intervention follow-up: 6 months	116 subjects with MS	↓ triglycerides ↑ HDL-C
High glycemic index and high glucose load foods	Nurses' Health Study [120]	Cross sectional	280 women	↑ triglycerides ↓ HDL-C
Increased intake of ω-3 fatty acids	Finnegan [121]	Intervention follow-up: 6 months	150 moderately hyperlipidemic subjects	↓ triglycerides
Inflammation				
Mediterranean diet	Esposito [35]	Intervention; follow-up: 2 years	180 subjects with MS	↓ CRP, ↓ IL-6, ↓ IL-7, ↓ IL-8
Physical activity				
Aerobic exercise training	HERITAGE Study [122]	Intervention follow-up: 20 weeks	621 sedentary healthy adults	↓ MS

Table 2 continued

	Study/ref.	Design	Sample	Outcome
Leisure-time physical exercise	Hu [51]	Prospective; follow-up: 19 years	47,840 adults	↓ CVD
	Berengo [123]	Prospective; follow-up: 20 years	32,677 adults	↓ CVD and total mortality
Vigorous vs. moderate physical activity	Laaksonen [124]	Prospective follow-up: 4 years	612 subjects without MS	↓ MS
Standing or walking around home	Nurses' Health Study [45]	Prospective follow-up: 6 years	50,277 women	↓ obesity ↓ risk of diabetes

MS metabolic syndrome, *CVD* cardiovascular disease, *MUFA* monounsaturated fatty acids

moderate-intensity exercise into their lifestyle. Unfortunately, studies have shown that compliance declines as recommended frequency of exercise increases [142]. Guidelines recommend regular and moderate regimens for exercise [143] such as 30-min per day of moderate-intensity physical activity. Increasing the level of physical activity (e.g., 1-hr daily) further enhances beneficial effects. One-hour a day walking or light jogging favours significant losses of abdominal (visceral) fat when performed in a non-restricted diet regimen [144]. Interestingly, beneficial effects on cardio-protection are achieved not only by leisure-time exercise, but also by physical activity in the occupational setting [145].

Efforts and commitments to promote smoking cessation, above all among young people, should be adopted. Programs on smoking cessation should especially concentrate on persons of lower educational level due to the fact that this habit is more common among people with lower educational level [63]. Benefit of smoking cessation are apparent as far as increase in HDL-cholesterol levels is considered, while no effect on glucose tolerance has been observed [146]. Body weight gain upon smoking cessation may vanish the beneficial effect, stressing the need for even stronger life-style modification in these subjects.

Conclusions

Given the widespread occurrence of MS, there is no doubt that treatment of MS should strongly lie on preventative programs aiming at life-style modification. Several intervention studies have demonstrated the beneficial effect of body weight control, healthy diet and regular physical activity. On a practical ground, a 10% reduction in body weight should be sought in all overweight subjects, a Mediterranean diet encouraged and 30 min walking a day implemented in everybody. As simple these measures may look, their effective implementation and maintenance still represent a formidable challenge. So, pharmacological intervention often represents a necessary option. In the DPP, metformin use in IGT subjects was associated with significant reduction of conversion to T2DM [28] and incidence of MS [103].

Given the serious health consequences of metabolic syndrome and its economic impact, greater attention must be directed to the prevention, identification, and treatment of underlying risk factors, mainly overweight and obesity. Primary prevention of metabolic syndrome cannot be accomplished without major lifestyle changes within society.

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