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A REVIEW OF METABOLIC SYNDROME: DIET, PHYSICAL ACTIVITY AND NATURAL REMEDIES

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SUMMARY

Metabolic syndrome (MetS) is a growing public health problem and is defined by the presence of at least three of five diagnostic criteria, which include impaired glucose metabolism, abdominal obesity, hypertension, high levels of triglycerides and low high-density lipoprotein cholesterol (HDL-C) levels. MetS increases the risk of type 2 diabetes (T2D), cardiovascular disease (CVD), non-alcoholic fatty liver disease (NAFLD), cancer and polycystic ovary syndrome (PCOS). In this narrative review, we describe the effects of diet, physical activity and natural remedies on the prevention and treatment of MetS, performing a literature search using PubMed and Google Scholar. The results of this work show that the Mediterranean diet, the energy-restricted Mediterranean diet and the healthy diet are promising dietary strategies for treating and preventing MetS. Other diets include the fat-modified diet, the carbohydrate-modified diet, the high-protein diet, intermittent fasting and the plant-based diet. Physical activity has beneficial effects on MetS, alone or in combination with a proper diet and natural remedies. Finally, natural remedies, such as unsaturated fatty acids, resveratrol, artichoke, berberine, probiotics and prebiotics, garlic, curcumin, pomegranate and olive polyphenols, may be helpful for the prevention and treatment of this condition. The results of many scientific studies described in this work should be confirmed. This narrative review shows that diet, physical activity and natural remedies are effective in preventing and treating MetS.

Key words
Metabolic syndrome; treatment; diet; physical activity; natural remedies.

Impact statement
Diet, physical activity and natural remedies are promising strategies for preventing and treating metabolic syndrome (MetS).

INTRODUCTION

Metabolic syndrome (MetS) encompasses different metabolic conditions and represents a growing public health problem worldwide. Many definitions of MetS are found in the scientific literature and the most commonly used are those of the World Health Organization (WHO) (1), the National Cholesterol Education Program (NCEP) Adult Treatment Panel III (ATP III) (2) and the International Diabetes Federation (IDF) (3). MetS diagnosis requires the presence of at least three of five diagnostic criteria, which include abdominal obesity, impaired glucose metabolism, high levels of triglycerides, hypertension and low high-density lipoprotein cholesterol (HDL-C) levels. Hyperglycemia or insulin resistance and abdominal obesity are essential criteria in the WHO and

IDF definitions, respectively. The NCEP ATP III and IDF definitions share the same cut-off values, except for abdominal obesity.

The prevalence of MetS varies by age, sex and ethnicity. This condition becomes more common with age and the prevalence of each MetS factor and their combinations differs between males and females. For example, obesity is more common in females than in males (4, 5). Individuals with MetS are at increased risk of different medical conditions, including cardiovascular disease (CVD), type 2 diabetes (T2D), cancer, non-alcoholic fatty liver disease (NAFLD) and polycystic ovary syndrome (PCOS). MetS is often due to inappropriate lifestyles, which include lack of physical activity and unhealthy diets, and a genetic predisposition (6, 7). Epigenetic modifications are of primary importance, as they can explain how genetics and environmental factors contribute to MetS (8).

In this narrative review, we describe the strategies for the prevention and treatment of MetS. We used the electronic databases, such as PubMed and Google Scholar, to find the scientific articles which show the role of nutrition, physical activity and natural remedies in MetS (**Figure 1**).

METABOLIC SYNDROME AND DIET

Healthy eating habits are relevant for the prevention and treatment of MetS and several studies have reported the beneficial effects of different types of diet on this condition.

Mediterranean diet and energy-restricted Mediterranean diet

The Mediterranean diet has been previously studied to find its role in MetS prevention and treatment. A research article by Babio *et al.* (9) showed that a Mediterranean diet which includes nuts or extra virgin olive oil can reverse MetS in a cohort of 3,392 individuals with this condition. They found a reversal of MetS in 958 individuals and a beneficial effect on hyperglycemia and central obesity. Another study showed the positive effect of this type of diet on MetS status in a sample of 424 individuals at risk of CVD (10). Riutord Sbert and colleagues (11) reported a decreased prevalence of MetS in 1,457 adults who followed the Mediterranean diet. Another study found that this type of diet is associated with a lower severity of MetS in a cohort of 5,739 overweight or obese individuals with MetS (12). Campanella and colleagues (13) showed that the Mediterranean diet, especially the Medi-

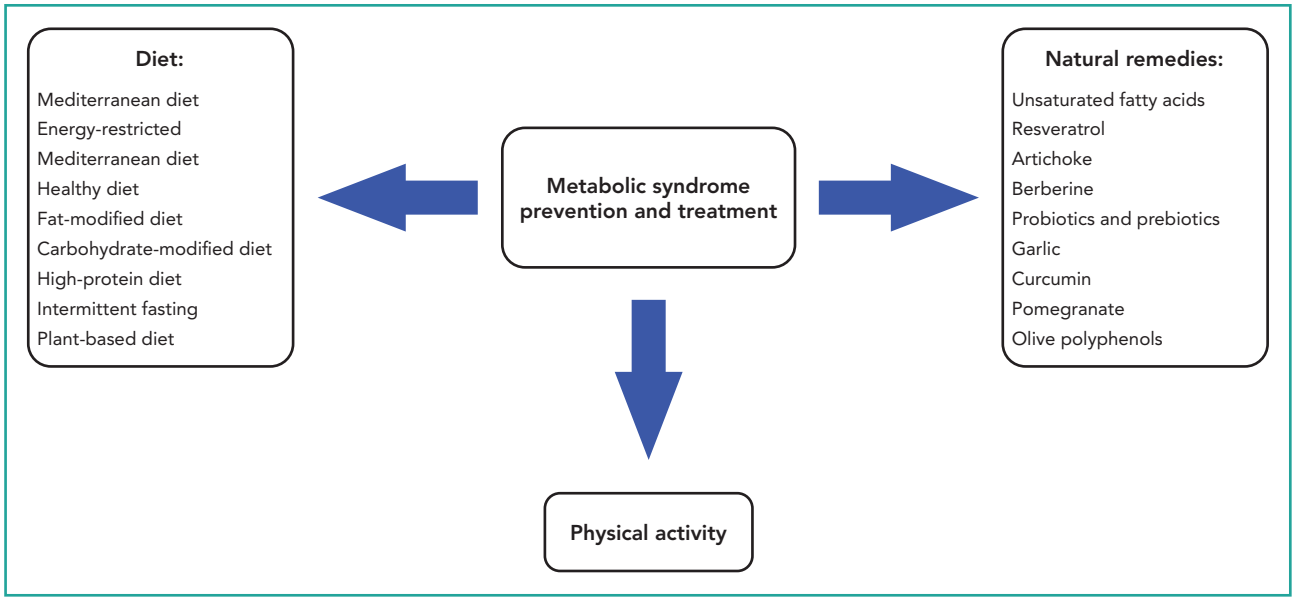

Figure 1. Metabolic syndrome. An illustration of the role of diet, natural remedies and physical activity in the prevention and treatment of this condition.

terranean low-glycemic index diet, is associated with lower levels of fasting remnant cholesterol, which is a predictor of CVD, in a sample of 237 individuals with MetS.

Most previous studies examined the effects of the energy-restricted Mediterranean diet on MetS. Two research articles found the beneficial effect of this type of diet in combination with physical activity on NAFLD and MetS in participants with these two conditions (14, 15). Álvarez-Álvarez and colleagues (16) showed a decreased risk of CVD in individuals following an energy-restricted Mediterranean diet, studying a sample of 6,874 overweight or obese participants with MetS. Other two studies found that this diet in combination with physical activity modifies the gut microbiota and has a beneficial effect on NAFLD (17) or cardiovascular health (18) in overweight or obese participants with MetS. Previous research articles showed the positive effect of an energy-restricted Mediterranean diet in combination with physical activity on body composition (19) and lipid profiles (20, 21) of overweight or obese individuals with MetS. Salas-Salvadó and colleagues (22) reported that an energy-restricted diet in combination with physical activity may exert beneficial effects on cardiovascular health and weight management in a cohort of 626 overweight or obese individuals with MetS.

Healthy diet

A diet characterized by healthy food intake is a promising choice for MetS prevention and treatment. Lankinen and colleagues (23) found the positive effect of a diet which includes fatty fish, bilberries and wholegrain products on HDL-C in individuals with MetS and impaired glucose metabolism. A study by Bub *et al.* (24) demonstrated that the intake of bioactive food is associated with increased HDL-C levels and decreased triglyceride levels in a sample of 167 individuals at risk of MetS. Another research article found the beneficial effect of food containing betaine or choline on cardiometabolic health, studying a cohort of 5,613 obese or overweight participants with MetS (25). Tremblay and colleagues (26) showed that high consumption of fibers improves metabolic health in 87 individuals with MetS. A previous study by Julibert *et al.* (27) found that the consumption of nuts may improve MetS, studying a sample of 5,800 obese or overweight participants with MetS. The moderate intake of red wine, which is high in polyphenols, has been found to decrease the prevalence of MetS in 5,801 individuals at risk of CVD (28). A study by Xiao *et al.* (29) showed that the intake of rice wine is associated with a decreased prevalence of MetS in a cohort of 37,582 individuals living in rural China. The high intake of ultra-processed food has been negatively associated with cardiometabolic health in a sample of 5,373 obese or overweight participants with MetS, providing evidence of the positive role of a healthy diet in MetS management (30). Low-fat milk and dairy products and yogurt have been found to have a beneficial effect on MetS prevention, studying a cohort of 1,868 individuals at risk of CVD (31). A previous study by Mohammadi-Sartang and colleagues (32) showed the positive effect of fortified yogurt intake on MetS factors in a sample of 87 overweight or obese individuals with MetS following an energy-restricted diet. Chen and colleagues (33) found that yogurt may have beneficial effects on insulin resistance and biomarkers of NAFLD in a cohort of 92 obese females with MetS and NAFLD.

Fat-modified diet

The beneficial effects of the fat-modified diet on MetS have been reported in previous studies. Egert and colleagues (34) found that an energy-restricted diet enriched with α-linolenic acid (ALA) ameliorates vascular and inflammatory biomarkers in a sample of 81 overweight or obese individuals with MetS. Another study showed the positive effect of a diet high in monounsaturated fatty acids (MUFAs) and a diet high in complex carbohydrates and low in fats with ω-3 long chain polyunsaturated fatty acids (PUFAs) supplements on insulin

resistance in individuals with MetS and insulin resistance (35). Two previous research articles showed the beneficial effect of diets rich in MUFAs on MetS and central obesity (36) or lipid-lipoprotein profile (37) in obese individuals with MetS or at risk of this condition. Diets rich in MUFAs or PUFAs have been reported to improve cholesterol function in obese participants at risk of MetS or with this condition (38).

Carbohydrate-modified diet and high-protein diet

A diet which includes healthy carbohydrates may exert a positive effect on MetS and CVD. Zamanillo-Campos and colleagues (39) found that this dietary strategy may reduce adiposity, studying a sample of 1,476 overweight or obese individuals with MetS. High consumption of wholegrain products and fibers has been described as the main factor. A study by Martínez-González *et al.* (40) demonstrated that high intake of healthy carbohydrates may reduce the risk of CVD in a sample of 5,373 overweight or obese participants with MetS.

The high-protein, low-glycemic index diet has been previously examined to find a possible beneficial effect on MetS. Two research articles showed that this dietary intervention may help to reduce weight, inflammatory biomarkers and insulin levels (41) or weight and leptin levels (42) in obese or overweight individuals with MetS.

A case report study by Bolos *et al.* (43) found that the ketogenic diet, which is characterized by low-carbohydrate and high-fat intake, may exert a positive effect on MetS and weight reduction in an obese adult male with MetS, following this diet combined with intermittent fasting. The results of this study should be confirmed.

Intermittent fasting

Intermittent fasting is a promising dietary strategy for preventing and treating different health conditions. This strategy has been studied to find possible beneficial effects on MetS. A previous research article showed that intermittent fasting has positive effects on weight reduction, HDL-C, triglycerides, systolic blood pressure and waist circumference in a sample of 100 individuals with MetS following an energy-restricted diet (44). Parvaresh and colleagues (45) found the beneficial effect of an alternate-day modified fasting diet, compared with an energy-restricted diet, on fasting plasma glucose, waist circumference, weight reduction and systolic blood pressure in a cohort of 69 overweight participants with MetS. A research article by Razavi *et al.* (46) demonstrated that this type of diet may exert a positive effect on weight management and coagulation and inflammatory biomarkers in a sample of 75 participants with MetS. Another study reported that a hepatic intermittent fasting diet plan is helpful in treating prediabetes and insulin resistance in 21 participants with MetS and insulin resistance or prediabetes (47). He and colleagues (48) showed that a time-restricted diet either alone or in combination with a low-carbohydrate diet may ameliorate MetS in individuals with this condition.

Plant-based diet

The health benefits of the plant-based diet have been reported in previous studies. Many studies have been focused on the benefits of the healthy plant-based diet. Oncina-Cánovas and colleagues (49) found that a pro-vegetarian diet, characterized by high intake of plant-derived food, and a pro-vegetarian diet which includes healthy food reduce the risk of CVD in a cohort of 6,439 overweight or obese individuals with MetS. Another study showed the beneficial effect of the healthful plant-based diet on MetS and waist circumference in a sample of 9,544 adult participants (50). A research article by Kim *et al.* (51) found a higher prevalence of MetS in individuals following an unhealthy plant-based diet, studying a cohort of 5,646 participants. Vajdi and colleagues (52) showed that an unhealthful plant-based diet may raise the risk of hyperglycemia in a sample of 347 obese participants. Another research article found that a healthy plant-based diet may lower the risk of central obesity and

MetS, studying a cohort of 10,013 adult participants (53).

METABOLIC SYNDROME AND PHYSICAL ACTIVITY

Physical activity has been reported to be a strategy for treating and preventing MetS. Previous studies showed that physical activity may be effective in reducing the prevalence of MetS in different study populations (11, 29, 54, 55, 56, 57, 58, 59, 60, 61, 62). Regular and high-intensity physical activity has been reported to reduce the prevalence of MetS, studying samples of 1,653 (63) and 27,788 (64) individuals. A research article by Pitsavos *et al.* (65) found that physical activity may have beneficial effects on coagulation and inflammatory biomarkers in a sample of 3,042 participants with or without MetS, highlighting the possible protective effect of this strategy on MetS by modulating coagulation and inflammation.
Previous studies demonstrated that physical activity may reduce the accumulation of visceral adipose tissue (66) and ameliorate body composition (67) in overweight or obese individuals with MetS. Another study found the beneficial effect of multi-component and power training programs using elastic bands on MetS in a sample of 72 overweight or obese elderly females with this condition (68). Two research articles showed the benefits of aerobic exercises in combination with resistance exercises on MetS in individuals with this condition (69) or with T2D and MetS (70). Physical activity may improve cardiovascular health in participants with MetS (71, 72). Another study found that moderate and high-intensity physical activity exerts a beneficial effect on CVD risk in a cohort of 5,776 overweight or obese individuals with MetS (73). Reljic and colleagues (74) showed the positive effect of low-volume high-intensity interval training on cardiometabolic and inflammatory biomarkers in a sample of 104 obese individuals with MetS. The severity of MetS has been reported to be decreased in participants with this condition (75) and in overweight or obese individuals with MetS (12) practicing physical activity. A study by Lau *et al.* (76) found the protective effect of Hatha yoga against MetS in participants with and without this condition. Another research article showed the anti-inflammatory activity of Hatha yoga in a sample of 97 individuals with MetS (77).

NATURAL REMEDIES FOR METABOLIC SYNDROME

The use of natural remedies may be an effective strategy for the treatment and prevention of MetS. Previous studies showed that different natural products may be used for these purposes. The results of many research articles should be confirmed.

Unsaturated fatty acids

Previous studies found the beneficial effect of unsaturated fatty acids on MetS. Lee and colleagues (78) reported that oral intake of encapsulated borage (*Borago officinalis* L.) oil in combination with echium (*Echium plantagineum* L.) oil may decrease low-density lipoprotein cholesterol (LDL-C) and total cholesterol, while encapsulated fish oil consumption may improve HDL-C and decrease hemoglobin A1c and triglycerides, studying a cohort of 59 individuals with MetS or T2D. Another study found the beneficial effect of the intake of encapsulated fish oil in combination with an energy-restricted diet on insulin and glucose levels and insulin resistance in a sample of 30 obese females with MetS (79). A research article by Venturini *et al.* (80) showed that the consumption of encapsulated ω-3 fish oil in combination with a diet enriched with extra virgin olive oil exerts antioxidant activity and ameliorates lipid profile in a sample of 102 individuals with MetS. Cicero and colleagues (81) reported the beneficial effect of dietary supplementation with PUFAs and red yeast rice on lipid profile in individuals with MetS and primary polygenic hypercholesterolemia. Another study found that the intake of skim

milk enriched with ω-3 PUFAs and oleate in combination with high-intensity aerobic training may ameliorate cardiometabolic health in a sample of 36 individuals with MetS (82). Tousoulis and colleagues (83) showed that encapsulated ω-3 PUFAs consumption improves cardiovascular health and lipid profile and exerts anti-inflammatory activity in a cohort of 29 individuals with MetS.

Artichoke

Previous studies reported that artichoke (*Cynara scolymus* L.) may be effective in the treatment of MetS. A research article found that the intake of artichoke leaf extract (ALE) may ameliorate cardiometabolic and NAFLD biomarkers in a sample of 100 individuals with MetS (84). Two previous studies showed the beneficial effect of ALE consumption on triglycerides in individuals with MetS (85, 86). Ebrahimi-Mameghani and colleagues (87) reported that oral intake of ALE may reduce insulin levels and insulin resistance in individuals with MetS. A research article by Rezazadeh *et al.* (88) found that ALE consumption may exert antioxidant activity, studying a sample of 68 individuals with MetS.

Resveratrol

Resveratrol is a natural polyphenol which exerts many health benefits. Previous research articles found that the intake of encapsulated resveratrol and δ-tocotrienol may ameliorate inflammatory, oxidative stress and cardiometabolic parameters (89) and MetS components through micro RNAs (miRNAs) modulation (90), studying samples of 82 participants with MetS. Chen and colleagues (91) reported that encapsulated resveratrol consumption exerts beneficial effects on the metabolism of lipids and glucose and insulin resistance in individuals with NAFLD. A previous study found that the intake of encapsulated resveratrol may ameliorate endothelial function in a sample of 30 overweight or obese individuals with mild insulin resistance and prediabetes (92).

Berberine

Berberine is a natural compound which has been studied in clinical trials related to MetS. Previous research articles reported the positive effect of the intake of berberine in combination with other compounds (i.e., monacolin K, policosanol, coenzyme Q10, folic acid and astaxanthin) on lipid profile and the risk of CVD in individuals with MetS (93, 94). Cicero and colleagues (95) found that the consumption of a nutraceutical combination containing tree turmeric (*Berberis aristata* DC.), banaba (*Lagerstroemia speciosa* L.), turmeric (*Curcuma longa* L.), folic acid, chromium picolinate and alpha-lipoic acid may ameliorate insulin resistance and lipid profile in a sample of 40 individuals with prediabetes. Another study showed the beneficial effects of the intake of berberine in combination with silymarin on cardiometabolic health in a cohort of 136 obese individuals with MetS and T2D (96).

Probiotics and prebiotics

Previous studies have reported the positive effect of probiotics and prebiotics on MetS. A research article by Rahimi *et al.* (97) found that the consumption of a synbiotic preparation may lower fasting blood glucose levels in a sample of 108 individuals with MetS. Another study reported the beneficial effect of the intake of a synbiotic preparation on insulin resistance, glucose and insulin levels, body mass index (BMI) and satiety in individuals with MetS following an energy-restricted diet (98). Tenorio-Jiménez and colleagues (99) showed that the intake of probiotics (*i.e.*, *Lactobacillus reuteri* V3401) may modify the gut microbiota and lower inflammation in a cohort of 53 participants with MetS following an energy-restricted diet in combination with physical activity. A previous study found that probiotics and prebiotics consumption has a beneficial effect on the prevalence of MetS and MetS components in a sample of 85 prediabetic participants (100).

Curcumin

Curcumin has many health-promoting properties and has been studied for its possible role

in the treatment of MetS. A previous study by Panahi *et al.* (101) found that oral intake of curcumin may have a beneficial effect on leptin and adiponectin levels in a cohort of 100 individuals with MetS. Di Pierro and colleagues (102) showed that curcumin consumption may be used in weight management programs, studying a sample of 44 overweight individuals with MetS. A research article found that oral intake of encapsulated turmeric in combination with black seeds (*Nigella sativa* L.) ameliorates MetS in a sample of 250 males with this condition (103). Bateni and colleagues (104) reported that the consumption of curcumin nanomicelle may lower triglyceride levels in individuals with MetS.

Garlic

Previous studies showed that garlic (*Allium sativum* L.) exerts beneficial effects on MetS. Matsumoto and colleagues (105) found that the intake of a garlic extract may improve cardiovascular health in a cohort of 55 individuals with MetS. A research article by Sangouni *et al.* (106) reported the positive effect of the consumption of a garlic supplement on MetS and NAFLD parameters, appetite and insulin resistance in participants with MetS. Another study found that the intake of a garlic supplement may ameliorate cardiometabolic health and gut transit time in a sample of 84 individuals with MetS (107).

Pomegranate

The benefits of pomegranate (*Punica granatum* L.) intake on MetS have been previously studied. Two research articles reported that oral intake of pomegranate juice exerts anti-inflammatory activity and has a beneficial effect on cardiovascular health in individuals with MetS (108, 109). A previous study by Esmaeilinezhad *et al.* (110) found that the consumption of synbiotic pomegranate juice may have beneficial effects on insulin levels, insulin resistance, body composition and weight management in a sample of 86 females with PCOS.

Olive polyphenols

Previous studies have shown the positive effect of olive polyphenols on MetS. A research article found that olive leaf polyphenols exert beneficial effects on glucose homeostasis in a sample of 45 overweight individuals (111). Sanchez-Rodriguez and colleagues (112) reported that olive oil with high polyphenolic content ameliorates parameters of endothelial function and MetS, studying a cohort of 51 participants. Two previous studies found the beneficial effects of extra virgin olive oil with high polyphenolic content on insulin resistance and glucose levels in healthy individuals (113) and on endothelial function in participants at risk of T2D (114).

CONCLUSIONS

This narrative review describes the role of diet, physical activity and natural remedies in the prevention and treatment of MetS. The Mediterranean diet, the energy-restricted Mediterranean diet and a diet characterized by high intake of healthy food have been shown to be effective in treating and preventing this condition. The fat-modified diet, the carbohydrate-modified diet, the high-protein diet, intermittent fasting and the plant-based diet are also promising strategies to consider for these purposes. Physical activity has been reported to be helpful for treating and preventing MetS, either alone or in combination with a proper diet and natural remedies. Unsaturated fatty acids, ALE, resveratrol, berberine, probiotics and prebiotics, curcumin, garlic, pomegranate and olive polyphenols are the natural remedies which have been previously studied for their beneficial effects on MetS. The results of many research articles reported in this review should be confirmed.

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ETHICS

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Conflict of interests
The Authors declare that they have no conflict of interests.

Availability of data and material
Data and material are available on request from the Authors.

Authors' contributions
ADN, FG, FP and PZ conceived the study. ADN searched the scientific literature and wrote the initial draft of the manuscript. All Authors discussed the results and contributed to the final version of the manuscript. All Co-authors read and approved the final manuscript.

Ethical approval
N/A.

REFERENCES
1. Alberti KG, Zimmet PZ. Definition, diagnosis and classification of diabetes mellitus and its complications. Part 1: diagnosis and classification of diabetes mellitus provisional report of a WHO consultation. Diabet Med. 1998;15(7):539-53. doi: 10.1002/(SICI)1096-9136(199807)15:7<539::AID-DIA668>3.0.CO;2-S.
2. 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(19):2486-97. doi: 10.1001/jama.285.19.2486.
3. Alberti KG, Zimmet P, Shaw J; IDF Epidemiology Task Force Consensus Group. The metabolic syndrome--a new worldwide definition. Lancet. 2005;366(9491):1059-62. doi: 10.1016/S0140-6736(05)67402-8.
4. Kuk JL, Ardern CI. Age and sex differences in the clustering of metabolic syndrome factors: association with mortality risk. Diabetes Care. 2010;33(11):2457-61. doi: 10.2337/dc10-0942.
5. Pradhan AD. Sex differences in the metabolic syndrome: implications for cardiovascular health in women. Clin Chem 2014;60(1):44-52. doi: 10.1373/clinchem.2013.202549.
6. Abou Ziki MD, Mani A. Metabolic syndrome: genetic insights into disease pathogenesis. Curr Opin Lipidol. 2016;27(2):162-71. doi: 10.1097/MOL.0000000000000276.
7. Mendrick DL, Diehl AM, Topor LS, Dietert RR, Will Y, La Merrill MA, et al. Metabolic syndrome and associated diseases: from the bench to the clinic. Toxicol Sci. 2018;162(1):36-42. doi: 10.1093/toxsci/kfx233.
8. Silva-Ochoa AD, Velasteguí E, Falconí IB, García-Solorzano VI, Rendón-Riofrio A, Sanguña-Soliz GA, et al. Metabolic syndrome: Nutri-epigenetic cause or consequence? Heliyon. 2023;9(11):e21106. doi: 10.1016/j.heliyon.2023.e21106.
9. Babio N, Toledo E, Estruch R, Ros E, Martínez-González MA, Castañer O, et al. Mediterranean diets and metabolic syndrome status in the PREDIMED randomized trial. CMAJ. 2014;186(17):E649-57. doi: 10.1503/cmaj.140764.
10. Mayneris-Perxachs J, Sala-Vila A, Chisaguano M, Castellote AI, Estruch R, Covas MI, et al. Effects of 1-year intervention with a Mediterranean diet on plasma fatty acid composition and metabolic syndrome in a population at high cardiovascular risk. PLoS One. 2014;9(3):e85202. doi: 10.1371/journal.pone.0085202.
11. Riutord Sbert P, Riutord B, Riutord N, Arroyo Bote S, López González ÁA, Ramírez Manent JI. Relationship between physical activity and adherence to the

mediterranean diet with metabolic syndrome, hypertriglyceridemic waist phenotype and hypertensive waist. Medicina Balear. 2022;37(6):33-8. doi: 10.3306/AJHS.2022.37.06.33.
12. Gallardo-Alfaro L, Bibiloni MDM, Mascaró CM, Montemayor S, Ruiz-Canela M, Salas-Salvadó J, et al. Leisure-time physical activity, sedentary behaviour and diet quality are associated with metabolic syndrome severity: the PREDIMED-plus study. Nutrients. 2020;12(4):1013. doi: 10.3390/nu12041013.
13. Campanella A, Iacovazzi PA, Misciagna G, Bonfiglio C, Mirizzi A, Franco I, et al. The effect of three Mediterranean diets on remnant cholesterol and non-alcoholic fatty liver disease: a secondary analysis. Nutrients. 2020;12(6):1674. doi: 10.3390/nu12061674.
14. Montemayor S, Bouzas C, Mascaró CM, Casares M, Llompart I, Abete I, et al. Effect of dietary and lifestyle interventions on the amelioration of NAFLD in patients with metabolic syndrome: the FLIPAN Study. Nutrients. 2022a;14(11):2223. doi: 10.3390/nu14112223.
15. Montemayor S, Mascaró CM, Ugarriza L, Casares M, Llompart I, Abete I, et al. Adherence to Mediterranean diet and NAFLD in patients with metabolic syndrome: the FLIPAN Study. Nutrients. 2022b;14(15):3186. doi: 10.3390/nu14153186.
16. Álvarez-Álvarez I, Martínez-González MÁ, Sánchez-Tainta A, Corella D, Díaz-López A, Fitó M, et al. Adherence to an energy-restricted Mediterranean diet score and prevalence of cardiovascular risk factors in the PREDIMED-Plus: A cross-sectional study. Rev Esp Cardiol. 2019;72(11):925-34. doi: 10.1016/j.rec.2018.08.010.
17. Gómez-Pérez AM, Ruiz-Limón P, Salas-Salvadó J, Vioque J, Corella D, Fitó M, et al. Gut microbiota in nonalcoholic fatty liver disease: a PREDIMED-Plus trial sub analysis. Gut Microbes. 2023;15(1):2223339. doi: 10.1080/19490976.2023.2223339.
18. Muralidharan J, Moreno-Indias I, Bulló M, Lopez JV, Corella D, Castañer O, et al. Effect on gut microbiota of a 1-y lifestyle intervention with Mediterranean diet compared with energy-reduced Mediterranean diet and physical activity promotion: PREDIMED-Plus Study. Am J Clin Nutr. 2021;114(3):1148-58. doi: 10.1093/ajcn/nqab150.
19. Konieczna J, Ruiz-Canela M, Galmes-Panades AM, Abete I, Babio N, Fiol M, et al. An energy-reduced Mediterranean diet, physical activity, and body composition: an interim subgroup analysis of the PREDIMED-Plus randomized clinical trial. JAMA Netw Open. 2023;6(10):e2337994. doi: 10.1001/jamanetworkopen.2023.37994.
20. Candás-Estébanez B, Fernández-Cidón B, Corbella E, Tebé C, Fanlo-Maresma M, Esteve-Luque V, et al. The impact of the Mediterranean diet and lifestyle intervention on lipoprotein subclass profiles among metabolic syndrome patients: findings of a randomized controlled trial. Int J Mol Sci. 2024;25(2):1338. doi: 10.3390/ijms25021338.
21. Sanllorente A, Soria-Florido MT, Castañer O, Lassale C, Salas-Salvadó J, Martínez-González MÁ, et al. A lifestyle intervention with an energy-restricted Mediterranean diet and physical activity enhances HDL function: a substudy of the PREDIMED-Plus randomized controlled trial. Am J Clin Nutr 2021;114(5):1666-74. doi: 10.1093/ajcn/nqab246.
22. Salas-Salvadó J, Díaz-López A, Ruiz-Canela M, Basora J, Fitó M, Corella D, et al. Effect of a lifestyle intervention program with energy-restricted mediterranean diet and exercise on weight loss and cardiovascular risk factors: one-year results of the PREDIMED-Plus trial. Diabetes Care. 2019;42(5):777-88. doi: 10.2337/dc18-0836.

23. Lankinen M, Kolehmainen M, Jääskeläinen T, Paananen J, Joukamo L, Kangas AJ, et al. Effects of whole grain, fish and bilberries on serum metabolic profile and lipid transfer protein activities: a randomized trial (Sysdimet). PLoS One. 2014;9(2):e90352. doi: 10.1371/journal.pone.0090352.
24. Bub A, Malpuech-Brugère C, Orfila C, Amat J, Arianna A, Blot A, et al. A dietary intervention of bioactive enriched foods aimed at adults at risk of metabolic syndrome: Protocol and results from PATHWAY-27 pilot study. Nutrients. 2019;11(8):1814. doi: 10.3390/nu11081814.
25. Díez-Ricote L, San-Cristobal R, Concejo MJ, Martínez-González MÁ, Corella D, Salas-Salvadó J, et al. One-year longitudinal association between changes in dietary choline or betaine intake and cardiometabolic variables in the PREvención con DIeta MEDiterránea-Plus (PREDIMED-Plus) trial. Am J Clin Nutr. 2022;116(6):1565-79. doi: 10.1093/ajcn/nqac255.
26. Tremblay A, Clinchamps M, Pereira B, Courteix D, Lesourd B, Chapier R, et al. Dietary fibres and the management of obesity and metabolic syndrome: the RESOLVE study. Nutrients 2020;12(10):2911. doi: 10.3390/nu12102911.
27. Julibert A, Del Mar Bibiloni M, Gallardo-Alfaro L, Abbate M, Martínez-González MÁ, Salas-Salvadó J, et al. Metabolic syndrome features and excess weight were inversely associated with nut consumption after 1-year follow-up in the PREDIMED-Plus study. J Nutr. 2020;150(12):3161-70. doi: 10.1093/jn/nxaa289.
28. Tresserra-Rimbau A, Medina-Remón A, Lamuela-Raventós RM, Bulló M, Salas-Salvadó J, Corella D, et al. Moderate red wine consumption is associated with a lower prevalence of the metabolic syndrome in the PREDIMED population. Br J Nutr. 2015;113(Suppl 2):S121-30. doi: 10.1017/S0007114514003262.
29. Xiao J, Wu CL, Gao YX, Wang SL, Wang L, Lu QY, et al. Prevalence of metabolic syndrome and its risk factors among rural adults in Nantong, China. Sci Rep. 2016b;6:38089. doi: 10.1038/srep38089.
30. González-Palacios S, Oncina-Cánovas A, García-de-la-Hera M, Martínez-González MÁ, Salas-Salvadó J, Corella D, et al. Increased ultra-processed food consumption is associated with worsening of cardiometabolic risk factors in adults with metabolic syndrome: Longitudinal analysis from a randomized trial. Atherosclerosis. 2023;377:12-23. doi: 10.1016/j.atherosclerosis.2023.05.022.
31. Babio N, Becerra-Tomás N, Martínez-González MÁ, Corella D, Estruch R, Ros E, et al. Consumption of yogurt, low-fat milk, and other low-fat dairy products is associated with lower risk of metabolic syndrome incidence in an elderly Mediterranean population. J Nutr. 2015;145(10):2308-16. doi: 10.3945/jn.115.214593.
32. Mohammadi-Sartang M, Bellissimo N, Totosy de Zepetnek JO, Brett NR, Mazloomi SM, Fararouie M, et al. The effect of daily fortified yogurt consumption on weight loss in adults with metabolic syndrome: A 10-week randomized controlled trial. Nutr Metab Cardiovasc Dis 2018;28(6):565-74. doi: 10.1016/j.numecd.2018.03.001.
33. Chen Y, Feng R, Yang X, Dai J, Huang M, Ji X, et al. Yogurt improves insulin resistance and liver fat in obese women with nonalcoholic fatty liver disease and metabolic syndrome: a randomized controlled trial. Am J Clin Nutr. 2019;109(6):1611-19. doi: 10.1093/ajcn/nqy358.
34. Egert S, Baxheinrich A, Lee-Barkey YH, Tschoepe D, Wahrburg U, Stratmann B. Effects of an energy-restricted diet rich in plant-derived α-linolenic acid on systemic inflammation and endothelial function in overweight-to-obese patients with metabolic syndrome traits. Br J Nutr. 2014;112(8):1315-22. doi: 10.1017/S0007114514002001.

35. Yubero-Serrano EM, Delgado-Lista J, Tierney AC, Perez-Martinez P, Garcia-Rios A, Alcala-Diaz JF, et al. Insulin resistance determines a differential response to changes in dietary fat modification on metabolic syndrome risk factors: the LIPGENE study. Am J Clin Nutr. 2015;102(6):1509-17. doi: 10.3945/ajcn.115.111286.
36. Liu X, Kris-Etherton PM, West SG, Lamarche B, Jenkins DJ, Fleming JA, et al. Effects of canola and high-oleic-acid canola oils on abdominal fat mass in individuals with central obesity. Obesity (Silver Spring). 2016;24(11):2261-68. doi: 10.1002/oby.21584.
37. Bowen KJ, Kris-Etherton PM, West SG, Fleming JA, Connelly PW, Lamarche B, et al. Diets enriched with conventional or high-oleic acid canola oils lower atherogenic lipids and lipoproteins compared to a diet with a Western fatty acid profile in adults with central adiposity. J Nutr. 2019;149(3):471-8. doi: 10.1093/jn/nxy307.
38. Liu X, Garban J, Jones PJ, Vanden Heuvel J, Lamarche B, Jenkins DJ, et al. Diets low in saturated fat with different unsaturated fatty acid profiles similarly increase serum-mediated cholesterol efflux from THP-1 macrophages in a population with or at risk for metabolic syndrome: the canola oil multicenter intervention trial. J Nutr. 2018;148(5):721-28. doi: 10.1093/jn/nxy040.
39. Zamanillo-Campos R, Chaplin A, Romaguera D, Abete I, Salas-Salvadó J, Martín V, et al. Longitudinal association of dietary carbohydrate quality with visceral fat deposition and other adiposity indicators. Clin Nutr. 2022;41(10):2264-74. doi: 10.1016/j.clnu.2022.08.008.
40. Martínez-González MA, Fernandez-Lazaro CI, Toledo E, Díaz-López A, Corella D, Goday A, et al. Carbohydrate quality changes and concurrent changes in cardiovascular risk factors: a longitudinal analysis in the PREDIMED-Plus randomized trial. Am J Clin Nutr. 2020;111(2):291-306. doi: 10.1093/ajcn/nqz298.
41. Kempf K, Röhling M, Banzer W, Braumann KM, Halle M, McCarthy D, et al. High-protein, low-glycaemic meal replacement decreases fasting insulin and inflammation markers-a 12-month subanalysis of the ACOORH trial. Nutrients. 2021;13(5):1433. doi: 10.3390/nu13051433.
42. Kempf K, Röhling M, Banzer W, Braumann KM, Halle M, Schaller N, et al. Early and strong leptin reduction is predictive for long-term weight loss during high-protein, low-glycaemic meal replacement-a subanalysis of the randomised-controlled ACOORH trial. Nutrients. 2022;14(12):2537. doi: 10.3390/nu14122537.
43. Bolos P, Ceana D, Buicu F. Ketogenic diet and intermittent fasting on patient with metabolic syndrome: case report. Acta Medica Transilvanica. 2023;28(1):4-6. Available from: https://www.amtsibiu.ro/Arhiva/2023/Nr1-en/2.Bolos_Paula.pdf. Accessed: Nov 21, 2024.
44. Micallef D. Physiological and therapeutic outcomes of intermittent fasting versus calorie-restriction diet in patients suffering from metabolic syndrome. MCAST J Applied Res Pract. 2019;3(1):4-19. doi: 10.5604/01.3001.0013.2067.
45. Parvaresh A, Razavi R, Abbasi B, Yaghoobloo K, Hassanzadeh A, Mohammadifard N, et al. Modified alternate-day fasting vs. calorie restriction in the treatment of patients with metabolic syndrome: A randomized clinical trial. Complement Ther Med. 2019;47:102187. doi: 10.1016/j.ctim.2019.08.021.
46. Razavi R, Parvaresh A, Abbasi B, Yaghoobloo K, Hassanzadeh A, Mohammadifard N, et al. The alternate-day fasting diet is a more effective approach than a calorie restriction diet on weight loss and hs-CRP levels. Int J Vitam Nutr Res. 2021;91(3-4):242-50. doi: 10.1024/0300-9831/a000623.
47. Rohner M, Heiz R, Feldhaus S, Bornstein SR. Hepatic-metabolite-based intermit-

tent fasting enables a sustained reduction in insulin resistance in type 2 diabetes and metabolic syndrome. Horm Metab Res. 2021;53(8):529-40. doi: 10.1055/a-1510-8896.
48. He M, Wang J, Liang Q, Li M, Guo H, Wang Y, et al. Time-restricted eating with or without low-carbohydrate diet reduces visceral fat and improves metabolic syndrome: a randomized trial. Cell Rep Med. 2022;3(10):100777. doi: 10.1016/j.xcrm.2022.100777.
49. Oncina-Cánovas A, Vioque J, González-Palacios S, Martínez-González MÁ, Salas-Salvadó J, Corella D, et al. Pro-vegetarian food patterns and cardiometabolic risk in the PREDIMED-Plus study: a cross-sectional baseline analysis. Eur J Nutr. 2022;61(1):357-72. doi: 10.1007/s00394-021-02647-4.
50. Jovanovic CES, Hoelscher DM, Chen B, Ranjit N, van den Berg AE. The associations of plant-based food and metabolic syndrome using NHANES 2015-16 data. J Public Health. 2023;45(1):e22-e29. doi: 10.1093/pubmed/fdab403.
51. Kim H, Lee K, Rebholz CM, Kim J. Plant-based diets and incident metabolic syndrome: Results from a South Korean prospective cohort study. PLoS Med. 2020;17(11):e1003371. doi: 10.1371/journal.pmed.1003371.
52. Vajdi M, Karimi A, Tousi AZ, Hosseini B, Nikniaz Z, Farhangi MA. Association between plant-based diets and metabolic syndrome in obese adults from Iran: a cross-sectional study. BMC Endocr Disord. 2023;23(1):109. doi: 10.1186/s12902-023-01358-7.
53. Huo Y, Cao S, Liu J, Zhang B, Xu K, Wang Y, et al. The Association between plant-based diet indices and metabolic syndrome in Chinese adults: longitudinal analyses from the China Health and Nutrition Survey. Nutrients. 2023;15(6):1341. doi: 10.3390/nu15061341.
54. Earnest CP, Johannsen NM, Swift DL, Gillison FB, Mikus CR, Lucia A, et al. Aerobic and strength training in concomitant metabolic syndrome and type 2 diabetes. Med Sci Sports Exerc. 2014;46(7):1293-301. doi: 10.1249/MSS.0000000000000242.
55. El Bilbeisi AH, Hosseini S, Djafarian K. The association between physical activity and the metabolic syndrome among type 2 diabetes patients in Gaza Strip, Palestine. Ethiop J Health Sci. 2017;27(3):273-82. doi: 10.4314/ejhs.v27i3.9.
56. Kang M, Joo M, Hong H, Kang H. Eating speed, physical activity, and cardiorespiratory fitness are independent predictors of metabolic syndrome in Korean university students. Nutrients. 2021;13(7):2420. doi: 10.3390/nu13072420.
57. Laaksonen DE, Lakka HM, Salonen JT, Niskanen LK, Rauramaa R, Lakka TA. Low levels of leisure-time physical activity and cardiorespiratory fitness predict development of metabolic syndrome. Diabetes Care. 2002;25(9):1612-18. doi: 10.2337/diacare.25.9.1612.
58. Lee J, Kim Y, Jeon JY. Association between physical activity and the prevalence of metabolic syndrome: from the Korean National Health and Nutrition Examination Survey, 1999-2012. SpringerPlus. 2016;5:1870. doi: 10.1186/s40064-016-3514-5.
59. Sagawa N, Rockette-Wagner B, Azuma K, Ueshima H, Hisamatsu T, Takamiya T, et al. Physical activity levels in American and Japanese men from the ERA-JUMP Study and associations with metabolic syndrome. J Sport Health Sci. 2020;9(2):170-78. doi: 10.1016/j.jshs.2019.09.007.
60. Wang P, Tsao L, Lin M, Lee C. Metabolic syndrome risk factors and physical activity in middle-aged women. International Journal of Studies in Nursing. 2019;4(4):70-8. doi: 10.20849/ijsn.v4i4.669.
61. Wu S, Fisher-Hoch SP, Reininger B, McCormick JB. Recommended levels of physical activity are associated with reduced risk of the metabolic syndrome in Mexican-Americans. PLoS One. 2016;11(4):e0152896. doi: 10.1371/journal.pone.0152896.

62. Xiao J, Shen C, Chu MJ, Gao YX, Xu GF, Huang JP, et al. Physical activity and sedentary behavior associated with components of metabolic syndrome among people in rural China. PLoS One. 2016a;11(1):e0147062. doi: 10.1371/journal.pone.0147062.
63. Hahn V, Halle M, Schmidt-Trucksäss A, Rathmann W, Meisinger C, Mielck A. Physical activity and the metabolic syndrome in elderly German men and women: results from the population-based KORA survey. Diabetes Care. 2009;32(3):511-3. doi: 10.2337/dc08-1285.
64. Jang YS, Joo HJ, Jung YH, Park EC, Jang SY. Association of the "weekend warrior" and other physical activity patterns with metabolic syndrome in the South Korean population. Int J Environ Res Public Health. 2022;19(20):13434. doi: 10.3390/ijerph192013434.
65. Pitsavos C, Panagiotakos DB, Chrysohoou C, Kavouras S, Stefanadis C. The associations between physical activity, inflammation, and coagulation markers, in people with metabolic syndrome: the ATTICA study. Eur J Cardiovasc Prev Rehabil. 2005;12(2):151-8. doi: 10.1097/01.hjr.0000164690.50200.43.
66. Galmes-Panades AM, Konieczna J, Abete I, Colom A, Rosique-Esteban N, Zulet MA, et al. Lifestyle factors and visceral adipose tissue: Results from the PREDIMED-PLUS study. PLoS One. 2019;14(1):e0210726. doi: 10.1371/journal.pone.0210726.
67. Galmes-Panades AM, Konieczna J, Varela-Mato V, Abete I, Babio N, Fiol M, et al. Targeting body composition in an older population: do changes in movement behaviours matter? Longitudinal analyses in the PREDIMED-Plus trial. BMC Med. 2021;19(1):3. doi: 10.1186/s12916-020-01847-9.
68. Gargallo P, Tamayo E, Jiménez-Martínez P, Juesas A, Casaña J, Benitez-Martinez JC, et al. Multicomponent and power training with elastic bands improve metabolic and inflammatory parameters, body composition and anthropometry, and physical function in older women with metabolic syndrome: A 20-week randomized, controlled trial. Exp Gerontol. 2024;185:112340. doi: 10.1016/j.exger.2023.112340.
69. Zhou Y, Wu W, Zou Y, Huang W, Lin S, Ye J, et al. Benefits of different combinations of aerobic and resistance exercise for improving plasma glucose and lipid metabolism and sleep quality among elderly patients with metabolic syndrome: a randomized controlled trial. Endocr J. 2022;69(7):819-30. doi: 10.1507/endocrj.EJ21-0589.
70. Amin M, Kerr D, Atiase Y, Samir MM, Driscoll A. Improving metabolic syndrome in Ghanaian adults with type 2 diabetes through a home-based physical activity program: a feasibility randomised controlled trial. Int J Environ Res Public Health. 2023;20(8):5518. doi: 10.3390/ijerph20085518.
71. Boudet G, Walther G, Courteix D, Obert P, Lesourd B, Pereira B, et al. Paradoxical dissociation between heart rate and heart rate variability following different modalities of exercise in individuals with metabolic syndrome: The RESOLVE study. Eur J Prev Cardiol. 2017;24(3):281-96. doi: 10.1177/2047487316679523.
72. Ekblom-Bak E, Halldin M, Vikström M, Stenling A, Gigante B, de Faire U, et al. Physical activity attenuates cardiovascular risk and mortality in men and women with and without the metabolic syndrome – a 20-year follow-up of a population-based cohort of 60-year-olds. Eur J Prev Cardiol. 2021;28(12):1376-85. doi: 10.1177/2047487320916596.
73. Rosique-Esteban N, Díaz-López A, Martínez-González MA, Corella D, Goday A, Martínez JA, et al. Leisure-time physical activity, sedentary behaviors, sleep, and cardiometabolic risk factors at baseline in the PREDIMED-PLUS intervention trial: A cross-sectional analysis. PLoS One. 2017;12(3):e0172253. doi: 10.1371/journal.pone.0172253.

74. Reljic D, Dieterich W, Herrmann HJ, Neurath MF, Zopf Y. "HIIT the inflammation": Comparative effects of low-volume interval training and resistance exercises on inflammatory indices in obese metabolic syndrome patients undergoing caloric restriction. Nutrients. 2022;14(10):1996. doi: 10.3390/nu14101996.
75. Haufe S, Kerling A, Protte G, Bayerle P, Stenner HT, Rolff S, et al. Telemonitoring-supported exercise training, metabolic syndrome severity, and work ability in company employees: a randomised controlled trial. Lancet Public Health. 2019;4(7):e343-e352. doi: 10.1016/S2468-2667(19)30075-1.
76. Lau C, Yu R, Woo J. Effects of a 12-week Hatha yoga intervention on metabolic risk and quality of life in Hong Kong Chinese adults with and without metabolic syndrome. PLoS One. 2015;10(6):e0130731. doi: 10.1371/journal.pone.0130731.
77. Supriya R, Yu AP, Lee PH, Lai CW, Cheng KK, Yau SY, et al. Yoga training modulates adipokines in adults with high-normal blood pressure and metabolic syndrome. Scand J Med Sci Sports. 2018;28(3):1130-8. doi: 10.1111/sms.13029.
78. Lee TC, Ivester P, Hester AG, Sergeant S, Case LD, Morgan T, et al. The impact of polyunsaturated fatty acid-based dietary supplements on disease biomarkers in a metabolic syndrome/diabetes population. Lipids Health Dis. 2014;13:196. doi: 10.1186/1476-511X-13-196.
79. Soares de Oliveira Carvalho AP, Kimi Uehara S, Nogueria Netto JF, Rosa G. Hypocaloric diet associated with the consumption of jam enriched with microencapsulated fish oil decreases insulin resistance. Nutr Hosp. 2014;29(5):1103-08. doi: 10.3305/nh.2014.29.5.6654.
80. Venturini D, Simão AN, Urbano MR, Dichi I. Effects of extra virgin olive oil and fish oil on lipid profile and oxidative stress in patients with metabolic syndrome. Nutrition. 2015;31(6):834-40. doi: 10.1016/j.nut.2014.12.016.
81. Cicero AF, Derosa G, Pisciotta L, Barbagallo C; SISA-PUFACOL Study Group. Testing the short-term efficacy of a lipid-lowering nutraceutical in the setting of clinical practice: a multicenter study. J Med Food. 2015;18(11):1270-73. doi: 10.1089/jmf.2015.0024.
82. Ortega JF, Morales-Palomo F, Fernandez-Elias V, Hamouti N, Bernardo FJ, Martin-Doimeadios RC, et al. Dietary supplementation with omega-3 fatty acids and oleate enhances exercise training effects in patients with metabolic syndrome. Obesity (Silver Spring). 2016;24(8):1704-11. doi: 10.1002/oby.21552.
83. Tousoulis D, Plastiras A, Siasos G, Oikonomou E, Verveniotis A, Kokkou E, et al. Omega-3 PUFAs improved endothelial function and arterial stiffness with a parallel antiinflammatory effect in adults with metabolic syndrome. Atherosclerosis. 2014;232(1):10-6. doi: 10.1016/j.atherosclerosis.2013.10.014.
84. Castellino G, Nikolic D, Magán-Fernández A, Malfa GA, Chianetta R, Patti AM, et al. Altilix® supplement containing chlorogenic acid and luteolin improved hepatic and cardiometabolic parameters in subjects with metabolic syndrome: A 6-month randomized, double-blind, placebo-controlled study. Nutrients. 2019;11(11):2580. doi: 10.3390/nu11112580.
85. Rezazadeh K, Rahmati-Yamchi M, Mohammadnejad L, Ebrahimi-Mameghani M, Delazar A. Effects of artichoke leaf extract supplementation on metabolic parameters in women with metabolic syndrome: Influence of TCF7L2-rs7903146 and FTO-rs9939609 polymorphisms. Phytother Res. 2018b;32(1):84-93. doi: 10.1002/ptr.5951.
86. Rezazadeh K, Rezazadeh F, Ebrahimi-Mamaghani M. The effect of artichoke leaf extract supplementation on lipid and CETP response in metabolic syndrome with respect to Taq 1B CETP polymorphism: A randomized, controlled clin-

ical trial. Eur J Integr Med. 2018;17:112-8. doi: 10.1016/j.eujim.2017.12.008.
87. Ebrahimi-Mameghani M, Asghari-Jafarabadi M, Rezazadeh K. TCF7L2-rs7903146 polymorphism modulates the effect of artichoke leaf extract supplementation on insulin resistance in metabolic syndrome: a randomized, double-blind, placebo-controlled trial. J Integr Med. 2018;16(5):329-34. doi: 10.1016/j.joim.2018.05.006.
88. Rezazadeh K, Aliashrafi S, Asghari-Jafarabadi M, Ebrahimi-Mameghani M. Antioxidant response to artichoke leaf extract supplementation in metabolic syndrome: A double-blind placebo-controlled randomized clinical trial. Clin Nutr. 2018;37(3):790-96. doi: 10.1016/j.clnu.2017.03.017.
89. Fatima S, Khan DA, Aamir M, Pervez MA, Fatima F. δ-Tocotrienol in combination with resveratrol improves the cardiometabolic risk factors and biomarkers in patients with metabolic syndrome: a randomized controlled trial. Metab Syndr Relat Disord. 2023;21(1):25-34. doi: 10.1089/met.2022.0052.
90. Fatima S, Khan DA, Fatima F, Aamir M, Ijaz A, Hafeez A. Role of δ-tocotrienol and resveratrol supplementation in the regulation of micro RNAs in patients with metabolic syndrome: A randomized controlled trial. Complement Ther Med. 2023;74:102950. doi: 10.1016/j.ctim.2023.102950.
91. Chen S, Zhao X, Ran L, Wan J, Wang X, Qin Y, et al. Resveratrol improves insulin resistance, glucose and lipid metabolism in patients with non-alcoholic fatty liver disease: a randomized controlled trial. Dig Liver Dis. 2015;47(3):226-32. doi: 10.1016/j.dld.2014.11.015.
92. Pollack RM, Barzilai N, Anghel V, Kulkarni AS, Golden A, O'Broin P, et al. Resveratrol improves vascular function and mitochondrial number but not glucose metabolism in older adults. J Gerontol A Biol Sci Med Sci. 2017;72(12):1703-09. doi: 10.1093/gerona/glx041.
93. Galletti F, Fazio V, Gentile M, Schillaci G, Pucci G, Battista F, et al. Efficacy of a nutraceutical combination on lipid metabolism in patients with metabolic syndrome: a multicenter, double blind, randomized, placebo-controlled trial. Lipids Health Dis. 2019;18(1):66. doi: 10.1186/s12944-019-1002-y.
94. Ruscica M, Gomaraschi M, Mombelli G, Macchi C, Bosisio R, Pazzucconi F, et al. Nutraceutical approach to moderate cardiometabolic risk: results of a randomized, double-blind and crossover study with Armolipid Plus. J Clin Lipidol. 2014;8(1):61-8. doi: 10.1016/j.jacl.2013.11.003.
95. Cicero AFG, Fogacci F, Morbini M, Colletti A, Bove M, Veronesi M, et al. Nutraceutical effects on glucose and lipid metabolism in patients with impaired fasting glucose: a pilot, double-blind, placebo-controlled, randomized clinical trial on a combined product. High Blood Press Cardiovasc Prev. 2017;24(3):283-8. doi: 10.1007/s40292-017-0206-3.
96. Guarino G, Strollo F, Carbone L, Della Corte T, Letizia M, Marino G, et al. Bioimpedance analysis, metabolic effects and safety of the association Berberis aristata/Silybum marianum: a 52-week double-blind, placebo-controlled study in obese patients with type 2 diabetes. J Biol Regul Homeost Agents. 2017;31(2):495-502. PMID: 28685558.
97. Rahimi F, Pasdar Y, Kaviani M, Abbasi S, Fry H, Hekmatdoost A, et al. Efficacy of synbiotic supplementation on the metabolic factors in patients with metabolic syndrome: a randomized, triple-blind, placebo-controlled trial. Int J Clin Pract. 2022;2022:2967977. doi: 10.1155/2022/2967977.
98. Rabiei S, Hedayati M, Rashidkhani B, Saadat N, Shakerhossini R. The effects of synbiotic supplementation on body mass index, metabolic and inflammatory biomarkers, and appetite in patients with metabolic syndrome: A tri-

ple-blind randomized controlled trial. J Diet Suppl. 2019;16(3):294-306. doi: 10.1080/19390211.2018.1455788.
99. Tenorio-Jiménez C, Martínez-Ramírez MJ, Del Castillo-Codes I, Arraiza-Irigoyen C, Tercero-Lozano M, Camacho J, et al. Lactobacillus reuteri V3401 reduces inflammatory biomarkers and modifies the gastrointestinal microbiome in adults with metabolic syndrome: the PROSIR study. Nutrients. 2019;11(8):1761. doi: 10.3390/nu11081761.
100. Kassaian N, Feizi A, Aminorroaya A, Amini M. Probiotic and synbiotic supplementation could improve metabolic syndrome in prediabetic adults: A randomized controlled trial. Diabetes Metab Syndr. 2019;13(5):2991-96. doi: 10.1016/j.dsx.2018.07.016.
101. Panahi Y, Hosseini MS, Khalili N, Naimi E, Soflaei SS, Majeed M, et al. Effects of supplementation with curcumin on serum adipokine concentrations: a randomized controlled trial. Nutrition. 2016;32(10):1116-22. doi: 10.1016/j.nut.2016.03.018.
102. Di Pierro F, Bressan A, Ranaldi D, Rapacioli G, Giacomelli L, Bertuccioli A. Potential role of bioavailable curcumin in weight loss and omental adipose tissue decrease: preliminary data of a randomized, controlled trial in overweight people with metabolic syndrome. Preliminary study. Eur Rev Med Pharmacol Sci. 2015;19(21):4195-202. PMID: 26592847.
103. Amin F, Islam N, Anila N, Gilani AH. Clinical efficacy of the co-administration of Turmeric and Black seeds (Kalongi) in metabolic syndrome - a double blind randomized controlled trial - TAK-MetS trial. Complement Ther Med. 2015;23(2):165-74. doi: 10.1016/j.ctim.2015.01.008.
104. Bateni Z, Rahimi HR, Hedayati M, Afsharian S, Goudarzi R, Sohrab G. The effects of nano-curcumin supplementation on glycemic control, blood pressure, lipid profile, and insulin resistance in patients with the metabolic syndrome: A randomized, double-blind clinical trial. Phytother Res. 2021;35(7):3945-53. doi: 10.1002/ptr.7109.
105. Matsumoto S, Nakanishi R, Li D, Alani A, Rezaeian P, Prabhu S, et al. Aged garlic extract reduces low attenuation plaque in coronary arteries of patients with metabolic syndrome in a prospective randomized double-blind study. J Nutr. 2016;146(2):427S-32S. doi: 10.3945/jn.114.202424.
106. Sangouni AA, Alizadeh M, Jamalzehi A, Parastouei K. Effects of garlic powder supplementation on metabolic syndrome components, insulin resistance, fatty liver index, and appetite in subjects with metabolic syndrome: A randomized clinical trial. Phytother Res. 2021;35(8):4433-41. doi: 10.1002/ptr.7146.
107. Sangouni AA, Alizadeh M, Jamalzehi A, Hosseinzadeh M, Parastouei K. Garlic supplementation improves intestinal transit time, lipid accumulation product and cardiometabolic indices in subjects with metabolic syndrome: A randomized controlled trial. Phytother Res. 2023;37(6):2305-14. doi: 10.1002/ptr.7741.
108. Kojadinovic MI, Arsic AC, Debeljak-Martacic JD, Konic-Ristic AI, Kardum ND, Popovic TB, et al. Consumption of pomegranate juice decreases blood lipid peroxidation and levels of arachidonic acid in women with metabolic syndrome. J Sci Food Agric. 2017;97(6):1798-804. doi: 10.1002/jsfa.7977.
109. Moazzen H, Alizadeh M. Effects of pomegranate juice on cardiovascular risk factors in patients with metabolic syndrome: a double-blinded, randomized crossover-controlled trial. Plant Foods Hum Nutr. 2017;72(2):126-33. doi: 10.1007/s11130-017-0605-6.
110. Esmaeilinezhad Z, Babajafari S, Sohrabi Z, Eskandari MH, Amooee S, Barati-Boldaji R. Effect of synbiotic pomegranate juice on glycemic, sex hormone profile and an-

thropometric indices in PCOS: A randomized, triple blind, controlled trial. Nutr Metab Cardiovasc Dis. 2019;29(2):201-08. doi: 10.1016/j.numecd.2018.07.002.
111. de Bock M, Derraik JG, Brennan CM, Biggs JB, Morgan PE, Hodgkinson SC, et al. Olive (Olea europaea L.) leaf polyphenols improve insulin sensitivity in middle-aged overweight men: a randomized, placebo-controlled, crossover trial. PLoS One. 2013;8(3):e57622. doi: 10.1371/journal.pone.0057622.
112. Sanchez-Rodriguez E, Lima-Cabello E, Biel-Glesson S, Fernandez-Navarro JR, Calleja MA, Roca M, et al. Effects of virgin olive oils differing in their bioactive compound contents on metabolic syndrome and endothelial functional risk biomarkers in healthy adults: a randomized double-blind controlled trial. Nutrients. 2018;10(5):626. doi: 10.3390/nu10050626.
113. D'Amore S, Vacca M, Cariello M, Graziano G, D'Orazio A, Salvia R, et al. Genes and miRNA expression signatures in peripheral blood mononuclear cells in healthy subjects and patients with metabolic syndrome after acute intake of extra virgin olive oil. Biochim Biophys Acta. 2016;1861(11):1671-80. doi: 10.1016/j.bbalip.2016.07.003.
114. Njike VY, Ayettey R, Treu JA, Doughty KN, Katz DL. Post-prandial effects of high-polyphenolic extra virgin olive oil on endothelial function in adults at risk for type 2 diabetes: A randomized controlled crossover trial. Int J Cardiol. 2021;330:171-6. doi: 10.1016/j.ijcard.2021.01.062.