

A Science-Based, Clinically Tested Dietary Approach for the Metabolic Syndrome

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Abstract

During the last decade, great strides have been made to delineate the importance of diet in the prevention and treatment of the metabolic syndrome. Dietary recommendations have emphasized a low-fat (“antiatherogenic”) diet as the first-line therapeutic approach. However, the complex etiology of the metabolic syndrome would seem to necessitate tailored dietary approaches beyond simple macronutrient modification. Current data have revealed varying biological effects of individual macronutrients within the same category, suggesting that adjusting dietary macronutrient percentages without considering their physiological impact may not be adequate. The concepts of glycemic index and glycemic load support the need for differentiation between various types of carbohydrates. Additionally, significant evidence to date indicates that metabolic syndrome biomarkers improve with dietary patterns rich in phytochemical complexity (e.g., Mediterranean diet). Taking these aspects into account, we designed a specific dietary approach consisting of foods found in the popularized Mediterranean diet, modified to include only those items that are low in glycemic load and grains (gluten) and are antiinflammatory. Initially based on scientific literature, this food plan has since been tested and adapted in our clinic over the past decade. This paper describes the rationale of the dietary program and provides an overview of data on its efficacy in individuals with metabolic syndrome.

Introduction

DESPITE DEBATE ABOUT ITS DEFINITION and significance,^{1,2} the metabolic syndrome is clinically relevant because it precedes a number of chronic diseases, including type 2 diabetes and cardiovascular disease (CVD).^{3,4} Recent estimates indicate that approximately 69 million (34.5%) American adults fit within the definition of metabolic syndrome established by the International Diabetes Federation (IDF).⁵ Ultimately, early intensive control of metabolic syndrome may produce better health outcomes and reduce the risk of chronic disease complications.⁶ Thus, an urgent need exists for strategies to prevent or reverse this epidemic.

Because the occurrence of metabolic syndrome is strongly correlated with lifestyle habits, dietary recommendations are one means to prevent or treat health consequences associated with this syndrome.^{7–10} Over time, consumption of a particular profile of foods may give rise to development of metabolic syndrome. Lower vegetable and fiber intake,¹¹ as well as high meat and alcohol consumption,¹² have been

associated with increased incidence of metabolic syndrome. Similarly, using data from three large epidemiological studies, Baxter et al.¹³ observed that dietary patterns high in meat and refined grains were correlated with greater prevalence of metabolic syndrome.

Because the maladaptive diet is, in part, responsible for the origin of metabolic syndrome, a rational therapy to reverse the condition would be to shift dietary habits away from those that are not health promoting. Leading organizations such as the National Heart, Lung, and Blood Institute (NHLBI) and American Heart Association (AHA) advocate dietary therapy as part of the first-line approach to addressing metabolic syndrome with the ultimate goal of reducing risk for atherosclerotic disease.⁴ Prescribed diets include those intended for weight loss that are primarily low in fat and, in particular, saturated fat.⁴ A number of intervention studies have assessed the role of dietary patterns on metabolic syndrome. Feldeisen and Tucker¹⁴ have compiled an excellent review on this topic, and as a result, the research in this area will not be extensively presented in this text. However, it is

worthwhile to mention that several of these dietary patterns, including the Mediterranean diet,¹⁵ Dietary Approaches to Stop Hypertension (DASH) diet,¹⁶ and even a whole grain-enriched hypocaloric diet¹⁷ have all been effective to some degree in reducing metabolic risks in populations with metabolic syndrome. The common feature of these dietary patterns is the inclusion of an array of diverse phytochemicals through the consumption of unprocessed foods such as whole grain, vegetables, and fruits. Hence, these and other studies suggest that the existing dietary model for metabolic syndrome should be revisited and assessed beyond macronutrient modification.¹⁸ The potential benefits of formulating a specific diet tailored to the individual metabolic syndrome parameters have been discussed.¹⁹

In this paper, we present a dietary approach (“*FirstLine Therapy*® Food Plan” or FLT Food Plan) built on a foundation of scientific principles related to prevention and treatment of metabolic syndrome. Furthermore, we modified the food plan based on a decade’s worth of clinical experience. Herein, clinical results from our studies and from an external study are presented.

The *FirstLine Therapy* (FLT) Food Plan

The *FirstLine Therapy* (FLT) Food Plan, formulated by researchers and clinicians at the Functional Medicine Research Center (Gig Harbor, WA), leverages the cumulative sum of well-researched dietary tenets, including the benefits of low glycemic load eating and a whole food pattern similar to the Mediterranean-style diet. Overall, foods selected for this program fulfill the following criteria (Table 1): (1) low in glycemic load (GL), (2) abundant in phytochemicals, (3) low in arachidonic acid, and thus, antiinflammatory, (4) contain negligible food additives such as trans fats, food dyes, or artificial sweeteners, and (5) limited grains, with gluten-containing grains minimally represented.

One of the strengths of this program is its successful outcome despite a lack of caloric restriction. Clinical observations have indicated that although regular eating times throughout the day are encouraged, fewer overall calories are consumed on a daily basis. Potential reasons for this seeming discrepancy could be due to the high-fiber content and low glycemic load of meals, resulting in increased satiety. On average, the FLT Food Plan provides a daily energy intake of 44–47% carbohydrates, 27–30% protein, and 25–27% fat with a total GL of no higher than 65. Consequently, this dietary approach would be consistent with guidelines for being low in fat (considered by contemporary guidelines to be 27–29 energy% from fat). These percentages, however, can be variable. Depending on vegetable consumption, carbohydrate intake may contribute as much as 50% to the daily energy intake. Fiber (insoluble and soluble combined) intake typically doubles on this plan relative to the baseline diet. The rationale for formulating a dietary approach beyond adjusting levels of macronutrients is due, in part, to the extensive research favoring the diversity and quality of individual macronutrients.

The FLT Food Plan is designed to incorporate the complexity found in plant-based eating patterns like the Mediterranean diet. Although not definitively proven, it would seem that phytochemicals, or plant-based, healthful nonnutritive substances, play a role in a diet for metabolic syndrome. The importance of phytochemicals for metabolic

syndrome is their role in restoring dysfunctional cellular signaling pathways by positively modulating insulin receptor binding, protein kinase activity, and genetic expression of inflammatory markers like nuclear factor- κ B.

Clinical Effects of the FLT Food Plan on Metabolic Syndrome Markers

Initially, the FLT Food Plan was tested together with a medical food containing soy protein and phytosterols against the standard of care, AHA Step 1 low-fat diet, in 53 overweight, postmenopausal, hypercholesterolemic women for 12 weeks.²⁰ Both groups were provided with target caloric intakes and a standard 150-minute exercise prescription to achieve weight loss of 1 to 2 pounds weekly. Even though these women did not have metabolic syndrome, postmenopausal women have increased susceptibility to CVD.²¹ When reviewing compliance data for both study arms, it was found that the group following the FLT Food Plan consumed fewer calories than the AHA group due to lack of hunger. Conversely, the AHA group consumed their recommended dietary intake, but often complained of hunger. Results indicated that the FLT Food Plan with accompanying medical food more favorably modified certain serum lipid parameters compared with the AHA diet (–15.8% in total cholesterol, $p = 0.0036$ between groups; –14.8% in low-density lipoprotein cholesterol [LDL-C], $p = 0.004$ between groups; and –44.8% in triacylglycerols, $p = 0.006$ between groups). Most importantly, the Framingham CVD risk score was reduced to a greater extent in the FLT group relative to the AHA group.

In a separate trial, we tested the ability of the diet to reduce metabolic syndrome markers in individuals with metabolic syndrome (Lerman et al., 2008). In 18 subjects with metabolic syndrome, 12 weeks of following the FLT Food Plan without caloric prescription plus a standard 150-minute aerobic exercise protocol resulted in a 14.3% decrease in triacylglycerols and a 4.8% reduction in fasting blood glucose. Triacylglycerols:high-density lipoprotein (TG:HDL), a common clinical marker of metabolic syndrome, had decreased 17.6% compared with baseline. By the end of the study period, the percentage of subjects meeting metabolic syndrome criteria dropped from 100% at baseline to 78%. Additionally, waist circumference had dropped, along with overall weight (–5.7 kg \pm 1.0 kg). The Framingham CVD risk score fell in these subjects from 16.0 \pm 3.0% at baseline to 13.1 \pm 2.7% at 12 weeks ($p = 0.011$). When the FLT Food Plan was coupled with a medical food high in soy protein and phytosterols, ($n = 23$) a 43% net resolution in metabolic syndrome was noted, along with significant improvements in blood lipids beyond diet alone. Hence, in conjunction with appropriate supplementary phytochemicals, the FLT Food Plan has the potential to impact biomarkers of metabolic syndrome dramatically within a short period of time.

Additionally, cravings for sweets, fast foods, fats, and carbohydrates decrease significantly within 2 weeks of following the FLT Food Plan in conjunction with moderate exercise and remain reduced at completion of the intervention (12 weeks). Hunger between breakfast, lunch, and dinner and general hunger throughout the day were also shown to be decreased in individuals following the program.

Finally, over a mean time period of 85.7 days, Robledo and Flynn²² report improvements in weight (–9.4 \pm 1.3 lb),

TABLE 1. FIRSTLINE THERAPY (FLT) FOOD PLAN GOALS AND THEIR SCIENTIFIC RATIONALE

<i>FLT Food Plan goal</i>	<i>Implementation</i>	<i>Scientific rationale</i>
Balance glycemic response	All foods on the plan have a low-to-moderate glycemic index. Daily glycemic load does not exceed 65.	Positive association exists between high glycemic load and chronic disease risk ^{24,25} ; meals high in glycemic index may lead to overeating. ²⁶
Reduce sweeteners	All sweeteners, except for agave nectar and stevia, are omitted from the food plan. Whole fruits, low in glycemic index, are encouraged.	Increased added sugars in the diet can lead to increased serum triacylglycerol concentrations. ²⁷ Dietary patterns encompassing low-calorie/diet soft drinks, sugar-sweetened beverages, and sugar-sweetened soft drinks have been associated with increased risk for metabolic syndrome and type 2 diabetes. ^{28–31}
Leverage phytochemical complexity of whole food patterns	Eating whole versus processed foods is strongly emphasized.	Increasing evidence indicates that whole foods-based dietary regimens rich in phytochemicals, such as the Mediterranean diet, are therapeutic for metabolic syndrome. ³²
Choose antiinflammatory fats (low arachidonic acid, higher amounts of monounsaturated fats)	High-fat animal foods are not allowed on the plan. Low-fat cheeses, milk, and meats are presented as optional replacements.	Inflammatory biomarkers are associated with metabolic syndrome. ³³ Higher arachidonic acid content in adipose tissue has been shown to be positively correlated with increasing risk of metabolic syndrome. ³⁴ The Mediterranean diet, shown to be efficacious in reducing metabolic syndrome biomarkers, consists of copious amounts of olive oil, high in monounsaturated fat.
Reduce grain (gluten) intake	Only one serving of whole grains is allowed daily.	Although the FLT Food Plan parallels much of the Mediterranean diet recommendations, it is different from the Mediterranean diet in its number of grain servings. It has been suggested that the standard Mediterranean diet may not be suitable for individuals with insulin resistance due to the high carbohydrate content. ³⁵ Additionally, keeping the diet low in allergens, particularly gluten, may be important for reducing inflammatory processes in metabolic syndrome. ^{36–38} A well established association exists between diabetes and celiac disease. ^{39,40}
Eat frequently	Five to six small meals are advocated daily.	Smaller, frequent meals eaten throughout the day have been shown to produce better blood glucose peaks. ^{41,42}
Eat mindfully	Individuals are made aware of signs of emotional eating and stressful eating. The importance of mindful eating is emphasized.	Mindfulness-based eating awareness can be helpful in reducing binge-eating behavior ⁴³ and has been shown to result in decreased insulin resistance. ⁴⁴
Make eating convenient and full of quality phytochemicals using a medical food	Medical foods specific for the cardiometabolic syndrome that leverage important phytochemicals, like soy protein, phytosterols, hops-derived <i>rho</i> iso alpha acids, and <i>Acacia nilotica</i> , are part of the FLT Food Plan, commonly at one or two servings daily.	Incorporation of a medical food into an eating regimen for those with metabolic syndrome enhances individual compliance with a program due to its convenience and ease of preparation. ^{45,46} Additionally, it can provide a concentrated source of phytochemicals specifically compiled to address the underlying pathologies of metabolic syndrome. ^{47–49}

TABLE 2. FIRSTLINE THERAPY (FLT) FOOD PLAN GUIDELINES FOR DAILY CONSUMPTION

<i>Food category</i>	<i>Average serving size</i>	<i>Daily recommendations</i>	<i>Examples</i>
Low GI* (<55) vegetables	½ cup (10–25 kcal)	At least 3 servings	Bell peppers, broccoli, celery, leafy greens of all types, mushrooms, tomatoes, zucchini
Moderate GI (55–70) vegetables	½ cup (45 kcal)	Only 1 serving	Carrots, turnips, beets, sweet potatoes, yams
Legumes	½ cup (110 kcal)	At least 1 serving	Canned or fresh beans (garbanzo, pinto, kidney, cannellini, fat-free refried beans, etc.)
Concentrated animal and vegetable protein sources	3 oz. (150 kcal)	Unlimited	Eggs, fish, poultry, lean cuts of beef (<5% fat), tofu, tempeh, low-fat cheeses such as cottage cheese, ricotta, mozzarella, and parmesan
Nuts and seeds	1 scant handful or 2 tablespoons of nut butter	1 serving	Almonds, walnuts, pecans, pistachios, sunflower seeds, sesame seeds, almond butter, peanut butter
Low GI fruits	Specific quantities for each fruit to equal 80 kcal	2 to 3 servings	Apple, blackberries, blueberries, cherries, grapes, grapefruit, tangerine, kiwi, mango, nectarine, peach, plum
Dairy products	6 oz (80 kcal)	Optional, but 2 to 3 servings maximum	Low-fat, plain, unsweetened yogurt, plain, unsweetened soymilk, non-fat milk
Fats and oils	1 teaspoon (40 kcal)	4 servings daily	Oils: Olive, flaxseed, canola, walnut; Mayonnaise made with canola or grapeseed oil
Whole grains	½ cup cooked (75–100 kcal)	Only 1 serving	Brown rice, barley, oatmeal (¾ cup), whole grain rye crackers, low-carb tortilla (2 small or 1 large)
Beverages		Unlimited	Decaffeinated or herbal teas, decaffeinated coffee, water
Condiments		Unlimited	Cinnamon, mustard, tamari soy sauce, vinegar, agave nectar, stevia, cooking spices (curcumin, dill, cumin, etc.)

Abbreviation: GI, glycemic index.

percent body fat ($-3.4 \pm 0.5\%$), systolic blood pressure (-8 ± 4 mm Hg), HDL (2.9 ± 2.4 mg/dL), and triacylglycerols (-34.4 ± 23.0 mg/dL) in 22 men and women following the FLT Food Plan, along with exercise and the addition of a medical food. In subsequent studies, we plan to monitor the performance of our dietary approach in a clinical trial for an extended period of time.

Net Resolution of Metabolic Syndrome With the FLT Food Plan Compared With Other Dietary Approaches

To our knowledge, this dietary regimen, complete with the addition of a medical food, is unique relative to other dietary patterns available for metabolic syndrome. Clinical

results have indicated its efficacy in subjects with metabolic syndrome, including reducing metabolic syndrome biomarkers and CVD risk. These results are in agreement with dietary patterns advocated by others.^{15,16,23} For example, Esposito et al.¹⁵ demonstrated a 48% net resolution in metabolic syndrome in subjects instructed to follow a Mediterranean diet for 2 years. The DASH eating plan emphasizes increased consumption of fruit, vegetables, low-fat dairy, and whole grains, which is quite similar to the Mediterranean diet. Azadbakht et al.¹⁶ found a 35% reduction in the prevalence of metabolic syndrome in individuals following the DASH diet compared with the 19% reduction in metabolic syndrome for those following a weight-reduction diet (500 kcal less than their caloric needs according to their weight) after 6 months. The lifestyle modification protocol established in the Diabetes Prevention Program Trial,²³ using a healthy low-calorie, low-fat diet and physical exercise of at least 150 minutes weekly, resulted in a 38% resolution of metabolic syndrome after 3 years. Within the relatively short period of 12 weeks, the FLT Food Plan together with 150 minutes of aerobic exercise can lead to 22% resolution of metabolic syndrome, and with the addition of a phytochemical-specific medical food, increases to a 43% resolution. These results suggest that this food plan is a relatively compelling approach to addressing the complicated etiology underlying metabolic syndrome. It will be advantageous to study this program in a long-term clinical study comparable to the duration of the aforementioned intervention trials (ranging from 6 months to 3 years) to determine results in individuals with metabolic syndrome.

Conclusion

Lifestyle modification, including changing dietary regimen, has been shown to have a positive effect on reducing the incidence of metabolic syndrome and type 2 diabetes. In an attempt to address metabolic syndrome from a nutritional perspective, we developed an easy-to-follow dietary program in our medical clinic that incorporated foundational concepts such as low glycemic load and leveraging the antiinflammatory whole foods pattern high in phytochemicals representative of the healthful Mediterranean diet. To enhance compliance and discourage overeating, the diet was modified further to exclude added sugars and limit grain intake. In addition to focusing on the constituents of the diet, individuals were counseled on their meal frequency and eating mindfully to ensure that blood sugar remained stable throughout the day and that they invested time and attention in eating. Clinical research on this program coupled with modest exercise demonstrates beneficial effects on the diagnostic criteria of metabolic syndrome. Further studies are needed to determine its long-term effect on the incidence of type 2 diabetes and CVD in individuals with metabolic syndrome.

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