

Weight Management



Food Plans & Dietary Recommendations

WEIGHT MANAGEMENT FOOD PLANS & DIETARY RECOMMENDATIONS

No allele variation

Variation in FTO Allele

Variation in AC4R Allele

Variation in FABP2 Allele

Variation in ADRB2 Allele

Variation in SH2B1 Allele

Combination of any of the Above Variations

Welcome to a new way of eating and managing weight. This guide provides both practitioners and patients with specific recommendations for losing and sustainably managing weight. This approach relies on genetic testing for the following gene variations known to impact weight gain and appetite:

- Human fat-mass and obesity associated gene (FTO)
- Melanocortin 4 Receptor (MC4R)
- Fatty acid binding protein 2 (FABP2)
- Beta-adrenoreceptor 2 (ADRB2)
- SH2B1 adapter protein 1 (SH2B1)

Food plans included in this guide rely on the primary components of a Mediterranean-style diet, which has been shown to have a positive impact on weight, heart health, and many other modern chronic diseased states.

This guide is split into two sections. The first section is for practitioners and provides an evidence-based summary of each food plan with specific macronutrient information. This section also provides suggestions for choosing the best food plan for an individual based on his/her genetic test results.

The second section is for patients, with separate chapters for each gene variant. Each patient chapter contains basic dietary guidance, a 7-day meal plan with recipes, and tools for creating future customized meal plans. Materials support both the weight loss phase of weight management as well as ongoing weight maintenance.

PRACTITIONER INFORMATION

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Features of All Food Plans

While the food plans provided in this booklet are allele-specific, all of the plans promote a healthy eating lifestyle and have the following features in common:

Whole foods – whole foods are emphasized over processed and refined foods. Whole foods generally provide higher nutrient density per calorie (Drewnowski, 2005), a particularly important feature when reducing calorie intake for weight loss.

Minimal sugar – Sugar in all forms, even fruit, is reduced to help maintain consistent blood glucose levels, improve insulin sensitivity and reduce inflammation. Refined sugar is discouraged because of its low nutrient density.

High fiber – High fiber whole grains, vegetables and fruits make up a large part of each food plan. A high fiber eating pattern helps to promote satiety, manage blood sugar, improve insulin resistance, and remove toxins from the body through more regular bowel movements.

Healthy, high quality fats – Healthy fats help to promote flexible and healthy cell membranes and support hormone and neurotransmitter production (McGuire & Beerman, 2013, p. 225). All food plans include lean meat proteins with an emphasis on cold water fish, known to be high in omega-3 fatty acids.

Lots of vegetables – Most plans contain at least 8 – 10 servings of vegetables per day. Not only do vegetables provide substantial fiber, phytonutrients within vegetables help ensure a wide range of micronutrients and minerals, reduce oxidative stress, and reduce inflammation.

Specific water, beverages, and supplements to support weight loss.

Each of these features is discussed in more detail below.

Whole Foods

Whole foods are the core of each recommended food plan. Whole foods are minimally processed and have higher nutrient density per calorie than most processed foods.

Minimal Sugar

Maintaining a relatively constant blood glucose level is important in maintaining the body's overall metabolic balance. The body expects and deals best with small increases in blood glucose after a meal.

When our stomachs begin to fill, a signal is transmitted to the pancreas to release insulin. Insulin's job is to "guide" glucose from the food that we eat into cells that need the energy. When our blood glucose gets too low, the liver begins using stored sugars (glycogen) and converting them into glucose to keep our blood glucose and energy levels constant.

If we eat a meal high in refined foods and sugar, this sugar quickly enters the bloodstream and overwhelms the insulin that's trying to get the sugar into the cells, causing high postprandial blood glucose levels. To address this issue, the body produces more and more insulin and insulin tries to feed the cells more and more sugar. At some point the cells no longer want more sugar - they have no need for it and they become less sensitive to insulin. This results in higher blood insulin levels.

Higher blood glucose and insulin increases low-grade, systemic inflammation, triggering the stress response and signaling the body to store the extra sugar as fat (Tateya, Kim, & Tamori, 2013).

The ebb and flow of blood glucose also affects how we feel. We may feel energized after a high sugar meal, but quickly lose that energy as our blood sugar quickly drops. This often leads to a cycle of eating more high-sugar foods or beverages or taking stimulants like caffeine to help ourselves wake up and function better.

High Fiber

Foods high in fiber take longer to digest, helping us feel full longer. In fact, we cannot digest plant fiber, which explains why it can help us feel satiated for a longer time.

Our diets contain two types of fiber: soluble and insoluble. Soluble fiber will combine with water and glucose slowing stomach emptying and reducing spikes in blood sugar. Soluble fiber also softens stools and binds cholesterol as it moves through the digestive tract, resulting in easier, more regular bowel movements and decreased blood cholesterol levels. Foods high in soluble fiber include yeast, oat bran, barley, psyllium, chia, marshmallow root and pectin found in fruits, vegetables, seeds, beans, lentils, squash, carrots and oat bran.

Insoluble fiber does not bind water and it increases stool frequency and bulk while acting like a sticky brush in the intestines, picking up and moving wastes and toxins out of the body. Insoluble fiber also provides food for the microbes that live in our large intestines. Our bodies contain more microbes than cells, and those in the gut play an important part in regulating many systems and functions of the body. Certain microbes digest insoluble fibers and release additional nutrients that are absorbed through our large intestine. Cellulose, hemicellulose and lignans are insoluble fiber, found in the outer coat of whole grains and vegetables.

Diets high in fiber have been shown to lower blood pressure, improve blood glucose control, aid weight loss, support the immune system, and improve bowel movement regularity, yet estimates suggest that adults in the U.S. eat less than half of recommended levels of fiber (Anderson et al., 2009). The United States Dietary Reference Intake for Total Fiber is from 30 - 38 g/day for men and from 21 - 25 g/day for women (Institute of Medicine, 2005).

Healthy, High-Quality Fats

In 1980, the U.S. government launched a low-fat campaign in an effort to reduce Americans' consumption of high fat foods. This campaign was hugely successful, resulting in the creation of many low-fat substitutes (i.e., salad dressings, cookies, etc.). However, heart disease in the U.S. did not decrease as expected (Mozaffarian, 2016). At the same time, Americans' gained more weight.

Fat is necessary for many of the body's functions, such as maintaining flexible and healthy cell membranes, ensuring balanced hormones, and supporting the stress response (Gropper & Smith, 2013, pp. 137–182); however, some types of fat can harm the body. For instance, artificial trans-fats are highly inflammatory and make cell membranes less flexible (Gropper & Smith, 2013, p. 162).

Saturated fats in high quantities, found primarily in meat and dairy products, also increase inflammation (Enos et al., 2013). It is the increased inflammation that causes the buildup of plaque in the blood vessels - not the saturated fat itself (Hansson, 2005).

Leaner meat products are included in all food plans to minimize saturated fat. Fish is suggested at least twice per week because it contains high quantities of beneficial omega-3 fatty acids. Omega-3 fatty acids reduce inflammation (Calder, 2006), an important first step in weight loss.

As with carbohydrates, eating minimally processed fats is the best option. The healthiest liquid oils will be cold pressed or unrefined. Liquid oils exposed to high temperatures are partially oxidized and can cause inflammation. For cooking at higher temperatures, coconut oil or butter are best. These are both saturated fats which means that they can stand up to higher heat with minimal oxidation.

Phytonutrients

Phytonutrients are 'plant nutrients'. Plants contain thousands of different nutrients that affect how our bodies function. Current estimates suggest that there are between 5,000 to 10,000 phytonutrients. Few phytonutrients have been extensively studied, and new discoveries are made regularly. Some phytonutrients are more familiar, such as resveratrol found in red wine and the skins of purple grapes, and lycopene found in tomatoes. It's possible to get some of these phytonutrients in supplement form, but research suggests that these nutrients work best in the body when they are eaten as a part of the whole plant (Liu, 2003).

Many phytonutrients are anti-inflammatory, meaning they help reduce inflammation in the body. Localized inflammation may be felt as swelling and pain, while systemic inflammation may be experienced as allergies, food sensitivities, diabetes, atherosclerosis, arthritis, Alzheimer's, fibromyalgia and migraines (Miller, 2016, p. 3). Studies have shown that systemic inflammation increases as percent body fat increases (Jung & Choi, 2014). When inflamed, the body tends to hold onto weight because it thinks that it's under stress and must prepare for famine or difficult times. Therefore, it's important that any weight loss plan include lots of vegetables to help the body reduce inflammation and signal the body that it's okay to lose weight.

Fruit and vegetable colors provide a lot of information about the types of phytonutrients they contain. When coming up with menu plans and shopping lists for the week, strive to get as many colors into your meals as possible. This is called "eating the rainbow."

The meals and snacks in all of the food plans are designed to provide many different phytonutrients and at least 8 - 12 servings of fruits and vegetables each day. Ideally, half your plate will contain vegetables at each meal or snack. The importance of vegetables cannot be overstated. When hungry and in doubt, always go for vegetables!

Food Groups

All food plans have been broken down into common "food groups" to help patients make the connection between more common foods and the general macronutrient designations of protein, fat and carbohydrate. Food groups used in all plans include: vegetables, fats/oils, proteins, whole grains, fruits, legumes, dairy, nuts/seeds and starchy vegetables. All food plan servings and recipes are based on these food groups.

Water & Beverages

Green Tea – There are conflicting studies on green tea and its effect on weight loss. Some studies have found that green tea may inhibit gastric and pancreatic lipases and stimulate thermogenesis. Decreased lipases will decrease the body's fat absorption, while stimulating thermogenesis increases resting metabolic rate, resulting in decreased body weight, waist circumference, and body fat mass. However, other studies have observed no effect. Although evidence with respect to weight loss is conflicting, it is reasonable to include green tea in a weight management program as it may aid weight loss and provide additional health benefits, such as reducing risk for cardiovascular disease and behavioral health. Brewed caffeinated green tea is suggested because of its higher catechin content than either instant or decaffeinated (Gaby, 2011, pp. 1266–1267).

Water – The Stanford A to Z study found that increasing water intake to greater than 1 liter/day supported weight loss in overweight premenopausal women who were following the Atkins, Zone or Ornish diets (Stookey, Constant, Popkin, & Gardner, 2008). Additionally, weight loss has been associated with an increase of organochlorine compounds in both the plasma and subcutaneous adipose tissue. Sufficient water intake, with fiber, is necessary to aid the body in regular bowel movements to clear these toxins (Chevrier et al., 2000).

Rooibos (Red Bush) Tea – Rooibos tea is high in vitamin C, providing strong antioxidant activity that may be supportive in weight loss.

Supplements

High Quality Multiple Vitamin Mineral Complex – Most Americans are deficient in an array of vitamins and minerals, from poor diet and reduced food/plant nutrient density. The U.S. 2015 Dietary Guidelines report indicates that vitamins A, C, D, E, folate, calcium and magnesium are under-consumed relative to the Estimated Average Requirement (EAR) (U.S. Office of Disease Prevention and Health Promotion, 2015). Most individuals in a chronic disease state, such as obesity or Type 2 diabetes, have insufficient levels of multiple vitamins and minerals that are necessary cofactors for biochemical reactions within the body.

Vitamin D – Vitamin D3 supplementation is suggested as vitamin D insufficiency is more common in obese individuals, likely due to decreased bioavailability (Wortsman, Matsuoka, Chen, Lu, & Holick, 2000). However, serum 25-OH-D levels should be tested prior to supplementing with Vitamin D3. Target serum levels for 25-OH-D should be within 40 – 70 ng/ml (Guilliams, 2014, p. 87). Genetic testing to evaluate Vitamin D receptor function is a consideration.

Curcumin – Systemic inflammation is typically higher in overweight and obese individuals, triggering the sympathetic nervous system, making it more difficult to reduce weight. Curcumin interacts directly with adipocytes, pancreatic cells, hepatic cells, macrophages and muscle cells to suppress inflammation. These actions can improve insulin sensitivity and maintain more stable blood glucose levels (Aggarwal, 2010).

Alpha Lipoic Acid (ALA) – a clinical trial found that 1800 mg/day of ALA over 20 weeks reduced body weight compared to placebo in patients with a BMI greater than 27 kg/m² (Koh et al., 2011).

Optional: Targeted Calories

Each food plan can be modified in multiple ways. Depending on your patient's current diet, you may wish to transition them to Mediterranean-style eating first without worrying about calorie intake. By reducing refined sugars, grains and other foods, eating healthy fats and increasing vegetable servings, many individuals will begin to lose weight without counting calories. Adopting this approach helps emphasize that this way of eating is a lifestyle change rather than a short-term "diet".

If you believe that counting calories is important for your patient, remember that a safe and sustainable rate of weight loss is about 2 - 3 lb./week. This can be achieved by subtracting 500 calories/day from your patient's Estimated Energy Requirement (EER) (Nelms, Sucher, Lacey, & Roth, 2010, p. 264).

Choosing the Best Food Plan

This guide contains six different food plans developed to support weight loss and weight management for individuals with variations in one or several of the following gene alleles: FTO, MC4R, FABP2, ADRB2 and SH2B1. There is also a Foundational Food Plan for individuals who have no variations in these specific alleles but need weight management guidance and support.

Throughout this guide, information is organized by specific allele variants (i.e., FTO, MCR4, FABP2, ADRB2 and SH2B1). Recognizing that variability is not necessarily limited to one gene, there is a chart (Table 1) to help you determine which food plan is the best starting point for individuals with multiple variant alleles.

Table 1: Flow Chart for Determining most applicable food plan when there are variations in more than one allele

| SH2B1 | FABp2 | ADRB2 | MC4R | FTO | Recommended Food Plan |
|-------|-------|-------|------|-----|------------------------|
| Y | Y | Y | Y | Y | SH2B1 Food Plan |
| Y | Y | Y | Y | N | SH2B1 Food Plan |
| Y | Y | Y | N | Y | SH2B1 Food Plan |
| Y | Y | Y | N | N | SH2B1 Food Plan |
| Y | Y | N | Y | Y | SH2B1 Food Plan |
| Y | Y | N | Y | N | SH2B1 Food Plan |
| Y | Y | N | N | Y | SH2B1 Food Plan |
| Y | Y | N | N | N | SH2B1 Food Plan |
| Y | N | Y | Y | Y | SH2B1 Food Plan |
| Y | N | Y | Y | N | SH2B1 Food Plan |
| Y | N | Y | N | Y | SH2B1 Food Plan |
| Y | N | Y | N | N | SH2B1 Food Plan |
| Y | N | N | Y | Y | SH2B1 Food Plan |
| Y | N | N | Y | N | SH2B1 Food Plan |
| Y | N | N | N | Y | SH2B1 Food Plan |
| Y | N | N | N | N | SH2B1 Food Plan |
| N | Y | Y | Y | Y | FABP2 Food Plan |
| N | Y | Y | Y | N | FABP2 Food Plan |
| N | Y | Y | N | Y | FABP2 Food Plan |
| N | Y | Y | N | N | FABP2 Food Plan |
| N | Y | N | Y | Y | FABP2 Food Plan |
| N | Y | N | Y | N | FABP2 Food Plan |
| N | Y | N | N | Y | FABP2 Food Plan |
| N | Y | N | N | N | FABP2 Food Plan |
| N | N | Y | Y | Y | SH2B1 Food Plan |
| N | N | Y | Y | N | FABP2 Food Plan |
| N | N | Y | N | Y | FABP2 Food Plan |
| N | N | Y | N | N | ADRB2 Food Plan |
| N | N | N | Y | Y | MC4R Food Plan |
| N | N | N | Y | N | MC4R Food Plan |
| N | N | N | N | Y | FTO Food Plan |
| N | N | N | N | N | Foundational Food Plan |

In general, recommendations are based on the number of requirements, or constraints, that need to be met. For example, the Foundational Food Plan has no real constraints aside from its macronutrient distribution, while the SH2B1 Food Plan has more constraints because it should ideally supply five or more meals per day, 20 – 30 g protein per meal, and contain foods with a glycemic index less than 55. Below is a list of the six food plans in order of fewest requirements to most requirements:

Foundational Food Plan – no extra requirements
 FTO Food Plan – 5+ meals/day, monounsaturated fats
 MC4R Food Plan – 5+ meals/day, low calorie density
 FABP2 Food Plan – Low fat, monounsaturated fat
 ADRB2 Food Plan – 20 – 30g protein/meal, carbohydrates < 50% of daily intake
 SH2B1 Food Plan – 5+ meals/day, 20 – 30g protein/meal, glycemic index < 55

The following sections describe each plan in detail, starting with who the plan is for, followed by plan features, macronutrient distribution, supplement recommendations, components of the customizable food plan (for 1200, 1500 and 1800 calories/day) and macronutrient information on the allele-specific 7-Day Meal Plans.

Foundational Food Plan

For: Those with no variation in the MC4R, FABP2, FTO, ADRB2 or SH2B1 genes

Features of the Foundational Food Plan

The Foundational Food Plan is the baseline plan from which all other food plans are derived. This plan is for those with no variation in the FTO, MC4R, FABP2, ADRB2, or SH2B1 genes. The Foundational Food Plan includes the following features to support sustainable weight loss and weight maintenance:

Limited fat intake. Moderately limiting dietary fat, while reducing sugars and refined carbohydrates, helps the body burn its own fat. In addition, fat is calorie dense so there are more calories for a given weight of fat than there are in either protein or carbohydrate.

High fiber intake. Foods high in fiber take longer to digest and improve feelings of fullness. Higher fiber also helps regulate blood sugar.

Foods that help increase metabolism. Increasing metabolism helps the body burn more energy. Eating increases metabolism, as does exercise. The Foundational Food Plan is packed with foods reported to increase metabolism, such as: berries, grapefruit, fish, celery, beans, coconut oil, green tea and spinach.

Macronutrient Distribution

All macronutrient recommendations are based on daily calorie intake (see Figure 1):

20% healthy fat, with an emphasis on monounsaturated and polyunsaturated fats over saturated fats
 30% lean protein
 50% carbohydrates in the form of whole grains, vegetables and fruits

Figure 1: Macronutrient Distribution for Foundational Food Plan

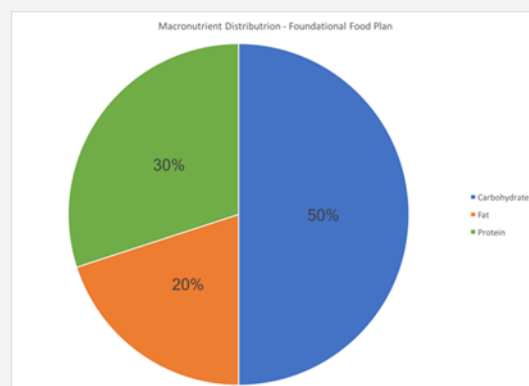


Table 2

| Food Group (servings) | Daily Calorie Target (kcal/day) | | |
|---------------------------|---------------------------------|------|------|
| | 1200 | 1500 | 1800 |
| Vegetables | 10 | 11 | 12 |
| Fats/Oils | 1 ½ | 1 ½ | 2 |
| Proteins | 8 | 9 | 10 |
| Whole Grains | 1 | 2 | 2 |
| Fruits | 1 | 2 | 2 |
| Legumes | 1 ½ | 1 ½ | 2 |
| Dairy | 1 | 1 ½ | 2 |
| Nuts/Seeds | ½ | 1 | 2 |
| Starchy Vegetables | ½ | ½ | 1 |

Customizable Foundational Food Plan

Use Table 2 as a guide for customizing the Foundational Food Plan. Food group servings per day are listed for 1200, 1500 or 1800 calories/day. These foods can be distributed in any way throughout the day, although it's recommended that protein and vegetables, in particular, be distributed fairly equally throughout the day to maintain blood sugar and minimize hunger.

Macronutrient Composition of Foundational 7-Day Meal Plan

| Nutrition Facts | | |
|---------------------------------------|------|-----|
| Daily intake – Foundational Food Plan | | |
| Calories | 1475 | |
| | g | % |
| Total Fat | 35.3 | 22 |
| Saturated Fat | 8.6 | 5.2 |
| Monounsaturated Fat | 11.8 | 7.2 |
| Polyunsaturated Fat | 8.8 | 5.4 |
| Total Carbohydrate | 199 | 54 |
| Dietary Fiber | 52.4 | 14 |
| Protein | 109 | 29 |
| Estimated Calorie Density | 1.1 | |

Estimated macronutrient composition of the Foundational 7-Day Meal Plan is summarized below, including values for saturated fat, monounsaturated fat, polyunsaturated fat, dietary fiber and calorie density. While total carbohydrate is 54% of total calories consumed, dietary fiber makes up 14%; therefore, net carbohydrates are 147 g, or 40%.

FTO Variant

For: Those with variation in the FTO gene

FTO, also known as the *human fat-mass and obesity associated gene*, is found on chromosome 16 and is one of the strongest risk factors for obesity. Individuals with both variant genes likely have 1.7x the increased risk of developing obesity compared to individuals not carrying this gene variant. FTO appears to play a key role in regulating energy metabolism; however, the exact mechanism remains to be determined. One theory is that the FTO gene is involved in making ghrelin, the hormone that stimulates feelings of hunger. If ghrelin continues to be produced after eating a regular meal, the brain receives the signal to keep eating; it's therefore easy to consume more food than needed. This risk may be seen in a preference for high calorie foods, in having a difficult time recognizing when enough food has been eaten, and coming back for seconds and thirds on a regular basis. Portion control is particularly important if usual satiety signals are misfiring.

Features of the FTO Food Plan

In addition to the Foundational Food Plan features, the FTO Food Plan includes the following features to support the preferences and common concerns associated with those with the FTO variant:

Limited fat intake. Moderately limiting dietary fat, while reducing sugars and refined carbohydrates helps the body burn its own fat. In addition, fat is calorie dense so there are more calories for a given weight of fat than there are in either protein or carbohydrate.

High fiber intake. Foods high in fiber take longer to digest and improve feelings of fullness. Higher fiber also helps regulate blood sugar.

Five moderate, balanced meals each day help improve fullness and reduce snacking.

Foods that help increase metabolism. Increasing metabolism helps the body burn more energy. Eating increases metabolism, as does exercise. The FTO Food plan is packed with foods reported to increase metabolism, such as: berries, grapefruit, fish, celery, beans, coconut oil, green tea and spinach.

Macronutrient Distribution

All macronutrient recommendations are based on daily calorie intake (see Figure 2):

20% healthy fat, with an emphasis on monounsaturated and polyunsaturated fats over saturated fats

25% lean protein

55% carbohydrates in the form of whole grains, vegetables and fruits

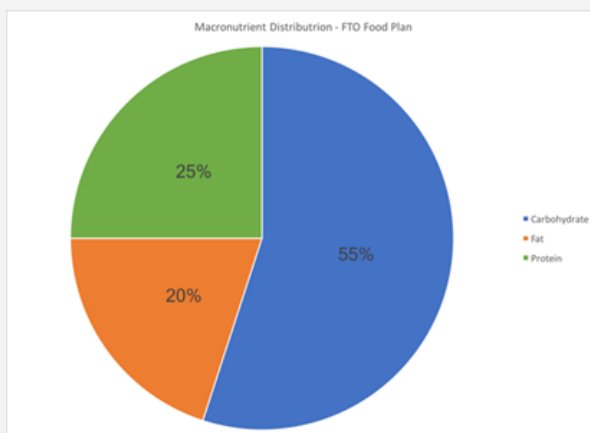


Figure 2: Macronutrient Distribution for FTO Food Plan

Table 3

| Food Group (servings) | Daily Calorie Target (kcal/day) | | |
|---------------------------|---------------------------------|------|------|
| | 1200 | 1500 | 1800 |
| Vegetables | 10 | 10 | 11 |
| Fats/Oils | 1 ½ | 2 | 2 |
| Proteins | 8 | 9 | 10 |
| Whole Grains | 1 | 1 ½ | 1 ½ |
| Fruits | 2 ½ | 2 ½ | 2 |
| Legumes | 1 | 2 | 3 |
| Dairy | ½ | 1 | 2 |
| Nuts/Seeds | ½ | 1 | 2 |
| Starchy Vegetables | ½ | ½ | 1 |

Customizable FTO Food Plan

Use Table 3 to customize the FTO Food Plan. Food group servings per day are listed for 1200, 1500 or 1800 calories/day. These foods can be distributed any way throughout the day, although it's recommended that protein and vegetables, in particular, be distributed fairly equally throughout the day to maintain blood sugar and minimize hunger.

Macronutrient Composition of FTO 7-Day Meal Plan

| Nutrition Facts | | |
|----------------------------------|--------------|-----|
| Daily intake | | |
| Calories | 1462 kcal | |
| | g | % |
| Total Fat | 33.6 | 21 |
| Saturated Fat | 7.2 | 4.3 |
| Monounsaturated Fat | 10.5 | 6.3 |
| Polyunsaturated Fat | 8.3 | 5 |
| Total Carbohydrate | 208 | 57 |
| Dietary Fiber | 52 | 15 |
| Protein | 103 | 28 |
| Estimated Calorie Density | 1.0 | |

Estimated macronutrient composition of the FTO 7-Day Meal Plan is summarized below, with estimated values for saturated fat, monounsaturated fat, polyunsaturated fat, dietary fiber and calorie density. While total carbohydrate is 57% of total calories consumed, dietary fiber makes up 15%; therefore, net carbohydrates are 156 g, or 43%.

MC4R Variant

For: Those with variations in the MC4R and/or FTO genes

MC4R, also known as the Melanocortin 4 Receptor, is a gene found on chromosome 18 and the receptor that this gene creates. The MC4R receptor is located in the hypothalamus, a region in the brain that is related to a number of different body functions, but in the case of MC4R, it is related to appetite and metabolism regulation. A variation in this gene causes individuals (referred to here as MC4R carriers), to have a tendency towards obesity and increased appetite. This is shown in a lowered basal metabolic rate, increased insulin levels, increased hunger, followed by a tendency to snack often.

Features of the MC4R Food Plan

In addition to the Foundational Food Plan features, the MC4R Food Plan includes the following features to support the preferences and common concerns associated with those who have this allele variant:

Limited fat intake. High fat diets may cause MC4R carriers to overeat. When a meal has a high fat content, MC4R carriers will eat more of that meal. Consuming even one high fat meal can rewire dietary habits to overeat for up to two weeks after returning to a controlled fat diet.

High fiber intake. Foods high in fiber take longer to digest and improve feelings of fullness. Higher fiber also helps regulate blood sugar.

Five moderate, balanced meals to support a healthy metabolism and to prevent overeating. MC4R carriers have a tendency to snack outside of mealtimes and also have difficulty restricting food intake so several regularly spaced meals can reduce this tendency.

Control carbohydrate intake. A higher level of carbohydrates frequently leads to greater obesity. MC4R carriers also have a tendency to experience higher insulin levels. Controlling carbohydrate intake helps to control food cravings, prevent excess carbohydrates from being stored as fat, and to help prevent development of insulin resistance and diabetes.

Macronutrient Distribution

All macronutrient recommendations are based on daily calorie intake (see Figure 3):

- 20% healthy fat, with an emphasis on monounsaturated and polyunsaturated fats over saturated fats
- 35% lean protein
- 45% carbohydrates in the form of whole grains, vegetables and fruits

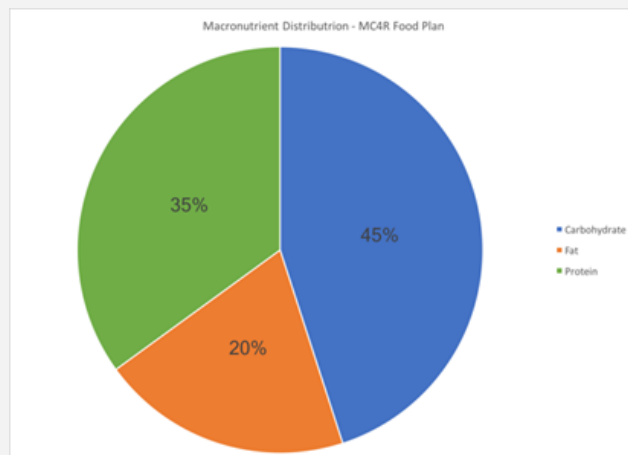


Figure 3: Macronutrient distribution for MC4R Food Plan

Table 4

| Food Group (servings) | Daily Calorie Target (kcal/day) | | |
|-----------------------|---------------------------------|------|------|
| | 1200 | 1500 | 1800 |
| Vegetables | 8 | 10 | 12 |
| Fats/Oils | 1 ½ | 2 | 2 ½ |
| Proteins | 8 | 10 | 12 |
| Whole Grains | 1 | 1 ½ | 2 |
| Fruits | ½ | 1 | 1 |
| Legumes | 1 | 2 | 2 ½ |
| Dairy | 1 ½ | 1 ½ | 1 ½ |
| Nuts/Seeds | ½ | 1 | 1 ½ |
| Starchy Vegetables | ½ | ½ | ½ |

Customizable MC4R Food Plan

Use Table 4 as a guide to customize the MC4R Food Plan. Food group servings per day are listed for 1200, 1500 or 1800 calories/day. These foods can be distributed any way throughout the day, although it's recommended that protein and vegetables, in particular, be distributed fairly equally throughout the day to maintain blood sugar and minimize hunger.

| Nutrition Facts | | |
|----------------------------------|-----------|-----|
| Daily intake | | |
| Calories | 1489 kcal | |
| | g | % |
| Total Fat | 33.9 | 20 |
| Saturated Fat | 7.8 | 4.8 |
| Monounsaturated Fat | 11.1 | 6.9 |
| Polyunsaturated Fat | 7.3 | 4.6 |
| Total Carbohydrate | 202 | 56 |
| Dietary Fiber | 51.4 | 15 |
| Protein | 111 | 30 |
| Estimated Calorie Density | 0.9 | |

Macronutrient Composition of MC4R 7-Day Meal Plan

Estimated macronutrient composition of the MC4R 7-Day Meal Plan is summarized below, with estimated values for saturated fat, mono-unsaturated fat, polyunsaturated fat, dietary fiber and calorie density. While total carbohydrate is 56% of total calories consumed, dietary fiber makes up 15%; therefore, net carbohydrates are 150 g, or 40%.

FABP2 Variant

For: Those with variation in the FABP2 and/or the ADRB2, MC4R, FTO genes

FABP2, also known as *fatty acid binding protein 2*, refers to a gene found on chromosome 4 and the protein that the gene creates. The function of the FABP2 protein is to move dietary fat from the intestines into small delivery vessels that travel to fat deposit sites around the body. Once at their location they release the fat into fat cells for storage. Fat molecules can also be sent from the intestines to the liver, but too much fat deposited in the liver can lead to inflammation, which may progress to scarring and irreversible damage. The variation in the FABP2 gene causes more fat to be transported to the belly, hips, thighs and other body areas for storage. The key to successful weight loss and health management in FABP2 variant carriers is to control how much and what types of fat are consumed.

Features of the FABP2 Food Plan

In addition to the Foundational Food Plan features, the FABP2 Food Plan includes the following features to support the preferences and common concerns associated with those who have this allele variant:

Limited fat intake. FABP2 delivers a higher amount of fat to the fat cells, so taking in less through the diet is important.

Higher intake of monounsaturated fats. By eating mainly monounsaturated fat instead of saturated fat and polyunsaturated fat the body receives signals to send the fat to the fat cells instead of to the liver. Excess fat in the liver leads to inflammation and high levels of insulin and glucose in the bloodstream which can then lead to weight gain, insulin resistance, metabolic syndrome, and eventually diabetes.

Lower carbohydrate intake. FABP2 carriers have a tendency towards higher insulin levels. By controlling fat and carbohydrate intake it is possible to reduce this trend. Choose complex carbohydrates that will digest slowly and also absorb fat.

High fiber intake. Foods high in fiber take longer to digest and improve feelings of fullness. Higher fiber also helps regulate blood sugar.

Macronutrient Distribution

All macronutrient recommendations are based on daily calorie intake (see Figure 4)

20% healthy fat, with an emphasis on monounsaturated and polyunsaturated fats over saturated fats

30% lean protein

50% carbohydrates in the form of whole grains, vegetables and fruits

Figure 4: Macronutrient distribution for FABP2 Food Plan

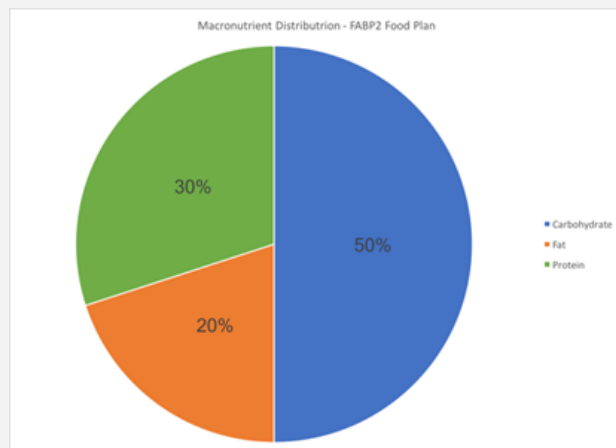


Table 5

| Food Group (servings) | Daily Calorie Target (kcal/day) | | |
|---------------------------|---------------------------------|------|------|
| | 1200 | 1500 | 1800 |
| Vegetables | 10 | 11 | 12 |
| Fats/Oils | 1 ½ | 2 | 2 ½ |
| Proteins | 8 | 9 | 10 |
| Whole Grains | 1 | 1 | 1 ½ |
| Fruits | 1 | 1 ½ | 2 |
| Legumes | 1 | 1 ½ | 2 |
| Dairy | 1 | 2 | 2 |
| Nuts/Seeds | 1 | 1 | 2 |
| Starchy Vegetables | 1 | 1 | 1 |

Customizable FABP2 Food Plan

Use Table 5 as a guide to customize the FABP2 Food Plan. Food group servings per day are listed for 1200, 1500 or 1800 calories/day. These foods can be distributed any way throughout the day, although it's recommended that protein and vegetables, in particular, be distributed fairly equally throughout the day to maintain blood sugar and minimize hunger.

| Nutrition Facts | | |
|----------------------------------|--------------|-----|
| Daily intake | | |
| Calories | 1477 kcal | |
| | g | % |
| Total Fat | 33.7 | 21 |
| Saturated Fat | 7.6 | 4.2 |
| Monounsaturated Fat | 11.6 | 6.4 |
| Polyunsaturated Fat | 9.3 | 5.1 |
| Total Carbohydrate | 209 | 57 |
| Dietary Fiber | 46.6 | 13 |
| Protein | 102 | 28 |
| Estimated Calorie Density | 1.0 | |

Macronutrient Composition of FABP2 7-Day Meal Plan

Estimated macronutrient composition of the FABP2 7-Day Meal Plan is summarized below, with estimated values for saturated fat, mono-unsaturated fat, polyunsaturated fat, dietary fiber and calorie density. While total carbohydrate is 57% of total calories consumed, dietary fiber makes up 13%; therefore, net carbohydrates are 163 g, or 44%.

ADRB2 Variant

For: Those with variation in ADRB2 and/or the MC4R, FTO genes

ADRB2, also known as *Beta-Adreno-Receptor 2*, refers to a gene found on chromosome 5 and the receptor that the gene creates. Many ADRB2 receptors are found in the liver and fat tissue. Here these receptors play an important role in the rate of release of glucose stored in the liver and muscle, in moving food through the digestive system, and in stimulating the release of insulin from the pancreas. These receptors have a significant influence on metabolism, especially when responding to persistent stress. Individuals with this variation, referred to here as ADRB2 carriers, are more likely to gain weight from eating carbohydrate. Although exercise is important for many body processes and does help regulate weight, research suggests that carriers of the ADRB2 variant will likely see greatest changes in weight from eating a low carbohydrate diet and fewer changes to weight from implementing an exercise regime.

Features of the ADRB2 Food Plan

In addition to the Foundational Food Plan features, the ADRB2 Food Plan includes the following features to support the preferences and common concerns associated with those who have this allele variant:

Lower carbohydrate intake. The ADRB2 variant and weight gain is strongly linked with a high carbohydrate diet. Carbohydrate will be quickly broken down and stored as fat, thus increasing weight. The variant can slow movement of food through the digestive tract so it is important to ensure that any dietary carbohydrate is high fiber, but with low calorie density.

Moderate fat intake. ADRB2 carriers are less sensitive to dietary fat; however, fat quality remains important.

High fiber intake. Foods high in fiber take longer to digest and improve feelings of fullness. Higher fiber also helps regulate blood sugar.

Macronutrient Distribution

All macronutrient recommendations are based on daily calorie intake (see Figure 5):

- 30% healthy fat, with an emphasis on monounsaturated and polyunsaturated fats over saturated fats
- 30% lean protein
- 40% carbohydrates in the form of whole grains, vegetables and fruits

Figure 5: Macronutrient Distribution for ADRB2 Food Plan

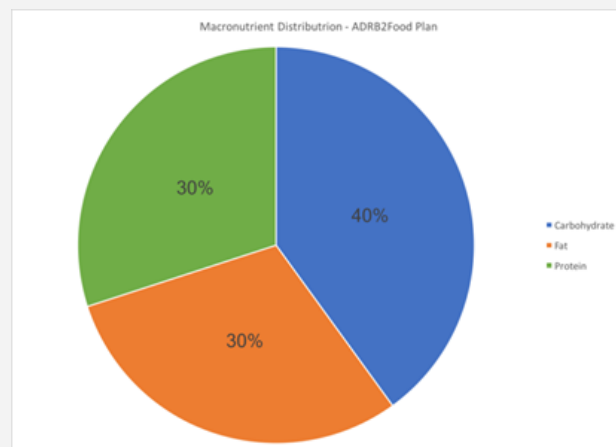


Table 6

| Food Group (servings) | Daily Calorie Target (kcal/day) | | |
|---------------------------|---------------------------------|------|------|
| | 1200 | 1500 | 1800 |
| Vegetables | 10 | 12 | 14 |
| Fats/Oils | 2 | 3 ½ | 5 |
| Proteins | 9 | 10 | 11 |
| Whole Grains | ½ | 1 | 1 |
| Fruits | ½ | ½ | 1 |
| Legumes | 1 | 1 | 1 ½ |
| Dairy | 1 | 1 | 1 |
| Nuts/Seeds | 2 | 2 | 3 |
| Starchy Vegetables | ½ | ½ | 1 |

Customizable ADRB2 Food Plan

Use Table 6 as a guide to customize the ADRB2 Food Plan. Food group servings per day are listed for 1200, 1500 or 1800 calories/day. These foods can be distributed any way throughout the day, although it's recommended that protein and vegetables, in particular, be distributed fairly equally throughout the day to maintain blood sugar and minimize hunger.

Macronutrient Composition of ADRB2 7-Day Meal Plan

Estimated macronutrient composition of the ADRB2 7-Day Meal Plan is summarized below, with estimated values for saturated fat, monounsaturated fat, polyunsaturated fat, dietary fiber and calorie density. While total carbohydrate is 43% of total calories consumed, dietary fiber makes up 12%; therefore, net carbohydrates are 107 g, or 31%.

| Nutrition Facts | | |
|----------------------------------|--------------|-----|
| Daily intake | | |
| Calories | 1462 kcal | |
| | g | % |
| Total Fat | 33.6 | 21 |
| Saturated Fat | 7.2 | 4.3 |
| Monounsaturated Fat | 10.5 | 6.3 |
| Polyunsaturated Fat | 8.3 | 5 |
| Total Carbohydrate | 208 | 57 |
| Dietary Fiber | 52 | 15 |
| Protein | 103 | 28 |
| Estimated Calorie Density | 1.0 | |

SH2B1 Variant

For: Those with variation in the SH2B1 genes and/or MC4R, FABP2, FTO, ADRB2 variations

SH2B1, also known as *SH2B adapter protein 1*, refers to a gene found on chromosome 5 and the protein that the gene creates. The function of the SH2B1 protein is to improve the balance of the body's hormones insulin and leptin. Insulin is made in the pancreas and helps to control blood sugar levels by signaling the liver, muscles and fat cells to take in glucose from the blood. Circulating levels of insulin are strongly influenced by the amount and type of fat and carbohydrates consumed. Sometimes the body can stop responding to insulin, a state known as insulin resistance. This results in high blood sugar levels and signals the early stages of diabetes. Leptin is involved in controlling hunger levels and, like insulin, the body can stop responding to it appropriately. Individuals with the variant in the SH2B1 gene are at increased risk for reduced response to both insulin and leptin. This variation increases the likelihood of weight gain as the body loses its ability to respond to insulin and leptin. The key to successful weight loss and health management in SH2B1 carriers is to control the amount of fat and carbohydrates consumed, to eat smaller meals more frequently to reduce the demand for insulin, and to exercise frequently to improve leptin signaling.

Features of the SH2B1 Food Plan

In addition to the Foundational Food Plan features, the SH2B1 Food Plan includes the following features to support the preferences and common concerns associated with those who have this allele variant:

Limited fat intake. For maintenance of healthy insulin levels.

Low glycemic carbohydrates. The goal is to keep the insulin response low, particularly in SH2B1 variant carriers because there is already an inappropriate response to existing insulin levels with this variant. Ideal: carbohydrates with a glycemic index ≤ 55 . Acceptable in moderation: carbohydrates with a glycemic index 55 – 70. Avoid as much as possible: Carbohydrates with a glycemic index greater than 70. A list of low, medium and high glycemic index foods is provided in the SH2B1 Patient section.

High fiber intake. Foods high in fiber take longer to digest and improve feelings of fullness. Higher fiber also helps regulate blood sugar.

Five moderate, balanced meals each day to improve fullness and help regulate insulin secretion.

Macronutrient Distribution

All macronutrient recommendations are based on daily calorie intake (see Figure 6):

- 20% healthy fat, with an emphasis on monounsaturated and polyunsaturated fats over saturated fats
- 35% lean protein
- 45% carbohydrates in the form of whole grains, vegetables and fruits

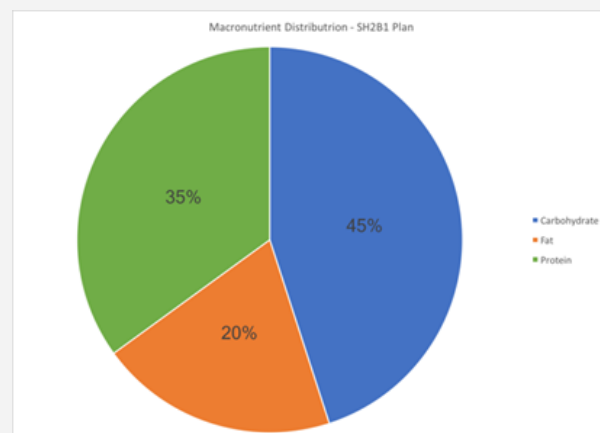


Figure 6: Macronutrient Distribution for SH2B1 Food Plan

Table 7

| Food Group (servings) | Daily Calorie Target (kcal/day) | | |
|---------------------------|---------------------------------|------|------|
| | 1200 | 1500 | 1800 |
| Vegetables | 10 | 10 | 10 |
| Fats/Oils | 1 ½ | 2 | 2 ½ |
| Proteins | 9 | 10 | 12 |
| Whole Grains | 1 | 1 | 1 ½ |
| Fruits | 1 | 1 | 1 ½ |
| Legumes | 1 | 2 | 2 |
| Dairy | 1 | 2 | 2 |
| Nuts/Seeds | ½ | 1 | 1 |
| Starchy Vegetables | ½ | ½ | 1 |

Customizable SH2B1 Food Plan

Use Table 7 as a guide for customizing the SH2B1 Food Plan. Food group servings per day are listed for 1200, 1500 or 1800 calories/day. These foods can be distributed any way throughout the day, although it's recommended that protein and vegetables, in particular, be distributed fairly equally throughout the day to maintain blood sugar and minimize hunger.

Macronutrient Composition of SH2B1 7-Day Meal Plan

Estimated macronutrient composition of the SH2B1 7-Day Meal Plan is summarized below, with estimated values for saturated fat, monounsaturated fat, polyunsaturated fat, dietary fiber and calorie density. While total carbohydrate is 52% of total calories consumed, dietary fiber makes up 13%; therefore, net carbohydrates are 139 g, or 40%.

| Nutrition Facts | | |
|----------------------------------|-----------|-----|
| Daily intake | | |
| Calories | 1404 kcal | |
| | g | % |
| Total Fat | 32.4 | 21 |
| Saturated Fat | 7.9 | 5.6 |
| Monounsaturated Fat | 10.3 | 7.3 |
| Polyunsaturated Fat | 7 | 5 |
| Total Carbohydrate | 183 | 52 |
| Dietary Fiber | 45 | 13 |
| Protein | 110 | 31 |
| Estimated Calorie Density | 0.9 | |

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