



THE CLINICAL APPLICATION OF
FASTING
VERSUS OTHER POPULAR DIETS

A Practitioner's Guide



DISCLAIMER
The information provided in this guide is meant to facilitate a discussion between the patient and healthcare practitioner, and is not intended to provide medical advice.

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Decades of research has shown that what we eat, how much we eat, and when we eat can influence our health.

As patients become savvier to nutrition trends, they may seek out more evidence-based answers to their nutrition questions and recommendations for a nutrition regimen that is personalized to their health goals.

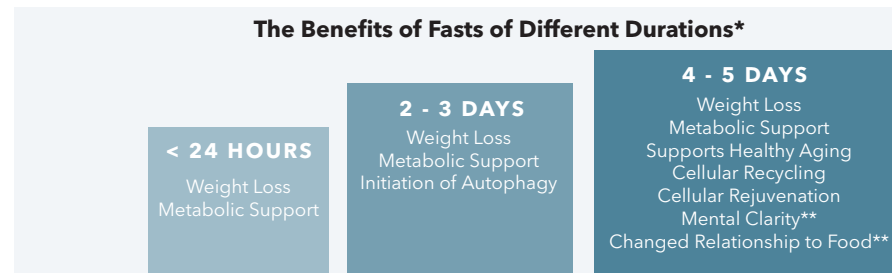
This guide aims to help clinicians be able to:

- 1 Incorporate fasting into a patient's nutrition plan
- 2 Recommend health-promoting foods to be consumed when not fasting
- 3 Differentiate the impact of fasting from popular approaches to weight loss, such as low-calorie, Mediterranean, and ketogenic diets

PART I: How To Incorporate Fasting Into a Patient's Nutrition Plan

THE BENEFITS OF FASTING

For hundreds of thousands of years, humanity lacked the abundance of food that we have today. Fasting was a routine part of life out of necessity. It later became a component of many spiritual and religious practices, and today it's growing in popularity due to its health benefits. The benefits of fasting differ based on the duration of the fast (see table below). Shorter-duration fasts are associated with metabolic support and weight loss while longer-duration fasts are associated with additional effects like cellular recycling and cellular rejuvenation.



While prolonged fasts of several days may be associated with the greatest number of health benefits, there are also significant health gains to be had from incorporating shorter fasts into patients' nutrition recommendations. In this section, we will discuss the benefits of **intermittent fasting** and **periodic fasting** and how both can be used to advance patients' health goals.

*Results may vary per individual. The presented information is taken from multiple studies, therefore overall averages are taken into consideration.

**Based on survey conducted by L-Nutra, June 2019. Data on file.

BENEFITS OF INTERMITTENT FASTING

Intermittent fasting (IF) can be defined as fasting for less than two days. While there are a variety of fasting methods within the category of IF, they are all based on eating patterns that alternate between intervals of eating and fasting.

DIFFERENT INTERMITTENT FASTING PATTERNS

TIME-RESTRICTED EATING (TRE)

This is a form of IF in which patients limit their feeding window to specific hours of the day. Popular combinations are 12:12 and 16:8.



ALTERNATE-DAY FASTING (ADF)

In this method of IF, patients freely eat for a day, fast the next day, and repeat.



5:2 DIET (5:2)

Patients following this IF pattern will consume their usual diet five days a week and fast or consume a very low-calorie diet for the other two days. Patients can choose the days that make the most sense for them, and the days do not need to be consecutive.



Each type of IF has been studied to determine its unique health benefits (summarized in the table below). While the fasting window is not long enough to cause the degree of cellular rejuvenation that is achieved through multi-day fasting, IF can still contribute to overall health by supporting weight loss, cardiovascular health, and metabolic health. Clearly, even incorporating shorter fasting windows can have positive implications for individuals' health and wellbeing.

Benefits of Different Styles Intermittent Fasting	
TYPE OF IF	ASSOCIATED BENEFITS
TRE	Weight loss, fat reduction, supports cardiovascular health as part of a healthy lifestyle
ADF	Weight loss, fat reduction, supports cardiovascular health as part of a healthy lifestyle
5:2	Weight loss, supports metabolic health

SUPPORTING INTERMITTENT FASTING WITH FOOD

While the fasting window in IF is relatively short, it can still be difficult for some individuals to adhere to. This is where fasting with food can be leveraged to help people extend their fasting window without foregoing all nutrition. A 2021 clinical trial of 105 healthy individuals tested whether Fast Bar -- a bar with a specific combination of plant-based macronutrients -- could extend ketosis in individuals observing TRE. They found that participants who consumed the fasting-mimicking bar after a 15-hour overnight fast had similar post-prandial glucose and ketone levels hourly for the next 4 hours, compared to individuals who consumed only water after the same fasting period. Long-term studies of Fast Bar have not yet been completed, so it's too soon to say if its ability to mimic a fasting state confers the same health benefits as forms of TRE where no food is consumed during the fasting window. What is known is that Fast Bar extends the physiological fasting window, likely making IF attainable for more individuals.

KEY TAKEAWAY

The fasting window in IF may be short, but it can still be an impactful strategy to support weight loss, metabolic health, and cardiovascular health as part of a healthy lifestyle.



LEVERAGING THE BENEFITS OF A PERIODIC FAST

What is Periodic Fasting?

Periodic fasting (PF) is fasting for more than two days, usually anywhere from three to seven consecutive days, that is done several times per year. Due to its extended duration, PF goes beyond providing weight loss and metabolic support to promote cellular rejuvenation and support a healthy-aging lifestyle.

Cellular Effects of Periodic Fasting

How does periodic fasting have such profound effects on the human body? Because food is not merely fuel. It's also a source of information for our cells, upregulating or downregulating pathways that influences the cell's function. For example, the consumption of amino acids, protein, and carbohydrates upregulate the cell's **nutrient-sensing pathways (NSPs)**, which include **mTOR** (mechanistic target of rapamycin), **IGF-1** (insulin-like growth factor 1), and **PKA** (protein-kinase A). The upregulation of the NSPs activates the cell's growth and aging mechanisms.

When in a fasting state, by contrast, NSPs are downregulated. When the NSPs are downregulated for several days, the cell enters a stress-resistant state and activates **autophagy**, the body's built-in mechanism for eliminating damaged or worn-out structures in the cell. Interestingly, the **2016 Nobel Prize in Physiology or Medicine** was given to the scientist who uncovered the mechanisms of autophagy. Periodic fasting is one way to activate this process and to support the cell's natural rejuvenation functions.

Cellular Response to Feeding vs. Fasting		
STATE	EFFECT ON NSPs	RESULTING EFFECTS
FED	Upregulated	Cell growth and aging functions activated
FASTING	Downregulated	Stress-resistance, antioxidant production, and autophagy functions activated

SUPPORTING PERIODIC FASTING WITH FOOD

Until relatively recently, water fasts were thought to be the only means to perform a multi-day fast; however, such a restrictive intervention is neither ideal nor necessary. First, the feelings of fatigue, headache, weakness, and hunger that a person can experience may be overwhelming, creating compliance issues. Second, prolonged water fasts can contribute to nutrient deficiencies, gallbladder dysfunction, hypoglycemia, hypotension, and the catabolism of lean muscle mass. These risks are not inconsequential and may pose risks to patients' health. Finally, water fasts, especially multi-day fasts, may simply be unsafe for some people due to underlying health conditions.

How are patients to carry out a periodic fast if water fasting poses so many risks? **The fasting mimicking diet (FMD)** is an alternative for those who want many of the benefits of a prolonged water fast without some of the drawbacks. The diet consists mostly of plant-based, unsaturated fats and restricts protein, simple carbohydrates, and total energy. FMD is the result of 20+ years of research and is designed to be a periodic, prolonged fast, meaning it lasts more than two days and is meant to be done more than once per year.

Key Characteristics of FMD

Fats Emphasis on plant-based, Omega-3 rich fats (44-46% of energy)	Carbohydrates Emphasis on complex carbs and fiber (43-47% of energy)
Protein Short-term restriction (9-11% of energy)	Total Energy Short-term restriction (700-1100 kcal/day)

Benefits of Fasting Mimicking Diets

FMD shows great promise as a safe and effective strategy to support healthy aging. In a clinical trial of 100 healthy individuals, one 5-day cycle of FMD resulted in five pounds of weight loss and a one-inch reduction of waist circumference. Three consecutive cycles (one cycle performed each month over three months) resulted in a reduction in trunk fat, weight, waist circumference, and BMI without causing a loss of lean body mass (see full findings in the table to the right).

These effects were largely maintained three months after the completion of the trial, indicating that although FMD is a short-term intervention, it can have significant, lasting benefits even three months later. No major adverse outcomes were reported in the trial. In a survey following the study, a majority of respondents stated that they had an improved relationship with food, improved mental clarity and energy, fewer cravings, and better portion control. Ongoing studies are examining the effects of additional FMD cycles to support cardiovascular health.



Summary of Outcomes in Clinical Trial and Post-Trial Survey of FMD

AFTER ONE CYCLE OF FMD

- Supports weight loss, a reduced waistline, and abdominal fat-driven weight loss
- A better relationship with food*
- Mental clarity*
- Improved energy levels*
- Fewer cravings*

AFTER 3-4 CYCLES OF FMD**

- Support of the natural process of autophagy – cellular clean-up and rejuvenation
- Supports overall metabolic health
- Weight loss (average of 5.7 – 7.8 pounds) with preserved lean body mass over 3-4 cycles
- Reduced waist circumference of 1.6 inches
- Supports cardiovascular health, as part of a healthy lifestyle

*Based on survey conducted by L-Nutra, June 2019. Data on file.

**Benefits seen in a clinical trial when FMD was used once a month for 3 to 4 consecutive months. Data on file.



KEY TAKEAWAY

FMD allows a person to consume a specific mix of nutrients without kicking the body out of a fasting state. Incorporating just 3-4 cycles of a 5-day FMD each year can provide many of the deeper health benefits of a periodic fast without requiring a water-only fast.

COMBINING INTERMITTENT FASTING WITH PERIODIC FASTING

IF and PF do not need to be mutually exclusive and can go hand-in-hand in patient protocols. For those patients who want to support their metabolism and weight loss journey on a consistent basis, daily adherence to IF can be beneficial. For patients seeking additional benefits like cellular rejuvenation, PF can be recommended up to once per month for three months or until desired results are achieved, then every three months for maintenance to support weight loss, healthy aging, and cellular rejuvenation. After completing PF, it is recommended to give the body at least 5-7 days to refuel before restarting IF. Please note: fasting is not appropriate for all patients. Please use your clinical judgment when assessing the medical history of each patient to determine if IF and/or PF are safe and suitable for their health goals and lifestyle.

WHAT TO EAT WHEN NOT FASTING?

1 Prioritize a Variety of Produce

Vegetables and fruits contain fiber, which is associated with numerous positive health benefits, including supporting metabolic health and maintaining healthy weight. The Institute of Medicine advises men and women to consume 38g and 25g of dietary fiber per day, respectively. It's also important to encourage patients to "eat the rainbow" and consume a variety of produce each day to get a greater diversity of vitamins, minerals, and phytochemicals.

2 Choose Plant-Based Proteins

Residents of Western countries tend to consume more protein than the recommended amount, and they often choose animal-based proteins like meat and dairy, which are associated with poor health outcomes when overconsumed. Encouraging patients to swap their animal-based proteins for plant-based alternatives could be beneficial for their health. Good sources of plant-based protein include nuts, seeds, beans, lentils, chickpeas, tofu, tempeh, and quinoa.

3 Consume Whole Grains

Whole grains retain more fiber, vitamins, minerals, phytonutrients, and healthy fats than refined grains during processing. It may be unsurprising that consuming more whole grains is associated with health benefits while a diet high in refined carbs - like the Standard American Diet - may be associated with poor health outcomes.

4 Switch to Unsaturated Fats

Unsaturated fats have been studied for their health-promoting benefits and should be a staple in patients' pantries. Olive oil, avocados, olives, nuts, seeds, and fish are good sources of unsaturated fat. Saturated fats such as butter, cream, lard, cheese, and fatty cuts of meat should be consumed in moderation as these are associated with negative health outcomes when overconsumed.

5 Hydrate with Water

Talking to your patients about their beverage choices is a key part of the discussion about their nutrition. Many Americans consume added sugar and calories by choosing juices, sodas, energy drinks, sports drinks, and sweetened teas. These may contribute to weight gain and other poor health outcomes when overconsumed. Choosing water, either still or sparkling, is the best way to hydrate.

KEY TAKEAWAY

A Mediterranean-style diet emphasizes foods with a highly nutritious profile. It has been studied for its many health benefits, including supporting healthy weight and metabolic health.

Patients are increasingly exposed to nutrition-related information from family, friends, and social media. Helping them understand the benefits and drawbacks of different diets is a key part of coaching them to adopt a nutrition protocol that is safe, appropriate, and aligned with their health goals. In this section, we'll discuss the ketogenic diet and the low-calorie diet, both of which are popular approaches to weight loss and metabolic support, and how they compare to a nutrition regimen that combines fasting with a Mediterranean-style diet.

KETOGENIC DIET

What is the Ketogenic Diet?

The classic **ketogenic (keto) diet**, which was originally designed for medical purposes, requires 4g of fat to be consumed for every 1g of carbohydrate and protein combined. However, the general public tends to label any low-carb, high-fat diet as ketogenic. The diet, when done correctly, causes the body to switch from glucose to ketones as the primary energy source, drawing on fat reserves for fuel. It has gained popularity with the public due to two possible side effects: weight loss and improved insulin sensitivity. As obesity and insulin resistance are implicated in a growing number of health conditions, more patients may start asking about the efficacy of trying keto.

Nutritional Profile of a Classic Ketogenic Diet

Fats	Carbohydrates	Protein	Total Energy
90% of Energy	2 - 4% of Energy	6 - 8% of Energy	No Restriction

How Does Keto Compare to Fasting?

1 Ease of Implementation

Keto is a lot more effort than either IF or FMD. It requires strict daily meal planning to maintain compliance. IF is far simpler as it only requires observance of certain meal times or days; not specific nutrients. While FMD does require that a specific mix of nutrients be consumed, a 5-day FMD program is available in a ready-made meal kit, making it easy to try.

2 Duration

Both keto and IF must be adhered to daily for weeks or months to bring about their intended effects. FMD, however, is designed to be followed for only five days, up to once per month.

3 Cellular Effects

Keto does not likely downregulate NSPs. While it restricts macronutrients that interact with NSPs, keto does not adequately restrict calories or protein, which also play a role in the cell signalling cascade. The fasting window in IF may allow the autophagy process to begin but is not long enough to fully carry this process out. FMD, however, supports cellular rejuvenation by downregulating NSPs long enough to both trigger and support several days of autophagy.

How Does Keto Compare to a Mediterranean-Style Diet?

1 Fiber and Micronutrient Adequacy

A key feature of the keto diet is the restriction of carbohydrates, which can put patients at risk of becoming deficient in nutrients like folate, thiamin, potassium, magnesium, and Vitamin E. It can also make it challenging for individuals to consume adequate fiber. As the Mediterranean diet emphasizes the consumption of plants, neither micronutrient deficiencies nor fiber deficiencies are risks.

2 Saturated vs. Unsaturated Fats

While the Mediterranean diet emphasizes the consumption of healthy unsaturated fats, a keto diet tends to include higher amounts of animal-based saturated fats, which may be harmful to cardiovascular health. In addition, the restrictions on keto make the diet both less sustainable than an everyday healthy diet and possibly detrimental to patient health.

A LOW-CALORIE DIET

What is a Low-Calorie Diet?

A **low-calorie diet** is generally accepted to be one that meets 70% of an individual's estimated caloric needs. It poses no other nutritional restrictions or recommendations. In addition to weight loss, patients may see other health benefits when following a low-calorie diet. For example, excess visceral fat loss is associated with improved cardiometabolic health.

Nutritional Profile of a Low-Calorie Diet

Carbohydrates, Protein, and Fats	Total Energy
No specific macronutrient mix; patients must only limit intake based on calories	Varies; typically 70% of estimated needs

How Does a Low-Calorie Diet Compare to Fasting?

1 Ease of Implementation

A low-calorie diet is the most simplistic way to think about achieving weight loss. It might be the most intuitively appealing approach to patients because choosing to consume smaller portions is more straightforward than, say, planning out the exact balance of macros one can consume. However, it may be difficult to adhere to as patients may experience hunger, fatigue, and frustration on a daily basis. IF, by contrast, requires no calorie counting or restriction, only a plan for meal timing. With the option to observe a fast as short as 12 hours and still obtain health benefits, IF may deliver similar results in a manner that may be safer and more feasible for individuals. As for a prolonged fast, FMD is available in a ready-made formulation that takes any planning out of the regimen. Though individuals may experience symptoms such as headache and fatigue while following FMD, these symptoms tend to be mild, improve with time, and are limited to just a few days.

2 Duration

A low-calorie diet and IF must both be adhered to daily over months or even longer. FMD, by contrast, is designed to be practiced just five days each month, up to once per month.

3 Cellular Effects

A low-calorie diet does not likely downregulate NSPs. It does not restrict protein, and the permissible calorie level is likely too great to initiate a cellular fasting state. IF may downregulate the NSPs for a brief time, but the fasting window is not long enough for autophagy to be carried out. FMD, however, supports cellular rejuvenation by downregulating NSPs long enough to trigger and carry out autophagy for several days.

How Does a Low-Calorie Diet Compare to a Mediterranean-Style Diet?

1 Energy Adequacy

A low-calorie diet by definition does not meet an individual's energy needs. The body compensates for energy restriction by slowing the metabolism. The metabolism is further slowed as muscle mass is lost along with fat, making weight loss more and more difficult to attain. The Mediterranean diet, by contrast, is not associated with calorie restriction, muscle loss, or negative effects on the metabolism.

2 Nutrient Density

A low-calorie diet does not help an individual learn how to eat in a healthy way. Patients may restrict portions without putting an emphasis on choosing the most nutrient-dense foods. This puts them at risk for nutrient deficiencies and sets them up for failure when they transition off the diet. A Mediterranean-style diet, by contrast, promotes nutrient-dense foods and an eating pattern that is sustainable long-term.



KEY TAKEAWAY

Keto and low-calorie diets are two nutrition patterns that patients may be interested in if they have goals such as weight loss and metabolic support. However, each approach has drawbacks that make fasting and the Mediterranean diet more appealing methods to achieve these goals.



CONCLUSION

Personalized nutrition can and should be a pillar of every patient treatment plan. Along with a Mediterranean-style diet, fasting can support metabolic and cardiovascular health, weight loss, and – unique to periodic fasting – cellular rejuvenation. This approach likely confers greater health benefits than keto or a low-calorie diet, both of which promise similar results and may be popular among patients.

The quick comparison table below may be useful to communicate the differences in each nutrition approach to patients in order to help them adopt a nutrition plan that meets their health goals and sets them up to adopt a healthy lifestyle.

Fasting Strategies vs. Popular Diets: A Comparison of Health Benefits*

	FMD	IF	MEDITERRANEAN	KETO	LOW-CALORIE
Supports Weight Loss	✓	✓	✓	✓	✓
Supports Metabolic Health	✓	✓	✓	?	?
Supports Autophagy and Cellular Rejuvenation	✓	X	X	X	X
Easy to Implement	✓	✓	✓	X	X
Short-term Intervention with Long-term Benefits	✓	X	X	X	X
Preserves Lean Body Mass	✓**	?***	?	?	?

✓ Evidence-Based X Not Supported By Evidence ? Inconclusive Data



KEY TAKEAWAY

The most profound difference between FMD and other nutrition approaches is that it supports autophagy and cellular rejuvenation.

*Data compiled through literature review. No head to head trials were conducted.

**Benefits seen in a clinical trial when FMD was used once a month for 3 consecutive months. See Wei et al. (2017).

***See Patikorn et al. (2021).